Australian Government
Department of Health and Ageing
National Health and Medical Research Council

A review of the evidence to address targeted questions to inform the revision of the Australian Dietary Guidelines

Evidence Statements

with

Summary of studies contributing to Statements, and cited references
Studies not sufficient to make a Statement, and cited references

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Contents

Abbreviations and acronyms

adjHR	adjusted hazard ratio
adjOR	adjusted odds ratio
BMC	bone mineral content
B	boy
CHO	carbohydrate
CHD	coronary heart disease
CVD	cardiovascular disease
DHA	docosahexaenoic acid
DEXA	dual energy X-ray absorptiometry
EtOH	alcohol
Hr	hour
HR	hazard ratio
Kcal	kilocalorie
kJ	kilojoule
F	female
FA	fatty acid
FO	fish oil
HT	hypertensive
LGA	large for gestational age
M	male
MI	myocardial infarction
Mo	month
n	no
NHMRC	National Health and Medical Research Council
O	neutral
NS	non-significant
NT	normotensive
OR	odds ratio
P	positive
PND	post natal depression
PUFA	polyunsaturated fatty acids
QUS	quantittive ultrasound
RR	relative risk
RCT	randomised controlled trial
SE	standard error
SEP	socio-economic position
SES	socio-economic status
SFA	short chain fatty acids
SGA	small for gestational age
SLR	systematic literature review
SOS	speed of sound
SRRE	summary relative risk estimate
UK	United Kingdom
USA	United States of America
Veg	vegetable
WCRF	World Cancer Research Fund
Wk	week
Wt	weight
WMD	weighted mean difference
y	yes
Yrs	years

Introduction

In 2008, the NHMRC tendered for systematic literature reviews to be undertaken to support the revision of the *Dietary Guidelines for Australians*. The details of the requested work and the methods employed are set out in the Process Report. The primary aim was to undertake a series of systematic reviews of the national and international literature from the year 2002 on the food-diet-health-disease inter-relationship for different population subgroups. In addition, information was sought on the following factors:

- Current national dietary habits and patterns and nutritional status;
- Physical activity, weight gain and dietary energy balance;
- Growth in infants, children and adolescents;
- The economic, physical and psychosocial barriers and enablers to achieving diets consistent with the dietary guidelines;
- Food safety, preparation and storage;
- Inter-relationship between diet and environmental sustainability;
- Current and past national food selection guides.

In brief, three types of reviews were commissioned, depending on the question being addressed:

- Systematic reviews, considering primary evidence from epidemiological and experimental studies, as well as reviews and meta analyses (but excluding editorial and other grey literature);
- Umbrella reviews, which only included reviews and meta analyses; and
- Narrative reviews, which may have also included information from secondary sources such as government reports.

The systematic and umbrella reviews were primarily conducted using the methods described in the NHMRC publication *"How to use the evidence: assessment and application of scientific evidence"*, and have resulted in body of evidence statements, graded depending on the strength, consistency, potential impact, generalisability and applicability of the evidence base. The narrative reviews are presented in a more traditional journal article style.

Details of the scope of the searches, including key populations, and outcomes were agreed with the NHMRC in March 2009. An expert medical librarian was employed to develop the detailed search strategies, conduct the searches in CINAHL, PREMEDLINE, MEDLINE, EBM REVIEWS, DARE, COCHRANE, PUBMED, PSYCHINFO, ERIC and SCIENCE DIRECT databases and provided each reviewer with an Endnote Library of retrieved studies. The search strategies of each review are given in detail in a separate document on searches of this report.

Limitations of the Reviews

These reviews should not be considered complete reviews of the relevant literature and readers need to bear in mind five key limitations:

Search Timeframe

Most of the reviews considered only evidence published from 2002, to provide an update on literature published since the last edition of the *Dietary Guidelines for Australians*. The searches were mostly carried out to April 2009, so more recent publications are generally not included unless specifically requested by the NHMRC. It is important therefore to realise that these are only update reviews, to be considered along with the evidence reviews summarised in the last *Dietary Guidelines*. In many cases, some of the most important literature was published before 2002 and is not considered in these reviews. Therefore evidence grades for these may be lower than would be anticipated with a time-unlimited literature review (e.g. for sugar and dental caries, where the diet disease relationship was well established prior to 2002).

Methods for Assessment of Evidence

The published NHMRC methods for literature reviews are primarily designed to be applied to assessment of the evidence of the effectiveness of medical interventions (primarily relying on randomised controlled trials) or diagnostic tests. In the case of examination of diet-health relationships, often there is a notable dearth of evidence from Level I and Level II studies (as is evidenced from the previous editions of the *Dietary Guidelines*), and much of the scientific evidence is observational, especially from prospective cohort studies. This poses particular challenges in balancing the evidence to reach public health conclusions.

It is rarely possible to conducted blinded intervention studies with whole foods or diets, and very few trials are conducted for long enough periods to assess long term health outcomes. Therefore Level III prospective cohort studies often provide more important evidence for the development of dietary guidelines than Level I evidence summarising small short-term randomised controlled trials. In some cases therefore, when assessing the overall evidence base used to establish grades for the evidence statements, a rating of excellent has been given when only Level III studies are available.

Umbrella Reviews

As noted, umbrella reviews did not include any primary studies. For a number of these reviews (e.g. U1.3 on Dietary Intake Data; U1.4 on Energy Balance) this severely limited the number of articles in the evidence base and important individual studies were not considered.

Cross Sectional Studies

Cross-sectional epidemiological studies are common in nutritional epidemiology but cannot be used as evidence of causation. They have therefore not been used in these reviews to inform the body of evidence statements because of their low rating in the NHMRC evidence hierarchy (Level IV evidence). It should be noted however that they were considered in evidence informing the last edition of the *Dietary Guidelines*.

Quantification of Dietary Exposure

For many of the evidence statements it was not possible to quantify exposure due to limitations in the dietary methodologies used in studies or the level of detail reported. For example, in many cohort studies quantiles of exposure are reported in relation to disease outcomes, but absolute intakes are not reported for the highest and lowest levels being compared.

1. FRUIT (S1.1 and S1.10)

Evidence Statements

1. FRUIT (S1.1 and S1.10)

Search results

The initial search of the databases included 3691 references for fruit and the specified disease outcomes. The detailed search is included in a separate document on searches. As there were 2714 duplicates with the vegetable database the two were combined in one Endnote library and coded as one. In all, 97 references concerning fruit and vegetables had data extracted and 57 papers were used to form the body of evidence statements for fruit. Sufficient evidence was found to make statements for fruit and cardiovascular disease, stroke, weight loss and obesity, type 2 diabetes and a range of cancers including gastric, breast, lung, colorectal, oesophageal and oral and nasopharyngeal, ovarian, endometrial and bladder cancer.

1.1 FRUIT and CORONARY HEART DISEASE

Does a particular intake of fruit affect the risk of coronary heart disease in adults?		
Evidence statement		Consumption of each additional daily serve of fruit is associated with a reduced risk of coronary heart disease.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	Level III evidence from two meta analyses each with 9 cohort studies (with most studies in common and medium risk bias) 2 individual cohorts (with low risk bias) and 1 case control (medium risk bias).
Consistency	Good	Two meta analyses and one cohort protective but 1 case control increased risk and other cohort describes protection when on a 40% - 55% energy from carbohydrate but not higher or lower.
Clinical impact	Good	Meta analyses protective for each additional serve fruit (7%).
Generalisability	Good	Populations from US Europe Japan.
Applicability	Excellent	Australian adults.

The studies used to make the body of evidence statements are shown in the Table 1.1. The two meta analyses are in agreement but have six of nine studies in common, with most studies being from the USA. The Japanese cohort study demonstrated a stronger association between fruit and cardiovascular disease. The analysis of the Nurses Health and Male Health Professionals cohorts stratified by the percentage energy from carbohydrate indicated that the protective effect is only found when

carbohydrate intakes are between 40% and 55% energy. The hospital-based case control study showing that fruit increases the risk of acute myocardial infarction was of a poorer quality because of the instrument used to measure fruit intake and the bias in selection of controls.

Summary: It is probable that consumption of each additional daily serve of fruit is associated with a reduced risk of coronary heart disease (Grade B). This is supported by two meta-analyses (Dauchet et al. 2006; He et al. 2007) of nine cohort studies in predominantly developed countries, concluding that increased protection of at least 7% was gained from each additional serve of fruit consumed per day. A further cohort study (Joshipura et al. 2008) found a protective effect only when carbohydrate intakes were between 40–55% of total energy intake.

References

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Joshipura, K. J., Hung, H.-C., Li, T. Y., Hu, F. B., Rimm, E. B., Stampfer, M. J., Colditz, G. & Willett, W. C. 2009, "Intakes of fruits, vegetables and carbohydrate and the risk of CVD", *Public Health Nutrition*, vol. 12, no. 1, pp. 115-21.

Rastogi, T., Reddy, K. S., Vaz, M., Spiegelman, D., Willett, W. C., Stampfer, M. J. & Ascherio, A. 2004, "Diet and risk of ischemic heart disease in India.[see comment]", *American Journal of Clinical Nutrition*, vol. 79, no. 4, pp. 582-92.

Takachi, R., Inoue, M., Ishihara, J., Kurahashi, N., Iwasaki, M., Sasazuki, S., Iso, H., Tsubono, Y. & Tsugane, S. 2008, "Fruit and vegetable intake and risk of total cancer and cardiovascular disease: Japan Public Health Center-Based Prospective Study", *American Journal of Epidemiology*, vol. 167, no. 1, pp. 59-70.

Table 1.1 Studies used to make evidence statement for fruit and cardiovascular disease.

Reference [1]	**Dauchet et al. 2006 [33]**	**He et al. 2007 [23]**	**Joshipura et al. 2008 [2546]**	**Takachi et al. 2008 [376]**	**Rastogi et al.2004 [1846]**
Type of study [2]	Meta analysis of cohort 9 cohorts	Meta analysis of cohort -12 (9 included)	Cohort	Cohort	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Decrease in RR with each additional serve of fruit (1-5 or more serves) and coronary heart disease	Intake of fruit of <1.3, 1.3–2.0 and >2.0 servings per day and coronary heart disease	Quintile of fruit by % energy from carbohydrate i.e. <40%,40-55% and >55% and cardiovascular disease	Quartiles of intake and cardiovascular disease outcomes	Serves of fruits and risk of acute myocardial infarction <1 serve, 1-2 serves, 2-3 serves, >3 serves per day
N [5]	91 379M 12 9701 F	278 459 M and F	38 918 M 70 870 F	77 891	350 cases and 700 controls (both from Indian hospitals)
Population/study information [6]	9 cohorts include 7 cohorts from the U.S. and 2 from Finland.	9 cohorts included long follow up in US and Europe	Nurses Health and Male Health Professionals	Japanese adult male and female	Hospital based Indian study
Quality [7]	0	0	P	P	0
Results [8]	RR 0.93 (95% CI 0.89-0.96) for each one portion increment fruit	RR for 1.3-2 (0.9), (95% CI 0.83-0.98) and >2 0.87 (0.8-0.95) vs <1.3 serves per day. No heterogeneity	quintile 5 vs quintile 1 for the moderate CHO group only RR 0.81 (95% CI 0.70-0.94). Risk was > 1 for low and high carbohydrate	quartile 4 vs quartile 1 for fruit HR 0.81(0.67-0.97)	For >3 serves fruit daily vs <1 serve RR 2.46 (95%CI 1.15-5.25) P for trend 0.03

Effect on risk (Increase/None/Protect)	Protect	Protect	None	Protect	Increase
Clinical importance [9]	1	1	1	1	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	n
Applicability	y	y	y	n	n

1.2 FRUIT and STROKE

Does a particular intake of fruit affect the risk of stroke?		
Evidence statement		Consumption of at least one and a half serves of fruit a day, ideally two and a half or more is associated with reduced risk of stroke.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	Level III evidence from 2 meta analysis of cohorts (medium risk bias, one with 4 studies and one with 6).
Consistency	Good	Both found significant protective effect.
Clinical impact	Good	Meta analyses showed 11% per serve and 28% protection for > 5. serves/
Generalisability	Good	US, Europe.
Applicability	Excellent	Australian adults of all age groups and both genders.
	ntllent	

The two meta analyses are summarized below in Table 1.2. They had three cohorts in common. Both found a protective effect.

Summary: It is probable that consumption of at least one and a half serves of fruit a day, ideally two and a half or more, is associated with a reduced risk of stroke (Grade B). Two meta-analyses (Dauchet et al. 2006; He et al. 2007) of a total of seven individual cohort studies concluded that increased protection of at least 11% was gained from each additional half-serve of fruit per day, with at least two and a half serves of fruit per day providing a protective effect of 28%.

References

Dauchet, L., Amouyel, P. & Dallongeville, J. 2005, "Fruit and vegetable consumption and risk of stroke: a meta analysis of cohort studies.[summary for patients in Neurology. 2005 Oct 25;65 (8):E17-8; PMID: 16247035]", *Neurology*, vol. 65, no. 8, pp. 1193-7.

He, F. J., Nowson, C. A. & MacGregor, G. A. 2006, "Fruit and vegetable consumption and stroke: meta-analysis of cohort studies.[see comment]", *Lancet*, vol. 367, no. 9507, pp. 320-6.

Table 1.2 Studies used to make the body of evidence for fruit and stroke

Reference [1]	**He et al. 2006 [42]**	**Dauchet et al. 2005 [44]**
Type of study [2]	Meta analysis of 6 cohorts	Meta analysis of 4 cohorts
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	<3 , 3-5 and to >5 serves fruit per day and stroke	Each additional serve of fruit up to 5 and stroke
N [5]	257,551 in total	90,513 M 141,536 F
Population/study information [6]	US and European cohorts	US cohorts and Danish
Quality [7]	0	0
Results [8]	RR for >5 serves veg vs <3 daily 0·72 (95% CI 0·66–0·79)	RR: 0.89 (95% CI 0.85-0.93) per additional serve
Effect on risk (Increase/None/Protect)	Protect	Protect
Clinical importance [9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicabilty	y	y

1.3 FRUIT and OBESITY

Does a particular intake of fruit affect the risk of weight gain and obesity?		
Evidence statement		Consumption of fruit is associated with a reduced risk of obesity and weight gain.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level II and III evidence 4 RCTs (low to medium risk bias) 5 cohorts (low to medium risk bias).
Consistency	Satisfactory	4 show protection; 5 no effect (but one of these was children 9 to 14 y).
Clinical impact	Satisfactory	For obesity prevention quintile 1 vs quintile 5 RR=0.74 (95% CI 0.69-0.86) P for trend <0.0001. For weight gain quintile 5 vs quintile 1 RR = 0.72 (95% CI 0.55-0.93) P for trend =0.01 in cohort studies. In regression models in 2 different studies fruit intake was an independent predictor of weight loss and weight gain.
Generalisability	Good	Similar populations include Nurses Health from the US.
Applicability	Excellent	Australian adults.

The evidence (see Table 1.3) concerning fruit and obesity and weight gain has limitations. There has only been one large cohort study in adults published from 2002 through 2009 that examined weight changes if fruit consumption changed. Women in the Nurses Health study increasing fruit consumption had a lower risk of weight gain. The other prospective studies were small - one study was in young children in the US and found that fruit consumption was negatively associated with change in BMI Z score but the changes were not statistically significant. Another cohort in Canada reported that fruit was inversely correlated with change in weight, fat and waist circumference and the other two cohorts failed to find significant protection. The remainder of the evidence comes from small randomized controlled trials of varying design that had different amounts of fruit averaging from two to four serves per day. From these randomized controlled trials it appears fruit can be included as part of a weight reduction diet and up to four pieces per day is satisfactory provided the overall diet is hypoenergetic.

Summary: The evidence suggests that consumption of fruit is associated with a reduced risk of obesity and weight gain (Grade C). The largest cohort study in adults (the Nurses' Health study) found increasing fruit consumption was clearly associated with a lower risk of weight gain (He et al. 2004); this was consistent with results from a smaller cohort study (Drapeau et al. 2004) and supported by results from a small cohort study of children (Field et al. 2003), although the change in BMI Z score

seen in the latter study was not statistically significant and two smaller cohort studies in adults did not find an association (Vioque et al. 2008; te Velde et al. 2007). The evidence from RCTs was inconsistent with two trials, including one of good quality (Sartorelli et al. 2008), showing protection (Conciecao de Oiveira et al. 2003) and two short-term trials not finding an effect (Rodriguez et al. 2005; Booth et al. 2008), although the RCTs suggested that up to four pieces of fruit a day can be part of a weight reduction diet if the overall diet is hypoenergetic.

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Conceição de Oliveira, M., Sichieri, R. & Sanchez Moura, A. 2003, "Weight Loss Associated With a Daily Intake of Three Apples or Three Pears Among Overweight Women", *Nutrition*, vol. 19, no. 3, pp. 253-256.

Drapeau, V., Despres, J.-P., Bouchard, C., Allard, L., Fournier, G., Leblanc, C. & Tremblay, A. 2004, "Modifications in food-group consumption are related to long-term body-weight changes", *American Journal of Clinical Nutrition*, vol. 80, no. 1, pp. 29-37.

Field, A. E., Gillman, M. W., Rosner, B., Rockett, H. R. & Colditz, G. A. 2003, "Association between fruit and vegetable intake and change in body mass index among a large sample of children and adolescents in the United States", *International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, vol. 27, no. 7, pp. 821-6.

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te Velde, S. J., Twisk, J. W. R. & Brug, J. 2007, "Tracking of fruit and vegetable consumption from adolescence into adulthood and its longitudinal association with overweight.[erratum appears in Br J Nutr. 2007 Oct;98(4):871]", *British Journal of Nutrition*, vol. 98, no. 2, pp. 431-8.

Vioque, J., Weinbrenner, T., Castello, A., Asensio, L. & de la Hera, M. G. 2008, "Intake of fruits and vegetables in relation to 10-year weight gain among Spanish adults", *Obesity*, vol. 16, no. 3, pp. 664-670.

Table 1.3 Studies used to make evidence statement for fruit and obesity.

Reference [1]	**Field 2003 [2036]**	**He et al. 2004 [1586]**	**Vioque et al. 2008 [4150]**	**te Velde et al. 2007 [518]**	**Drapeau et al. 2004 [7938]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Servings of fruit per day and change in BMI Z score	Change in serves of fruit by quintile -1.27; -0.29; 0.22; 0.8 and 1.86 median change for fruit; and outcome is obesity or weight gain	Quintiles of fruit intake <149 g/day, 149–248 g per day, 249–386 g per day >386 g per day, and weight gain of more than the average i.e. 3.4 kg over 10 years	Quartiles fruit intakes tracked over 24 years and longitudinal change in BMI and sum of skinfolds (reference is the highest quartile)	Changes in food groups consumption in the predictability of weight gain and changes in % body fat and waist circumference after 6 years
N [5]	6 715 B 8 203 G	74,063 F	206 M and F	168 M and F	248 M and F
Population/study information [6]	US boys and girls 9 to 14 yrs	US Nurses Health cohort	Healthy sub sample Spanish Valenica cohort age 15 yrs to 80 yrs	Amsterdam Growth and Health Longitudinal Study followed from 13 to 36 yrs	Quebec family study
Quality [7]	P	P	P	0	P
Results [8]	Adjusted change for annual change in fruit intake -0.006 (-0.018-0.006) for girls and 0.004 (-0.01-0.02) boys	Quintile 5 and quintile 1 fruit and obesity RR 0.76 (95% CI 0.56-0.95) and P for trend< 0.0007 For weight gain quintile 5 vs quintile 1 RR 0.73 (95% CI 0.56-0.95) P for trend <0.03	Quintile 5 vs quintile 1 OR 0.62 (95% CI 0.18- 2.1) P for trend 0.211	NS for fruit and BMI at 36yrs but sum of skinfolds for lowest quartile predictive of lower skinfolds -3·65 (95% CI -6·47, -0·83) (sex adjusted)	Fruit inversely correlated with change in weight (P=0.03), body fat (P=0.03), change in waist circumference (P=0.03)

Effect on risk Increase/None/Protect	None	Protect	None	None	Protect
Clinical importance [9]	2	1	2	2	1
Clinical relevance [10]	2	1	2	2	2
Generalisability	y to children	y to F	y	n	n
Applicability	y to children	y to F	y	y	y

Table 1.3 Studies used to make evidence statement for fruit and obesity (cont).

Reference [1]	**Sartorelli et al. 2008 [97]**	**Conceicao de Oliveira et al. 2003 [7687]**	**Rodriguez et al. 2005 [7883]**	**Booth et al. 2008 [5944]**
Type of study [2]	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	80 overweight adults individualized energy restricted diet that included at least 2 serves of fruit per day and advice for 30 mins of walking. Outcome is weight loss	12 week trial randomly assigned to be in a fruit group (then randomized to consume either 3 pears or 3 apples per day) or an oat group with 3 oat cookies per day	Energy restricted diet for 8 weeks to assess if inclusion of fruit alters weight loss. The comparison is 13.8% energy as fructose vs 4.0% energy as fructose and 25.9 g fibre vs 15.8 g fibre	Two 12 week weight reduction diets, one with four serves fruit/day and increased targets for vegetables and dairy (WELL diet) the other a Low Fat diet (control). Control ate 0.7 serves less fruit
N [5]	80 adults	26 in fruit group and 9 in oat group at the end of the trial (49 total at commencement)	15 obese F in test (7 on high fruit and 8 on low fruit) and 5 lean women as controls	27 in intervention group, 27 in control group
Population/study information [6]	Brazilian mean age (±SD) 46.5 ± 9.5 yrs, mean BMI 29 ± 3 kg/m^2 at baseline	Conducted in Brazilian F aged 30 to 50 yrs with BMI>25 kg/m^2	Conducted in Spain Mean BMI 34.9 kg/m^2 and mean age 32yrs.	All subjects Australian M mean age 47.7 yrs

Quality [7]	0	P	0	P
Results [8]	Iincrease of 100 g per day of fruits represented a body weight loss of 300 g (P <0.05)	The fruit group lost 1.22 kg (95% CI 0.44 –1.85), whereas the oat group had a non-significant weight loss of 0.88 kg (0.37–2.13). The difference between the two groups was statistically significant (P = 0.004).	Both diets resulted in weight loss. 6.9 kg on low fruit and 6.6 on high fruit. i.e NS difference and none detected in any other metabolic parameters Mean energy intake about 1300 kcal	WELL subject lost 4.8 +/- 3.3 kg and Low Fat control 4.6 +/- 3.1 kg P=0.83
Effect on risk Increase/None/Protect	Protect	Protect	None	None
Clinical importance [9]	2	2	3	4
Clinical relevance [10]	2	2	2	2
Generalisability	y	y limited	n	n
Applicability	y	n	n	n

1.4 FRUIT and DIABETES TYPE 2

Does a particular intake of fruit affect the risk of type 2 diabetes?		
Evidence statement		Consumption of fruit is not associated with risk of type 2 diabetes.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 meta analyses of cohorts (4 studies) and 1 cohort.
Consistency	Satisfactory	Meta analysis and 1 European cohort no protection.
Clinical impact	Poor	HR ranges 0.7-1.01.
Generalisability	Good	US and Finland.
Applicability	Good	Applicable to Australian adults.

One meta analysis of US and Europeans cohorts with four studies and an additional cohort from EPIC (both studies of good quality) were used to form the evidence (see Table 1.4). The meta-analysis showed no significant protection but the EPIC cohort did. The evidence statement is based on five cohorts and additional studies are needed to further guide evidence.

Summary: The evidence suggests that consumption of fruit is not associated with risk of type 2 diabetes (Hamer & Chida 2007; Harding et al. 2008) (Grade C). However, as seen for vegetables, given the evidence suggesting association between consumption of fruit and reduced risk of obesity and weight gain, further long-term studies may be required in this area.

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Table 1.4 Studies used to make the body of evidence statement for fruit and diabetes.

Reference [1]	**Hamer et al. 2007 [18]**	**Harding et al. 2008 [225]**
Type of study [2]	Systematic review of 4 cohorts	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Examine subjects consuming 3 or more serves fruit vs those consuming less and diabetes type 2	Quintile of fruit and incident diabetes type 2
N [5]	167 128	21 831
Population/study information [6]	6 to 23 years follow up includes US and Finnish cohorts	EPIC in UK males and females
Quality [7]	P	P
Results [8]	RR for 3 or more serves vs < 3 serves fruit 1.01 (95% CI 0.88–1.15)	OR for quintile 5 vs quintile 1 RR 0.7 (95% CI 0.54-0.9)
Effect on risk (Increase/None/Protect)	None	Protect
Clinical importance [9]	2	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicabilty	y	y

1.5 FRUIT and CANCER

Does a particular intake of fruit affect the risk of gastric cancer?		
Evidence Statement		Consumption of fruit is associated with reduced risk of gastric cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled analysis (7 cohorts and 24 case control medium risk bias) 4 cohort (low to medium risk bias) and 3 case control (low to medium risk bias).
Consistency	Poor	4 show significant protection (including pooled analysis and 4 do not.
Clinical impact	Satisfactory	Reduction in risk ranged from 25% to 47%.
Generalisability	Good	Populations from US Italy Poland Japan and Sweden.
Applicability	Good	For Australian adults.

The pooled analysis and four cohort studies and the four case control studies contributing to the body of evidence are in Table 1.5. Based largely on the pooled analysis a protective effect is suggested. Only one of the newer cohort studies reported protection and this was in Japanese adults and the quality of this study was rated neutral because of the strong possibility of measurement bias due to the assessment of fruit intake. The study from the EPIC cohort and a Swedish and US study failed to find protective effects. It is noted that gastric cancer is more common in Japan. The case control studies included one in Japanese women with a negative outcome and two in Europe with a positive outcome. In the World Cancer Research Report it was concluded that it was probable that fruits were protective.

Summary: There is inconclusive evidence that consumption of fruit is associated with reduced risk for gastric cancer (Grade D) as there is but with lower consistency across studies, with a number of studies including cohort, case control and pooled analysis, showing an inverse association (Kobayashi et al. 2002; Lissowska et al. 2004; Lucenteforte et al. 2008; Riboli & Norat 2003) but other cohort and case control studies not finding an association (Gonzales et al. 2006; Larsson et al. 2006; George et al. 2009; Ito et al. 2003).

References

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Table 1.5 Studies used to make evidence statements for fruit and gastric cancer

Reference [1]	**Riboli and Norat 2003 [1993]**	**Kobayashi et al. 2002 [2229]**	**Gonzalez et al.2006 [1207]**	**Larsson 2006 [1036]**
Type of study [2]	Pooled cohorts (7) and case controls (24)	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Each 100 g fruit additional and gastric cancer	Quintiles of fruit intake and gastric cancer	Quartiles of fruit intake and incident gastric cancers	Serves of fruit <1; 1.0 to 1.4; 1.5-2.4 and >=2.5 per day and gastric cancer
N [5]	Uncertain	19,304 M 20,689 F	521,457	45,338 M 36,664 F
Population/ study information [6]	Asian US and European cohorts	Japanese cohort adult	Part of EPIC	Swedish cohort males and females
Quality [7]	0	0	P	P
Results [8]	RR 0.74 (95% CI 0.69-0.81) for an increase of 100 g per day (some heterogeneity)	significant effect for fruit if consumed more than once per week RR 0.70 (95% CI 0.49-1.00)	quartile 4 vs quartile 1 fruit RR 0.99 (95% CI 0.68–1.42)	no effect for 2.5 serves fruit. RR 0.86 (95% CI 0.52-1.43)
Effect on risk (Increase/None/ Protect)	Protect	Protect	None	None
Clinical importance[9]	1	1	2	2
Clinical relevance [10]	1	1	1	1
Generalisability	y	limited	y	y
Applicability	y	limited	y	y

Table 1.5 Studies used to make evidence statements for fruit and gastric cancer (cont.)

Reference [1]	**George et al. 2009 [2574]**	**Lissowska et al. 2004 [6757]**	**Lucenteforte et al. 2008 [2698]**	**Ito et al. 2003 [3676]**
Type of study [2]	Cohort	Case control	Case control	Case control
Level of evidence [3]	IIII-2	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of fruit and incidence gastric cancer	Quartiles of Intake of fresh fruit and incidence of gastric cancer	Quintiles of intake of fruit and gastric cancer	Fruit intake by quartiles and gastric cancers
N [5]	195 229 F 288 109 M	274 cases 463 controls	230 cases 547 controls	508 cases 36 490 controls
Population/ study information [6]	US adults M and F	Polish adults - a well defined population study base	Italian adults 22 to 80 yrs. Hospital controls ie poorly defined study base	Japanese F >30 yrs, hospital controls i.e. poorly defined study base
Quality [7]	P	P	0	0
Results [8]	Quintile 5 vs quintile 1 fruit RR 0.75 (95% CI 0.43, 1.31) for women and 1.15 (95% CI 0.85, 1.55) for men	Fruits (including juice) OR 0.53(95% CI 0.33-0.86) P for trend P=0.02	Fruit highest vs lowest quintile OR 0.53(95% CI 0.3-0.93) P for trend NS	Fruit everyday OR 0.68 (95% CI 0.40-1.16) but the P for trend across quartiles was significant (P< 0.001)
Effect on risk (Increase/None/ Protect)	None	Protect	Protect	None
Clinical importance[9]	2	1	1	2
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	n
Applicabilty	y	y	y	n

1.6 FRUIT and BREAST CANCER

Does a particular intake of fruit affect the risk of breast cancer?		
Evidence Statement		Consumption of fruit is not associated with risk of breast cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled analysis of 8 case control and 10 cohort studies (medium risk bias 2 cohort (low risk bias) and 4 case control (low to medium risk bias).
Consistency	Good	Pooled analysis, both cohorts and 2 case control no effect; 1 case control protective and one protective for menopausal but not premenopausal.
Clinical impact	Poor	No significance.
Generalisability	Good	In European US and Asian populations and both menopausal and premenopausal women.
Applicability	Good	Applicable to Australian adult women.

The pooled analysis showed no protective effect of fruit per additional 100g per day. Two cohorts and four case control studies were used to make the body of evidence statements for fruit and breast cancer, see Table 1.6. Only one case control study found a significant protective effect and this was for daily fruit consumption in Polish people. The two cohort studies conducted in the US and Europe included populations with higher fruit consumption such that intakes for lower quintiles were similar intakes to the higher consumption levels in the case control study. The World Cancer Research Fund report concluded that no dietary factors were protective.

Summary: Consumption of fruit is not associated with risk of breast cancer (George et al. 2009; Van Gils 2009; Kruk 2007; Malin et al. 2003; Gaudet et al. 2004; Hermann et al. 2002) (Grade C)

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Table 1.6 Studies used to make evidence statement for fruit and breast cancer

Reference [1]	**Riboli and Norat 2003 [1993]**	**George et al. 2009 [2574]**	**Van Gils 2009 [1511]**	**Kruk J 2007 [2738]**
Type of study [2]	Pooled cohorts (10) case controls (25)	Cohort	Cohort	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Per additional 100 g fruit and breast cancer with 8 case control and 10 cohort studies pooled	Quintile of fruit intake and incident breast cancer	Quintile of intake for fruit 115 g 171 g 229 g 277 g 372 g per day and breast cancer	Fruit <5 serves per week; 5-6 serves per week; more than 7 serves per week and breast cancer according to menopausal status.
N [5]	Not specified	195 229 F	285 526	858 cases 1085 controls
Population/study information [6]	Asian US and European cohorts	US F >50yrs	EPIC F aged 25- 70 yrs	F aged 28-78 yrs in Poland
Quality [7]	0	P	P	P
Results [8]	Fruit shows no protection RR 0.99 (95% CI 0.90-1.0)	NS effect for fruit RR Q5 1.01 (95% CI 0.8-1.28) and NS trend effect	RR quintile 5 vs quintile 1 for fruit RR 1.09 (95% CI, 0.94-1.25)	For menopausal breast cancer OR 0.62 (95% CI 0.47-0.81) P for trend P<0.0012 and for premenopausal 0.6 (0.43-0.85) P for trend P<0.002 for one serve fruit per day vs 5 serves or less per week
Effect on risk	None	None	None	Protect
Clinical importance [9]	1	2	4	1
Clinical relevance [10]	2	1	1	1
Generalisability	y	y	y	y
Applicabilty	y	y	y	y

Table 1.6 Studies used to make evidence statement for fruit and breast cancer (cont.)

Reference [1]	**Malin et al. 2003 [2078]**	**Gaudet et al. 2004 [1650]**	**Hermann et al. 2002[2141]**
Type of study [2]	Case control	Case control	Case control
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Quintile of intake of total and subtypes fruit and risk of breast cancer	Quintile of intake of fruit and risk of breast cancer by menopausal status	Association between premenopausal breast cancer and German diet including g fruit per day- fruit by quartiles
N [5]	1459 cases 1556 controls	1463 cases 1500 controls	355 cases 838 controls
Population/study information [6]	Women aged 25-64 yrs in Shangai	Study in US and Bahamas and was population based	F <51 yrs hospital based in Germany
Quality [7]	P	0	0
Results [8]	OR NS for fruits but significant effect for bananas OR 0.73 (0.58-0.93) quintile 5 vs quintile 1 and showed a significant trend across quintiles	NS reduction in OR or P for trend across quintiles for premenopausal For post menopausal quintile 5 vs quintile 1 OR 0.72 (95 % CI 0.53–0.99)	No significant effect for fruit. OR quartile 4 (>368g per day) 1.13 (95% CI 0.77–1.66)
Effect on risk	None	None/Protect	None
Clinical importance [9]	4	1	3
Clinical relevance [10]	1	1	1
Generalisability	y limited	y	y
Applicabilty	y limited	y	y

1.7 FRUIT and LUNG CANCER

Does a particular intake of fruit affect the risk of lung cancer?		
Evidence Statement		Consumption of fruit is associated with reduced risk of lung cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 2 pooled analyses of cohorts and case control (one of 8 cohorts and one of 25 case control and 11 cohorts and medium risk bias) 5 cohorts (low to medium risk bias) and 4 case control (low to medium risk bias).
Consistency	Poor	2 pooled analyses protective for fruit; 1 cohort (EPIC) protective 4 cohorts and 4 case controls no protection.
Clinical impact	Satisfactory	15% to 23% reduction in the pooled meta analysis.
Generalisability	Good	Nurses Health, Adventist Health, ATBC, Canadian breast cancer Health Professionals Iowa Netherlands New York State in cohorts.
Applicability	Good	Australian adults.

The two pooled cohorts, five cohort studies and four case control studies contributing to the body of evidence are in Table 1.7. The two pooled analyses indicated that fruit is protective of lung cancer as did the EPIC cohort study but most of the studies published since the pooled analyses have failed to demonstrate a protective effect. The pooled analyses include 16 cohort and 25 case control studies and it is difficult for the newer studies to negate this finding with the backing of the EPIC cohort. Thus the evidence statement is that the association is protective but the newer studies indicate the evidence may not be trusted to guide decision making. The World Cancer Research Fund report concluded that it was probable that fruits were protective.

Summary: Consumption of fruit is associated with a reduced risk of lung cancer (Grade D). However a *substantial* effect on risk is unlikely given the initially strong and consistent evidence from pooled analysis, in 2003 (Smith Warner et al. 2003; Riboli & Norat 2003), with the exception of the EPIC study (Miller et al. 2007) is not well supported by more recent cohort (George et al. 2009; Liu et al. 2004; Skuladottir 2004; Wright 2004) studies or case-control studies (Dosil-Diaz 2008; Ruano-Ravina et al. 2002; Rylander et al. 2006; Marchand et al. 2009).

References

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Table 1.7 Studies used to make evidence statements for fruit and lung cancer

Reference [1]	**Smith Warner et al. 2003 [1954]**	**Riboli and Norat 2003 [1993]**	**George et al. 2009 [2574]**	**Liu et al. 2004 [1826]**
Type of study [2]	Pooled analysis (8 cohorts)	Pooled cohorts (10) case controls(25)	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of fruit (155 to 354 fruit g per day) and lung cancer	Fruit and lung cancer with 25 case control and 10 cohort studies pooled	Fruit by quintile and incident lung cancer	Fruit intake as low (mean <=31.6g per day) medium (mean <=95.5 g per day) and high (mean >=138.4g per day) and lung cancer
N [5]	8 cohorts 28,0419 F 149,862 M	Not specified	195,229 F 288,109 M	42,224 (cohort 1) and 51,114 (cohort 2)
Population/ study information [6]	US European cohorts Follow up 6 to 16 years	Asian US and European cohorts	US adults M and F	Japanese men and women JPHC study
Quality [7]	0	0	P	0
Results [8]	Total fruits lowered risk across quintiles p for trend <0.001 RR 0.77; 95% CI 0.67–0.87 for quintile 5 vs quintile1;	Fruit appears to protect against lung cancer RR 0.85 (95% CI 0.78-0.92)	NS protection from fruit for females quintile 5 vs quintile 1 RR 0.89 (95% CI 0.77, 1.02) and for males 0.91 (95% CI 0.81, 1.01)	No significant effect found and RR above 1
Effect on risk (Increase/None /Protect)	Protect	Protect	None	None
Clinical importance[9]	1	1	2	4
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 1.7 Studies used to make evidence statements for fruit and lung cancer (cont.)

Reference [1]	**Skuladottir 2004 [1808]**	**Wright M et al. 2008 [190]**	**Dosil-Diaz et al. (2008) [298]**	**Ruano-Ravina et al. 2002 [2187]**
Type of study [2]	Cohort	Cohort	Case control	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Quartiles of fruit 5 to 40 g; 41-88 g; 89-164 g 165-643 g per day and incident lung cancer	Quintiles of fruit and subtypes and lung cancer	Fruit intake and lung cancer. Total fruit oranges, apples bananas and pears. Compared <1serve per week 1-6 per week and >= 1 per day	FFQ to assess fruit and subtypes in 20 years prior to diagnosis of lung cancer
N [5]	27,178 M 29,875 F (1993-1997)	472,081 M and F	295 cases, 322 controls	163 cases and 241 controls
Population/ study information [6]	Danish population 50 to 64 yrs	US M and F from age 50 to 71 yrs	M and F, aged >35 yrs, Spain hospital based controls	Minimum age was 35yrs Spain population based controls
Quality [7]	P	P	0	P
Results [8]	No significant effect for fruit. For quartile 4 RR 0.86 (95% CI 0.59-1.26)	NS effect for fruit. For men RR 0.93 (95% CI 0.83-1.04) and women RR 0.97(95% CI 0.84-1.11). Subgroup of apple group RR 0.82 (95% CI 0.73-0.91) for men but NS for women	OR for fruit 1.49 (95% CI 0.81–2.73) one or more/day and no significant effect for individual fruits.	Fruit intake offered no protection with OR 2.16 (1.02-4.58) for once/day vs less than once/week and no significant protection was found for subtypes.
Effect on risk (Increase/None /Protect)	None	None but for apple in men	None	None
Clinical importance[9]	2	2	4	3
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 1.7 Studies used to make evidence statements for fruit and lung cancer (cont.)

Reference [1]	**Rylander et al. 2006 [1265]**	**Marchand et al. 2009 [2238]**	**Miller et al. 2007 [1906]**
Type of study [2]	Case-control	Case-control	Cohort
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Fruit intake's association with lung cancer in smokers, former smokers and non smokers	Fruit intake by tertile and lung cancer	Quintiles of intake of fruit and lung cancer Fruit median g per day for F 68.6; 142.4; 218.2; 308.6; 490.4; for M 41.2; 102.3; 165.9; 265.4; 486.4.
N [5]	177 F 359 M 916 controls (M/F)	109 male cases, 227 controls, F had to be excluded as incident cases so low	478,021 M and F
Population/ study information [6]	Conducted in Sweden. Adults less < 75 yrs. Population based controls.	Conducted in New Caledonia	The EPIC study
Quality [7]	0	0	P
Results [8]	Fruit intake offered no protection for non-smokers OR 0.99 (0.36-2.74).	Fruit OR 0.7 (95% CI 0.4-1.5) or tertile 3 vs 1. P for trend NS	Quintile 5 vs quintile 1 for fruit HR 0.60 (95% CI 0.46–0.78), P for trend 0.0099.
Effect on risk (Increase/None /Protect)	None	None	Protect
Clinical importance[9]	2	2	1
Clinical relevance [10]	1	1	1
Generalisability	n	n	y
Applicability	n	n	y

1.8 FRUIT and COLORECTAL CANCER

Does a particular intake of fruit affect the risk of colorectal cancer?		
Evidence Statement		Consumption of fruit is not associated with risk of colorectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 2 pooled analyses of 14 cohort studies and of 31 studies (15 case control and 16 cohort, with medium risk bias) 2 cohorts and 2 case control (low to medium risk).
Consistency	Good	4 of 6 studies find no effect for fruit but 2 case control found a protective effect for fruit.
Clinical impact	Poor	No effect.
Generalisability	Good	US and European cohorts and cases and some Asian populations.
Applicability	Good	Australian adults.

The six studies used to build the evidence statements are shown in Table 1.8. The pooled cohorts showed a slight protection but the confidence intervals for relative risk crossed 1.0. The single cohort studies showed no protection and it was only the case control studies, of neutral and negative quality because of selection and/or measurement bias that demonstrated protection. The World Cancer Research Fund report made no conclusions about fruit but stated dietary fibre is probably protective.

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Table 1.8 Studies used to make evidence statements for fruit and colorectal cancer

Reference [1]	**Koushik et al. 2007 [20]**	**Riboli and Norat 2003 [1993]**	**Sato et al. 2005 [1424]**
Type of study [2]	Pooled cohort analysis (14)	Pooled cohorts and case controls (31)	Cohort
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of fruit intake (<100 g to > 400 g) and colon cancer	Intake of fruit and decreased risk per 100 g intake on colorectal cancer	Quartiles of fruit and incident colorectal cancer
N [5]	756 ,217 in cohort 5838 cases 14 studies	Not specified	47,605 M and F (41 835 included in analysis)
Population/study information [6]	6 to 20 yrs US and Europe	US and Europe	Japanese 40 to 64 yrs
Quality [7]	0	0	P
Results [8]	Quintile 5 highest vs quintile 1 lowest fruit RR 0.93 (95% CI 0.85-1.02)	For an increase in fruit intake of 100 g per day from 15 case control studies RR 0.93 (95% CI 0.87-0.99) and from 16 cohort RR 0.96 (95% CI 0.90-1.01)	Quartile 4 vs quartile 1 RR 1.45 (95% CI 0.85–2.47).
Effect on risk (Increase/None/Protect)	None	None	None
Clinical importance[9]	2	2	4
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

Table 1.8 Studies used to make evidence statements for fruit and colorectal cancer (cont.)

Reference [1]	**George et al. 2009 [2574]**	**Wu et al. 2009 [119]**	**Oh et al. 2005 [3383]**
Type of study [2]	Cohort	Case-control	Case-control
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Quintile of fruit intake and then incidence for all cancers and then for individual cancers	Tertile of fruit intake and risk of colorectal adenoma	Tertiles of fruit intake and risk of polyps or colorectal cancer
N [5]	195 229 F 288 109 M	764 cases 1517 controls	49 cases cancer, 87 cases of polyps 134 controls
Population/study information [6]	US adults M and F	US adult M and F Hospital based study so poorly defined study base	Korea – hospital based study so poorly defined study base
Quality [7]	P	0	N
Results [8]	Quintile 5 vs quintile 1 RR 0.93 (0.79, 1.09)	Tertile 3 vs tertile 1 OR 0.66 (95% CI 0.51–0.86) for total fruits, 0.64 (95% CI 0.47–0.87) for berries, and 0.72 (95% CI 0.56–0.92) for fruit juice	Tertile 3 vs tertile 1 (> 276.5 g vs <140 g) OR 0.38 (95% CI 0.2-0.74)
Effect on risk (Increase/None/Protect)	None	Protect	Protect
Clinical importance[9]	2	1	1
Clinical relevance [10]	1	2	2
Generalisable	y	n	n
Applicable	y	n	n

1.9 FRUIT and OESOPHAGEAL CANCER

Does a particular intake of fruit affect the risk of oesophageal cancer?		
Evidence statement		Consumption of fruit is associated with reduced risk of oesophageal cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled analysis (medium risk bias); 3 cohorts and 1 case control (low risk bias).
Consistency	Poor	1 pooled analysis showed a positive effect; 2 cohorts no effect; 1 cohort and 1 case control a positive effect for fruit.
Clinical impact	Good	If pooled analysis correct 28% for each additional 100 g fruit.
Generalisability	Good	Includes European and US populations.
Applicability	Good	Yes for adult men and women in Australia.

The five studies used to make the evidence statement are shown in Table 1.9. The case control studies indicate protection with fruit intake as seen in the pooled analyses and subsequent case control study. The findings from the US cohort showed significant protection from squamous cell carcinoma. The EPIC study showed a 6% decrease but the confidence interval was wide and crossed 1. Average follow up for the US cohort study was about five years and for EPIC 6.5 years. There were more incident cancers in the US population. The World Cancer Research Fund report stated that it was probable that fruits were protective.

Summary: While positive findings were reported across five studies (including pooled cohort and case control and cohort studies) (Freedman et al. 2007; Riboli & Norat 2003; Gonzales et al. 2006; George et al. 2009) and a smaller case control study (Anderson et al. 2007) there were quality issues apparent with one meta-analysis (Riboli & Norat 2003), therefore it was inconclusive that consumption of fruit is associated with decreased risk of oesophageal cancer (Grade D).

References

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Table 1.9 Studies used to make evidence statement for fruit and oesophageal cancer

Reference [1]	**Riboli and Norat 2003 [1993]**	**Freedman et al. 2007 [427]**	**Gonzalez et al. 2006 [1207]**	**George et al. 2009 [2574]**	**Anderson et al. 2007 [7807]**
Type of study [2]	Pooled cohorts and case controls – 15 studies	Cohort	Cohort	Cohort	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Intake of fruit and decreased risk per 100 g intake on oesophageal cancer	Quintiles of fruit intake incident oesophageal cancer	Tertiles of fruit intake and incident oesophageal adenocarcinoma	Quintile of fruit and then incidence for all cancers and then for individual cancers	Tertiles for weekly fruit consumption and oesophageal adenocarcinoma
N [5]	Not specified	490 802 subjects (566 407 initial sample)	521 457 M and F	195 229 F 288 109 M	227 with Oesophageal Adenocarcinoma and 260 controls
Population/study information [6]	Asian US and European (15 studies)	US NIH American Association of Retired Persons study M and F >=50 yrs	Part of European Investigation into cancer EPIC	US adults M and F	Population based in Ireland (FINBAR study)
Quality [7]	0	P	P	P	P
Results [8]	Each additional 100 g fruit RR 0.72 (95% CI 0.62-0.83) based on case control	Total fruit 0.46 (0.21-1.0) P for trend 0.03. for squamous cell carcinoma but for adenocarcinoma RR 1.04 (95% CI 0.64-1.69)	Tertile 1 vs tertile 3 RR 0.94 (95% CI 0.49–1.80)	Quintile 5 vs quintile 1 RR 1.09 (95% CI 0.54-2.2)	Tertile 1 (<5 per week) vs tertile 3 (>20 per week. OR 0.5 (95% CI 0.3-0.86) NS for trend effect

Effect on risk (Increase/None/Protect)	Protect	Protect	None	None	Protect
Clinical importance [9]	1	1	2	4	1
Clinical relevance [10]	1	1	1	1	1
Generalisable	y	y	y	y	y
Applicable	y	y	y	y	y

1.10 FRUIT and ORAL and NASOPHARYNGEAL CANCERS

Does a particular intake of fruit affect the risk of oral and nasopharyngeal cancer?		
Evidence Statement		Consumption of fruit is associated with a reduced risk of oral and nasopharyngeal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled cohort (medium risk bias with 9 studies) and 4 case control (medium to high risk bias).
Consistency	Good	4/5 found fruit protective.
Clinical impact	Good	As much as 50% reduction.
Generalisability	Good	European US and Asian.
Applicability	Good	Adult Australians.

The pooled analysis and three of the four case control studies used to make the evidence statements show protection (see Table 1.10). The quality of the study showing no significant effect was very poor. Comparisons were by Mann Whitney U test of intakes with no logistic regression modeling to yield an odds ratio. The studies also indicate that protection may be more for current or ever smokers than non-smokers. Most studies adjust for smoking and alcohol that are known risk factors. The World Cancer Research Fund report stated that it was probable that fruits protected against oral cancer.

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Table 1.10 Studies used to make evidence statement for fruit and oral and nasopharyngeal cancer

Reference [1]	**Riboli and Norat 2003 [1993]**	**Kreimer et al. 2006 [1217]**	**Guneri et al. 2005 [1322]**	**Heck et al. 2008 [2657]**	**Escribano Uzcudun et al. 2002 [7999]**
Type of study [2]	Pooled cohorts and case controls 9 studies	Case control	Case control	Case control	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Intake of fruit and decreased risk per 100 g intake on oral and pharyngeal cancer	Quartiles of fruit and oral and oropharyngeal squamous cell carcinomas	Comparison of weekly fruit intake in cases of oral cancer and controls	Quartiles of fruit intake and hypopharyngeal cancer	Fruit intake included with many risk factors for pharyngeal cancer
N [5]	Not specified	1670 cases, 1732 controls	79 cases, 61 controls	513 cases, 713 controls	232 cases, 232 controls
Population/study information [6]	Asian US and European cohorts 9 case control studies	Hospital based in 9 countries (IARC group) Italy Spain Australia, Canada, Poland Northern Ireland, India, Sudan, Cuba	Clinic based study in young Turkish adults	Indian hospital based study	Hospital based study in Madrid, Spain
Quality [7]	0	0	N	0	0
Results [8]	Each additional 100 g per day fruit RR 0.53 (95% CI 0.37-76)	Quartile 4 vs quartile 1 OR 0.7 (95% CI 0.5-0.9) P for trend <0.001.	NS association. ORs not calculated in normal manner	Ever smoked tobacco highest quartile vs lowest of fruit intake OR 0.37 (95% CI 0.20–0.69) for never smokers OR 0.56 (95% CI 0.20 1.55)	Deficient dietary intake of fruit and fruit juice OR 4.4 (95% CI 2.0–9.4)

Effect on risk (Increase/None/Protect)	Protect	Protect	None	Protect	Protect
Clinical importance[9]	1	1	n/a	1	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	n	n	y
Applicability	y	y	n	smokers only	n

1.11 FRUIT and OVARIAN CANCER

Does a particular intake of fruit affect the risk of ovarian cancer?		
Evidence statement		Consumption of fruit is not associated with risk of ovarian cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled analysis of 12 cohorts (low risk bias); and 1 cohort (low risk bias).
Consistency	Excellent	Pooled analysis showed no effect; 1 cohort no effect.
Clinical impact	Poor	No protection.
Generalisability	Good	Includes European and US studies.
Applicability	Good	Yes for adult women in Australia.

The pooled analysis and cohort are summarized in Table 1.11. In European and US women there is no evidence of protection from fruit consumption.

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Table 1.11 Studies used to make evidence statement for fruit and ovarian cancer

Reference [1]	**Koushik et al. 2005 [1345]**	**Schulz 2005 [1308]**
Type of study [2]	Pooled cohort analysis (12) ovarian cancer	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Quartiles of fruit <100 to >400 g per day and ovarian cancer	Looking at 80 g increments of total fruit and ovarian cancer
N [5]	560,441 cohort 2130 cases	325,640 F
Population/study information [6]	US and European cohorts including Nurse Health, Netherlands, Swedish Mammography	EPIC cohort
Quality [7]	0	P
Results [8]	Quartile 4 vs quartile 1 veg intake RR 1.06 (95% CI 0.92-1.21)	Per additional 80 g veg HR 1.08 (95% CI 0.99, 1.18)
Effect on risk (Increase/None/ Protect)	None	None
Clinical importance [9]	4	4
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

1.12 FRUIT and ENDOMETRIAL CANCER

Does a particular intake of fruit affect the risk of endometrial cancer?		
Evidence statement		Consumption of fruit is not associated with risk of endometrial cancer.
Grade		**C**
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled analysis of 10 studies (only 4 included in RR) and 1 cohort (low risk bias) and 2 cases. control (medium risk bias)
Consistency	Excellent	No protection.
Clinical impact	Poor	No protection.
Generalisability	Good	Includes European and US studies.
Applicability	Good	Yes for adult women in Australia.

The meta analysis, cohort and case control studies used to make the body of evidence are shown in Table 1.12. All studies agree that there is no protection from fruit but further studies are indicated. The World Cancer Research Fund report also concluded there was no supportive evidence for fruit offering protection.

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Table 1.12 Studies used to make the body of evidence statement for fruit and endometrial cancer

Reference [1]	**Bandera et al. 2007 [4633]**	**McCullough M et al. 2007 [454]**	**Bravi et al. 2009 [2829]**	**Yeh et al. 2009 [8110]**
Type of study [2]	Meta analysis 10 studies included	Cohort	Case-control	Case-control
Level of evidence [3]	III-2	3	III-2	III-2
Intervention/ comparator [4]	Dose response per 100 g fruit and endometrial cancer	Quintiles veg up to more than 2.7 serves and incident endometrial cancer	Fruit and endometrial cancer risk	Quartile of fruit intake risk of endometrial cancer
N [5]	Varied from 2951 to 3255 cases	41,400	454 cases and 908 controls	541 cases and 541 controls
Population/ study information [6]	US Europe and Asia this is the WCRF systematic review	US W median age 63yrs Cancer Prevention 2 Cohort	In Italy - hospital based controls	Hospital based in US
Quality [7]	P	P	0	0
Results [8]	For additional 100g fruit per day RR 0.94 (95% CI 0.86-1.02) only 4 studies	For highest vs lowest tertile fruit RR 1.24, (95% CI 0.90,1.70)	For an increment of one serving of fruit OR 0.83 (95% CI 0.55 -1.24)	For quartile 4 vs quartile 1 fruit intake OR 1.10 (0.74–1.62)
Effect on risk (Increase/None/ Protect)	None	None	None	None
Clinical importance [9]	2	4	2	4
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	n	y
Applicability	y	y	n	y

FRUIT - subtypes

Search results

The initial search of the databases included 3691 references for fruit and the specified disease outcomes. The detailed search is included in a separate document on searches. As there were 2714 duplicates with the fruit database the two were combined in one Endnote library and coded as one. All 97 references concerning fruit and vegetables had data extracted and 4 papers were used to form the body of evidence statements for subtypes of fruit. Sufficient evidence was found to make a statement for citrus fruit and pancreatic cancer, fruits and colorectal cancer.

1.13 CITRUS FRUIT and PANCREATIC CANCER

Does a particular intake of citrus fruit affect the risk of pancreatic cancer?		
Evidence Statement		Consumption of citrus fruit is associated with reduced risk of pancreatic cancer
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 meta analysis of 9 studies (4 case control and 5 cohort (medium risk bias) plus 1 cohort (low risk bias).
Consistency	Poor	The pooled analysis shows protection but reliant on the case control studies. The single cohort study shows an increased risk.
Clinical impact	Good	Reduction of risk 17%.
Generalisability	Good	Studies in Europe USA and Asia.
Applicability	Good	Applies to Australian adults.

The systematic review with pooled odds ratio indicates that citrus fruits are protective but it is noted that this is largely because of positive findings with the case control rather than the cohort studies. The EPIC cohort investigation finds an increased risk and as this is the largest prospective trial into cancer and fruit consumption the results cannot easily be dismissed. This means that the evidence base cannot guide practice but alerts researchers to the need for further study of this association.

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Table 1.13 Studies used to make the body of evidence statement for citrus fruit and pancreatic cancer.

Reference [1]	**Bae et al. 2009 [8035]**	**Vreiling et al. 2009 [86]**
Type of study [2]	Systematic review with pooled estimate (9 cohort, 4 case control)	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Citrus fruits and pancreatic cancer	Quartile of intake <8g per day 8–29 g per day; 29–68 g per day; >68 g per day and incident pancreatic cancer
N [5]	9 (5 cohort and 4 case control) 1894 cases and 6257 controls/ 4783case/1,478,925 in cohorts	142,759M 335,821 F
Population/study information [6]	European Japan and US; cohorts followed for 6.8 to 14 years	EPIC cohort mean age 51 yrs
Quality [7]	0	P
Results [8]	Inverse association RR 0.83 (0.7-0.98) but effects only found in case control from seldom to almost daily	No association of pancreatic cancer with citrus fruit highest quartile vs lowest quartile RR 1.12 (95% CI 0.86–1.45)
Effect on risk (Increase/None/ Protect)	Protect	None
Clinical importance [9]	1	4
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

1.14 FRUIT by sub type and COLORECTAL CANCER

Does a particular intake of fruit affect the risk of colorectal cancer?		
Evidence Statement		Consumption of fruit of most subtypes is not associated with colorectal cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from1 meta analysis of 14 cohort studies (medium risk bias) plus 1 case control study (medium risk bias).
Consistency	Satisfactory	The pooled analysis show no protection except for bananas.
Clinical impact	Poor	Only reduction found for bananas of about 10%.
Generalisability	Good	Studies in Europe and USA.
Applicability	Good	Applies to Australian adults.

As was found for total fruits, no subtype of fruit was demonstrated to provide protection from colorectal cancer with the exception of bananas in the pooled analysis. The protective effect of bananas has been reported previously. See Table 1.14.

References

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Wu, H., Dai, Q., Shrubsole, M. J., Ness, R. M., Schlundt, D., Smalley, W. E., Chen, H., Li, M., Shyr, Y., Zheng, W., , W. 2009, "Fruit and vegetable intakes are associated with lower risk of colorectal adenomas", *Journal of Nutrition*, vol. 139, no. 2, pp. 340-4.

Table 1.14 Studies used to make the body of evidence statement for citrus fruit and colorectal cancer.

Reference [1]	**Koushik et al. 2007 [20]**	**Wu et al. 2009 [119]**
Type of study [2]	Pooled cohort analysis colon cancer (14 studies)	Case-control
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Quintiles of fruit intake (<100g to > 400g) and colon cancer	Fruit subtypes intake by tertile and risk of colorectal adenoma
N [5]	756217 in cohort 5838 cases 14 studies	764 cases 1517 controls
Population/study information [6]	Europe and US. Follow up 6 to 20 years	US adult males and females Hospital based study
Quality [7]	0	0
Results [8]	Highest (1/2 or 1 serving per day) vs nil apples/pears RR 0.98 (0.88-1.10) melon RR 0.98 (0.88-1.10) oranges RR 1.00 (0.89- 1.11) grapefruit RR 0.96 (0.81- 1.13) bananas RR 0.88 (0.78-0.99) peaches RR 0.97 (0.75-1.24)	Tertile 3 vs tertile 1 OR citrus fruit 0.83 (95% CI 0.63-1.10) OR melon 1.10 (95% CI 0.86-1.39)
Effect on risk (Increase/None/ Protect)	None except for bananas	None
Clinical importance [9]	1 for bananas	2 citrus/4 melon
Clinical relevance [10]	1	1
Generalisability	y	n
Applicability	y	n

2. VEGETABLES (S1.1 and S1.10)

Evidence Statements

2. VEGETABLES (S1.1 and S1.10)

Search results

The initial search of the databases included 4667 references for vegetables and the specified disease outcomes. The detailed search is included in a separate document on searches. As there were 2714 duplicates with the fruit database the two were combined in one Endnote library and coded as one. In all, 97 references concerning fruit and vegetables had data extracted and 58 papers were used to form the body of evidence statements for vegetables. Sufficient evidence was found to make statements for vegetables and cardiovascular disease, stroke, obesity diabetes and a range of cancers including gastric, breast, lung, colorectal, oesophageal and oral and nasopharyngeal, endometrial, ovarian and bladder cancer.

2.1 VEGETABLES and CORONARY HEART DISEASE

Does a particular intake of vegetables affect the risk of coronary heart disease?		
Evidence Statement		Consumption of each additional daily serve of vegetables is associated with a reduced risk of coronary heart disease.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from two meta analyses each with 9 cohort studies (with most studies in common and medium risk bias and 2 cohort (low risk bias) and 1 case control and one RCT (medium risk bias).
Consistency	Good	Meta analyses and case control and RCT protective (and in each study) but cohort studies show no effect.
Clinical impact	Good	15 to 25% reduction with additional serve.
Generalisability	Good	US, Europe.
Applicability	Excellent	Australian adults of both sexes.

The studies used to make the body of evidence statements are shown in the Table 2.1 below. The two meta analyses are in agreement but have six of nine studies in common, with most studies being from the USA. The Japanese cohort study demonstrated no association between vegetables and cardiovascular disease and the analysis of the Nurses Health and Male Health Professionals cohorts stratified by the percentage energy from carbohydrate indicated that the protective effect is only found when carbohydrate intakes are less than 40% energy. The hospital-based case control study showing that vegetables markedly decrease the risk of acute myocardial infarction was of a poorer quality with selection and measurement bias. The RCT is also of a poorer quality and only for six

weeks with measurement of surrogate outcomes of blood lipids but it reinforces the finding that vegetable consumption may protect from cardiovascular disease.

Summary: It is probable that each additional daily serve of vegetables is associated with a reduced risk of coronary heart disease (Grade B) with consistent reporting of protective effects from meta-analysis (Dauchet et al. 2006; He et al. 2007) supported by other individual studies (Rastogi et al. 2004; Rodriguez-Rodriguez et al. 2007). These findings were not supported by two cohort studies (Joshipura et al. 2008; Takashchi et al. 2008) although a protective effect was seen in the Nurses Health and Male Health Professionals study (Joshipura et al. 2008) when carbohydrate intakes were less than 40% energy intake.

References

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He, F. J., Nowson, C. A., Lucas, M. & MacGregor, G. A. 2007, "Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies", *Journal of Human Hypertension*, vol. 21, no. 9, pp. 717-28.

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Rastogi, T., Reddy, K. S., Vaz, M., Spiegelman, D., Willett, W. C., Stampfer, M. J. & Ascherio, A. 2004, "Diet and risk of ischemic heart disease in India.[see comment]", *American Journal of Clinical Nutrition*, vol. 79, no. 4, pp. 582-92.

Rodríguez-Rodríguez, E., Ortega, R. M., López-Sobaler, A. M., Andrés, P., Aparicio, A., Bermejo, L. M. & García-González, L. 2007, "Restricted-energy diets rich in vegetables or cereals improve cardiovascular risk factors in overweight/obese women", *Nutrition Research*, vol. 27, no. 6, pp. 313-320.

Takachi, R., Inoue, M., Ishihara, J., Kurahashi, N., Iwasaki, M., Sasazuki, S., Iso, H., Tsubono, Y. & Tsugane, S. 2008, "Fruit and vegetable intake and risk of total cancer and cardiovascular disease: Japan Public Health Center-Based Prospective Study", *American Journal of Epidemiology*, vol. 167, no. 1, pp. 59-70.

Table 2.1 Studies used to make evidence statement for vegetables and coronary heart disease

Reference [1]	**Dauchet et al. 2006 [33]**	**He et al. 2007 [23]**	**Joshipura et al. 2008 [2546]**	**Takachi et al. 2008 [376]**	**Rastogi et al. 2004 [1846]**	**Rodriguez-Rodriguez et al. 2007 [3123]**
Type of study [2]	Meta analysis of cohort - 9 cohorts	Meta analysis of cohort -12	Cohort	Cohort	Case-control	RCT
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	II
Intervention/ comparator [4]	Decrease in RR with each additional serve of vegetables (1-5 or more serves) and coronary heart disease	Intake of vegetables of <1.7, 1.7-3.0 and >3.0 servings/day and coronary heart disease	Quintile of vegetable by % energy from carbohydrate i.e. <40%, 40-55% and >55% and cardiovascular disease	Quartiles of intake and cardiovascular disease outcomes	Serves of veg and risk of acute myocardial infarction <1 serve, 1-2 serves, 2-3 serves, >3 serves/day	Energy restricted diet rich in either cereal or vegetable, and cardiovascular disease risk factors
N [5]	82,524 M 117,108 F	278,459 (M and F)	38,918 M 70,870 F	77,891	350 cases and 700 controls (both from Indian hospitals)	57 overweight females 29 in cereal group and 8 in veg group
Population/study information [6]	9 cohorts include 7 cohorts from the U.S. and 2 from Finland but only 7 used in the metanalysis.	9 cohorts included long follow up in US and Europe	Nurses Health and Male Health Professionals	Japanese adult M and F	Hospital based Indian study	Subjects in veg group encouraged to increase intake of veg (at least 3 times per day), salad at lunch and dinner and veg as a main course in one meal
Quality [7]	0	0	P	P	0	0
Results [8]	Veg and CHD mortality RR 0.74 (95%CI 0.75-0.84) P for trend <0.0001	For <1.7 serves veg vs >3 serves per day RR 0.84 (95% CI	Quintile 5 vs quintile 1 NS effect but trend across quintiles for low	HR for quartile 4 vs quartile 1 0.97 (95% CI 0.82-1.15) P for trend NS	For < 1 serve vs >3 serves per day OR 0.33 (95%CI 0.33-0.82) P for trend	LDL chol significantly decreased (P<0.05) from 2.89 to 2.61 mmol/L in veg group after 6 weeks.

	and fatal and nonfatal MI RR 0.95 (95%CI 0.92-0.99) P<0.006)	0.76–0.92)	CHO group RR 0.82 for an increment of 3 servings per day (95% CI 0.68, 0.99);		<0.006	
Effect on risk (Increase/None/ Protect)	Protect	Protect	None	None	Protect	Protect
Clinical importance [9]	1	1	2	2	1	1
Clinical relevance [10]	1	1	1	1	1	2
Generalisability	Y	y	y	y	n	n
Applicability	Y	y	y	n	n	n

2.2 VEGETABLES and OBESITY

Does a particular intake of vegetables affect the risk of weight gain and/or obesity?		
Evidence statement		Consumption of vegetables is associated with reduced risk of weight gain.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 4 cohorts (4 studies, low risk bias) and 2 RCTs of weight loss diets.
Consistency	Good	2 cohorts in adults and 1 RCT show protection and one cohort tracking BMI from childhood protection in girls (not boys), 1 cohort in children no effect and 1 RCT of weight reduction diet no effect.
Clinical impact	Satisfactory	RR in adult cohorts 0.18 to 0.76 for weight gain.
Generalisability	Good	US and European and one Australian study.
Applicability	Excellent	Applicable to Australian adults.

The cohort studies generally showed a protective effect of increasing vegetable intake and decreased weight gain with the exception of the study in children that used change in BMI Z score. See Table 2.2.

Summary: The evidence suggests that consumption of vegetables is associated with a reduced risk of weight gain (Grade C) (He et al. 2004), although different measures of changing body weight have been applied, different age groups have been studied (Sartorelli et al. 2008; Vioque et al. 2008 ; te Velde et al. 2007) and results have not been consistent (Field et al. 2003).

References

Booth, A., Nowson, C., Worsley, A., Margerison, C. & Jorna, M. 2008, "Dietary approaches for weight loss with increased intakes of fruit, vegetables and dairy products", *Nutrition & Dietetics*, vol. 65, no. 2, pp. 115-120.

Field, A. E., Gillman, M. W., Rosner, B., Rockett, H. R. & Colditz, G. A. 2003, "Association between fruit and vegetable intake and change in body mass index among a large sample of children and adolescents in the United States", *International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, vol. 27, no. 7, pp. 821-6.

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Sartorelli, D. S., Franco, L. J., Cardoso, M. A., Sartorelli, D. S., Franco, L. J. & Cardoso, M. A. 2008, "High intake of fruits and vegetables predicts weight loss in Brazilian overweight adults", *Nutrition Research*, vol. 28, no. 4, pp. 233-8.

te Velde, S. J., Twisk, J. W., Brug, J., te Velde, S. J., Twisk, J. W. R. & Brug, J. 2007, "Tracking of fruit and vegetable consumption from adolescence into adulthood and its longitudinal association with overweight.[erratum appears in Br J Nutr. 2007 Oct;98(4):871]", *British Journal of Nutrition*, vol. 98, no. 2, pp. 431-8.

Vioque, J., Weinbrenner, T., Castello, A., Asensio, L. & de la Hera, M. G. 2008, "Intake of fruits and vegetables in relation to 10-year weight gain among Spanish adults", *Obesity*, vol. 16, no. 3, pp. 664-670.

Table 2.2 Studies used to make evidence statement for vegetables and obesity

Reference [1]	**Field 2003 [2036]**	**He et al. 2004 [1586]**	**Sartorelli et al. 2008 [97]**	**Booth et al. 2008 [5944]**	**Vioque et al. 2008 [4150]**	**te Velde et al. 2007 [518]**
Type of study [2]	Cohort	Cohort	RCT	RCT	Cohort	Cohort
Level of evidence [3]	III-2	III-2	II	II	III-2	III-2
Intervention/ comparator [4]	Servings of veg per day and change in BMI Z score over 3 years	change in serves veg by quintile - 1.72; -0.40; 0.36; 1.21; 2.8 for veg; and outcome is obesity or weight gain	80 overweight adults individualized energy restricted diet that included at least 5 serves of veg per day and advice for 30 mins of walking. Outcome is weight loss	Comparing 2 diets in terms of greater loss of weight one with additional fruit and veg and dairy and one low fat	Quintiles of veg intake <166 g per day; 166–243 g per day; 244–333 g per day ; >333 g per day and weight gain of more than the average ie 3.4 kg over 10 years	Quartiles veg intakes tracked over 24 years and longitudinal change in BMI and sum of skinfolds (reference is the highest quartile)
N [5]	8203 G 6715 B	74 063	80 adults	27 in intervention group, 27 in control group	206 M and F	168 M and F
Population/study information [6]	US 9 to 14 yrs B and G	US Nurses Health	Brazilian mean age (±SD) 46.5 ± 9.5 yrs, mean BMI 29 ± 3 kg/m^2 at baseline	2 diets - WELL (Weight loss, Exercise, Lower blood pressure and Longevity) with double fruit (4 serves) and veg (4 serves) vs low fat diet for 12 weeks	Healthy sub sample Spanish Valenica cohort age 15 - 80 yrs	Amsterdam Growth and Health Longitudinal Study followed from 13 to 36 yrs

Quality [7]	P	P	0	P	P	0
Results [8]	Adjusted change BMI Z score with veg intake 0.005 (95% CI -0.009-0.019) girls and -0.007 (95% CI -0.027-0.013) for boys	Significant for veg quintile 5 RR 0.84 (95% 0.75-0.93) P for trend 0.0002 and obesity For weight gain veg quintile 5 significant RR 0.76 (95% CI 0.59-0.99) P for trend=0.05	Veg intake increased by 82 g to 260 g per day and veg intake was a significant predictor of weight loss beta = −0.00497 (CI −0.008; −0.002) r^2 = 0.137 P =0.003	WELL subjects lost 4.8 +/-3.3kg and Low Fat 4.6 +/- 3.1kg P=0.83	Quintile 5 vs quintile 1 OR 0.18 (95% CI 0.05–0.66) P trend = 0.017).	For girls being in lowest quartile veg intake was predictive of higher BMI Q1 0·480 (95% CI 0·180-0·779) and skinfolds 4·41 (95% CI 1·89-6·93) but NS for boys
Effect on risk (Increase/None/ Protect)	None	Protect	Protect	None	Protect	Protect (girls only)
Clinical importance [9]	2	1	1	4	1	1
Clinical relevance [10]	2	1	2	2	1	1
Generalisability	y	y	y	n	y	n
Applicability	y	y	y	n	y	y

2.3 VEGETABLES and TYPE 2 DIABETES

Does a particular intake of vegetables affect the risk of type 2 diabetes?		
Evidence statement		Consumption of vegetables is not associated with reduced risk of type 2 diabetes.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 meta analyses of cohorts (4 studies, low risk bias) and 2 cohorts.
Consistency	Satisfactory	Meta analysis and 1 European cohort no protection. One Chinese cohort protective for vegetables (women only).
Clinical impact	Satisfactory	HR ranges 0.7-0.97.
Generalisability	Good	Chinese women US women and Finland.
Applicability	Excellent	Applicable to Australian adults.

One meta analysis of US and Europeans cohorts with 4 studies and an additional cohort from EPIC (both studies of good quality) failed to find any relationship but the Chinese women's cohort showed a protective effect. It may be that these women are different to Australian women and lifestyle conditions. See Table 2.3.

Summary: The evidence suggests that consumption of vegetables does not appear to be directly associated with a risk of Type 2 diabetes (Grade C) (Hamer et al. 2007, Harding et al. 2008, Villegas et al. 2008).However, as there is a strong relationship between Type 2 diabetes and body weight, this suggests longer-term studies may be required to further investigate the effect of consumption of vegetables on risk of type 2 diabetes.

References

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Table 2.3 Studies used to make evidence statement for vegetables and type 2 diabetes

Reference [1]	**Hamer et al. 2007 [18]**	**Harding et al. 2008 [225]**	**Villegas et al.l 2008 [336]**
Type of study [2]	Systematic review of 4 cohorts	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Examine subjects consuming 3 or more serves veg vs those consuming less and diabetes type 2	Quintile of veg and incident diabetes type 2	Quintiles of intake of veg 121.5g ;181.6 g; 236g 302.6, 428 g and incident Type 2 diabetes total veg and subtypes
N [5]	167,128	21,831	74,942
Population/study information [6]	6 to 23 yrs includes US and Finnish cohorts	EPIC in UK M and F	Chinese F 40 to 70 yrs
Quality [7]	P	P	P
Results [8]	RR for 3 or more serves vs < 3 serves vegs 0.97 (95% CI 0.86–1.10, p=0.59)	OR for quintile 5 vs quintile 1 veg 0.80 (95% CI 0.62-1.03)	HR 0.72 (95% CI 0.61-0.85) is significantly lower for quintile 5 vs quintile 1 Dose response P<0.001
Effect on risk (Increase/None/Protect)	None	None	Protect
Clinical importance [9]	2	2	1
Clinical relevance [10]	1	1	1
Generalisability	y	y	y only women
Applicabilty	y	y	y

2.4 VEGETABLES and STROKE

Does a particular intake of vegetables affect the risk of stroke?		
Evidence statement		Consumption of vegetables is associated with reduced risk of stroke.
Grade		B Additional methodological consideration noted that if the two systematice reviews of cohort are unpicked then it would be found the conbimed effect of the cohort studies would be protective. The systematic review by He is the stroonger study as it contains all of the studies that Dauchet included (although it does not present data for vegetables alone as is included by Gillman, but this was a smallish study which would not have made much impact overall). Another key difference is that He presents results as >5 vs <3 per day. Thus the evidence statement should be upgraded from D to B.
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 2 meta analyses of cohorts (medium risk bias, one with 4 studies and one with 5).
Consistency	Good	One found significant protection the other did not.
Clinical impact	Good	One meta analysis showed 20 % risk reduction but other did not.
Generalisability	Good	US, Europe.
Applicability	Excellent	Australian adults of all age groups and both genders.

The two meta analyses are summarized below. They had three cohorts in common but the addition of the Finnish cohort and Dutch cohort in one analysis resulted in a finding of protection in one and the other failed to find a significant effect. For this reason the evidence statement cannot be used to guide judgement and more studies are needed. See Table 2.4.

References

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He, F. J., Nowson, C. A. & MacGregor, G. A. 2006, "Fruit and vegetable consumption and stroke: meta-analysis of cohort studies.[see comment]", *Lancet*, vol. 367, no. 9507, pp. 320-6.

Table 2.4 Studies used to make evidence statement for vegetables and stroke

Reference [1]	**He et al. 2006 [42]**	**Dauchet et al. 2005 [44]**
Type of study [2]	Meta analysis of 5 cohorts	Meta analysis of 4 cohorts
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	<3 , 3-5 and to >5 serves veg per day and stroke	Each additional serve of vegetables up to 5 and stroke
N [5]	257,551 in total	90,513 M 141,536 F
Population/study information [6]	US Japanese and European cohorts	US cohorts and Danish
Quality [7]	0	0
Results [8]	RR for >5 serves veg vs <3 per day 0·81 (95% CI 0·72–0·90)	RR: 0.97 (95% CI 0.92 to 1.02); per additional serve
Effect on risk (Increase/None/Protect)	Protect	None
Clinical importance [9]	1	2
Clinical relevance [10]	1	1
Generalisability	y	y
Applicabilty	y	y

2.5 VEGETABLES and GASTRIC CANCER

Does a particular intake of vegetables affect the risk of gastric cancer?		
Evidence statement		Consumption of vegetables is associated with reduced risk of gastric cancer.
Grade		D The methodologist noted that the null finding of the study undertaken by Gonzalezof 0.5 millin needs to be given greater weight – either to say any association is unclear – or weak evidence for no association (grade D overall).
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence 1 meta analysis (5 cohort 17 case control medium risk bias) 4 cohorts (low to medium risk bias) and 3 case controls (low to medium risk bias).
Consistency	Poor	Meta analysis and 2 cohorts positive for vegetable; 2 positive case controls and 2 cohort and 1 case control no effect.
Clinical impact	Good	Reduction approximately 20% to 25%.
Generalisability	Good	Studies in Japan, Sweden, Poland, US.
Applicability	Excellent	Applicable to Australian adults.

The meta analysis included 22 studies, 17 of which were case controls. Two additional case control studies also found a protective effect. The findings from the single cohort studies were equivocal but the meta analysis showed protection. The two cohort studies that failed to find protection included EPIC and the newer cohort of older adults from the National Institute of Health American Association of Retired Persons. The World Cancer Research Fund report stated that it was probable that non starchy vegetables were protective. See Table 2.5.

References

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Table 2.5 Studies used to make evidence statement for vegetables and gastric cancer

Reference [1]	**Riboli and Norat 2003 [1993]**	**Kobayashi et al. 2002 [2229]**	**Gonzalez et al. 2006 [1207]**	**Larsson 2006 [1036]**
Type of study [2]	Pooled cohorts (5) and case controls (17)	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Each 100 g veg additional and gastric cancer	Quintiles of veg intake and gastric cancer	Quartiles of veg intake and incident gastric cancers	<1; 1.0 to 1.4; 1.5-2.4 and >=2.5 serves vegetables per day and gastric cancer
N [5]	Uncertain	19 304 M 20 689 F	521 457	45 338 M 36 664 F
Population/study information [6]	Asian US and European cohorts	Japanese cohort adult	Part of EPIC	Swedish cohort M and F
Quality [7]	0	0	P	P
Results [8]	0.81 (0.75, 0.87) for an increase of 100 g per day (some heterogeneity	RR quintile 5 vs quintile 1 of total veg consumption 0.75 (95% CI 0.59–0.99)	RR for quartile 4 vs quartile 1 of veg consumption 1.15 (95% CI 0.78–1.70)	>2.5 serves per day of veg <had HR of 0.56 (95% CI, 0.34-0.93) vs <1 serve per day
Effect on risk (Increase/None/ Protect)	Protect	Protect	None	Protect
Clinical importance[9]	1	1	4	1
Clinical relevance [10]	1	1	1	1
Generalisability	y	limited	y	y
Applicability	y	limited	y	y

Table 2.5 Studies used to make evidence statement for vegetables and gastric cancer (cont.)

Reference [1]	**George et al. 2009 [2574]**	**Lissowska et al. 2004 [6757]**	**Lucenteforte et al. 2008 [2698]**	**Ito et al. 2003 [3676]**
Type of study [2]	Cohort	Case control	Case control	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Vegetables by quintile and then incidence for all cancers and then for individual cancers	Quartiles of intake of vegetables and incidence of stomach cancer	Quintiles of veg intake of fruit and stomach cancer	Veg intake and gastric cancers
N [5]	195 229 F	274 cases 463 controls	230 cases 547 controls	508 cases 36 490 controls
Population/study information [6]	US National Institutes of Health (NIH)–AARP Diet and Health Study	Polish M and F a well defined population study base	Italian Hospital controls ie poorly defined study base	F >30 yrs, poorly defined study base Japanese hospital
Quality [7]	P	P	0	0
Results [8]	RR for quintile 5 vs quintile 1 veg intake 0.86 (95% CI 0.47, 1.58) for women 0.93 (0.69, 1.25) for men	RR for quartile 4 vs quartile 1 for veg intake 0.83 (0.52–1.33)	OR highest quintile vs lowest 0.47 (95% CI 0.27-0.81); P for trend <0.01	Raw veg every day vs less OR 0.50(95% C I0.36-0.71) P for trend P<0.001;
Effect on risk (Increase/None/ Protect)	None	None	Protect	Protect
Clinical importance[9]	2	2	1	1
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	n
Applicability	y	y	y	n

2.6 VEGETABLES and BREAST CANCER

Does a particular intake of vegetables affect the risk of breast cancer?		
Evidence statement		Consumption of vegetables is not associated with reduced risk of breast cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 meta analysis 2 cohorts (low to medium risk bias) and 4 case controls (low to medium risk bias).
Consistency	Poor	Meta analysis small protective effect,1 cohort no effect and 1 increased risk; 1 case control no effect and 3 case controls protective effect.
Clinical impact	Poor	Only 4% protection from meta analysis.
Generalisability	Good	In European US and Asian populations and both menopausal and premenopausal women.
Applicability	Excellent	For Australian adult women.

The studies used to form the body of evidence are shown below. The meta analysis (pooled analysis) of 20 studies, 10 cohort and 10 case control, demonstrates a small protective effect with a RR of 0.96 similar to the RR reported in the results from the EPIC cohort RR 0.98. The findings from the case control studies were equivocal with three protective and one no effect. The other cohort of American retirees showed a slight increase in risk with RR 1.08. Thus it appears that if there is any protective effect of vegetables it is likely very small and further studies are needed. The World Cancer Research Fund also considered there to be no support for a protective effect. See Table 2.6.

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Table 2.6 Studies used to make evidence statement for vegetables and breast cancer

Reference [1]	**Riboli and Norat 2003 [1993]**	**George et al. 2009 [2574]**	**Van Gils 2009 [1511]**	**Kruk J. 2007 [2738]**	**Malin et al. 2003 [2078]**	**Gaudet et al. 2004 [1650]**	**Hermann et al. 2002 [2141]**
Type of study [2]	20 pooled cohorts (10) and case controls (10)	Cohort	Cohort	Case control	Case control	Case control	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Veg by each additional 100 g per day and breast cancer	Veg by quintile and then incidence for all cancers and then for individual cancers	Quintile of intake for veg 112 g; 144 g; 171 g ; 205 g; 245 mean g per day and breast cancer	Veg intake in three groups <4 serves per week 4-6 serves per week more than 7 serves per week and breast ca according to menopausal status.	Quintile of Intake of total and subtypes veg and risk of breast cancer	Quintile of intake of veg and risk of breast cancer by menopausal status	Association between premenopausal breast cancer and German diet including g veg per day as quartiles
N [5]	Uncertain	195,229 F	285,526	858 cases 1085 controls in Poland	1459 cases 1556 controls in Shangai cohort study (nested case control)	1463 cases 1500 controls	355 cases 838 controls
Population/study information [6]	Asian US and European cohorts	US women NIH AARP	EPIC women 25 to 70 yrs	Women aged 28-78 yrs, Histologically confirmed breast cancer	Women aged 25-64yrs in Shangai	Study in US and Bahamas and was population based	Women <51 yrs hospital based in Germany

Quality [7]	0	P	P	P	P	0	0
Results [8]	RR for an additional 100 g veg per day 0.96 (95% CI 0.94- 0.98)	RR for quintile 5 vs quintile 1 veg intake 1.08 (95% CI 1.00-1.18, P for trend 0.009)	RR for quintile 5 vs quintile 1 veg intake 0.98 (95% CI 0.84-1.14, P for trend NS)	menopausal OR 0.58 (95% CI 0.44-0.47, P for trend P<0.0001) for veg at least once per day vs less than 4 per week and premenopausal 0.59 (95% CI 0.41-0.84, P for trend P<0.0018)	OR for quintile 5 vs quintile 1 for veg intake 1.05 (95% CI 0.81–1.40, P for trend = 0.81)	Among postmenopausal women OR for quintile 5 vs quintile 1 veg intake 0.63 (95% CI 0.46–0.86, P for trend < 0.01)	OR for quartile 4 vs quartile 1 veg intake 0.64 (95% CI 0.43–0.96, P for trend = 0.034).
Effect on risk (Increase/None/ Protect)	Protect	Increase	None	Protect	None	Protect	Protect
Clinical importance [9]	1	2	2	1	4	1	1
Clinical relevance [10]	1	1	1	1	1	1	1
Generalisability	y	y	y	y	y limited	y menopausal	y
Applicability	y	y	y	y	y limited	y	y

2.7 VEGETABLES and LUNG CANCER

Does a particular intake of vegetables affect the risk of lung cancer?		
Evidence statement		Consumption of vegetables is associated with reduced risk of lung cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 2 meta analyses of cohorts (one of 8 cohorts, and 1 with 11 cohorts and 25 case control (medium risk bias) 5 cohorts (low to medium risk bias) and 4 case control (low to medium risk bias).
Consistency	Poor	2 pooled meta analyses protective, 1 cohort and 2 case control protective, 3 cohort and 2 case control no protection, 1 cohort protection for men only.
Clinical impact	Satisfactory	The pooled analyses indicate a decrease in risk of about 10%.
Generalisability	Good	Nurses Health, Adventist Health, ATBC, Canadian breast cancer Health Professionals Iowa Netherlands New York State in cohorts.
Applicability	Excellent	Australian adults.

The two pooled cohorts, five cohort studies and four case control studies contributing to the body of evidence are in Table 2.7. The two pooled analyses indicated that vegetable consumption is protective of lung cancer but the studies published since 2003 have been equivocal. The World Cancer Research Fund concluded that foods containing carotenoids might be protective. In the current review the case control studies indicate protection but the cohort studies are less likely to do so. It may be that longer follow up is needed. Two studies report on the same cohort the NIH American Association of Retired Persons but report slightly different RR such that in one study a small protective effect was found for males. Thus the evidence statement is that the association is protective but the newer cohort studies indicate the evidence may not be trusted to guide decision making.

Summary: There is limited evidence that consumption of vegetables is associated with risk of lung cancer.

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Table 2.7 Studies used to make evidence statement for vegetables and lung cancer.

Reference [1]	**Smith Warner et al. 2003 [1954]**	**Riboli and Norat 2003 [1993]**	**George et al. 2009 [2574]**	**Liu et al. 2004 [1826]**	**Skuladottir 2004 [1808]**	**Wright M et al. 2008 [190]**	**Miller et al. 2007 [1906]**	**Dosil-Diaz et al. 2008 [298]**	**Ruano-Ravina et al. 2002 [2187]**	**Rylander et al. 2006 [1265]**	**Marchand et al. 2009 [2238]**
Type of study [2]	Pooled analysis (8 cohorts)	Pooled cohorts (11) and case controls (25)	Cohort	Cohort	Cohort	Cohort	Cohort	Case control	Case-control	Case-control	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of veg (94 to 293 g per day veg) and lung cancer	Each additional 100 g veg per day and lung cancer	Veg by quintile and then incidence for all cancers and then for individual cancers	Thirds of vegetable intake incident lung cancer	Quartiles veg 17-68 g; 60-120; 121-170; 171-479 and incident lung cancer	Quintiles of veg and subtypes and lung cancer	Quintiles of intake Vegetables and lung cancer vegetable median g/day for F 78.1; 130.7; 185.4; 260.1; 402.5; for M 56.9; 106.0; 152.4; 222.0; 385.9	Veg intake < 5 per week; 5-6 per week and >=1 per day on the risk of lung cancer	Vegetable and subtypes in 20 years prior to diagnosis of lung cancer	Veg intake association with lung cancer in smokers, former smokers and non smokers	Tertile of veg consumption and lung cancer
N [5]	8 cohorts 280 419 F 149 862 M	Uncertain	195,229 F 288,109 M	42,224 (cohort 1) and 51	27,178 M 29,875 F	47,2081 M and F	478,021 M and F	295 cases 322	163 cases 241 controls	177 F and 359 M and 916	109 M cases 227 controls

				114 (cohort 2)				controls		controls (M/F)	
Population/study information [6]	US Canada Netherlands	Asian US and European cohorts	US adults male and female retirees NIH AARP	Japanese men and women	Danish 50 to 64 yrs	US male and female retirees from age 50 to 71 yrs NIH AARP	The EPIC study	Men and women, >35 yrs, Spain hospital based controls	Conducted in Spain minimum age limit was 35 yrs Population based controls	Conducted in Sweden. All adults less than 75 yrs. Population based controls.	New Caledonia
Quality [7]	0	0	P	0	P	P	P	0	P	0	0
Results [8]	RR for quintile 5 vs quintile 1 for veg intake 0.88 (95% CI 0.78–1.00) p for trend 0.12).	RR for each additional 100g per day 0.89 (95% CI 0.82, 0.93)	Men quintile 5 vs quintile 1 veg intake 0.87 (95% CI 0.78, 0.96) P for trend 0.024 for women RR 1.08 (95 CI 0.94, 1.23) P for trend =0.219	RR for high consumers vs low consumers of veg 1.03 (95% CI 0.81–1.30)	A significant protection for highest intake of veg i.e. 171 to 479 g per day RR 0.67(95% CI 0.46-0.97)	Men RR of quintile 5 vs quintile 1 0.93 (95% CI 0.83, 1.03) Women 1.05 (95% CI 0.92, 1.21)	For veg HR 1.00 (95% CI 0.76–1.30) p for trend 0.8528	OR for >=1 per day vs <5 per week 0.50 (95% CI 0.30-0.83)	OR for veg more than once per day vs less than once per week 0.64 (95% CI 0.3-1.36)	Lowest OR found for non-smokers 0.37 (95% CI 0.15-0.97) and smokers 0.49 (95% CI 0.29-0.82) for former smokers 0.59 (95% CI 0.28-1.28)	OR for highest tertile vs lowest 1.4 (95% CI 0.7–2.9)
Effect on risk (Increase/ None/ Protect)	Protect	Protect	Protect for men None for women	None	Protect	None	None	Protect	None	Protect	None
Clinical	1	1	1 (M)and	4	1	2	2	1	2	1	4

importance [9]			4(F)								
Clinical relevance [10]	1	1	1	1	1	1	1	1	1	1	1
Generalisability	y	y	y	y	y	y	y	y	n	n	n
Applicabilty	y	y	y	y	y	y	y	y	n	n	n

2.8 VEGETABLES and COLORECTAL CANCER

Does a particular intake of vegetables affect the risk of colorectal cancer?		
Evidence statement		Consumption of vegetables is not associated with risk of colorectal cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 2 pooled analyses of cohorts and case control (one with 14 cohort studies and one with 27 studies (10 cohort 17 case control0, with medium risk bias) 5 cohorts and 5 case control (low to medium risk).
Consistency	Poor	Pooled analysis of cohorts found protection but result was non-significant other pooled analysis significant protection 2/2 cohorts no effect, 1/3case control no effect 2/3 case control protective.
Clinical impact	Satisfactory	Protection from pooled analyses is less than 10% reduction.
Generalisability	Good	US and European cohorts and cases some Asian.
Applicability	Good	Australian adults.

The seven studies used to build the evidence statements are shown in Table 2.8. The pooled cohorts showed a small protection but the confidence intervals for relative risk crossed 1.0 in Koushik's analysis. The other pooled analysis contained 17 case control studies and 10 cohorts but when study designs were examined separately only the case control studies showed a significant reduction in relative risk and there was significant heterogeneity of findings among them. The single cohort studies showed no protection but the case control studies, of neutral and negative quality because of selection and/or measurement bias, demonstrated protection. It appears that case control studies are indicative of protection but cohorts are not. The World Cancer Research Fund report could make no claims for a probable or convincing protective effect.

Summary: The association between consumption of vegetables and colorectal cancer is unclear.

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Table 2.8 Studies used to make evidence statement for vegetables and colorectal cancer.

Reference [1]	**Koushik et al. 2007 [20]**	**Riboli and Norat 2003 [1993]**	**Sato et al. 2004 [2005]**	**George et al. 2009 [2574]**	**Wu et al. 2009 [119]**	**Oh et al. 2005 [3383]**	**Hara et al. 2003 [1928]**
Type of study [2]	Pooled cohort analysis colon cancer (14 studies)	Pooled cohorts (10) and case controls (17)	Cohort	Cohort	Case-control	Case-control	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of veg intake (<100g to > 400g) and colon cancer	Intake of veg and decreased risk per 100 g intake on colorectal cancer	Quartiles of veg and incident colorectal cancer	Veg intake by quintile and then incidence for all cancers and then for individual cancers	Veg intake by tertile and risk of colorectal adenoma	Tertiles of veg intake and (<130; 130-221; >221 g per day risk of polyps or colorectal cancer	Tertiles of veg intake and risk of colorectal cancer.
N [5]	756217	Uncertain	47605 M and F (41835 included in analysis)	195229 F 288109 M	764 cases, 1517 controls	49 cases cancer, 87 cases polyps 134 controls	115 cases, 230 controls
Population/study information [6]	US European	US and Europe Asian	Japanese 40 to 64 y	US adults male and female	US adults Hospital based study	Hospital based study in Korea	Hospital based case control study in Japan
Quality [7]	0	0	P	P	0	0	N
Results [8]	Quintile 5 vs quintile 1 fruit RR 0.94 (95% CI 0.86-1.02)	For additional 100g veg per day RR 0.91 (95% CI 0.86, 0.97)	Quartile 4 vs quartile 1 veg intake RR 1.24 (95% CI 0.79–1.95)	Q5 vs Q1 RR 0.87 (95% CI 0.74, 1.02)	Tertile 3 vs tertile 1 OR 0.94 (95% CI 0.72–1.22)	Tertile 3 vs tertile 1 for veg intake OR 0.34, (95% CI 0.16-0.71)	Tertile 3 vs tertile 1 of veg intake RR 0.22 (95% CI 0.08–0.66)
Effect on risk (Increase/None/Protect)	None	Protect	None	None	None	Protect	Protect
Clinical importance[9]	2	1	4	2	1	1	1

Clinical relevance [10]	1	1	1	1	2	2	1
Generalisability	y	y	y	y	n	n	n
Applicability	y	y	y	y	n	n	n

2.9 VEGETABLES and OESOPHAGEAL CANCER

Does a particular intake of vegetables affect the risk of oesophageal cancer?		
Evidence statement		Consumption of vegetables is not associated with reduced risk of oesophageal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 pooled analysis of 1 cohort 12 case control (medium risk bias); 3 cohorts and 1 case control (low risk bias).
Consistency	Good	1 meta analysis showed a positive effect; 3 cohorts no effect; 1 case control no effect.
Clinical impact	Satisfactory	If pooled analysis correct 10% for veg.
Generalisability	Good	Includes European and US studies.
Applicability	Excellent	Yes for adult men and women in Australia.

The five studies used to make the evidence statement are shown in Table 2.9 below. The case control studies indicate protection with vegetable intake as seen in the pooled analyses but a subsequent case control study demonstrated none. The three cohort studies include the EPIC population in which non significant reduction in risk was noted and the other two both use the NIH American Association of Retired Persons cohort. Both analyses find no significant effects but in one study the author looks at squamous cell and adenocarcinoma separately and it appears that risk of squamous cell could be modulated by vegetables intake but the confidence interval is wide and includes values above 1.0. The World Cancer Research Fund report concluded it was probable that non starchy vegetables were protective.

References

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Riboli, E. & Norat, T. 2003, "Epidemiologic evidence of the protective effect of fruit and vegetables on cancer risk", *American Journal of Clinical Nutrition*, vol. 78, no. 3 Suppl, pp. 559S-569S.

Table 2.9 Studies used to make evidence statement for vegetables and oesophageal cancer.

Reference [1]	**Riboli and Norat 2003 [1993]**	**Freedman et al. 2007 [427]**	**Gonzalez et al. 2006 [1207]**	**George et al. 2009 [2574]**	**Anderson et al. 2007 [7807]**
Type of study [2]	Pooled cohorts (1) and case controls (12)	Cohort	Cohort	cohort	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Additional 100g veg per day and risk of oesophageal cancer	Quintiles veg (0.7 servings to 3.2) serves per day (median) of intake and incident oesophageal cancer	Tertiles of veg intake (range from mean of 110 to 250 g per day) and incident oesophageal cancers	Veg by quintile and then incidence for all cancers and then for individual cancers	Veg intake (,12 ;12-17; >17 serves per week and risk Barrett's oesophagus (BO) and oesophageal adenocarcinoma (OA)
N [5]	Asian US and European cohorts	490 802 subjects M and F	521 457	288 109 M 195 229 F	224 with BO 227 with OA 260 controls
Population/study information [6]	Uncertain	US NIH AARP retired persons cohort >=50	Part of EPIC	US NIH AARP retired persons cohort >=50	Population based in Ireland (FINBAR study)
Quality [7]	0	P	P	P	P
Results [8]	Each additional 100 g veg RR 0.89 (95% CI 0.82- 0.97)	Differentiated by 2 types cancer squamous cell RR 0.57 (95% CI 0.28-1.18) and for adenocarcinoma 0.92 (95% CI 0.57-1.50)	For each additional 100 g veg per day the HR 0.72 (95% CI 0.32–1.64)	Quintile 5 vs quintile 1 veg intake RR 1.04 (95% CI 0.78, 1.39) for men RR 1.21 (95% CI 0.54- 2.71) for women	More than 17 portions veg per week. Adenocarcinoma OR 1.49 (95% CI 0.89 - 2.48)

Effect on risk (Increase/None/ Protect)	Protect	None	None	None	None
Clinical importance[9]	1	2	2	4	4
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

2.10 VEGETABLES and ORAL and NASOPHARYNGEAL CANCERS

Does a particular intake of vegetables affect the risk of oral and nasopharyngeal cancer?		
Evidence statement		Consumption of vegetables is associated with a reduced risk of oral and nasopharyngeal cancers.
Grade		C
Evidence statement		Consumption of preserved vegetables is associated with increased risk of oral and nasopharyngeal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence 2 pooled/meta analyses of case control studies (medium risk bias with 12 studies; low risk bias with 16 studies) larger one is about preserved and non-preserved veg; 4 case controls.
Consistency	Good	Most report vegetables protective; meta analysis of preserved (i.e. salted dried fermented and pickled) vegetables found double the risk of cancer.
Clinical impact	Satisfactory	Estimates range from <5% reduction to more than 40%.
Generalisability	Good	European US and Asian.
Applicability	Good	Adult Australians for vegetables but preserved vegetables are not commonly consumed in Australia.

The two pooled analyses and four case control studies used to make the evidence statements are shown in Table 2.10. Different studies are used in the two pooled analyses with that of Riboli being mostly US and European studies and those in Gallicchio all from Asia. The additional case control studies reported are of varying quality with all showing protection with the exception of the study that divided smokers/ever smokers and non smokers finding that protection was limited to the smokers. Most of the other case control studies here have adjusted for smoking and alcohol that are known risk factors. The World Cancer Research Report concluded that non starchy vegetables were probably protective.

References

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Table 2.10 Studies used to make evidence statement for vegetables and oral and nasopharyngeal cancer.

Reference [1]	**Riboli and Norat 2003 [1993]**	**Gallicchio et al. 2006 [37]**	**Kreimer et al. 2006 [1217]**	**Guneri et al. 2005 [1322]**	**Heck et al. 2008 [2657]**	**Escribano Uzcudun et al. 2002 [7999]**
Type of study [2]	Pooled analysis case controls (12)	Meta analysis of case control (16 studies)	Case control	Case control	Case control	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Each additional 100 g veg and risk of oral and pharyngeal cancer	Highest and lowest intakes of preserved and non-preserved veg and nasopharyngeal cancer	Quartiles of veg intake and oral and oropharyngeal SCCs	Comparison of weekly veg intake in cases of oral cancer and controls	Quartiles of veg intake and hypopharyngeal cancer	Veg intake included with many risk factors for pharyngeal cancer
N [5]	Uncertain	3074 cases nasopharyngeal cancer 4131 controls	1670 cases 1732 controls	79 cases 61 controls	513 cases 713 controls	232 cases 232 controls
Population/study information [6]	Asian US and European cohorts	Asian case control studies	Hospital based in 9 countries Italy Spain Australia, Canada, Poland Northern Ireland, India, Sudan, Cuba	Clinic based study in young Turkish adults	Indian hospital based study	Hospital based study in Madrid, Spain
Quality [7]	0	P	P	N	0	0
Results [8]	Each additional 100 g veg per day RR 0.84 (95% CI 0.67-1.07)	Highest vs lowest for preserved OR 2.04 (95% CI 1.43-2.92) non preserved OR 0.64 (95% CI	Quintile 5 vs quintile 1 veg intake OR 0.7 (0.6-1.0) P for trend <0.001.	OR with raw veg 0.745 but no CIs	Ever smoked quartile 4 vs quartile 1 OR 0.40 (95% CI 0.18- 0.87) for never smokers	OR 3.8 (95% CI 1.5–9.1 P=0.0001) for deficient intake of raw vegetables

		0.48-0.85)			OR 0.96 (95% CI 0.30- 3.06)	
Effect on risk (Increase/None/ Protect)	None	Increase pickled protect non pickled	Protect	Protect	Protect for smokers only; none for nonsmokers	Protect
Clinical importance [9]	2	1	1	1	2	1
Clinical relevance [10]	1	1	1	1	1	1
Generalisability	Y	y	y	n	n	y
Applicability	Y	y - mainly Asian	y	n	n	n

2.11 VEGETABLES and OVARIAN CANCER

Does a particular intake of vegetables affect the risk of ovarian cancer?		
Evidence statement		Consumption of vegetables is not associated with reduced risk of ovarian cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 1 pooled analysis of 12 cohorts (low risk bias); and 1 cohort (low risk bias).
Consistency	Excellent	Pooled analysis showed no effect; 1 cohort no effect.
Clinical impact	Poor	No protection.
Generalisability	Good	Includes European and US studies.
Applicability	Good/excellent	Yes for adult women in Australia.

The pooled analysis and cohort are summarized in Table 2.11 below. In European and US women there is no evidence of protection from vegetable consumption. The World Cancer Research Fund reported no probable or convincing evidence that vegetable intake reduced risk of ovarian cancer.

References

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Table 2.11 Studies used to make evidence statement for vegetables and ovarian cancer

Reference [1]	**Koushik et al. 2005 [1345]**	**Schulz 2005 [1308]**
Type of study [2]	Pooled cohort analysis (12) ovarian cancer	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	**Quartiles of veg <100 to >400 g per day and ovarian cancer**	**Looking at 80 g increments of vegetables and ovarian cancer**
N [5]	560,441 cohort 2130 cases	325,640 females
Population/study information [6]	US and European cohorts including Nurse Health, Netherlands, Swedish Mammography	EPIC cohort
Quality [7]	0	P
Results [8]	Quartile 4 vs quartile 1 veg RR 0.9(95% CI 0.78-1.04)	Per additional 80 g veg HR 0.92 (95% CI 0.76, 1.11)
Effect on risk (Increase/None/ Protect)	None	None
Clinical importance [9]	2	2
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

2.12 VEGETABLES and ENDOMETRIAL CANCER

Does a particular intake of vegetables affect the risk of endometrial cancer?		
Evidence statement		Consumption of vegetables is not associated with reduced risk of endometrial cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 1 pooled analysis of 8 studies and 1 cohort (low risk bias) and 2 case controls (medium risk bias).
Consistency	Satisfactory	Pooled analysis showed no effect; 1 cohort no effect; 2 case controls protection.
Clinical impact	Poor	No protection.
Generalisability	Good	Includes European and US studies.
Applicability	Good/Excellent	Yes for adult women in Australia.

The meta analysis, cohort and case control studies used to make the body of evidence are shown in Table 2.12 below. The meta analysis and cohort study were in agreement but both case control studies which were of a poorer quality because of possible selection and measurement bias showed protective effects. There are issues about the generalisability of the case control studies so the statement is based on the meta analysis. The World Cancer Research Fund reported no convincing or probable protective effects of diet but some suggestion that non-starchy vegetables might decrease risk of endometrial cancer.

References

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Table 2.12 Studies used to make evidence statement for vegetables and endometrial cancer

Reference [1]	**Bandera et al. 2007 [4633]**	**McCullough M et al. 2007 [454]**	**Bravi et al. 2009 [2829]**	**Yeh et al. 2009 [8110]**
Type of study [2]	Meta analysis 8 studies included	Cohort	Case-control	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Dose response per 100 g veg and endometrial cancer	Quintiles veg up to more 2.6 serves and incident endometrial cancer	Veg and endometrial cancer risk	Quartile of veg intake risk of endometrial cancer
N [5]	Varied from 2951 to 3255 cases	41,400	454 cases 908 controls	541 cases 541 controls
Population/ study information [6]	US Europe and Asia this is the WCRF systematic review	US women median age 63 Cancer Prevention 2 Cohort	In Italy - hospital based controls	Hospital based in US
Quality [7]	P	P	0	0
Results [8]	Per 100 g veg RR 0.90(95% CI 0.86-0.95) But had to exclude some studies so per 100g 0.94(95% CI 0.86-1.02) for 5 studies	For highest vs lowest tertile veg intake RR 1.21 (95% CI: 0.89, 1.65);	For an increment of one serving of veg OR 0.83 (95% CI 0.72-0.95).	For quartile 4 vs quartile 1 OR, 0.51; (95% CI, 0.34–0.75)
Effect on risk (Increase/None/ Protect)	None	None	Protect	Protect
Clinical importance [9]	2	4	1	1
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	n	y
Applicability	y	y	n	y

VEGETABLES - subtypes

Search results

The initial search of the databases included 3691 references for vegetables and the specified disease outcomes. The detailed search is included in a separate document on searches. As there were 2714 duplicates with the fruit database the two were combined in one Endnote library and coded as one. In all 97 references concerning fruit and vegetables had data extracted and 8 papers were used to form the body of evidence statements for subtypes of vegetables. Sufficient evidence was found to make statements for tomatoes and prostate cancer, cruciferous vegetables and lung cancer, and subtypes of vegetables and colorectal cancer.

2.13 TOMATOES and PROSTATE CANCER

Does a particular intake of tomatoes affect the risk of prostate cancer?		
Evidence Statement		Consumption of one to two serves per day of tomato is associated with a reduced risk of prostate cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 meta analysis one of 3 cohorts and 7 case control studies (medium risk bias) plus 1 cohort study (low risk bias).
Consistency	Satisfactory	review positive for tomato (high intake) but the one large cohort found no effect.
Clinical impact	Good	10-20% reduction found in meta analysis for tomato.
Generalisability	Good	Most studies in US, some in Europe.
Applicability	Good/excellent	Australian adult men.

The meta analyses provide the basis for the recommendation. When the case control and cohort studies within the meta analysis were analysed separately both demonstrate a protective effect with the association strongest for cohort studies. The discrepancy with the individual cohort study may relate to the serving size. The upper quintile was 37.3 g per 1000 kcal that is less than the 200 g daily serve that the meta analysis considers protective. See Table 2.13.

The Food and Drug Administration published their scientific evidence review concerning health claims and tomatoes (Kavanaugh et al.) and included and two cohorts, 11 case control and two ecological studies. Both of these cohorts were included in the Etminan review and four of the case control studies were in common. The FDA acknowledges that the cohort studies show protection but only three of nine case control studies indicated significant protection. ‘FDA concluded that there was very limited credible evidence for qualified health claims for tomatoes and/or tomato sauce and a reduced risk for prostate cancer provided that the qualified health claims were appropriately

worded so as to not mislead consumers.' The World Cancer Research Fund report claimed that lycopene rich foods were probably protective.

References

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Table 2.13 Studies used to make evidence statement on tomatoes and prostate cancer

Reference [1]	**Etminan et al. 2004 [1854]**	**Stram et al. 2006 [1051]**
Type of study [2]	Systematic review for 3 cohorts and 7 case control	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Quintiles of tomato intake (raw and cooked separately) and prostate neoplasm	Quintiles of tomato intake (g/1000kcal) <12 g; 12-18.2 g 18.2-25.4 g; 25.4-37.3 g and >37.3 g/1000kcal and incident prostate cancer
N [5]	8940 cases/ 102,192	82,486
Population/study information [6]	North America and Europe	US multiethnic cohort males
Quality [7]	0	P
Results [8]	Highest vs lowest quintile raw tomato per day RR 0.89 (0.80– 1.00) and for cooked tomato RR 0.81 (0.71– 0.92)	Highest vs lowest quintile tomato intake RR 1.02 (95% CI 0.92-1.14) P for trend NS
Effect on risk (Increase/None/ Protect)	Protect	None
Clinical importance [9]	1	4
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	n

2.14 CRUCIFEROUS VEGETABLES and LUNG CANCER

Does a particular intake of cruciferous vegetables affect the risk of lung cancer?		
Evidence Statement		Consumption of cruciferous vegetables is associated with reduced risk of lung cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from1 meta analysis of 30 studies (23 case control and 7 cohort (low risk bias) plus 1 cohort (low risk bias) and 1 case control (medium risk bias).
Consistency	Good	Meta analysis and case control protective. Cohort no effect.
Clinical impact	Good	Reduction at least 10%.
Generalisability	Good	Studies in Europe USA Asia and Australia.
Applicability	Good/Excellent	Applies to Australian adults.

The evidence statement is based on the meta analysis in particular the case control studies, with the two additional studies located supporting the evidence. In the meta analysis the measures of association for case control and cohort are both positive but with a stronger reduction found in the case control studies (21% reduction). Similarly the additional case control study from Spain finds a significant reduction in risk. However, the pooled RR from the seven cohort studies and the additional cohort study find a 10% reduction in risk but the confidence intervals include no effect and harmful values. The meta analysis also examined protection from lung cancer by genotype and it seems that the protection is genotypic specific. See Table 2.14.

References

Dosil-Díaz, O., Ruano-Ravina, A., Gestal-Otero, J. J. & Barros-Dios, J. M. 2008, "Consumption of fruit and vegetables and risk of lung cancer: A case-control study in Galicia, Spain", *Nutrition*, vol. 24, no. 5, pp. 407-413.

Lam, T. K., Gallicchio, L., Lindsley, K., Shiels, M., Hammond, E., Tao, X. G., Chen, L., Robinson, K. A., Caulfield, L. E., Herman, J. G., Guallar, E., Alberg, A. J., Lam, T. K., Gallicchio, L., Lindsley, K., Shiels, M., Hammond, E., Tao, X. G., Chen, L., Robinson, K. A., Caulfield, L. E., Herman, J. G., Guallar, E. & Alberg, A. J. 2009, "Cruciferous vegetable consumption and lung cancer risk: a systematic review", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 18, no. 1, pp. 184-95.

Wright, M. E., Park, Y., Subar, A. F., Freedman, N. D., Albanes, D., Hollenbeck, A., Leitzmann, M. F. & Schatzkin, A. 2008, “Intakes of fruit, vegetables, and specific botanical groups in relation to

lung cancer risk in the NIH-AARP Diet and Health Study", *American Journal of Epidemiology*, vol. 168, no. 9, pp. 1024-1034.

Table 2.14 Studies used to make evidence statement on cruciferous vegetables and lung cancer

Reference [1]	**Lam et al. 2009 [2545]**	**Wright M et al. 2008 [190]**	**Dosil Diaz et al. 2008 [298]**
Type of study [2]	Meta analysis of 7 cohort and 23 case control studies	Cohort	Case control
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	From never to daily consumption of cruciferous vegetables and lung cancer	Quintiles of cruciferous veg intake and lung cancer	Cabbage intake < 1 per month; <1 per month – 1 per week; >1 per week on the risk of lung cancer
N [5]	More than 700,000 M and F	472,081 M and F	295 cases 322 controls
Population/study information [6]	European, Asian and US studies 4 to 12 years follow up for cohorts.	US male and female retirees from age 50 to 71 y NIH AARP	Men and women, >35 yrs, Spain hospital based controls
Quality [7]	P	P	0
Results [8]	Pooled OR 0.78 (95% CI 0.7-0.88) case control; pooled RR 0.83 for cohort (95% CI 0.62-1.08) highest versus lowest strongest inverse association was among those with homozygous deletion for GSTM1 and GSTT1. OR 0.41; 95% CI 0.26-0.65)	Men RR of quintile 5 (0.5g/1000kcal per day) vs quintile 1 (0.03 g/1000kcal) 0.92 (95% CI 0.83, 1.02) Women 1.0 (95% CI 0.87, 1.14)	OR for > 1 per week vs <1 per month 0.53 (95% CI 0.29-0.99) and 1 per month to 1 per week OR 0.49 (95% CI 0.28-0.86)
Effect on risk (Increase/None/ Protect)	Protect	None	Protect
Clinical importance [9]	1	2	1
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

2.15 VEGETABLE by sub type and COLORECTAL CANCER

Does a particular intake of vegetables by subtype affect the risk of colorectal cancer?		
Evidence Statement		Consumption of cruciferous vegetables, carrots, potatoes and beans and lentils is not associated with risk of colorectal cancer.
Grade		C
Evidence Statement		Consumption of more than one serving per week of spinach is associated with reduced risk of colorectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from1 meta analysis of 14 cohort studies (medium risk bias) plus 2 case control studies (medium risk bias).
Consistency	Satisfactory	The pooled analysis showed no protection except for spinach and perhaps green leafy in general.
Clinical impact	Satisfactory	Only reduction found for spinach of about 10%.
Generalisability	Good	Studies in Europe and USA.
Applicability	Good/Excellent	Applies to Australian adults.

As was found for total vegetables, no subtype of vegetables was demonstrated to provide protection from colorectal cancer with the exception of spinach in the pooled analysis and green leafy in one case control. Koushik et al. report that the inverse association with spinach has been reported consistently. See Table 2.15.

References

Hara, M., Hanaoka, T., Kobayashi, M., Otani, T., Adachi, H. Y., Montani, A., Natsukawa, S., Shaura, K., Koizumi, Y., Kasuga, Y., Matsuzawa, T., Ikekawa, T., Sasaki, S., Tsugane, S. 2003, "Cruciferous vegetables, mushrooms, and gastrointestinal cancer risks in a multicenter, hospital-based case-control study in Japan", *Nutrition & Cancer*, vol. 46, no. 2, pp. 138-47.

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Wolk, A., Zeleniuch-Jacquotte, A., Zhang, S. M. & Smith-Warner, S. A. 2007, "Fruits, vegetables, and colon cancer risk in a pooled analysis of 14 cohort studies", *Journal of the National Cancer Institute*, vol. 99, no. 19, pp. 1471-1483.

Wu, H., Dai, Q., Shrubsole, M. J., Ness, R. M., Schlundt, D., Smalley, W. E., Chen, H., Li, M., Shyr, Y., Zheng, W., , W. 2009, "Fruit and vegetable intakes are associated with lower risk of colorectal adenomas", *Journal of Nutrition*, vol. 139, no. 2, pp. 340-4.

Table 2.15 Studies used to make evidence statement on vegetables by subtype and colorectal cancer

Reference [1]	**Koushik et al. 2007 [20]**	**Wu et al. 2009 [119]**	**Hara et al. 2003 [1928]**
Type of study [2]	Pooled cohort analysis colon cancer (14 studies)	Case-control	Case control
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Four groupings of veg subtype intake and colon cancer	Veg sub types intake by tertile and risk of colorectal adenoma	Tertiles of cruciferous veg intake and risk of colorectal cancer
N [5]	756,217 in cohort 5838 cases 14 studies	764 cases 1517 controls	115 cases 230 controls
Population/study information [6]	European and US cohorts and 6 to 20 years	US adult males and females Hospital based study	Hospital based case control study in Japanese hospital
Quality [7]	0	0	0
Results [8]	Highest (1/2 or 1 serving per day) vs nil broccoli RR 0.95 (0.85 to 1.05) brussels sprouts RR 1.03 (0.82 to 1.29) cabbage RR 1.08 (0.97 to 1.21) carrots RR 0.87 (0.75 to 1.01) spinach RR 0.89 (0.82 to 0.97) beans and lentils RR 1.00 (0.90 to 1.11) potatoes RR 1.02 (0.86 to 1.21)	Tertile 3 vs tertile 1 cruciferous OR 0.94 (95% CI 0.73–1.20) green leafy OR 0.74 (95% CI 0.58-0.96)	Tertile 3 vs tertile 1 of cruciferous veg intake OR 0.64 (0.25–1.63)
Effect on risk (Increase/None/ Protect)	None except for spinach	None for cruciferous Protect for green leafy	None
Clinical importance [9]	1 for spinach	2 cruciferous/1 green leafy	2
Clinical relevance [10]	1	2	1
Generalisability	y	n	n
Applicability	y	n	n

STUDIES NOT INCLUDED IN BOE as < 5 studies

CRUCIFEROUS VEGETABLES and BLADDER CANCER

Hospital-based case-control study examined relationship of primary bladder cancer with usual intake of raw and cooked cruciferous vegetables. A strong inverse association between bladder cancer risk and raw cruciferous vegetable intake (OR for highest versus lowest category = 0.64 (95% CI 0.42-0.97, P trend = 0.003) was found but there were no significant associations for fruit, total vegetables, or total cruciferous vegetables. (Tang 2008)

ALLIUM VEGETABLES and GASTRIC CANCER

The associations between allium vegetable consumption and stomach cancer were examined in a large population-based case-control study in China (Shangai and Qingdao). After adjusting for matching variables, education, body mass index, pack-years of smoking, alcohol drinking, salt intake, and fruit and vegetable intake, inverse relationships were observed between frequency of onion intake and stomach cancer for never vs often ie OR 0.66 (95% CI 0.42-1.02, P for trend 0.04) for Shangai province and OR 0.14 (95% CI 0.03-0.71, P<0.02) for Qingdao province. (Setiawan et al. 2005). The World Cancer Research Fund reported that allium vegetables are probably protective.

GREEN LEAFY VEGETABLES and GALLBLADDER CANCER

A case-control study of the relationship between three levels of vegetable intake and the risk of gallbladder cancer showed an inverse association was for amaranth OR of 3.45 for the low vs. high level of consumption OR 2.14 for spinach, OR1.86 for bathua, OR1.02 for bengalgram leaves, OR2.26 for cabbage, OR3.06 for fenugreek leaves, OR1.95 for mustard leaves and OR1.44 for radish leaves. (Rai et al. 2006)

SUBTYPES OF VEGETABLES and PROSTATE CANCER

Cruciferous vegetables

The association between cruciferous vegetable intake and risk of prostate cancer in the Health Professionals Follow-Up cohort Study was investigated. Overall, no association between baseline intake of cruciferous vegetables and risk of prostate cancer RR 0.93 (95% CI 0.82-1.05) for ≥5 versus ≤1 serving/week; P for trend = 0.30 was found.

No association between prostate cancer risk and intake of fruits and vegetables was found in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. Risk of extraprostatic prostate cancer (stage III or IV tumors) decreased with increasing vegetable intake RR = 0.41 (95% CI 0.22 - 0.74) for high versus low intake; P trend = .01 mainly explained by intake of cruciferous vegetables (RR = 0.60 (95% CI 0.36 - 0.98) for high versus low intake). (Kirsh 2007)

In a West Australian cohort a decreased prostate cancer risk was observed with increasing intakes of vitamin C-rich vegetables, including bell peppers and broccoli but fruit and other vegetables did not appear to be important factors. (Ambrosini et al. 2008)

Allium vegetables

In a population-based, case-control study conducted in Shanghai, China the association between intake of allium vegetables and the risk of prostate cancer was investigated. Men in the highest of three intake categories of total allium vegetables (>10.0 g/day) had OR 0.51 (95% CI 0.34 - 0.76, P trend <.001) of prostate cancer than those in the lowest category (<2.2 g/day). (Hsing et al. 2002)

3. FRUIT AND VEGETABLES
(S1.1 and S1.10)

Evidence Statements

3. FRUIT AND VEGETABLES (S1.1 AND S1.10)

While fruit and vegetables have been analysed as separate food groups in question S1.1 for some of the retrieved papers they were studied in combination. This chapter details these studies.

Search results

The initial search of the data bases included 3691 references for fruit and 4667 references for vegetables and the specified disease outcomes. The detailed search is included in a separate document on searches. As there were 2714 duplicates the two data bases were combined in one Endnote library and coded as one. In all, 97 references concerning fruit and vegetables had data extracted and 16 papers were used to form the body of evidence statements for fruit and vegetables combined. More comprehensive evidence statements are available for fruit and vegetables intakes measured individually. Sufficient evidence was found to make statements for fruit and vegetables and risk of cardiovascular disease, stroke, type 2 diabetes and a range of cancers including lung, colorectal and ovarian cancer.

3.1 FRUIT and VEGETABLES and CORONARY HEART DISEASE

Does a particular intake of fruit and vegetables affect the risk of coronary heart disease in adults?		
Evidence statement		Consumption of each additional daily serve of fruit and vegetables is associated with a reduced risk of coronary heart disease.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 2 meta analyses cohorts (of 9 cohorts and 12 cohorts) (medium risk bias) and 3 coho rts (low risk bias).
Consistency	Good	2 meta analyses agree with protection, 3 cohorts no effect. One cohort was in Japanese and may not be applicable. The other cohort was looking at associations in those with low medium or high carbohydrate intakes and may not be most appropriate design to examine the relationship. The other cohort looked at CVD mortality.
Clinical impact	Good	RR 0.96 (95% CI 0.93-0.99) for each additional serve fruit & vegetables in one meta analysis; <3 serves vs >5 serves per day RR 0.83 (95% CI 0.77-0.89, dose response P<0.0001) in other meta analysis.
Generalisability	Good	Populations in cohorts from US Europe and Japan.
Applicability	Excellent	Australian adults.

The studies used to make the body of evidence statements are shown in Table 3.1. The two meta analyses are in agreement but have six of nine studies in common, with most studies being from the USA. The Japanese cohort study demonstrated no association between fruit and vegetable consumption and cardiovascular disease and the analysis of the Nurses Health and Male Health Professionals cohorts stratified by the percentage energy from carbohydrate indicated no significant protective effect. The other US cohort showed protection but the upper 95% CI for HR was 1.06.

References

Dauchet, L., Amouyel, P., Hercberg, S. & Dallongeville, J. 2006, "Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies", *Journal of Nutrition*, vol. 136, no. 10, pp. 2588-93.

Genkinger, J. M., Platz, E. A., Hoffman, S. C., Comstock, G. W., Helzlsouer, K. J., Genkinger, J. M., Platz, E. A., Hoffman, S. C., Comstock, G. W. & Helzlsouer, K. J. 2004, "Fruit, vegetable, and antioxidant intake and all-cause, cancer, and cardiovascular disease mortality in a community-dwelling population in Washington County, Maryland", *American Journal of Epidemiology*, vol. 160, no. 12, pp. 1223-33.

He, F. J., Nowson, C. A., Lucas, M. & MacGregor, G. A. 2007, "Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies", *Journal of Human Hypertension*, vol. 21, no. 9, pp. 717-28.

Joshipura, K. J., Hung, H.-C., Li, T. Y., Hu, F. B., Rimm, E. B., Stampfer, M. J., Colditz, G. & Willett, W. C. 2009, "Intakes of fruits, vegetables and carbohydrate and the risk of CVD", *Public Health Nutrition*, vol. 12, no. 1, pp. 115-21.

Takachi, R., Inoue, M., Ishihara, J., Kurahashi, N., Iwasaki, M., Sasazuki, S., Iso, H., Tsubono, Y. & Tsugane, S. 2008, "Fruit and vegetable intake and risk of total cancer and cardiovascular disease: Japan Public Health Center-based Prospective Study", *American Journal of Epidemiology*, vol. 167, no. 1, pp. 59-70.

Table 3.1 Studies used to make evidence statement on fruit and vegetables and coronary heart disease

Reference [1]	**Dauchet et al. 2006 [33]**	**He et al. 2007 [23]**	**Joshipura et al. 2008 [2546]**	**Takachi et al. 2008 [376]**	**Genkinger et al. 2004 [1566]**
Type of study [2]	Meta analysis of 9 cohorts	Meta analysis of 12 cohorts	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Each additional serve of fruit and veg and RR of CHD MI and mortality	<3 or 3-5 or >5 serves of fruit and veg and CHD	Quintile of fruit and veg (and by % energy from CHO i.e. <40%, 40 to 55% and >55% and CVD	Quartiles of intake of fruit and veg i.e. 186 g; 335g; 482 g; 733 g per day median and CVD outcomes	Quintiles of fruit & veg median serves 0.87 serves; 1.61 serves; 2.31 serves; 3.21 serves; 4.89 serves outcome is CVD mortality
N [5]	48,039 M 127,316 F	278,459 M and F	38,918 M 70,870 F	77,891 M and F	6151 (910 deaths)
Population/study information [6]	Only 6/9 cohorts used for fruit and veg meta analysis. All are US	Long follow up in US and Europe	Nurses Health and Male Health Professionals	Japanese adult male and female	Community living adult men and women in US
Quality [7]	0	0	P	P	P
Results [8]	RR 0.96 (0.93-0.99, Trend P < 0.0027) for fruit and veg	RR <3 vs >5 RR 0.83(0.77-0.89, P<0.0001) for fruit and veg combined	No significant effects for total fruit and veg at any of the three carbohydrate intakes	NS effect for fruit and veg RR 0.90 (95% CI 0.75- 1.07)	HR for quintile 5 vs. quintile 1 but DR NS cardiovascular disease 0.76(0.54-1.06, p=0.15)
Effect on risk (Increase/None/ Protect)	Protect	Protect	None	None	None

Clinical importance [9]	1	1	2	2	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	n	y

3.2 FRUIT and VEGETABLES and STROKE

Does a particular intake of fruit and vegetables affect the risk of stroke in adults?		
Evidence statement		Consumption of each additional daily serve of fruit and vegetables is associated with a reduced risk of stroke.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	Level III evidence from 2 meta analyses cohorts (of 7 cohorts and 9 cohorts) (medium risk bias).
Consistency	Good	Both meta analyses agree with protection.
Clinical impact	Good	For each additional serve daily the RR is 0.95 (95% CI 0.92-0.79).
Generalisability	Good	US Europe.
Applicability	Excellent	Australian adults.

Two meta analyses with seven cohorts in common confirm that fruit and vegetables protect against stroke. The two have approached the comparison in slightly different ways. He et al. indicate that more than five serves daily (a serve of fruit was 80 g and of vegetables 77g) results in 26% decrease in risk and Dauchet et al. reach a similar conclusion stating that each additional serve daily (106 g) decreases the risk by 5%. See Table 3.2.

References

Dauchet, L., Amouyel, P. & Dallongeville, J. 2005, "Fruit and vegetable consumption and risk of stroke: a meta-analysis of cohort studies", *Neurology*, vol. 65, no. 8, pp. 1193-1197.

He, F. J., Nowson, C. A., Lucas, M. & MacGregor, G. A. 2007, "Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies", *Journal of Human Hypertension*, vol. 21, no. 9, pp. 717-28.

Table 3.2 Studies used to make evidence statement for fruit and vegetables and stroke

Reference [1]	**He et al. 2006 [42]**	**Dauchet et al. 2005 [44]**
Type of study [2]	Meta analysis of cohort 9 studies	Meta analysis of 7 cohorts
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	RR <3 serves to >5 fruit and veg serves per day and stroke	Decrease in RR per additional serve per serve, to 8 or more of fruit and veg and stroke
N [5]	257,551	90,513 M 141,536 F
Population/study information [6]	US Japanese and European cohorts	Includes US Europe and Japan cohorts
Quality [7]	0	0
Results [8]	RR 0.89 (0.83 to 0.97) for 3 to 5 serves and 0.74(0.69-0.79) for >5 serves fruit and veg	RR 0.95 (0.92-0.97) for each additional portion fruit and veg
Effect on risk (Increase/None/ Protect)	Protect	Protect
Clinical importance [9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicablility	y	y

3.3 FRUIT and VEGETABLES and TYPE 2 DIABETES

Does a particular intake of fruit and vegetables affect the risk of type 2 diabetes in adults?		
Evidence Statement		Consumption of 5 or more serves fruit and vegetables per day is not associated with risk of type 2 diabetes.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 meta analysis of cohorts (4 studies and low risk bias) and 1 cohort.
Consistency	Satisfactory	
Clinical impact	Satisfactory	OR range from
Generalisability	Good	USA and Europe.
Applicability	Excellent	Applicable to Australian adults.

The meta analysis has only four studies based in the USA, see Table 3.3. For these four studies the RR ranged from 0.6 to 1.3. The pooled estimate was 0.96 for the highest quintile. The two largest cohorts in the meta analysis have approximately 35,000 and 38,000 women and in both these studies no significant protection was demonstrated. The additional cohort study comes from the EPIC cohort and includes both men and women. This did demonstrate protection but on the basis of five cohorts the overall finding is no protective association of fruit and vegetables with type 2 diabetes. Additional studies are needed especially with cohorts that include both men and women as the lack of association stems largely from studies in women. The serving size is in the range of 92 to 106 g per serve.

References

Hamer, M., Chida, Y. 2007, "Intake of fruit, vegetables, and antioxidants and risk of type 2 diabetes: systematic review and meta-analysis", *Journal of Hypertension*, vol. 25, no. 12, pp. 2361-9.

Harding, A.-H., Wareham, N. J., Bingham, S. A., Khaw, K., Luben, R., Welch, A. & Forouhi, N. G. 2008, "Plasma vitamin C level, fruit and vegetable consumption, and the risk of new-onset type 2 diabetes mellitus: the European prospective investigation of cancer--Norfolk prospective study.[see comment]", *Archives of Internal Medicine*, vol. 168, no. 14, pp. 1493-9.

Table 3.3 Studies used to make evidence statement for fruit and vegetables and type 2 diabetes

Reference [1]	**Hamer et al. 2007 [18]**	**Harding et al. 2008 [225]**
Type of study [2]	Systematic review of 4 cohorts	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Serves of fruit and veg (lowest intake vs 5 or more) and diabetes type 2. One serve is 106 g	Fruit and veg and incident diabetes type 2**;** quintile of intake: quintile 1 289g M 382g F per day quintile 5 459g M 550g F per day
N [5]	167,128	21,831
Population/study information [6]	All US and follow-up 6 to 23 years	EPIC in UK male and females
Quality [7]	P	P
Results [8]	RR of type 2 diabetes for five or more servings of fruit and veg daily was 0.96 (95% CI 0.79–1.17, P = 0.96)	OR top quintile fruit and veg 0.78(0.60-1.00)
Effect on risk (Increase/None/ Protect)	None	Protect
Clinical importance [9]	2	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

3.4 FRUIT and VEGETABLES and COLORECTAL CANCER

Does a particular intake of fruit and/or vegetables affect the risk of colorectal cancer in adults?		
Evidence Statement		Consumption of fruit and vegetables is not associated with risk of colorectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 1 pooled analysis of cohorts (14 studies) and 1 cohort (low risk bias).
Consistency	Good	Pooled analysis shows a protective effect but it is not significant. The Japanese cohort found a non significant increased risk.
Clinical impact	Poor	RR 0.91 (pooled analysis) and 1.05 (cohort) but CIs cross 1.0.
Generalisability	Good	US and European cohorts and Japanese.
Applicability	Excellent	Australian adults.

The pooled analysis indicated small protection but this was not significant. The Japanese cohort found no protection. The pooled analysis compared low intakes with those four times as large and 800 g is more than five average serves of fruit and vegetables. In the Japanese cohort the difference between lowest intake and highest was not as marked but would constitute 1.5 to 2 extra serves. See Table 3.4.

Fruit and vegetable intake was not reported as a convincing or protective factor for colorectal cancer in the World Cancer Research Fund report with only limited suggestion of reduction in risk with non-starchy vegetables and fruit intake.

References

Koushik, A., Hunter, D. J., Spiegelman, D., Beeson, W. L., Pa, Buring, J. E., Calle, E. E., Cho, E., Fraser, G. E., Freudenheim, J. L., Fuchs, C. S., Giovannucci, E. L., Goldbohm, R. A., Harnack, L., Jacobs, D. R., Jr., Kato, I., Krogh, V., Larsson, S. C., Leitzmann, M. F., Marshall, J. R., McCullough, M. L., Miller, A. B., Pietinen, P., Rohan, T. E., Schatzkin, A., Sieri, S., Virtanen, M. J., Wolk, A., Zeleniuch-Jacquotte, A., Zhang, S. M. & Smith-Warner, S. A. 2007, "Fruits, vegetables, and colon cancer risk in a pooled analysis of 14 cohort studies", *Journal of the National Cancer Institute*, vol. 99, no. 19, pp. 1471-1483.

Sato, Y., Tsubono, Y., Nakaya, N., Ogawa, K., Kurashima, K., Kuriyama, S., Hozawa, A., Nishino, Y., Shibuya, D., Tsuji, I., I. 2005, "Fruit and vegetable consumption and risk of colorectal cancer in Japan: The Miyagi Cohort Study", *Public Health Nutrition*, vol. 8, no. 3, pp. 309-14.

Table 3.4 Studies used to make evidence statement for fruit and vegetables and colorectal cancer

Reference [1]	**Koushik et al. 2007 [20]**	**Sato et al. 2004 [2005]**
Type of study [2]	Pooled analysis 14 cohorts	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Quintiles of fruit and veg quintile 1 <200g; quintile5 > 800g daily and colon cancer	Quintiles of fruit and veg intake quintile 1<=534g daily; quintile 5 >=698g daily and incident colorectal cancer
N [5]	756 217 in cohort 5838 cases	41 835 males and females
Population/study information [6]	US, Canadian and European cohorts follow up 6 to 20 years	Japanese 40 to 64 yrs
Quality [7]	0	p
Results [8]	Highest vs lowest fruit and veg RR 0.91 (0.82-1.01, P trend = 0.19)	No protective effects of fruit and veg RR 1.05 (0.64–1.75, for quintile 5 P for trend 0.90)
Effect on risk (Increase/None/ Protect)	None	None
Clinical importance [9]	2	4
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

3.5 FRUIT and VEGETABLES and LUNG CANCER

Does a particular intake of fruit and vegetables affect the risk of lung cancer in adults?		
Evidence statement		Consumption of fruit and vegetables is associated with a reduced risk of lung cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from meta analyses of 8 cohorts and case control (medium risk bias) 2 cohorts (low to medium risk bias).
Consistency	Satisfactory	Pooled RR from 8 cohorts shows protection but the 2 cohorts showed no protection.
Clinical impact	Good	May be up to 20% reduction.
Generalisability	Good	US, Canadian, European and Japanese cohorts.
Applicability	Excellent	Australian adults.

The pooled analysis of eight cohorts indicates protection and the North American and Dutch populations included are likely generalizable to Australians. The more recent cohort study from the US is an older population. The RR indicates reduction but the confidence interval includes harmful effects. The number of serves is high so unlikely to be the reason for these findings. The Japanese cohort had lower consumptions. See Table 3.5.

References

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Table 3.5 Studies used to make evidence statement for fruit and vegetables and lung cancer

Reference [1]	**Smith Warner et al. 2003 [1954]**	**Wright M et al. 2008 [190]**	**Liu et al. 2004 [1826]**
Type of study [2]	Meta analysis of cohorts (i.e. pooled analysis of 8 cohorts)	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of fruit and veg intake and lung cancer	Quintiles of fruit and veg lung cancer results by gender. Quintiles as number of serves per 1000kcal	Thirds of vegetable intake <1 day per week, 1-2 days per week and 3-4 days per week and incident lung cancer
N [5]	149 862 M 280 419 F	472 081 M and F	42 224 (cohort 1) 51 114 (cohort 2)
Population/study information [6]	US Canada and Netherlands follow up 6 to 16 years	US male and female from age 50 to 71 yrs NIH-AARP cohort	Japanese men and women
Quality [7]	0	P	0
Results [8]	RR for quintile 5 0.79 (95% CI 0.69–0.90) P for trend 0.001	Males RR quintile 5 (i.e. more than 4.3 serves per 1000kcal) 0.93 (95% CI 0.83-1.04). Females RR quintile 5 (i.e. more than 5.4 serves per 1000kcal) 0.98 (0.85-1.13)	Highest intake RR 1.10 (95% CI 0.79–1.52)
Effect on risk (Increase/None/ Protect)	Protect	None	None
Clinical importance [9]	1	2	4
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	n

3.6 FRUIT and VEGETABLES and OVARIAN CANCER

Does a particular intake of fruit and vegetables affect the risk of ovarian cancer in adult women?		
Evidence statement		Consumption of fruit and vegetables is not associated with risk of ovarian cancer.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	Level III evidence from 1 pooled analysis of 12 cohorts (medium risk bias); and 1 cohort (low risk bias). Over 1 million women in study.
Consistency	Good	Pooled analysis showed no effect; 1 cohort no effect.
Clinical impact	Good	No protection.
Generalisability	Good	Includes European and US studies.
Applicability	Excellent	Yes for adult women in Australia.

The pooled analysis and cohort are summarized in the Table 3.6. In European and US women there is no evidence of protection from fruit and vegetable consumption.

References

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Table 3.6 Studies used to make evidence statement for fruit and vegetables and ovarian cancer

Reference [1]	**Koushik et al. 2005 [1345]**	**Schulz 2005 [1308]**
Type of study [2]	Pooled cohort analysis (12) ovarian cancer	Cohort
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Quartiles of fruit veg <200 to >= 800 g per day and ovarian cancer	Looking at 80 g increments of total vegetables ovarian cancer
N [5]	560,441 cohort 2130 cases	325,640 females
Population/study information [6]	US and European cohorts including Nurse Health, Netherlands, Swedish Mammography	EPIC cohort
Quality [7]	0	P
Results [8]	>800 g vs <200 fruit and veg RR 0.95 (95% CI 0.79-1.15) P for trend 0.64	Per additional 80 g fruit and veg daily HR 1.02 (95% CI 0.95-1.10)
Effect on risk (Increase/None/ Protect)	None	None
Clinical importance [9]	2	3
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

Studies not included in body of evidence as there were < 5 studies

FRUIT and VEGETABLES and BLOOD PRESSURE

Both an RCT (John et al. 2002) and cohort study (Miura et al. 2004) report that higher fruit and vegetable intakes protect against increases in systolic and diastolic blood pressure in normotensives.

FRUIT and VEGETABLES and MENTAL HEALTH

A total of 8085 non demented participants aged 65 and over were enrolled in the Three-City cohort study in France. Daily consumption of fruits and vegetables was associated with a decreased risk of all cause dementia HR 0.72 (95% CI 0.53-0.97) in fully adjusted models (Barberger-Gateau et al. 2007).

FRUIT and VEGETABLES and EYE HEALTH

Using the Nurses' Health Study and men in the Health Professionals Follow-up Study the association of fruit and vegetables with age related maculopathy was studied. Participants who consumed three or more servings per day of fruits had a pooled RR of 0.64 (95% CI 0.44-0.93) P value for trend =0.004 compared with those who consumed less than 1.5 servings per day. Intakes of vegetables were not strongly related to maculopathy. (Cho et al. 2004)

Using the Womens Health Study the relationship between incident cataract and fruit and vegetable intake was examined. Compared with women in the lowest quintile of fruit and vegetable intake, women with highest intakes had a RR of 0.83 (95% CI 0.70-0.99, P for trend 0.048). (Christen et al. 2005)

FRUIT and VEGETABLES and BONE HEALTH

In the Norfolk English arm of EPIC the rate of change in bone mineral density was assessed an average of three years apart (range 2-5 years) and relationship with fruit and vegetable intake. There was no effect of fruits and vegetables, combined or separately, on rate of BMD loss. (Kaptoge 2003)

A longitudinal study in children studied the relationship of total-body bone mineral content (TBBMC) in boys and girls from childhood to late adolescence and found that vegetable and fruit intakes were significant independent environmental predictors of TBBMC in boys but not in girls. (Vatanparast 2005)

FRUIT and VEGETABLES and HEAD and NECK CANCER

The NIH-AARP (American Association of Retired People) Diet and Health cohort study found an inverse association between total fruit and vegetable intake and head and neck cancer risk (per serving per day per 1000 calories, HR 0.94 (95% CI 0.89-0.99). The association was stronger for vegetables (fifth vs. first quintile: HR 0.65 (95% CI 0.50-0.85) than for fruits (fifth vs. first quintile: HR 0.87 (95% CI 0.68-1.11). (Freedman et al. 2008)

FRUIT and VEGETABLES and UPPER AERODIGESTIVE CANCERS

In the European Investigation into Cancer and Nutrition (EPIC) cohort study cases of squamous cell carcinoma of the oral cavity, pharynx, larynx, and esophagus were identified and relationships with intakes of fruit and vegetables examined. A significant inverse association with combined total fruits and vegetables intake RR 0.91 (95% CI 0.83-1.00) per 80 g/d of consumption, and nearly significant inverse associations in separate analyses with total fruits and total vegetables intake RR 0.97 (95% CI 0.92-1.02) and RR 0.89 (95% CI 0.78-1.02) per 40 g/day of consumption) were found. (Boeing et al. 2006)

In the Iowa Womens Health cohort study significant inverse associations were observed for the highest compared to the lowest tertile of yellow/orange vegetables RR 0.58 (95% CI 0.39-0.87). (Kasum 2002)

Another European study with a case control design consumption of fruits OR per increasing tertile 0.68 (95% CI 0.62-0.75) and vegetables OR per increasing tertile 0.73 (95% CI 0.66-0.81) were associated with a reduced risk. (Lagiou 2009)

On the basis of the three studies it seems fruit and vegetables might be protective. Refer to the studies by site within the main BOE statements.

FRUIT and VEGETABLES and LARYNGEAL CANCER

Case-control study conducted in Northern Italy found significant inverse associations of raw vegetables (OR 0.2), cooked vegetables (OR 0.3), citrus fruit (OR 0.6) and other fruit (OR 0.5) and laryngeal cancer. (Bossetti et al. 2002)

FRUIT and VEGETABLES and SALIVARY GLAND CANCER

A population-based case-control study in Canada examined primary cancer of the salivary gland and relationship with diet. No significant associations with fruit or vegetables intake were found. (Forrest et al. 2008)

FRUIT and VEGETABLES and RENAL CANCER

A US population based case-control study showed decreased renal cell carcinoma risk with vegetable consumption OR 0.56 (95% CI 0.35-0.88); but not for fruit consumption. (Dolwick Grieb et al. 2009)

The association between fruits and vegetables and risk of renal cell carcinoma was also studies in a cohort of Swedish women. Women consuming five or more servings of fruit and vegetables daily had RR 0.59 (95% CI 0.26-1.34) in comparison to them consuming less than once daily. (Rashidkhani 2005)

In the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study no significant associations between fruit and vegetable consumption and renal cell carcinoma risk were observed despite a wide range of intake. The RR 0.97 (95% CI 0.85-1.11) per 40 g increase in vegetable intake, 1.03 (0.97-1.08) per 40 g increase in fruit intake, and 1.02 (0.93-1.11) per 80 g

increase in fruit and vegetable intake combined (Weikert 2006). The evidence is inconclusive but there does not appear to be a strong protective relationship.

FRUIT and VEGETABLES and PROSTATE CANCER

Two case control studies one in New York and one in Bombay both investigated fruit and vegetable intake and prostate cancer. Compared with New York men in the lowest quartile of total vegetable intake those in the highest quartile of intake had OR 0.53 (95% CI 0.36-0.79). (McCann et al. 2005) In the Indian study for those who consumed more than 3 kg per week had OR (95% CI 0.3-0.6) P trend =0.001 compared to those who consumed less than 2 kg per week. (Sunny et al. 2005)

FRUIT and VEGETABLES and LIVER CANCER

In a Japanese cohort study consumption of vegetables, green-yellow and green leafy vegetables was inversely associated with the risk of hepatocellular carcinoma, with HR for the highest vs lowest tertile of intake 0.61 (95% CI 0.36-1.03) P trend = 0.07, 0.65 (95% CI 0.39-1.08) P trend =0.06 and 0.59 (95% CI=0.35-1.01, P trend = 0.04 respectively. (Kurahashi 2009)

Another Japanese cohort study examined the relationship between vegetable consumption and the risk of death from liver cancer. Vegetable consumption was classified into three groups: "once per week or less," "2-4 times per week" and "daily intake." In males, the HRs of liver cancer deaths were 0.61 (95% CI 0.33-1.14) and 0.25 (95% CI 0.11-0.59) in the "2-4 times per week" and "daily intake" groups, respectively. In females, the multivariate HRs were 0.44 (95% CI 0.13-1.51) and 0.51 (95% CI 0.16-1.69), respectively. (Pham et al. 2006)

FRUIT and VEGETABLES and PANCREATIC CANCER

The association of the consumption of fruits and vegetables intake and with pancreatic cancer risk was examined in European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. HR (95% CI) for the highest versus the lowest quartile were 0.92 (0.68-1.25) for total fruit and vegetables combined, 0.99 (0.73-1.33) for total vegetables, and 1.02 (0.77-1.36) for total fruits. (Vrieling et al. 2009)

The associations of overall consumption of fruits and vegetables with the incidence of pancreatic cancer among women and men in the Swedish Mammography Cohort and the Cohort of Swedish Men were also studies. The HRs for the highest compared with the lowest category of intake were 1.13 (95% CI 0.66-1.94) for total fruits and vegetables, 1.10 (95% CI 0.64-1.88) for total fruits, and 1.08 (95% CI 0.63-1.85) for total vegetables. (Larsson et al. 2006)

The study of total vegetables intake and pancreatic cancer in the Hawaii-Los Angeles Multiethnic Cohort Study showed total vegetable intake was not associated with pancreatic cancer risk, nor was intake of vegetable subgroups. (Nothlings et al. 2007)

On the basis of these three studies it appears that higher consumption of fruit and vegetables is not associated with decreased risk of pancreatic cancer.

FRUIT and VEGETABLES and ORAL CANCER

A case control study examining combined (but not individual) fruit and vegetable intake found if >= three portions consumed per day OR 0.6 (95% CI 0.3-1.3) for males and for females OR 0.3 (95% CI 0.1-0.7) compared with two or less. (Llewellyn et al. 2004)

FRUIT and VEGETABLES and OBESITY

Evidence statements have been formed for fruit and for vegetables but these two randomised controlled trials only examined intake as a combined entity.

Whybro et al. (2006) found no change in weight when subjects were allocated to an additional 0 g, 300 g or 600 g fruit and vegetable per day. Ello-Martin compared a reduced fat diet with a reduced fat diet enriched in fruit and vegetables and reported those with the additional fruit and vegetables, had a significantly different weight loss (P = 0.002).

4. MEAT (S1.1 and S1.6)

Evidence Statements

4. MEAT (S1.1 & S1.6)

Search results

The initial search of the databases included 1664 references for meat and the specified disease outcomes. The detailed search is included in a separate document on searches. In all, 63 references concerning meat had data extracted and 29 (WCRF was counted as a single reference) papers were used to form the body of evidence statements for meat. The definition of fresh red meat provided by NHMRC was as follows:

Red meat for this review includes 'fresh red meat' taken from the 'carcass of any cattle, sheep, goat, buffalo, kangaroo, camel, deer, goat, pig or rabbit' and includes the 'muscle component only; it excludes offal such as liver and kidney and processed red meat'.

A significant number of papers had to be excluded from the SLR based upon this definition of red meat, or the inability to separate the data for fresh red meat from processed meat. To preserve the rigor of this definition and outcome of this review a number of large international cohort studies were therefore excluded. We acknowledge that some of the meta analyses included in this SLR did include studies which may have not met this definition for fresh red meat strictly because we were not able to remove those studies from the meta analyses undertaken by those reviewers. This includes important systematic reviews such as the WCRF report, which the reviewers felt could not be excluded based on the substantive and comprehensive nature of these well-resourced meta analyses.

The study by Sinha et al. did not meet the criteria for inclusion in this review based on the red meat included in the study i.e. all types of beef and pork, including bacon, beef, cold cuts, ham, hamburger, hot dogs, liver, pork, sausage, steak and meats in foods such as pizza, chilli, lasagne and stew. However, it is a recently published very large cohort study in over half a million people which examined all cause mortality. Therefore, although the red meat category in the study does include processed meats, it is worth acknowledging the findings in a cautionary manner. The Hazard Ratios for All Cause mortality, based on quintiles (1 = lowest, 5 = highest) of red meat intake, for men and women were as follows:

Men: Q1=1; Q2=1.08; Q3=1.17; Q4=1.28; Q5=1.36 P for trend <0.001
Women: Q1=1; Q2=1.07; Q3=1.11; Q4=1.20; Q5=1.25 P for trend <0.001

Despite the study's limitation based on the red meat definition, it is worth noting that its results for colon cancer outcomes are consistent with the BOE arising from the current review.

Sufficient evidence was found to make statements for fresh red meat and the following cancers; bladder, pancreatic, prostate, breast, lung, renal and colorectal.

**NOTE: Studies rated as negative quality were not included in body of evidence statements.

4.1 MEAT and BLADDER CANCER

Does a particular intake of meat affect the risk of bladder cancer in adults?		
Evidence statement		Consumption of fresh red meat 1 to 6 times per week (or an intake range of 14-70 g/1000 Calories/d) is not associated with risk of bladder cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 systematic review / meta analysis (of case control studies), 1 cohort and 1 case control with low risk of bias.
Consistency	Good	All studies fail to show a relationship of meat consumption with bladder cancer outcomes.
Clinical impact	Satisfactory	HRs (95% CI) in the range of 1.00-1.11 (0.71,1.52) and OR (95% CI) 0.8-1.1 (0.6, 1.5), doesn't include any clinically important effects.
Generalisability	Satisfactory	Population in body of evidence differ but it's sensible to apply evidence to Australian mid-aged population.
Applicability	Excellent	Dietary intake similar to Australian population.

The systematic review, cohort and case control study contributing to the body of evidence are shown in Table 4.1. The systematic review (World Cancer Research Fund) only included two case-control studies, one of which was Italian and the other Uruguayan. The cohort study was from Sweden (Swedish Mammography Cohort) and the other case control from Spain. Despite differences in population groups, study design (including definition and level of red meat intake) and quality of the studies contributing to the body of evidence, all failed to show an increased risk of bladder cancer according to fresh red meat consumption.

Reference

García-Closas, R., M. García-Closas, et al. 2007, "Food, nutrient and heterocyclic amine intake and the risk of bladder cancer", *European Journal of Cancer*, vol. 43, no. 11, pp. 1731-1740.

Larsson, S. C., J. E. Johansson, et al. 2009, "Meat intake and bladder cancer risk in a Swedish prospective cohort", *Cancer Causes & Control*, vol. 20, no. 1, pp. 35-40.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*, vol., no.

Table 4.1 Studies used to make evidence statements for meat and bladder cancer

Reference [1]	**Bekkering 2006 WCRF - Bladder**	**Larsson et al. 2009 [611]**	**Garcia-Closas et al. 2007 [1533]**
Type of study [2]	Systematic Review	Cohort	Case control
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Red meat / servings per week	Red meat / 0-3 servings/month, 1-4 servings/week, ≥5 servings/week	Red meat intake included beef, veal, lamb, pork. Intake measured in quintiles: quintile 1 = <20g/d (median g/d/kcal = 14), quintile 2 = 20-32g/d (median g/d/kcal = 26), quintile 3 = 33-43g/d (median g/d/kcal = 37), quintile 4 = 44-58g/d (median g/d/kcal = 50), quintile 5 = >58g/d (median g/d/kcal = 70).
N [5]	Not reported	82 002	912 cases 873 controls
Population/study information [6]	International, adults, females, males	Swedish participants from Swedish Mammography Cohort (SMC) n=39 227 & Cohort of Swedish Men (COSM) n=48 850, free from cancer and completed FFQ in 1997. Mean follow-up 9.4 years. Incident cases of bladder cancer identified in Swedish cancer registries. Swedish men and women with mean age 62.2	Spanish subjects: Age (mean±SD): 65.3±10.2yrs (cases); 64.0±9.9yrs (controls). All Caucasian (except 1 case & 1 control). 88% cases & 89% controls were male. Smokers: 85.5% cases vs 72.4% controls
Quality [7]	O - Neutral	P - Yes confident in results	P - confident in results
Results [8]	No associations could be found. Results couldn't be pooled because of different adjustments. Italy: unadjusted OR (95% CI) 1.04 (1.02,1.08) per servings per week increase. Uruguay adjusted OR (95% CI) 1.03 (1.00, 1.07) per servings per week	No association between meat intake and risk of bladder cancer. HR (95% CI) after adjusting for 6 factors: 1-4 servings/wk: 1.11(0.81-1.52); ≥5 servings/wk: 1.00(0.71-1.41)	Red meat intake was not significantly associated with risk of bladder cancer. P trend = 0.09. All OR 95% CIs go through 1.

	increase.		
Effect on Risk (Increase/None/Protect)	Varies - None and Increase	None	None
Clinical importance [9]	2	2	2
Clinical relevance [10]	1	1	1
Generalisability	Y	Y	Y
Applicability	Y	Y	Y

4.2 MEAT and PANCREATIC CANCER

Does a particular intake of meat affect the risk of pancreatic cancer in adults?		
Evidence statement		Consumption of 30-200grams of fresh red meat per day is not associated with risk of pancreatic cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 systematic review/meta analysis (of cohorts and case controls) and 1 case control study (both low risk of bias). Age populations 21-85 years.
Consistency	Satisfactory	Some inconsistency (Meta analysis of cohorts - no effect; meta-analysis of case-controls - increased risk; 1 case control - increased risk for beef/lamb and regular hamburger patty). Variability may be due to heterogeneity of meat definitions.
Clinical impact	Satisfactory	Detrimental Pooled RR for 20g increment/d (95% CI) 1.00-1.11 (0.92, 1.40) in cohort studies and 1.11 (1.08-1.15) in case control studies.
Generalisability	Good	Population in body of evidence differ but it is sensible to apply evidence to Australian mid-aged population.
Applicability	Good	Dietary intake similar to Australian population but variability in agricultural methods.

The meta analysis and case control study contributing to the body of evidence statement are shown in Table 4.2. Although there is some inconsistency in the evidence base, the strongest evidence (based on the WCRF meta-analysis of cohort studies) does not support an increased risk of pancreatic cancer. This analysis however was only based on two cohort studies. In contrast, the WCRF meta-analysis of case control studies (three studies included) did suggest some increased risk, as did the USA-based case control study with respect to consumption of beef or lamb and regular hamburger patties. Given the limited number of studies and inconsistencies in findings, some caution is required in interpreting the current evidence.

NB – There was one negative quality cohort study from Japan not included in the BOE (based on risk of bias from the method used to assess dietary intake) that also failed to show any significant relationship between red meat intake and increased risk of pancreatic cancer mortality.

References

Chan, J. M., F. Wang, et al. 2007, "Pancreatic cancer, animal protein and dietary fat in a population-based study, San Francisco Bay Area, California", *Cancer Causes & Control*, vol. 18, no. 10, pp. 1153-67.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*, vol., no.

Table 4.2 Studies used to make evidence statements for meat and pancreatic cancer

Reference [1]	**Forman 2006 WCRF - Pancreas**	**Chan et al. 2007 [8]**
Type of study [2]	Meta Analysis	Case control
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Red meat consumption and pancreatic cancer risk; risk assessed per 20g incremental increases in intake	Dietary intake of beef/lamb as main dish (4-6oz), pork as main dish (4-6oz), beef/pork/lamb as a sandwich or mixed dish (1 whole), regular hamburger (1 patty), lean/extra lean hamburger (1 patty). Subjects from USA
N [5]	Red meat: 7 cohorts (only 2 used for meta analysis); 4 case-controls Beef: 2 cohorts (only 1 used for meta analysis); 7 case-controls (only 7 used in meta-analysis)	Cases: 532 Controls: 1701
Population/study information [6]	Male, female, international, adults	Age range: 21-85yrs, For Cases: 85% between 50-79yrs, 55% men: 45% women, 83% white, 95% non Hispanic origin, 53% BMI <25, 37% BMI 25-29.9, 86% no history of diabetes
Quality [7]	Positive	P - confident in results
Results [8]	Pooled estimates of relative risk: Red meat: 1.0 (95% CI: 0.95-1.05; p=0.9) per 20g/day (cohort studies) Red meat: 1.11 (95% CI: 1.08-1.15; p<0.001) per 20g/day (case control studies) Beef: 1.13 (0.92–1.39) per 20 g/day (cohort studies) Beef: 1.22 (1.06-1.40) per 20 g/day (case-control)	Adjusted ORs (adjusted for multiple confounders): Beef/lamb as main dish (<1/month vs ≥5 serves/wk): OR 2.2 (1.0-4.5) *P* trend = 0.03 Pork as a main dish (<1/month vs ≥2 serves/week: OR 0.6 (0.3-1.1) *P* trend = 0.2 Regular hamburger patty (<1/month vs ≥2/week) OR 1.7 (1.2-2.4). *p* for trend =0.005 Lean hamburger patty <1/month vs ≥2/week OR 1.4 (0.9-2.3), *p*=0.1
Effect on Risk (Increase/None/Protect)	None	Increase Beef/lamb; None Pork; Increase Regular Hamburger patty; None Lean Hamburger patty
Clinical importance [9]	4	4

Clinical relevance [10]	l	l
Generalisability	y	y
Applicability	y	y

4.3 MEAT and PROSTATE CANCER

Does a particular intake of meat affect the risk of prostate cancer in adults?		
Evidence statement		Consumption of fresh red meat, irrespective of frequency or serving size, is not associated with risk of prostate cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from 1 meta analysis and 1 systematic review (cohorts/case-controls) with low to moderate risk of bias and 1 cohort study with low risk of bias.
Consistency	Good	Generally consistent, but mostly no effect (no effect from meta-analysis of cohort studies; no effect from 18 studies in systematic review; 1 no effect cohort study; 1 slight increased risk meta-analysis of case-control studies).
Clinical impact	Satisfactory	RRs generally consistent with null value (1.0) however 95% CI range is wide (0.59-2.99).
Generalisability	Satisfactory	Some differences in populations with respect to ethnicity/culture and level of red meat consumption but it is sensible to apply this evidence to the target population.
Applicability	Satisfactory	The Australian meat supply / meat composition differs from other countries (agricultural/environmental factors). Types of meats eaten in Australia also differ from other countries. Heterogeneity in definition of red meat between studies (which may have included processed meat and different cooking methods) also reduces applicability.

The systematic review, meta-analysis and cohort study contributing to the body of evidence are shown in Table 4.3. The evidence predominantly involves studies from the USA, however Asian, European, Asian and Australian populations have also been included. Despite differences in the definition of red meat definition and level of intake between studies, the strongest evidence (based on the WCRF meta analyses of cohort studies, prospective cohorts from the systematic review and the positive quality USA cohort study) does not support an increased risk of prostate cancer according to level of red meat consumption.

References

Koutros, S., A. J. Cross, et al. 2008, "Meat and meat mutagens and risk of prostate cancer in the Agricultural Health Study", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 17, no. 1, pp. 80-7.

Mori, M., N. Masumori, et al. 2009, "Traditional Japanese diet and prostate cancer", *Molecular Nutrition & Food Research*, vol. 53, no. 2, pp. 191-200.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*, vol., no.

Table 4.3 Studies used to make evidence statements for meat and prostate cancer

Reference [1]	**Bekkering 2006 WCRF - Prostate**	**Mori et al. 2009 [495]**	**Koutros et al. 2008 [1165]**
Type of study [2]	Meta Analyses	Systematic Review	Cohort
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Red meat / 0.2 -13 serves per week	Red meat / varies but compares lowest to highest intakes	Meat / Median (g/d): Red meat 23.2-122.3; Beef steaks: 4.2-63.0; Pork chops/ham steaks: 3.3-28.6
N [5]	Included under "Red meat" - 13: 6 prospective cohorts, 2 nested case control, 5 case control (not all included in meta-analysis)	28,679	23,080
Population/study information [6]	Male, female, international, adults	Studies: USA x 8, Puerto Rico x 1, Taiwan x 2, Japan x 1, Australia x 1, Netherlands x 1, New Zealand x 1, Canada x 2, Uruguay x 1	Agricultural Health Study - includes licensed pesticide applicators from Iowa and North Carolina USA. Mean age over the 5 quintiles: 45.6-52.4yrs. 197,017 person-years of follow-up
Quality [7]	Positive	O - Neutral	P - Very confident in results
Results [8]	Summary estimate and 95% CI's per servings per week: 0.98 (0.97-1.0) (adjusted) - cohort studies 1.07 (1.00- 1.15) (adjusted) - same population case control studies random effects model Aggressive/advanced prostate cancer cases: 1.0 (0.97, 1.03) - cohort studies	Only 2 of 19 articles revealed significantly positive relationship between red meat and prostate cancer risk. Cross et al. 2005 (USA) RR (95% CI) 1.42 (1.05,1.92); Norrish et al. 1999 (NZ) RR (95% CI) 1.68 (1.02,2.77). General OR range for studies showing no effect: 0.95-1.7 with general 95% CI range of 0.6-3.4	No association observed for any meat items and risk of prostate cancer. RR (95% CI) total red meat: quintile 1 1.00, quintile 5 1.10 (0.85-1.43) p=0.92; beef steaks: quintile 1 1.00, Q5 1.03 (0.71-1.49) p=0.90; pork quintile 1 1.00, quintile 5 1.00 (0.76-1.29) p=0.98
Effect on Risk	None	Varies, most were - None	None

(Increase/None/Protect)			
Clinical importance [9]	4	2	2
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

4.4 MEAT and BREAST CANCER

Does a particular intake of meat affect the risk of breast cancer in adults?		
Evidence statement		Consumption of 60-90g fresh red meat per day is not associated with risk of breast cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	All Level III studies with moderate risk of bias (1 meta-analysis within a systematic review of 3 cohort; 6 case-controls plus 4 cohort, 4 case control studies).
Consistency	Poor	Evidence is inconsistent (One meta-analysis shows no relationship for cohort studies and only just significant for case-control studies). The primary research is variable (4 no effect; 3 increased risk, 1 varied).
Clinical impact	Satisfactory	HRs (95% CI) in range of 1.05-1.41 (0.93, 1.81) and RRs (95% CI) in range of 0.98-1.64 (0.92, 2.93), includes clinically important effects. ORs (95%CI) in range of 0.82-1.24 (0.60-1.62), P trend range 0.35-0.91 for NO RISK; 1.49-2.96 (1.04-2.78) for RISK, P trend range 0.016-0.003.
Generalisability	Good	Populations in body of evidence are similar to the Australian population.
Applicability	Good	Applicable to Australian females, despite variability in different agricultural methods.

The systematic review, four cohort and four case control studies contributing to the body of evidence are shown in Table 4.4. The systematic review (World Cancer Research Fund) included three cohort and six case-controls studies n a meta-analysis and found no association with breast cancer. Of the four cohort studies, two were undertaken in the Nurses Health study but in different age groups and after different lengths of follow-up with the longer follow up (18 years) in the mid–aged women showing no effect while the 12 year follow-up in women showed no effect for red meat including lamb and beef and but an increase risk for higher intakes of pork. Of the four case-control studies, three had positive quality and two of these showed no effect with increased red meat. Despite differences in population groups, study design (including definition and level of red meat intake) and quality of the studies contributing to the body of evidence, the inclusion of the meta-analysis weights the results towards no increased risk of breast cancer according to fresh red meat consumption.

NB – There were two negative quality studies not included in the body of evidence. (Linos 2008, Petro-Nustas 2002)

References

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Dai, Q., X. O. Shu, et al. 2002, "Consumption of animal foods, cooking methods, and risk of breast cancer", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 11, no. 9, pp. 801-8.

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Holmes, M. D., G. A. Colditz, et al. 2003, "Meat, fish and egg intake and risk of breast cancer", *International Journal of Cancer*, vol. 104, no. 2, pp. 221-7.

Kabat, G. C., A. J. Cross, et al. 2009, "Meat intake and meat preparation in relation to risk of postmenopausal breast cancer in the NIH-AARP diet and health study", *International Journal of Cancer*, vol. 124, no. 10, pp. 2430-5.

Mignone, L. I., E. Giovannucci, et al. 2009, "Meat consumption, heterocyclic amines, NAT2, and the risk of breast cancer", *Nutrition & Cancer*, vol. 61, no. 1, pp. 36-46.

Taylor, E. F., V. J. Burley, et al. 2007, "Meat consumption and risk of breast cancer in the UK Women's Cohort Study.[erratum appears in Br J Cancer. 2007 Jun 4;96(11):1780]", *British Journal of Cancer*, vol. 96, no. 7, pp. 1139-46.

van der Hel, O. L., P. H. Peeters, et al. 2004, "GSTM1 null genotype, red meat consumption and breast cancer risk (The Netherlands)", *Cancer Causes & Control*, vol. 15, no. 3, pp. 295-303.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*, vol., no.

Table 4.4 Studies used to make evidence based statements for meat and breast cancer

Reference [1]	**WCRF - Breast**	**Taylor et al. 2007 [1204]**	**Kabat et al. 2009 [1129]**	**Cho et al. 2006 [1222]**	**Holmes et al. 2003 [1347]**
Type of study [2]	Systematic Review	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Red meat/ increasing amounts (variably defined)	Red meat/ none to low <32 g per day medium 32-57 g per day high >57 g per day intakes	Red meat/ ≤13 g/1000 kcal 13-21.9 g/1000 kcal, 21.9-31.1 g/1000 kcal, 31.3-43.7 g/1000 kcal, >43.7 g/1000 kcal per day	Red meat / Servings <1/mo 1-≤2/mo >2/mo-≤1/wk >1-≤3/wk >3/wk	Red meat / From never up to 6 or more times/day
N [5]	unknown	33 725	120 755	90 659	88 647
Population/study information [6]	International, adults, females	UK Women's Cohort Study. Women 35 - 69 yrs in 1995-1998. Median follow-up of 8 years	NIH-AARP Diet and Health Study cohort. 8 year follow-up. Mean age 62.4yrs	Nurses' Health Study II -Female registered nurses, 25-42yrs, living in 1 of 14 U.S. states, (diagnosed with breast cancer - mean±SD: 43.0±4.5yrs). 12 yr follow-up	Nurses' Health Study - Age: mean±SD: 46.7±7.2yrs, 18 years follow-up
Quality [7]	O - Neutral	P - Yes confident	P - Yes confident	P - Yes confident	P - Yes confident

		in results	in results	in results	in results
Results [8]	Case-control results suggest a positive association with increased risk breast cancer and red meat intake but this is not supported by the cohort studies. No association with menopausal status. Cohort Pooled RR (95% CI): 1.02 (0.98,1.07) for an increased meat consumption of 5 times/month	Postmenopausal women consuming red meat are at increased risk of breast cancer. HR (95% CI) after adjusting for 10 factors: Red meat: none 1.00, high (>57g/d) 1.41 (1.11, 1.81) p=0.007 trend, p=0.0577 effect modification by menopausal status	No association between a high intake of red meat in premenopausal women and increased risk of breast cancer. HR (95% CI) after adjusting for 15 factors: Red meat: quintile 1 1.00, quintile 5 1.05 (0.93-1.18) p=0.66	Higher red meat intake may be a risk factor for ER+/PR+ breast cancer among premenopausal women. RR (95% CI) after adjusting for 11 factors: Beef/lamb as main dish: <1/mo 1.00, >1/wk 1.30 (0.93-1.90) p=0.03; Pork as main dish: <1/mo 1.00, >1/wk 1.81 (1.21-2.70) p=0.005; Beef/pork/lamb sandwich or mixed dish: <1/mo 1.00, >3/wk 1.64 (0.92-2.93) p=0.35	No evidence that red meat intake during mid-life and later was associated with risk of breast cancer. RR (95% CI) after adjusting for 14 factors: All women: Beef/pork/lamb sandwich: ≤0.07 serves/d 1.00, ≥0.27 serves/d 1.00 (0.90-1.11) p=0.85; Beef/pork/lamb mixed dish: ≤0.14 serves/d 1.00, ≥0.45 serves/d 0.98 (1.87-1.09) p=0.99
Effect on risk (Increase/None/Protect)	None	Increase	None	Mixed (no effect or increased)	None
Clinical importance [9]	2	4	2	4	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 4.4 Studies used to make evidence based statements for meat and breast cancer (cont.)

Reference [1]	**van der Hel et al. 2004 [1321]**	**Dai et al. 2002 [1375]**	**Hermann et al. 2002 [1065]**	**Mignone et al. 2009 [645]**
Type of study [2]	Nested case control	Case control	Case control	Case control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Fresh red meat (g per day) in groups of <30 g per day (reference group 30-44 g per day ≥45 g per day	Red meat (g per day) in groups ≤28.6 g per day ≤44.6 g per day ≤62.2 g per day , ≤87.1 g per day >87.1 g per day OR quintiles 1-5	Red meat included beef, pork and lamb. Red meat quartiles: 0, 1-21g/d, 22-39g/d, 40-64g/d, ≥65g/d.	Red meat (<2 servings/wk; 2-<3 servings/wk; 3-<4 servings/wk; 4-<5 servings/wk; 5+ servings/wk). Serving size information not assessed, so medium portion assigned - Middle aged women: 84g hamburger, 85g steak. Older women: 70g hamburger; 84g steak.
N [5]	251 cases 300 controls - frequency matched on age, town and menopausal status	1459 cases 1556 controls	cases 355 controls 838	2686 cases 3508 controls
Population/study information [6]	Women aged 20-59 yrs, Dutch towns	Women aged 25-64 yrs who were newly diagnosed with breast cancer from Aug 1996 to Mar 1998, from Shanghai, China	Women aged: cases: 42.6±5.48; controls: 42.6±5.77. Age range: 24-52 yrs. Germany	The Collaborative Breast Cancer Study (CBCS). Mean age of both cases and controls is 55yrs. 40% premenopausal, 97% European ancestry
Quality [7]	P - confident in results	0 - Neutral	P - confident in results	P - confident in results

Results [8]	No relation between any type of meat (including fresh red meat) consumption and breast cancer risk. Fresh red meat 30-44g/d OR 1.31(0.83-2.05), ≥45g/d OR 1.30(0.83-2.02).	Positive association with red meat and breast cancer, particularly in women with higher BMI and WHR (especially postmenopausal women). If never used deep fried cooking: >87.1g/d OR 1.49 (1.04-2.15) Trend test: P=0.11. Quintile 5 for Red meat: OR 1.53 (1.19-1.96) Trend P=0.003.	Breast cancer risk increased with a higher consumption of red meat (P for trend = 0.016); women with the highest consumption level had an 85% elevated breast cancer risk compared with the lowest quartile (95% CI 1.23-2.78). When only premenopausal women considered, positive association with meat intake were even stronger.	No association of breast cancer with consumption of red meat (P for trend: 0.91 (all women); 0.55 (premenopausal); 0.35 (postmenopausal). All OR 95% CI pass through 1.
Effect on risk (Increase/None/Protect)	None	Increase	Increase	None
Clinical importance [9]	2	4	4	2
Clinical relevance [10]	1	1	1	1
Generalisability	Y	N	Y	Y
Applicability	Y	N	Y	Y

4.5 MEAT and LUNG CANCER

Does a particular intake of meat affect the risk of lung cancer in adults?		
Evidence statement		Consumption of fresh red meat is associated with increased risk of lung cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from systematic review of cohorts and case controls (low to moderate risk of bias), 3 case controls (moderate risk of bias) and 1 case control (moderate to high risk of bias).
Consistency	Poor	Cohort study and 7/8 case-control studies in systematic review - higher risk; 2 individual case controls - no effect; 2 case controls -increased risk (but not for all types lung cancer). Inconsistency may be explained by differences in study design, eg definition of red meat and level of exposure/consumption (which is highly variable between studies).
Clinical impact	Satisfactory	Increased risk ORs and HRs in the general range of 1.20-2.0 (95% CIs in the general range of 0.7-3.0).
Generalisability	Good	Some differences in populations with respect to ethnicity/culture and level of red meat consumption but it is sensible to apply this evidence to the target population.
Applicability	Satisfactory	Meta-analysis may have included studies that included processed meat within the definition of red meat. The Australian meat supply, type and composition differ from other countries (agricultural/environmental factors).

The systematic review and four individual case control studies contributing to the body of evidence are shown in Table 4.5. Although the cohort study and 7/8 case control studies from the WCRF systematic review showed increase risk, odds ratios were highly variable with wide confidence intervals, limiting strength of this association. One high quality case control study from Italy did also however show increased risk. The two case control studies (also from European populations) that failed to show increased risk tended to be of lesser quality, rated as neutral due to greater potential for bias in selection of controls and assessment of dietary intake. Definitions of red meat intake were not always described clearly from studies included in the evidence base, with heterogeneity in these definitions likely to have impacted on consistency of findings. Importantly, most results were adjusted for smoking as a major confounder for lung cancer.

It was not possible to quantify a dose-response relationship based on the current body of evidence.

References

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Lam, T. K., A. J. Cross, et al. 2009, "Intakes of red meat, processed meat, and meat mutagens increase lung cancer risk", *Cancer Research*, vol. 69, no. 3, pp. 932-9.

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Table 4.5 Studies used to make evidence statements for meat and lung cancer

Reference [1]	**Alberg 2006 - WCRF Lung**	**Dosil-Diaz 2007 [114]**	**Lam 2009 [551]**	**Kubik 2002 [368]**	**Zatloukal 2003 [1629]**
Type of study [2]	Systematic review	Case-Control	Case-Control	Case-Control	Case-Control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Red meat consumption and lung cancer mortality and incidence. Level of red meat intake not well defined (results generally reported as highest versus lowest intake)	Lung cancer incidence according to beef intake (beef cutlets and steak) - high (>2x serves per week) vs. low intake (< once per wk)	Lung cancer incidence according to fresh red meat consumption including beef steaks, hamburgers, pork chops and veal chop/cutlets.	Risk of different types of lung cancer according to red meat consumption (types of red meat included not detailed)	Risk of different types of lung cancer according to red meat consumption (types of red meat included not detailed)
N [5]	10 (1 cohort, 9 case-control) - Total participant n unclear from report	335 cases 337 controls	1903 cases 2073 controls	269 cases 1079 controls	145 adenocarcinoma cases 221 other types lung cancer cases 1642 controls
Population/study information [6]	M and F adults international,	Spain. M and F aged >35. Cases = histologically confirmed lung or oropharyngeal cancer combined from 3 different case control studies. Dietary intake assessed using 74 item FFQ - 11 items for meat intake	Italy. M and F Cases = incident cases of primary lung cancer (either pathologically or cytologically confirmed or identified via clinical history and imaging). Controls = randomly selected from population database and matched with controls for age,	Prague, Czech Republic. Women. Cases as above, from Prague University Hospital. Controls=hospital based (family/friends of other hospitalised patients).	Prague, Czech Republic. Women. Cases as above, from Prague University Hospital. Controls=hospital based (family/friends of other hospitalised patients).

			gender and residence.		
Quality [7]	Neutral	Neutral	Positive	Neutral	Negative
Results [8]	No aggregate / meta-analysis results reported. ORs highly variable with range of 0.9->12.0: (95% CIs 0.46->10); total red meat OR in general range 1.2-1.9 (0.7-3). RR for cohort study (total red meat) 1.6 (95% CI 1.0-2.6) for 1.4 vs. 9 serves/wk. Overall there is some indication that higher total red meat and beef consumption may be linked with lung cancer incidence with 7/8 studies indicating increased risk. CIs are quite wide however, limiting the overall strength of this association.	Adjusted model OR (95% CI) beef consumption (high = >2x serves per week vs. low = < once per wk): 1.89 (0.94–3.82, p for trend =0.54)	Fully adjusted model OR (95% CI) for fresh red meat consumption tortile (F/M): 0.36/0.55 vs. 3.5/2.7 serves per wk: 1.9 (1.5–2.2, p for trend <0.001)	OR (95% CI) for never/monthly consumption vs. daily/several times weekly for all cancer cases: 1.53 (0.94–2.48), p for trend not given	OR (95% CI) for never/monthly consumption vs. daily/several times weekly: Adenocarcinoma: 1.21 (0.68-2.15), p for trend =0.240 Other lung ca's: 1.81 (1.04-3.18, p for trend =0.042)
Effect on Risk (Increase/None/Protect)	Varies - majority Increase	None	Increase	None	For lung cancers other than adenocarcinoma - Increase Adenocarcinoma - None
Clinical importance [9]	4	4	4	4	4

Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

4.6 MEAT and RENAL CANCER

Does a particular intake of meat affect the risk of renal cancer in adults?		
Evidence statement		Consumption of fresh red meat is associated with risk of renal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	3 meta analyses Level III studies (cohort and/or case controls) with low to moderate risk of bias and 1 case control.
Consistency	Satisfactory	Some inconsistency but overall trend for no effect (2 meta analyses) or slight increased risk (1 meta-analysis) with higher levels of meat consumption. Inconsistency might be due to differences in included studies for each meta-analysis and heterogeneity between studies (e.g. definition of red meat, level of consumption).
Clinical impact	Poor	ORs generally in the direction of no effect to increased risk (1.01-1.3 with 95% CI range 0.86-1.63). Confounder adjusted ORs generally <1.06 (95% CI range 0.91-1.15).
Generalisability	Good	Some differences in populations with respect to ethnicity/culture and level of red meat consumption but it is sensible to apply this evidence to the target population.
Applicability	Satisfactory	Meta analyses may have included studies that included processed meat within the definition of red meat. The Australian meat supply, type and composition differ from other countries (agricultural/environmental factors).

The three meta analyses and one case control study contributing to the body of evidence are shown in Table 4.6. These studies cover a wide range of populations, including the USA, UK, Europe, Asia and Australia. Point estimates and confidence intervals were very close to, or crossed 1, for the two highest quality and most robust meta analyses (WCRF and Alexander 2009). Definitions of red meat intake and differences in study populations may help to explain inconsistencies in findings between the meta analyses. Of note, significant heterogeneity was found for both analyses that reported aggregated results. Heterogeneity was diminished however when only studies appropriately adjusted for confounders (eg smoking, BMI) were included in analysis, as per Alexander 2009. Although the USA case control study showed a highly significant increased risk for women, this is largely negated by evidence from the more robust meta analyses which indicate no effect.

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Grieb, S. M., R. P. Theis, et al. 2009, "Food groups and renal cell carcinoma: results from a case-control study", *Journal of the American Dietetic Association*, vol. 109, no. 4, pp. 656-67.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*, vol., no.

Table 4.6: Studies used to make evidence statements for meat and renal cancer

Reference [1]	**Mayer 2006 - WCRF Report**	**Alexander 2009 a [1127]**	**Faramawi 2007 [1210]**	**Grieb 2009 [1130]**
Type of study [2]	Meta Analyses	Meta Analyses	Meta Analyses	Case-Control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Red meat / <2 -up to 10 serves per week	Red meat / low versus high intake (amoounts vary)	Red meat consumption / tertiles, quartiles or quintiles	Red meat (including beef steaks, pot roasts and ground meat) / <once / wk up to 5 or more times/wk
N [5]	5 case control. Total participant n unclear.	11 (7 case-control, 3 cohort and 1 pooled analysis (from 13 international cohorts)). Total participant n unclear. The pooled analysis (Lee 2008) included 530 469 women and 244 483 men.	6 case-control Total participant n unclear. Several large (>5000) case control studies included.	335 cases 337 controls
Population/study information [6]	M and F adults international	M and F adults international (including Australia, UK, Europe, USA and Canada)	M and F adults international	M and F (wide age range <50 - >80) from Florida / Georgia USA. Cases histologically confirmed renal cell carcinoma diagnosis between 2000-2004 Controls matched from population (identified using random digit dialling). Diet measured using validated 70 item Block FFQ assessing previous yr / yr prior to diagnosis intake.
Quality [7]	Positive - extensive protocol followed as per WCRF systematic literature review	Neutral. Only Medline searched. Quality assessment of included	Neutral. Key limitations are that quality and validity of included studies not assessed/reported; and	Positive

	process guidelines. Articles quality checked and only those with sufficient data included in meta-analysis	studies unclear. However, still better quality than Faramawi 2007.	not all included studies were adjusted for smoking or BMI.	
Results [8]	Summary relative risk not included (due to small number of studies with key design differences). Studies from same population: Unadjusted RR: 1.02 (1-1.04) Adjusted RR: 1.06 (1-1.13) Studies from not same population Unadjusted RR: 1.18 (1.08-1.30) Adjusted RR: 1.01 (0.971-1.05)	Summary relative risk estimate (highest vs lowest intakes): 1.12 (95% CI 0.98-1.29) Heterogeneity p=0.015 For sub analysis of studies that adjusted for smoking, BMI and energy intake (n=5): SRRE: 1.02 (0.91-1.15), heterogeneity p=0.181.	Pooled RR (highest vs lowest intakes) random effects model: 1.30 (1.03-1.63); p not reported. Heterogeneity p=0.06	Adjusted odds ratio for combined M/F according to lowest vs. highest red meat intake (<1 week vs. >5 serves/wk) = 4.43 (2.02-9.75); p for trend 0.001 AOR men (<1 serve/wk vs. >3 serves) = 2.08 (1.08-4.00); p for trend 0.22 AOR women (<1 serve/wk vs. >3 serves) = 3.04 (1.60-5.79); 0.001
Effect on Risk (Increase/None/Protect)	None to slight Increased	None	Increase	Increase
Clinical importance [9]	4	4	4	4
Clinical relevance [10]	1	1	1	1
Generalisability	Y	Y	Y	Y
Applicability	Y	Y	Y	Y

4.7 MEAT and COLORECTAL CANCER

Does a particular intake of meat affect the risk of colorectal cancer in adults?		
Evidence statement		Consumption of (greater than, at least 100-120g/d) fresh red meat is associated with an increased risk of colorectal cancer.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	Three neutral quality meta analyses of cohort, or cohort and case-control studies (Level III evidence) and 6 major cohort studies (Level III) (5 positive, 1 neutral quality) with low risk of bias. Only 1 positive quality case-control study.
Consistency	Good	Meta analyses all support an increased risk for colorectal cancer with increased meat consumption (RR range 1.24-1.43), as does one case control study OR 2.2(1.2-4.2). All 6 recent cohort studies show no increased risk overall. One nested case-control in Nurses Health Cohort (Chan et al., 2005) showed increased risk only for rapid acetylators (NAT2) OR 3.10 (1.10-8.18). Recent cohort studies included in this review from the Netherlands, Japan, China, Canada and the US. Diverse populations may explain the inconsistencies as majority of previous studies have been from Europe and the USA. Forest plots from meta analyses show most of the included cohort studies had wide CIs around the point estimates, which were only slightly greater than one. A major inconsistency occurs with the definition of red meat. While cohort studies in this review were limited to those where fresh red meat was reported separately and mostly included meats described as "fresh muscle meats", other definitions of "red meat" from excluded papers included ham, bacon, liver, sausage, hamburger, offal etc. Meta analyses will have included papers which include these items within their definition of red meat.
Clinical impact	Good	Reported RRs (1.24-1.43) from meta analyses have potential to make significant impact on colorectal cancer risk if it indeed relates to fresh red meat consumption, but evidence tends to be inconsistent.
Generalisability	Good	All of the studies examined are randomly selected community samples from large cohort studies, though from varied countries and ethnicity profiles. American and European studies most generalisable. There seems to be a larger representation of women-only studies in the recent

		cohorts.
Applicability	Satisfactory	This is limited due to the heterogeneity associated with the definition of red meat for most studies and the major differences in the meat supply and types of meat eaten in Australia compared with other countries.

Three meta analyses within systematic reviews, six cohorts (one with a nested case-control of a genetically defined sub-group) and one additional case-control study contributed to the body of evidence and are shown in Table 4.7. For Dose-Response, all three meta analyses (two of cohort studies and one of case-control studies) consistently demonstrated an increased risk of colorectal cancer with increasing meat consumption. This dose-response relationship was quantitated in the table below for all three. Reporting varied from increased relative risk per additional one serve per day and increased relative risk per increase of 100g/d in one meta-analysis; to increased relative risk for highest versus lowest consmers and increased relative risk for a increase of 120g/d in two meta analyses. All six recent cohort studies show no increased risk overall. A major inconsistency occurs with the definition of red meat. While cohort studies in this review were limited to those where fresh red meat was reported separately and mostly included meats described as "fresh muscle meats", other definitions of "red meat" from excluded papers included ham, bacon, liver, sausage, hamburger, offal etc. Meta analyses will have included papers which include these items within their definition of red meat. A large cohort study (Sinha et al 2009) did find a positive association, but was not included due to issues with definition of red meat (as above). The WCRF reported a convincing relationship between red and processed meat and increased risk of colorectal cancer (WCRF 2007).

NB – There were 2 negative quality studies not included in the BOE (Marques-Videl 2006, Truswell 2002).

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Table 4.7 Studies used to make evidence statements for meat and colorectal cancer

Reference [1]	**WCRF Colorectal Ca 2007**	**Larsson &Wolk, 2006 [1224]**	**Norat et al., 2002 [1389]**	**Brink et al. (2005) [1289]**	**Chan et al., 2005 [1288]**	**Oba et al., 2006 [1227]**	**Lee et al., 2009 [481]**	**Kabat et al., 2007 [1191]**	**Sato et al., 2006 [1240]**	**Seow et al., 2002 [1364]**
Type of study [2]	Meta-analysis	Meta-analysis	Meta-analysis	Cohort	Nested Case-control within Cohort	Cohort	Cohort	Cohort	Cohort	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Colorectal incidence	Colorectal Ca incidence	Colorectal Cancer incidence or mortality	Beef and Pork intake	Beef, Pork or Lamb as main meal	Fresh beef and pork intakes	Red Meat (including beef and pork)	Red Meat, total iron, heme iron, meat iron	Fresh Beef and Pork intake (frequency only)	Exposure - red meat (including pork, lamb, beef and mutton)
N [5]	Not specified	1,042,824 total; almost 8000 incident cases	Not Reported	2948 sub-cohort participants ; 448 colon ca cases; 160 rectal cancer cases	183 incident cases, 443 matched controls among cohort of 32,826	Total Cohort: 13,894 men, 16.327 women. Incident colon cancer cases: men 111, women 102	Total cohort: 73.224; 394 incident cases colorectal cancer (colon=236, rectal=158)	Total cohort: 49,654; colorectal cases 617 (colon 428, rectal 195)	41,835 (20,174 men, 21,661 women). 474 incident cases colorectal cancer (280 colon cancers, 198 rectal	121 Cases; 222 controls

									cancers, 4 cases colon+rectal cancer)	
Population/study information [6]	Men and Women from major international cohort studies	Men and women from major international cohort studies	Men and Women from cohort and case-control studies	The Netherlands Cohort Study, men and women 55-69 yrs at baseline	Nurses Cohort, women 30-55 yrs at baseline	Japanese Takayama Cohort, men and women 35+ years at baseline	Shanghai Women's Health Study, Chinese women 40-70 years at baseline	Canadian National Breast Screening Study (Women 40-59 years)	Japanese men and women from Miyagi Cohort Study	Male and Female Chinese Singaporeans >=40 years
Quality [7]	Neutral	Neutral	Neutral	P	P	P	P	0	P	P
Results [8]	RR 1.43 (1.06,1.94) for an increase of 1 serve per day of red meat; RR 1.29 (1.05,1.59) for an increase of 100g/d of red meat	RR=1.28 (1.15,1.42) for highest vs lowest consumption groups; RR=1.28 (1.18,1.39) for an increase of 120g/d	High intake of red meat associated with moderate but significant increase in colorectal cancer risk. RR 1.35 (1.21-1.51) for highest vs lowest	No significant association for fresh beef or pork intake with either colon or rectal cancer, neither overall or with K-ras mutation status.	No assoc of red meat with colorectal cancer incidence overall. OR 3.10(1.10-8.18) for rapid acetylators, no assoc for slow acetylators. OR for high red meat, NAT2 and	No association found with colon cancer and red meat intake for men or women	No association of CRC risk and red meat intake	No sig association of CRC risk for red meat, total iron, heme iron or meat iron.	No association of CRC risk and either fresh beef or Pork intake (frequency).	Significant positive association of highest vs lowest tertile of red meat intake (portions) with CRC incidence [OR 2.2 (1.2-4.2)], but portions not defined. Relationship was modified by vegetable intake (again portions not defined). OR for highest tertile of red meat and low vegetable intake 2.6 (1.0-6.7)

			quartile intakes. RR 1.24 (1.08-1.41) for increase in 120g/d.		smoking >35 pack years was 17.6 (2.0-158.3					
Effect on Risk (Increase/None/Protect)	Increase	Increase	Increase	None	None	None	None	None	None	Increase
Clinical importance [9]	4	4	4	4	2	4	3	3	3	4
Clinical relevance [10]	1	1	1	1	1	1	1	1	1	1
Generalisability	y	y	y	y	n	n	n	y	n	n
Applicability	y	y	y	y	n	n	n	y	n	n

Summary of Studies not included in BOE statements for Meat:
Data was extracted from papers for the following outcomes but there was an inadequate evidence base to create BOE statements.

Iron status:
Two RCT studies (1 Level II and 1 Level III, both of positive quality) in different population sub-groups but both consistent for higher iron stores with higher intakes of bioavailable iron (Snetselaar 2004 Wells 2003).

Hypertension:
Two studies (both Level III, one positive and one neutral quality). Cohort study (Miura 2004) showed increasing Hypertension with increasing red meat while RCT (Nowson 2009) showed reduced BP on a low DASH diet including lean red meat.

Mental Health:
Two studies (both Level III, one positive, one neutral quality) in older people. Neither study showed an association with meat intake and mental health (Barberger-Gateau 2002, Almeida 2006).

Type 2 Diabetes:
One study (Level III, positive quality) in Shaghai women showing no clear linear relationship of meat intake with Type 2 diabetes incidence (Villegas 2006). Modest positive association with meat intake for overweight women and modest negative association for normal weight women.

Cardiovascular Disease:
Three studies (2 Level III small RCTs and 1 Level III medium cohort, 2 positive and 1 neutral quality). One large cohort study had to be excluded based on the definition of red meat (Sinha 2009). While there was major variability in the study designs, none showed an increased risk of CVD with meat intake. The cohort study (Wagemakers 2009) showed no increase in the main CVD risk factors with increasing meat intake, while the RCTs (Rubio 2003, Melanson 2003) showed no adverse effects on lipid profiles of including lean red meat.

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5. DAIRY (S1.1 and Cat 2 S2.6)

Evidence Statements

5. DAIRY (S1.1 & Cat 2 S2.6)

Search results

The search of the databases included 2738 references for dairy and the specified disease outcomes. An additional 18 studies were found by reviewing reference lists of retrieved studies and through hard copies submitted from external sources. Unless otherwise specified, throughout this document dairy consumption is defined as the total consumption of cheese, milk, and yoghurt. Unless specified in the narrative and the data extraction table, butter was not included as a dairy food. Due to few studies that examined high fat dairy foods versus low fat dairy foods, the body of evidence statements include dairy foods of varying fat levels unless otherwise specified. The detailed search is included in a separate document on searches. Data was extracted from 53 references concerning dairy foods, and 38 publications were used to form the final body of evidence statements. Sufficient evidence was found to make statements for the relationships between dairy foods and bone health, hip fracture, heart disease, stroke, hypertension, type 2 diabetes, metabolic syndrome, obesity, social equity, and colorectal, rectal, renal cell, prostate, breast, and endometrial cancers. Evidence was found on the following factors, but was not strong enough to develop a body of evidence statement: mental health (two cohort studies), lipid profile in adults (two randomised controlled trials), lipid profile in infants (three randomised controlled trials), adiposity in children (one randomised controlled trial), dental health (one cohort), child growth (one cohort study), pancreatic cancer (one cohort study), ovarian cancer (one cohort study), dairy consumption during pregnancy and size of infant (one cohort study), and the effect of nutrition education on dairy consumption (two randomised controlled trials).

5.1 DAIRY and BONE HEALTH

Does a particular intake of dairy affect bone health?		
Evidence statement		Consumption of dairy products (particularly milk) is associated with improved bone mineral density
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	One systematic review (1 N) (of 4 cross-sectional studies, 3 randomised controlled trials); 1 small cohort study in pregnant women (1 P) and 4 randomised controlled trials: (one in boys aged 13-17 y (1 0), one in men (1 P), one in younger women (18-30y) and one in post-menopausal women (2 P)).
Consistency	Good	2 of 3 RCTs in the first systematic review reported a significant association. In the systematic review included in the second systematic review, 6 studies reported no effect, 5 reported a positive effect, and 1 reported a negative effect. 3 of 4 additional RCTs and the 1 additional cohort study reported a significant association between milk consumption and bone health.
Clinical impact	N/A	Study outcomes and populations were varied and no summary statistic can be provided.
Generalisability	Excellent	Systematic review included studies from Australia, USA, The Netherlands, China; additional studies conducted in Canada, China, France, UK, USA.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL.

The Lanou 2005 systematic review was of poor quality and did not critically analyse included studies. This review focused on calcium intake rather than dairy food intake and its conclusion does not support our body of evidence statement. Examining only the included studies within the Lanou review that evaluated dairy intake and had high level evidence (i.e. cross-sectional studies were excluded), two of three randomised controlled trials in this review reported a positive association between either milk or dairy intake and increase in total bone mineral content and lumbar spine bone mineral density. Therefore, using only the data from the review that is directly applicable to our body of evidence statement (high level evidence and examining dairy food consumption), the results are in support of our body of evidence statement. The Alvarez-León 2008 review was also of poor quality and did not include sufficient detail of the studies included and did not contribute to the body of evidence statement.

This review reported that of 12 randomised controlled trials, six reported no effect, five reported a positive effect, and one reported a negative effect.

Three of four additional randomised controlled trials found some association between milk or dairy consumption and reduced markers of bone turnover or increased whole body bone mineral density. The three studies that reported a significant effect were conducted in adolescent boys (12 week intervention of low fat milk with 18 month follow-up), postmenopausal women (six week intervention of skim milk), and women aged 18-30y (12 month intervention of dairy foods). The study that reported no effect was conducted in men and had a 12 week treatment period of skim milk, but only bone mineral content, not bone mineral density or markers of bone turnover, was measured in this study. The cohort was small (n=307), and was conducted in pregnant women. This study reported an association between greater milk consumption before pregnancy and a reduction in loss of bone mass during pregnancy. Because the retrieved studies were conducted in populations of varying ages and measured different markers of bone health, the body of evidence overall is assessed as fairly weak. Because most of the included studies examined milk rather than dairy, the body of evidence statement is based on milk, and includes milk of all fat levels.

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Table 5.1 Studies used to make evidence statement for dairy and bone health

Reference [1]	**Lanou 2005 [R14]**	**Alvarez-Leon 2006 [R36]**	**Hartman 2007 [2277]**	**Bonjour 2008 [850]**
Type of study [2]	Systematic review of 4 cross-sectional, 3 RCTs	Non-systematic review of 1 systematic review	RCT	RCT
Level of evidence	Level I	Level I	Level II	Level II
Intervention/ comparator [4]	Effect of dairy products on bone mineralisation.	Effect of dairy or milk consumption on bone health.	(1) Resistance training + 500ml cow's milk (fat free) vs. (2) Resistance training + 500ml soy milk (fat free - macronutrient matched) consumed immediately after exercise and then 1h after exercise vs (3) Control (resistance training + 500ml maltodextrin based drink). Outcome is bone mineral content (BMC).	4 week adaptation period of 250ml skim milk followed by either (1) additional 500ml skimmed milk (600mg calcium) per day + standardised background diet (total of 1200mg calcium/d), or (2) no additional skim milk + standardised background diet (total of 600mg calcium/d) – cross-over design. Outcomes are dietary intake, blood biochemistry (PTH, CTX, PINP, osteocalcin, BAP, IGF-I, creatinine, albumin, total protein, vit D).
N [5]	Not given	Number of subjects not provided. SR included 12 RCTs and cohort studies.	Interv 1=18, Interv 2=19, Control =19	n=30, cross over design (15+15)
Population/ study information	USA, Australia, The Netherlands, China; Children, adolescents, and young adults aged 1 to 25y.	Popluation characteristics not reported.	Men aged 18-30y, Canada. 12 week follow up.	Postmenopausal women in France of normal to low bone mineral density. 6 week follow up.
Quality [7]	N.	N	P	P
Results [8]	Review conclusions:	SR found 6 studies reported	There were no significant	Skim milk supplementation

	"available evidence does not support nutritional guidelines focused specifically on *increasing* milk or other dairy product intake for promoting child and adolescent bone mineralisation." There is not enough data on the effect of dairy on bone mineralisation in children under the age of 7. However, when only studies examining dairy food consumption as opposed to calcium intake were examined, 1 of 4 cross-sectional studies and 2 of 3 randomised controlled trials reported a positive association between dairy intake and bone health.	no effect, 5 reported a positive effect, 1 reported a negative effect. Most beneficial effect in women under age 30y and with milk (rather than dairy in general). No statistics reported.	differences in BMC between the fat free cow's milk, soy milk, or control groups after the 12 wk intervention, and no significant change within any group after treatment compared to before treatment. Change in BMC – cow's milk: 1.7%, soy milk: 0.8%, control: 0.6%.	providing a calcium intake of 1105mg/d can reduce markers of bone turnover in postmenopausal women in 6 weeks. Compared to no milk supplementation, skim milk supplementation resulted in a reduction in serum PTH (-3.2pg/mL, P=0.0054), carboxy terminal crosslinked telopeptide of type I collagen (-624pmol/L, P=0.0001), propeptide of type I procollagen (-5.5ng/mL, P=0.0092), and osteocalcin (-2.8ng/mL, P=0.0014). There were no changes in bone alkaline phosphatise (0µg/mL) or insulin-like growth factor-1 (+6.7ng/mL, P=NS).
Effect on risk	Protect	Protect	None	Protect
Importance	Not reported	1	1	1
Relevance	1	1	2	2
Generalisability	Yes	Yes	Yes	Yes
Applicability	Yes	Yes	No	Yes

Table 5.1 Studies used to make evidence statement for dairy and bone health (cont.)

Reference [1]	**Volek 2003 [2385]**	**Javaid 2005 [243]**	**Teegarden 2005 [R34]**
Type of study [2]	RCT	Cohort	RCT
Level of evidence	Level II	Level III	Level II
Intervention/ comparator [4]	Effect of 3 servings (708mL) of 1% fluid milk per day compared to 3 servings of unfortified apple and grape juice supplementation on bone mineral density and bone mineral content.	Effect of milk intake on bone mass lost during pregnancy. Outcomes = speed of sound (SOS), broadband ultrasound attenuation (BUA), and calcaneal width, measured at heel using quantitative ultrasound.	Effect of high dairy group (goal of 1200-1300 mg of calcium per day from dairy foods) vs medium dairy group (goal of 1000-1100mg of calcium/d from dairy foods) vs control (maintain current dietary consumption of <800mg calcium per day) on total body, spine, and total hip bone mineral density (BMD) and bone mineral content (BMC) (measured with DEXA). Administered intervention with dietary counseling and monitored with daily food records.
N [5]	28	307	High dairy group: 29 not using OCP, 19 using OCP; Medium dairy group: 25 not using OCP, 20 using OCP; Control group: 24 not using OCP, 18 using OCP.
Population/ study information [6]	Healthy boys aged 13-17 yrs participating in resistance training program; USA; 12 wk interval, 18 month follow up.	Pregnant women aged 20-34 yrs; Southampton, UK; 22 wk follow up.	Young, healthy women in USA aged 18-30 yrs with calcium intakes <800 mg per day. 57 of 135 on oral contraceptive pill (OCP). Mean age ranged from 19.5-21.1 yrs among the groups. 12 month follow-up.
Quality [7]	0	P.	P
Results [8]	Supplementation with 3 servings of 1% milk per day resulted in a greater increase in whole body bone mineral density compared to supplementation with juice in physically active adolescent boys: milk group:	Milk consumption during pregnancy was not associated with a change in QUS. Compared to women who drank <1 pint of milk per day pre-pregnancy, women who drank	There was no difference in spine BMD in control vs medium dairy group vs high dairy group in OCP nonusers (P=0.14). Loss of 1.33% in spine BMD in control, OCP user group and gain of 0.67% in combined medium and high dairy, OCP user groups (P=0.002). Increased dairy

	1.126g/cm^2 ± 1.167 at wk 0 and 1.154 ± 0.172 at wk 12, juice group: 1.111g/cm^2 ± 0.089 at wk 0 and 1.125 ± 0.087 at wk 12, P=0.017. BMD at specific sites and BMC at specific sites or whole body were not significantly difference between groups.	>1 pint milk per day preserved calcaneal SOS during pregnancy (β=0.3, 95% CI 0.07-0.6, P=0.01), indicating less loss of bone mass.	intake improved total hip BMD and BMC and protected OCP users from both total hip and spine BMD loss.
Effect on risk	Protect	Pregnancy: none; Pre-pregnancy: protect	Protect
Importance	1	1	1
Relevance	2	2	2
Generalisable	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

5.2 DAIRY and HIP FRACTURE

Does a particular intake of dairy affect the risk of hip fracture in adults?		
Evidence statement		Consumption of less than 1 serving* of milk per day during adult life is not associated with risk of osteoporotic or hip fracture.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	One meta-analysis derived from 6 prospective cohort studies including Australian data. One additional cohort study (Nurses' Health Study) of over 27 000 post-menopausal women.
Consistency	Excellent	Studies were consistent.
Clinical impact	Poor	The meta-analysis data indicates the relative risk was not significant: relative risk of osteoporotic fracture for low milk intake = 1.06 (95% CI 0.95-1.19); relative risk of hip fracture for low milk intake = 1.10 (95% CI 0.83-1.47). The cohort data indicates a relative risk of hip fracture for >1.5 servings of milk/day = 0.83 (95% CI 0.61-1.10).
Generalisability	Excellent	Western populations: Australia, USA, Europe, Canada.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL.

The meta analysis and large cohort study are in agreement, both concluding that milk consumption during adult life is not associated with reduced risk of hip fracture. It is important that more studies have been conducted in women compared to men. The meta-analysis did not conduct a systematic search, but instead included six cohort studies known to the meta-analysis authors. The pooled statistic from meta-analysis found no increased risk of fracture in participants who consumed <1 serving of milk/day compared to the rest of the population. The Nurses' Health Study reported the consumption of >1.5 servings of milk/day in women, but also found no association with risk of hip fracture. The term "milk" includes full fat, low fat, and fat free milk.

References

Feskanich, D., Willett, W. C. & Colditz, G. A. 2003, "Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women", *American Journal of Clinical Nutrition*, vol. 77, no. 2, pp. 504-11.

Kanis, J. A., Johansson, H., Oden, A., De Laet, C., Johnell, O., Eisman, J. A., Mc Closkey, E., Mellstrom, D., Pols, H., Reeve, J., Silman, A. & Tenenhouse, A. 2005, "A meta-analysis of milk intake and fracture risk: low utility for case finding", *Osteoporosis International*, vol. 16, no. 7, pp. 799-804.

Table 5.2 Studies used to make evidence statement for dairy and hip fracture.

Reference [1]	**Kanis 2005 [5]**	**Feskanich 2003 [427]**
Type of study [2]	Meta-analysis of 6 prospective cohort studies	Cohort
Level of evidence [3]	Level I	Level II
Intervention/ comparator [4]	Effect of low milk intake (<1 glass milk per day) on risk of osteoporotic and hip fracture	Effect of milk consumption (quintiles: <1 times per wk, 1-3.9 times per wk, 4-6.9 times per wk, 1-1.4 times per day, and ≥ 1.5 times per day) on risk of hip fracture.
N [5]	39,563	72,337 in entire cohort, 27,632 identified in 1980 as meeting qualifications for this study, 603 cases of hip fracture.
Population/study information [6]	Europe, Australia, Canada; M (31%) and F (69%); Adults.	Post-menopausal women, US (Nurses Health Study), 98% white. 18 years total, follow-up every 2 years.
Quality [7]	0	P.
Results [8]	Overall, a low intake of milk (<1 glass milk per day) was not significantly associated with an increased risk of either osteoporotic fracture adj RR 1.06 (95% CI 0.95-1.19) or hip fracture adj RR 1.10 (95% CI 0.83-1.47) in either men or women. The size of a glass of milk was not standardised in this study, but 1 glass is generally equivalent to approximately 240mL.	Milk consumption was not associated with a reduced risk of hip fracture in post-menopausal women: adj RR for >1.5 servings milk per day (>360mL per day) = 0.83 (95% CI 0.61-1.10). P for trend = 0.21.
Effect on risk (Increase/None/Protect)	None	None
Importance [9]	3	3
Relevance [10]	5	1
Generalisable	Yes	Yes
Applicability	Yes	Yes

5.3 DAIRY and HEART DISEASE

Does a particular intake of dairy affect the risk of cardiovascular disease in adults?		
Evidence statement		Consumption of at least 2 servings* per day dairy foods (milk, yoghurt, and cheese) is associated with reduced risk of ischemic heart disease and myocardial infarction.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	One recent meta-analysis (neutral quality) evaluating 11 prospective studies (ischemic heart disease) and 4 case-control studies (myocardial infarction). One earlier meta-analysis (2004) of similar studies (7 cohort studies, 2 case-control studies) by the same authors (1 P).
Consistency	Satisfactory	For ischemic heart disease, the 2008 meta-analysis found a protective effect with dairy consumption. Results of individual studies included in meta-analysis were mixed: 4 found a protective association, 10 found no association, and 1 found increased risk. For myocardial infarction, the meta-analysis found a protective effect and all individual studies found a nonsignificant, protective effect.
Clinical impact	Satisfactory	Meta-analysis of highest quartile/quintile of dairy food intake and relative risk of ischemic heart disease: 0.91 (95% CI 0.82-1.00) including whole milk; 0.84 (95% CI 0.76-0.93) including low fat milk (low fat milk data includes females only). Meta-analysis of highest quartile/quintile of dairy food intake and relative risk of myocardial infarction: 0.83 (95% CI 0.66-0.99).
Generalisability	Excellent	Included western populations, such as USA, UK, Italy, and Canada.
Applicability	Good	Evidence for low fat milk is only available for women

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

The two meta analyses are in agreement for the association between dairy consumption and risk of ischemic heart disease, but have many studies in common and are written by the same authors. The 2008 study examines both dairy and milk consumption, while the 2004 study examines only milk consumption. The 2008 meta analysis includes all but one of the seven cohort studies in the 2004 meta analysis on ischemic heart disease, and adds four additional prospective studies. Therefore, the 2008 meta analysis influences the body of evidence statement to a greater degree, but the 2004 study is still included for reference. Although the association with ischemic heart disease appears stronger with low fat milk compared to whole milk, only one study included in the meta-analysis made this comparison, and data is available in females only. Data may be confounded by the varying levels of fat in dairy

foods in the other studies. In addition, three studies included in the meta analysis reported dietary or dairy calcium rather than dairy food intake, potentially further confounding the data.

Only the 2008 publication examined the association between dairy consumption and risk of myocardial infarction. Four case-control studies were included in the meta-analysis. Although none of the individual studies reported significant results, all found a slightly protective effect, and the meta-analysis statistic showed a significant, protective effect.

Because meta analysis statistics provide strong evidence, this body of evidence statement can be used to guide practice in most situations. The definition of the highest and lowest quartile/quintile of dairy intake is variable and is not always defined. When defined, it ranged from >0.5 to >2 servings/d for highest quartile/quintile, and none to <1 serving/d for lowest quartile/quintile. Therefore, it is difficult to include a serving size in the body of evidence statement. However, if this is required, a safe estimate is a recommendation of at least two servings of dairy foods/day (including milk, yoghurt, cheese of varying fat levels).

References

Elwood, P. C., Givens, D. I., Beswick, A. D., Fehily, A. M., Pickering, J. E. & Gallacher, J. 2008, "The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer", *Journal of the American College of Nutrition*, vol. 27, no. 6, pp. 723S-734.

Elwood, P. C., Pickering, J. E., Hughes, J., Fehily, A. M. & Ness, A. R. 2004, "Milk drinking, ischaemic heart disease and ischaemic stroke II. Evidence from cohort studies", *European Journal of Clinical Nutrition*, vol. 58, pp. 718-724.

Table 5.3 Studies used to make evidence statements for dairy and heart disease.

Reference [1]	**Elwood 2004 [R1]**	**Elwood 2008 [2533]**
Type of study [2]	Meta analysis of 7 cohort studies and 2 case-control studies examining ischemic heart disease.	Meta analysis of 11 cohort studies examining ischemic heart disease, meta-analysis of 4 case-control studies examining myocardial infarction.
Level of evidence [3]	Level I	Level I
Intervention/ comparator [4]	Effect of milk intake (usually highest quintile or quartile compared to lowest quintile or quartile; definition of quintile/quartile varied among studies and were not defined in the meta-analysis) on ischemic heart disease.	Effect of milk and dairy consumption (usually highest quintile or quartile ("milk drunk" to 480mL per day) compared to lowest quintile or quartile (none to <240mL per day)) on myocardial infarction and ischemic heart disease.
N [5]	Cohort studies: n=399 762; Case-control studies: n=1921	1 861 185
Population/study information [6]	M and F adults; Continental USA, UK, The Netherlands, Italy; Smokers and non-smokers.	M and F adults; USA, UK, The Netherlands, Japan, Canada; Smokers and non-smokers.
Quality [7]	P	0
Results [8]	Ischemic heart disease: RR 0.87 (95% CI 0.74-1.03).	The analysis provides some evidence of a beneficial effect of milk and dairy on myocardial infarction and ischemic heart disease. RR of myocardial infarction 0.83 (95% CI 0.66-0.99), RR of ischemic heart disease of 0.91 (95% CI 0.82-1.00) for high fat milk, RR of ischemic heart disease of 0.84 (95% CI 0.76-0.93) for low fat milk.
Effect on risk (Increase/None/Protect)	Protect	Protect
Importance [9]	2	2
Relevance [10]	1	1
Generalisable	Yes	Yes
Applicability	Yes	Yes

5.4 DAIRY and STROKE

Does a particular intake of dairy affect the risk of stroke in adults?		
Evidence statement		Consumption of 2 or more servings* of dairy foods per day is associated with reduced risk of stroke.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	One meta-analysis evaluating 7 prospective studies, and 1 earlier meta-analysis (2004) of similar studies (5 prospective studies) by the same authors (1 P, 1 0). One additional large cohort examined the effect of dairy fat (1 P).
Consistency	Excellent	Reviews, all individual studies in reviews, and additional cohort were all consistent.
Clinical impact	Good	Relative risk for highest quartile/quintile of dairy food intake = 0.79 (95% CI 0.75-0.82). More than 1 serving of high fat dairy foods/day had no association: RR 1.23 (95% CI 0.74-2.03).
Generalisability	Excellent	Populations include USA, UK, and Japan.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

The two meta analyses are in agreement, both concluding that a diet high in dairy foods may reduce the risk of stroke, but they have most studies in common and are written by the same authors. The 2008 study examines both dairy and milk consumption, while the 2004 study examines only milk consumption. The 2008 meta-analysis includes all five of the studies in the 2004 meta-analysis, and adds two additional prospective studies. Therefore the 2008 meta-analysis influences the body of evidence statement to a greater degree, but the 2004 study is included for reference. The definition of the highest and lowest quartile/quintile of dairy intake is variable and is not always defined. When defined, it ranged from >0.5 to >2 servings/d for highest quartile/quintile, and none to <0.67 serving/d for lowest quartile/quintile. Data may be confounded by the varying levels of fat in dairy foods. In addition, three of the seven studies included in the 2008 meta-analysis report dairy calcium rather than dairy food intake, potentially further confounding the data. The additional systematic review was of poor quality and did not provide many details, but was in agreement with the findings of the two meta analyses, reporting two studies that found men who do not consume milk have twice the risk of stroke compared to men who consume ≥ 2 glasses of milk/d. The cohort study (Health Professionals Follow-up Study) found there was no increase in incidence of stroke in US men who consume >one serving of high fat dairy product per day compared to those who consume <one per week. Dairy food in the body

of evidence statement is defined as all milk, yoghurt, and cheese of varying fat levels. No weighting was given to the review by Alvarez-León (2006) due to poor quality.

References

Alvarez-León, E. E., Román-Viñas, B. & Serra-Majem, L. 2006, "Dairy products and health: a review of the epidemiological evidence", *British Journal of Nutrition*, vol. 96, no. Suppl 1, pp. S94-S99.

Elwood, P. C., Givens, D. I., Beswick, A. D., Fehily, A. M., Pickering, J. E. & Gallacher, J. 2008, "The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer", *Journal of the American College of Nutrition*, vol. 27, no. 6, pp. 723S-734.

He, K., Merchant, A., Rimm, E. B., Rosner, B. A., Stampfer, M. J., Willett, W. C. & Ascherio, A. 2003, "Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study", *British Medical Journal*, vol. 327, no. 7418, pp. 777-82.

Table 5.4 Studies used to make evidence statement for dairy and stroke.

Reference [1]	**Elwood 2008 [2533]**	**Elwood 2004 [1]**	**Alvarez-Leon 2006 [R36]**	**He 2003 [5]**
Type of study [2]	Meta-analysis of 7 prospective studies	Meta-analysis of 5 prospective studies	Non-systematic review of 1 systematic review.	Cohort
Level of evidence [3]	I	I	I	II
Intervention/ comparator [4]	Effect of milk and dairy consumption (usually highest quintile or quartile (>0.5 to >2 servings per day) compared to lowest quintile or quartile (none to <0.67 serving per day)) on risk of stroke.	Effect of milk intake (usually highest quintile or quartile compared to lowest quintile or quartile; definition of quintile/quartile varied among studies and were not defined in the meta-analysis) on risk of stroke.	Relationship between milk consumption and incidence of stroke.	Effect of high fat dairy foods (<1 per wk vs >1 per day) intake and risk of stroke.
N [5]	1,861,185	Cohort studies: n=399,762; Case-control studies: n=1,921	Number of subjects not provided. SR included 2 studies on dairy (type of study not reported) and was published in 2001.	43 732 total, including 455 cases of ischemic stroke, 125 cases of haemorrhagic stroke, and 145 cases of stroke of unknown type
Population/study information [6]	M and F adults; USA, UK, Hawaiians (Japanese ancestry), Japan; Smokers and non-smokers	M and F adults; Continental USA, UK, Japan, Hawaii (Japanese ancestry); Smokers and non-smokers	Men in US (no other details provided).	US men in health profession aged 40-75y in 1986; Excluded those with history of DM or CVD; 14 year follow up.
Quality [7]	0	P	N	P

Results [8]	The analysis provides some evidence of a beneficial effect of milk and dairy on stroke. RR 0.79 (95% CI 0.75-0.82) for highest intake vs lowest intake.	RR of stroke 0.83 (95% CI 0.77-0.90) for highest intake vs lowest intake.	2 studies reported men who do not consume milk have 2x increased risk of stroke compared to men who consume ≥ 2 glasses of milk per day (480ml milk per day), P<0.05. No further statistics reported.	There was no association between intake of high fat dairy and incidence of stroke in males. RR 1.23 (95% CI 0.74-2.03) for highest intake vs lowest intake.
Effect on risk (Increase/None/Protect)	Protect	Protect	Protect	None
Importance [9]	2	2	1	3
Relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

5.5 DAIRY and HYPERTENSION

Does a particular intake of dairy affect the risk of hypertension in adults?		
Evidence statement		Consumption of 3 servings of low fat dairy foods is associated with reduced risk of hypertension
Grade		B
Evidence statement		Consumption of 3 servings of any dairy foods a day is associated with reduced risk of hypertension
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory/Good	One review (1 N) and one large and four small cohort studies (5 P). (Good for low fat dairy foods)
Consistency	Good	The systematic review and 4 of the 5 additional cohort studies reported a protective effect of either total dairy or low fat dairy on change in blood pressure or development of hypertension. 1 cohort study reported no association for either total or low fat dairy.
Clinical impact	Excellent	Odds and risk ratios for development of hypertension ranged from 0.81 to 1.11 for total dairy intake; odds and risk ratios ranged from 0.46-0.89 for low fat dairy intake (confidence intervals not crossing 1).
Generalisability	Excellent	Western populations, including Denmark, USA, and Spain.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

The review was of poor quality and included one systematic review examining dairy foods, published in 2003; the number of studies or number of participants in this review was not reported. No weighting was given to the review by Alvarez-León (2006) due to poor quality. The included review reported that compared to a diet high in fruits and vegetables but low in dairy foods, consumption of 3-4 servings of dairy foods per day can lower systolic blood pressure by -2.7 mmHg (97.5% CI -4.6 - -0.9) and diastolic BP by -1.9 mmHg (97.5% CI -3.3 - -0.6). One small cohort study also examined change in blood

pressure, and reported a protective effect with 2.5 servings of low fat dairy per day, but no effect with high fat dairy. The remaining four cohort studies examined development of hypertension, with three reporting a protective effect from one to two servings of low fat dairy per day (including the large cohort) and two reporting a protective effect from one to three servings of total dairy per day (one of these studies included butter in their definition of total dairy). Two of these studies examined specific types of dairy products, reporting a significant effect with consumption of one serving of milk or milk drinks and two servings of skim milk per day, but no association with yoghurt or cheese. The final cohort reported no significant association between either total dairy (three servings per day), low fat dairy (two servings per day), or high fat dairy (one serving per day) intake and development of hypertension. Low fat in Australia is defined as ≤ 1.5 g fat/100 g milk and ≤ 3 g fat/100 g cheese or yoghurt.

References

Alonso, A., Beunza, J. J., Delgado-Rodríguez, M., Martínez, J. A. & Martínez-González, M. A. 2005, "Low-fat dairy consumption and reduced risk of hypertension: the Seguimiento Universidad de Navarra (SUN) cohort", *American Journal of Clinical Nutrition*, vol. 82, no. 5, pp. 972-979.

Alvarez-León, E. E., Román-Viñas, B. & Serra-Majem, L. 2006, "Dairy products and health: a review of the epidemiological evidence", *British Journal of Nutrition*, vol. 96, no. Suppl 1, pp. S94-S99.

Engberink, M. F., Geleijnse, J. M., de Jong, N., Smit, H. A., Kok, F. J. & Verschuren, W. M. M. 2009, "Dairy intake, blood pressure, and incident hypertension in a general Dutch population", *Journal of Nutrition*, vol. 139, no. 3, pp. 582-7.

Pereira, M. A., Jacobs, D. R. J., VanHorn, L., Slattery, M. L., Kartashov, A. I. & Ludwig, D. S. 2002, "Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study", *Journal of the American Medical Association*, vol. 287, no. 16, pp. 2081-2089.

Toledo, E., Delgado-Rodríguez, M., Estruch, R., Salas-Salvadó, J., Corella, D., Gomez-Gracia, E., Fiol, M., Lamuela-Raventós, R. M., Schröder, H., Arós, F., Ros, E., Ruíz-Gutiérrez, V., Lapetra, J., Conde-Herrera, M., Sáez, G., Vinyoles, E. & Martínez-González, M. A. 2009, "Low-fat dairy products and blood pressure: follow-up of 2290 older persons at high cardiovascular risk participating in the PREDIMED study", *British Journal of Nutrition*, vol. 101, no. 1, pp. 59-67.

Wang, L., Manson, J. E., Buring, J. E., Lee, I. & Sesso, H. D. 2008, "Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged and older women", *Hypertension*, vol. 51, no. 4, pp. 1073-1079.

Table 5.5 Studies used to make evidence statement for dairy and hypertension

Reference [1]	**Engberink 2009 [672]**	**Pereira 2002 [10]**	**Alvarez-Leon 2006 [R36]**
Type of study [2]	Cohort	Cohort	Non-systematic review of 1 systematic review
Level of evidence	Level II	Level II	Level I
Intervention/ comparator [4]	Relationship between intake of total dairy (quintiles: median 765 g per day vs. 110 g per day), low fat dairy (quintiles: median 507 g per day vs 21 g per day), and high fat dairy (quintiles: median 186 g per day vs 27 g per day) and development of hypertension.	Effect of dairy consumption (1 serving per day of total dairy, reduced fat dairy, high fat dairy, milk and milk drinks, cheese and sour cream, butter and cream, dairy-based desserts, and yoghurt) on development of elevated blood pressure.	Effect of dairy or milk consumption on risk of hypertension.
N [5]	3454	3157 including 923 who were overweight	Number of subjects not provided. Number of studies in SR not provided.
Population/study information [6]	Denmark; M and F aged 20-65 yrs (mean 49 yrs). 5 year follow up. Participants from an original cross-sectional study were followed up after 5 years for incidence of hypertension.	CARDIA study; USA; Black and white young adults aged 18-30 yrs. Follow up of 10 yrs.	Population characteristics not reported.
Quality [7]	P	P	N
Results [8]	No association between total adj OR 1.11 (95% CI 0.85-1.44), low fat adj OR 0.82 (95% CI 0.64-1.06) or high fat dairy adj OR 1.19 (95% CI 0.92-1.54) and risk of hypertension was found.	Association between high dairy intake and low risk of development of elevated blood pressure in young, overweight, black and white men and women. Adj OR for elevated blood pressure with 1 serving per day of total dairy products 0.81 (95% CI 0.71-0.93), reduced fat dairy products 0.79 (95% CI 0.64-0.98), high fat dairy products 0.84 (95% CI 0.71-0.99), milk and milk drinks 0.80	SR reported 3-4 servings of dairy products per day can lower systolic BP by -2.7 mmHg (97.5% CI -4.6 to -0.9) and diastolic BP by -1.9 mmHg (97.5% CI -3.3 to -0.6), compared to a diet rich in fruits and vegetables but low in dairy products.

		(95% CI 0.64-0.99), cheese and sour cream 0.67 (95% CI 0.43-1.06), butter and cream 0.86 (95% CI 0.70-1.05), dairy-based desserts 0.37 (95% CI 0.12-1.13), yoghurt 0.78 (95% CI 0.22-2.72). The OR was similar for blacks and whites and for men and women. This inverse association was not seen in subjects who were of normal weight at baseline.	
Effect on risk	None	Protect	Protect
Importance [9]	3	1	1
Relevance [10]	2	1	1
Generalisable	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

Table 5.5 Studies used to make evidence statement for dairy and hypertension (cont.)

Reference [1]	**Alonso 2005 [R31]**	**Toledo 2009 [R23]**	**Wang 2008 [R20]**
Type of study [2]	Cohort	Cohort	Cohort
Level of evidence	Level II	Level II	Level II
Intervention/ comparator [4]	Relationship between total dairy, low fat dairy, and whole fat dairy consumption (5th quintile vs 1st quintile) and development of hypertension.	Relationship between dairy food consumption (quintiles of intake of low fat dairy and whole fat dairy) and change in systolic and diastolic blood pressure over 12 months.	Relationship between total dairy food, low fat dairy food, high fat dairy food, skim milk, low fat yoghurt, and low fat cottage cheese consumption and the development of hypertension over 10 years.
N [5]	6686 at baseline	2290	28 886 total, with 8710 cases of incident hypertension developing over the 10 yrs.
Population/study information [6]	University of Navarra Follow-up Study. Former students of University of Navarra, registered nurses from some Spanish provinces, university graduates from other associations. Spain. Aged 20-90 yrs at baseline. 3-5 yrs follow-up.	Men aged 55-80 yrs and women aged 60-80 yrs with no history of CVD but at high cardiovascular risk. Spain. 12 month follow-up.	Women's Health Study - female health professionals in US older than age 45 yrs. Mean age 53.8 yrs. 10 yr follow-up.
Quality [7]	P	P	P
Results [8]	Total dairy food consumption (P=0.12) and whole fat dairy food consumption (P=0.44) were not associated with development of hypertension. Low fat dairy food consumption was associated with a reduced risk of hypertension: adj HR 0.46 (95% CI 0.26-0.84, P trend = 0.02).	Consumption of low fat dairy consumption (mean 632 g per day (quintile 5) vs mean 3 g per day (quintile 1)) is associated with reduced systolic blood pressure (-4.2 mm Hg, (95% CI -6.9 - -1.4, P=0.01) and diastolic blood pressure (-1.8 mm Hg (95% CI -3.2 - -0.4, P=0.09). There was no association between whole fat dairy food consumption and systolic (P=0.84) or diastolic (P=0.61) blood	Adj RR of hypertension for 5th quintile (2.99-22.1 servings per day) compared to 1st quintile (0-0.85 servings per day of total dairy food intake 0.86 (95% CI 0.79-0.94, P trend = 0.003). Adj RR of hypertension for 5th quintile (2-9.6 servings per day) compared to 1st quintile (0-0.27 servings per day) of low fat dairy food intake = 0.89 (95% CI 0.81-0.98, P trend = 0.01). No association between hypertension and high fat dairy consumption (P trend = 0.13). Adj RR of

		pressure.	hypertension for 5th quintile (≥ 2 servings per day) compared to 1st quintile (<1 serving per month) of skim milk intake = 0.93 (95% CI 0.86-1.01, P trend = 0.002). No association between hypertension and low fat yoghurt (P trend = 0.36) or low fat cottage cheese consumption (P trend = 0.33). Effect of total dairy is heavily influence by skim milk intake.
Effect on risk	Protect for low fat dairy, none for total dairy or whole fat dairy.	Protect for low fat dairy, none for whole fat dairy.	Protect for total dairy, low fat dairy, and skim milk. None for high fat dairy, yoghurt, and cottage cheese.
Importance [9]	1	1	1
Relevance [10]	1	1	1
Generalisable	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

5.6 DAIRY and TYPE 2 DIABETES

Does a particular intake of dairy affect the risk of type 2 diabetes?		
Evidence statement		Consumption of at least 1.5 servings* of dairy foods (milk, youghurt, cheese) per day is associated with reduced risk of type 2 diabetes.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Two meta analyses (2 0), each evaluating 4 prospective studies. One small cohort study (1 P) examining insulin resistance syndrome.
Consistency	Satisfactory	Both meta analyses reported a significant protective correlation. The individual studies in the meta analyses were mixed, with 3 reporting a significant protective correlation, and 2 reporting no significant effect. The additional cohort study reported a protective effect in overweight subjects only.
Clinical impact	Satisfactory	Meta-analysis reported a relative risk for high dairy intake of 0.92 (0.86-0.97).
Generalisability	Excellent	Western populations, including USA and UK.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

Although the pooled statistics of both meta analyses report a significant protective association between risk of type 2 diabetes and high dairy food intake compared to low dairy food intake, only three of the five individual studies found significant results. Each of the two meta analyses examined four prospective studies. Three of these studies appeared in both meta analyses. Yet each meta-analysis differed as each had selected different odds ratios from the component studies. For example, while the Elwood 2008 study selected from one paper the odds ratio for skim milk intake, the Pittas 2007 study selected the odds ratio for total low fat dairy. From another component study, the Elwood 2008 study selected the odds ratio for quintiles of dietary calcium intake while the Pittas 2007 study selected the odds ratio for intake of low fat dairy. The definition of the highest and lowest quartile/quintile of dairy intake is variable, ranging from >0.29 to >4.1 servings per day for the highest grouping, and none to <0.5 serving per day for lowest grouping. The small cohort study supports the result of the meta-analysis, finding an inverse association between high dairy consumption (>35 servings per week) and the insulin resistance syndrome among overweight young adults in the US, but not among those of a healthy weight (this study included butter in their definition of dairy). Therefore, there is support for a

protective relationship between dairy intake (including milk, cheese, and yoghurt of varying fat levels) and risk of type 2 diabetes, and the recommendation can be trusted to guide practice in most situations.

References

Elwood, P. C., Givens, D. I., Beswick, A. D., Fehily, A. M., Pickering, J. E. & Gallacher, J. 2008, "The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer", *Journal of the American College of Nutrition*, vol. 27, no. 6, pp. 723S-734.

Pereira, M. A., Jacobs, D. R. J., VanHorn, L., Slattery, M. L., Kartashov, A. I. & Ludwig, D. S. 2002, "Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study", *Journal of the American Medical Association*, vol. 287, no. 16, pp. 2081-2089.

Pittas, A. G., Lau, J., Hu, F. B. & Dawson-Hughes, B. 2007, "The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis", *Journal of Clinical Endocrinology and Metabolism*, vol. 92, no. 6, pp. 2017-2029.

Table 5.6 Studies used to make evidence statements for dairy and type 2 diabetes

Reference [1]	**Elwood 2008 [2533]**	**Pereira 2002 [10]**	**Pittas 2007 [R33]**
Type of study [2]	Meta analysis of 4 prospective studies	Cohort	Meta analysis of 4 prospective studies
Level of evidence [3]	I	II	I
Intervention/ comparator [4]	Effect of milk and dairy consumption (ranging from >0.29 to >2 servings per day for highest quartile/quintile, and none to <0.14 serving per day for lowest quartile/quintile) on risk of type 2 diabetes.	Effect of dairy consumption (0-10 servings per wk versus >35 servings per wk) on insulin resistance syndrome and abnormal glucose homeostasis. Dairy = milk, milk drinks, butter, cream, cheese (90%) and yoghurt, dips, ice cream, pudding, other dairy-based desserts (10%).	Relationship between dairy intake and development of type 2 diabetes. High intake compared to low intake - high intake ranged from >1-5 servings per day and low intake ranged from 0 to <1.5 servings per day.
N [5]	1,861,185	3157, including 923 who were overweight	203,402
Population/study information [6]	M and F adults USA and UK Smokers and nonsmokers.	CARDIA study; USA; Black and white young adults aged 18-30y.	M and F in USA (Health Professionals Follow-Up Study, Women's Health Study, Nurses' Health Study, Black Women's Health Study)
Quality [7]	0	P	0
Results [8]	The analysis provides some evidence of a beneficial effect of milk and dairy on diabetes (RR 0.92 (95% CI 0.86-0.97).	OR for one serving of dairy products per day in overweight subjects was 0.83 (95% CI 0.73-0.95) for abnormal glucose homeostasis and 0.79 (95% CI 0.72-0.88) for insulin resistance syndrome. The OR was similar for blacks and whites and for men and women. Inverse association was limited to high fat dairy only for abnormal glucose homeostasis, but was for both low fat and high fat products for insulin resistance syndrome. This inverse association was not seen in subjects who	There was an inverse association between dairy intake (highest intake vs lowest intake) and incident type 2 diabetes: summary OR 0.86 (95% CI 0.79-0.93). OR based on adjusted data from individual studies.

		were of normal weight at baseline.	
Effect on risk (Increase/None/Protect)	Protect	Protect if overweight, none if healthy weight.	Protect
Clinical importance [9]	2	1	
Clinical relevance [10]	1	1	
Generalisable	Yes	Yes	
Applicability	Yes	Yes	

5.7 DAIRY and METABOLIC SYNDROME

Does a particular intake of dairy affect the risk of metabolic syndrome?		
Evidence statement		Consumption of 2-4 serves* of dairy foods per day is associated with reduced risk of metabolic syndrome.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	One meta-analysis (1 0) evaluating 4 case-control studies. 1 additional cohort study (1 P).
Consistency	Good	3 of the 4 case-control studies and the additional cohort study reported a significant protective effect.
Clinical impact	Excellent	Relative risk for highest quartile/quintile of dairy intake = 0.74 (95% CI 0.64-0.84).
Generalisability	Excellent	Populations include France, USA, UK, and Iran.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

Of the four case-control studies included in the meta-analysis, two reported reduced incidence of metabolic syndrome in participants who consumed two servings of milk per day (males) or ≥ 3.1 servings of dairy per day, one found reduced incidence in males but not females consuming > 4 servings of dairy per day, and the last reported reduced risk in females who consumed >3 servings of dairy/day, but no association with consumption of >1.08 servings of milk/day. Data may be confounded by varied levels of fat in dairy foods. Overall, the highest category of intake ranged from >1.08 servings of milk to ≥ 4 servings of dairy per day, and the lowest category of intake ranged from <0.13 servings of milk to <1.7 servings of dairy per day. The additional cohort study found reduced development of metabolic syndrome in participants who consumed a mean of 3.3 servings of dairy per day compared to those who consumed 0.3 servings of dairy per day. As the meta analysis included case-control studies only, care must be taken when applying this recommendation to practice.

References

Elwood, P. C., Givens, D. I., Beswick, A. D., Fehily, A. M., Pickering, J. E. & Gallacher, J. 2008, "The survival advantage of milk and dairy consumption: an overview of evidence from cohort studies of vascular diseases, diabetes and cancer", *Journal of the American College of Nutrition*, vol. 27, no. 6, pp. 723S-734.

Lutsey, P. L., Steffen, L. M. & Stevens, J. 2008, "Dietary intake and the development of the metabolic syndrome: the Atherosclerosis Risk in Communities study", *Circulation*, vol. 117, no. 6, pp. 754-761.

Table 5.7 Studies used to make evidence statements for dairy and metabolic syndrome

Reference [1]	**Elwood 2008 [2533]**	**Lutsey 2008 [R25]**
Type of study [2]	Meta analysis of 4 case-control studies.	Cohort
Level of evidence [3]	II	II
Intervention/ comparator [4]	Effect of milk and dairy consumption (highest intake (>1.08 to ≥ 4 servings/d) compared to lowest intake (<1.7 to <0.13 servings/d)) on risk of metabolic syndrome.	Relationship between dairy consumption (top quintile vs bottom quintile) and development of metabolic syndrome over 9 years.
N [5]	1,861,185	9514
Population/study information [6]	M and F adults France, Iran, USA, UK Smokers and nonsmokers.	Free-living subjects in the USA (NC, MS, MN, MD). Cohort reexamined every 3 years and followed for 9 years. Atherosclerosis Risk in Communities (ARIC). White and black men and women aged 45-64 yrs at baseline.
Quality [7]	0	P
Results [8]	The analysis provides some evidence of a beneficial effect of milk and dairy on metabolic syndrome. RR 0.74 (95% CI 0.64-0.84) for highest category of dairy intake compared to lowest category.	Quintile 5 intake of dairy products 3.30 servings per day compared to quintile 1 intake 0.28 servings per day, adj HR for metabolic syndrome in M and F 0.87 (95% CI 0.77-0.98) P trend=0.006. Individual dairy foods were not associated with incidence of metabolic syndrome (statistics not reported).
Effect on risk (Increase/None/Protect)	Protect	Protect
Clinical importance [9]	2	1
Clinical relevance [10]	1	1
Generalisable	Yes	Yes
Applicability	Yes	Yes

5.8 DAIRY and OBESITY

Does a particular intake of dairy affect the risk of obesity?		
Evidence statement		Consumption of dairy foods is not associated with weight change or risk of obesity.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Two systematic reviews (2 N), the first including 6 randomised controlled trials of 765 adults (with 71 men only). The second review included 10 randomised controlled trials in adults who were mainly overweight or obese. In addition there was 1 small randomised controlled trial (1 P) of a 12 week intervention in overweight or obese subjects, and 3 cohort studies (3 P), with 9 to 12 year follow-ups, in normal and overweight adults.
Consistency	Satisfactory	Both systematic reviews, the RCT, and 1 cohort study found no association. 2 cohort studies found no association with low fat dairy products. One found a protective effect of whole milk and cheese consumption in postmenopausal women, and one found a protective effect of high fat dairy product consumption in overweight subjects but not in subjects at a healthy weight.
Clinical impact	Satisfactory	Most studies found no association. In the two studies reporting an association, OR ranged from 0.70 to 0.85 for high fat dairy products.
Generalisability	Excellent	Western populations, including Australia, USA, and Sweden; China.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

Both systematic reviews included similar studies, but are of poor quality. The reviews did not analyse the quality of component studies and included studies that were not designed to examine weight change as an outcome. The reviews did not report BMI or examine development of overweight or obesity. In addition, one of the reviews had very limiting inclusion criteria (excluding studies when authors failed to respond to their email enquiries). This review probably therefore did not include all relevant studies. Regardless, both systematic reviews concluded there was no effect on change in body weight with an intervention to increase consumption of dairy foods. Of the six randomised controlled trials of adults included in the Barr 2003 review, one reported greater weight loss in postmenopausal Chinese women

supplemented with low fat milk powder compared to controls, four found no effect of dairy intake on weight change in women in the US and Australia, and one reported greater weight gain in US men and women supplemented with two cups of low fat milk (the author did not disclose that this final study was examining the use of milk as a supplement to provide additional nutrition in the elderly, and was not focused on weight loss). The Lanou 2008 review reported similar findings in their stratification of studies without energy restriction, and included four of the six studies in the Barr review. Of the six randomised controlled trials of overweight or obese adults included in the Lanou 2008 review that involved energy restriction, three studies reported no effect of high dairy consumption on weight change, and three studies (by the same author) reported weight loss in the study groups with high dairy intake. However, the three studies that reported an outcome of weight loss did not examine baseline energy intake or change in energy intake during the intervention period, so it cannot be determined if energy intakes were equivalent among groups.

The cohort studies and randomised controlled trial also reported mixed results. Only one reported development of obesity, while the others reported change in weight and did not report BMI. The large cohort study in peri-menopausal and early menopausal Swedish women found an inverse association between having a mean weight gain of at least one kg per year and a daily intake of ≥ 1 serving of whole milk, but no association with low fat milk. A small cohort study found an inverse association between total and high fat dairy intake and obesity in overweight young adults in the US, but not in young adults at a healthy weight and not with low fat dairy (this study included butter in their definitions of total dairy and high fat dairy). The third cohort study, the Health Professionals Follow-Up Study, also found no association with change in weight. Finally, the randomised controlled trial reported no difference in weight change between an intervention of 296 mL milk per day compared to two different forms of calcium supplements or a placebo. Therefore, there is weak evidence of an association in women who consume at least one serving of full fat dairy daily, but this cannot be extended to the rest of the population or to dairy products of all fat levels.

Of the 10 studies included in the Lanou 2008 review that were published after 2002 (meeting the NHMRC search criteria), only two were recovered in the original NHMRC search, indicating a possible gap in the NHMRC search criteria on this topic. Due to the poor quality of the systematic reviews and the inconsistency of the additional cohorts and the randomised controlled trial, no evidence statement can be developed on this topic until an improved systematic review is performed.

S.2.6. What is the dose response relationship between different types of milk intake and weight change in adults?

Because both systematic reviews were of poor quality and did not critically analyse the included studies, only the two cohort studies (Rosell 2006, Pereira 2002) and one randomised controlled trial (Wagner 2007) that examine milk and were retrieved by our search are discussed here. Only Rosell 2006 compared different types of milk. Rosell monitored the weight change of healthy weight and overweight women, finding that consuming ≥ 1 serving per day of whole milk compared to < 1 serving

per day resulted in a reduced likelihood of weight gain greater than 1 kg per year OR 0.85 (95% CI 0.73-0.99), but found no significant effect of ≥ 1 serving per day of either medium fat or low fat milk. Pereira 2002 reported a reduced risk of the development of obesity OR 0.83 (95% CI 0.68-1.00) in overweight young adults consuming one serving of milk and milk drinks per day, but found no effect in the total cohort including both healthy weight and overweight young adults. The type of milk was not examined. Wagner 2007 compared the addition of approximately 2.5 servings per day (the exact dose is not reported; this value is calculated from the amount of calcium provided) of milk (1% fat) to calcium supplementation or a placebo, finding no difference in weight change among the groups. No other types of milk were examined in this study. Because only one study examined the type of milk in relation to change in weight, no body of evidence statement can be developed on this topic.

References

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Table 5.8 Studies used to make evidence statement for dairy and obesity

Reference [1]	**Barr 2003 [R6]**	**Lanou 2008 [R28]**	**Wagner 2007 [103]**
Type of study [2]	Systematic Review of 6 RCTs	Systematic review of 10 RCTs	RCT
Level of evidence	Level I	Level I	Level II
Intervention/ comparator	Effect of dairy consumption on body weight change.	Effect of increasing dairy foods or calcium intake from dairy foods on change in weight. Divided into studies without energy restriction and studies with energy restriction.	(1) Diet with 500 kcal deficit + exercise 3x/wk + Ca lactate vs (2) Diet with 500 kcal deficit + exercise 3x/wk plus Ca phosphate vs (3) Diet with 500 kcal deficit + exercise 3x/wk + 10 oz (250g) milk (1% fat) vs (4) Diet with 500 kcal deficit + exercise 3x/wk + placebo. Outcome = change in body weight.
N [5]	221 adolescent girls 765 adult women 71 men	Studies without energy restriction: number of subjects in each individual study ranged from 34 to 200, total not reported. Studies with energy restriction: 271 subjects.	12 in calcium lactate group 16 in calcium phosphate group 17 in milk group 13 in placebo group
Population/study information [6]	US, Australia, New Zealand, UK, China; 72% adult female (premenopausal and postmenopausal), 7% adult male, 21% adolescent female. Follow up of 12 weeks to 3 years.	Without energy restriction: adults. With energy restriction: overweight or obese adults in Australia (1) and US (5).	Pre-menopausal adult women who were overweight or obese, BMI 25-45. Mean age 36-42 yrs. 12 week follow up. Ohio, USA.
Quality [7]	N	N	P.
Results [8]	Increased dairy consumption is not related to a change in body weight. No quantitative data reported.	In studies without energy restriction (n=4): 1 study reported weight gain with milk supplementation (not mentioned in this review, the study was examining the use of milk as a	Weight change did not differ between any of the groups. Milk did not effect weight change.

		supplement to provide additional nutrition in the elderly). 3 studies reported no effect of high dairy consumption on weight change. In studies with energy restriction (n=6), 3 studies reported no effect of high dairy consumption on weight change, and 3 studies (by the same author) reported weight loss in the study groups with high dairy intake. In these 3 studies reporting an effect, baseline energy intake and change in energy intake during intervention period were not reported, so cannot determine if energy intakes were equivalent among groups. Overall, authors conclude that increased dairy or calcium consumption does not aid in weight loss.	
Effect on risk	None	None	None
Importance [9]	3	3	3
Relevance [10]	1	1	1
Generalisable	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

Table 5.8 Studies used to make evidence statement for dairy and obesity (cont.)

Reference [1]	**Rosell 2006 [2237]**	**Pereira 2002 [R10]**	**Rajpathak 2006 [R11]**
Type of study [2]	Cohort	Cohort	Cohort
Level of evidence	Level II	Level II	Level II
Intervention/ comparator	Effect of dairy consumption (<1 versus ≥ 1 servings per day) on odds ratio for a mean weight gain of ≥ 1 kg per year during the 7-9 yrs follow-up.	Effect of dairy consumption (0-10 versus >35 servings dairy per wk) on risk of obesity. Dairy = milk, milk drinks, butter, cream, cheese (90%) and yoghurt, dips, ice cream, pudding, other dairy-based desserts (10%).	Dairy consumption and mean 12 yr weight change. Total dairy intake: 4.3 vs 0.7 servings per day. High fat dairy intake: 2.8 vs 0.2 servings per day. Low fat dairy intake: 2.6 vs 0.1 servings per day.
N [5]	19,352	3157, including 923 who were overweight	23,504 at baseline 19,615 for change of intake analysis
Population/study information [6]	Peri-menopausal and early menopausal women in central Sweden (a population vulnerable to weight gain), aged 40-55years at baseline. BMI ~20-28. Follow up of 9 years.	CARDIA study; USA; Black and white young adults aged 18-30 yrs. Follow up of 10 years.	Men aged 40-75 yrs from the Health Professionals Follow-Up Study, USA; BMI of ~25. 12 year follow up.
Quality [7]	P	P	P
Results [8]	There was an inverse association between having a mean weight gain of ≥1kg per year and habitual intake of ≥ 1 serving per day of whole milk or whole sour milk adj OR 0.85 (95% CI 0.73-0.99) and cheese adj OR 0.70 (95% CI 0.59-0.84). There was no association with medium-fat milk adj OR 0.90 (95% CI 0.74-1.10) or low fat milk or sour milk adj OR 1.03 (95% CI	There was an association between high dairy intake and low risk of development of obesity in young, overweight, black and white men and women. For overweight subjects at baseline, adj OR for obesity with 1 serving of total dairy products per day: 0.82 (95% CI 0.72-0.93), reduced fat dairy products per day: 0.84 (95% CI 0.70-1.02), high fat dairy products per day: 0.84 (95% CI 0.73-0.97), milk and milk drinks per day: 0.83 (95% CI 0.68-1.00), cheese	Baseline high fat dairy intake in the higher quintiles was associated with lower weight gain (2.86kg ± 0.11 for highest quintile, 3.24kg ± 0.11 for lowest quintile, adj P for trend = 0.03). Subjects who increased dairy consumption during the study period had greater weight gain over the 12 years (3.14kg ± 0.11 for highest quintile, 2.57kg ± 0.13 for lowest quintile, adj P for trend = 0.001).

	0.90-1.18).	and sour cream per day: 0.85 (95% CI 0.72-1.02), butter and cream per day: 0.85 (95% CI 0.72-0.93), dairy based desserts per day: 0.63 (95% CI 0.24-1.64), yoghurt per day: 0.47 (95% CI 0.16-1.43). The OR was similar for blacks and whites and for men and women. This inverse association was not seen in healthy weight subjects.	Overall, higher intake of dairy products was not associated with less weight gain in men.
Effect on risk	None for low fat milk products. Protect for whole milk.	Protect for high fat dairy. None for low fat dairy. Overweight only.	None
Importance [9]	1	1	3
Relevance [10]	1	1	1
Generalisable	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

5.9 DAIRY and CHILD BODY MASS INDEX

Does a particular intake of dairy affect BMI in children?		
Evidence statement		Consumption of milk is not associated with BMI or BMI change in childhood.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	One systematic review (1 N) including 3 randomised controlled trials of 221 adolescent girls. 6 cohort studies (2 P, 4 0) examining milk intake, 4 measuring change in BMI and 1 measuring BMI. One cohort study examining both milk and cheese intake.
Consistency	Satisfactory	Most of the studies examining milk are in agreement: 5 reported no effect, 1 reported a protective effect, 1 reported increased risk. Only 1 study examined cheese intake, so consistency cannot be evaluated.
Clinical impact	Poor	There was no association found.
Generalisability	Excellent	Western populations, including US, Australia, New Zealand, and UK; China.
Applicability	Excellent	Directly applicable.

Of the three randomised controlled trials of children included in the systematic review, none found any association between milk or dairy supplementation and weight change. This systematic review was of poor quality because due to its limiting inclusion criteria, it likely did not include all relevant studies. Of the six additional cohort studies, one reported lower fat mass accumulation in UK children consuming one serving of milk per day, four found no association between milk consumption and BMI or BMI change in adolescents and children, and one found greater weight gain in US adolescents consuming >3 servings of milk daily. One study examined cheese intake in preschool children, reporting a positive relationship between frequency of cheese consumption and incidence of overweight or obesity. From these studies, it appears there is no association between milk intake and BMI or BMI change in childhood, and there is very weak evidence for an association between cheese consumption and risk of overweight. There is not enough evidence to extend this statement to include all dairy foods.

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Table 5.9 Studies used to make evidence statement for dairy and child body mass index

Reference [1]	**Barr 2003 [6]**	**Berkey 2004 [338]**	**Berkey 2005 [257]**
Type of study [2]	Systematic review of 3 RCTs	Cohort	Cohort
Level of evidence [3]	Level I	Level II	Level II
Intervention/ comparator [4]	Effect of dairy consumption on body weight change	Effect of milk (1.75-2.25 servings per day) on 1 year change in BMI	Effect of milk, dietary calcium, and dietary fat on 1 year change in BMI
N [5]	221 adolescent girls, 765 adult women, 71 men	16,771	16,771
Population/study information [6]	US, Australia, New Zealand, UK, China; 72% adult female (premenopausal and postmenopausal), 7% adult male, 21% adolescent female. Follow up of 12 weeks to 3 years.	Girls and boys aged 9-14 at start of study; 94.7% white; 23.2% of boys and 17.5% of boys were overweight; 7.2% of boys and 8.6% of girls were very lean at baseline. 2 year follow up. USA.	Children of participants in the Nurses' Health Study II aged 9-14 yrs at baseline; Boys and girls; 94.7% white; USA.
Quality [7]	N	0	0
Results [8]	Increased dairy consumption is not related to a change in body weight. Increased dairy consumption is not related to a change in body weight. No quantitative data reported.	Average milk intake significantly declined each year. There was a non-significant positive association between milk intake and change in BMI over 1 yr in both boys and girls (P=0.056 and P=0.077, respectively), when energy intake is not adjusted. This association was weakened with energy adjustment (P=0.320 for boys and P=0.153 for girls).	High milk intake (>3 servings per day) was associated with weight gain compared to lower milk intake (<0.5 serving per day): For boys, β=0.019 kg/m^2 ± 0.009, P=0.03. For girls, β=0.015 kg/m^2 ± 0.007, P=0.04. This association was reduced when adjusted for energy intake, but still remained significant for skim milk in girls adj β 0.020 kg/m^2 (95% CI 0.001-0.039) P<0.1). There was no association between dairy fat intake and weight gain.

Effect on risk (Increase/None/Protect)	None	None	Increase for skim milk. None for other milks.
Importance [9]	3	3	1
Relevance [10]	1	1	1
Generalisability	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

Table 5.9 Studies used to make evidence statement for dairy and child body mass index (cont.)

Reference [1]	**Huus 2009 [754]**	**Johnson 2007 [1546]**	**Newby 2004 [2000]**	**Striegel-Moore 2006 [1801]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	Level II	Level III	Level II	Level II
Intervention/ comparator [4]	16,058 babies at birth (74% of babies born in region at that time) enrolled in cohort at food frequency and BMI recorded at 2.5 and 5 yrs of age. Dairy intake of 1 serving per day versus <1 serving per week.	Relationship between milk consumption (1 serving per day) and change in fat mass over 4 yrs.	Effect of milk intake (ounce per day) on change in weight and change in BMI.	Effect of intake of milk (100 per day) on BMI.
N [5]	8763 at 2.5 years 7356 at 5 years of age	521	1345	2371
Population/study information [6]	Children born in Sweden followed from birth to 5 yrs. Baseline=48% boys, 52% girls, maternal age 29.6 yrs, Uni degree mother 31.7%, single parent 2.1%.	Children, followed from age 5 to 9 in United Kingdom. 4 year follow up.	Low-income preschool children aged 2-5 yrs in North Dakota WIC program; 83% white. 6-12 month follow up.	Girls in the US aged 9-10 yrs at start of study; Black or white non-Hispanic; 10 year follow-up.
Quality [7]	0	P	0	P
Results [8]	Frequency of consumption of cheese at 2.5 yrs was positively associated with overweight and obesity at 5 yrs. Frequency of milk consumption was not associated with overweight and obesity. Results should be interpreted with caution as statistics were poorly	Milk consumption was associated with a reduction in fat mass accumulation at age 5 (-0.51 (95% -0.86 to -0.16) and age 7 (-0.35 (95% CI -0.57 to -0.14) in the fully adjusted analyses (P<0.01), but not in the unadjusted	There was no association between milk intake and change in weight (adj β=0.00lb ± 0.01, P=0.86) or change in BMI (adj β=0.00 kg/m^2 ± 0.00, P=0.93).	Girls' milk intake reduced by greater than 25% during the 10 years. There was no association between milk intake and BMI (-0.002 kg/m^2, SE 0.006).

	explained and poorly reported.	analyses (P=0.06 at age 5, P=0.10 at age 7).		
Effect on risk (Increase/None/Protect)	Increase for cheese. None for milk.	Protect	None	None
Importance [9]	2	2	3	1
Relevance [10]	2	2	1	2
Generalisable	No	Yes	Yes	Yes
Applicability	No	Yes	Yes	Yes

5.10 DAIRY and SOCIAL EQUITY

Does social equity affect dairy intake?		
Evidence statement		Higher occupational level is associated with consumption of cheese and skim milk.
Grade		B
Evidence statement		Higher educational level is associated with consumption of cheese.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	One meta-analysis (1 P) of 12 population-based studies examining differences in intake of whole milk, skim milk, and cheese in relation to education (12 studies) and occupational (9 studies) level in European populations.
Consistency	Good	The meta-analysis reported a positive relationship between both cheese and skim milk consumption and occupational level. 8 of the 9 included studies reported a positive association between cheese consumption and occupational level in men and women, with 5 being significant in men and 3 being significant in women. Results of individual studies examining the relationship with skim milk consumption were not reported, so consistency cannot be evaluated.
Clinical impact	N/A	No health outcomes.
Generalisability	Excellent	Western Europe.
Applicability	Good	Food types and occupations may differ in Australia.

The meta analysis was of high quality and collected data on cheese and milk consumption in western European subjects with a range of education (12 studies) and occupation (nine studies) levels. The term "cheese" includes non-fat, low-fat, and full-fat cheeses. The review did not examine total dairy consumption. The pooled statistics indicated a significant, positive relationship with cheese consumption, but not total milk consumption, and both education and occupation level in men and women. When the highest category of education and occupation was compared to the lowest category of education and occupation measured, those in the highest level consumed significantly more cheese. There was also a significant, positive relationship between skim milk consumption and occupation level, but only four individual studies made this comparison and the association was not consistent with education level.

References

Sanchez-Villegas, A., Martinez, J. A., Prattala, R., Toledo, E., Roos, G., Martinez-Gonzalez, M. A. & FAIR-97-3096 Group. 2003, "A systematic review of socioeconomic differences in food habits in Europe: consumption of cheese and milk", *European Journal of Clinical Nutrition*, vol. 57, no. 8, pp. 917-29.

Table 5.10 Studies used to make evidence statement for dairy and social equity

Reference [1]	**Sanchez-Villegas 2003 [1917]**
Type of study [2]	Meta-analysis of 12 population-based studies.
Level of evidence [3]	I
Intervention/ comparator [4]	Relationship between occupational level (highest category vs lowest category) and educational level (highest category vs lowest category) on cheese and milk consumption (g per day).
N [5]	Education: 61,814; Occupation: 20,143
Population/ study information [6]	Finland, Norway, Sweden, Estonia, Denmark, Ireland, The Netherlands, Germany, Spain; Males and females; Adults (11-85 yrs).
Quality [7]	P
Results [8]	There was a significant, positive relationship between cheese consumption and education (men: +6.76 g per day (95% CI 3.40-10.12), women: +9.03 g per day (95% CI 7.06-11.00)) and occupation level (men: +4.56 g per day (95% CI 2.13-7.00), women: +5.08g per day (95% CI 3.65-6.50)). There was no significant association between milk consumption and education or occupation level in either women or men. In addition, there was a positive, significant relationship between skimmed milk and occupation level (men: +32.89g per day (95% CI 15.68-50.10), women: +35.04g/d (95% CI 9.09-61.00)), but not education level.
Effect on risk (Increase/None/Protect)	N/A
Importance [9]	1
Relevance [10]	2
Generalisability	yes
Applicability	yes

5.11 DAIRY and COLORECTAL CANCER

Does a particular intake of dairy affect the risk of colorectal cancer?		
Evidence statement		Consumption of more than 1 serving* of dairy per day, especially milk, is associated with a reduced risk of colorectal cancer.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	Two Level I studies for colorectal cancer (2 P). One meta-analysis is particularly robust, having used a sample of >500,000 based on original data of 10 cohorts. The other (of 14 cohort studies and 13 case-control studies) was based on published studies and was funded by the National Dairy Council. One additional recent, large cohort study in Chinese women that provides further evidence.
Consistency	Good	All studies included in the meta-analysis were fairly consistent except for a study published by Kune et al. (1987). This study was conducted in Australia, introduced a large amount of heterogeneity into the meta-analysis, and found a 2.37 times (95% CI 1.57-3.58) increased risk of colorectal cancer among high-dairy consumers.
Clinical impact	Good	RR of colorectal cancer with >250mg milk/d = 0.88 (95% CI 0.79-0.99). RR of colorectal cancer with total dairy consumption = 0.84 (95% CI 0.75-0.95). The fat content of milk must be considered.
Generalisability	Excellent	Western populations, including Australia, USA, and western Europe.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

The two meta analyses are in agreement, reporting an inverse association between both milk and dairy food intake and risk of colorectal cancer in adults. One meta analysis is particularly robust, using original data from a sample of >500,000 (Pooling Project of Prospective Studies of Diet and Cancer). Although there was no attempt to include studies in addition to the Pooling Project, the individual cohorts evaluated are understood to be reputable, and provide the benefit of analysing individual data rather than published literature. This study reported a reduced incidence of colorectal cancer with the consumption of ≥ 250 g milk per day compared to <70g per day. No association was found with

consumption of cheese or yoghurt. The other meta-analysis was funded by the National Dairy Council and reported pooled data of 14 cohort studies and pooled data of 13 case-control studies. The results of the individual studies are almost consistent except for one study published by Kune et al. (1987) and conducted in Australia. This case-control study introduces a large amount of heterogeneity into the meta analysis, and reports a 2.37 times increased risk of colorectal cancer among high-dairy consumers. The authors of the meta analysis reported a significant inverse association between colorectal cancer and milk intake among case-control studies only when this outlier is removed. Meta analysis of the cohort studies consistently found inverse relationships between colorectal and colon cancer and milk and dairy intake. In addition, the recently published cohort study includes over 73,000 women in China, reporting a small inverse association between >200g daily milk intake and incidence of colon cancer (P=0.05), but no association with colorectal cancer. This body of evidence statement is stronger for milk intake than for total dairy intake. This body of evidence statement is consistent with the WCRF report that indicates that it is "probable" that milk is protective against colo-rectal cancer.

References

Cho, E., Smith-Warner, S. A., Spiegelman, D., Beeson, W. L., van den Brandt, P. A., Colditz, G. A., Folsom, A. R., Fraser, G. E., Freudenheim, J. L., Giovannucci, E., Goldbohm, R. A., Graham, S., Miller, A. B., Pietinen, P., Potter, J. D., Rohan, T. E., Terry, P., Toniolo, P., Virtanen, M. J., Willett, W. C., Wolk, A., Wu, K., Yaun, S.-S., Zeleniuch-Jacquotte, A. & Hunter, D. J. 2004, "Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies", *Journal of the National Cancer Institute*, vol. 96, no. 13, pp. 1015-22.

Huncharek, M., Muscat, J. & Kupelnick, B. 2009, "Colorectal cancer risk and dietary intake of calcium, vitamin D, and dairy products: a meta-analysis of 26,335 cases from 60 observational studies", *Nutrition & Cancer*, vol. 61, no. 1, pp. 47-69.

Lee, S.-A., Shu, X. O., Yang, G., Li, H., Gao, Y.-T. & Zheng, W. 2009, "Animal origin foods and colorectal cancer risk: a report from the Shanghai Women's Health Study", *Nutrition & Cancer*, vol. 61, no. 2, pp. 194-205.

Table 5.11 Studies used to make evidence statement for dairy and colorectal cancer

Reference [1]	**Cho 2004 [334]**	**Huncharek 2009 [736]**	**Lee 2009 [659]**
Type of study [2]	Meta-analysis of 10 cohorts (used original data, not published data)	Meta-analysis of 14 cohort studies and 13 case-control studies	Cohort
Level of evidence [3]	Level I	Level I	Level II
Intervention/ comparator [4]	Effect of milk intake (<70 compared to >250 g per day) on risk of colorectal cancer.	Effect of milk and dairy intake ("high" vs "low" intake quartiles) on colorectal cancer risk.	Effect of milk intake (0 compared to >200g milk day) on risk of colorectal cancer.
N [5]	534,536	10,294	73,224 total, with 394 incident cases of colorectal cancer (colon = 236; rectal = 158) diagnosed
Population/study information [6]	M and F adults USA, Finland, Canada, Netherlands, Sweden; Smokers and non-smokers.	M and F Norway, Finland, The Netherlands, USA, France, Japan, Sweden, Italy, Switzerland, Singapore, Australia, Argentina.	Women aged 40- 70y of age from Shanghai Women's Health Study. Mean follow up 7.4 yrs.
Quality [7]	P	P	P
Results [8]	Milk consumption was inversely related to risk of colorectal cancer: RR 0.88 (95% CI 0.79-0.99) for consumption of >250 g milk per day. Supports hypothesis that moderate milk intake can reduce risk of colorectal cancer. There was no association between risk of colorectal cancer and cheese or yoghurt consumption.	There is an inverse relationship between milk/dairy intake and risk of colorectal cancer. Data from cohort studies: RR for colon or colorectal cancer and milk consumption 0.90 (95% CI 0.83-0.97); RR for colon cancer only and milk consumption 0.78 (95% CI 0.67-0.92), RR for colorectal cancer and total dairy consumption 0.84 (95% CI 0.75-0.95). Data from case-control studies: RR for colon or colorectal cancer and milk consumption 0.90 (95% CI 0.81-1.00), excluding Kune et al. data; RR for	Milk intake was inversely associated with the risk of colon cancer (RR=0.8, 95% CI 0.4-1.3, P trend=0.05). RR for colorectal cancer = 0.8(95% CI 0.5-1.2, P trend=0.09).

		colorectal cancer and total dairy consumption 0.90 (95% CI 0.78-1.04).	
Effect on risk (Increase/None/Protect)	Protect	Protect	Protect
Clinical importance [9]	1	1	1
Clinical relevance [10]	1	1	1
Generalisability	Yes	Yes	Yes
Applicability	Yes	Yes	Yes

5.12 DAIRY and RECTAL CANCER

Does a particular intake of dairy affect the risk of rectal cancer?		
Evidence statement		Consumption of more than 1 serving* of milk per day is associated with reduced risk of rectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Excellent	Two Level I studies on rectal cancer (2 P): one is very strong and uses a sample of >500,000 and original data from 10 cohorts, one is slightly weaker and evaluates published studies (7 cohort studies and 3 case-control studies). One additional cohort (1 P) study examines unpasteurised milk.
Consistency	Satisfactory	The high quality meta-analysis found a protective effect from milk consumption, while the slightly lower quality meta-analysis found no association. The additional cohort study found a protective effect from unpasteurised milk consumption.
Clinical impact	Good	Relative risk of rectal cancer for intake of ≥ 250g milk/day = 0.80 (95% CI 0.66-0.96), but nonsignificant relative risks for high cheese and high yoghurt consumption.
Generalisability	Excellent	Western populations, including Australia, USA, and western Europe.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL

The two meta analyses are conflicting. One meta analysis is of higher quality and influences the body of evidence statement to a greater degree. The high quality meta analysis uses original data from a sample of >500,000 (Pooling Project of Prospective Studies of Diet and Cancer), and reports a reduced incidence of rectal cancer with the consumption of ≥ 250 g milk per day compared to <70 g milk per day. No association was found with high intake of cheese or yoghurt. The other meta-analysis was funded by the National Dairy Council. This study included seven cohort and three case-control studies examining the relationship between milk intake and rectal cancer, but found no significant relationship. The additional cohort study examines the relationship between unpasteurised milk consumption as a child and later development of cancers. The results are consistent with the high quality meta analysis, but no specific statement can be made on the effect of unpasteurised milk consumption as the study design lacked sufficient detail.

References

Cho, E., Smith-Warner, S. A., Spiegelman, D., Beeson, W. L., van den Brandt, P. A., Colditz, G. A., Folsom, A. R., Fraser, G. E., Freudenheim, J. L., Giovannucci, E., Goldbohm, R. A., Graham, S., Miller, A. B., Pietinen, P., Potter, J. D., Rohan, T. E., Terry, P., Toniolo, P., Virtanen, M. J., Willett, W. C., Wolk, A., Wu, K., Yaun, S.-S., Zeleniuch-Jacquotte, A. & Hunter, D. J. 2004, "Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies", *Journal of the National Cancer Institute*, vol. 96, no. 13, pp. 1015-22.

Huncharek, M., Muscat, J. & Kupelnick, B. 2009, "Colorectal cancer risk and dietary intake of calcium, vitamin d, and dairy products: a meta-analysis of 26,335 cases from 60 observational studies", *Nutrition & Cancer*, vol. 61, no. 1, pp. 47-69.

Sellers, T. A., Vierkant, R. A., Djeu, J., Celis, E., Wang, A. H., Kumar, N. & Cerhan, J. R. 2008, "Unpasteurized milk consumption and subsequent risk of cancer", *Cancer Causes & Control*, vol. 19, no. 8, pp. 805-11.

Table 5.12 Studies used to make evidence statement for dairy and rectal cancer

Reference [1]	**Cho 2004 [334]**	**Huncharek 2009 [736]**	**Sellers 2008 [846]**
Type of study [2]	Meta analysis of 10 cohorts (used original data, not published study data)	Meta analysis of 7 cohort and 3 case-control studies	Cohort
Level of evidence [3]	Level I	Level I	Level II
Intervention/ comparator [4]	Effect of milk intake (<70 compared to >250g per day) on risk of rectal cancer	Effect of milk intake ("high" vs "low" intake) on rectal cancer risk	Risk of cancers and unpasteurised milk consumption
N [5]	534,536	10,294	22,808
Population/study information [6]	M and F adults USA, Finland, Canada, Netherlands, Sweden; Smokers and non-smokers	M and F Norway, Finland, The Netherlands, USA, France, Japan, Sweden, Italy, Switzerland, Singapore, Australia, Argentina	Iowa, USA; Post menopausal women aged 55-69 yrs; Follow-up: 11 yrs
Quality [7]	P	P	P
Results [8]	Milk consumption was inversely related to risk of rectal cancer: RR 0.80 (95% CI 0.66-0.96) for consumption of >250g milk per day. There was no association between risk of rectal cancer and consumption of cheese or yoghurt.	There is no association between milk intake and risk of rectal cancer. RR of rectal cancer with milk consumption from cohort data 0.95 (95% CI 0.80-1.14). RR of rectal cancer with milk consumption from case-control data 1.01 (95% CI 0.79-1.28).	The only site specific cancer that was found to be associated with unpasteurized milk consumption was rectal cancer: RR (only as a child) 0.66, 95% CI: 0.39-1.11 p=0.02) or RR (as a child and an adult) 0.26 (95% CI 0.1–0.68).
Effect on risk (Increase/None/Protect)	Protect for milk, none for yoghurt and cheese.	None	Protect
Clinical importance [9]	1	1	2
Clinical relevance [10]	1	1	1
Generalisable	Yes	Yes	Yes
Applicability	Yes	Yes	No

5.13 DAIRY and RENAL CANCER

Does a particular intake of dairy affect the risk of renal cancer?		
Evidence statement		Consumption of 3 or more servings* of milk per day is not associated with risk of renal cell cancer.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	One meta-analysis (1 P) of 13 prospective studies examining intake of milk.
Consistency	Good	One meta-analysis, but consistency among studies was not well reported.
Clinical impact	Poor	There was no observed effect of milk on renal cell cancer, so impact is limited. Relative risk for multivariate analysis for high milk consumption = 1.00 (95% CI 0.94-1.06).
Generalisability	Excellent	Western populations, including USA, Finland, Canada, Netherlands, and Sweden.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL.

The meta analysis uses original data from the Pooling Project of Prospective Studies of Diet and Cancer, and includes a sample of nearly 800,000 from 13 prospective studies. While there was no attempt to include studies in addition to the Pooling Project, the individual cohorts included are understood to be reputable, and provide the benefit of analysing individual data rather than published literature. No association was found between milk consumption (≥ 3 glasses per day compared to <1) and renal cell cancer risk. The lack of association remained when whole milk and reduced fat milk were analysed separately. Because the results of individual studies were not reported, consistency among studies cannot be evaluated.

The WCRF reportdoes not examine the relationship between dairy and renal cancer.

References

Lee, J. E., Hunter, D. J., Spiegelman, D., Adami, H. O., Bernstein, L., van den Brandt, P. A., Buring, J. E., Cho, E., English, D., Folsom, A. R., Freudenheim, J. L., Gile, G. G., Giovannucci, E., Horn-Ross, P. L., Leitzmann, M., Marshall, J. R., Männistö, S., McCullough, M. L., Miller, A. B., Parker, A. S., Pietinen, P., Rodriguez, C., Rohan, T. E., Schatzkin, A., Schouten, L. J., Willett, W. C., Wolk, A., Zhang, S. M. & Smith-Warner, S. A. 2007, "Intakes of coffee, tea, milk, soda and juice and renal cell cancer in a pooled analysis of 13 prospective studies", *International Journal of Cancer*, vol. 121, no. 10, pp. 2246-53.

Table 5.13 Studies used to make evidence statement for dairy and renal cancer.

Reference [1]	**Lee 2007 [7]**
Type of study [2]	Meta analysis of 13 cohort studies
Level of evidence [3]	Level I
Intervention/ comparator [4]	Effect of milk consumption (≥ 3 servings per day compared to <1 serving per day) on risk of renal cell cancer.
N [5]	530,469 women total 244,483 men total 709 renal cell cancer cases in women 769 renal cell cancer cases in men
Population/study information [6]	M and F adults USA, Finland, Canada, Netherlands, Sweden. Smokers and non-smokers.
Quality [7]	P
Results [8]	There was no association found between ≥ 3 servings of milk/d and renal cell cancer risk. The lack of association remained when whole milk and reduced fat milk were analysed separately.
Effect on risk (Increase/None/Protect)	None
Clinical importance [9]	3
Clinical relevance [10]	1
Generalisability	Yes
Applicability	Yes

5.14 DAIRY and PROSTATE CANCER

Does a particular intake of dairy affect the risk of prostate cancer?		
Evidence statement		Consumption of milk is associated with increased risk of prostate cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	One non-systematic review (1 N) of 1 meta-analysis (2004, of 11 case-control studies) and 1 systematic review (2004, of 27 cohort and intervention studies).
Consistency	Poor	Meta-analysis reported increased risk, systematic review reported inconclusive evidence and cannot determine an association. Results of individual studies were not reported.
Clinical impact	Good	MA reported increased risk of prostate cancer in higher vs lower consumers of milk: adj OR = 1.56 (95% CI 1.30-1.83); intake of milk not reported.
Generalisability	Poor	Assume a wide variety of populations due to the inclusion of 38 individual studies between the meta-analysis and systematic review, but specific populations were not reported.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL.

The poor quality review included one meta-analysis and one systematic review and did not provide sufficient detail on the included studies. The included meta-analysis, published in 2004, reported an increased risk of prostate cancer in participants who consumed higher vs lower amounts of milk adjOR 1.56 (95% CI 1.30-1.83), but the level of milk consumption not reported. The included systematic review, also published in 2004, concluded that the evidence was too inconclusive to determine a relationship between dairy consumption and prostate cancer. Therefore, this body of evidence statement is weak and must be applied with caution. This weak body of evidence statement is consistent with the WCRF report that indicates that while diets high in calcium are a "probable" cause of prostate cancer, there is limited evidence suggesting that high consumption of milk and dairy products are causative.

References

Alvarez-León, E. E., Román-Viñas, B. & Serra-Majem, L. 2006, "Dairy products and health: a review of the epidemiological evidence", *British Journal of Nutrition*, vol. 96, no. Suppl 1, pp. S94-S99.

Table 5.14 Studies used to make evidence statement for dairy and prostate cancer

Reference [1]	**Alvarez-Leon 2006 [R36]**
Type of study [2]	Non-systematic review of 1 meta-analysis and 1 systematic review.
Level of evidence [3]	Level I
Intervention/ comparator [4]	Effect of milk consumption on risk of prostate cancer.
N [5]	Number of subjects not provided. MA included 11 case-control studies; SR included 27 prospective cohorts and intervention studies.
Population/study information [6]	Popluation characteristics not reported.
Quality [7]	N
Results [8]	MA reported increased risk of prostate cancer in higher vs lower consumers of milk: unadjOR 1.68 (95% CI 1.34-2.12), adjOR 1.56 (95% CI 1.30-1.83); intake of milk not reported. SR reported available evidence remains limited or inconclusive.
Effect on risk (Increase/None/Protect)	Increase
Clinical importance [9]	1
Clinical relevance [10]	1
Generalisability	Yes
Applicability	Yes

5.15 DAIRY and BREAST CANCER

Does a particular intake of dairy affect the risk of breast cancer?		
Evidence statement		Mean consumption of 1 serving* of dairy food per day is not associated with the risk of breast cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	One meta-analysis of 8 prospective studies (1 P), and one non-systematic review (1 N).
Consistency	Satisfactory	The meta-analysis reported no association, but results of individual studies were not reported so consistency cannot be assessed. The systematic review included one meta-analysis that reported increased risk with high dairy food consumption, and included one systematic review that reported no association.
Clinical impact	Satisfactory	There was no association in the meta-analysis. The systematic review reported a relative risk of 1.17 (95% CI 1.04-1.30) for high dairy food consumption.
Generalisability	Excellent	All studies were in women. Western populations.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

The meta analysis examining breast cancer uses original data from the Pooling Project of Prospective Studies of Diet and Cancer, and includes a sample of over 350,000. While there was no attempt to include studies in addition to the Pooling Project, the individual cohorts included are understood to be reputable, and provide the benefit of analysing individual data rather than published literature. The meta analysis found no association between breast cancer incidence and either dairy solids or dairy fluids (highest quartile of intake compared to lowest quartile). Quartile intakes were not reported, but the 95th percentile for intake of total dairy fluids for the individual studies ranged from 555-1101 g per day, mean intakes ranged from 203-262 g per day, and 5th percentile intakes ranged from 0-32 g per day. 95th percentile intakes for total dairy solids for the individual studies ranged from 70-111 g per day, mean intakes ranged from 23-34 g per day, and 5th percentile intakes ranged from 0-6 g per day. Butter was included in the category of dairy solids. The additional poor quality systematic review included one meta-analysis from 1993 and one systematic review from 2004. The meta-analysis from 1993 reported an increased risk of breast cancer with high dairy food consumption RR 1.17 (95% CI 1.04-1.30), but intakes of dairy were not reported. The systematic review from 2004 reported that the evidence was too inconsistent to determine an association between intake of dairy foods and development of breast cancer. Although this systematic review is of poor quality, it introduces inconsistency to the association,

so care must be taken when using this evidence to guide practice. This WCRF report does not make any statement about dairy and breast cancer.

References

Alvarez-León, E. E., Román-Viñas, B. & Serra-Majem, L. 2006, "Dairy products and health: a review of the epidemiological evidence", *British Journal of Nutrition*, vol. 96, no. Suppl 1, pp. S94-S99.

Missmer, S. A., Smith-Warner, S. A., Spiegelman, D., Yaun, S. S., Adami, H. O., Beeson, W. L., van den Brandt, P. A., Fraser, G. E., Freudenheim, J. L., Goldbohm, R. A., Graham, S., Kushi, L. H., Miller, A. B., Potter, J. D., Rohan, T. E., Speizer, F. E., Toniolo, P., Willett, W. C., Wolk, A., Zeleniuch-Jacquotte, A. & Hunter, D. J. 2002, "Meat and dairy food consumption and breast cancer: a pooled analysis of cohort studies", *International Journal of Epidemiology*, vol. 31, no. 1, pp. 78-85.

Table 5.15 Studies used to make evidence statement for dairy and breast cancer

Reference [1]	**Missmer 2002 [8]**	**Alvarez-Leon 2006 [R36]**
Type of study [2]	Meta analysis of 8 cohort studies	Non-systematic review of 1 MA and 1 SR
Level of evidence [3]	Level I	Level I
Intervention/ comparator [4]	Effect of intake of dairy fluids (whole cream, whipped cream, custard or pudding, ice cream, milk – skim, 0.5%, 1%, 2%, and whole, evaporated milk, buttermilk, sherbet, ice milk, sour cream, yoghurt – light and regular, yoghurt dressing) and dairy solids (butter, cheese – high and low fat, hard, cottage cheese, ricotta cheese, cream cheese, and other) (4th quartile vs 1st quartile, and 100 g per day) on risk of breast cancer.	Effect of dairy food or milk consumption on incidence of breast cancer.
N [5]	351,041 total 7379 cases	Number of subjects not provided. MA included 5 cohort and 12 case-control studies. Number of studies in SR not reported.
Population/study information [6]	8 large prospective studies from Pooling Project of Prospective Studies of Diet and Cancer with a 5-11 year follow up.	Population characteristics not reported. MA done in Canada.
Quality [7]	P	N
Results [8]	There was no significant association between intake of dairy fluids or dairy solids and risk of breast cancer. Adj RR for dairy fluids (highest quartile vs lowest quartile) 0.93 (95% CI 0.84-1.03, P=0.09). Adj RR for dairy solids (highest quartile vs lowest quartile) 1.01 (95% CI 0.93-1.09, P=0.94). Quartile intakes were not reported, but 95th percentile for total dairy fluids for the individual studies ranged from 555-1101 gper day, mean intakes ranged from 203-262 g per day, and 5th percentile intakes ranged from 0-32 g per day. 95th percentile intakes for total dairy solids for the individual studies ranged from 70-111 g per day, mean intakes ranged from	MA (Boyd 1993) reported increased risk of breast cancer with greater intakes of milk: RR 1.17 (95% CI 1.04-1.30), but intake of milk not reported. SR reported no consistent evidence for an association between the consumption of dairy foods and breast cancer risk.

	23-34 g per day, and 5th percentile intakes ranged from 0-6 g per day	
Effect on risk (Increase/None/Protect)	None	Increase for one study, none for the other study
Clinical importance [9]	3	1
Clinical relevance [10]	1	1
Generalisability	Yes	Yes
Applicability	Yes	Yes

5.16 DAIRY and ENDOMETRIAL CANCER

Does a particular intake of dairy affect the risk of endometrial cancer?		
Evidence statement		Consuming dairy food is not associated with risk of endometrial cancer
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	One meta-analysis of 1 cohort study and 8 case-control studies (1 P).
Consistency	Good	One meta-analysis. All but one individual study found no association between dairy intake and endometrial cancer.
Clinical impact	Poor	There were no associations. Pooled OR = 0.97 (95% CI 0.93-1.01) per serving of dairy/day.
Generalisability	Excellent	All studies were in women. Western populations.
Applicability	Excellent	Directly applicable.

*1 serving of milk = 240mL, 1 serving of yoghurt = 240mL, 1 serving of cheese = 45g.

The meta analysis examining endometrial cancer included one cohort study and eight case-control studies (three hospital-based and five population-based) with data on dairy intake (sample of just over 32,000). Both the pooled analysis and most individual studies were consistent, finding no association between total dairy food intake and risk of endometrial cancer. One individual study reported a significant association. Intake levels in individual studies were not reported in this review. This body of evidence statement is consistent with the WCRF report that indicates that there is no convincing or probable evidence suggesting that high consumption of milk and dairy products are causative of endometrial cancer.

References

Bandera, E. V., Kushi, L. H., Moore, D. F., Gifkins, D. M. & McCullough, M. L. 2007, "Consumption of animal foods and endometrial cancer risk: a systematic literature review and meta-analysis", *Cancer Causes and Control*, vol. 18, no. 9, pp. 967-988.

Table 5.16 Studies used to make evidence statement for dairy and endometrial cancer

Reference [1]	**Bandera 2007 [13]**
Type of study [2]	Meta analysis of 1 cohort and 8 case-control studies
Level of evidence [3]	Level I
Intervention/ comparator [4]	Effect of dairy food consumption (highest category compared to lowest category – specific levels were not reported) on risk of endometrial cancer.
N [5]	32,013 total with data on dairy 2881 cases with data on dairy
Population/study information [6]	USA, Sweden, Greece, Mexico; Ages 18-84; Females
Quality [7]	P
Results [8]	There was no association found between total dairy food intake and incidence of endometrial cancer. Pooled OR 0.97 (95% CI 0.93-1.01) per serving of dairy per day.
Effect on risk (Increase/None/Protect)	None
Clinical importance [9]	3
Clinical relevance [10]	1
Generalisability	Yes
Applicability	Yes

S1.1/S2.6 Dairy

Summary of studies not included in Body of Evidence statements

Dairy and Mental Health

One small cohort study (n=1449, positive quality) in men and women in Finland reported no association between fat intake from milk products and development of dementia over a 21 year follow-up (Laitinen 2006).

One small cohort study (n=601, neutral quality) in men in Western Australia aged >80 yrs reported that regular consumption of full-cream milk is inversely related to successful mental health aging (unadj OR 0.63 (95% CI 0.45-0.89) (Almeida 2006).

Dairy and Lipid Profile in Adults

One RCT (positive quality) of 14 healthy men in Denmark compared the effect of consumption of 1.5L whole milk, 205g cheese, or 64g butter, and reported that there were no differences in the cholesterolemic effect, postprandial glucose response, or postprandial insulin response of diets containing whole milk and butter. However, LDL cholesterol was lower after the cheese diet compared to the other diets (P=0.098), but this must be verified through additional studies (Tholstrup 2004).

One RCT (positive quality) of 41 healthy adults in New Zealand reported that compared to three to six servings of cow's milk products per day, the same consumption of sheep's milk products resulted in a reduction in plasma total cholesterol, HDL cholesterol, and LDL cholesterol (Skeaff 2004).

Dairy and Lipid Profile in Infants

One randomised controlled trial of healthy infants in Belgium (n=189, positive quality) reported that ad libitum consumption of infant milk formula with 0.6 g/100 mL of GOS/lcFOS (9:1) did not affect serum cholesterol levels compared to control formula. Total cholesterol and LDL cholesterol in breast-fed infants were higher compared to formula-fed infants ($p<0.016$) (Alliet 2007).

Two randomised controlled trials of healthy infants in the USA compared the effect of consumption of regular infant formula versus infant formula supplemented with 40-100 mg/L cholesterol versus breast milk. Demmers 2005 (neutral quality) reported that plasma cholesterol concentrations were higher and cholesterol synthesis was lower at 4 months in the groups with a higher intake of dietary cholesterol (n=47). At 12 months, Bayley 2002 (neutral quality) did not see a change in cholesterol synthesis, plasma total cholesterol, or plasma LDL cholesterol levels in the groups with a higher intake of dietary cholesterol (n=49), and Demmers did not see the differences maintained at 18 months. This suggests there is "no imprinting of cholesterol biosynthesis," and that differences in plasma lipid profiles before the introduction of solid foods do not last (Demmers 2005).

Dairy and Adiposity in Children

One randomised controlled trial (positive quality) of 90 overweight children in Chile reported that an intervention of nutrition education and 200g milk per day reduced the consumption of sugar-sweetened beverages (P<0.0001). There was no change in body fat, but there was an increase in lean body mass in the intervention group (P=0.04) (Albala 2008).

Dairy and Dental Health

One cohort study (positive quality) of 695 newborn infants in the USA followed through age 5 yrs reported that compared to children without dental caries, children with dental caries had lower median intakes of milk at 2 and 3 years of age (P<0.05). Low intakes of non-milk dairy foods (cheese+yoghurt+dairy desserts) compared to high intakes of non-milk dairy foods were associated with fewer teeth having caries (P<0.05) (Marshall 2003).

Dairy and Child Growth

One large cohort study (neutral quality) of 16,491 healthy infants reported that compared to breast milk, formula and other milks increased weight and length growth during infancy from three months to 12 months. There was no difference in growth among infants receiving whole cow's milk compared to formula (Kramer 2004).

Dairy and Pancreatic Cancer

One large cohort study following 88,802 women in the USA (Nurses Health Study, positive quality) for 18 years reported 178 cases of pancreatic cancer (Michaud 2003). There was no association between total dairy product intake (first quartile (13g/d) versus fourth quartile (91g/d)) and pancreatic cancer risk (adj RR 1.04 (95% CI 0.62-1.77). There was also no association between intake of specific types of dairy foods (skim milk, hard cheese, butter) and pancreatic cancer risk.

Dairy and Ovarian Cancer

One large cohort study of 61,084 women in Sweden (Swedish Mammography Cohort, positive quality) followed for 13 years revealed 66 incident cases of invasive epithelial ovarian cancer (Larsson 2004). High intakes of lactose and milk were associated with an increased risk of serous ovarian cancer but not of other subtypes of ovarian cancer. The adjusted relative risk for serous epithelial tumours was: 2.0 (95% CI 1.1-3.7) for >4 servings total dairy per day, 2.0 (95% CI 1.1-3.7) for >2 servings total milk per day, 1.4 (95% CI 0.9-2.2) for >1 serving total yoghurt per day, 1.1 (95% CI 0.7-1.9) for >2 servings cheese per day.

Dairy and Dairy Consumption During Pregnancy and Size of Infant

One large cohort (positive quality) of 50 117 pregnant women in Denmark reported that mother's milk intake while pregnant is positively associated with a reduced risk of small for gestational age (adjOR for

>6 glasses of milk/day vs none = 0.51 (95% CI 0.39-0.65) P<0.001), an increased risk of large for gestational age (adjOR for >6 glasses milk per day vs none 1.59 (95% CI 1.16-2.16, P<0.001), and an increased mean birth weight, abdominal circumference, placental weight, birth length, and head circumference (adjusted for gestational age at birth) (Olsen 2007).

Dairy and Effect of Nutrition Education on Dairy Consumption

One randomised controlled trial (n=38 for intervention, positive quality) of men and women >70 yrs of age in the USA intervened with an individualised home based nutrition education and behaviour change program focused on five servings of fruit and vegetables per day and three servings of calcium rich foods per day. The intensive individual nutrition education, counselling, and support increased intake of calcium-rich foods in this elderly population. The intervention group reached 0.9 ± 0.21 servings of milk or dairy per day and 0.3 ± 0.06 servings of cheese per day (P<0.05) (Bernstein 2002).

One randomised controlled trial (positive quality) of boys and girls aged 8-11 years in the USA reported that children who received intensive nutrition education consumed significantly more low fat milk and more calcium per day than the control group (Friedman 2007).

S2.6 What is the dose response relationship between different types of milk intake and weight change in adults?

See Dairy topic chapter.

References

Included Studies (not contributing to BOE) - Dairy

Alliet, P., Scholtens, P., Raes, M., Hensen, K., Jongen, H., Rummens, J.-L., Boehm, G. & Vandenplas, Y. 2007, "Effect of prebiotic galacto-oligosaccharide, long-chain fructo-oligosaccharide infant formula on serum cholesterol and triacylglycerol levels", *Nutrition*, vol. 23, no. 10, pp. 719-723.

Almeida, O. P., Norman, P., Hankey, G., Jamrozik, K. & Flicker, L. 2006, " Successful Mental Health Aging: Results From a Longitudinal Study of Older Australian Men", *American Journal of Geriatric Psychiatry.* , vol. 14, no. 1, pp. 27-35.

Bayley, T. M., Alasmi, M., Thorkelson, T., Jones, P. J., Corcoran, J., Krug-Wispe, S., Tsang, R. C., 2002, "Longer term effects of early dietary cholesterol level on synthesis and circulating cholesterol concentrations in human infants", *Metabolism: Clinical & Experimental*, vol. 51, no. 1, pp. 25-33.

Bernstein, M. A., Nelson, M. E., Tucker, K. L., Layne, J., Johnson, E., Nuernberger, A., Castaneda, C., Judge, J. O., Buchner, D. & Singh, M. F. 2002, "A Home-Based Nutrition Intervention to Increase Consumption of Fruits, Vegetables, and Calcium-Rich Foods in Community Dwelling Elders", *Journal of the American Dietetic Association*, vol. 102, no. 10, pp. 1421-1427.

Demmers, T. A., Jones, P. J. H., Wang, Y., Krug, S., Creutzinger, V. & Heubi, J. E. 2005, "Effects of

early cholesterol intake on cholesterol biosynthesis and plasma lipids among infants until 18 months of age", *Pediatrics*, vol. 115, no. 6, pp. 1594-601.

Elwood, P. C., Pickering, J. E. & Fehily, A. M. 2007, "Milk and dairy consumption, diabetes and the metabolic syndrome: the Caerphilly prospective study", *Journal of Epidemiology & Community Health*, vol. 61, no. 8, pp. 695-698.

Friedman, L. A., Snetselaar, L., Stumbo, P., Van Horn, L., Singh, B. & Barton, B. A. 2007, "Influence of Intervention on Beverage Choices: Trends in the Dietary Intervention Study in Children (DISC)", *Journal of the American Dietetic Association*, vol. 107, no. 4, pp. 586-594.

Kramer, M. S., Guo, T., Platt, R. W., Vanilovich, I., Sevkovskaya, Z., Dzikovich, I., Michaelsen, K. F. & Dewey, K. 2004, "Feeding effects on growth during infancy", *Journal of Pediatrics*, vol. 145, no. 5, pp. 600-605.

Laitinen, M. H., Ngandu, T., Rovio, S., Helkala, E.-L., Uusitalo, U., Viitanen, M., Nissinen, A., Tuomilehto, J., Soininen, H. & Kivipelto, M. 2006, "Fat Intake at Midlife and Risk of Dementia and Alzheimer's Disease: A Population-Based Study", *Dementia and Geriatric Cognitive Disorders.* , vol. 22, no. 1, pp. 99-107.

Larsson, S. C., Bergkvist, L. & Wolk, A. 2004, "Milk and lactose intakes and ovarian cancer risk in the Swedish Mammography Cohort", *American Journal of Clinical Nutrition*, vol. 80, no. 5, pp. 1353-7.

Marshall, T. A., Levy, S. M., Broffitt, B., Warren, J. J., Eichenberger-Gilmore, J. M., Burns, T. L. & Stumbo, P. J. 2003, "Dental caries and beverage consumption in young children", *Pediatrics*, vol. 112, no. 3, pp. e184-91.

Michaud, D. S., Giovannucci, E., Willett, W. C., Colditz, G. A. & Fuchs, C. S. 2003, "Dietary meat, dairy products, fat, and cholesterol and pancreatic cancer risk in a prospective study", *American Journal of Epidemiology*, vol. 157, no. 12, pp. 1115-25.

Olsen, S. F., Halldorsson, T. I., Willett, W. C., Knudsen, V. K., Gillman, M. W., Mikkelsen, T. B. & Olsen, J. 2007, "Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study", *American Journal of Clinical Nutrition*, vol. 86, no. 4, pp. 1104-1110.

Skeaff, C. M., Williscroft, K., Mann, J. & Chisholm, A. 2004, "Replacing cows' with sheep's dairy fat lowers plasma cholesterol concentration in participants consuming dairy fat-rich diets", *European Journal of Clinical Nutrition*, vol. 58, no. 2, pp. 250-7.

Tholstrup, T., Hoy, C.-E., Andersen, L. N., Christensen, R. D. K. & Sandstrom, B. 2004, "Does fat in milk, butter and cheese affect blood lipids and cholesterol differently?", *Journal of the American College of Nutrition*, vol. 23, no. 2, pp. 169-76.

6. CEREALS (S1.1)

Evidence Statements

6. CEREALS (S1.1)

Search Results

The initial search of the data bases included 2693 references for cereals generally (S1.1) and wholegrain and refined cereals (S1.9) and the specified disease outcomes. The detailed searches are included in a separate document on searches. As there were many duplicates, the two searches were combined into one Endnote library and coded as one. 193 references were retrieved for detailed review and 144 references had data extracted. 54 papers were used to form the body of evidence statements for cereals. Sufficient evidence (i.e. at least five different studies) was only found to make statements for adults aged 19+yrs for cereals generally and cancer, cardiovascular disease, weight gain and obesity, and type 2 diabetes. For the effect of wholegrain or refined grain cereals separately, sufficient evidence was only available for colorectal cancer, cardiovascular disease, weight gain and obesity, and type 2 diabetes. There was inadequate evidence to make statements for any other disease states or other age of sex groups. No data was available to make any statements for children or adolescents.

The term 'wholegrain food' is problematic, with definitions varying between countries. The US Food and Drug Administration permits health claims on foods that contain at least 51% of whole grains (including milled products). The most commonly used definition in research (Jacobs et al. 1998) defines wholegrain foods as those containing 25% or more of wholegrains and includes some foods such as bran-based cereals that do not meet the FSANZ definition of wholegrain: "*wholegrain means the intact grain or the dehulled, ground, milled, cracked or flaked grain where the constituents – endosperm, germ and bran – are present in such proportions that represent the typical ratio of those fractions occurring in the whole cereal, and includes wholemeal*". This same definition is supported by Go Grain in Australia (http://www.gograins.com.au/display.php?menuId=wholegrains).

Nonetheless many of the best epidemiological studies have used the Jacobs et al. (1998) definition, and such studies have been included in this review, on the assumption that if a health relationship is found for a more lenient definition, then it will also be found for foods with a higher proportion of wholegrain ingredients.

6.1 CEREALS and CANCER

Does a particular intake of cereal foods affect the risk of cancer in adults?		
Evidence Statement		Consumption of wholegrain cereal foods is associated with reduced risk of cancer in adults.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 Level I studies (a review of 7 other reviews of all cancers); 1 Level II study; 2 Level III studies with low risk of bias.
Consistency	Satisfactory	Some inconsistency (2 Protect; 2 No effect; 0 Increase risk).
Clinical impact	Satisfactory	Protective ORs generally in range 0.40-0.70.
Generalisability	Good	Populations in body of evidence differ but it is sensible to apply this evidence to the target population.
Applicability	Good	Levels of intake in normal range of Australian intake of wholegrain cereals.

The studies used to make the body of evidence statement are listed below and summarised in Table 6.1.

RCTs of interventions with wheat bran supplementation have been included in this evidence base because bran cereals are regarded as wholegrain cereals in most epidemiological studies (although they do not meet the FSANZ definition of a wholegrain food). The two meta analyses both reviewed prevention of colorectal adenomas and carcinomas and have one study in common, but used different publications of different data analysis of the results. The most recent analysis of high fibre cereal intervention finds a protective effect for men but not women. A reduced risk was also reported in two recent case-control studies. A list of studies with specific cancers (too few to make body of evidence statements) is given at the end of this section. The various case-control and cohort studies of other cancer types report diets with higher cereal content associated with reduced risk for gastric, small intestinal and thyroid cancers. There seems to be no relationship with prostate cancer risk.

In the 2007 World Cancer Research Fund report the following statements were made about Cereal Foods and Cancer:

<u>Cereals Generally</u>

The evidence was too limited in amount, consistency, or quality to draw any conclusions

Given the evidence from the most recent meta analysis (Jacobs et al. 2006) and the very large case-control study (LaVecchia et al. 2003), an evidence statement can be supported, but the level of consistency in the data limits the overall evidence rating to Grade D.

References

Engeset, D., Dyachenko, A., Ciampi, A. & Lund, E. 2009, "Dietary patterns and risk of cancer of various sites in the Norwegian European Prospective Investigation into Cancer and Nutrition cohort: the Norwegian Women and Cancer study." *European Journal of Cancer Prevention,* vol. 18, no. 1, pp. 69-75

Jacobs, E., Lanza, E., Alberts, D., Hsu, C., Jiang, R., Schatzkin, A. et al. 2006, "Fiber, sex, and colorectal adenoma: results of a pooled analysis." *American Journal of Clinical Nutrition,* vol. 83, no. 2, pp. 343-9.

La Vecchia, C., Chatenoud, L., Negri, E., & Franceschi, S. 2003, "Wholegrain cereals and cancer in Italy." *Proceedings of the Nutrition Society*, vol. 62, pp. 45-49.

Prentice, R., Thomson, C., Caan, B., Hubbell, F., Anderson, G., Beresford, S. et al. 2007, "Low-fat dietary pattern and cancer incidence in the Women's Health Initiative Dietary Modification Randomized Controlled Trial." *Journal of the National Cancer Institute,* vol 99, no. 20, pp. 1534-43.

Williams, M. & Hord H. 2005, "The role of dietary factors in cancer prevention: beyond fruits and vegetables." *Nutrition in Clinical Practice,* vol. 20, no. 4, pp. 451-459.

6.2 CEREALS and COLORECTAL CANCER

Does a particular intake of refined or wholegrain forms of cereals affect the risk of colorectal cancer in adults?		
Evidence statement		Consumption of 1-3 serves per day of cereals high in fibre is associated with reduced risk of colorectal cancer in adults*.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	3 Level I studies; 3 Level III studies.
Consistency	Satisfactory	Most studies consistent with favourable or no effect of wholegrains (2 Level I and 2 Level III studies Protective; 1 Level I and 1 Level III No effect). 2 studies report no effect of refined grains.
Clinical impact	Good	Protective ORs for wholegrain generally in range 0.6-0.88.
Generalisability	Satisfactory	Populations in body of evidence differ but it is sensible to apply this evidence to the target population.
Applicability	Good	Levels of intake in normal range of Australian intake of wholegrain cereals.
***** One serve of cereal defined as 1 slice bread, 1 cup cereal or cooked grain; 1 item serve of muffin, cracker or pancake.***		

The studies used to make the body of evidence statements are listed below and summarised in Table 6.1.

RCTs of interventions with wheat bran supplementation have been included in this evidence base because bran cereals are regarded as wholegrain cereals in most epidemiological studies (although they do not meet the FSANZ definition of a wholegrain food). The two meta analyses which reviewed the effect of wheat bran cereal on prevention of colorectal adenomas and carcinomas have one study in common, but used different publications of different data analysis of the results. The 2002 meta analysis found no effect of bran supplementation on colorectal cancer. The more recent analysis of the two largest intervention trials finds a protective effect for men but not women. The other non-systematic review of Williams and Hord concludes that the strongest evidence linking specific foods with decreased cancer risk is for fruits, vegetables and wholegrain.

Two recent case control studies report differing results. Deneo-Pellegrino et al. reported a modest increased risk with total grain consumption but the confidence interval included 1.0. The very large PLCO Cancers Screening Trial (with 3591 cases) found an OR of 0.88 across quintiles of dietary fibre from cereals and the NIH-AARP Diet and Health Cohort Study (2974 cases) found a similar

OR of 0.86, but notes that wholegrain but not refined grain was associated with modest risk reduction. The lower level of consistency in the data limits the overall evidence rating to Grade C.

Since the evidence is based on a mixture of studies of cereal fibre (including RCTs with bran supplementation) and studies of wholegrain intake in cohort studies it is concluded that a statement about cereals high in fibre is more appropriate than wholegrain per se. However, increasing wholegrain consumption would increase cereal fibre intake.

The evidence statement is consistent with the 2007 World Cancer Research Fund report in which the following statement was made about Cereal Foods and Colorectal Cancer:

Food Containing Dietary Fibre

Foods containing dietary fibre probably protect against colorectal cancer.

The level of one to three serves used in the evidence statement derives from the third and highest quintile levels in the paper by Schatzkin (1.2 serves per 1000 Kcal in quintile 5).

References

Asano, T. & McLeod, R. 2002, "Dietary fibre for the prevention of colorectal adenomas and carcinomas", *Cochrane Database of Systematic Reviews*, vol. 22, no. CD003430.

Deneo-Pellegrini, H., Boffetta, P., De Stefani, E., Ronco, A., Brennan, P. & Mendilaharsu, M. 2002, "Plant foods and differences between colon and rectal cancers", *European Journal of Cancer Prevention,* vol. 11, no. 4, pp. 369-75.

Jacobs, E., Lanza, E., Alberts, D., Hsu, C., Jiang, R., Schatzkin, A. et al. 2006, "Fiber, sex, and colorectal adenoma: results of a pooled analysis", *American Journal of Clinical Nutrition,* vol. 83, no. 2, pp. 343-9.

La Vecchia, C., Chatenoud, L., Negri, E., & Franceschi, S. 2003, "Wholegrain cereals and cancer in Italy", *Proceedings of the Nutrition Society*, vol. 62, pp. 45-49.

Peters, U., Sinha, R., Chatterjee, N., Subar, A., Ziegler, R., Kulldorff, M. et al. 2003, "Dietary fiber and colorectal adenoma in a colorectal cancer early detection program", *Lancet,* vol. 361, pp. 1491-95.

Schatzkin, A., Mouw, T., Park, Y., Subar, A., Kipnis, V., Hollenbeck, A. et al. 2007, "Dietary fiber and whole-grain consumption in relation to colorectal cancer in the NIH-AARP Diet and Health Study", *American Journal of Clinical Nutrition,* vol. 85, no. 5, pp. 1353-60.

Table 6.1 Summary of studies of cereals and Cancer

	A	B	C	D	E	F	G	H
1	**Reference [1]**	**Asano Cochrane 2002 [570]**	**Jacobs AJCN 2006 [263]**	**Williams &Hord Nutr Clin Prac 2005 [2812]**	**Prentice JNCI 2007 [121]**	**LaVecchia ProcNutrSoc 2003 [2565]**	**Engeset EJCancPrev 2009 [740]**	**Deneo-Pellegrino EJCPrev 2002 [551]**
2	**Type of study [2]**	Meta-analysis (5 RCTs)	Meta-analysis (2 RCTs)	Non-systematic Review (7 other reviews)	RCT	Case-control	Cohort	Case-control
3	**Level of evidence [3]**	1	1	1	11	111-2	111-2	111-2
4	**Intervention/ comparator [4]**	Dietary fibre and wheat bran - **Colorectal cancer**	Wheat bran - **colorectal cancer**	Whole grain foods - **all cancers**	Low fat diet + veg&fruit (≥5 serves/d) and grains (≥6 serves/day) for 6 years - **all cancers**	Intake measured with questionnaire of frequency of consumption of WG food (bread or pasta) in 3 levels: rarely, 1-3d/week,or >3d/week. Outcome: **all confirmed cancers**	Six different clusters of dietary patterns, including "Bread" (17% of cohort)/**Total and breast cance**r over 7 years	Energy adjusted OR of **colorectal cancer** calculated by multiple logisitic regression, using quartiles of intake. Results presented for total grains, and rice, polenta, pasta and white bread. Quintile levels not reported
5	**N [5]**	3642(dietary fibre); 1195(wheat bran)	3209	not reported	1954 intervention; 29294 control	11,990cases; 10,058 controls	1348 cases; 34,353 in cohort	484 cases; 14542 controls
6	**Population/study information [6]**	M+F, USA, 10 European countries, Canada and Australia; 40-85y	M+F; US; 40-80y; BMI 27±4; 92% Caucasian	not reported	US Postmenopausal women aged 50-79y	Italy; M+W 45-74y	Norway; Women mean age 48y	Uruguay M+W 30-89y
7	**Quality [7]**	P	P	N	P	0	P	0
8	**Results [8]**	No evidence of protective effect for recurrent adenoma	For men, but not women, the intervention of a low fat higher fibre diet with cereals was associated with a statistically significant reduced adenoma recurrence: OR: 0.81 (0.67, 0.98) p<0.03.	The strongest evidence linking specific foods to decrease cancer risk include the consumption of fruits, and vegetables and whole grains	No evidence of any relationship between total grain consumption and invasive cancer risk in postmenopausal women.	Consistent pattern of inverse relationship between wholegrain foods and risk of cancer OR were 0.3-0.5 for digestive, respiratory and colon, 0.6 for rectum and liver, 0.4 for bladder and kidney, 0.7 for ovary, 0.5 for non-Hodgkins lymphoma (all p<0.01)	There was no significant association between dietary patterns and cancer risk, including the Bread pattern.	Total grains showed increased risk (OR1.4, 95% CI 1.0-1.9; p=0.02). Rice a slight protective effect (OR 0.7, 95%CI 0.5-0.9; p+0.006) but s no effect with polenta or pasta. White bread was associated with elevated risk in women only (OR 2.8, 95%CI 1.7-4.7)
9	**Effect on risk (Increase/None/Protect)**	None	Protect	Protect	None	Protect	None	None
10	**Clinical importance [9]**	3	1	1	3	1	3	4
11	**Clinical relevance [10]**	1	1	1	1	1	1	1
12	**Generalisable**	Yes	Yes	Yes	Yes	Uncertain	No	No
13	**Applicable**	Yes	Yes	Yes	Yes	Yes	Yes	Yes

6.3 CEREALS and CARDIOVASCULAR DISEASE

Does the consumption of particular levels of cereal foods affect the risk of CVD in adults?		
Evidence Statement		Consumption of cereal foods (especially wholegrains and those with fibre from oats or barley) is associated with a reduced risk of cardiovascular disease in adults.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	2 Level I studies (1 meta-analysis of 10 RCTs and one systematic review of 14RCTs, 9 cohort and 5 cross-sectional studies); 5 Level II studies; 10 Level III studies.
Consistency	Good	Most studies consistent (14 Protect; 3 No effect; None increased risk).
Clinical impact	Good	Substantial protective OR of cereals (total, wholegrain or cereal fibre) in meta analyses and cohort studies of around 30% reduction in CVD risk.
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to Australian healthcare context with few caveats.

The studies used to make the body of evidence statements are listed below and summarised in Table 6.2.

Three meta analyses all report a protective effect of cereal fibre with an estimated 25% reduction of coronary death risk for each 10g increment in cereal fibre calculated by Pereira et al. (2004). Almost all the RCTs have been conducted with oats, and there is evidence of beneficial lowering of levels of LDL and total cholesterol levels, but longer term studies and with other grains are needed. The other systematic reviews of cohort and cross-sectional studies consistently report significant effects. Most studies are about wholegrain consumption particularly, rather than cereals generally.

Intervention studies with oats and barley show beneficial effects but there is no clear association with wheat consumption. Nonetheless there is a strong body of evidence from cohort studies of the protective effect of wholegrain foods in general, which in the studies from the US are primarily wheat-based, and therefore relevant to the Australian diet. Therefore the evidence statement is not restricted to cereal foods high in soluble fibre.

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6.4 CEREALS and CARDIOVASCULAR DISEASE

Does a particular intake of refined and wholegrain forms of cereals affect the risk of CVD in adults?		
Evidence Statement		Consumption of 1-3 serves per day of wholegrain cereals is associated with a reduced risk of cardiovascular disease*
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent (wholegrains) Satisfactory (refined grains)	2 Level I studies (1 meta-analysis of 10 RCTs; 1 systematic review of 14 RCTs, 9 cohort and 5 cross-sectional studies); 2 Level II studies; 7 Level III studies.
Consistency	Good	Almost all report a favourable effect of Wholegrain cereals (10 Protect; 1 No effect; 0 Increase). The no effect study was with a liquid meal product. Three Level III studies report no association with refined grain intake.
Clinical impact	Good	Protective OR for wholegrain of approximately 0.70 in meta analyses.
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to Australian healthcare context with few caveats.
**** Note:*** One serve of cereal defined as 1 slice bread, 1 cup cereal or cooked grain; 1 item serve of muffin, cracker or pancake.		

The 11 studies used to make this body of evidence statements are listed below and summarised in Table 6.2 (which also includes seven other studies about cereals in general).

The three meta analyses all report an association of reduced risk of CVD with wholegrain food consumption. The most recent systematic review (DeMoura 2008) concludes three serves a day is associated with a 30-48% risk reduction and in seven of the cohort studies summarised in that review there was a significant reduction in relative risk from 1 serve of wholegrain per day. Therefore the evidence statement above refers to consumption of one to three serves per day.

Three other systematic reviews all conclude that evidence from epidemiological studies show CVD risk reduction with consumption of wholegrain foods. Definitions of wholegrain foods vary from requiring 25% to 51% wholegrain ingredients. Using the few studies employing the stricter FDA definition of 51%, the body of evidence was insufficient to draw conclusions. However most observational studies, such as the Iowa Women's Health Study, the Physicians Health Study and the Nurses Health study use the lower definition and since they report an association, the effect is also likely to be present for foods with a higher percentage of wholegrain.

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Table6.2. Summary of studies of cereals and CVD

	A	B	C	D	E	F	G
1	**Reference [1]**	**Kelly Cochrane 2007 [2075]**	**Anderson ProcNutSoc 2003 [2829]**	**Pereira ArchIntMed 2004 [2464]**	**DeMoura ILSI 2008 [2574]**	**Flight Eur J Clin Nutr 2006 [212]**	**Jacobs CurrAthRep 2004 [375]**
2	**Type of study [2]**	Meta-analysis (10 RCT)	Meta-analysis (5 cohort)	Meta-analysis (10 cohort)	Systematic Review (14RCT, 9 cohort, 5 cross-sectional)	Systematic Review (9 cohort)	Systematic Review (13 cohort)
3	**Level of evidence [3]**	I	III-2	III-2	I	III-2	lll-2
4	**Intervention/ comparator [4]**	Wholegrain cereals and CHD - 8/10 studies with oats only	Wholegrains & cereal fibre and CVD	Cereal fibre and CHD	Wholegrain intake and CVD surrogate endpoints	Cereals and WG and CVD	Wholegrain and CVD
5	**N [5]**	924	77,002	336,244	20045	325303 (WG and CHD); 310278 (cereal fibre and CHD)	405,613
6	**Population/study information [6]**	M+W; USA and Finland; 30-60 years; 6 with participants with elevated cholesterol	M+W, USA, 25-69y	M+W; USA and Europe; 35-99y	M+F, 20-61y, mean BMI 19-34, in USA, Sweden, Germany, UK and Japan	M+W, US and Europe. Ages and BMI not given	M+W, US and Europe. Ages and BMI not given
7	**Quality [7]**	P	N	P	0	0	N
8	**Results [8]**	Weighted mean diff of -0.19mmol/L TC (CI: -.31 to -0,10; p=0.0001) and -0.018mmol/L LDL (CI: -0.28 to -.09; p<0.0001) oatmeal vs RG diets. Some evidence that oatmeal foods can lower TC and LDL, but need longer studies and studies with other grains.	RR Wholegrains = 0.71 (0.48;0.94). RR Cereal fibre = 0.90 (0.80-1.10)	Consumption of dietary fibre from cereals is inversely associated with risk of coronary heart disease. Each 10g increment of cereal fibre is associated with a 25% reduction in coronary deaths RR 0.75 (0.63-0.91; p=0.003)	All observational studies, regardless of grain, show a protective assoc between WG & CVD. 3 serves / day associated with 30-48% less risk. Intervention studies with oats & barley but not wheat, show up to 15-20% reduction in TC and LDL levels	Prospective epidem studies show WG foods reduce risk of CHD. Whether all grain are equal cannot be concluded from these studies, nor the effect of different parts of the grain. Many studies don't show independent effect of fibre on CHD events or deaths	All 13 studies report significant CVD risk reduction with consumption of WG foods. OR: 0.56-0.86
9	**Effect on risk (Increase/None/Protect)**	Protect (oats)	Protect	Protect	Protect	Protect	Protect
10	**Clinical importance [9]**	1	1	1	1	1	1
11	**Clinical relevance [10]**	1	1	1	1	1	1
12	**Generalisable**	Yes	Yes	Yes	Yes	Yes	Yes
13	**Applicable**	Yes	Yes	Yes	Yes	Yes	Yes

	G	H	I	J	K	L	M
1	**Jacobs CurrAthRep 2004 [375]**	**Truswell EurJClinNut 2002 [596]**	**Berg AnnNutrMetab 2003 [450]**	**Katcher AJCN 2008 [98]**	**Ortega IntJVitMinRes 2006 [191]**	**Rave BrJNutr 2007 [122]**	**Djousse ArchIntMed 2007 [2120]**
2	Systematic Review (13 cohort)	Systematic Review (36 RCT wheat fibre; 36 RCT oats; 7 cohort)	RCT	RCT	RCT	RCT	Cohort
3	III-2	II	II	II	II	II	III-2
4	Wholegrain and CVD	Cereal grains and CHD	Fat modified and calorie restricted diet with addition of 35-50g oat bran daily (providing 5g soluble fibre) incorporated in bread, sauces and desserts, for 4 weeks	Inclusion of at least 5 serves of wholegrain foods in a hypocaloric (-500kcal/d) diet - 12 week study. Size of serves not specified	20% hypocaloric diet + increased cereals (Special K cereals and bars) and other CHO for a min 3x per day). Difference achieved approx one extra serve: 4.07 to 4.94 serves per day (p<0.01) - 6 week study. Size of serves not specified	Hypoenergetic diet with 200g wholegrain based diet product (WG) made up as a drink replacing 2 meals a day to provide 21.4g dietary fibre - 8 week study	Q1 (0 serves/week) vs Q5 (7+ serves/week) of breakfast cereal;
5	405,613	36RCT wheat fibre; 38RCT oats; 7 prospective cohort studies	99	25	36	36	1018 cases Heart Failure identified over 19.6y in cohort of 21376
6	M+W, US and Europe. Ages and BMI not given	M+W; USA, Finland and Norway (cohort studies); age range not stated	German hospital: Males aged 30-65 with increased risk CVD (BMI 27.5-35 and total cholesterol >150mg/dl). Mean age 53y; mean BMI 30.	US, adults with metabolic syndrome (BMI>30 and 3 or more NCEP criteria), aged 20-65y. Mean age 45y	Spain. Women aged 20-35y with BMI 24-35 (mean 28)	Germany. Obese (BMI >29 to <40); adults aged 18-70 with elevated fasting blood glucose (6.1-7.1 mmol/L)	US Male Physicians Health Study; mean age 53.7y (range 40-86y); mean BMI 24.1-25.1
7	N	0	0	P	0	P	0
8	All 13 studies report significant CVD risk reduction with consumption of WG foods. OR: 0.56-0.86	There is no clear association between total cereal consumption and CHD. Wheat fibre does not lower cholesterol but the majority of human trials with oats found modest reduction in total and LDL cholesterol	TC: -12.0mg/dl (p<0.05); LDL -14.1mg/dl (p<0.01); ApoB -11.0mg/dl (p<0.01)	Change in C reactive protein; -2.4 vs +0.2mg/L P=0.01. No significant differences in blood lipids, PAI-1, TNF or IL-6	Significant reduction in % energy from fat (28.2 vs 32.6%; p<0.05) and increase in fibre (19.3 vs 25.1g/d; p<0.001).	No significant improvements in total, LDL or HDL cholesterol (all p>0.05)	HR for highest total breakfast cereal intake vs lowest was 0.71 (0.60-0.85). All effect was due WG cereal (HR 0.72 [0.59-0.88], not RG cereal (HR 0.83 [0.58-1,18]).
9	Protect	Protect (oats)	Protects (oat)	Protect	Protect	None	Protect
10	1	1	1	1	2	3	1
11	1	1	2	1	1	2	1
12	Yes	Yes	Yes	Uncertain	Yes	Yes	Yes
13	Yes	Yes	Yes	Yes	Yes	No	Yes

	N	O	P	Q	R
1	**Erkkila AmHeartJ 2005 [303]**	**Liu JAmCollNutr 2002 [2568]**	**Liu AJCN 2003 [2569]**	**Nettleton JADA 2008 [34]**	**Negri EJCN 2003 [497]**
2	Cohort	Cohort	Cohort (included in the Pereira review)	Cohort	Case-Control
3	III-2	III-2	III-2	III-2	III-2
4	MCAD and mean percent stenosis (%S), controlled for age, BMI, smoking, medication, HRT, diabetes, alcohol, energy intake, sat and PUFA intake, lipids and BP. Comparing <3 or >3g cereal fibre /1000cal/d. Median intake of 6 serves WG foods per week (serve s	Quintiles of intake of cereal fibre (Q1: 3g/d; Q5 6.5g/d)	Serves per week of breakfast cereals (from Never to ≥1 serve/d)	Number of serves of WG food per day (defined as 1 slice bread, 1 cup cereal or cooked grain; 1 item serve of muffin, cracker or pancake)	Tertiles of cereal fibre derived from various food groups in diet
5	248 followed for 3.2y	570 incident cases of CVD in cohort of 38480 followed 6 years	3114 total deaths (1381 due to CVD; 146 due to stroke) in cohort of 86190 followed 5.5y	1140 cases of incident Heart Failure, in cohort of 14,153 followed 13.3y	507 cases; 478 controls
6	US. Postmenopausal women; mean age 65±6y, with established CAD, in the ERAT trial	USA; Women's Health Study; women aged 45-75y (men 54) BMI: 26	US Physicians Health Study; males, aged 40-84y	US, ARIC study; M+W; aged 45-64y	Italy; patients with first episode of non-fatal acute myocardial infarction (AMI) admitted to a network of Milan hospitals 1995-1999; M+W 25-79y mean age 61y
7	P	P	P	0	P
8	Change in MCAD was smaller in women with higher cereal fibre intake (-0.04±0.02 vs -0.09±0.02). Non significant trend to lower change in %S. Effect was found with WG but not RG	RR of Incident CVD, adjusted for age, smoking, PA, alcohol, HRT, smoking, BMI, vitamin supplements, Hx MI and energy intake was 1.11 (0.84-1.46) p=0.38. Total fibre but not cereal fibre inversely associated	CVD specific mortality inversely associated with WG (but not refined grain) breakfast cereal intake. RR WG cereals = 0.80(0.66-0.97; p=0.008); RR Refined grain cereals = 1.04 (0.84-1.27; p=0.37)	Whole grain intake was significantly less in those with incident HF (p<0.001). HR for 1 serving per day of WG cereal was 0.92 (0.86-0.98) p<0.05	OR of AMI by tertile of cereal fibre intake; 1.12 (0.71-1.77). Fruit but not cereal or vegetable fibre associated with reduced risk of AMI
9	Protect	None	Protect (WG); None (RG)	Protect	None
10	1	3	1	1	2
11	2	1	1	1	1
12	Yes	Yes	Yes	Yes	Yes
13	Yes	Yes	Yes	Yes	Yes

6.5 CEREALS and OBESITY

Does a particular intake of cereal foods affect the risk of weight gain and obesity in adults?		
Evidence Statement		Consumption of 3-5 serves per day of cereal foods (mainly wholegrain) is associated with a reduced risk of weight gain (Note: original evidence statement has been merged with the following statement in the Dietary Guidelines- the original wording stated: Consumption of 5 serves per day of cereal foods (mainly wholegrain) is associated with a reduced risk of weight gain.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	1 Level I study (reviewing 11 RTCs, 8 cohort and 17 cross-sectional studies); 8 Level II studies; 2 Level III studies with low risk of bias.
Consistency	Satisfactory	Some inconsistency. Mostly favourable effect of all cereal foods (7 Protect; 4 No effect; 0 Increase).
Clinical impact	Satisfactory	Moderately protective OR of all cereals in cohort studies approximately 0.80 for significant weight gain.
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to Australian healthcare context with few caveats.
**** Note:*** One serve of cereal defined as 1 slice bread, 1 cup cereal or cooked grain; 1 item serve of muffin, cracker or pancake.		

The studies used to make the body of evidence statements are listed below and summarised in Table 6.3. The nine RCTs are all for limited time periods and mostly use wholegrain foods. The three reviews of cohort and cross-sectional studies (de la Hunty 2007, Harland 2008, and Williams 2008) all conclude that there is an association between cereal intake and reduced risk of weight gain or overweight. In the Multiple Risk Factor Intervention trial those achieved the greatest weight loss were those who had the largest increases in bread and cereal consumption, and in the EPIC study, bread and cereal consumption significantly predicted weight loss (Williams 2008). A study of at least five serves per day of wholegrain foods in a hypocaloric diet led to significantly greater reduction of abdominal body fat, but there have been no studies since 2002 examining the effect of higher intakes.

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6.6 CEREALS and OBESITY

Does a particular intake of refined and wholegrain forms of cereals affect the risk of weight gain and obesity in adults?		
Evidence Statement		(Note: original evidence statement has been merged with the previous statement and grading increased from C to B in the Dietary Guidelines- the original wording stated: Consumption of 3 serves of wholegrain cereals per day is associated with a reduced risk of weight gain*).
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	1 Level I study (reviewing 11 RTCs, 8 cohort and 17 cross-sectional studies); 5 Level II studies; 2 Level III studies with low risk of bias.
Consistency	Satisfactory	Some inconsistency. Mostly favourable effect of wholegrain cereals (6 Protect; 2 No effect; 0 Increase). Only 3 studies report refined grain effect: 1 Increase; 2 no effect.
Clinical impact	Satisfactory	Moderately protective OR of wholegrain in cohort studies approximately 0.80 for significant weight gain. Effect in short term studies ranges 0-1.3kg greater loss in weight loss diet over 3 months. Possible increased risk of significant weight gain with high intake of refined cereals.
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to Australian healthcare context with few caveats. * ***Note***: One serve of cereal defined as 1 slice bread, 1 cup cereal or cooked grain; 1 item serve of muffin, cracker or pancake.

The studies used to make the body of evidence statements are listed below and summarised in Table 6.3. The meta-analysis of 11 cohort studies on the relationship between wholegrain consumption and body reported a mean BMI reduction of 0.63 between highest (≥3 serves per day) and lowest intakes of wholegrain foods (Harland 2008). There is not sufficient data to evaluate the effect of lower levels of intake. There is no evidence that changing from refined to wholegrain foods without energy restriction will lead to weight loss, but a study of at least 5 serves per day of cereals foods in a hypocaloric diet led to significantly greater reduction of abdominal body fat with wholegrain vs refined grain cereals (Katcher 2008). There are insufficient studies to make an evidence statement related to the effect of consumption of refined cereals.

In the 2007 World Cancer Research Fund Report, the following statements were made about Cereal Foods and Obesity (which are consistent with an Evidence Statement about wholegrain cereals):

Wholegrain cereals and cereal products

Wholegrain cereals and cereal products are assessed here as high-fibre foods and as a marker for low energy-dense foods. For this reason no separate judgement is made for wholegrain cereals and cereal products.

The evidence, compelling on physiological grounds and supported by experimental and observational evidence, is for diets with plenty of low energy-dense foods to limit weight gain.

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Table 6.3 Summary of studies of cereals and obesity

	A	B	C	D	E	F	G
1	**Reference [1]**	**de La Hunty NutBull 2007 [2036]**	**Harland Pub Health Nutr 2008 [64]**	**Williams Nutr Rev 2008**	**Andersson J Nutr 2007 [166]**	**Aston Int J Obes 2008 [570]**	**Behall J Am Diet Assoc 2006 [971]**
2	**Type of study [2]**	Systematic Review (1RCT, 1 cohort, 3 cross-sectional)	Meta-analysis (11 cohort)	Systematic Review (11 RCT, 8 cohort, 17 cross-sectional)	RCT	RCT	RCT
3	**Level of evidence [3]**	III-2	III-2	1	II	II	II
4	**Intervention/ comparator [4]**	Regular breakfast cereal consumption and BMI	Wholegrain consumption and measure of body weight	Cereal consumption and measures of body weight	Two six week periods of diet intervention including 7 serves per day of wholegrain (>50%) or refined grain products (3 bread slices, 2 crispbread slices, 1 portion muesli, 1 portion pasta)	Two 12-week periods with high or low GI foods in habitual diet (mean diff 28 GI units inl foods provided -bread, breakfast cereals, rice, pasta, potatoes). Target diff 12 GI units	AHA Step 1 diet for 2 weeks, followed by three 5-week periods of diets with same total fiber but different grain sources: 20% energy (1) whole wheat and brown rice, (2) half barley & half whole wheat and brown rice, or (3) barley only
5	**N [5]**	49,519	119,829	129,047 (8 cohort);790 (11 RCT)	30	19	25
6	**Population/study information [6]**	M+F; USA, UK, Spain, France; 43,642 adults 19-84y 5887 children 4-15; rarely or never eat - daily consumers	M+F; US, UK, Scandinavia, Iran; Age 13-98y,	M+W healthy or overweight adults in intervention studies in US and Europe and Australia	M+F; 35-70y; BMI 26-35 in Sweden	Women 34-65y BMI>25 and fasting plasma insulin >50pmol/L, weight stable in UK	US M+W Healthy subjects (7 men, 9 premenopausal women, 9 postmenopausal women) mean ages 43y, 47y, 50y respectively
7	**Quality [7]**	0	P	P	P	P	P
8	**Results [8]**	Consistent assoc between breakfast cereal consumption and a healthy weight (5/5 for increased risk of BMA>25; 4/5 for increased BMI), but limited evidence on a proposed mechanism that suggest causality	Mean BMI reduction of 0.63 (CI: 0.46-0.80), p<0.001, between lowest and highest intakes of WG; WC was reduced by 2.7 (0.2,5.2)cm (p<0.03); WHR was reduced by 0.023 (0.016,0.030), p<0.0001).	Cohorts show WG help reduce weight gain. High RG may cause WC increases in women. Nurses Health: more RG likely to become obese (OR1.18;p<0.0001) or major weight gain (OR1.26;p=0.04). No evidence changing RG to WG w/o energy restriction leads to wt loss.	No evidence of significant benefit of WG substitution on BMI in healthy moderately overweight adults (BMI change over 6 weeks; 0.3 vs 0.2kg; p=0.046)	No evidence of beneficial effect of change to low GI cereals on body weight, waist circumference % body fat, or satiety.	Increase consumption of wholegrain diets from insoluble or soluble sources resulted in greater decreases in body weight (-0.8kg in 5 weeks; p<0.05)
9	**Effect on risk (Increase/None/Protect)**	Protect	Protect	Protect (WG); Possible effect (RG)	None	None	Protect
10	**Clinical importance [9]**	2	1	2	4	4	1
11	**Clinical relevance [10]**	1	1	1	2	1	2
12	**Generalisable**	Yes	Yes	Yes	Yes	Yes	Yes
13	**Applicable**	Yes	Yes	No	No	Yes	Yes

	H	I	J	K	L	M	N
1	**Freeland Appetite 2009 [1609]**	**Gilhooly Aging Clin Exp Res 2008 [2]**	**Hallfrisch Nutr Res 2003 [923]**	**Hamedani Am J Clin Nutr 2009 [2693]**	**Katcher Am J Clin Nutr 2008 [98]**	**Lightowler Nutr Bull 2009 [2731]**	**Ortega Int J Vit Min Res 2006 [191]**
2	RCT	RCT	RCT	RCT	RCT	RCT	RCT
3	II	II	II	II	II	II	II
4	Breakfast of high fibre wheat cereal (90g providing 41g fibre) made up in liquid with oil and whey vs Low Fibre control - 2 hour study	20g extra dietary fibre per day from a high wheat fibre breakfast cereal, in a 30% calorie restricted diet (total 44g fibre per day). All food provided for first 24 weeks	AHA Step 1 diet for 2 weeks then three 5-week periods with different WG: (1) whole wheat and brown rice (soluble fibre from barley), (2) half barley & half whole wheat and brown rice (extra 3g soluble fibre), or (3) barley(extra 6g soluble fibre)	60 g serve of high fibre cereal (28g) served with 250mL milk after overnight fast; followed 3 h later with ad lib pizza meal (vs low fibre cereal) - 4.5h study	Inclusion of at least 5 serves of wholegrain foods in a hypocaloric (-500kcal/d) diet - 12 week study	2 x 45g serves/d of low fibre (1.7g) cereal (1 for breakfast; 1 for lunch) with 125mL low fat milk for 2 weeks; then breakfast only for further 6 weeks. Ad lib rest of the day. Comparisons had choice of 3 cereals: 1 low fibre and 2 higher	20% hypocaloric diet with increased consumption of cereals (Special K cereal and bars) and other CHO for a min 3x per day). Difference achieved approx one extra serve: 4.07 to 4.94 serves per day (p<0.01) - vs extra consumption of vegetables (3 serves/d)
5	17	16	21	32	25	23	36
6	Canadian healthy non smoking males ages 18-35y (mean 25) with BMI 20-27 (mean 23.4)	US; Healthy overweight (BMI 25-30) men and women aged 20-42y	US 16 men mean age 47±10y; mean BMI 26.7; BP: 120/74 and mildly hypercholesterolemic	Canada; Healthy M+W adults aged 20-26y with normal BMI and not restrained eaters	US; M+W, mean age 46y, BMI 36	UK: 54 Healthy overweight subjects 20-60 years (mean 45) with BMI 25-35 (19M; 35W)	Spanish women aged 20-35y with BMI 24-35
7	P	P	N	P	P	0	0
8	A serving of 41g insoluble fibre at breakfast reduces food intake independently of volume and weight at 60 minutes (0.9Mj; p=0.004) but this effect is not maintained at 120minutes (0.1Mj; p=0.2). Hunger and fullness did not differ between treatments.	No significant difference between groups in energy intake (p=0.51) or weight change (p=0.96) or satisfaction with amount of food (p=0.08)	No evidence of effect of grain type on weight over 5 week period (p>0.05)	A HF breakfast supports cumulative reduction in energy intake (-92kcal at breakfast and lunch; p=0.01) and higher satiety value per kilojoule (-17 vs -10; p<0.01)	Significantly greater decreases in abdominal body fat % with WG vs RG (-2.2 vs -0.9; p=0.03) over 12 week period	Loss of >1kg in 53% all subjects at 2 weeks. Greater loss at 6 weeks in variety cereal group compared to single cereal (-0.6kg vs -2.0kg) and sig change from baseline at 6 weeks in VC group (p<0.01). Significant difference in waist circumference from base	Increased consumption of low fibre breakfast cereals in hypocaloric diet may reduce percentage energy from fat in the diet to a greater extent than increasing vegetable intake (28.2% vs 32.6%; p<0.05), but had no effect on W:H ratio or skinfolds
9	Protect	None	None	Protect	Protect	Protect	None
10	3	3	2	1	1	2	3
11	2	2	1	1	1	1	2
12	Yes	No	Yes	Yes	Yes	Yes	Yes
13	Yes	No	Yes	Yes	Yes	No	Yes

	O	P	Q	R
1	**Ortega Eur J Clin Nutr 2007 [187]**	**Rodgriguez Pub Health Nutr 2009 [14]**	**Waller J Am Coll Nutr 2004 [387]**	**Huus Acta Pediatr 2009 [1]**
2	RCT	RCT	RCT	Cohort
3	II	II	II	III-2
4	20% hypocaloric diet with increased consumption of cereals (Special K cereal and bars) and other CHO for a min 3x per day). Difference achieved approx one extra serve: 4.07 to 4.94 serves per day (p<0.01) - vs extra consumption of vegetables (3 serves/d)	Hypoenergetic diet (20% deficit) with increased consumption of WG cereals (cereal at breakfast and dinner, plus a cereal bar as mid-morning snack) - versus extra 3 serves of vegetables in controls - 6 weeks study	Subjects instructed to eat 1 cup of RTEC with 2/3 cup low fat milk, at least 90 minutes after dinner (from a selection of Kellogg cereals providing 1.0-1.5g dietary fibre per cup) - controls continued normal diet - 4 weeks study	Highest (Daily) vs lowest (<1x/week) consumption of porridge and risk of overweight over 2.5y
5	36	29	29	7,356
6	Spanish women aged 20-35y with BMI 24-35	Spanish women aged 20-35y with BMI 24-35	US adults aged 18-65y, BMI ≥25, who endorsed a question that snacking after dinner contributed to their weight problem	Sweden; Children recruited to the ABIS (All babies in SE Sweden) study from 1997-1999; studied at age 5
7	0	P	0	0
8	Both groups lost weight but the cereal group lost significantly more weight over 6 weeks (-2.8 vs -2.0kg; p<0.001)	Subjective feelings of satiety were better on the cereal vs vegetable supplemented diet (0.3 vs 0.2 cm/kcal; p=0.006). Higher cereal content may assist in compliance to low energy diet	There was a trend to more weight loss with compliers but not statistically significant (-1.85 vs 1.17 kg over 4 weeks; p=0.06).	Consumption of porridge daily at age 2.5y was negatively associated with being overweight or obese at age 5y (OR 0.55: 0.36-0.85)
9	Protect	Protect	None	Protect
10	2	2	3	1
11	1	5	1	2
12	Yes	Yes	No	Yes
13	Yes	Yes	No	Yes

6.7 CEREALS and TYPE 2 DIABETES

Is the consumption of particular levels of cereal foods beneficial or detrimental with respect to Type 2 Diabetes in adults?		
Evidence Statement		Consumption of cereal foods (especially 3 serves a day of wholegrains) is associated with reduced risk of type 2 diabetes (Note was combined with following evidence statement in the Dietary Guidelines: the original wording was: Consumption of cereal foods (especially wholegrains) is associated with reduced risk of Type 2 Diabetes).
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	1 Level I study (reviewing 9 RCTS, 6 cohort and 5 cross-sectional); 4 Level II studies (surrogate outcomes only); 6 Level III studies.
Consistency	Good	Most studies consistent (8 Protect; 2 No effect; 1 increased risk with white bread only).
Clinical impact	Good	Moderately protective OR of wholegrain from 0.57-0.85 in reviews and cohort studies and 0.38 for total grain. No significant effect with refined grain.
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to Australian healthcare context with few caveats.

The studies used to make the body of evidence statements are listed below and summarised in Table 6.4. Most of the studies have examined wholegrain rather than total cereal intakes and all four systematic reviews conclude that intake of wholegrain is inversely associated with type 2 diabetes risk. One US cohort study reported a lower incidence of type 2 diabetes in those with the highest quintile of fibre intake for all cereal sources (Krishnan et al. 2007). One Australia study reports no relationship between numbers of cereal serves per week and incidence of type 2 diabetes (Hodge et al. 2004). The few RCTs have mostly examined effects on insulin and other surrogate markers, with variable results, rather than incidence.

References

Andersson, A., Tengblad, S., Karlstrom, B., Kamal-Eldin, A., Landberg, R., Basu, S. et al. 2007, "Whole-grain foods do not affect insulin sensitivity or markers of lipid peroxidation and

inflammation in healthy, moderately overweight subjects", *Journal of Nutrition*, vol. 137, no. 6, pp. 1401-7.

De Moura, F. 2008, "Whole grain intake and cardiovascular disease and whole grain intake and diabetes review", Life Sciences Research Office, Bethesda MA.

de Munter, J., Hu, F., Spiegelman, D., Franz, M., van Dam, R. 2007, "Whole grain, bran, and germ intake and risk of type 2 diabetes: a prospective cohort study and systematic review", *PLoS Medicine / Public Library of Science*, vol. 4, no. 8, pp. e261. (Note: contains systematic review *and* prospective cohort study).

Henry, C., Lightowler, H., Tydeman, E., Skeath, R. 2006, "Use of low-glycaemic index bread to reduce 24-h blood glucose: implications for dietary advice to non-diabetic and diabetic subjects", *International Journal of Food Sciences & Nutrition,* vol. 57, no. 3-4, pp. 273-8.

Hodge, A., English, D., O'Dea K. & Giles, G. 2004, "Glycemic index and dietary fiber and the risk of type 2 diabetes", *Diabetes Care*, vol. 27, no. 11, pp.2701-6.

Krishnan, S., Rosenberg, L., Singer, M., Hu, F., Djousse, L., Cupples, L. et al. 2007, "Glycemic index, glycemic load, and cereal fiber intake and risk of type 2 diabetes in US black women", *Archives of Internal Medicine*, vol. 167, no. 21, pp. 2304-9.

Pereira, M., Jacobs, D., Pins, J., Raatz, S., Gross, M., Slavin, J. et al. 2002, "Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults", *American Journal of Clinical Nutrition,* vol. 75, no. 5, pp. 848-855.

Priebe, M., van Binsbergen, J., de Vos, R., Vonk R. 2008, "Whole grain foods for the prevention of type 2 diabetes mellitus", *Cochrane Database of Systematic Reviews,* vol. 1.

Rave, K., Roggen, K. Dellweg, S., Heise, T. & Tom Dieck, H.,2007, "Improvement of insulin resistance after diet with a whole-grain based dietary product: results of a randomized, controlled cross-over study in obese subjects with elevated fasting blood glucose", *British Journal of Nutrition*, vol. 98, no. 5, pp.929-36.

Venn, B. & Mann J. 2004, "Cereal grains, legumes and diabetes", *European Journal of Clinical Nutrition*, vol. 58, no. 11, pp. 1443-61.

6.8 CEREALS and TYPE 2 DIABETES

Is there an association between intakes of refined and wholegrain forms of cereals and reduced risk of Type 2 Diabetes in adults?		
Evidence Statement		. (Note- this evidence statement has been combined with the previous statement in the Dietary Guidelines. Original statement was:Consumption of 3 serves per day of wholegrain cereals is associated with reduced risk of Type 2 Diabetes)
Grade		**C**
Component	**Rating**	**Notes**
Evidence Base	Good	1 Level I study (reviewing 9 RCTS, 6 cohort and 5 cross-sectional); 4 Level II studies (surrogate outcomes only); 6 Level III studies.
Consistency	Satisfactory	Most studies consistent about wholegrain (9 Protect; 2 No effect). Less consistent about refined grain.
Clinical impact	Good	Moderately protective OR of wholegrain from 0.57-0.85 in reviews and cohort studies. Two show no significant effect with refined grain - one protective (OR 0.69) and one increased risk (OR 1.11).
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to Australian healthcare context with few caveats.

The studies used to make the body of evidence statements are listed below and summarised in Table 6.4. All four systematic reviews support the protective effect of wholegrains and that the risk reduction is evident even when foods with as little as 25% whole grain are consumed (Venn and Mann 2004). The most recent concluded that, while the evidence is suggestive rather than conclusive, overall epidemiological studies show a 21-42% reduction in the incidence of type 2 diabetes associated with the consumption of 3 serves of wholegrain per day (DeMoura 2008). There were only four studies that provided data on the effect of refined cereals; the results were contradictory and too few to make an Evidence Statement.

References

Andersson, A., Tengblad, S., Karlstrom, B., Kamal-Eldin, A., Landberg, R., Basu, S. et al. 2007, "Whole-grain foods do not affect insulin sensitivity or markers of lipid peroxidation and inflammation in healthy, moderately overweight subjects", *Journal of Nutrition*, vol. 137, no. 6, pp. 1401-7.

De Moura, F. 2008, "Whole grain intake and cardiovascular disease and whole grain intake and diabetes review", Life Sciences Research Office, Bethesda MA.

de Munter, J., Hu, F., Spiegelman, D., Franz, M., van Dam, R. 2007, "Whole grain, bran, and germ intake and risk of type 2 diabetes: a prospective cohort study and systematic review", *PLoS Medicine / Public Library of Science*, vol. 4, no. 8, pp. e261. (Note: contains systematic review *and* prospective cohort study).

Henry, C., Lightowler, H., Tydeman, E., Skeath, R. 2006, "Use of low-glycaemic index bread to reduce 24-h blood glucose: implications for dietary advice to non-diabetic and diabetic subjects", *International Journal of Food Sciences & Nutrition,* vol. 57, no. 3-4, pp. 273-8.

Hodge, A., English, D., O'Dea K. & Giles, G. 2004, "Glycemic index and dietary fiber and the risk of type 2 diabetes", *Diabetes Care*, vol. 27, no. 11, pp.2701-6.

Krishnan, S., Rosenberg, L., Singer, M., Hu, F., Djousse, L., Cupples, L. et al. 2007, "Glycemic index, glycemic load, and cereal fiber intake and risk of type 2 diabetes in US black women", *Archives of Internal Medicine*, vol. 167, no. 21, pp. 2304-9.

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Rave, K., Roggen, K. Dellweg, S., Heise, T. & Tom Dieck, H.,2007, "Improvement of insulin resistance after diet with a whole-grain based dietary product: results of a randomized, controlled cross-over study in obese subjects with elevated fasting blood glucose", *British Journal of Nutrition*, vol. 98, no. 5, pp.929-36.

Venn, B. & Mann J. 2004, "Cereal grains, legumes and diabetes", *European Journal of Clinical Nutrition*, vol. 58, no. 11, pp. 1443-61.

Table 6.4 Summary of studies of cereals and Type 2 Diabetes

	A	B	C	D	E	F
1	**Reference [1]**	**DeMunter PLOSMed 2007 [136]**	**Priebe Cochrane 2008 [882]**	**DeMoura ILSI 2008 [2574]**	**Venn EJCN 2004 [370]**	**Andersson JNutr 2007 [166]**
2	**Type of study [2]**	Systematic Review (5 cohort)	Systematic Review (1 RCT and 11 cohort)	Systematic Review (9 RCT; 6 cohort; 5 cross-sectional)	Systematic Review (4 cohort studies)	RCT
3	**Level of evidence [3]**	III-2	III-2	1	III-2	II
4	**Intervention/ comparator [4]**	Whole grain intake and T2D	Wholegrain intake and T2D	Wholegrain intake and T2D surrogate endpoints	Wholegrain intake and T2D	Two six week periods of diet intervention including 7 serves per day of wholegrain (>50%) or refined grain products (3 bread slices, 2 crispbread slices, 1 portion muesli, 1 portion pasta) vs energy matched refined grain diet
5	**N [5]**	286,126	335,061	373,703	158,723	30
6	**Population/study information [6]**	M+W; USA and Finland; Aged 21-75y	M+W, USA and Finland; 21-75y; freeliving persons without pre-existing diabetes	M+F, 20-61y, BMI 19-88, in USA, Sweden, Finland, Canada, Slovakia, Germany, and UK	M+W; USA and Finland	Sweden; M+F; 35-70y; BMI 26-35
7	**Quality [7]**	P	P	0	0	P
8	**Results [8]**	A two-serving per day increment in wholegrain consumption was associated with a 21% decrease in the risk of T2DM after adjustment for potential confounders and BMI	36% of studies did not adjust for relevant confounders. Intake of WG inversely associated with T2DM risk with RR from 0.67-0.79 (95%CI 0.65-0.96). Intake of cereal fibre was also inversely associated: RR 0.37-0.79. All studies showed effect in same direct	Evidence on WG and T2DM is suggestive but inconclusive. Short term studies of WG & insulin response are inconsistent. Overall, epidemiological studies show a 21-42% reduction in the incidence of T2D associated with the consumption of 3 serves WG/d	Highest vs lowest intakes of WG, RR of developing T2D ranges from 0.65 to 0.73. Strong evidence that a variety of WGs helps in prevention and treatment of T2DM. Not clear which components of WG are responsible but WG has benefits beyond effect of fibre	After 6 weeks there was no significant difference between test and controls in insulin sensitivity (6.5 vs 6.9 M/I; p=0.79) or blood glucose (5.3 vs 5.2 mmol/L; p=0,28)
9	**Effect on risk (Increase/None/Protect)**	Protect	Protect	Protect	Protect	None
10	**Clinical importance [9]**	1	1	1	1	4
11	**Clinical relevance [10]**	1	1	1	1	2
12	**Generalisable**	Yes	Yes	Yes	Yes	Yes
13	**Applicable**	Yes	Yes	Yes	Yes	No

	G	H	I	J	K	L
1	**Henry IntJFoodSciNutr 2006 [201]**	**Pereira AJCN 2002 [2192]**	**Rave BrJNutr 2009 [122]**	**deMunter PLOSMed 2007 [136]**	**Hodge Diab Care 2004 [372]**	**Krishnan ArchIntMed 2007 [108]**
2	RCT	RCT	RCT	Cohort	Cohort	Cohort
3	II	II	II	III-2	III-2	III-2
4	Changing type of bread in diet to low glycemic index multi-seed (54 or 49) versus white bread (GI=71) in control; all other food provided and identical - 2 day study	An isoenergetic diet containing 6-10 servings of wholegrain foods - providing 28.0g fibre/d vs 6-10 serves refined grain (18.8g fibre/d) - 12 week study	Hypoenergetic diet with 200g wholegrain based diet product (WG) made up as a drink replacing 2 meals a day to provide 21.4g dietary fibre vs meal replacement drink with same fibre using mostly inulin - 8 week study	Quintiles of Wholegrain intake (3.2 - 45.6g/d) and incidence of T2D	Quartiles of numbers of serves per week. Q5 ≥7 serves white bread or ≥41 serves cereals/week; Q1 <0.5 serves white bread or <20 serves cereals per week	Quintiles of cereal fibre: Q5: 7.6g/d - Q1:1.7g/d
5	10	12	36	4747 incident cases in cohort of 161737 over 18y	365 incident cases of T2D in cohort of 31641 over 4 years	1938 incident cases T2D in cohort of 40078 over 8 years
6	UK: healthy Caucasians (5 males; 5 females); mean age 23; mean BMI 22.7	US: Healthy overweight or obese adults 21-65y, BMI 26-36 free of diabetes or CVD	Germany: Obese (BMI >29 to <40); adults aged 18-70 with elevated fasting blood glucose (6.1-7.1 mmol/L)	US: Women aged 37-65y in Nurses Health Study 1, 26-46y	Australia: Melbourne Collaborative Cohort Study. M+W, aged 40-69y without diabetes; BMI 25-8-26.6	US Women in Black Women's Health Study; aged 21-69y (median 38y); approx 30% with BMI >30
7	0	P	P	P	P	P
8	No impact of change to low GI bread choices on 24-h mean glucose in healthy young adults. Int vs Control: 4.4 vs 4.8 mmol/L; p=0.135	Fasting insulin was 10% lower during consumption of wholegrain vs refined grain. (mean difference -15±5.5 pmol/L; p=0.03. Improved insulin sensitivity on WG: rate of glucose infusion higher by $0.07x10^{-4}$ mmol/kg/min/pmol/L (CI: 0.003 -0.144)	HOMA-IR score showed better improvement after WG diet (-1.0 vs +4.3; p=0.049)	After multiple adjustment, RR (Q5 vs Q1) was 0.75 (0.68-0.83) in NHS1, and 0.86 (0.72-1.02) in NHS2. Similar results for bran and germ. RR for 40g increment in WG (= difference between 5th and 95th%) was 0.70 (0.62-0.79) in NHS1 and 0.83 (0.70-0.98).	OR Q4vsQ1: cereal: 1.05 (0.73-1.52), white bread 1.13(0.86-1.50). OR increase of one serve white bread per week 1.11 (1.02-1.22)	IRR: 0.82 (0.70-0.96); p=0.01
9	None	Protect	Protect	Protect	None (total cereals); Increase (White bread)	Protect
10	3	1	1	2	2	1
11	5	2	2	1	1	1
12	No	Yes	Yes	Yes	Yes	No
13	Yes	Yes	No	Yes	Yes	Yes

Summary of studies not included in Body of Evidence statements

The following diet-health relationships had too few studies to develop a body of evidence statement.

Cereals and Bone Mineral Density

One RCT (positive quality), a sub-study of a three year wheat bran fibre trial (n=113), found no significant differences in bone loss over three years with 13g more fibre per day (Chen 2004).

One Cross-sectional US study with men aged 69 yrs+ using cluster analysis found men in fruit/veg/cereal group had significantly higher bone mineral density (Tucker 2002).

Cereals and Blood Pressure

Two RCTs (positive quality) examining effect of oat supplementation. No significant effect of 14 g of fibre from oats (vs wheat) on 24h ambulatory BP in 18 subjects with elevated BP (Davy 2002). In a study with 43 hypertensive patients on medication, 2 serves of oats/day led to greater reduction in medication than two serves of wheat cereal (Pins 2002).

Cereals and Stroke

Two cohort studies of positive quality. In an ARIC study of 11,940 US adults, there was no association of either wholegrains or refined grains with ischemic stroke incidence (Steffen 2003). In the Nurses Health Study (78,770 US females), highest vs lowest cereal fibre quintile was associated with reduced of risk hemorrhagic (RR=0.51), but not ischemic, stroke (Oh 2005).

Cereals and Mental Health

One Finnish cross-sectional study of 6243 adults reported no association between mental health scores and consumption of dark bread or porridge cereals (Sarlio-Larteenkorva 2004).

Cereals and Dental Health

One cohort study (the US Health Professionals Follow-Up Study of 31,160 adults) found the risk of periodontitis was negatively associated with consumption of wholegrains and cereal fibre (RR=0.77). There was no association with refined grain consumption (Merchant 2006).

Cereals and Asthma

Two cross-sectional studies. One positive quality Dutch study of 598 children aged 8-13 yrs reported intake of wholegrains was inversely associated with asthma: OR=0.43 (Tabak 2006). One negative quality Indian study of 3000 children aged 6-14 yrs reported increased risk of wheeze or asthma with consumption of pasta or noodles at least once a week (OR=2.99), but no other cereal foods were reported (Awasthi 2004).

Cereals and High Iron Stores

One cross-sectional study (Framingham Heart Study) of 614 IS adults reported consumption of at least seven serves of wholegrains per week was inversely associated with high iron stores: OR=0.23 (Fleming 2002).

Cereals and Bowel Function

Two RCTs conducted in Finland with high fibre rye bread (compared to low fibre white wheat bread) reported rye bread improved transit time and stool frequency and consistency (Grasten 2007; Hongisto 2006).

Cereals and type 2 diabetes

One US cohort study (Diabetes Autoimmunity Study of the Young), examining 34 incident cases of Islet Autoimmunity in a cohort of 1183 children at increased risk of DM, reported first exposure of children to any cereal between one to three months or after six months increased risk - but not with exposure in the four to six month period (Norris 2003).

Cereals and Breast Cancer

One positive quality Danish cohort study of 25 278 postmenopausal women reported no relationship between incidence of breast cancer and intakes of rye, oatmeal or wholegrain bread (Egeberg 2009).

One positive quality Italian case-control study of 5783 women used principal component analysis and identified five dietary patterns. The group with highest bread and pasta consumption had highest risk of breast cancer OR=1.23 (Edefonti 2009).

Cereals and Prostate Cancer

Four case-control studies; two report some increased risk, two report no association.

- Australian study with 993 subjects using principal component analysis reported increased OR with Western Diet pattern (with high intake of white bread), but many cereals in other diet patterns too (Ambrosini 2008).
- One Italian study with 650 subjects using logistic regression models reported no association with cereal or bread consumption (Gallus 2007).
- Another Italian study with 1369 cases and 14 351 controls reported significant increased risk with highest vs lowest quintile consumption of bread (OR-1.69), but no association with rice or pasta (Bravi 2006).
- A Jamaican study of 408 men reported no relationship with consumption of white bread or refined cereals (Jackson 2009).

Cereals and Renal Cell Cancer

Three case-control studies.

- One US study with 672 subjects reported increased highest quartile consumption of white bread was associated with higher risk in women but not men. No association with rye or wholewheat breads (Dolwik-Grieb 2009).
- One Italian study with 2301 subjects reported no trend in risk across quintiles of fibre intake from grains (Galeone 2007).
- Another Italian study of the same 2301 subjects using logistic regression reported a significant risk trend across quintiles of consumption of bread (OR=1.94) and pasta and rice (OR1.29) (Bravi 2006).

Cereals and Gastric Cancer

One cohort study in 10 European countries with 312 incident gastric adenocarcinomas by quartiles of cereal fibre intake found a possible protective effect of cereal fibre (HR=0.69) but not vegetable or fruit fibre (Mendez 2007).

One Polish case-control study 837 subjects reported increased risk with refined grain consumption (OR=1.89) but not with wholegrains (Lissowska 2004).

Cereals and Aerodigestive Cancer

One US cohort study (Iowa Women's Health Study) reported a significant protective association with wholegrain consumption between highest and lowest tertiles (OR=0.53) but not with refined grain consumption (Kasum 2002).

Cereals and Thyroid Cancer

One neutral quality Greek case-control study with 251 subjects reported a protective association between pasta intake and risk of thyroid cancer, with OR=0.76 with pasta consumption at least four times per month (Markaki 2003).

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7. LEGUMES (S1.1)

Evidence Statements

7. LEGUMES (S1.1)

Search results

The initial search of the databases included 1259 references for legumes; of these 952 mapped to soy and 265 mapped to legumes and the specified disease outcomes. Many of the studies concerned isoflavone protein isolates which were excluded because they do not pertain to legume foods. The detailed search is included in a separate document on searches. In all, 28 references concerning legumes had data extracted and 15 papers were used to form the body of evidence statements for legumes. Sufficient evidence was found to make statements for legumes and cancer (breast and prostate and colorectal) and legumes and cholesterol.

7.1 LEGUMES and BREAST CANCER

Does a particular intake of legumes affect the risk of breast cancer?		
Evidence statement		Consumption of legumes, especially soy foods, is associated with reduced risk of breast cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level II and III evidence from 1 x RCT study with low risk of bias and 5 x III-2 studies (2 meta analyses of cohorts/case controls (medium risk bias), 2 cohort, 1 case-control) Most studies soy.
Consistency	Good	Some inconsistency but mostly protective effect including 2 meta analyses, 1 case control and 1 cohort. RCT and other cohort no effect.
Clinical impact	Satisfactory	Moderate clinical impact RR 0.45 to 0.86.
Generalisability	Good	Range of populations both pre and post menopausal women.
Applicability	Satisfactory	Many studies conducted in Asian countries with higher consumption of legumes, especially soy foods.

Both meta analyses found a protective effect but Trock et al. (2006) caution the effect is modest. The RCT showed no effect, however only an unproven surrogate of breast density was used. In the cohort study finding no effect in Japanese women, some limitations of the food frequency questions may have lead to misclassification of the intake group. The World Cancer Research Fund reported no convincing or probable protection from foods.

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Table 7.1 Summary of studies of legumes and breast cancer

Reference [1]	**Trock 2006 [1025]**	**Qin 2006 [7]**	**Maskarinec et al. 2004 [613]**	**Kim et al. 2008 [26]**	**Nishio et al. 2007 [118]**	**Wu et al. 2008 [52]**
Type of study [2]	Meta-analysis of 6 cohorts /12 case-control	Meta-analysis of 7 cohort/ 14 case-control	RCT	case control	cohort	cohort
Level of evidence [3]	III-2	III-2	II	III-2	III-2	III-2
Intervention/ comparator [4]	No/low vs high soy protein intake and breast cancer.	Low vs high soyfood (or isoflavone) consumption and breast cancer.	Intake of 2 daily servings of soy foods (a serving equated to products providing ~ 25 mg isoflavones) versus usual diet and breast density.	Quintiles of tofu and soy intake Quintiles of soy protein: quintile 1 (<4.24 g per day), quintile 2 (4.25-6.34 g per day), quintile 3 (6.35-8.09 g per day), quintile 4 (8.10-10.54 g per day), quintile 5 (≥ 10.55 g per day) and breast cancer).	Soy intake - tertiles (tofu: ≤ 2 per week; 3-4 per week; almost daily) (boiled beans: almost never; 1-2 per month; ≥ 1 per week) (miso soup: not daily; 1 cup per day; ≥ 2 cups per day) and breast cancer.	Soy intake: below and above median intakes of soy foods (< 10.6 mg isoflavones per 1000 kcal; ≥ 10.6 mg isoflavones per 1000 kcal) and breast cancer.
N [5]	979,348	>388,2947 participants	220	362 cases 362 controls	30,454	35,303
Population/study information [6]	Asian and Western countries, pre- and post-menopausal (although some studies did not	Asia (Japan, China, Singapore), USA, Europe women.	Premenopausal US women; Age: ~40-50 yrs.	Korean women Mean age: ~46yrs; Country: Korea; Cases: Histologically confirmed breast cancer.	40 to 79 yrs Japanese women; Japan Collaborative Cohort (JACC) Study.	Singaporean women; age: 45-74yrs; Singapore Chinese Health Study.

	stratify by menopausal status).					
Quality [7]	0	0	p	p	0	p
Results [8]	Small reduction in breast cancer risk with high soy intake vs low intake OR 0.86 (95% CI 0.75-0.99).	Pooled RR of breast cancer for soyfood intake was 0.75 (95% CI 0.59-0.95). Isoflavone intake was RR 0.81; (95% CI 0.67-0.99).	Change in mammographic density: P-value (between intervention and control groups) = 0.27.	Soy protein intake between cases and controls: p < 0.01. Crude OR (and 95% CI) of Ca breast according to soy protein: Quintile 1: 1.0; quintile 2: 0.66 (0.40-1.06); quintile 3: 0.58 (0.36-0.93); quintile 4: 0.55 (0.34-0.88), quintile 5: 0.45 (0.28-0.72); P for trend < 0.01.	No association found between soy food consumption and breast cancer.	> Median intakes of soy foods RR 0.82 (95% CI 0.7-0.97); postmenopausal women RR 0.74 (0.61-0.90) but NS for premenopausal women.
Effect on risk (Increase/None/ Protect)	Protect	Protect	None	Protect	None	Protect
Clinical importance [9]	1	1	3	1	3	1
Clinical relevance [10]	1	1	5	1	n/a	1
Generalisability	y	y	n	y	y	y
Applicability	y	y	n	y	n	n

7.2 LEGUMES and PROSTATE CANCER

Does a particular intake of legumes affect the risk of prostate cancer?		
Evidence statement		Consumption of soy foods is associated with reduced risk of prostate cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence 1 meta analyses of 5 cohorts/9 case controls (medium risk bias) and 1 cohort.
Consistency	Satisfactory	Meta analyses shows protective effect but for soy food; cohort study of legumes no effect.
Clinical impact	Satisfactory	Moderate clinical impact RR 0.75.
Generalisability	Good	Range of populations European US and Asian.
Applicability	Good	Findings are only for soy and not legumes.

The meta analysis is for soy foods but the cohort study examines sources of protein food and protein rich foods and prostate mortality. Legume consumption ranged from none to about one cup daily. The confidence intervals around the RR are very wide because the cohort size is small. The World Cancer Research Fund concluded no convincing or probable decrease in risk but there was limited suggestive evidence for legumes having a protective effect.

References

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Table 7.2 Summary of studies of legumes and prostate cancer

Reference [1]	Yan & Spitznagel 2009 [498]	Smit et al. 2007 [119]
Type of study [2]	Meta-analysis of 5 cohort/9 case-control studies.	Cohort.
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Soy intake highest vs lowest and prostate cancer.	Intake of legumes (quartiles: 0 serves; 1-2 serves; 3 serves; 4 serves; where 1/4 cup is a serving of legumes) and prostate cancer.
N [5]	171,487	9824
Population/study information [6]	Men US, Japan, China, Scotland, Canada, Taiwan.	35 - 79yrs Puerto Rican men; Puerto Rico Heart Health Program recruited (1964).
Quality [7]	0	p
Results [8]	Soy consumption and prostate cancer: combined RR of 0.74 (95% CI 0.63-0.89; P = 0.01).	quartile 4 vs quartile 1 RR 1.06 (95% CI 0.48–2.32) P value for trend 0.93.
Effect on risk (Increase/None/ Protect)	Protect	None
Clinical importance [9]	1	4
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	n

7.3 LEGUMES and COLORECTAL CANCER

Does a particular intake of legumes affect the risk of colorectal cancer?		
Evidence statement		Consumption of legume foods is associated with reduced risk of colorectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence 4 cohort studies and 1 case control.
Consistency	Satisfactory	All show protection but in one case it is only at one cancer site and for males and in the other only females showed protection.
Clinical impact	Satisfactory	Reduction of 30%.
Generalisability	Satisfactory	Three Asian studies, one US and one Paraguay.
Applicability	Satisfactory	Findings are in Asian populations who may have different intakes and one US study of women.

Three of the studies indicate that legume and/or soy foods are protective. However, in one cohort measuring soy the effect was only significant for the proximal colon and in another study measuring soy intake the effect was only significant for females. Both studies that measured legume intake found a reduced risk with higher consumption of legumes. The World Cancer Research Fund report does not list legume foods as a convincing or probable factor but states foods containing fibre probably decrease the risk of colorectal cancer.

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Table 7.3 Summary of studies of legumes and colorectal cancer

Reference [1]	**Akter et al. 2008 [37]**	**Michels et al. 2006 [217]**	**Yang et al. 2009 [1089]**	**Oba et al. 2007 [1170]**	**Deneo-Pellegrini et al. 2002 [463]**
Type of study [2]	cohort	cohort	cohort	cohort	case control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Dietary soy intake (Quartiles) and colorectal cancer.	Legume consumption (quintiles: ≤ 3; 4; 5; 6; ≥ 7 servings/day) and colorectal adenomas.	Soy food intake (Tertiles: ≤ 12.8 g/d; 12.9-21.0 g/d; > 21.0 g/d) and colorectal cancer.	Soy product and isoflavone intake (Tertiles: low, middle and high intake have different values for M and F) and colon cancer.	Quartiles of pulses/all legumes) intake and colorectal cancer.
N [5]	83,063	34,467	68,412	30,221	484 cases 1452 hospital based controls
Population/study information [6]	M and F 45-74 yrs Japan Public Health Center-Based Prospective Study.	F 30-55 yrs Nurses Health Study.	F 40-70 yrs Shanghai Women's Health Study.	M and F ≥ 35 yrs Japan Takayama study.	M and F 30-89 yrs (largest proportion aged 70-79 yrs) Uruguay Cases having microscopically verified adenocarcinomas of colon and rectum. Controls admitted to hospital for conditions not related with tobacco

					smoking, alcohol drinking, and without recent changes in the diet.
Quality [7]	p	p	p	p	0
Results [8]	No significant association for colorectal cancer but by site sub analyses in males proximal colon cancer reduced HR for quintile 4 vs quintile1 : soy food HR 0.51(95% CI 0.3-0.87).	Females consuming ≥ 4 serves legumes per wk OR 0.67 (95% CI 0.51-0.90) P trend = 0.005 vs lowest intake group.	Women in tertile 3 had RR 0.67 (95% CI 0.49-0.90) vs tertile 1 (P for trend = 0.008).	Females tertile 3 vs. tertile 1 HR 0.56 (95% CI 0.34–0.92) vs (P trend =0.04) for soy food intakes. Males NS.	OR (95% CI) of colorectal cancer for quartiles of legume intake: quartile 1: 1.0; quartile 2: 0.9 (0.7-1.3); quartile 3: 0.9 (0.7-1.2); quartile 4: 0.7 (0.5-0.9); P-value for trend = 0.03.
Effect on risk (Increase/None/ Protect)	None/protect	protect	protect	protect for females only	protect
Clinical importance [9]	1	1	1	1 females only	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	n
Applicability	n	y	n	n	n

7.4 LEGUMES and HYPERCHOLESTEROLAEMIA

Does a particular intake of legumes affect the risk of hypercholesterolaemia?		
Evidence statement		Consumption of soy foods is associated with reduced total cholesterol and LDL-cholesterol.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level I and II evidence from one meta analysis of 30 RCTs (10 of soy foods and 20 of isolated soy protein) and 1 RCT.
Consistency	Good	Meta analyses showed total and LDL cholesterol decreased.
Clinical impact	Satisfactory	Total cholesterol and LDL-cholesterol are more consistently lowered by soy protein. Total cholesterol reduced (-0.160 to -0.306 mmol/L) with 25 g soy protein per day.
Generalisability	Good	Mostly in Western countries and both male and female adults.
Applicability	Satisfactory	May have lower applicability in the context of the Australian diet.

The literature concerning blood lipids and legumes was exclusively soy and soy products. There were insufficient papers to make a body of evidence for legumes and cardiovascular disease outcomes per se, hence the statement on the surrogate of blood lipids. The meta analysis provides support for the cholesterol lowering effects of soy protein. Three other meta analyses were located but all or almost all the studies included used isoflavone rich protein isolates rather than food (Weggeman, Taku, Zhan), whereas the meta analysis of Harland included 10 of 30 studies which were not using isoflavones isolates. Each of these 10 studies demonstrated decreases in LDL cholesterol although this was not always statistically significant. It seems that the isoflavone component is the active and important biological constituent for the effect of soy foods.

References

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Table 7.4 Summary of studies of legumes and hypercholesterolaemia

Reference [1]	**Harland et al. 2008 [1]**	**Azadbakht et al. 2007 [1147]**
Type of study [2]	Meta-analysis of 30 RCT	RCT
Level of evidence [3]	I	II
Intervention/ comparator [4]	15-40 g soy protein and total LDL and HDL cholesterol.	Control vs 30 g soy nut vs 30 g soy protein diet and blood lipids.
N [5]	2913	42
Population/study information [6]	M and F age range approx. 27-67 yrs European North American and Asian average BMI <30 baseline total cholesterol range 4.57-7.03 mmol/L.	F; postmenopausal women with metabolic syndrome; Tehran, Iran.
Quality [7]	P	p
Results [8]	No dose response effect on standard difference in mean HDL-C, LDL-C, Total C or Triglycerides, with soya protein intakes of 15-40 g. Approx. 25 g soy protein intake lead to decreased LDL-C: -0.233 mmol/l (95% CI -0.306 to -0.160); increased HDL-C: 0.071 mmol/L (95% CI -0.002 to 0.144); decreased TG: -0.081 mmol/l (95% CI -0.158 to -0.001); and decreased TC: -0.217 mmol/l (95% CI -0.291to -0.142).	LDL-C: $p < 0.01$ (all 3 diet periods significantly different to each other; soy nut < soy protein < control); TC: $p < 0.01$ (all 3 diet periods significantly different to each other; soy nut < soy protein < control).
Effect on risk (Increase/None/ Protect)	Protect	None
Clinical importance [9]	1 (LDL-C, TC, TG) & 2 (HDL-C)	1
Clinical relevance [10]	2	2
Generalisabilty	y	n
Applicability	y	n

STUDIES NOT INCLUDED IN BOE as < 5 studies

SOY FOOD and BONE FRACTURE

In the Shanghai Women's Health Study, a cohort study of approximately 75,000 Chinese women aged 40 to 70 yrs, examined the relationship between usual soy food consumption and fracture incidence was examined in 24 403 postmenopausal women who had no history of fracture. The relative risks (95% confidence intervals) of fracture for quintile 5 vs quintile 1 was 0.63 (0.53-0.76) across quintiles of soy protein intake ($P < .001$ for trend). The inverse association was more pronounced among women within 10 years of menopause (Zhang et al. 2005).

SOY-PROTEIN RICH FOODS and WEIGHT LOSS

47 overweight women (body mass index 28 to 33, aged 25 to 49 yrs) were allocated to decrease their caloric intake by 500 kcal per day for a period of 12 weeks with or without the addition of 15 g soy protein per 1000 kcal. The addition of soy protein did not result in any additional weight loss or improvements in blood lipids compared to weight loss diet alone (St Onge et al. 2007).

Conversely, in a trial with 45 g of soy protein as part of a 1200 kcal diet vs a control low calorie diet with two thirds animal sources of protein, body weight, body mass index, body fat percentage, and waist circumference significantly decreased in both groups ($P < 0.05$) but the decrease in body fat percentage in the soy group 2.2% (95% CI 1.6 –2.8) was greater than that in the traditional group 1.4% (95% Cl 0.1 to 2.8). Serum total and LDL cholesterol concentrations decreased more in the soy-based diet group ($P < 0.05$) (Liao et al. 2007).

In a study with 90 obese subjects a low fat diet that included soy protein improved body composition in overweight and obese people, losing fat but preserving muscle mass compared with traditional lifestyle measures (Deibert et al. 2004).

LEGUMES and CEREBRAL INFARCTION

A Costa Rican case control study to assess the relationship of beans intake and myocardial infarction reported an odds ratio of 0.62; (95% CI 0.45-0.88) for those consuming one or more serves per day (Kabagambe et al. 2005).

A Japanese cohort study of 40,462 Japanese (40 to 59 yrs old) found the multivariable hazard ratios and 95% confidence limits for soy intake five times or more per week versus zero to two times per week were 0.64 (0.43 - 0.95) for risk of cerebral infarct and 0.55 (0.26 - 1.09) for risk of myocardial infarction, and 0.31 (0.13 - 0.74) for cardiovascular disease mortality. Similar but weaker inverse associations were observed between intake of miso soup and beans and risk of cardiovascular disease mortality (Kokubo et al. 2007).

SOY INTAKE and CANCER

The relationship between intake of soy products and death from stomach cancer was examined in a cohort of men and women in Japan. After seven years of follow-up, 121 deaths from stomach cancer (81 men and 40 women) occurred among 30,304 (13,880 men and 16,424 women) participants. In men, risk of death from stomach cancer for highest compared to the lowest tertile of total soy product intake was HR 0.50 (95% CI 0.26-0.93, P for trend=0.03). In women HR for the highest compared to the lowest tertiles of total soy product intake was 0.49; (95% CI 0.22-1.13) (Nagata et al. 2002).

The relationship of soy foods and hepatocellular carcinoma was studied in a case control design in atomic bomb survivors. The adjusted OR for high versus low consumers of miso soup was 0.5 (95% CI 0.14-1.55) and the adjusted OR for tofu was 0.9 (95% CI 0.20-3.51) (Sharpe et al. 2005).

CHICK PEAS and METABOLIC SYNDROME

19 men were assigned to either a chick pea based diet or a wheat based diet for six weeks but the study failed to show significant differences in plasma glucose, insulin, or HOMA either in the fasting state or after a glucose load after being on the chick pea diet. This was despite short term effects observed after a single chick pea meal (Nestel et al. 2004).

SOY and HYPERTENSION

Three RCTs looked at soy intake as soy nuts, soy cereal or soy milk. Substituting soy nuts for nonsoy protein improved BP (Welty et al. 2007) and substituting soy milk for cows milk also lowered blood pressure (Rivas et al. 2002), but the other RCT of soy cereal showed no effect (Teede et al. 2006). A cohort study in Chinese women found soy protein intake was inversely associated with both systolic and diastolic blood pressure (Yang et al. 2005).

References

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8. NUTS AND SEEDS (S1.1)

Evidence Statements

8. NUTS AND SEEDS (S1.1)

Search results

The initial search of the databases included 1475 references for nuts and seeds and the specified disease outcomes. The detailed search is included in a separate document on searches. In all, 17 references concerning nuts and seeds had data extracted but only seven papers were of high enough study design to be used to form the body of evidence statements for nuts and seeds. Sufficient evidence was found to make statements for nuts and seeds and obesity and cardiovascular disease only.

The WCRF report describes the evidence on nuts and seeds and the relationship with cancer as insubstantial. They report that the evidence was too limited in amount, consistency, or quality to draw any conclusions. Our evaluation supports this conclusion.

8.1 NUTS AND SEEDS and OBESITY

Does a particular intake of nuts and seeds affect the risk of obesity in adults?		
Evidence statement		Consumption of nuts (65-110 g / day) does not lead to weight gain in the short-term.
Grade		**C**
Component	**Rating**	**Notes**
Evidence Base	Good	In total 6 Level II studies (RCT's) analysed (6P), but all short-term and no cohort studies.
Consistency	Good	Some minor inconsistency but mostly no effect on BMI (RCT's: 5 No effect, 1 minor negative). Variability may be due to differing types of nuts, lengths of study or population group.
Clinical impact	Satisfactory	Range- 65-110 g of whole nuts per day has some protective effect on maintaining body weight. Having 40 g of seeds showed a small positive effect on weight change with a significant reduction in BMI or no effect on weight change. Results are mostly consistent for demonstrating that the consumption of nuts does not result in weight gain. Results were neutral for gain in weight in 5 of the 6 RCT's and 1 RCT showing a slight but insignificant gain in weight.
Generalisability	Good	Most studies generalisable. Note sample sizes for most

		studies were small (4 of 6 nut RCT studies < 50, 2 of 6 nut RCT studies > 50).
Applicability	Good	Likely to be applicable to Australian population. Some studies included a range of ethnic groups. 1 study was specific to post menopausal women and 1 study was specific to older men.

The six RCTs contributing to the body of evidence are shown in Table 8.1.

There were six RCTs, all of a positive quality, regarding nut consumption (65-110 g) with four of six RCTs investigating the consumption of nuts (one on pistachio, two on almond, one on walnut) of relatively short-term duration (three – eight weeks) and with a small number of participants (n= 21- 44). All studies included men and women, except one which included men only, and all the studies were from the USA except one from Turkey. Results were mostly consistent for no effect on body weight.

Two of the six RCTs were of a longer-term intervention period (six months) with a larger number of participants and with a wide age range and both were from the USA. Both studies reported little weight change overall. One RCT included walnuts as part of the energy intake (one on walnuts, n= 90, age 30-72 yrs) and reported a small but insignificant weight gain. One RCT (one on almonds, n = 81, age 25-70 yrs) did not include dietary advice about inclusion of the nuts and reported that almonds in the diet did not lead to statistically or biologically significant changes in body weight, but that the small increase in weight gain could become biologically significant if it were to continue to increase.

References

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Spaccarotella, K. J., P. M. Kris-Etherton, et al. 2008, "The effect of walnut intake on factors related to prostate and vascular health in older men", *Nutrition Journal*, vol. 7, no., pp. 13-13.

Table 8.1 Studies used to make evidence statements for nuts and seeds and obesity

Reference [1]	**Kocyigit 2006 J [891]**	**Hyson et al. 2002 [149]**	**Sabaté 2003 [386]**	**Spaccarotella et al. 2008 [413]**	**Sabate et al. 2007 [219]**	**Fraser et al. 2002 [1499]**
Type of study [2]	RCT	RCT	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II	II	II
Intervention/ comparator [4]	Pistachio Nuts (20% EI pistachios)/ Obesity.	Nuts (Whole Almonds or Almond Oil 50% fat intake)/ Obesity.	Almonds (high almond 20% EI and low almond diet 10% V's Step 1 diet)/ Obesity.	75 g Walnuts (24% of energy intake)/ Obesity.	Walnuts (28–56 g) consumption during the study period of 6 months (approx 12% Energy intake). Mean daily walnut consumption was 35 g during the walnut-supplemented diet.	Almonds (15% of daily energy for each individual). On average, 54.3 g or 76.4 kJ (319.8 calories) per day (about 40–50 nuts), and the range was 59.9 to 99.9 kJ per day. 12 month study.
N [5]	22 intervention; 22 control.	22 completed	25 completed	21 completed	90	100 subjects were initially enrolled, 81 completed.
Population/study information [6]	Healthy subjects 20 women and 24 men. A total of 60 volunteer subjects who worked as doctors and nurses at the Research Hospital, University of Harran, Sanliurfa, Turkey.	M and F Normocholesterolemic (plasma cholesterol <5.2mm/L, +/ 10%) normal weight, non smokers, free of allergies and dietary restrictions, no medications known to alter metabolism. Mean age 43.5 +/- 8yrs, mean BMI 23.7 +/- 1.2kg/m^2.	Healthy subjects, mean age 41 +/- 13 yrs. 4 ethnic groups white (100, Hispanic (7), Asian (5), African American (3).	Men recruited from the community. Healthy, non-smoking men who resided in central Pennsylvania, US. The average age was 65.9 yrs (range was 55 to 75 yrs). Participants had total PSA ≥ 2.0	50 females and 40 males, aged 30 to 72 yrs (mean 54·3 (SD 10·6) years).	M and F

				ng/mL (2.0 µg/L), but they did not have clinically diagnosed prostate cancer. Study was a 2-period cross-over in which the men received 2 treatments in random order. Study period was 8 wks on either walnut diet or usual diet, followed by a 2 wk break, then men switched diets for another 8wks. All men completed the study.		
Quality [7]	P	P	P	P		
Results [8]	(65-75 g per day of Pistachio nuts). Modifying the diet through the consumption of pistachio nuts (20% EI) did not result in significant wt change (P>0.05).	Whole almonds (66 g per day +/-5 g) or almond oil (35 g per day +/-2g) for 6 wks given as 50% fat daily did not result in significant changes in weight. Inclusion of whole almonds or almond oil in diet lowers plasma lipids.	Incorporating an average of 54.3 g almonds per day (76 kJ per day) in the diet for 6 mo did not result in significant weight changes in healthy adults. For blood lipids, 68 g of almonds (20% energy). Inclusion of	In the intervention group, 75 g walnuts per day for 8 wks did not result in any significant treatment effects on weight change and in the control group, the men on the usual diet	Walnuts (28–56 g) consumption during the study period. Mean daily walnut consumption was 35 g during the walnut-supplemented diet. The walnut-supplemented diet	During the almond feeding period, average body weight increased by 0.40 (kg) (p 0.09). The weight change depended on baseline BMI (p 0.05), and only those

			almonds (20% of energy) in usual or prescribed cholesterol diets may benefit both healthy and persons with hypercholesterolemia by reducing serum and total and LDL concentrations.	lost 1.36 ± 0.39kg (p=0.001). Mean weight was 84.8 ± 2.9 kg at the screening visit, 83.4 ± 2.8 kg at the end of the usual diet and 84.3± 2.9 kg at the end of the walnut supplemented diet. No effect on serum concentrations of triglycerides, total cholesterol, LDL cholesterol.	resulted in greater daily energy intake (557 kJ (133 kcal)), which should theoretically have led to a weight gain of 3·1 kg over the 6-month period. For all participants, walnut supplementation increased weight (0·4 (SE 0·1) kg), BMI (0·2 (SE 0·1) kg/m^2). But, after adjusting for energy differences between the control and walnut-supplemented diets, no significant differences were observed in body weight or body composition parameters, except for BMI (0·1 (SE 0·1) kg/m^2).The findings show that regular walnut	initially in the lower BMI tertiles experienced small weight gains with the almonds.

					intake resulted in weight gain much lower than expected and which became non-significant after controlling for differences in energy intake.	
Clinical importance [9]	2	2	2	2	2	2
Clinical relevance [10]	2	2	2	2	2	2
Generalisability	Yes	yes	yes	Yes	Yes	Yes
Applicability	yes	yes	yes	Yes	Yes	Yes
[NOTES]					The findings show that regular walnut intake (approx 12%EI) for 6mnths resulted in weight gain much lower than expected and which became non-significant after controlling for differences in energy intake.	Almond feeding(15% EI) for 6 months increased body weight slightly and mostly in those with lower BMI's.

8.2 NUTS AND SEEDS and CARDIOVASCULAR DISEASE

Body of Evidence and Statement for nuts and seeds and cardiovascular disease

Does a particular intake of nuts and seeds affect the risk of cardiovascular disease in adults?		
Evidence statement		Consumption of nuts (65-110 g per day) reduces cholesterol levels.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Excellent	5 Level II studies (RCT's) all 5 of Positive quality.
Consistency	Satisfactory	Some inconsistency but mostly favourable effect on blood lipids (RCT's: 5 protect, 2 No effect). Variability may be due to differing types of nuts, lengths of study or population group.
Clinical impact	Satisfactory	Range 65-110 g of whole nuts per day has some protective effect on some blood lipids. One study showed similar benefits of either 61-71g almonds or 33-37 g almond oil. Having 40 g of seeds per day showed some or little effect on blood lipids. Results are mostly consistent for lowering total cholesterol (3 of 4 RCT's for nut consumption significantly lowered Total Chol and 1 was neutral; 1 of 2 RCT's for flaxseed consumption significantly lowered Total Chol), LDL Cholesterol (3 of 5 RCT's lower LDL Chol and 2 of 5 was neutral), Triglycerides (3 of 5 RCT's lower trig and 2 of 5 are neutral) and Apo-A/Apo-B (3 of 4 studies increased Apo-A/Apo-B and 1 of 4 was neutral). Results were neutral for HDL cholesterol with 2 of 4 RCT's increasing HDL Chol and 2of 4 having a neutral effect.
Generalisability	Good	Most studies generalisable. Note sample sizes for all studies were small (6 studies < 50, 1 study > 50).
Applicability	Good	Likely to be applicable to Australian population. Some studies included a range of ethnic groups. 1 study was specific to post menopausal women and 1 study was specific to older men.

The five RCT's contributing to the body of evidence are shown in Table 8.2. These studies investigating the consumption of nuts (65-110 g; two on almond, one on walnut, one on pistachio, one on peanuts) were of relatively short-term duration (three to eight weeks) with a relatively small number of participants (n=21-44). Four studies were from the USA and one was from Turkey. Results were mostly consistent with four of the five RCTs reporting favourable effects on blood lipids. These studies all included men and women. The RCT which did not show any benefit on blood lipids included only men.

References

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Kocyigit, A., A. A. Koylu, et al. 2006, "Effects of pistachio nuts consumption on plasma lipid profile and oxidative status in healthy volunteers", *Nutrition, Metabolism and Cardiovascular Diseases*, vol. 16, no. 3, pp. 202-209.

Sabaté, J., E. Haddad, et al. 2003, "Serum lipid response to the graduated enrichment of a Step I diet with almonds: a randomized feeding trial", *American Journal of Clinical Nutrition*, vol. 77, no. 6, pp. 1379-1384.

Spaccarotella, K. J., P. M. Kris-Etherton, et al. 2008, "The effect of walnut intake on factors related to prostate and vascular health in older men", *Nutrition Journal*, vol. 7, no., pp. 13-13.

Table 8.2 Studies used to make evidence statements for nuts and seeds and CVD

Reference [1]	**Kocyigit 2005 [891]**	**Hyson et al. 2002 [149]**	**Sabaté 2003 [386]**	**Alper & Mattes 2003 [126]**	**Spaccarotella et al. 2008. [413]**
Type of study [2]	RCT	RCT	RCT	RCT	RCT
Level of evidence [3]	11	11	11	11	II
Intervention/ comparator [4]	Pistachio Nuts (20% EI pistachios)/ CVD.	Nuts (Whole Almonds or Almond Oil 50% fat intake)/ CVD.	Almonds (high almond 20% EI and low almond diet 10% V's Step 1 diet)/ CVD.	Peanuts (3 diets; free feeding, added or substituted)/ CVD.	75g Walnuts (24% of energy intake)/ CVD.
N [5]	22 intervention; 22 control	22 completed	25 completed	15	21 completed
Population/study information [6]	Healthy subjects (n=44; 20 women and 24 men). A total of 60 volunteer subjects who worked as doctors and nurses at the Research Hospital, University of Harran, Sanliurfa, Turkey.	Normocholesterolemic (plasma cholesterol <5.2mm/L, +/ 10%) men and women, normal weight, non smokers, free of allergies and dietary restrictions, no medications known to alter metabolism. Mean age 43.5 +/- 8yrs, mean BMI 23.7 +/- 1.2kg/m^2.	Healthy subjects mean age 41 +/- 13 yrs, 4 ethnic groups white (100, Hispanic (7), Asian (5), African American (3).	Healthy adults recruited from the community. Seven non-pregnant or lactating female and eight male adults (33 +/- 9 yrs).	Subjects recruited from the community. Healthy, non-smoking men who resided in central Pennsylvania, US. Average age 65.9 yrs (55 -75 yrs). Mean weight 84.8 ± 2.9 kg. Participants had total PSA ≥ 2.0 ng/mL (2.0 µg/L), but they did not have clinically diagnosed prostate cancer. All completed the 8-week intervention.

Quality [7]	P	P	P	P	P
Results [8]	65-75 g per day Pistachio nuts. Modifying the diet through the consumption of pistachio nuts (20% EI) may raise AOP and improve Total cholesterol and HDL cholesterol.	Whole almonds 66 g +/- 5 g per day or almond oil 35 g +/-2g per day. Inclusion of whole almonds or almond oil in diet lowers plasma lipids.	68 g of almonds (20% energy). Inclusion of almonds (20% of energy) in usual or prescribed cholesterol diets may benefit both healthy and persons with hypercholesterolemia by reducing serum and total and LDL concentrations.	Peanuts 68 g-110 g per day for 8 weeks lowers triglycerides levels.	75 g walnuts per day for 8 wks did not result in any significant treatment effects on serum concentrations of triglycerides, total cholesterol, LDL cholesterol.
Clinical importance [9]	2	2	2	2	2
Clinical relevance [10]	2	2	2	2	2
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y
Effect on risk (Increase/None/Protect)	Protect	Protect	Protect	Protect	None

Summary of studies not included in Body of Evidence statements

Nuts and Seeds and Obesity

Two RCTs (both positive quality) investigated seeds (flaxseed, 40g/d), one from the USA and one from Canada. One showed no change in body weight in post-menopausal women (n=36; 12-week intervention) and one RCT reported a significant reduction in BMI in menopausal women (n=179; 12-month intervention).

Nuts and Seeds and Cardiovascular Disease

Two studies from the male Physicians' Health Study (USA cohort study). One study assessed association between nut consumption and incident heart failure (n=20,976). No association was found according to nut consumption of zero versus ≥ 2 serves per week (HR 1.01, p for trend 0.64) (Djousse 2008). The other study assessed association between nut consumption and sudden cardiac death (n=21,454). An inverse association between nut consumption and total cardiovascular disease death was suggested (RR 0.53; p for trend 0.01) for ≥ 2 serves per week versus <1 serve per month (Albert 2002). These studies were not included in the evidence statement due to having very different endpoints when compared with the included RCTs but the results support the regular consumption of nuts.

Two small pre-test / post-test studies, one from USA (positive quality) and one from Brazil (negative quality). The USA study (n=20) investigated addition of almonds (100g per day) to habitual diet for 4 weeks men and women and reported reductions in total cholesterol (p=0.0001), LDL (p=0.0001) and HDL cholesterol (p=0.0002) (Lovejoy 2002). This is consistent with the other studies supporting regular nut consumption. The other study (n=15) investigated diets supplemented with Brazil nuts (45 g per day) for 15 days reported no changes in LDL, HDL, triacylglycerols or apolipoproteins (Strunz 2008). The Brazilian study was not included in the body of evidence statement due to being of a negative quality rating and limited generalisability related to sample selection and small sample size.

One cross-sectional study (positive quality). This study of 6080 adults from the USA reported that intake of nuts and seeds five or more times per week was associated with lower levels of the inflammatory markers interleukin-6 (p=0.05) and fibrinogen (p=0.03). There was also a trend for lower CRP (p=0.06) (Jiang 2006).

Two RCTs (positive quality), investigated diets supplemented with flaxseed (40 g per day); one for 12 months in menopausal Canadian women and the other for three months in postmenopausal women from the USA. The study in postmenopausal women found that flaxseed reduced total cholesterol by 6% (<0.05) and Apo-A and B by 6 and 7.5% respectively (Lucas 2002). The other found that flaxseed supplementation 40 g of flaxseed per day for 12 months reduced Apo-A1 by 4.4% (p=0.006) and Apo-B by 3% (p=0.054) (Dodin 2008).

Nuts and Seeds and Hypertension

One cohort study of positive quality (Physicians' Health Study) reported an association between nut consumption and a lower risk of hypertension in USA male physicians (HR 0.82; p for trend 0.014 when comparing a zero nut intake with ≥ 7 serves per week). When stratified by BMI, this association remained for subjects within the healthy weight range (BMI < 25kg/m^2) but not for subjects classified as overweight or obese (Djousse 2009).

Nuts and Seeds and Colorectal Cancer

One positive quality European cohort study (EPIC study); n= 478,040. Results suggested no significant protective association on colorectal cancer risk for men and women combined. Sub-analysis by gender however showed that a daily intake of nuts and seeds (average of 16 g per day) was associated with reduced incidence of colon cancer in women relative to non-consumers (HR 0.69; p for trend 0.04) (Jenab 2004).

Nuts and Seeds and Prostate Cancer

One randomised control trial (cross-over study) of positive quality from USA. Investigated 2000 kcal diet supplemented with walnuts (75 g per day) for eight weeks in 21 men. No significant changes occurred in prostate specific antigen levels, suggesting that walnut supplementation does not increase prostate cancer risk (Spaccarotella 2008).

Nuts and Seeds and Asthma

One positive quality cohort study from the Netherlands (n=4146; 2806 included in nuts analysis). This study investigated the association between frequency of nut consumption during pregnancy and prevalence of childhood asthma symptoms. Results suggested increased risk of daily versus rare consumption of nut products (OR 1.47) however this association was not found for nut intake per se (OR 1.00) (Willers 2008).

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9. FISH (S1.1)

Evidence Statements

9. FISH (S1.1)

Search results

The initial search of the data bases included 3272 references for fish and the specified disease outcomes. The detailed search is included in a separate document on searches. In all, 81 references concerning fish had data extracted and 60 papers were used to form the body of evidence statements for fish. Sufficient evidence was found to make statements for fish and cardiovascular disease, dementia, depression, eye disease, stroke, breast cancer, colorectal cancer, prostate cancer and renal cancer.

In the WCRF report, the following two statements were made for fish and this has been compared to the body of evidence statements made here.

1. There is limited evidence suggesting that high fish intakes decrease the risk for cancers of the Colorectum. Our finding was that consumption of fish is not associated with risk of colo-rectal cancer.
2. There is possible evidence that diets relatively high in Cantonese-style salted fish increase the risk of cancers of the naso-pharynx. This was noted in the body of evidence on sodium and cancer.

9.1 FISH and CARDIOVASCULAR DISEASE

Does a particular intake of fish affect the risk of cardiovascular disease in adults?		
Evidence statement		Consumption of at least two serves a week is associated with reduced risk of mortality from cardiovascular disease, and with reduced incidence of cardiovascular disease
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	23 studies, all Level III-2 (7 systematic reviews of cohorts, 2 non-randomised CT, 11 cohort studies and 3 case-control studies). Quality of evidence moderate (Systematic reviews 3 Neutral, 4 Negative, NRCT= 1 negative, 1 neutral, Cohorts: 9 positive, 2 neutral Case-Control: 1 positive 2 neutral).
Consistency	Satisfactory	Definitions of CVD varied across studies and within systematic reviews and several different outcomes were examined. Main contributing studies to outcomes were: Mortality: 4 systematic reviews showed a protective effect with higher intake. Of 7 cohorts, only one showed a protective effect with higher fish intakes. Total Incidence: one systematic review showed a protective effect, 2 cohort showed no association and one a protective effect. One case-control showed no association. Myocardial Infarction: one cohort showed no effect and one a protective effect, 2 case-controls showed a protective effect. Cardiac arrest: one cohort showed no association. Heart failure: one cohort showed no effect, one a protective effect. Atrial fibrilation: one cohort showed no effect. Blood lipids: 2 controlled trials showed no effect. N.B: Three systematic reviews included variable outcomes with no synthesis of results, so no clear overall results reported.
Clinical impact	Satisfactory	Inconsistent findings. Clinical significance varied across studies. Exposure/Intervention lengths varied. When a protective effect is shown for a higher intake, commonly >2 serves/week (or approximately 300g/week with OR 0.6-0.75).
Generalisability	Good	Most studies generalisable. Except for three cohorts in high fish consuming populations, all but one study specific to the adult

		population (mostly mix of adults and older adults). Some cohort studies gender specific, and many studies in systematic reviews gender specific.
Applicability	Good	Several studies in "high fish consuming" countries. One study in Australia showed no effect.

The systematic reviews, cohort studies, case-control studies and controlled trials used to make the body of evidence statements are shown in Table 9.1. Four negative or neutral quality systematic reviews showed protection from high intake of fish for cardiovascular disease mortality. However, the study by Gochfeld examined the dose-response curve in recognition that both benefits and harm must be related to dose. The benefit threshold for pregnant women in relation to birth weight was 8-15 g per day maternal fish intake and for adults, the cardiovascular benefits commenced at around 7.5-22.5 g per day. The review by Koning showed that consuming small quantities of fish was associated with a 17% reduction in CHD mortality risk, with each additional serving per week associated with a further reduction in this risk of 3.9%. Small quantities of fish consumption were associated with risk reductions in nonfatal MI risk by 27%, but additional fish consumption conferred no incremental benefits.

Six cohort studies, five of which were of high quality, demonstrated that fish intake had no effect on cardiovascular disease mortality. Two of the studies were undertaken in high fish consuming populations, one of which looked at sudden death only. Only one of the cohort studies was conducted in Australia. One high quality cohort study demonstrated that high fish consumption was associated with lower cardiovascular disease mortality, but demonstrated the relationship for women only.

For cardiovascular disease morbidity, one neutral quality meta-analysis demonstrated a protective effect from high fish consumption. The review included 19 studies, conducted in Italy, USA, Japan, Spain, Netherlands, Finland, China and Denmark. Twelve of the 19 studies included a single gender. The three cohort studies, and one case-control study were all of high quality, but only one study, which was conducted in Japan, demonstrated increased fish intake is associated with protection from cardiovascular disease incidence. For incidence of myocardial infarction, cardiac arrest, atrial fibrillation and high blood lipids, there were a small number of case-control and cohort studies with inconsistent results.

Summary for reduced risk of mortality from cardiovascular disease : This evidence is based on the findings of three consistent systematic reviews of cohort and case control studies of the relationship between fish consumption and cardiovascular disease mortality (Konig et al, 2005; Whelton wt al, 2004; He et al, 2004;), although this protective effect was not observed in six cohort studies (Kaushik 2008; Streppel 2008; Iso 2006; Nakamura 2005; Ness 2005; Folsom 2004;) in which hazard ratio, as distinct from risk ratio, was reported in the results; one additional cohort study did observe a protective effect for women (Jarvinen 2006).

Summary for reduced incidence of cardiovascular disease: This evidence is based on the findings of one systematic review (Whelton et al, 2004;) and one cohort study (Yamagishi et al, 2008;), although two case control studies (Viratanen et al, 2008; Iso et al, 2006) did not demonstrate this association.

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Table 9.1 Studies used to make evidence statements for fish and cardiovascular disease (mortality)

Reference [1]	**Gochfeld 2005 [281]**	**Konig 2005 [2023]**	**Whelton 2004 [385]**	**He 2004 [374]**	**Kaushik 2008 [85]**	**Streppel 2008 [12]**	**Iso 2006 [753]**	**Jarvinen 2006 [220]**	**Nakamura 2005 [2176]**	**Ness 2005 [624]**	**Folsom 2004 [342]**
Type of study [2]	Systematic Review of Cohort	Systematic Review of Cohort	Meta analysis of Cohort	Meta analysis of Cohort	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Fish intake (varied across studies)/Benefit by risk and dose curve for CVD	Fish intake (varied across studies)/CVD mortality	Fish intake (Mean 36g/day or 2.2 servings/week)	Fish intake (varied across studies)/CHD mortality	Frequency of fish consumption. Gp 1: Less than once per week, Gp2: Once per week, Gp3: At least twice per week, Gp4: At least one per week/CVD mortality	Cumulative average fish consumption /fish vs. non-fish consumers/CVD mortality	Quintiles of intake (g/day). Gp 1: 23g/d Gp2: 51g/d, Gp 3: 78g/d, Gp4: 114g/d, Gp5: 180g/d/Sudden cardiac death	Males: Gp1 ≤11g/d, Gp2 12-21g/d, Gp3: 22-35g/d. Gp4: 26-62g/d Gp5:≥63g/d. Females:Gp1 ≤8g/d, Gp2 9-15g/d, Gp3 16-24g/d, Gp4 25-40gg/d Gp5 ≥41g/d /CVD mortality	Frequency of intake. 2 or more times/day, About 1 time/day, about 1 time per 2 days, about 1 to 2 times/week, <1/week	Quartiles of intake (g). Gp 1 (low): Range: 0-6.9, Mean 1.8 (2.4), Gp 2: Range: 7-15.7, Mean (11.3 (2.5), Gp 3: Range: 15.8-29.2, Mean: 21.6 (3.9), Gp 4: Range: 29.2-148.9, Mean: 44.5 (15.5)/CVD Mortality	Quintiles of servings/week. Gp 1: <0.5, Gp 2: 0.5 to <1, Gp 3: 1.0-1.5, >1/5 to <2.5, ≥2.5 serves/week
N [5]	8 studies, number of particpants unclear	7 studies 157,925 participants	19 studies 228,864 participants	13 studies 222,364 participants	2897	1373	41 578	5220	8879	4028	41 836
Population/study information [6]	Adults Length of follow-up unclear. 4 studies male only 1 study	Adults 5 studies all male, 1 study all females. 6-30 years follow-up	Adults 22 to 87 yrs. Men only (n=9), Women only (n=2). 4-30	Adults, 16-79 yrs, Men only (n=8), women only	Adults aged ≥49 yrs. Australia. 10 yrs follow-up	Men born between 1900 and 1919 residing in Zupthen The	M and F 40-59 years in 1990 Japanese 11 yrs follow-up	≥15 yrs Finland. mean 21.5 yrs follow-up	M and F ≥30 yrs Japan 19 yrs follow-up	1352 families living in 16 areas of England	F 55-69 yrs in 1986 USA 11 yrs follow-up

	females only.		yrs follow-up	(n=1). 6-30 yrs follow-up		Netherlands for at least 5 yrs in 1960s. ≥ 40 yrs follow-up				and Scotland (1937-1939), data on 4999 children aged 0 to 19 yrs. 61-63 yrs follow-up	
Quality [7]	N	0	0	0	P	0	P	P	P	P	P
Results [8]	Composite benefits risk by dose curve:Choosing fish low in MeHg and PCBs and high in PUFA is clearly desirable. Duration of pregnancy and birth weight improve at a benefit threshold of about 8-15 g/day maternal fish intake. Meta analyses reveal adult	CHD mortality risk (dose-response curve). Intercept point: -0.17 (-0.25 to -0.088). Central estimate: -0.039 (-0.066 to -0.011). Consuming small quantities of fish was associated with a 17% reduction in CHD mortality risk, with each additional serving per	Relative Risk of Fatal CHD by level of fish consumption per week. Any: (n=13) 0.83 (0.76-0.9) p<0.005. <2: (n=9) 0.83 (0.75-0.92) p<0.005. 2-<4 (n=11) 0.75 (0.62-0.92) p<0.01. 2-<4 (n=11) 0.75 (0.62-0.92) p<0.01.	Pooled Relative Risk (95% CI) for fish consumption 1/week vs <1/month. 0.85 (0.76-0.96)	Hazard ratio (95% CI) Gp 1: 1 (ref) Gp 2: 0.88 (0.60-1.28) Gp 3: 0.91 (0.64-1.28) Gp 4: 0.89 (0.67-1.13)Fish intake had no effec t on CHD mortality	HR (95% CI) Although trend for effect, risk is not statistically significant therefore fish intake has no effect on:CHD Death Gp1: 1.00 Gp2: 0.73 (0.47-1.13) p-value 0.16) Sudden CHD Death Gp 1: 1.00 Gp 2: 0.89 (0.34-2.30)	HR (95% CI) Gp 1:1 (ref), Gp 2: 0.40 (0.13-1.19), Gp 3: 1.38 (0.59-3.22) Gp 4: 1.05 (0.42-2.64), Gp 5: 1.06 (0.42-2.76) p=0.31	Men Total fish Gp 1: 1 (ref) Gp 2: 1.07 (0.75-1.52) Gp 3: 1.09 (0.77-1.56) Gp 4: 0.98 (0.69-1.39) Gp 5: 1.00 (0.70-1.43) p=0.83 Seawater fish. Gp 1: 1 (ref), Gp 2: 0.98 (0.70-1.39), Gp3: 1.0 (0.71-1.41), Gp4:0.82 (0.58-1.19), Gp5: 1.09 (0.77-1.54) p=	HR (95% CI) Gp 1: 0.91 (0.33-2.35) Gp 2: 0.91 (0.53-1.62) Gp3: 1.07 (0.66-1.76), Gp 4 : 1 (ref), Gp 5: 1.47 (0.64-3.39) p=0.54 No association between frequency of fish consumption and CHD death	RR (95% CI) Gp 1: 1 (ref), Gp 2: 0.99 (0.68-1.43), Gp 3: 0.85 (0.58-1.25), Gp 4: 1.18 (0.80-1.76) p=0.6. No association between level of fish intake and CHD mortality	CVD Mortality Gp 1: 1 (Ref), Gp 2 1.03 (0.85-1.23), Gp 3: 0.86 (0.73-1.02), Gp4: 0.79 (0.63-0.99), Gp 5: 0.95 (0.78-1.15) p=0.11 CHD Mortality. Gp 1: 1 (ref), Gp 2: 1.11 (0.87-1.42), Gp 3: 0.86 (0.69-1.08), Gp4: 0.75 (0.55-0.94), Gp 5: 1.04 (0.80-1.34) p=
Effect on risk (Increase/None /Protect)	Not applicable	Protect	Protect	Protect	None	None	None	None for men. Protect for women for total fish only	None	None	None
Clinical importance [9]	1	1	1	1	2	2	3	1	3	3	2

Clinical relevance [10]	1	1	1	1	1	1	1	1	1	1	1
Generalisability	y	y	y	y	y	y	n	y	n	y	y
Applicability	n	y	y	y	y	y	y	y	y	y	y

Table 9.2 Studies used to make evidence statements for fish and cardiovascular disease various (mortality and incidence).

Reference [1]	**Carrol 2002 [655]**	**Bourre 2007 [1651]**	**Undeland 2004 [669]**
Type of study [2]	Systematic Review of Cohort	Systematic review	Systematic Review of Cohort
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	Fish intake (varied across studies)/CVD outcome variable across studies	Fish intake (unclear)/CVD outcomes variable across studies	Fish intake (varied across studies)/Variable CVD outcomes
N [5]	5 studies with 113 341 participants	Number of sudies and participants unclear	36 studies with 769 115 participants
Population/study information [6]	Adults. 4 studies males only, 1 study females only.Length of follow-up 10.5-30 yrs.	Population and follow-up unclear,	Adults, Age unclear. 20 studies male only, 3 females only. Follow-up 0 to 30 yrs
Quality [7]	N	N	0
Results [8]	All studies show protective effect, but on different outcomes (CHD incidence, CHD death, MI mortality etc)	Not clearly reported	Mixed effect across studies and on different outcomes (e.g. CHD risk, CHD mortality, MI, stroke etc)
Effect on risk (Increase/None/Protect)	Protect	Unclear	Unclear
Clinical importance [9]	1	4	3
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

Table 9.3 Studies used to make evidence statements for fish and cardiovascular disease incidence

Reference [1]	**Whelton 2004 [385]**	**Viratanen 2008 [3179]**	**Yamagishi 2008 [1150]**	**Iso 2006 [753]**	**Panagiotakos 2005 [2087]**
Type of study [2]	Meta analysis of Cohort	Cohort	Cohort	Cohort	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Fish intake (Mean 36 g per day or 2.2 servings per week)/CVD incidence.	Cumulative frequency of fish consumption/quintiles of fish consumption. Gp 1: <1 serve per month, Gp2: 1-3 per month Gp3: 2-4 per week Gp4: ≥5 per week/Total CVD incidence.	Quintiles of intake. Gp 1 0-27 g per day, Gp2: 27 to 39 g per day, Gp3: 39 to 53 g per day, Gp4: 53 to 72 g per day, Gp5: 72 to 229 g per day/ Total CVD Incidence.	Quintiles of intake (g per day). Gp 1: 23 g per day Gp2: 51 g per day Gp 3: 78 g per day Gp4: 114 g per day Gp5: 180 g per day /CHD incidence.	Weekly fish consumption Gp 1: Never Gp 2: Low (<150g/week) Gp3: Moderate (150-300g/wk) Gp4: High (>300g/wk)/ Incidence of coronary disease.
N [5]	19 studies with 228 864 participants	40,230	57,972	41,578	1926 (848 cases)
Population/study information [6]	Adults 22-87 yrs. Men only (n=9), Women only (n=2). Follow-up 4-30 yrs.	Male health professionals, 40-75 yrs in 1986. 16 yrs follow-up.	40-79 years at baseline, from 34 Japanese communities. Mean follow-up 12.7 yrs.	M and F 40 to 59 years (in 1990) Japanese Follow-up 11 yrs.	Greek, Males and females, Cases: First event of MI, Controls: randomly selected CVD free matched to patients by age, sex and region.
Quality [7]	0	P	P	P	P
Results [8]	RR of Total CHD by level of fish consumption per week Any: (n=12) 0.86 (0.81-0.92) p<0.005. <2: (n=7) 0.85 (0.80-	All fish Gp 1 1 (Ref) Gp 2 0.90 (0.77-1.05) Gp 3 0.86 (0.75-0.98) Gp 4 0.85 (0.73-0.99) Gp 5 1.04 (0.87-1.25) Tuna	HR (95% CI) Gp 1 1 (ref), Gp 2 0.93 (0.81-1.06) Gp 3 0.91 (0.79-1.05) Gp 4 0.86 (0.75-1.00) Gp5 0.82 (0.71-0.95) p=0.007	HR (95% CI) Gp 1 1 (ref) Gp 2 0.71 (0.48-1.06) Gp 3 0.93 (0.63-1.38) Gp 4 0.83 (0.53-1.30), Gp5 0.63 (0.38-1.04) p=0.25	OR (95% CI) Gp 1 1 (Ref) Gp 2 0.62 (0.412-0.871) Gp 3 1.10 (0.679-1.793) Gp 4 1.01 (0.554-

	0.91) p<0.005. 2-<4 (n=9) 0.83 (0.69-0.99) p<0.05. ≥4 (n=7) 0.84 (0.70-1.01) p<0.10	Gp 1 1 (ref) Gp 2 0.96 (0.87-1.04) Gp 3 0.94 (0.86-1.04) Gp 4 0.98 (0.87-1.10) p=0.84 Dark meat fish Gp 1 1 (ref) Gp 2 0.96			1.741)
Effect on risk (Increase/None/Protect)	Protect	None	Protect	None	None
Clinical importance [9]	1	3	1	2	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	n	n	y
Applicability	y	y	y	y	y

Table 9.4 Studies used to make evidence statements for fish and cardiovascular disease (other outcomes)

	Myocardial infarction				Cardiac arrest	Heart failure		Atrial fibrilation	Blood lipids	
Reference [1]	**Yamagishi 2008 [1150]**	**Iso 2006 [753]**	**Tavani 2004 [2344]**	**Martinez-Gonzalez 2002 [542]**	**Yamagishi 2008 [1150]**	**Yamagishi 2008 [1150]**	**Nettleton 2008 [618]**	**Brouwer 2006 [1895]**	**Din 2008 [1312]**	**Li 2004 [370]**
Type of study [2]	Cohort	Cohort	Case-control	Case-control	Cohort	Cohort	Cohort	Cohort	Non-randomised control trial	Non-randomised control trial
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Quintiles of intake. Gp 1 0-27g per day Gp2 27- 39 g per day Gp3 39 to 53 g per day Gp4 53 to 72 g per day Gp5 72 to 229 g per day/ Total MI incidence	Quintiles of intake Gp 1 23 g per day Gp2 51 g per day Gp 3 78 g per day Gp4 114 g per day Gp5 180g per day /Total and definite MI incidence	Fish portions per week: Gp 1<1. Gp 2 1 , Gp 3: >1/Acute MI Incidence	Quintiles of fish intake (g/day) Gp 1: <60g, Gp2: 60-77g, Gp 3: 77-106g, Gp 4: 106-142, Gp 5>142/Acute MI incidence	Quintiles of intake. Gp 1 0-27g/d, Gp2: 27 to 39g/d, Gp3: 39 to 53g/d, Gp4: 53 to 72 g/d, Gp5: 72 to 229g/d/ Total MI incidence	Quintiles of intake. Gp 1 0-27g/d, Gp2: 27 to 39g/d, Gp3: 39 to 53g/d, Gp4: 53 to 72 g/d, Gp5: 72 to 229g/d/ Heart failure incidence	Fish intake unclear/ Risk of incident heart failure	Gp1: <0g/d, Gp2: 0-20g/d, Gp3 ≥20g/d/Atrial Fibrilation	500g Mackerel/week (~1g EPA & DHA) for 4 weeks vs. No intervention/ Blood lipds	NCEP Step 2 Diet (High Fish). Fish served 8/week, chicken or turkey 4 times vs NCEP Step 2 (Low fish) vs Standard American Diet/ Blood lipids
N [5]	57 972	41 578	1602 (558 cases)	342 (171 cases)	57 972	57 972	14 000	5184	28	22
Population/study information [6]	40-79 yrs at baseline, from 34 Japanese communities. Mean follow-up 12.7 yrs.	M and F Japanese 40-59 yrs (in 1990). Follow-up 11 yrs.	Italian F 17-70 yrs 3 case-control studies, case=first episodic MI, Control: no hx of CVD.	M and F >80 years.	40-79 yrs at baseline, from 34 Japanese communities. Mean follow-up 12.7 yrs.	40-79 y-rs at baseline, from 34 Japanese communities. Mean follow-up 12.7 years.	M and F 45- 64 yrs African American and white.	M 2105 F 3079 ≥55 yrs Dutch Mean 67.4 ±7.7yrs Mean follow-up 6.4 yrs.	Healthy males 21-28 yrs. No follow-up beyond intervention.	Adults >40 yrs. No follow-up beyond intervention.
Quality [7]	P	P	0	0	P	P	0	P	P	0
Results [8]	HR (95% CI) Gp 1 1 (ref) Gp 2 0.87 (0.62-1.23) Gp 3 1.10 (0.79-1.54) Gp 4: 0.87 (0.61-1.34), Gp 5 0.77 (0.53-1.10) p=0.22.	HR (95% CI): Total MI Gp 1 1 (ref) Gp 2 0.81 (0.54-1.20) Gp 3 0.85 (0.55-1.31) Gp 4 0.78 (0.48-1.27) Gp5 0.47 (0.26-0.85) p=0.03 Definite MI. Gp 1 1 (ref), Gp 2 0.70 (0.46-1.07) Gp 3 0.74	OR (95% CI) Gp 1: 1 (ref) Gp 2: 0.8 (0.6-1.1) Gp 3: 0.7 (0.5-0.9) p=0.014.	OR (95% CI) Gp 1: 1 ref Gp 2: 0.41 (0.15-1.10) Gp 3: 0.28 (0.1-0.77) Gp 4: 0.55 (0.20-1.51) Gp 5: 0.31 (0.11-0.85) Three upper quintiles vs lowest quintile: 0.36 (0.15-0.87) Three upper quintiles vs lowest quintile (adjusted) 0.37 (0.13-1.03).	HR (95% CI) Gp 1: 1 (ref), Gp 2: 1.44 (0.79-2.62), Gp 3: 1.49 (0.81-2.72), Gp 4: 0.90 (0.46-1.76), Gp 5: 0.73 (0.36-1.46). p=0.16.	HR (95% CI) Gp 1: 1 (ref), Gp 2 : 0.83 (0.59-1.17), Gp 3: 0.63 (0.43-0.91) Gp4: 0.72 (0.50-1.03), Gp 5: 0.76 (0.53-1.09).	Model 1: 0.99 (0.82-1.19) Model 2: 0.99 (0.97-1.23)	Gp 1: 1 (ref) Gp 2: 1.08 (0.81-1.42), Gp 3: 1.17 (0.87-1.57) No association between level of fish intake and incident atrial fibrillation.	Intervention had no effect on totalcholesterol, HDL-cholesterol, LDL-cholesterol or triglycerides (data were not shown).	Both NCP diets showed significant Improvements in blood lipid profile compared to standard american diet, but no difference between each other.

		(0.47-1.16) Gp 4 0.72 (0.44-1.21) Gp 5 0.44 (0.24-0.								
Effect on risk (Increase/None/Protect)	None	Protect	Protect	Protect	None	Protect	None	None	None	Protect
Clinical importance [9]	2	1	1	1	2	2	1	2	3	3
Clinical relevance [10]	1	1	1	1	1	1	1	2	2	2
Generalisability	n	n	y	y	n	n	y	y	y	y
Applicability	y	y	y	y	y	y	y	y	y	y

9.2 FISH and DEMENTIA

Does a particular intake of fish affect the risk of dementia in adults?		
Evidence statement		Consumption of fish more than once per week is associated with a reduced risk of developing dementia in older adults.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	Several Level II and III-2 studies (7 cohorts 4O, 3P) with 2 systematic reviews (1P, 1O that included the 3 cohort studies that were the same, but for different outcomes) with low to moderate risk of bias.
Consistency	Good	Highly consistent that there is weak to moderate effect of fish consumption (at least once a week versus none) on reducing risk for total dementia (All Protect, 2 for NON-APOE carriers only; None showed an increased risk).
Clinical impact	Good	Protective OR was in range 0.30 (0.1-0.9) to 0.73 (0.52-1.03) but No Effect for specific vascular DM 0.7 (0.2-2.8), significant P for trend (5 cohorts & both systematic reviews). No effect for APOE carriers. No effect for fried fish on pre-clinical indicators.
Generalisability	Good/Excellent	Populations in body of evidence can be contextualised to older Australian men and women (>50 years).
Applicability	Excellent	Directly applicable to mid-aged to older adults.

The studies used to make the body of evidence statements are shown in Table 9.5. There are two systematic reviews that have three overlapping cohorts studies included within them. However, one examined dementia in general as an outcome and the other examined Alzheimer's disease specifically as an outcome. Both reviews demonstrated a protective effect for fish consumption of at least once week. The results for the seven cohorts published subsequently to the reviews are all consistent and demonstrate protection for fish consumption for both cognitive decline (four cohorts) and dementia (three cohorts). The only exception was in two studies that stratified results based on presence of the ApoE allele (one for cognitive decline and one for dementia). For those who were carriers of the ApoE allele, fish did not offer protection. The greatest effect on risk reduction was for consumption of total fish (any type estimated together) once a week or more frequently compared to consuming no fish at all. This relationship has been demonstrated for total fish intake (all studies) and fatty fish intake (only in two studies; one for cognitive decline and one for dementia in non-ApoE carriers). However, inclusion criteria for the "fish/seafood" questions across food frequency questionnaires varied considerably between studies, and this limited the ability to make more specific

recommendations on fish type. For the two studies that estimated "fried" fish intake (one on dementia and one on brain white matter grade) as a separate category of fish (including fish burgers), only one study comprehensively examined analyses for specific fish sub-types including eel and shellfish. There is no body of evidence statement made for cognitive decline, given there were only four studies. The studies on cognitive decline did not contribute to the body of evidence statement for dementia.

Summary: The two systematic reviews identified have three overlapping cohorts studies included within them. However, one (McLean, 2005) examined dementia in general as an outcome and the other (Weih 2007) examined Alzheimer's disease specifically as an outcome. Both reviews demonstrated a protective effect for fish consumption of at least once a week. The results for the seven cohorts published subsequently to the reviews are all consistent and demonstrate protection for fish consumption for both cognitive decline (Kalmijn 2004; Virtanen 2008; van Gelder 2007; Morris 2005) and dementia (Barberger-Gateau 2007; Larrieu 2004; Huang 2005). The only exception was in two studies (Barberger-Gateau 2007; Huang, 2005) that stratified results base on presence of the ApoE allele (one for cognitive decline and one for dementia). For those who were carriers of the ApoE allele fish did not offer protection. The greatest effect on risk reduction was for consumption of total fish (any type estimated together) once a week or more frequently compared to consuming no fish at all. However, the definition for what is included in the "fish/seafood" questions across the various food frequency questionnaires does vary considerably between studies limiting the ability to make more specific recommendations on fish type.

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Weih, M., J. Wiltfang, et al. 2007, "Non-pharmacologic prevention of Alzheimer's disease: nutritional and life-style risk factors", *Journal of Neural Transmission*, vol. 114, no. 9, pp. 1187-97.

Table 9.5 Studies used to make evidence statements for fish and dementia

Reference [1]	**Weih 2007 [3285]**	**McLean 2005 [307]**	**Barberger-Gateau 2007 [633]**	**Larrieu 2004 [2883]**	**Kalmijn 2004 [401]**	**Virtanen 2008 [678]**	**van Gelder 2007 [144]**	**Huang 2005 [2879]**	**Morris 2005 [253]**
Type of study [2]	Systematic Review	Systematic Review	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	111-2 (3 cohort studies)	111-2 (3 prospective cohorts as per Weih)	111-2	111-2	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	fish intake by tertiles, quintiles or frequency at least once per wk / Alzheimers Disease, measured by validated questionnaires	fish intake by tertiles, quintiles or frequency at least once per wk / Dementia, measured by validated questionnaires	Fish / frequent consumer defined as eating seafood at least once/wk	Fish / Quartiles of intake	Mean (95% CI) grams of fish and fatty fish/ day for normal cognitive function = 11.0 (10.5-11.6g fish per day) and 3.1 (2.9-3.3 g fatty fish per day) and for impaired (lowest 10%) cognitive function = 9.8 (8.2-11.5 g fish per day) and 2.3 (1.7-2.9g fatty fish per day) / Cognition measured by neuropsychological test battery measuring global cognitive function and specific cognitive domains	Fish <1 per mth to ≥3 per wk & Fried fish 1 per mth to ≥1 per wk; 2xMRIs 2 yrs apart	Fish consumption (yes or no and tertiles of 0, 0–20 and >20 g/d); Mini-Mental State Examination	Quartiles of fish category intakes from <0.25 serves per wk up to ≥4 per wk/ MMSE & other questionnaires	Fish meals per week: Gp 1 0 meals per week Gp 2 1 meal per wk Gp 3 ≥2 meals per week/Cognitive decline
N [5]	>6000	>6000	>8000	>3700	>1600	>2000	210	>2200	3718

Population/study information [6]	M and F >51 yrs	All age groups, predominantly older adults	3 City Cohort Study, Older adults in France >65 yrs	PAQUID, adults >65 yrs France	mid to older age adults 45-70 yrs	medicare eligible Older (≥65y) in USA	Zuphten Elderly study, men >70y	Cardiovascular Health Cognition Study	Adults ≥ 65 yrs Chicago
Quality [7]	O	P	P	O	O	P	O	P	O
Results [8]	Dose response (significant trend) in 2 studies with RR from 0.3 (0.1-0.9) for upper tertile to 0.69 (0.47-1.01) for ≤1/wk; One with no significant trend BUT RR = 0.4 (0.2-0.9) for upper quintile	Non AD dementia Mulivariate RR 0.73 (0.52-1.03); Total dementia RR 0.3 (0.1-0.9) for highest tertile only & for vascular component dementia 0.7 (0.2-2.8) for highest tertile	For frequent fish consumption, there was a 25% lower risk of dementia with borderline significance HR 0.75 (0.54 - 1.04, p=0.08), when stratified by ApoE, NON-ApoE carriers HR 0.60 (0.41-0.89, p<0.01), but not significant for carriers.	When fish consumers dichotomized into "fish < 1/wk" vs. "fish ≥1/wk" incidence was lower in the fish ≥1/wk. Adjusted for age and sex those eating fish at least 1/wk had a RR for developing dementia in the next 7 years of 0.66 (95%CI 0.46-0.92); when education added to adj RR=0.73 (95%CI 0.52-1.03). For AD adjusted for	Per SD increase in fatty fish (4 g/day) intake, the risk of impaired overall cognitive function and speed was decreased by 23% and 29% OR 0.77 (95% CI 0.6-0.97) and OR 0.71 (95% CI 0.55-0.92, p<0.05).	Multivariate adj RR for one or more subclinical infarcts was lower for tuna/other fish _3 times per week, cf. once per month RR 0.74 (95% CI 0.54–1.01) p _ 0.06, p trend _ 0.03). Tuna/other fish consumption also showed trends toward lower incidence of subclinical infarcts and better white matter grade, but not with sulcal and ventricular grades,	From multivariate linear regression, mean cognitive decline in fish non-consumers -1.2 (95%CI -1.9--0.6) versus fish consumers -0.3 (-0.6-0.1), P= 0.01 P for trend for 5yr cognitive decline by tertile, P=0.07.	Tuna/other non-fried fish ≥4 times/week protects against incident dementia (HR 0.63, 95% CI: 0.44 to 0.90) and AD (HR 0.56, 95% CI: 0.34 to 0.91), but not after adjusting for education and income. Fatty fish had little or no association for individuals with APOE ε4 (HR for two to four servings per week 0.91, 95% CI: 0.48 to 1.71), but was associated with significantly lower hazard	Annual rate of decline in cognitive score (standardised unit per year) by number of fish meals per week. Gp 1: -1.01 Gp 2: -0.09 (p=0.03) Gp 3: -0.088 (p=0.04)

				age and sex RR= 0.68 (95%CI 0.46-1.01) and when education added to adjusted then RR= 0.77 (95%CI 0.52-1.14).		markers of brain atrophy. No associations between fried fish consumption and any subclinical brain abnormalities.		ratios for those without the allele (HR for two to four servings per week 0.60, 95% CI 0.40 to 0.89). After controlling for age at baseline, minority status, sex, energy, BMI, and region, the association remained significant for APOE ε4– negative individuals. However, adding education and income to the models attenuated the association	
Effect on Risk (Increase/None/Protect)	Protect	Protect	Protect for non-ApoE carriers	Protect	Protect	Protect	Protect	Protect for non-ApoE carriers	Protect
Clinical importance [9]	1	1	1	2	1	1	2	2	1
Clinical relevance [10]	1	1	1	1	1	1	1	2	2
Generalisability	y	y	y	y	y	y	y	y	y
Applicability	y	y	y	n	y	y	y	y	y

9.3 FISH and DEPRESSION

Does a particular intake of fish affect the risk of depression in adults?		
Evidence statement		Consumption of at least one serve of fish a week is not associated with reduced risk of depression.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Poor	1 neutral systematic review (that included 1 cohort study and other lower level designs) plus 6 Level III-2 studies (5 cohort, 1 case-control). 6 studies had a moderate to high risk of bias and 1 cohort with low risk of bias. 3 cross-sectional studies within sys r/v (2P, 1O) not included.
Consistency	Good	Consistent that there is no effect of fish consumption on risk of depression (6 no-effect cohort studies; 1 increase risk (for those with a high baseline fish intake who then increased their fish intake further).
Clinical impact	Poor	Most of the confidence intervals around the odds ratios cross one with the two multivariate regression analyses not significant.
Generalisability	Good	Populations in body of evidence relevant to older Australian men (>50y), mid aged adults (35y +/- 4y) and pregnant/postpartum women (2 studies).
Applicability	Excellent	Applicable to the populations above, with some caveats.

The studies used to make the body of evidence statements are shown in Table 9.6. The only systematic review located was of neutral quality and the studies within it were of low level design. There were six additional Level III-2 studies included but only two of these were of positive quality. Six of the seven studies consistently reported no relationship between fish and risk of depression with the only one that did was in a subgroup within the study who had a high baseline fish intake and then subsequently increased their intake further. It is important to note that two of the studies (1, 4) were conducted on postpartum depression (one cohort neutral quality and one case-control positive quality) and both showed no effect.

Summary: One systematic review (Sontrop 2006) and two prospective cohort (Colangelo 2009; Kyrozis 2008) and one retrospective cohort study (Schieper 2009) did not show a relationship; the one cohort study (Sanchez-Villegas 2007) that did show a relationship, recruited a subgroup within the study that had a high baseline fish intake and subsequently increased their intake further**.**

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Table 9.6 Studies used to make evidence statement for fish and depression

Reference [1]	**Sontrop 2006 [824]**	**Sanchez-Villegas 2007 [116]**	**Schieper 2009 [1006]**	**Colangelo 2009 [1016]**	**Kyrozis 2008 [1121]**	**Miyake 2006 [2873]**	**Browne 2006 [2878]**
Type of study [2]	Systematic Review (1 cohort, 3 cross-sectional)	Cohort	Retrospective Cohort	Cohort	Cohort	Cohort	Case-Control
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	low fish intake (definition varies) versus higher intake / depression mesured by questionnaire, not always validated.	Fish (including oily fish) quintiles from median of 36 g per day (quintile1) to 162 g per day (quintile 5).	Frequency of fish intake assessed and converted to a dimensionless score (max 48). Mean (range) intake 8.5 (0-44).	Intake divided into quintiles; only baseline mean (SD) intakes reported as Men 0.7 (1.2) serves per week, Women 0.5 (0.9) serves per week.	Baseline only:mean (SD) fish+seafood g per day:men 26.4 (16.3), women 24.2 (14.9).	Fish Intake (g per day) by quartile: Q1 23.1g, Q2.37.9g, Q3 51.4g, Q4 72.9g.	No fish versus Any fish.
N [5]	>30,000	7900	241 only of original sample >1800	3300	610 >60y	865 pregnant	41 cases, 39 controls
Population/study information [6]	29 133 Finnish men 50-69 yrs followed median 6 yrs other 3 studies cross-sectional.	young to mid aged University graduates 28-57 yrs.	older adults from Netherlands, mean age 60 yrs (37-88 yrs).	M and F mean 35 +/-4 yrs CARDIA study 4 USA communities (includes African-Americans).	Older adults from Greece.	fish intake during pregnancy and postpartum depression in Japan.	fish intake during pregnancy and postpartum depression.
Quality [7]	O	O	O	P	O	N	P
Results [8]	For the cohort study: no association with baseline fish intake and	lower risk only for moderate to high intakes (quintiles 3	No association, p=0.5; no	No trend for men or women, ORs from 1.0 (0.83 to	Logistic regression not	No association and no	Logistic regression p>0.29

	self-reported feelings of depression in last 3mth. Note use of an invalidated tool to measure "depressed mood" & inclusion of earlier reports of depressed mood in the prediction model would have attenuated associations.	and 4) median fish intakes of 85 to 112 g per day; ORs of 0.49 to 0.95. Note that when change in fish intake tested those with high baseline who had increased intake had increased risk (ORs 1.10 to 2.22).	trend data reported.	1.43) to 0.97 (0.73-1.28).	significant p>0.5	trend, OR 1.2 to 0.89 and wide CIs.	
Effect on risk (Increase/None/Protect)	None	Increased Risk Only on a secondary analysis for those who changed intake) and Protect.	None	None	None	None	None
Clinical importance [9]	1	4	3	2	4	3	3
Clinical relevance [10]	1	2	2	2	2	2	2
Generalisability		y	y	y	y	y	y
Applicability		y	y	y	y	y	y

9.4 FISH and AGE RELATED MACULAR DEGENERATION

Does a particular intake of fish affect the risk of age related macular degeneration in adults?		
Evidence statement		Consumption of fish two or more times per week is associated with reduced risk of age-related macular degeneration.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 positive quality systematic review of 3 case-control, 3 cohort and 3 cross-sectional studies (Level III-2) including meta-analysis.
Consistency	Excellent	Meta-analysis for both early and late onset age related macular degeneration were not statistically heterogeneous (I^2 : 11.2% (p=0.002) and 0% (p<0.01).
Clinical impact	Good	OR = 0.76 (0.64-0.90) and OR = 0.67 (0.53-0.85), therefore moderate to high impact at follow-up from 5 to 12 years.
Generalisability	Good	Middle aged to older adults (>49 years).
Applicability	Good	Applicable to Australia adults.

The study used to make the body of evidence statement is shown in Table 9.7. This positive quality systematic review included nine heterogeneous studies (three cohort, three cross-sectional, three case-control) and included 88 974 participants, including 3203 cases of age related macular degeneration.

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Table 9.7 Studies used to make evidence statement for fish and age related macular degeneration

Reference [1]	Chong 2008 [59]
Type of study [2]	Systematic Review of Cohort, Case Control and Cross-sectional with meta-analysis.
Level of evidence [3]	III-2
Intervention/ comparator [4]	Fish intake varied across studies/ Early and late age-related macular degeneration.
N [5]	9 studies (3 cohort, 3 cross-sectional, 3 case-control). 88 974 participants, including 3203 cases of age related macular degeneration .
Population/study information [6]	Adults (>49 years)
Quality [7]	P
Results [8]	1. Fish intake and early AMD from 3 cohort studies & 3 cross-sectional studies - fixed effects. OR = 0.76 (0.64-0.90); I-squared for heterogenity, P=0.002 2. Fish intake and late AMD from 1 cohort studies, 3 case-control studies & 2 cross-sectional studies - fixed effects. OR = 0.67 (0.53-0.85); I-squared for heterogenity, P=0.001. Fish 2 or more times per week may be protective against age related macular degeneration.
Effect on risk (Increase/None/Protect)	Protect
Clinical importance [9]	1
Clinical relevance [10]	1
Generalisability	y
Applicability	y

9.5 FISH and STROKE

Does a particular intake of fish affect the risk of stroke in adults?		
Evidence statement		Consumption of fish at least twice a week is associated with a reduced risk of stroke
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	3 systematic reviews (2 negative, 1 positive quality) and 7 Level III cohort studies with low to moderate risk of bias.
Consistency	Satisfactory	All 3 systematic review consistent for protection but heterogenity across the 7 cohorts (3 Protect, 1 increase, 3 no effect. Variability accounted for variation in dietary methodology and study quality.
Clinical impact	Good	Protective ORs for total stroke incidence generally in range 0.50-1.0
Generalisability	Good	Populations in body of evidence can be contextualised to the Australian mid-aged population.
Applicability	Excellent	The study showing increased risk for fried fish/ burgers included analysis showing a protective effect for other "non-fried" fish.

The studies used to make the body of evidence statements are shown in Table 9.8. The three systematic reviews were consistent for protection from total stroke associated with higher fish consumption with moderate to substantial reductions (15% to 30%) in risk for total stroke compared to the lowest fish intake levels. The study showing an increased risk for stroke with higher fish consumption (8) was of positive quality but had a major flaw in the dietary methodology and measured total household intake using a household inventory with intake averaged across all household members and is likely to have confounded the association. When stroke categories were examined specifically, most commonly there were no associations with hemorrhagic stroke. Of the three cohorts showing no effect, two were from Japan where fish intakes reach higher levels than in Australia which may confound associations.

Summary: Three systematic reviews (Bouzan et al, 2005; Ding et al, 2006; Gochfeld et al, 2005;) found that higher fish consumption was associated with reduced risk of stroke. One cohort study showed an increased risk for stroke with higher fish consumption (Yamagishi et al, 2008), however the definition of fish in that study included fried fish and fried fish burgers and measured total household intake using a household inventory with intake averaged across all household members- these methodological issues are likely to have confounded results.

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Table 9.8 Studies used to make evidence statements for fish and stroke

Ness 2005 [624]	**Folsom 2004 [342]**	**Nakamura 2005 [2176]**	**Yamagishi 2008 [1150]**
Cohort	Cohort	Cohort	Cohort
III-2	III-2	III-2	III-2
Quartiles of intake (g). Gp 1 (low): Range: 0-6.9, Mean 1.8 (2.4), Gp 2: Range: 7-15.7, Mean (11.3 (2.5), Gp 3: Range: 15.8- 29.2, Mean: 21.6 (3.9), Gp 4: Range: 29.2-148.9, Mean: 44.5 (15.5)/Stroke Mortality	Quintiles of servings/week. Gp 1: <0.5, Gp 2: 0.5 to <1, Gp 3: 1.0-1.5, >1/5 to <2.5, ≥2.5 serves/week /Stroke mortality	Frequency of intake. 2 or more times/day, About 1 time/day, about 1 time per 2 days, about 1 to 2 times/week, <1/week/ Stroke mortality, cerebral haemorrhage and cerebral infarction	Quintiles of intake. Gp 1 0-27g/d, Gp2: 27 to 39g/d, Gp3: 39 to 53g/d, Gp4: 53 to 72 g/d, Gp5: 72 to 229g/d/ Total stroke, intraparenchymal hemmorhage, subarachnoid hemarrhage, ischemic stroke
4028	41836	8879	57972
1352 families living in 16 areas of England and Scotland (1937-1939), data on 4999 children aged 0 to 19 years. 61 to 63 years of follow-up	Women aged 55-69 in 1986, US, Follow-up: 11 years	Males and Females aged 30 years+, Japan, Follow-up 19 years	40 to 79 years at baseline, from 34 Japanese communities. Mean follow-up 12.7 years
P	P	P	P
RR (95% CI) Gp 1: 1 (ref), Gp 2: 0.79 (0.39-1.60), Gp 3: 1.13 (0.58-2.18), Gp 4: 2.01 (1.09 to 3.69) p=0.01. Higher fish intake associated with higher stroke mortality	Stroke Mortality: Gp 1: 1 (Ref), Gp 2: 1.30 (0.86-1.96), Gp 3: 0.95 (0.64-1.41), Gp 4:0.90 (0.53-1.53), Gp 5:1.06 (0.67-1.67). P=0.65.	Stroke death: Gp 1: 1.26 (0.70-2.29), Gp 2: 1.20 (0.82-1.75) Gp3: 1.09 (0.78-1.53), Gp 4 : 1 (ref), Gp 5: 1.34 (0.73-2.44) p=0.52. Cerebral hemorrhage death. Gp 1: 0.92 (0.20), Gp 2: 0.99 (0.38-2.56), Gp 3: 1.77 (0.84-3.69) Gp 4: 1 (ref), Gp 5: 0.55 (0.0	Total stroke. Gp 1: 1 (ref), Gp 2:0.95 (0.78-1.16), Gp 3: 0.93 (0.76-1.14) Gp 4: 0.92 (0.75-1.14) Gp 5: 0.91 (0.74-1.13) p=0.40 Intraparenchymal hemorrhage Gp 1: 1 (ref), Gp 2: 0.93 (0.62-1.40, Gp 3: 0.91 (0.60-1.39), Gp 4: 0.78 (0.50-1.21), Gp 5: 0.95 (
Increase	None	None	None
1	2	2	2
1	1	1	1
Y	Y	N	N
Y	Y	Y	Y

9.6 FISH and BREAST CANCER

Does a particular intake of fish affect the risk of breast cancer in adults?		
Evidence statement		Consumption of fish is not associated with risk of breast cancer.
Grade		D
Component	**Rating**	
Evidence Base	Poor	7 studies all Level III-2.breast cancer. 2 systematic reviews of cohorts (1 negative, 1 neutral quality), 2 cohort studies (both positive quality) and 3 case-control (all neutral quality).
Consistency	Satisfactory	The 2 systematic reviews provided no clear results or conclusive evidence, 2 cohort studies showed no association, 2 case control showed no association, 1 case control showed protective effect of not-fried fish intake (>1 serve per year) and 1 case-control showed increased risk with smoked fish in pre-menopause.
Clinical impact	Satisfactory	Most CI cross 1 in case-controls/cohorts and no meta-analysis/synthesis of results in systematic reviews.
Generalisability	Good	All studies in adults. .Some studies among high fish consuming populations with fish consumption patterns much higher than in Australia.
Applicability	Good	Applicable to Australia adults.

The studies used to make the body of evidence statements are shown in Table 9.9. Two systematic reviews, of negative and neutral quality, provided no synthesis of the evidence and concluded from a narrative summary that the evidence is not conclusive in relation to fish consumption and breast cancer risk. Two high quality cohort studies, and three neutral quality case-control studies conducted throughout Europe, in the US, Canada and Uruguay, demonstrated no effect of total fish consumption on breast cancer risk. One case-control demonstrated an increase risk of breast cancer with high fried fish consumption, and decreased risk with high non-fried fish consumption.

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Table 9.9 Studies used to make evidence statements for fish and breast cancer

Reference [1]	[1356]	Terry 2004 [338]	Folsom 2004 [342]	Engeset 2006 [217]	Hu 2008 [69]	Terry 2002 [490]	[2678]
Type of study [2]	Systematic review ofcohort studies	Systematic review of cohort studies	Cohort	Cohort study	Case-control	Case-control	Case-control
[3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Level of evidence [3]	Fish intake (unclear)/breast cancer risk	Fish intake (variable across studies)/Breast cancer risk	Frequency of fish intake per week Gp 1: <0.5, Gp 2: 0.5 to <1, Gp 3: 1.0-1.5, >1/5 to <2.5, ≥2.5 serves/week /Breast cancer	Quintile of intake (g/day). Total Mean Intake: 38.37g/day, Gp 1: 5.54g Gp2: 17.94 Gp3: 30.5, Gp4: 48, Gp5: 96.77/Breast cancer incidence	Fish intake per week (oz) Gp 1 (Low) ≤2, Gp2: 3-4 Gp3: ≥5/ Breast cancer incidence	Fish servings per week Gp 1L 0 to ≤0.5, Gp 2: >0.5 to ≤1, Gp 3: >1 to ≤2 gp 4: >2 to ≤3.5, Gp 5: >3.5/ Breast cancer incidence	Fried fish intake (per year) Gp 1: Low 0 serves per week, Gp 2: Mid 1-52, Gp 3:≥ 53 Not fried fish
[3]	~6 studies	9 studies	41836	310,671	7041 (2363 cases)	4085 (2085 cases)	333 (111 cases)
Level of evidence [3]	Adults, length of follow-up unclear	Adult. Length of follow-up unclear	Women aged 55 to 65 years, Iowa, 11 years of follow-up	Female EPIC, 35 to 70 years of age, general population living in 10 EPIC countries. Followed up for 6 to 12 years	Canadian adults	Swedish, Post-meopausal women aged 50 to 74 years	Uruguanian Women
[3]	N	O	P	P	0	0	0
Level of evidence [3]	Evidence not synthesised.	Evidence not synthesised. Concluded evidence not conclusive	RR of breast cancer incidence Gp 1: 1 (ref) Gp 2: 0.96 (0.90-1.16) Gp 3: 0.91 (0.77-1.08) Gp 4: 0.97 (0.79-1.19) Gp 5: 0.92 (0.76-	Total fish consumption Gp 1: 1 (ref) Gp 2: 0.99 (0.9-1.10), Gp 3: 0.98 (0.89-1.09), Gp 4: 0.98 (0.88-1.09) Gp 5: 1.07 (0.95-1.20) p=0.36 Total fish pre-menopausal women Gp 1: 1 (ref), Gp 2: 0.89 (0.71, 1.12), Gp 3: 1.08	BREAST CANCER Total Fish Gp 1: Ref 1.0 Gp 2: 1.0 (0.9-1.2) Gp 3: 1.1 (1.0-1.3) p=0.17 Fresh fish Gp 1 1.0 (ref) Gp 2: 1.0 (0.8-1.2) Gp3: 1.1(0.9-1.4)	Total fish Gp 1: 1 (ref), Gp 2:1.12 (0.761.69), Gp 3: 0.97 (0.68-1.38) Gp 4: 0).93 (0.65-1.32), Gp 5: 0.88 p=0.15 Fatty fish Gp 1: 1 (ref), Gp 2: 0.95 (0.78-1.14), Gp 3: 0.94 (0.78-1.13), Gp	Total fish Gp 1: 1 (ref) Gp 2: 0.52 (0.26-1.05), Gp 3: 0.79 (0.44-1.42) Fried fish Gp 1: 1 (ref), Gp 2: 1.35 (0.72-2.54), Gp 3: 1.99 (1.02-3.88)
Level of evidence [3]	Unclear	Unclear	None	None	None - except for smoked fish for premenopause	None	None for total. Increased for fried fish.
[3]	3	3	3	2	3	2	1
[3]	1	1	1	1	1	1	1
Level of evidence [3]	Y	Y	Y	Y	Y	Y	N
Level of evidence [3]	Y	Y	Y	Y	Y	Y	Y

9.7 FISH and COLORECTAL CANCER

Does a particular intake of fish affect the risk of colorectal cancer in adults?		
Evidence statement		Consumption of fish is not associated with risk of colorectal cancer.
Grade		D
Component	**Rating**	
Evidence Base	Poor	8 studies, all Level III-2. 1 systematic review of cohorts of negative quality , 2 cohort studies (both positive quality) and 5 case-control studies (all of neutral quality).
Consistency	Satisfactory	Systematic review showed no association, 2 cohort studies showed no association, 3 of the case-control studies demonstrated no associations and 2 case-control demonstrated protective effect at higher levels of intake (1 or more servings weekly and >4/week).
Clinical impact	Poor	Most CI cross one and no meta-analysis for systematic review.
Generalisability	Good	All studies in adults. Several studies gender specific. Some studies among high fish consuming populations with fish consumption patterns much higher than in Australia.
Applicability	Good	Applicable to Australia adults.

The studies used to make the body of evidence statements are shown 9.10. One negative quality systematic review with no synthesis of results concluded in a narrative summary that there is no association between fish intake and colorectal cancer risk. Two high quality cohort studies, including women only from Norway and China, showed fish intake had no effect on colon or colorectal cancer respectively. Five neutral quality, case-control studies produced inconclusive results. Three case-control studies demonstrated no effect of fish intake on colorectal cancer. One study demonstrated a protective effect of high fish consumption (not defined) on colorectal cancer incidence in Korean adults. Another study of Japanese adults demonstrated high fish consumption (>4 per week) was protective against colon cancer for males and rectal cancer for females.

Table 9.10 Studies used to make evidence statements for fish and colorectal cancer

Reference [1]	**Marques-Vidal 2006 [711]**	**Engeset 2007 [620]**	**Lee 2009 [3017]**	**Yang 2003 [469]**	**Hu 2008 [69]**	**Jedrychowski 2008, [3040]**	**Oh 2005 [2073]**	**Busstra 2003 [444]**
Type of study [2]	Systematic review of cohort study	Cohort study	Cohort study	Case-control	Case-control	Case-control	Case-control	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Fish intake (variable across studies)/ colo-rectal cancer risk	Tertiles of total fish (g per day): Gp 1 (T1): Mean fish: 46.2 (44.1), Gp 2 (T2): 92.6 (92.9), Gp 3 (T3): 167.2 (172.2)/ Colon cancer incidence	Quintiles of fish intake (g per day). Range mean of intake not reported./ Incidence of rectum, colon and colo-rectal cancer	Raw/cooked fish: 1<time per wk, 1-2 times per wk, 3-4 per week, >4 per week. Dried salted fish: <1 per wk, 1-2 per wk, >3 per wk/ Incidence of colon and rectal cancer	Fish intake per week (oz) Gp 1: (Low) ≤2, Gp2: 3-4 Gp3: ≥5	Gp 1: Very Low intake Gp 2:low intake Gp3: Medium Gp3: High intake/ Colon and rectum cancer	Tertiles of fish intake (g per day) Gp 1: 0, Gp 2 0-41g/d Gp 3: 41-90g/d/ Colo-rectal cancer risk	Frequency fish Gp1: <1 per month, Gp 2: 1 per month-1 per wk Gp3: >1 per wk Total fish intake (g per day) Gp 1: <6.4 Gp2: 6.4-14.0 Gp3: ≥14/ Colo-rectal cancer risk
N [5]	541,374 12 studies	63,914	73,244	48,436 1550 cases	8213 1727 Colon 1447 Rectum	1329 584 cases	270 136 cases	109 52 cases
Population/study information [6]	Adults. Follow-up 3.3 to 24 yrs	F 40-71 yrs. Norway, assume	75000, F 40-70 yrs, Shanghai China,	M and F 40-75 yrs Japan	M and F adults Canadian	M and F adults Korea	M and F 30-70 yrs	Dutch-speaking Western

		Adults Follow-up 5-8 yrs	follow-up mean 7.4 years				Koreans	Europeans diagnosed before 75 years. The Netherlands
Quality [7]	N	P	P	0	0	0	0	0
Results [8]	No pooled analysis, narrative summary. No association between fish intake and colo-rectal cancer.	RR (95% CI) Total fish. Gp 1: 1 (ref), Gp 2: 0.93 (0.66-1.31), Gp 3: 1.28 (0.90-1.81) p=0.14 Fish product Gp 1 1 (ref), Gp 2: 0.76 (0.55-1.05) Gp 3: 0.96 (0.69-1.32) p=0.81 Fatty fish Gp 1: 1 (ref), Gp2: 1.21 (0.88-1.66), Gp 3:1.22 (0.88-1.71) p=0.24 Lean fish Gp 1: 1 (ref) Gp 2: 1.05 (0.75-1.49),	TOTAL FISH Colorectal cancer Gp 1 Ref, Gp 2: 1.2, Gp 3: 1.2, Gp 4: 1.5, Gp 5 1.3 (0.9-1.9) p=0.21 Colon cancer Gp 1 Ref, Gp2: 1.1. Gp 3: 1.0 Gp 4: 1.4, Gp5: 1.4 (0.9-2.1) p=0.59 Rectal Cancer Gp 1 ref, Gp2: 1.3, Gp 3: 1.5, Gp 4: 1.5, Gp 5: 1.3 (0.7- 2.4) p=0.35 MARINE FISH Colorectal cancer Gp 1: Ref, Gp 2: 0.7, Gp 3: 0.8, Gp4: 1.1, Gp 5: 1.0 (0.7-1.4)	Frequent raw/cooked fish intake was associated with a decreased risk of male colon cancer, OR=0.68 (95% CI 0.47–0.99) and marginal decrease for female rectal cancer, OR=0.58 (95% CI 0.31–1.07) (highest vs lowest frequency).There was no significant association between overall frequent dried/salted fish intake and risk of colorectal cancer with ORs around 1 for	RR Colon Ca (95% CI) Total Fish: Gp 1: Ref 1.0; Gp 2: 0.9 (0.7-1.2); Gp 3: 1.0 (0.8-1.3) p=0.67; Fresh fish: Gp 1 1.0 (ref); Gp 2: 0.9 (0.7-1.1); Gp3: 1.0 (0.8-1.3) p=0.90 Smoked fish: Gp 1: 1 ref; Gp 2: 0.9 (0.8-1.1); Gp 3: 1.3 (0.8-2.0) p=0.92 RR Rectum Ca (95% CI). Total	RR Colo-rectal Ca (95% CI) Gp 1: 1.0 (Ref): Gp 2: 0.74 (0.54-1.01) p=0.06; Gp 3: 0.73 (0.53-1.0) p=0.05; Gp 4: 0.71 (0.51-0.98) P=0.043	RR Colorectal cancer: Gp 1: Ref, Gp 2: 0.93 (0.74-1.78) p=0.2309, Gp 3: 2.01 (0.97-4.18) p=0.0563	RR of colo-rectal cancer (95% CI); Frequency of fish: Gp 1: Ref (1.0); Gp 2: 0.6 (0.2,1.8); Gp 3: 0.5 (0.2-1.6) p=0.25 Total fish intake: Gp 1: 1.0; Gp 2: 0.4 (0.2-1.3); Gp3: 0.4 (0.2, 1.3) p=0.12

		Gp 3: 1.23 (0.88, 1.71) p=0.22	p=0.34 Colon cancer Gp 1: Ref, Gp 2: 0.5, Gp 3: 0.7, Gp4: 1.1, Gp 5: 0.8 (0.5-1.2) p=0.52 Rectal cancer Gp 1: Ref, Gp 2: 0.9, Gp 3: 1.0, Gp4: 1.2, Gp 5: 1.4 (0.8-2.3) p=0.39 FRESH WATER FISH Gp 1: Ref, Gp 2: 1.0, Gp 3: 0.8, Gp4: 1.0, Gp 5: 0.9 (0.6-1.2) p=0.67 Colon cancer Gp 1: Ref, Gp 2: 0.9, Gp 3: 0.7, Gp4: 0.8, Gp 5: 0.8 (0.5-1.2) p=0.55 Rectal cancer Gp 1: Ref, Gp 2: 1.0, Gp 3: 1.0, Gp4: 1.4, Gp 5: 1.0 (0.6-1.7) p=0.95 EEL	both men and women.	fish: Gp 1: 1.0 ref;Gp 2: 0.9 (0.7-1.1); Gp 3: 0.9 (0.7-1.2) p=0.94 Fresh fish: Gp 1: 1.0 (Ref); Gp 2: 0.9 (0.7-1.1); Gp 3: 0.9 (0.6-1.1) p=0.34 Smoked fish: Gp 1: 1.0 (Ref); Gp 2: 1.0 (0.8-1.2): Gp 3: 1.3(0.8-2.1) p=0.40			

			Gp 1: Ref, Gp 2: 1.1, Gp 3: 1.4, Gp4: 1.2, Gp 5: 1.3 (0.9-1.7) p=0.01 Colon cancer Gp 1: Ref, Gp 2: 1.0, Gp 3: 1.2, Gp4: 1.0, Gp 5: 1.4 (0.9-2.1) p=0.05 Rectal cancer Gp 1: Ref, Gp 2: 1.3, Gp 3: 1.7, Gp4: 1.5, Gp 5: 1.1 (0.6-1.0) p=0.03 SHRIMP Gp 1: Ref, Gp 2: 0.9, Gp 3: 1.3, Gp4: 1.0, Gp 5: 1.3 (1.0-1.3) p=0.06 Colon cancer Gp 1: Ref, Gp 2: 0.8, Gp 3: 1.1, Gp4: 1.1, Gp 5: 1.4 (0.9-2.1) p=0.04 Rectal cancer Gp 1: Ref, Gp 2: 1.0, Gp 3: 1.6, Gp4: 0.9, Gp 5:					

			1.3 (0.7-2.2) p=0.03 SHELLFISH Gp 1: Ref, Gp 2: 1.1, Gp 3: 1.3 (1.0-1.6) p=0.04 Colon cancer Gp 1: Ref, Gp 2: 1.2, Gp 3:1.4 (1.1-1.9) p=0.03 Rectal cancer Gp 1: Ref, Gp 2: 1.0, Gp 3: 1.1 (0.8-1.6) ,p=0.52. No overall association between total consumption of fish and colo-rectal cancer. Association between CRC and consumption of eel and shellfish .					
Effect on risk (Increase/None/Protect)	None	None	None for total fish. Protect for eel and shellfish.	Yes (male colon, female rectal)	None	Protect	None	None
Clinical importance [9]	3	2	3	1	3	1	2	2
Clinical relevance [10]	1	1	1	1	1	1	1	1

Generalisability	y	y	y	y	y	y	y	y
Applicability	y	y	y	y	y	y	y	y

9.8 FISH and PROSTATE CANCER

Does a particular intake of fish affect the risk of prostate cancer in adults?		
Evidence statement		Consumption of fish is not associated with risk of prostate cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Poor	7 Studies all Level III-2. 3 systematic reviews (2 of cohorts and 1 of cohorts and case-controls), 2 of negative and 1 neutral quality. 4 case-control studies all of neutral quality. Therefore moderate to high risk of bias.
Consistency	Poor	Systematic reviews (3) state evidence inconclusive, 2 case-controls show no association, 1 shows an increased risk for smoked fish and 2 show protection, at higher levels of intake (≥4 serves per week, serving size not specified).
Clinical impact	Poor	Most CI cross one in case-controls and no meta-analysis/synthesis of results in systematic reviews.
Generalisability	Satisfactory	All studies in adults. Some studies among high fish consuming populations with fish consumption patterns much higher than in Australia.
Applicability	Good	Applicable to Australia adults.

The studies used to make the body of evidence statements are shown in 9.11. The three systematic reviews of negative or neutral quality presented results in narrative summary only, and overall reported that the evidence is inconclusive in relation to fish intake and prostate cancer risk. The four case-control studies, of neutral quality, were also inconclusive with two finding no effect and two a protective effect of higher fish consumption on prostate cancer risk. Three of the four case-control studies were conducted in Canada, the other Japan.

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Table 9.11 Studies used to make evidence statements for fish and prostate cancer

Reference [1]	**Astorg 2004 [379]**	**Mori 2009 [3031]**	**Terry 2004 [338]**	**Hu 2008 [69]**	**Mina [582]**	**Sonoda 2004 [395]**	**Amin 2008 [3223]**
Type of study [2]	Systematic review of case control and cohort	Systematic review of cohort studies	Systematic review of cohort studies	Case-control	Case-control	Case-control	Case-control
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Fish intake (variable across studies)/Prostate cancer risk	Fish intake (variable across studies)/Prostate cancer risk	Fish intake (variable across studies)/Prostate cancer risk	Fish intake previous 2 years, and 20 years earlier.I ntake per week (oz) Gp 1 (Low) ≤2, Gp2: 3-4 Gp3: ≥5	Fish intake previous 2 years, and whether different 20 years earlier. Frequency of consumption Fresh and canned fish: Gp 1: 0 Gp2: 1-3/month Gp3: 1/week Gp 4: 2 or more/week. Preserved fish: Gp1: 0, Gp 2: 1-2/month, Gp 3: 1 or more/week	Usual fish intake in past 5 years. Gp 1: ≤47.3g/d, Gp2: 47.3-75.7g/d Gp3: 75.7-130.7g/d Gp4:≥130.7g/d/ Prostate cancer incidence	Fish intake: Gp 1: 1/wk Gp2: 2/wk, Gp3: 3/wk Gp4: 4/wk Gp5: Data missing/Prostate cancer incidence
N [5]	Number of participants unclear. 10 studies.	Number of participants unclear. 13 studies.	9 studies	1799 Cases, 5039 Controls	1534 Cases, 1607 Controls	140 Cases 140 Controls	386 Cases, 292 controls
Population/study information [6]	Male. Adults. Follow-up	Male, Adults. Follow-up ranged	Adult males. Length of	Canadian adults aged 20	Canadian Males aged	Japanese, Males, Aged	Canadian Males Aged >60 years

	ranged from 0-21.4 years	from 0- 30 years	follow-up unclear	to 76 years	20 to 79 years	59 to 73 years	
Quality [7]	O	N	N	0	0	0	0
Results [8]	Evidence not synthesised only narrative summary. Majority of studies show no significant association between fish intake and all stages of prostate cancer. However two more recent studies show a significant association between fatal or metastatic prostate cancer and fish consumption.	Evidence not synthesised, only a narrative summary. No clear conclusion regarding association between fish intake and prostate cancer risk	Evidence not synthesised. Concluded evidence not conclusive	OR (95% CI) Total Fish Gp 1: Ref 1.0 Gp 2: 0.8 (0.7-1.0) Gp 3: 0.8 (0.7-1.0) p=0.08 Fresh fish Gp 1 1.0 (ref) Gp 2: 1.0 (0.8-1.3) Gp3: 1.1(0.8-1.4) p=0.65 Smoked fish Gp 1: 1 ref Gp 2: 0.7 (0.6-0.9) Gp 3: 0.7 (0.4-1.2) p=0.002	OR (95% CI) FRESH AND CANNED FISH Gp 1: 1 Ref Gp 2: 1.09 (0.85-1.39) Gp 3: 1.04 (0.82-1.32) Gp4: 1.10 (0.84-1.42) PRESERVED FISH Gp 1: 1 Ref Gp 2: 0.78 (0.64-0.95) Gp 3: 0.70 (0.61-1.02)	OR (95% CI) Gp 1: 1 (Ref) Gp 2: 1.04 (0.53-2.02) Gp 3: 0.79 (0.38-1.59) Gp 4: 0.45 (0.2-1.02) p=0.04	OR (95% CI) Gp 1: 1.0 (Ref) Gp 2: 1.23 (0.67-1.45) Gp 3: 0.97 (0.95-1.56) Gp 4: 0.77 (0.26-0.91) Gp 5: 0.54 (0.32-0.89) p=0.017
Effect on risk (Increase/None/Protect)	None and Increase	Unclear	Unclear	None for total and fresh fish. Increase for smoked fish	None	Protect	Protect
Clinical importance [9]	3	3	3	2	2	2	1
Clinical relevance [10]	1	1	1	1	1	1	1
Generalisability	y	y	y	y	y	n	y
Applicability	y	y	y	y	y	y	y

9.9 FISH and RENAL CANCER

Does a particular intake of fish affect the risk of renal cancer in adults?		
Evidence statement		Consumption of fish is not associated with risk of renal cell cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	2 studies both Level III-2. 1 pooled analysis of cohorts of positive quality and 1 case control study of neutral quality.
Consistency	Good	All studies showed no association between fish consumption and the occurrence of renal cell carcinomas.
Clinical impact	Poor	All CI cross one.
Generalisability	Good	Both studies in adults.
Applicability	Good	Applicable to Australian adults.

The studies used to make the body of evidence statements are shown in Table 9.12. There was one neutral quality pooled analysis of prospective cohort studies (Lee 2008) that aggregated results from >500,000 women and 240,000 men. When fish was reported by quintiles of intake it found no association between risk and fish consumption. The single neutral quality case-control study gave consistent results.

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Table 9.12: Studies used to make evidence statements for fish and renal cancer

Reference [1]	Lee 2008 [3182]	Hu 2008 [69]
Type of study [2]	Pooled analysis of cohort studies	Case control
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Quintiles of intake (g/day)	Fresh, frozen or canned smoked, salted or dried fish intake per week (oz) Gp 1 (Low) ≤2, Gp2: 3-4 Gp3: ≥5/ Renal cancer incidence
N [5]	530469 women and 244483 men	6384 (1345 cases)
Population/study information [6]	Adults, 13 cohort studies	Canadian male and female adults.
Quality [7]	P	0
Results [8]	Intakes of seafood were not associated with the risk of renal call cancer. Multivariable relative risk <11g.day seafood: 1.06 (0.88-1.28), 11 to <16g/day seafood: 1.00 (referrent) 16 to <48g day seafood: 1.03 (0.86- 1.23), ≥48g/day seafood: 1.05 (0.82-1.3	OR 95% CI Total Fish Gp 1: Ref 1.0 Gp 2: 1.0 (0.8-1.2) Gp 3: 1.0 (0.8-1.2) p=0.8 Fresh fish Gp 1 1.0 (ref) Gp 2: 0.9 (0.8-1.1) Gp3: 1.0 (0.8-1.2) p=0.77 Smoked fish Gp 1: 1 ref Gp 2: 1.0 (0.8-1.1) Gp 3: 1.1 (0.7-1.6) p=0.79
Effect on risk (Increase/None/Protect)	None	None
Clinical importance [9]	3	2
Clinical relevance [10]	1	1
Generalisable	Y	Y
Applicable	Y	Y

Summary of Studies not included in body of evidence statements for Fish:
Data was extracted from papers for the following outcomes but there was inadequate evidence base to create body of evidence statements.

Fish and All Cause Mortality
Four cohort studies examined the relationship between frequency of fish consumption and relative risk of death. The follow-up period varied from 11 years in a US study of women aged 55-69 years [342], to 19 year follow-up in Japanese adults aged 30+ years [2176]; 61 to 63 years follow-up in families from UK; to 16 year follow-up in male health professional aged 40-75 years [3179]. None of the studies found any significant associations.

Fish and Cancer Outcomes
All Cause Cancer
Two Level III-2 cohort studies [3179], [342] examining frequency of fish consumption and all cause cancer mortality, both showed no relationship between increasing consumption and risk of cancer mortality.

Thyroid Cancer
One Level III-2 systematic of cohort studies on thyroid cancer in adults [3101] and one case-control study [2770] in women examining thyroid cancer.

The systematic review included three studies related to fish consumption. It reported that frequent intake of cooked fish was inversely associated with non-differentiated type of cancer (OR 0.74, 0.59-0.93) and that frequent intake of salty fish showed a similar tendency. It also reported that the highest intake of cooked fish was associated with total cases of gastric cancer (0.60, 0.40-0.90).

In the case-control study [(n= 594 (302 cases)]the only significant difference between groups was for a significantly greater risk of PAPILLARY THYROID CANCER for those consuming salt water fish a few times a week or more; [Saltwater fish Gp 1: 1 (ref) Gp 2: 0.8 (0.4-1.8) Gp 3: 0.7 (0.3-1.5) Gp 4:0.3 (0.1-1.0) p=0.006].

Skin Cancer

One Level III-2 cohort study examining oily fish intake and skin cancer incidence in adults in Nambour, Qld [2959] and one case-control study [38] in Italian adults examining melanoma incidence.

The Australian cohort study found Relative risk ratios (95% CI) of actinic keratosis counts (AKTs) in 1996 relative to 1992 for oily fish intake were:-

Gp2/Gp1 0.74 (0.53, 1.05) and for Gp3/Gp 1: 0.72 (0.55, 0.95)

Compared with those with the lowest intake tertile, the ratios of prevalent AKTs among participants with intermediate and the highest intakes of oily fish decreased by 26% and 28%

In the case-control study the Odds ratio (95% CI) of cutaneous melanoma was: - Fish. Gp 1: 1 (ref), Gp 2: 0.65 (0.43-0.97)

Fish rich in Omega 3: Gp 1: 1 (ref), Gp 2: 0.52 (0.34-0.78)

Shellfish Gp 1: 1 (ref), Gp 2: 0.53 (0.31-0.89)

Lung Cancer

Two case-control studies [69, 1513], one in Canadian adults and one in Spanish adults with one showing a reduced risk for sardine, whit fish, blue fish and total fish consumption [1513] and the other only for smoked fish [69].

Ovarian Cancer

Two case-control studies [69, 2420], one in Canadian adults and one in Italian women with one showing increased risk for the highest tertile of total fish intake [2420] and the other only for smoked fish [69].

Bladder Cancer

Two case-control studies [69, 1528], one in Canadian adults and one in Spanish adults and neither showed any significant associations.

Testicular Cancer, Brain Cancer, Non-Hodgkin's Lymphoma and Leukaemia

One case-control study [69] in Canadian adults. The OR (95% CI) were:-

The were some associations between total, fresh or smoked fish and risk of Non-Hodgkin's Lymphoma and Leukaemia, as follows:-

Testicular Cancer: OR (95% CI)

Total Fish: Gp 1: Ref 1.0; Gp 2: 0.9 (0.7-1.2); Gp 3: 0.8 (0.6-1.1) p=0.10

Fresh fish: Gp 1 1.0 (ref); Gp 2: 0.8 (0.6-1.1); Gp3: 0.8 (0.5-1.3) p=0.29

Smoked fish: Gp 1: 1 ref; Gp 2: 0.9 (0.7-1.2); Gp 3: 0.6 (0.2-1.8) p=0.24

***Brain Cancer*:** OR 95% CI

Total Fish: Gp 1: Ref 1.0; Gp 2: 0.9(0.7-1.1); Gp 3: 0.8 (0.6-1.0) p=0.08

Fresh fish: Gp 1 1.0 (ref); Gp 2: 0.8 (0.7-1.0); Gp3: 0.7 (0.5-0.9) p=0.01

Smoked fish: Gp 1: 1 ref; Gp 2: 0.9 (0.8-1.1); Gp 3: 0.8 (0.4-1.3) p=0.22

Non-Hodgkin's Lymphoma: OR 95% CI

Total Fish; Gp 1: Ref 1.0; Gp 2: 1.1 (0.9=1.3); Gp 3: 0.9 (0.7-1.1) p=0.10

Fresh fish: Gp 1 1.0 (ref); Gp 2: 1.1 (0.9-1.3); Gp3: 0.9 (0.7-1.1) p=0.27

Smoked fish: Gp 1: 1 ref; Gp 2: 0.8 (0.7-1.0); Gp 3: 0.9 (0.6-1.4) p=0.05

Leukaemia; OR 95% CI

Total Fish: Gp 1: Ref 1.0; Gp 2: 0.9 (0.8-1.2); Gp 3: 0.8 (0.6-1.0) p=0.08

Fresh fish: Gp 1 1.0 (ref); Gp 2: 0.9 (0.8-1.2); Gp3: 0.8 (0.6-1.0) p=0.04

Smoked fish: Gp 1: 1 ref; Gp 2: 0.9 (0.8-1.1); Gp 3: 0.6 (0.3-1.1) p=0.10

Pancreatic Cancer

One case-control study [69] in Canadian adults. The was no association between total, fresh or smoked fish and risk of pancreatic cancer.

Oral Cancer

One case-control study [552] in Italian adults. The OR was only reported as 0.447 and it was unclear how fish intake was categorised.

Endometrial Cancer

One case-control study [552] in post-menopausal Swedish women. The OR (95% CI) were:-

Fatty fish: Gp 1: 1.0 (ref), Gp 2: 1.0 (0.8-1.3), Gp 3: 0.8 (0.6-1.09), Gp 4: 0.6 (0.5-0.8) p=0.0002

Lean fish: Gp 1: 1.0 (ref), Gp 2: 1.0 (0.7-1.3), Gp 3: 0.9 (0.7-1.2), Gp 4: 1.0 (0.8-1.3) p=0.72

Total fish Gp 1: 1.0 (ref), Gp 2: 1.0 (0.8-1.2), Gp 3 0.8 (0.6-1.0), Gp 4: 0.8 (0.6-1.0) p=0.05

Gastric Cancer

One case-control study [627] in Japanese females which found that frequent intake of cooked fish was inversely associated with non-differentiated type of cancer (OR 0.74, 0.59-0.93), and that frequent intake of salty fish had a similar tendency. The highest intake of cooked fish was associated with total cases of gastric cancer (0.60 0.40-0.90).

Fish and Hypertension

On cohort in pregnant women in the USA [1472]which found ther was no relationship between fish consumption and pregnancy Pre-eclampsia, Odds ratio (95% CI)
:0.91 (0.75–1.09) or Gestational Hypertension: 1.04 (0.94–1.15).

Fish and Allergic Disease

Two cohort studies [769, 3133], one in pregnant German women and their offspring [769] and the other in Swedish infants [3133].

The German study examined the mother's fish intake (<1time/week versus 1-2 times per week) in the last 4 weeks of pregnancy versus used doctor diagnosed eczema, any allergens, food allergens and inhalant allergens as outcomes, in child at 2 years of age. The odds ratio (95% CI) of Doctor diagnosed eczema: 0.75 (0.57-0.98) p<0.05; any allergens: 1.02 (0.73-1.43); Food allergens: 1.01

(0.69-1.48); Inhalant allergens 0.94 (0.56-1.57) suggests a protective effect. High fish consumption during the last 4 weeks of pregnancy decreased the risk of eczema in childhood (2 years of age).

The Swedish study used self reported eczema and found Odds ratio (95% CI) of eczema for age at introduction of fish:
Gp 1: 1.1 (0.4-2.9); Gp 2: 0.7 (0.6-0.9); Gp 3: 0.6 (0.5-0.7); Gp 4: 1 (Ref);
Odds ratio (95% CI) eczema for frequency of fish consumption:
Gp 1: 1 (Ref); Gp 2: 0.88 (0.64-1.20); Gp 3: 0.86 (0.62-1.20); Gp 4: 1.32 (0.86-2.02); Gp 5: 2.73 (1.80-4.13);
Odds ratio (95% CI) eczema for usually eats lean fish, 0.81 (0.68-0.97).

Fish and Infant Cognition

There were three cohort studies examining fish consumption and infant cognitive outcomes. The VIVA cohort [771] of 135 mother-infant pairs found that each extra fish serve/wk was associated with higher visual recognition memory (VRM) score 2.9 (95%CI 0.2 to 5.4). When mercury was added to the model as a potential confounder, this VRM score increased to 4.0 (95%CI 1.3 to 6.7) points higher.

Two studies reported outcomes from the AVON cohort. The first in 7421 mother-infant pairs [369] examined the relationship between fish consumption and validated developmental questionnaires at 15 and 18 months. The found an OR of 0.7 for low test score and 1.4 for language for high scores, with some items significant, and with a significant P for incresaing consumption of fish. The second [773] in 8764 at the six month follow-up and 5000 at the eight year old follow-up examined fish comsumption against validated scale domains for gross motor, fine motor, communication, and social skills, completed by parents when their child was six, 18, 30 & 42 months at follow-up. Significant OR were found for full IQ and verbal ability with a significant P for incresaing consumption of fish.

Fish and Socio-economic status

The researchers investigated how socio-demographic factors influenced fish consumption by examining consumption of total, fried and “recommended” fish types (white and oily fish, and shellfish) over 11 years in participants aged 39–59 years (n= 8358), in the Whitehall II study. Over the follow-up there was a significant increase in consumption of ‘recommended’ (mean: 1·85 to 2·22 portions/week) and total fish (mean: 2·32 to 2·65 portions/week) and a decreasing trend in fried-fish intake (mean: 0·47 to 0·43 portions/week). Recommended, fried and total fish consumption differed by occupational status, ethnicity, marital status and sex. They found that recommended-fish, fried-fish and total fish consumption differed by occupational status, ethnicity, marital status and sex, but only ethnicity had a significant impact on trajectories of age-related fish intake. The intake of recommended and total fish was higher in women than in men, in South Asian than in white participants, but was lower in black compared with white participants and in low and middle employment grade compared higher employment grade.

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10. POULTRY (S1.1)

Evidence Statements

10. POULTRY (S1.1)

Search Results

The initial search of the databases included 936 references for poultry generally and the specified disease outcomes. The detailed searches are included in a separate document. There were 24 duplicates. 136 references concerning poultry had data extracted and nine papers were used to form the body of evidence statements for poultry. Sufficient evidence (i.e. at least five different studies) was only found to make statements for adults aged 19 years or older for poultry and breast cancer and colorectal cancer. There was inadequate evidence to make statements for any other disease states or other age and sex groups. No data was available to make any statements for children or adolescents.

The 2007 World Cancer Research Fund report concluded that the evidence was too limited in amount, consistency or quality to draw any conclusions about the relationship between poultry and cancer risk. However in the goals and recommendations it is suggested that "*people who eat flesh foods are advised to prefer poultry, and all types of fish, to red meat".*

10.1 POULTRY and BREAST CANCER

Does a particular intake of poultry affect the risk of breast cancer in adults?		
Evidence Statement		Consumption of poultry at least once per week is not associated with risk of breast cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 Level III-2 Systematic Review (of negative quality) and 3 Level III-2 case-control studies (2 of neutral, 1 of negative quality).
Consistency	Poor	Inconsistent results. The systematic review (1 case control, 2 cohort studies specific to poultry) showed an increased risk, 2 case-control studies showed a protective effect while 1 case-control showed no effect.
Clinical impact	Poor	Mostly no clinically important effects. Outcomes related to level of intake are widely varied and include poultry with and without skin (primarily chicken).
Generalisability	Satisfactory	Wide range of population types addressed (Chinese, US, Uruguayan) but difficult to generalise to Australian women. Adults only.
Applicability	Satisfactory	Probably applicable to the Australian context with some caveats.

The studies used to make the body of evidence statement are listed below and summarised in Table 10.1. The systematic review considered poultry to be a causative food group for breast cancer risk, though only three studies were specific to this food group. An inverse association with breast cancer risk was also identified in a Chinese case-control study, though this specifically focussed on calcium intake from poultry. Similarly, a Uruguayan case-control study found protective effects from skinless poultry and increased risk with consumption of chicken skin. No association was found for US women when considering the number of servings of poultry per week. There appears to be no clear relationship for poultry with breast cancer risk.

References

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Boyapati, S., Shu, X., Jin, F., Dai, Q., Ruan, Z., Gao, Y. et al. 2003, "Dietary calcium intake and breast cancer risk among Chinese women in Shanghai." *Nutrition & Cancer*, vol. 46, no. 1, pp. 38-43.

Mignone, L., Giovannucci, E., Newcomb, P., Titus-Ernstoff, L., Trentham-Dietz, A., Hampton, J. M. et al. 2009, "Meat consumption, heterocyclic amines, NAT2, and the risk of breast cancer." *Nutrition & Cancer*, vol. 61, no. 1, pp. 36-46.

Ronco, A., De Stéfani, E. & Fabra, A. 2003, "White meat intake and the risk of breast cancer: a case-control study in Montevideo, Uruguay." *Nutrition Research*, vol. 23, no. 2, pp. 151-162.

Table 10.1 Studies used to make evidence statements for poultry and Breast Cancer

Reference [1]	Bissonauth et al 2008 [265]	Boyapati et al 2003 [676]	Mignone et al 2009 [818]	Ronco et al 2003 [531]
Type of study [2]	Systematic Review; 13 studies (3 related to poultry: 2 cohort and 1 case-control)	Case-Control	Case-Control	Case-Control
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	No poultry vs any poultry/ **Breast cancer**	Frequency of poultry consumption vs other meat consumption/ **Breast cancer**	No poultry vs any poultry and frequency of consumption/ **Breast cancer**	Type and frequency of poultry consumption/ **Breast cancer**
N [5]	14,291 cohort; 114 cases, 280 controls	1459 / 1556	2686/ 3508	103/ 111
Population/study information [6]	Adult females, ages not given; USA and Italy	Chinese women aged 25-64yrs	US women aged 20-69yrs	Uruguayan women undergoing routine mammography assessment and belonging to mid-high SE class
Quality [7]	N	O	N	O
Results [8]	Two studies - no association, 1 study inverses association. The amino acid content of white meat may support better immune function.	Calcium from poultry inversely associated with breast cancer risk P<0.01.	Inverse trend for servings per week of chicken (P=0.05) for premenopausal women though not significant when adjusted for total chicken intake among premenopausal women (OR 0.68). No association of breast cancer with consumption of chicken	Increased risk with consumption of chicken skin (OR 1.54, CI 0.86-2.77), significant inverse association for skinless chicken (OR 0.42, CI 0.23-0.79), significant positive correlations (case-control) for chicken with skin and fried fish (0.230, p<0.0001), and skinless chicken and not fried fish (0.165, p<0.01), significant negative correlations for chicken with skin and skinless chicken (0.544, p<0.001), outcome case-control significantly positively correlated with chicken with skin (0.183, p<0.001) and negatively with skinless chicken (0.233, p<0.001). Outcome of breast cancer positively correlated with chicken with skin and negatively with skinless chicken
Effect on risk (Increase/None/Protect)	2 cohort studies with no association, 1 case-control with inverse association.	Protect	None	Protect (skinless chicken); Increase (skin and fried chicken)
Clinical importance [9]	3	2	4	2
Clinical relevance [10]	4	3	4	2
Generalisability	Yes	No	No	No
Applicability	No	No	Yes	Yes

10.2 POULTRY and COLORECTAL CANCER

Does a particular intake of poultry affect the risk of colorectal cancer in adults?		
Evidence Statement		Consumption of poultry at least once per week is not associated with risk of colorectal cancer.
Grade of recommendation		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 Level III-2 systematic review (of 11 cohort studies) and 4 Level III-2 case-control studies (3 of neutral and 1 of negative quality) relate to colorectal cancer.
Consistency	Satisfactory	The relationship appears to show no effect (2 Protect; 3 None; In the systematic review 9/11 studies showed no effect.
Clinical impact	Poor	Mostly no clinically important effects. Outcomes related to level of intake are widely varied and include poultry with and without skin (primarily chicken).
Generalisability	Good	Populations studied in the body of evidence are similar to the target audience of the guidelines.
Applicability	Good	Applicable to the Australian healthcare context with few caveats.

The studies used to make the body of evidence statements are listed below and summarised in Table 10.2. One case-control study found increased consumption of poultry provides a protective effect OR 0.5 (CI 0.3-0.9, P=0.03) though addressed a period of 30 years prior to sigmoidectomy. A case-control study addressing genetic polymorphisms found no effect and similarly a case-control study addressing cooking method also found no effect. The systematic review found small differences generally of no effect though the age groups varied widely.

References

Marques-Vidal, P., Ravasco, P. & Camilo, M. 2006, "Foodstuffs and colorectal cancer risk: a review." *Clinical Nutrition*, vol. 25, no. 1, pp. 14-36.

Chiu, B. & Gapstur, S. 2004, "Changes in diet during adult life and risk of colorectal adenomas." *Nutrition & Cancer*, vol. 49, no. 1, pp.49-58.

Joshi, A, Corral, R., Siegmund, K., Haile, R., Le Marchand, L., Martinez, M. et al. 2009, "Red meat and poultry intake, polymorphisms in the nucleotide excision repair and mismatch repair pathways and colorectal cancer risk." *Carcinogenesis*, vol. 30, no. 3, pp. 472-9.

Hansen, R., Sørensen, M., Tjønneland, A., Overvad, K., Wallin, H., Raaschou-Nielsen, O. et al. 2007, "XPA A23G, XPC Lys939Gln, XPD Lys751Gln and XPD Asp312Asn polymorphisms,

interactions with smoking, alcohol and dietary factors, and risk of colorectal cancer." *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis,* vol. 619, no. 1-2, pp. 68-80.

Hu, J., La Vecchia, C., Desmeules, M., Negri, E., Mery, L. 2008, "Meat and fish consumption and cancer in Canada." *Nutrition & Cancer*, vol. 60, no. 3, pp. 313-324.

Table 10.2 Studies used to make evidence statements for poultry and Colorectal Cancer

Reference [1]	Marques-Vidal et al 2006 [754]	Chiu et al 2004 [641]	Joshi et al 2009 [138]	Hansen et al 2007 [302]	Hu et al 2008 [815]
Type of study [2]	Systematic Review; 53 studies (11 poultry), cohort only	Case-Control	Case-Control	Case-Control	Case-Control
Level of evidence [3]	III-2	III-2	III-1	III-2	III-2
Intervention/ comparator [4]	No poultry vs any poultry /**Colorectal cancer**	No poultry vs any poultry before and after diagnosis/ **Colorectal cancer**	Cooking method and frequency of consumption per week/ **Colorectal cancer**	No poultry vs any poultry/ **Colorectal cancer**	Frequency of poultry consumption/ **All cancer**
N [5]	470,754	146 /226	1055/ 389	405/ 810	19732/ 5039
Population/study information [6]	M+F, 15-79y, USA, Finland, Sweden, Japan	Primarily active and retired US military officers and their families aged 18-74yrs	US persons with and without Colorectal cancer	Persons born in Denmark aged 50-64yrs/ DCH Danish prospective study	Canadian participants with and without cancer
Quality [7]	O	O	O	O	N
Results [8]	Nine studies - no relationship, two studies- positive relationship with rectal cancer only. Meat consumption deleterious to colorectal cancer risk	chicken/turkey consumption 1yr before sigmoidoscopy (P=0.03) OR 0.5 CI 0.3-0.9. Reduced risk with high intake of chicken/turkey	2.0+/-3.1 servings of cooked poultry per week, 30.7% lightly browned, 44.6% medium browned, 24.7% heavily browned for cases; 2.1+/-3.1 servings of cooked poultry per week, 30.2% lightly browned, 45.7% medium browned, 24.1% heavily browned for controls. No association between cooked poultry and risk of colorectal cancer	Intake of red meat, processed meat, fish and poultry comparable between cases and controls and no significant association with XPCLys939Gln polymorphism or other environmental variables and poultry consumption. No impact of poultry consumption on polymorphisms associated with colorectal cancer	High intake of poultry inversely related to colon cancer risk (OR 0.6) rectal cancer risk (OR 0.6) prostate cancer (OR 0.5) leukemia (OR 0.7), no association with lung, kidney, bladder, brain and non-Hodgkin's lymphoma. When considered with other demographic variables a 30% reduction in risk of stomach cancer (OR 0.7) and an inverse risk of lung cancer (OR 0.7). Poultry consumption not negatively associated with increased cancer risk
Effect on risk (Increase/None/Protect)	None	Protect	None	None`	Protect
Clinical importance [9]	3	2	4	3	2
Clinical relevance [10]	4	1	1	1	3
Generalisability	Yes	No	No	No	No
Applicability	No	Yes	No	Yes	Yes

Summary of studies not included in Body of Evidence statements

The following diet-health relationships had too few studies to develop a body of evidence statement.

Poultry and Hypertension

Two cohort studies (Level III-2) of neutral quality examining poultry and hypertension. There were inconsistent results (Two increase - one for animal protein generally; one no effect). The results included clinically unimportant outcomes with no clear relationship between poultry and hypertension HR 1.16 (0.87-1.38). The Chicago Western Electric Study demonstrated a significant change in diastolic blood pressure with consumption of poultry more than 8 times per month in older males n=2107 (Miura et al. 2004), while the CARDIA study found no association between poultry consumption and elevated blood pressure in younger adult females n=4304 (Steffen et al. 2005).

Poultry and Cardiovascular disease

Two cohort studies (Level III-2) of mixed quality (one negative, one positive) and one RCT study (Level II) of positive quality. Inconsistent findings (one protect; three none). No overall associations with poultry consumption in adults and inverse association in adolescents OR in cohort studies: 0.89-1.01; no significant association. Studies comprised different ethnic backgrounds/cultures not generalisable to the Australian population due to differing farming/cooking practices.

- 8-9% decrease in LDL on poultry diet, 25% decreased in TG, 28-29% reduction in VLDL ($p<0.05$). Favourable changes to CVD risk factors seen despite protein source (Beauchesne-Rondeau et al. 2003)
- Eating patterns may explain CVD risk factors and marital status though no specific association for poultry 0.89 Wilks lambda ($p=0.24$) (Yannakoulia et al. 2008)
- Non significant negative associations of poultry consumption 1.7 times per week and serum GGT (Lee et al. 2004).

Poultry and obesity

Two studies of neutral (Level II) and negative quality. Inconsistent outcomes (one protect; one none). The weight loss was not related to poultry consumption but rather whole of diet effects. Only overweight women were considered in one study premenopause (Melanson et al. 2003); the other in postmenopausal women:

- Significant difference ($p<0.05$) of -6.0+/-0.5 kg and -4.1+/-2.5% body fat and in chicken group. Successful weight loss regardless of type of meat protein consumed (Melanson et al. 2003)
- Greater change in body mass and BMI for chicken vs. carbohydrate based diet. BMI- Beef: -2.5+/-1.1 kgm^{-2}, Chick: -2.0+/-1.2 kgm^{-2}, Carb: -2.1+/-0.7 kgm^{-2} ($p<0.05$) (Mahon et al. 2007).

Poultry and eye health

One Level III-2 cohort study of neutral quality. No relationship between poultry intake and early macular degeneration (OR 1.13). OR intake ≥3.5 times per week vs ≤ once per week: 1.13 (CI 0.95-1.36, P=0.228) early AMD (definition 1); 1.02 (CI 0.81-1.28, P=0.9220 early AMD (definition 2); 0.43 (CI 0.20-0.91, P=0.007) for late. Total chicken intake was not associated with early macular degeneration but may be protective for late AMD. No clinically important effects for less than once per week up to 3.5 times per week. Older adults n=6734 only, although applicable to the Australian context (Chong, 2009).

Poultry and type 2 diabetes mellitus

Two Level III-2 studies (one cohort study and one case-control of negative quality) (Villegas et al. 2006, Karlinski et al. 2008) and two Level II RCT studies (de Mello et al. 2006, Gross et al. 2002) of positive quality measuring changes of intermediate markers in subjects with diabetes. Consistent effects (four protect), but many outcomes were related to outcome measures such as renal function or lipids in patients with diabetes, not incidence of diabetes. Limited: cohort study linked infrequent consumption (<once per week) with risk of type 2 diabetes but confidence intervals include 1.0. Improved outcome measures in RCTs with regular intake. Cohort included women only (Villegas et al. 2006). RCTs with persons with established diabetes (de Mello et al. 2006; Gross et al. 2002), though potentially applicable to Australian population due to high incidence.

Poultry and renal cancer

One Level III-2 Review relating to renal cancer (13 cohort studies). Compared to referent intake of 14-20 g per day, <14 g per day, RR 1.14 (CI 0.96-1.35), ≥ 606 g per day RR 1.28 (CI 0.88-1.87). Increase of two servings per week RR 1.03 (CI 0.94-1.11) P<0.05. (Lee et al. 2008). No association of poultry and renal cancer.

Poultry and bladder cancer

Two Level III-2 pooled cohort study for bladder cancer. Total of 82,002 participants, both Swedish women born between 1914-1948 and men born 1918-1952, from the Swedish Mammography Cohort and a Cohort of Swedish Men. <2 servings poultry per week HR 1.00 , ≥2 servings poultry per wk 1.01 (0.78-1.23) p=0.78 (Larsson et al. 2009). n= 808/ 135 893 US men and women from Health Professionals Follow-up Study and Nurses Health Study. Chicken without skin more than five times per week is related to increased risk of bladder cancer OR 1.52 (1.09-2.11) for women and 1.45 (0.96-2.17) for men (P=0.01), but no significant increase at intakes of two to four times per week (OR 1.03 and 1.02) (Michaud et al. 2006). No significant association for poultry intake and incidence of bladder cancer.

Poultry and lung cancer

Two Level III-2 case-control studies for lung cancer (inconsistent outcomes: one protect, one increase risk). Persons living in the territory of New Caledonia for >5 years and aged >18 years n= 228/ 305. High levels of consumption associated with decreased lung cancer risk OR 0.5 (CI 0.3-1.0) (Marchand et al. 2002). Prague adults 25-89 years, n= 269/ 1079. Poultry consumption associated with squamous, small and large cell lung cancer OR 8.37 (CI 1.05-66.89) (Kubik et al. 2002).

Poultry and ovarian cancer

One Level III-2 case-control study for ovarian cancer showing a protective effect. US women 40-85 years, n=124 cases and n=696 controls. Reduced risk for highest intakes (>1189 g per month) of consumption of poultry OR0.45 (CI 0.22-0.92) (McCann et al. 2003).

Poultry and prostate cancer

One Level III-2 case-control study for prostate cancer showing increased risk. Italian study of n=369 cases and n=1451 controls. Increased risk of benign prostatic hyperplasia with poultry consumption OR 1.39 (CI 1.00-1.91) (Bravi et al. 2006).

References

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Bravi, F., Bosetti, C., Dal Maso, L., Talamini, R., Montella, M., Negri, E., Ramazzotti, V., Franceschi, S. & La Vecchia, C. 2006, "Food groups and risk of benign prostatic hyperplasia", *Urology*, vol. 67, no. 1, pp. 73-79.**Excluded: <5 studies**

Chong, E. W., Simpson, J. A., Robman, L. D., Hodge, A. M., Aung, K. Z., English, D. R., Giles, G. G. & Guymer, R. H. 2009, "Red Meat and Chicken Consumption and Its Association With Age-related Macular Degeneration", *American Journal of Epidemiology*, vol. 169, no. 7, pp. 867-876.**Excluded: <5 studies**

de Mello, V. D. F., Zelmanovitz, T., Perassolo, M. S., Azevedo, M. J. & Gross, J. L. 2006, "Withdrawal of red meat from the usual diet reduces albuminuria and improves serum fatty acid profile in type 2 diabetes patients with macroalbuminuria", *American Journal of Clinical Nutrition*, vol. 83, no. 5, pp. 1032-8.**Excluded: <5 studies**

Gross, J. L., Zelmanovitz, T., Moulin, C. C., De Mello, V., Perassolo, M., Leitão, C., Hoefel, A., Paggi, A. & Azevedo, M. J. 2002, "Effect of a chicken-based diet on renal function and lipid profile in patients with type 2 diabetes: a randomized crossover trial", *Diabetes Care*, vol. 25, no. 4, pp. 645-

651.**Excluded: <5 studies**

Karlinski, M., Mrozikiewicz-Rakowska, B., Krasnodebski, P. & Karnafel, W. 2008, "Diet under 18 years of age and type 2 diabetes", **Excluded: <5 studies**

Kubik, A. K., Zatloukal, P., Tomasek, L. & Petruzelka, L. 2002, "Lung cancer risk among Czech women: A case-control study", *Preventive Medicine: An International Journal Devoted to Practice and Theory*, vol. 34, no. 4, pp. 436-444.**Excluded: <5 studies**

Larsson, S. C., Johansson, J.-E., Andersson, S.-O. & Wolk, A. 2009, "Meat intake and bladder cancer risk in a Swedish prospective cohort", *Cancer Causes & Control*, vol. 20, no. 1, pp. 35-40.**Excluded: <5 studies**

Lee, D., Steffen, L. M. & Jacobs, D. R., Jr. 2004, "Association between serum gamma-glutamyltransferase and dietary factors: the Coronary Artery Risk Development in Young Adults (CARDIA) Study", *American Journal of Clinical Nutrition*, vol. 79, no. 4, pp. 600-605.**Excluded: <5 studies**

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Mahon, A. K., Flynn, M. G., Stewart, L. K., McFarlin, B. K., Iglay, H. B., Mattes, R. D., Lyle, R. M., Considine, R. V. & Campbell, W. W. 2007, "Protein intake during energy restriction: effects on body composition and markers of metabolic and cardiovascular health in postmenopausal women", *Journal of the American College of Nutrition*, vol. 26, no. 2, pp. 182-9.**Excluded: <5 studies**

Marchand, J., Luce, D., Goldberg, P., Bugel, I., Salomon, C. & Goldberg, M. 2002, "Dietary factors and the risk of lung cancer in New Caledonia (South Pacific)", *Nutrition & Cancer*, vol. 42, no. 1, pp. 18-24.**Excluded: <5 studies**

McCann, S. E., Freudenheim, J. L., Marshall, J. R. & Graham, S. 2003, "Risk of human ovarian cancer is related to dietary intake of selected nutrients, phytochemicals and food groups", *Journal of Nutrition*, vol. 133, no. 6, pp. 1937-42.**Excluded: <5 studies**

Melanson, K., Gootman, J., Myrdal, A., Kline, G. & Rippe, J. M. 2003, "Weight loss and total lipid profile changes in overweight women consuming beef or chicken as the primary protein source", *Nutrition*, vol. 19, no. 5, pp. 409-414.**Excluded: <5 studies**

Michaud, D. S., Holick, C. N., Giovannucci, E. & Stampfer, M. J. 2006, "Meat intake and bladder

cancer risk in 2 prospective cohort studies", *American Journal of Clinical Nutrition*, vol. 84, no. 5, pp. 1177-1183.**Excluded: <5 studies**

Miura, K., Greenland, P., Stamler, J., Liu, K., Daviglus, M. L. & Nakagawa, H. 2004, "Relation of vegetable, fruit, and meat intake to 7-year blood pressure change in middle-aged men: the Chicago Western Electric Study", *American Journal of Epidemiology*, vol. 159, no. 6, pp. 572-580.**Excluded: <5 studies**

Steffen, L. M., Kroenke, C. H., Yu, X., Pereira, M. A., Slattery, M. L., Van Horn, L., Gross, M. D. & Jacobs, D. R., Jr. 2005, "Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study", *American Journal of Clinical Nutrition*, vol. 82, no. 6, pp. 1169-77. **Excluded: <5 studies**

Villegas, R., Shu, X. O., Gao, Y.-T., Yang, G., Cai, H., Li, H. & Zheng, W. 2006, "The association of meat intake and the risk of type 2 diabetes may be modified by body weight", *International Journal of Medical Sciences*, vol. 3, no. 4, pp. 152-9.**Excluded: <5 studies**

Yannakoulia, M., Panagiotakos, D., Pitsavos, C., Skoumas, Y. & Stafanadis, C. 2008, "Eating patterns may mediate the association between marital status, body mass index, and blood cholesterol levels in apparently healthy men and women from the ATTICA study", *Social Science & Medicine*, vol. 66, no. 11, pp. 2230-2239.**Excluded: <5 studies**

11. EGGS (SI.1)

Evidence Statements

11. EGGS (S1.1)

Search results

The initial search of the data bases included 1138 references for eggs and the specified disease outcomes. The detailed search is included in a separate document on searches. From the Endnote database, 35 references concerning eggs had data extracted and 31 papers were used to form the body of evidence statements for eggs. Sufficient evidence was found to make statements for eggs and cardiovascular disease and cancer.

11.1 EGGS and CORONARY HEART DISEASE

Does a particular intake of eggs affect the risk of coronary heart disease in adults?		
Evidence statement		Consumption of eggs daily is not associated with increased risk of coronary heart disease.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Excellent	13 Level II trials (RCTs – mostly positive studies, only 3 neutral studies), 1 Level III-1 study (positive) and 5 Level III-2 studies (1 neutral, remainder positive). 2 cross-sectional and 1 pre-test post test study not extracted.
Consistency	Good	Fairly consistent that there is no effect of egg consumption on risk of CVD (15 No Effect (11 RCT studies, 1 III-1 study, 3 cohort studies); 4 showed increased risk (2 cohort studies and 2 RCT showed slight increases in one measure of blood lipids).
Clinical impact	Poor	Majority of ORs cross 1 or p value not significant for differences between groups for RCTs.
Generalisability	Good	Populations in body of evidence relevant to adults of most ages and genders and also include Australian Aborigines, infants and older people.
Applicability	Excellent	Directly applicable to Australian healthcare context.

The studies used to make the body of evidence statements are shown in Table 11.1. There was fairly consistent evidence that there is no effect of egg consumption on risk of cardiovascular disease. Fifteen of the 19 studies agreed that there was no effect (11 of these were RCTs, three were cohort studies and one was a non-RCT). Only four studies showed an increased risk (two cohort studies and two RCTs, the RCTs only having one blood measure change significantly between groups). Based on these studies, no effect can be claimed.

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Table 11.1 Studies used to make evidence statement for eggs and cardiovascular disease

Reference [1]	**Lee et al. 2003 [5]**	**Vislocky et al. 2009 [28]**	**Wenzel 2006 [80]**	**Makrides 2002 [37]**
Type of study [2]	RCT (cross over)	RCT	Pseudorandomised CT	Block RCT
Level of evidence [3]	II	II	III-I	II
Intervention/ comparator [4]	National Cholesterol Education Program step 1 diet & either: no egg; 12 regular eggs per wk; and 12 omega-3 enriched eggs per wk/ blood lipids.	A 6 wk endurance training program and either: 12 eggs per wk or 0 eggs per wk / blood lipids.	12 week intervention and either: 1) sugar capsule per day; 2) 6 eggs per wk containing 331ug lutein & zeaxanthin; 3) 6 eggs per wk containing 964ug lutein or zeaxanthin/ changes in lipid levels and macular pigment optical density.	7 mth intervention and either: 1) Four n-3 egg yolks per wk; 2) Four regular egg yolks per wk; 3) no dietary intervention/ blood lipids.
N [5]	16	12	8	44-47
Population/study information [6]	M and F 19, 31, 51; US; Hypercholesterolaemic, non-smokers, not regular blood donors, not on meds to reduce cholesterol, not allergic to eggs; 6 wk intervention, 6 wk washout, 2 wk diet stabilisation; changes in blood cholesterol levels measured; no follow up.	M and F 18 – 30 yrs US with no GI disorders, no use of sports supplements or anabolic steriods or weekly exercise >90 mins total. 2 wks of diet intervention and 6 wks of diet and endurance training; changes in blood cholesterol levels measured; no follow up.	24 US F 24 - 59 yrs no egg allergy, no history of heart or GI disease, no diabetes, not current smoker, BMI < 30, TC/HDL < 5 were assigned to sugar tablet, or 6 eggs per wk for 12 weeks (eggs had lower or greater carotenoid concentrations) - changes in lipid levels and macular pigment optical density; no follow up.	6 mth old Australian infants born at term with birth wts >2.5 kg and no known protein intolerances or allergies. Assigned to n-3 egg, no diet intervention or regular egg for 7 mths. TC changes examined. No follow up.
Quality [7]	Positive	Positive	Neutral	Neutral

Results [8]	No significant differences between groups for Total, LDL, HDL cholesterol or triglycerides (p>0.05). Cholesterol responders (n=3) had 0.4-0.5mmol/L increase in TC in regular egg group (p<0.05).	No significant differences between groups for Total, LDL, HDL cholesterol or triglycerides (p>0.05). HDL improved with endurance training but an unrelated finding.	Between group calculations not done. Lipid levels did not change, except sugar pill group had 0.27mmol/L increase from baseline.	No differences in TC levels between interventions.
Effect on risk (Increase/None/Protect)	None	None	None	None
Clinical importance [9]	4	4	3	3
Clinical relevance [10]	2	2	2	2
Generalisability	n- hypercholesterolaemic	y	y	y
Applicability	y	y	y	y

Table 11.1 Studies used to make evidence statement for eggs and cardiovascular disease (cont.)

Reference [1]	**Katz 2005 [851]**	**Vander Wal 2008 [252]**	**Harman 2008 [59]**	**Rose 2006 [696]**
Type of study [2]	RCT (crossover)	Block RCT (by gender)	RCT	RCT (cross over)
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	6 wk intervention with either: 1) 2 eggs per day; and 2) 60g oats per day / BP, blood lipids, wt.	8 wk intervention and either: 1) Bagel breakfast with usual diet; 2) Egg breakfast (2 eggs 5 times per wk) with usual diet; 3) Bagel breakfast weight loss diet; 4) Egg breakfast wt loss diet/ wt, quality of life, blood lipids.	12 wk intervention and either: 1) 2 eggs per day on wt loss diet or 2) no eggs on a wt loss diet/ wt, blood lipids.	21 day intervention and either: 1) liquid egg breakfast or 2) standard breakfast/ wt, glucose, blood lipids, BP.

N [5]	49	35; 39	24	15
Population/study information [6]	M and F 36-73 yrs US not currently using HRT, non-smokers, no known coronary artery or other vascular disease, no vasoactive medication use, no regular use of Vit E or fibre supps, not hypercholesterolaemic. Lipids, Wt, BP and endothelial function tested. No follow up.	20 - 60 yrs, US; Inclusion criteria: BMI >25, <50; <5% wt loss in prior 3 mths; not unstable cardiac conditions, no major systemic illnesses, no hx drug abuse or eating disorders, no uncontrolled diabetes or hypothyroidism, no familial hyperlipidaemia, no conditions contraindicating wt loss and no allergy or dislike of eggs. Wt, lipids, quality of life tested. No follow up.	M and F aged 18-55yrs UK with BMI <35, TC <6.5mmol/L, Trigs<3; no medical condition affecting lipids, willing to eat eggs, no supps, <3kg wt loss in prior 2 mths. Wt, lipids tested. No follow up.	M 30 – 65 yrs M31, M51, Canada, Inclusion criteria: with trigs > 1mmol/L, with no fish or fish oil capsules in prior 2 wks, not taking lipid meds. Wt, glucose, BP and serum lipids tested. No follow up.
Quality [7]	Positive	Positive	Positive	Positive
Results [8]	Flow mediated vasodilation decreased in both groups equally. No changes in lipids (203.8 - 205.3 mg/dl), LDL (124.8 to 129.1), wt or BP during egg intervention and no differences between oat intervention except for lower TC and LDL in oats (but oat results are unrelated).	No significant differences in quality of life or blood lipids between eggs and bagel groups. Wt loss and BMI loss 61-65% greater on egg diet than bagel diet (~1kg, 0.5BMI), 34% more waist, 16% more body fat than bagel group - minimal loss in egg and bagel groups.	No significant differences between eggs and no eggs group for wt loss or lipid levels (2 eggs per day Wt (kg) 12 wks 77.6±16; Body fat (%) 12 wks 33.3±7.9; No eggs/d Wt 12 wks 76.4±14.7; Body fat 31.2±8.9).	No significant differences in wt, glucose, lipids and BP except for trigs 0.3 mmol lower on egg breakfast and 9mmHg lower systolic BP on egg breakfast. Egg breakfast Mean diff (95%CI) - TC -3.6 (-12.7-5.5); LDL 7 (-1.4 -15.4); HDL 3.5 (1-5.9); Trigs -53.1 (-77.7- -28.5), wt 0.2 (-2.3-3.1); BMI 0.0 (-0.4-0.5), sys

				BP -9.0 (-14.4- -3.6); dias BP -6.5 (-10.5- -2.6); Control breakfast Mean diff (95%CI) - TC -10.9 (-22.3-0.6); LDL -5.8 (-61.7- 10.8); HDL 3.1 (0.2 - 5.9); trigs -25.4 (-61.7 - 10.8), wt -0.1 (-1 -0.9); BMI -0.02 (-0.2 - 0.1), sys BP - 0.8 (-9 -7.3); dias BP -0.2 (-6.8 - 6.4).
Effect on risk (Increase/None/Protect)	None	None	None	None
Clinical importance [9]	3	3	3	CVD - 2; others - 3
Clinical relevance [10]	2 - CVD; 1 - HT, Ob	2 - CVD; 1 - Ob, H&W	1 - Ob, 2 - CVD	1 - Ob, T2D, HT; 2 - CVD
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 11.1 Studies used to make evidence statement for eggs and cardiovascular disease (cont.)

Reference [1]	**Ohman, 2008 [237]**	**Nakamura 2004 [16]**	**Djousse 2008 [13]**	**Nakamura 2006 [17]**
Type of study [2]	RCT (cross over)	Cohort	Cohort	Cohort
Level of evidence [3]	II	III-2	III-2	III-2
Intervention/ comparator [4]	1 month intervention and either: 1) n-3 enriched egg/day or 2) regular egg per day plus usual diet for both groups./ glucose, blood lipids.	≥2 eggs per day, 1 per day, 0.5 per day, 1-2 eggs per wk or seldom egg intake/ stroke, cancer, IHD deaths.	≥7 eggs per wk, 5-6 per wk, 2-4 eggs per wk, 1egg per wk/ MI or stroke deaths.	Egg consumption: <1 day per wk, 1-2 days per wk, 3-4 day per wk, Almost daily/ non-fatal myocardial infarction and CHD death.
N [5]	19	9263	21327	116638

Population/study information [6]	Health Swedish Caucasian volunteers M and F aged over 45 yrs, without medication that influences inflammatory parameters or blood lipids, no known malignancies.	14 yr follow up looking at egg consumption and mortality from all cause, IHD, stroke and cancer in Japanese female adults. Egg intake assessed through FFQ and death certificate used to assess cause of death. NIPPON Data 80.	US male physicians; M31, M51, M65. Average of 20 yr follow up looking at egg consumption patterns and all cause, MI, and stroke related deaths. Egg intake assessed through FFQ and death certificate used to assess cause of death. Physician's Health study.	Japan; M and F 31, 51, 65; Follow up for 7-11 yrs looking at egg consumption patterns and CHD events (including non-fatal myocardial infarction and CHD death). Japan Public health centre-based prospective study.
Quality [7]	Neutral	Positive	Positive	Positive
Results [8]	No between group analysis. Glucose decreased during n-3 intervention and blood lipids were maintained with both regular and n-3 egg. n-3 egg - Before and after intervention: TC (mmol/L) 6.25±0.3 to 6.22±0.3; HDL 1.42±0.1 to 1.49±0.1; LDL 3.92±0.24 to 3.85±0.26; Trigs 1.44±0.16 to 1.42±0.12; LDL/HDL 2.92±0.26 to 2.71±0.22, Glucose (mmol/L) 5.4±0.22 to 5.21±0.17; Regular egg- Before and after	No relationship between egg consumption and stroke, cancer and IHD deaths. 1-2 eggs per wk in females had lower risk of all cause death than those who consume 1egg per day, but no relationship in males.	No relationship between egg consumption and stroke or MI deaths. All cause death higher in those consuming at least 7eggs per wk and even higher in those with baseline diabetes. Hazard ratio not different between egg consumption levels, even when adjusted for a range of confounding variables.	Eating eggs more frequency, up to almost daily, was not associated with an increase in CHD incidence for middle-aged Japanese men and women (hazard ratios not significantly different). Subjects with hypercholesterolaemia were less frequently in frequent egg consumption groups, probably because they avoided eating eggs.

	intervention: TC (mmol/L) 6.25±0.3 to 6.22±0.3; HDL 1.45±0.1 to 1.48±0.1; LDL 3.89±0.24 to 3.88±0.24; Trigs 1.48±0.14 to 1.45±0.16; LDL/HDL 2.84±0.23 to 2.80±0.25, Glucose (mmol/L) 5.4±0.22 to 5.21±0.17.			
Effect on risk (Increase/None/Protect)	None - CVD;	None for each cause of death, Increase for all cause mortality when adjusted for covariates.	None for each cause of death, Increase for all cause mortality when adjusted for covariates.	None
Clinical importance [9]	CVD - 3;	3	3	3
Clinical relevance [10]	CVD - 2;	1	1	1
Generalisability	y	n - Japanese cohort- different lifestyle and genetic makeup.	n - males only and educated.	n - Japanese cohort- different lifestyle and genetic makeup.
Applicability	y	y	y	y

Table 11.1 Studies used to make evidence statement for eggs and cardiovascular disease (cont.)

Reference [1]	**Maki, 2003 [120]**	**Gillingham 2005 [793]**	**Sindelar 2004 [908]**
Type of study [2]	RCT	RCT	RCT
Level of evidence [3]	II	II	II
Intervention/ comparator [4]	10 DHA-enriched eggs per wk for 6 wks or 10 regular eggs per wk for 6 wks/ blood lipids.	2 DHA-enriched or regular eggs daily for 21 days each/ blood lipids.	1 n-3 enriched or regular egg daily for 6 of 7 days per wk for 4 wks/ blood lipids.
N [5]	77, 76	15	12
Population/study	US; 6 wk intervention for adults	Canada; 21 day intervention for	US; 4 wk intervention for

information [6]	aged 21-80 yrs. Randomised to either 10 DHA eggs or 10 regular eggs per wk. Blood lipid levels assessed at wk 6.	adult males treated with statin medications who are hypercholesterolaemic aged 35-78 yrs. Randomised crossover trial to either 2 DHA eggs per day or 2 regular eggs per day for 21 days. Blood lipid levels assessed at 21 days. 6 wk washout.	physically active adults mean age 33(7) yrs and BMI 24(3). Randomised crossover trial to 6 n-3 eggs per wk or 6 regular eggs per wk with 4 wk washout. Blood lipid levels assessed at 4 wks.
Quality [7]	Positive	Neutral	Positive
Results [8]	No significant differences between interventions in % changes from baseline for TC, HDL, non-HDL and trigs. Median LDL increased during DHA egg treatment 5.9%(CI -22.3 - 72.5%) compared to regular egg 2.3%(CI -37.5-34.9) p = 0.047 When separated further into <>BMI 30, no differences in lipid levels seen, but trigs and HDL came close to significance.	No differences in lipid levels between two interventions. HDL increased by 4.5% from baseline to 21 days in DHA enriched egg intervention arm. Day 0 - 22: TC: 4.62(0.26) to 4.76(0.22); LDL 2.54(0.18) to 2.76(0.17); HDL 1.10(0.11) to 1.15(0.12); Trigs 0.62(0.16) to 0.52(0.13); NonHDL 3.52(0.27) to 3.61(0.22). Control: Day 0 to 22: TC: 4.71(0.26) to 4.67(0.22); LDL 2.64(0.17) to 2.59(0.14); HDL 1.07(0.12) to 1.11(0.13); Trigs 0.59(0.17) to 0.63(0.15); NonHDL 3.64(0.29) to 3.56(0.22).	No differences in lipid levels between two interventions or from baseline to 4 wks within each intervention. Except that trigs increased 19mg/dl in n-3 group compared to regular egg group (and approx same from baseline within n-3 egg group). Actual numbers not provided - TC, LDL & HDL did not change significantly within the diet treatments. Serum trigs was higher with n-3 PUFA-enriched eggs 86.54 (5.84) mg/dL than with conventional eggs 67.56(5.48).
Effect on risk (Increase/None/Protect)	None	None - HDL increased by 4.5% during n-3 egg intervention.	None (except 19mg/dl increase in trigs in n-3 group).
Clinical importance [9]	3	3	3
Clinical relevance [10]	2	2	2
Generalisability	y	n - males on statins with hypercholesterolaemia attending a heart clinic.	y - except were physically active.

Applicability	y	y	y

Table 11.1 Studies used to make evidence statement for eggs and cardiovascular disease (cont.)

Reference [1]	**Burke 2007 [289]**	**Nettleton 2008 [486]**	**Chakrabarty 2002, 2004 [123,107]**	**Goodrow 2006 [81]**
Type of study [2]	Cohort	Cohort	RCT	RCT
Level of evidence [3]	III-2	III-2	II	II
Intervention/ comparator [4]	≤8 eggs per month; > 8 eggs per month / CHD rates.	1 egg per day or <1egg per day/ hospitalised heart failure.	1 egg per day or 0 eggs per day for 8 weeks.	1 egg per day or 0 eggs per day for 5 wks/ blood lipids.
N [5]	F 256 M 258	14,153	34	33
Population/study information [6]	Australia; M and F 19,31,51,65; Follow up for 13-15 yrs looking at egg consumption patterns and CHD rates. Aboriginal Australians aged 15-88 yrs.	US; M and F, 51; 13 yr follow up for adults aged 45-64 yrs looking at egg consumption patterns and hospitalised heart failure (fatal or non-fatal). African-American and white adults sampled. Atjerosclerosis Risk in Communities study.	8 wk follow up for Indian adults aged 24-26 yrs who were predominantly vegetarian: randomised crossover trial to either 1 egg per day or 0 eggs per day. Blood lipid levels assessed at baseline, 4 and 8 wks.	US; 5 wk intervention for older adults aged 60-96yrs. Randomised crossover to either 1 egg per day or 0 eggs per day. Blood lipid levels and lutein and zeaxanthin levels assessed at 5 wks.
Quality [7]	Positive	Positive	Positive	Positive
Results [8]	Egg consumption > 8 per month had Hazard ratio of 2.59 (CI 1.11- 6.04) compared to lesser egg consumption/mth (p= 0.03).	Participants with heart failure (HF) had 0.37(0.01) serves of eggs which was higher than nonHF participants 0.29(0.003) p<0.001). 1 daily egg led to increased	No differences in lipid levels between egg and no-egg consumers, except TC/HDL increased by 0.34. 12 subjects had 15 - 73% increases in LDL cholesterol. "Knowing the	No differences in lipid levels between egg and no egg consumers at 5 weeks. At 5 wks: Serum TC, LDL, HDL and TG concentrations during the egg and no egg

		risk of HF RR=1.23 (CI 1.08-1.41).	response of an individual [to dietary cholesterol] may be important before making egg consumption a regular habit."	interventions did not differ. Study did not provide numbers but TC ~ 5mmol/L, LDL ~3; HDL & Trigs ~1.3 for both groups at 5 weeks.
Effect on risk (Increase/None/Protect)	**Increase**	**Increase**	**None** (cholesterol responders may be at increased risk)	**None**
Clinical importance [9]	1	1	3	3
Clinical relevance [10]	1	1	2	2
Generalisability	No - generalisable to Australian Aborigines only	Yes - although African Americans might be genetically different but not entire sample.	No - Indian subjects plus predominantly vegetarian subjects - not reflective of usual Australian diet and lifestyle.	Yes - for older caucasians.
Applicability	Yes	Yes	Yes	Yes

11.2 EGGS and CANCER

Does a particular intake of eggs effect the risk of cancer?		
Evidence Statement		Consumption of eggs is not associated with risk of cancer risk.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	2 Level III studies (reviews of cohort or case control studies) and 10 Level III-2 studies (2 cohort and 8 case control studies); 1 cross sectional study retrieved but not extracted.
Consistency	Poor	Evidence is inconsistent - 5 studies (including both Level I reviews) showed no or little evidence of an association between egg consumption and cancer risk while 6 others showed an increased risk and 1 showed a protective effect. Different sites of cancer were analysed which may explain the inconsistent findings.
Clinical impact	Satisfactory	Only one Case-Control study had clear confidence intervals above 1: study of benign prostatic hyperplasia, OR 1.53 (1.24-1.89) in T3 vs. T1 (doses not reported).
Generalisability	Satisfactory	Population studies in body of evidence differ to target population but it is clinically sensible to apply this evidence to target population.
Applicability	Satisfactory	Probably applicable to Australian healthcare context with some caveats.

The two reviews, two cohort and eight case control studies contributing to the body of evidence are in Table 11.2. There was generally only one study located on each type of cancer, with the exception of ovarian cancer (three papers found) and brain tumour (two papers located). Articles that have examined cancer, bladder and colorectal cancer did not find an association between cancer and egg consumption. Evidence regarding the association between egg consumption and ovarian cancer was mixed. One meta analysis and one case control study in ovarian cancer found no association, however one case-control study found an positive association. Both brain tumour articles found an increased risk of cancer with increased egg consumption. Increased frequency of egg consumption was association with an increased risk of pancreatic, lung and prostate cancer and a decreased risk of gastric cancer. Whether an association between egg consumption and cancer exists may be dependent on cancer site. More evidence on each specific site is needed to confirm any associations found.

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Table11.2 Studies used to make body of evidence for eggs and cancer

Reference [1]	**Nakamura 2004 [16]**	**Brinkman 2008 [259]**	**Genkinger 2006 [91]**	**Lee 2009 [155]**	**Chan 2007 [72]**
Type of study [2]	Cohort	Systematic Review of mixed studies (primarily cohort and case control) studies	Pooled analysis of 12 cohort studies - meta-analysis of cohort studies	Cohort	Case control study
Level of evidence [3]	III-2	1	1	III-2	III-2
Intervention/ comparator [4]	≥2 eggs per day, 1 per day, 0.5 per day, 1-2 eggs per wk or seldom egg intake/ stroke, cancer, IHD deaths.	Egg consumption - levels not specified/ incidence of bladder cancer.	Egg consumption - intakes of >50 g per day (~1 egg per day) to <6.25 g per day./ incidence of ovarian cancer.	Quintiles of egg consumption / incidence of colorectal cancer.	Quartiles of egg consumption (lowest 1/4ile was comparator) + >1 per month, <1 per month; / incidence of pancreatic cancer.
N [5]	9263	Data not provided	553,217 participants across 12 cohort studies	73,225 1576 cases)	523 cases 1701 controls
Population/study information [6]	14 yr follow up looking at egg consumption and mortality from all cause, IHD, stroke and cancer in Japanese female adults. Egg intake assessed through FFQ and death certificate used to assess cause of death. NIPPON	Cases of bladder cancer and controls from countries including Serbia, Japan, Uruguay; M and F 19,31,51,65	12 cohorts of women from Nth America and Western Europe were pooled and analysed for risk of ovarian cancer. Follow up minimum of 7 yrs to 22 yrs. F 19,31,51,65	Women aged 40 to 70 yrs living in one of 7 urban communities of Shanghai, China. Women with hx of cancer at baseline, with extreme total EI, lacking detailed information on cancer and lost to follow up were excluded from	Individuals with incident adenocarcinoma of exocrine pancreas in San Francisco Bay area between 21-85 yrs, alive, complete interview in English. FFQ for intake of eggs assessed. Quartile and dose of eggs per year prior to diagnosis assessed.

	Data 80.			analysis. Quintile of egg intake using FFQ and relationship to incidence of colorectal cancer tested. Shanghai Women's Health Study.	
Quality [7]	Positive	Positive	Neutral	Positive	Positive
Results [8]	No relationship between egg consumption and stroke, cancer and IHD deaths. 1-2 eggs per wk in females had lower risk of all cause death than those who consume 1egg per day, but no relationship in males.	6 studies on association between egg and bladder cancer were found. 3 had no association, 2 had a positive association and 1 had a negative association. A carcinogenic effect between bladder cancer and egg consumption, on the basis of these findings, was deemed "possible".	Egg consumption was not associated with ovarian cancer risk (pooled multivariate RR 1.18 (CI 0.89-1.57) p = 0.52 (intake of >50g/d of eggs to <6.25g/d of eggs). When examined continuously, higher intakes of eggs were associated with a slightly higher risk of ovarian cancer (pooled mutlivariate RR for a 50g/d increment 1.11 (CI 0.99-1.24). Similar associations were observed for endometrioid (1.31 (CI 0.87-1.98), mucinous (1.12, 0.60-	No significant association between colorectal cancer and quintiles of egg consumption - even though fifth quintile of egg consumers in colorectal cancer showed a trend for increased risk. Colorectal - Q1 ref; Q2 1.3; Q3 1.3; Q4 1.0; Q5 1.4 (1.1-2) p = 0.57. Colon Q1 Ref; Q2 1.5, Q3 1.5, Q4 0.8, Q5 1.5 (1.0-2.3) p =0.57. Rectal - Q1 Ref, Q2 1.0, Q3 0.9, Q4 1.1, Q5 1.4 (0.9-2.2) p = 0.85.	Significant association for frequency of egg intakes per month but no clear dose response relationship with cancer incidence. M and F all covariates adjusted for: Q2 1.4 (1.0-1.9); Q3 1.6 (1.2-2.1); Q4 1.4 (1.0-2.0) p=0.1; 1-3 per month 1.2 (0.8-1.7); 1 per wk 1.4 (1.0-2.1); 2-4 per wk 1.7(1.2-2.3); 1.6(1.0-2.4) p<0.05

			2.10) and serous (1.12 (CI 0.91-1.37) ovarian cancers.		
Effect on risk (Increase/None/Protect)	None for each cause of death, Increase for all cause mortality when adjusted for covariates.	None - evidence still unclear of an effect.	None	None	Increase
Clinical importance [9]	3	2	3	3	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	n - Japanese cohort- different lifestyle and genetic makeup.	n - different lifestyles and genetic makeups of countries studied.	y	n - women only and Chinese.	y
Applicability	y	y	y	Y	y

Table11.2 Studies used to make body of evidence for eggs and cancer (cont.)

Reference [1]	**Stefani 2004 [238]**	**Terry 2009 [427]**	**Hu 2002 [1112]**	**Pogoda 2009 [426]**
Type of study [2]	Case control study	Case control study	Case control study	Case control study
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Tertiles of egg consumption / incidence of gastric carcinoma.	Quartiles of egg consumption / incidence of brain cancer.	Quartiles of egg consumption / incidence of lung cancer.	Quartiles of materal egg consumption / incidence of paediatric brain tumour incidence in offspring.
N [5]	240 cases 960 controls	1548 cases 2486 controls	161 cases 483 controls	1218 cases 2223 controls
Population/study information [6]	Uruguay; Cases - newly diagnosed	Subjects aged 20 to 80, controls matched for age	US F19,31,51,65	I0, I7, C1, C4, B9, G9, B14, G14, M19, W19;

	and microscopically confirmed gastric carcinoma admitted to hospital in one of 4 major hospitals of Montevideo. Controls - patients at same hospitals with non-neoplastic disease; no recent changes to diet; diseases not related to smoking or alcohol. Tertile egg consumption assessed using non-validated FFQ.	and gender (5 trials = population matched; 3 trials = frequency matched), 8 study centres in 6 countries. Quartile egg consumption assessed against brain cancer.	Incident lung cancer cases identified by cancer registries between 1994 and 1997 in eight Canadian provinces and had never smoked. Controls were frequency matched with an age/sex distribution similar to that of all cancer cases. Majority of participants were aged 40 and above, had a healthy to slightly overweight BMI, had 9 - 13 yrs of education and were intermediate or high social class.	Pediatric brain tumors from 9 study centres - Australia, Canada, France, Israel, Italy, Spain and US - diagnosis age ranged from birth to 19 yrs, controls were frequency matched to cases in all US centres and Paris, otherwise were individually matched (region of residence, age, sex and geographic area).
Quality [7]	Neutral	Neutral	Positive	Neutral
Results [8]	Significantly lower risk of gastric cancer with higher tertiles of egg consumption (p = 0.0001) Tertile 2 - OR (CI): 0.67 (0.47-0.97) ; Tertile 3 - 0.48 (0.33-0.69). No differences in ORs for individual genders.	Increased risk of all tumours, Glioma, Astro-cytoma, Oligodendro-glioma with egg consumption at highest quartile (OR 1.6-1.8). No relationship with oligodendro-glioma and meningioma.	Significant effect (p=0.04); Q2: 1 (0.5-2); Q3 1.8 (1 - 3.3); egg consumption frequency: Q1 = half an egg or less per wk; Q2 = 0.6-1eggs/wk; Q3 >3 eggs per wk Cases: 2.47eggs per wk; Controls 3 eggs per wk.	Eggs/dairy: All tumors: Q2 = 1.0 (0.8-1.3), Q3 1.1 (0.8-1.5), Q4 1.2 (1.0-1.5); Astroglials 1.0 (0.7 - 1.4), 1.2 (0.9-1.5), 1.3 (1-1.7); PNETs 1.3 (1-1.6); 1.6 (1-2.7), 1.6 (1-2.4). Pilocytic astrocytomas, Other astrocytomas were only tumor subtypes significantly associated with egg/dairy intake. Pilocytic astrocytoma p = 0.02; Other Astrocytoma

				p = 0.001; All tumors p = 0.04; Astroglials p = 0.01; PNETs p = 0.049
Effect on risk (Increase/None/Protect)	Protect - although no dose provided.	Increase - although no dose provided.	Increase - >3 eggs per wk.	Increase - although no dose provided and eggs and dairy were combined together.
Clinical importance [9]	1	2	2	2
Clinical relevance [10]	1	1	1	1
Generalisability	n - Uruguay considered culturally different.	y - geographic location may limit generalisabilty - but is across 6 different countries.	n -women only.	y - for younger ages.
Applicability	y	y	Y	y

Table11.2 Studies used to make body of evidence for eggs and cancer (cont.)

Reference [1]	**Pirozzo 2002 [125]**	**Pan 2004 [112]**	**Bravi 2006 [784]**
Type of study [2]	Case control study	Case control study	Case control study
Level of evidence [3]	III-2	III-2	III-2
Intervention/ comparator [4]	More than 2 per wk; 1-2 per wk; 1 per fortnight to <1 per wk, <1 per fortnight/ incidence of primary epithelial ovarian cancer.	Quartiles of egg consumption / incident ovarian cancer.	Tertiles of egg consumption/ incidence of benign prostatic hyperplasia.
N [5]	717 cases 806 controls in total	442 cases 2135 controls	1369 cases 1451 controls
Population/study information [6]	Australia; Girls 14 yrs, Women 19,31,51,65 yrs; Histologically confirmed incident cases of primary epithelial ovarian cancer registered in all major gynaecological oncology	Canada – Women 19,31,51,65 yrs; All ovarian cancer cases were histologically confirmed by ICD for oncology; cases were incident cancer newly diagnosed beween	Italy, M 31,51,65; Benign prostatic hyperplasia diagnosed btwn 1991 and 2002 in four Italian areas, younger than 75 yrs, admitted to major teaching and

	treatment centres in 3 Australian sites (aged between 18 and 79 yrs and competent to complete a questionnaire) were invited to participate. Controls were selected from electoral roll by a random procedure yielding an age and regional distribution similar to that of cases.	1994 and 1997 in 7 participating provinces; cases identified within 1 - 3 months of diagnosis; controls frequency matched to overall case group to select population controls with similar age and sex distribution - a random sample within various province databases were taken. National Enhanced Cancer Surveillance system.	general hospitals in study areas and surgically treated for BPH diagnosed no longer than 1 year prior to interview. Needle biopsy to confirm BPH.
Quality [7]	Positive	Neutral	Neutral
Results [8]	OR (CI) - >2 per wk 1.82 (1.3-2.55); 1-2 per wk 1.71 (1.25-2.35); 1 per fortnight - <1 per wk 1.40 (0.99-1.98), <1 per fortnight 1.0, p<0.001.	OR (CI range) - Q4: 1.3 (0.96-1.73); Q3: 1 (0.73-1.39); Q2: 0.96 (0.68-1.35); p = 0.13.	OR (CI range) - T3: 1.43 (1.18-1.74); T2 1.53 (1.24-1.89); p = 0.0007.
Effect on risk (Increase/None/Protect)	Increase - at least 1 egg per wk.	None	Increase - although no dose provided.
Clinical importance [9]	2	3	1
Clinical relevance [10]	1	1	1
Generalisability	y	y	Y
Applicability	y	y	Y

INCLUDED STUDIES not in BOE with < 5 studies

EGGS and STROKE

A cohort study in Japan reported that eggs were independently associated with a decreased risk of stroke mortality (Sauvaget et al. 2003).

EGGS and ATOPIC DISEASE

This review determined there was insufficient evidence to suggest avoidance of eggs during pregnancy to avoid later egg allergy in the offspring (Kramer 2006).

EGGS and DEPRESSION

A cohort study in Japan failed to find any relationship between egg consumption and post natal depression (Miyake et al. 2006).

EGGS and DIABETES

Cohort study of association of egg consumption with incident type 2 diabetes conducted in US. Compared with no egg consumption, multivariable adjusted hazard ratios for type 2 diabetes were 1.09 (95% CI 0.87-1.37), 1.09 (0.88-1.34), 1.18 (0.95-1.45), 1.46 (1.14-1.86), and 1.58 (1.25-2.01) for consumption of <1, 1, 2-4, 5-6, and >/=7 eggs per week, respectively, in men (P for trend <0.0001). Corresponding multivariable hazard ratios for women were 1.06 (0.92-1.22), 0.97 (0.83-1.12), 1.19 (1.03-1.38), 1.18 (0.88-1.58), and 1.77 (1.28-2.43), respectively (P for trend <0.0001) (Djoussa et al. 2009).

References

Djoussa, L., Gaziano, J. M., Buring, J. E. & Lee, I. M. 2009, "Egg consumption and risk of type 2 diabetes in men and women", *Diabetes Care*, vol. 32, no. 2, pp. 295-300.**Excluded: <5 studies**

Kramer Michael, S. & Kakuma, R. 2006, "Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child", *Cochrane Database of Systematic Reviews*, vol., no. 3.**Excluded: <5 studies**

Miyake, Y., Sasaki, S., Yokoyama, T., Tanaka, K., Ohya, Y., Fukushima, W., Saito, K., Ohfuji, S., Kiyohara, C. & Hirota, Y. 2006, "Risk of postpartum depression in relation to dietary fish and fat intake in Japan: The Osaka Maternal and Child Health Study", *Psychological Medicine*, vol. 36, no. 12, pp. 1727-1735.**Excluded: <5 studies**

Sauvaget, C., Nagano, J., Allen, N., Grant, E. J. & Beral, V. 2003, "Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study.[see comment]", *International Journal of Epidemiology*, vol. 32, no. 4, pp. 536-43.**Excluded: <5 studies**

12. FATS AND OILS (S1.1)

Evidence Statements

12. FATS AND OILS (S1.1)

Search results

The initial search of the data bases included 5501 references for fats and oils and the specified disease outcomes. The detailed search is included in a separate document on searches. In all, 501 references concerning fats and oils had data extracted and 51 papers were used to form the body of evidence statements for fats and oils. Sufficient evidence was found to make statements for fats and oils and cardiovascular disease, weight loss and obesity, type 2 diabetes, hypertension, incidence of cancer and in particular breast and endometrial cancer and mental health. While every effort was made to exclude clinical populations, if it was felt that the systematic review population was representative of the Australian population in general. The review was included even though some of the population may have had hyperlipidemia or impaired glucose tolerance.

In the WCRF report, the following three statements were made for Fats and Oils and this has been compared to the body of evidence statements made here.

1. There is limited evidence suggesting that diets relatively high in fats and oils (total and any type) increases the risk for lung cancer and breast cancer (postmenopause).
   Our evaluation could only be made for omega-3 fats and this supports the above conclusion.

2. There is limited evidence suggesting that exposure to foods containing animal fats increases the risk for cancers of the Colorectum.
   There were not enough recent studies to allow an evaluation for fat intake and colo-rectal cancer.

3. There is limited evidence suggesting evidence that exposure to butter increases the risk for lung cancer.
   There was only one case-control study included that examined lung cancer risk and therefore did not allow a body of evidence statement to be made for this outcome.

12.1 FATS AND OILS and CARDIOVASCULAR DISEASE

Does a particular intake of fat/oil affect the risk of Cardiovascular Disease?		
Evidence statement		Consumption of long chain polyunsaturated fatty acids is associated with reduced mortality from cardiovascular disease
Grade		D
Component	Rating	Notes
Evidence Base	Satisfactory	11 systematic review of predominantly RCTs (Quality rating; 5P, 4O, 2N).
Consistency	Satisfactory	Some inconsistency for effects of fatty acid (FA) on risk markers of CVD and CVD mortality. Most effects are for saturated fatty acids on plasma cholesterol and for long chain (omega-3) on plasma trigkycerides. Consistent trends on mortality and total CVD events.
Clinical impact	Poor	8 reviews are on biomarkers or risk factors for CVD (LCn-3 PUFA) and TG -27 (95% CI -33- -20) mg/dL; LDL and omega-3; 6 (95% CI 3- 8) mg/dL, the other three look at total mortality or mortality from cardiovascular events (omega-3 and total mortality RR 0.87 (95% CI 0.73-.03); n-3 PUFA and combined cardiovascular events RR 0.95 (95% CI 0.82-1.12), and then secondary outcomes on singlular and combined cardiac events.
Generalisability	Good	Wide range of poulations in the reviews, which were all adults. Wide range of omega-3 doses.
Applicability	Excellent	Applicable to the Australian health setting, most data from America and Europe.

The studies included in the body of evidence statements are shown in Table 12.1. The studies included in the body of evidence table are all systematic reviews (Quality rating; 5P; 3O; 2N). The evidence from three systematic reviews (Hooper et al. 2004, Struder et al. 2005, and Wang et al. 2006) supports a neutral effect on mortality from cardiovascular disease related to omega-3 PUFA intake of up to 7 grams per day. No data was supplied from studies of greater than 7 g per day omega-3 fatty acids. The other eight systematic reviews focused on surrogate markers of cardiovascular disease such as lipid profiles. Six of these reviews support a protective effect of omega-3 PUFA on triglycerides and a neutral or small detrimental effect on total cholesterol, LDL cholesterol and HDL cholesterol. There is little good evidence on vegetable origin omega-3 PUFA and cardiovascular disease. There is little new data on the other fatty acids and cardiovascular disease.

Two cohort studies (both O) of infant diet and cardiovascular disease. One, (Ohlund et al., 2008) looked at infant diet and then serum cholesterol over a six month period and found that PUFA is protective of lipid profile, and that the quality of the fat is important in an infant diet. The second cohort (Ness et al. 2005) measured childhood diet and followed up after 30 and 50 years with mortality data in adults. SFA and total fat in childhood diet was found to be protective of all causes of mortality and deaths attributable to cardiovascular disease. The second of these studies findings are not consistent with adult disease findings. These studies are summarized in the Summary of Not Included Studies.

The results need to be interpreted with caution because some of the systematic reviews included subjects who had already experienced a CVD event and were secondary prevention trials. These studies could not be removed from the review and/or meta-analysis and therefore the generalisability is only satisfactory.

References

Balk, E. M., Lichtenstein, A. H., Chung, M., Kupelnick, B., Chew, P., & Lau, J. 2006, "Effects of omega-3 fatty acids on coronary restenosis, intima-media thickness, and exercise tolerance: A systematic review", *Atherosclerosis*, vol. 184, no. 2, pp. 237-246.

Balk, E. M., Lichtenstein, A. H., Chung, M., Kupelnick, B., Chew, P., & Lau, J. 2006, "Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk: A systematic review", *Atherosclerosis*, vol. 189, no. 1, pp. 19-30.

Castro, I. A., Barroso, L. P., & Sinnecker, P. 2005, "Functional foods for coronary heart disease risk reduction: a meta-analysis using a multivariate approach", *American Journal of Clinical Nutrition*, vol. 82

Eslick, G. D., Howe, P. R. C., Smith, C., Priest, R., & Bensoussan, A. "Benefits of fish oil supplementation in hyperlipidemia: a systematic review and meta-analysis", *International Journal of Cardiology*, vol. In Press, Corrected Proof.

Hooper, L., Harrison, R. A., Summerbell, D. C., Moore, H., Worthington, H. V., Ness, A., Capps, N., Davey, S. G., Riemersma, R., & Ebrahim, S. 2004, "Omega 3 fatty acids for prevention and treatment of cardiovascular disease", *Cochrane Database of Systematic Reviews*, vol., no. 4, pp. CD003177.

Lee, K. W. & Lip, G. Y. H. 2003, "Effects of lifestyle on hemostasis, fibrinolysis, and platelet reactivity: a systematic review", *Archives of Internal Medicine*, vol. 163, no. 19, pp. 2368-2392.

Mensink, R. P., Zock, P. L., Kester, A. D. M., & Katan, M. B. 2003, "Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a

meta-analysis of 60 controlled trials", *American Journal of Clinical Nutrition*, vol. 77, no. 5, pp. 1146-1155.

Struder Marco, B. M., Leimenstoll Bernd, Glass Tracy R., & Bucher Heiner C. 2005, "Effect of Different Antilipid Agents and Diets on Mortality", *Archives of Internal Medicine*, vol. 165, no., pp. 725-30.

Wang, C., Harris, W. S., Chung, M., Lichtenstein, A. H., Balk, E. M., Kupelnick, B., Jordan, H. S.,& Lau, J. 2006, "n-3 Fatty acids from fish or fish-oil supplements, but not alpha-linolenic acid, benefit cardiovascular disease outcomes in primary- and secondary-prevention studies: a systematic review", *American Journal of Clinical Nutrition*, vol. 84, no. 1, pp. 5-17.

Wendland, E., Farmer, A., Glasziou, P.,& Neil, A. 2006, "Effect of alpha linolenic acid on cardiovascular risk markers: a systematic review", *Heart*, vol. 92, no. 2, pp. 166-169.

Table 12.1 Studies used to make evidence statement for fats and oils and the risk of cardiovascular disease

Reference [1]	**Balk et al. 2006 [1415]**	**Wendland et al. 2005 [3898]**	**Hooper et al. 2004. [5608]**
Type of study [2]	Systematic review RCTs	Systematic review RCT	Systematic review RCT and cohort studies, no case control studies used
Level of evidence [3]	I	I	I
Intervention/ comparator [4]	LChain-3PUFA 0.8 - .4g/day Larger the dose the better the effect For plant oil supplements or margarine (4.5-5 g ALA) for med diet (2g/day omega-3 FA).	No doses recorded	Most studies provided dietary supplement, one a liquid emulsion and one an enriched margarine, three provided dietary advice and one dietary advice + food supplement. Supplementation generally with FO, but five studies provided plant based, doses of FO ranged from 0.4 - 7g per day.
N [5]	Lipids : total cholesterol (FO - 7853; ALA - 1089); LDL (FO - 6969; ALA - 700); HDL (FO - 7353; ALA - 700);TG (FO - 7803; ALA - 700) FBS: (FO 1427; ALA - 52) HBA1c: (FO - 578; ALA - 0) CRP: (FO - 73; ALA - 18).	744 in meta-analysis	36, 913 48 RCT (111 papers)
Population/study information [6]	52 RCT of generally healthy, had DM, HT, dyslipidemia, or CVD. Supplementation or general dietary methodology but not >6g/day omega-3 reporting on serum	M and F adult Wide age range Generally healthy to risk factors for CVD, type 2 diabetes and overweight.	Adults with or without CVD, including those with increased risk of ca.

	markers of CVD risk.		
Quality [7]	Positive	Neutral, no mention of quality assurance of papers	Positive: allocation concealment, participant blinding, provide blinding and outcome assessor blinding
Results [8] - Systematic Reviews - RCT	LCn-3 PUFA significant net improvement on TG -27 (95% CI -33- -20) mg/dL;↑FO dose 1g/day associated with a 8 mg/dL ↓TG. HDL: significant net improvement of 1.6 (95% CI 0.8- 2.3) mg/dL. No dose or duration associated with FO and HDL. LDL: significant net worsening of 6 (95% CI 3-8) mg/dL. No dose or duration associated with FO and LDL. No effect on TC. ALA Singh et al. found large effect - study is problematic. All other studies showed small effect ≤2mg/dL net change on TC, LDL and HDL.	629 participants for TG. Significant heterogeneity. Random effect model showed pooled mean differences of 0.01 mmol/L for TG. HDL in 661 participants, pooled mean difference was -0.01 mmol/L ($p<0.01$) not heterogeneous. NS weight, TC, LDL, VLDL.	Relative risk of death of those randomised to n-3 PUFA arm of 0.87 (95% CI 0.-1.03) compared to control heterogeneity 0.04.sensitivity analysis (removing all studies without low summary risk of bias, relative risk of 0.98 (95% CI 0.7 - 1.36) heterogeneity 0.57. No significant effect of n-3 PUFA on combined cardiovascular events RR 0.95 (95% CI 0.82-.12) heterogeneity <0.0001) removing studies with moderate to high risk of bias improved heterogeneity RR 1.09 (95% CI 0.87 -1.37, heterogeneity 0.07) NS on Cardiovascular death, fatal and non fatal MI, sudden death, stroke, heart failure, angina, PVE, revascularisation. NS on risk factors of CVD e.g. weight, TC, HDL, BP (diastolic. & systolic.) TG reduced by n-3 PUFA WMD -0.40mmol/L; (95% CI -0.56- -0.23, heterogeneity 0.003). Greater effect seen at higher dose > 4.5g EPA/DHA.day-1. LDL

			significantly raised by n-3 PUFA WMD 0.13 mmol/L (95%CI 0.03-0.22, heterogeneity 0.58).
Results [8] - Systematic Review - cohort			Meta analysis of cohort studies showed increased dose of n-3 PUFA significantly reduces cardiovascular deaths, with significant heterogeneity. cohort studies suggest a reduced risk of fatal MI in participants choosing to consume more n-3 PUFA, RR 0.42 (95% CI 0.21 - 1.82) meta analysis from only one study. No significant effect of n-3 PUFA on non fatal MI shown. Pooling of cohort studies suggests that increased n-3 PUFA reduces sudden death, RR 0.44 (95% CI 0.21 - 0.91) data form one study. NS or no data for other outcomes.
Clinical importance [9]	1	2	3
Clinical relevance [10]	2	2	1
Effect of risk(increase/none/protect)	Protect - risk factors CVD measured.	None - risk factors CVD.	RCT - none total mortality, corhort - protective total mortality.
Generalisability	y	y(?)	y
Applicability	y	y(?)	y
Comment		No quality assessment, makes the generalisablity and applicability harder to assess.	RCT and Cohort data are not consistent.

Table 12.1 Studies used to make evidence statement for fats and oils and the risk of cardiovascular disease (cont.)

Reference [1]	**Mensink et al. 2003 [3966]**	**Struder et al. 2005 [5609]**	**Balk et al 2006 [1615]**
Type of study [2]	Systematic review of the parallel, crossover, or latin square design, must have a control group.	Systematic review of RCT.	Systematic review of RCT.
Level of evidence [3]	III	I	I
Intervention/ comparator [4]	Mean intake of fat of energy = 34.3% (4-5 - 53%); SFA 10.2% (2.2 - 24.4%); MUFA 13.5% (1.5-39.8%); PUFA 8.8% (0.6-28.8%). trans FA consumed from 0.0 - 10.9% of energy		Doses <6 g/day included in review
N [5]	159 diet data points from 1672 participants.	All trials > 1000 per group, In total 137,140 in interventions and 138,976 in controls. Only reporting on the small amount in the primary prevention studies.	22 studies 12 RCT for coronary artery restenosis after PTCA (4 additional studies also evaluated FO), 1 RCT for carotid IMT, 3 RCT in exercise tolerance.
Population/study information [6]	F:M = 30:70; test diets fed for 13 - 91 days; mean pre-study cholesterol values (from 40 studies) = 3.7 - 6.5 mmol/L. Mean age = 21 - 72 years; analysis showed that participant or study characteristics were a factor in results. Excluding inpatient and liquid diet studies did not change the results.		not reported.
Quality [7]	Neutral,	Positive	Positive used two reviewers,

	no quality assessment of papers/studies included.		quality and applicability assessed papers and a systematic search strategy.
Results [8] - Systematic Reviews - RCT	TC: HDL ratio unchanged for SFA→CHO; TC: HDL ↓ if SFA or CHO → cis unsaturated FA. *cis*MUFA small significant LDL ↓ relative to CHO. All FA ↑ HDL relative to CHO, SFA more than unsaturated FA (i.e. replace SFA with MUFA for 1% of energy→↓HDL 0.002mmol/L). Replace CHO with any FA ↓ TG. Replace CHO with SFA did not ↓ apoB, but cis unsaturated FA did, higher for PUFAs. Lauric acid highest ↑ TC and LDL effect, also ↓ TC:HDL relative to CHO. HDL-raising effect of SFA relative to CHO decreased with increasing chain length to from Lauric 0.027 mmol/L per % energy Stearic with approx 0% mmol/L per % energy. Trans 18:1 had largest effect on TC: HDL (replace SFA ↓ 0.019; cis MUFA ↓0.048; cis PUFA ↓ 0.054), & does not increase HDL or apo A-1 relative to CHO. Replacing trans fats with unsaturated FA from unhydrogenated oils most	Average relative reduction in levels of total cholesterol for n-3 FA (2%: -2 to 9%); diet (10%: 1 - 24%). Relative mortality reduced for n-3 FA 0.77 (95% CI 0.63 - 0.94, heterogeneity = 0.1, I2 = 53%; 95% UI 14-75%). Insufficient evidence to support a beneficial effect of n-3 FA in primary prevention of CHD. Risk ratios for cardiac deaths for n-3 FA 0.68 (95% CI 0.52-0.9, P=0.001, I2 = 66%, 95% UI 37 - 81%) reduced to 0.7 (95% CI 0.61-0.8, P=0.47, I2=0%, 95% UI 0-60%) removing Burr et al. n-3 FA reduce risk of overall mortality and mortality from cardiac arrest in patients with existing CHD only. 140 (95% CI 87-538) patients in a primary prevention situation need to be treated to save 1 death. In appropriate doses n-3 FA reduce TG levels, and are associated with a reduction in overall mortality. n-3 FA lower total cholesterol level to	May be net reduced coronary artery restenosis with FO supplementation. Across all studies (preferentially including analyses of patient rather than lesions, luminal loss over % stenosis and 50% stenosis over 70%) meta-analysis showed reduction of 13% RR 0.87 (95% CI 0.73-1.05, p=0.16). No real effect for dose n-3 PUFA shown. NS IMT and exercise tolerance largely due to wide variety in doses n-3 PUFA, methodology and populations.

	effective measure to improve blood cholesterol Replacing SFA with CHO depends on effect of body weight. Replace SFA with cis unsaturated FA may reduce CHD risk.	a very small extent, therefore their beneficial effect is mediated by other means.	
Results [8] - Systematic Review - cohort			
Clinical importance [9]	2	2	3
Clinical relevance [10]	2	1	2
Effect of risk(increase/none/protect)	Protect - risk factors CVD.	Protect - risk factors CVD, none total mortality.	None - rick factors of CVD.
Generalisability	y	y	y - Small numbers in some studies.
Applicability	y	y	n- Secondary prevention trials included.
Comment	Replacing trans fats with unsaturated FA from unhydrogenated oils most effective measure to improve blood cholesterol. Replacing SFA with CHO depends on effect of body weight. Replace SFA with cis unsaturated FA may reduce CAD risk.		

Table 12.1 Studies used to make evidence statement for fats and oils and the risk of cardiovascular disease (cont.)

Reference [1]	**Wang et al. 2006 [4673]**	**Eslick et al. 2007 [822]**	**Lee et al. 2003 [3979]**	**Castro et al. 2005 [4227]**
Type of study [2]	Systematic review of RCT and observational studies.	Systematic review of RCT.	(Semi) Systematic review, intervention and cross-sectional.	Meta analysis, Placebo controlled and randomised, cross over, or parallel design.
Level of evidence [3]	III	I	III-2	I
Intervention/ comparator [4]	For RCT: 10 mL Flaxseed oil (5.5 g ALA/d) for 1 yr vs. sunflower seed oil (0.14g ALA/d) for 1 yr.	Omega-3 supplementation vs. placebo. Different FO formulation used, 8 studies used DHA and 39 used EPA.	Omega - FA on markers of thrombogenisis. 23 studies, from 1985 - 2001. 2 cross-sectional; 10 double blind randomised (DBR), 3 randomised with control, 8 supplementation or food given and pre and post tested.	Received n-3 PUFA, soluble fibre or phytosterols. Treatment > 10 days.
N [5]	46 studies in total; 1 RCT, 25 prospective cohort studies and 7 case-control studies. a) 1 RCT - 13 578 participants b) large cohort studies >340 00 participants.	47 in final analysis. Cholesterol: 16 511; HDL 15 106; LDL 14 009; TG 15 492.	23 studies from 1985 - 2001.	84.28 ± 147.32 subjects n= 159 studies.
Population/study information [6]	For RCT adults 50 - 59; cohort population adults.	M and F adults with CVD risk factors. Majority of studies contained males mean age=49.	Cross sectional = 15 283 subjects; DBR from n=6 to n=60; randomised from n= 8 to n=29; pre and post form n=5 -	Human healthy.

			n=76	
Quality [7]	Positive: quality assessment	Positive	Negative	Negative, no quality check on papers, complicated stats, no discussion on if they should really be combined into one data set.
Results [8] - Systematic Reviews - RCT	1°-prevention trials. ALA RCT reported no significant cardiac benefits from ALA supplementation but overall very low CVD event rate (<1%) in control group. Background fish and fish oil intake was high. Significant reductions after multivariant adjustment in one or more of CVD outcomes investigated.	FBTG -0.34 mmol/L (95% CI -0.41- -0.27) from a mean baseline TG of 1.44mmol/L, clinically significant TG lowering effect in doses of 3.25g/day (1.9g EPA and 1.35g DHA per day). NS for total cholesterol, HDL or LDL Cholesterol.	Coagulation: no agreement for clotting factors (FVII or FVIII vWf. Fibrinolysis: inconsistent data, 1 decrease, most no change and some increase on PAI-1 and tPA antigen - mostly tpA decrease with FO (no vegetable origin). Platelet activity: inconsistent data.	Five independent variables (number of patients per study, dose, age, BMI, and treatment length) and four dependent variables (%change blood TC, LDL, HDL and TG) organised into a matrix, and converted to linear correlation units. Multivariate statistical approach. The general dietary interventions promoted a average net reduction in cholesterol (3.57%), LDL (3.88%), and TG (11.50%) and net increase in HLD (1.97%). n-3 PUFA lowered TG, but raised Total, LDL and HDL cholesterol, independent of dose, number of patients per

				study, age and BMI but was associated with treatment length. Mainly the authors wanted a combined therapy approach. Only reported the dietary results here.
Results [8] - Systematic Review - cohort	3 large prospective cohort studies > 50,000 participants reported significant reductions in all cause mortality. One cohort of women (41,836) marine n-3 FA not associated with total mortality but secondary analysis of ALA showed inverse association with total mortality after multivariate adjustments. cardiac death. Two prospective cohort studies reported on n-3 and cardiac death, one found no association with either ALA or EPA+DHA. MI: 5 cohorts and 1 case control. One cohort of female nurses showed higher EPA+DHA		NA	

	showed reduced rate of non fatal MI (31% higher to lower intake).			
Clinical importance [9]	3	2	3	3
Clinical relevance [10]	1	2	2	3
Effect of risk (increase/none/protect)	RCT none, Cohort protect	protect - risk factors of CVD		Y
Generalisablity	y	y	y	y
Applicability	y	n - Secondary prevention trials included.	n - Secondary prevention included in comments.	y
Comment	Only primary prevention data was extracted. Cohort and RCT evidence are not consistent.	Only primary prevention data extracted.	Authors note these are predominantly secondary prevention trials, that the effect of n-3 PUFA may be more antiarrhythmic rather than antithrombotic and the data is inconsistent so more needs done to investigate the variability in results published.	No new data here, n-3 PUFA mostly on TG.

12.2 FATS AND OILS and OBESITY

Does a particular intake of fats and oils affect the risk of obesity?		
Evidence statement		Consumption of a low fat diet (20-25% energy) is not associated with weight gain
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	6 Level II studies (all RCTs of low fat diets; quality all P, 2 Protect (both post-menopausal women), 3 No effect in (1 in University students, 2 in children) but 1 Protect for one Parent group in the same study with no effect for children). 3 Cohorts (2P, 1O) all no effect on risk (2 in adults and 1 in children).
Consistency	Poor	Some inconsistency is explained by life stage of subjects. No effect seen for children in 2 RCTs and 1 cohort. Protection seen for post-menopausal women in 2 RCTs and Parents in 1RCT, but no effect seen in the two adults cohorts. No effect seen for University students with a cafeteria style breakfast.
Clinical impact	Satisfactory	No effect for children. Small but important reduced risk in weight gain in some adults studies (2 population based RCTs post menopausal women; BMI change 0.3 (SE 0.03) kg/m^2; $p<0.001$).
Generalisability	Good	The populations are similar to the target population (i.e. Western, predominantly white Caucasian, men and menopausal women).
Applicability	Good	Results from the 4 large population-based RCTs are highly applicable.

The evidence concerning fats and oils and obesity and weight gain has some inconsistencies. Five Level II RCT (Quality rating: 5 P) are of relevance to the body of evidence statement on fats and oils and obesity. Two of the Level II RCT were (both P) trials. Child data (Two large RCTs) was neutral, post menopausal women data two large RCT) were protective. The cohort data used in the body of evidence statement was similar to the RCT data, mostly a neutral effect on weight gain.

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Table 12.2 Studies used to make evidence statement for fats and oils and the risk of obesity.

Reference [1]	**Donnelly et al. 2008**	**Akuamoah-Boateng et al. 2007**	**Bhargava & Guthrie 2002**	**Soares et al. 2004**
Type of study [2]	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Cafeteria-based intervention in University students with participants randomised to one of three levels of dietary fat. Low fat (LF): <25% of total energy as fat; Moderate fat (MF): 28-32% of total energy as fat; High fat (HF): >35% energy as fat.	Provision of peanut, olive, safflower or no oil everyday for 8 weeks delivered as a milkshake.	Nutrition education to reduce fat intake (to ~20% energy from fat), especially saturated fat intake, and to increase the consumption of fruits, grain products and vegetables, as led by a nutritionist vs. a copy of the American Dietary Guidelines.	Paired comparison of 2 high-fat, isoenergetic, mixed test meals, 1-4 weeks apart. Major fat source = cream (CREAM) or extra virgin olive oil (EVOO). Resting metabolic rate (RMR), diet-induced thermogenesis and substrate oxidation rates over 5 hours were measured.
N [5]	Randomised: LF n=105, MF n=98, HF n=102; Completed LF n=90, MF n=86, HF n=102	Peanut oil n=32, Olive oil n=32, Safflower oil n=33, Control n=2	Intervention n=575, Control n=351	n=12
Population/study information [6]	M 163, F 97; Mean age at baseline: Males 19.1 ± 1.4yrs; Females 18.6 ± 0.9yrs; BMI <25: 25-29.9: >30 = 65: 32: 4	Males (n=63) and nonlactating females (n=66), from Brazil (n=32), Ghana (n=64) and the US (n=33), BMI 18-25kg/m^2	Postmenopausal women 50-79 yrs, weight 76 ± 12.7kg at baseline, 57% white, 34% black, 9% Hispanic / Meetings held weekly in groups of 8-15 for the first 6 weeks, then bi-weekly, then once per month for a total of 12 months.	Postmenopausal women aged 57–73 (mean 64 ±4.5)yrs, BMI 21·9–38·3 (31.4 ±4.8) kg/m^2, Australian women.

Quality [7]	P	P	P	P
Results [8]	Weight change: LF: 0.1 ± 3.1kg (P>0.05); MF: 0.8 ± 2.5kg (P=0.009); HF: 1.0 ± 2.2kg (P=0.0002). Collinearity of fat with total energy intake. Total energy predicted weight (P=0.0025), not % fat.	Weight increased in all intervention groups (<1kg, P<0.05).	Significant (P<0·05) reductions between 0 & 12 months in energy and saturated, mono- and poly-unsaturated fats for both groups; reductions were greater for the intervention group. Mean body weight, waist and hip circumference in the intervention group were	The change in RER (P=0·018) and carbohydrate oxidation (P=0·023) was lower following the EVOO meal. Postprandial fat oxidation was significantly suppressed following the CREAM meal, but not after the EVOO meal. Hence change in fat oxidation was significant.
Clinical importance [9]	The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.
Clinical relevance [10]	Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	Evidence of an effect on proven surrogate outcomes but for a different intervention.
Effect of risk (increase/none/protect)	Increase for moderate and high fat	increase for high fat	protective	none
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 12.2 Studies used to make evidence statement for fats and oils and the risk of obesity (cont.)

Reference [1]	**Kamphuis et al. 2003**	**Bendixen et al. 2004**	**Bes-Rastrollo et al. 2006**	**Chaput et al. 2008**	**Baric et al. 2002**
Type of study [2]	RCT	RCT	Cohort	Cohort	Cohort
Level of evidence [3]	II	II	III-3	III-3	III-3
Intervention/ comparator [4]	Randomised, crossover trial: Two 36 hr sessions in a respiratory chamber for indirect calorimetry, energy expenditure, and substrate oxidation measurements comparing diacylglycerol (DG)-rich oil and triacylglycerol(TG)-rich oil.	Each subject participated in 4 different tests (1 conventional fat (rapeseed oil) and 3 modified fats (lipase-structured fat, chemically structured fat, and physically mixed fat) separated by 2–4 wks in a randomized, double-blind, 4-way, crossover design.	Quintiles of grams of olive oil Consumption at baseline.	Baseline total fat intake, highest vs lowest intake.	Fat intake % kJ/day and quartiles of Sat Fat intake % kJ.
N [5]	12	11	5356 free from obesity at baseline	184	233
Population/study information [6]	Healthy, nonsmoking women, 34.5 ± 9.4yrs, BMI 23-30 kg/m^2, weight stable, no medications, modest alcohol intake at most,	Healthy Danish men, Mean age: 25.1 ± 0.5 yrs, BMI 22.5 ± 0.6 (range: 18.9–25.0)kg/m^2.	Healthy Spanish adults.	M and F 21-64 yrs.	Children aged 7-10yrs.

	unrestrained eaters.				
Quality [7]	P	P	P	P	O
Results [8]	No difference between groups for energy balance (both slightly positive) and expenditure. Fat oxidation was higher with the DG treatment than with the TG treatment ($P<0.05$). Lower scores for hunger, appetite, estimates of prospective food intake and desire.	Appetite sensations (satiety, hunger, fullness, and prospective food consumption, thirst, comfort, and desire to eat something fatty or something savory) and ad libitum energy intakes did not differ between test oils ($P>0.05$). EE increased after all 4 tests.	In this free-living Mediterranean cohort with high between subject variability in olive oil consumption, no significant positive associations between oilve oil consumption and weight change was found. The risk of obesity is not increased in subjects who follow an olive oil-rich Mediterranean food pattern.	Those in the highest dietary fat group had greater baseline body weight, BMI and abdominal circumference, but this was not significantly different after adjustments for covariates. Mean change in body weight over 6y and waist circumference did not differ.	No significant difference between BMI or anthropometric measures in children by fat intake %kJ/day.
Clinical importance [9]	The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	The confidence interval does not include any clinically important effects.	The confidence interval does not include any clinically important effects.	The confidence interval does not include any clinically important effects.
Clinical relevance [10]	Evidence of an effect on a surrogate outcome	Evidence of an effect on proven surrogate	Evidence confined to unproven surrogate	Evidence confined to unproven surrogate	Evidence confined to unproven surrogate

	that has been shown to be predictive of patient-relevant outcomes for the same intervention.	outcomes but for a different intervention.	outcomes.	outcomes.	outcomes.
Effect of risk (increase/none/protect)	none	none	none	none	none
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

12.3 FATS AND OILS and TYPE 2 DIABETES

Does a particular intake of fat/oil affect the risk of type 2 diabetes mellitus		
Evidence statement		Consumption of fat is not associated with risk of type 2 diabetes in the short term.
Grade		D
Evidence statement		Consumption of long chain fatty acids (from 0.4 to 6g/day) is not associated with fasting plasma glucose or insulin concentrations.
Grade		C
Evidence statement		Manipulating fatty acid intake profile or total intake of fat (up to 50% of energy intake) is not associated with fasting plasma glucose or insulin concentrations.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Two systematic reviews of RCT (Quality rating: 1P, 10) and 14 Level II studies (all RCT, quality rating 12P, 2N) of relevance with 12 no effect, 1 protect and 1 increased risk. However, these are short-term interventions (up to 8 weeks) and measuring surrogate markers of type 2 diabetes only.
Consistency	Good	Most studies gave similar results. In Systematic reviews, any inconsistency arose from a particular study that had been commonly criticised.
Clinical impact	Poor	The data is largely based on RCTs of small numbers of participants and short duration using surrogate marker that demonstrated improvements commonly of <5%.
Generalisability	Good	Populations studied were generally similar to the target population for the review.
Applicability	Good	Applicable to the Australian health care context with the caveat that all the studies were of different types and doses of fat and were over very small time frames.

The evidence concerning fats and oils and their relationship with risk factors for development of type 2 diabetes is based on two systematic reviews (Quality rating: 1P; 52 RCT included, 1 O, 47 RCT included) and 14 RCTs (12 P; 2 O). The evidence was consistent, except for one of the systematic reviews (Wendland et al. 2006) of questionable quality. The evidence indicates that fats and oils, across a wide range of types and amounts and in the short term (up to 8 weeks), have no impact predominantly

on fasting plasma glucose and insulin, and in the short term, predominantly up to 8 weeks, are not associated with risk of development of type 2 diabetes.

The effect sizes are detailed in the table below with the systematic review highlighting that these are commonly of a small magnitude when found.

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Table 12.3 Studies used to make evidence statement for fats and oils and the risk of type 2 diabetes

Reference [1]	**Berry et al. 2007 [151]**	**Tholstrup et al 2006 [3955]**	**Tomonobu et al 2006 [1624]**	**Nosaka et al. 2002 [536]**	**Owen & Wolever 2003 [2213]**	**Rueda-Clausen et al, 2007 [1383]**
Type of study [2]	RCT	RCT	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II	II	II
Intervention/ comparator [4]	High stearic acid randomised shea blend (higher SFA) vs. unrandomised shea blend (randomized = random interesterification=increases SFA).	115 g fat per day from test butter high in vaccenic acid (3.6 g vaccenic acid per day) vs. low in vaccenic acid.	Test meal of 10g DAG vs. TAG.	40 g per day of MCT vs. LCT (common edible oil, blended rapeseed oil, soybean oil).	Impact of test meals of varying fat content (0,5,10,20 or 40 g fat) on blood gluscose between 15 min-2 hours.	Potato soup meal containing 60ml of one of three different vegetable oils (olive/soybean/plam), either fresh, 10 fries or 20 fries.
N [5]	20	22/20	43	11/11.	12 (crossover)	10 (crossover)
Population/study information [6]	16 healthy male subjects; age 26.8 (8.0) years; weight 74.8 (10.9) kg; BMI 23.7 (3.7); 3week run-in period with low-stearic acid diet then randomised to consume 1 of 2 test fats (unrandomised or stearic acid-rich fat). test meal of 50g test fat followed by 3week high-stearic acid dietary period (30g of same test fat in test meal). subjects then crossed over after 4 week washout perid with low-stearic acid diet. subjects then returned to	42 healthy men; high vaccenic group: mean age 25.2 years; height 181.5 cm; weight 76.1 kg; BMI 23.0; low vaccenic group: mean age 26.1 years; height 182.3 cm; weight 74.8 kg; BMI 22.5; outcomes: macronutrient intakes; cholesterol; TG;	Healthy Japanese men (36) & postmenopausal women (7) with fasting TAG 1.13-2.83 mmol/L at time of screening; age 43 (28-57) years; Height 166.8 (1.46.4-181.1) cm; weight 70.7 (52.3-92.8) kg; BMI 25.3 (19.8-30.3); 6 hours	MCT: 11 men; age 37.8 (73.82) years; weight 67.0 (12.2); height 170.4 (6.7) cm; BMI 22.9 (3.0); energy intake 2350 (520); fat intake 76.0 (14.5); MCT intake 0.3 (0.3); LCT: 11 men; age 33.4 (5.2) years; weight 67.4 (9.5) kg; height 170.2	Non-diabetic, 10 East Asians, 7 females, age 28.6 (3.5) years, BMI 21.4 (0.6); 5 test meals on separate mornings after 10-14 hour fast, separated by at least 2 days. 100g white bread test meal with either 0,5,10,20 or 40g fat (from Becel non-	M age 20.8 (2.4) years; weight 66.2 (9.8) kg; BMI 21.9 (2.6); fasting glucose 89.4 (7.03); total chol 118 (22.7) mg/dl; meals administered once a week, first meal in the morning. 24 hour recall weekly to evaluate changes in diet during the study. SFA content (fresh) olive 14.28%; soybean 16.24; palm 43.6: MUFA: olive

	normal diet and subsequent study conducted after 4 week washout, then test meal of 50g unrandomised stearic acid-rich fat or oleic acid-rich fat, separated by >= 1 week.	CRP; insulin; glucose; FA profiles; intervention for 5 weeks.	for test meal; crossover after 2 weeks washout; serum glucose and insulin (measured at 0,2,3,4,6 hours after ingestion of test meal).	(5.3) cm; BMI 23.2 (2.6); energy intake 2290 (370) kJ; fat intake 73.6 (12.6); MCT intake 0.3 (0.2); 4weeks follow-up; outcomes: diet intake, serum chol & TG, liver function, hemocytes, renal function, serum electrolytes, glucose metabolism, lipid metabolism.	hydrogenated margarine); finger prick capillary blood samples at fasting, 15, 30, 45, 60, 90 and 120 minutes; blood glucose concentrations; IAUC; 2 hour postprandial, 5 tests at least 2 days apart.	77.77%, soybean 24.4%, palm 46.4; PUFA: olive 6.55%, soybean 52.78, palm 9.97l; follow up 9 weeks (9 tests x 1 per week).
Quality [7]	Positive - no ITT, no blinding/ not stated, methods of randomisation not stated, these limitations not discussed.	Positive - randomised, double blind, no ITT, withdrawals not described.	Positive - double blind, randomised, no ITT, did not report compliance, postprandiol measurements only.	Positive - double blind however did not discuss recruitment and withdrawals.	Neutral - unsure how recruited and if selection of 12 particiapnts free from bias, no blinding, unclear if withdrawals, small sample size.	Positive - not stated if dropouts, small sample size, double blind.

Results [8] - T2D	Insulin NS; glucose NS; HOMA-IR NS.	Insulin NS; glucose NS.	Insulin NS; glucose NS.	Insulin NS; glucose NS.	Data not in tables - figures only; Mean blood glucose was significnatly higher after the 0, 5, 10 g fat meals than after the 40 g fat meal, and at 45 min higher after the 0,5 g than 40 g.	Glucose NS.
Clinical importance [9]	3	3	3	3	2	3
Clinical relevance [10]	2	2	2	2	2	2
Effect of risk (increase/none/protect)	None	None	None	None	Increase	None
Generalisability	y	y	y	y	y	y
Applicability	y	y	y	y	y	y

Table 12.3 Studies used to make evidence statement for fats and oils and the risk of type 2 diabetes (cont.)

Reference [1]	**Nicholls et al. 2006 [3557]**	**Eckel et al. 2006 [3399]**	**Kratz et al. 2002 [527]**	**Tahvonen et al. 2005 [1810]**
Type of study [2]	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Postprandial effect of safflower oil (high	Isocaloric high fat (50% fat) vs high-	Refined olive oil (high MUFA) vs. rapeseed oil	3 g per day of black current seed oil vs. 2.8

	PUFA) vs. coconut oil (high SFA).	carbohydrate (55% CHO).	(high MUFA & ALA) vs. sunflower oil (high in n6 PUFA).	g per day of FO for 4 weeks each.
N [5]	14 (crossover)	39 (crossover)	19/19/17	15 (crossover)
Population/study information [6]	M and F age 29.5 (2.3) years; BMI 23.6(0.8); subjects attended on 2 occasions separated by 1 months; consumed isocaloric meals of a slice of carrot cake and milkshake containing 1g fat/kg body weight; safflower oil (SFA 8.8%; MUFA 13.6%, PUFA 75%) vs. coconut oil (SFA 89.6%; MUFA 5.8%, PUFA 1.9%); follow-up: 6h postprandial with 1 month between tests.	M and F 25-36 years; BMI range 18.7-50.2; follow-up: 4 years (annual weight and body composition); cross-over study; 15 days isocaloric high fat (50% fat) and high-carbohydrate (55%CHO) with 4-6 week washout period; usual dietary patterns assess using the Diet Habit Survey.	M and F 25.7(5.4) years; weight 71.6(10.5)kg; BMI 23.0(2.3); serum insulin 54(24); serum glucose 4.3(0.4); HBA1c 4.09(0.27); LDL 2.97(0.78); HDL1.48(0.49); TG 0.87(2.46); all participants received baseline high fat/high SFA diet for 2 wks, then randomly assigned to one of 3 high-fat dietary treatments for 2 wks: refined olive oil (high MUFA), rapeseed oil (high MUFA & ALA), sunflower oil (high in n6 PUFA).	F 18-45 24.1(5.0) years; BMI 18.5-25 21.2(1.8); plasma glucose 4.98(0.24); chol 4.32(0.45); HDL 1.48(0.29); LDL 2.4(0.38); TG 0.98(0.47); 4 week periods of either 3g per day of black current seed oil or 2.8g per day of fish oil separated by 4 week washout period.
Quality [7]	Positive - small sample size, not stated if dropouts, double blind.	Positive - blinding not possible, method of randomisation not stated but crossover so still said groups comparable, mixed model procedure (includes drop-	Positive- assume no blinding as not stated and difficult to achieve, no ITT analysis, ? Selection free from bias - only college studies included, therefore not	Positive - unsure if withdrawals, small sample size, Unsure if errors in insulin results as description does not match table.

		outs/missing data).	relective of population, however said yes as answered other questions.	
Results [8] - T2D	Insulin NS between meals (between time points p=0.0002).	S1 insulin sensitivity NS.	Insulin NS; glucose NS; HBA1c NS (between treatment groups) differences found between timepoints.	Insulin NS; glucose: BC oil period: before 4.9(0.4), after 5.0(0.2), FO period: before 5.0(0.3), after 4.8(0.2) p<0.001 for difference in change between both, p<0.05 for difference before/after for FO but NS for BCO.
Clinical importance [9]	3	3	3	2
Clinical relevance [10]	2	2	2	2
Effect of risk (increase/none/protect)	None	None	None	None
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 12.3 Studies used to make evidence statement for fats and oils and the risk of type 2 diabetes (cont.)

Reference [1]	**Lovegrove et al. 2004 [4638]**	**Damsgaard et al. 2008 [4160]**	**Balk et al. 2006 [1415]**	**Wendland et al. 2005 [3898]**
Type of study [2]	RCT	RCT	Systematic review	Systematic review
Level of evidence [3]	II	II	I	I
Intervention/	Fish oil capsules (4x1g/d)	5ml per day fish oil vs.	Doses of fish oil against	

comparator [4]	for 12 wks vs. olive oil capsules (4x1g/d).	olive oil (OO) for 8 weeks. Within each group also alocated to use fats with a high LA content (S/B - sunflower and Becal) or low -LA content (R/K - rapeseed oil, rapeseed oil enriched butter spread).	placebo (often olive oil) and doses of ALA against placebo. Supplementation or general dietary methodology to gain increased intake of FO or ALA but not >6g/day omega 3.	
N [5]	44 Europeans; 40 Indo-Asians (stratefied randomisation to FO/OO, but numbers not specified).	66= OO: S/B (16) R/K (17); FO S/B (17) R/K (14).	Total numbers of participants in studies-lipids: total cholesterol (FO = 7853; ALA =1089); LDL (FO = 6969; ALA = 700); HDL (FO= 7353; ALA =700);TG (FO= 7803; ALA =700) FBS: (FO =1427; ALA =52) HBA1c: (FO =578; ALA = 0) CRP: (FO = 73; ALA =18).	744
Population/study information [6]	25-70 years, (demographics not by oils but ethnicity) Europeans: age 48.7(12.4), BMI 25.7(3.2), SBP 121(18), DBP 74(10), waist circumference cm 89.1(11.9), energy 2531(507), fat 34(7)%E; Indo-Asians: age 46.9(11.2), BMI 25.9(3.1),	M 18-40 years.		M and F adults Wide age range Generally healthy to risk factors for CVD, NIDDM and overweight.

	SBP 122(16), DBP 78(11), waist circumference cm 88.6(10.5), energy 2391(591), fat 37(5)%E; 2wk run in period where all subjects took 4x1g capsules of olive oil/d (2 with breakfast, 2 dinner), then randomised to fish oil group - 4x1g capsules/d for 12 wks (each capsule provided 367mg EPC/ 225mg DHA).			
Quality [7]	Neutral - double blind. Did not outline how many in each of the oil groups as only provided numbers of each ethnic group. No ITT.	Postive - double blinding, good description but no ITT.		Neutral, no assessment of papers for quality.
Results [8] - T2D	Insulin NS for FO vs. OO (p=0.05 for ethnicity); HOMA-IR NS for FO vs. OO (p=0.04 for ethnicity); HBA1c NS.	Fish oil group with high LA intake signficnatly increased glucose after intervention while low LA sginficnatly increased insulin after intervention. Therefore the type of fat had a significant impact at p=0.05.		Fixed effect analysis used showed a significant (p< 0.01) reduction in mean difference of 0.20 mmol/L (-0.30, -0.10 mmol/L) FPG with supplementation with ALA.
Clinical importance [9]	2	3		1* if it is true
Clinical relevance [10]	2	2		2 Note: no attempt to compare dose of ALA in review. Limitations include the small size of

				the trials, no methods of randomisation were discussed, not all were blinded, sometimes the data could not be pooled.
Effect of risk (increase/none/protect)	none	protective		protective
Generalisability	y	y		y
Applicability	y	y		y

12.4 FATS AND OILS and HYPERTENSION

Does a particular intake of fat/oil affect the risk of hypertension?		
Evidence statement		Consumption of fat, irrespective of amount or type, is not associated with hypertension.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Six Level II (Quality rating: 5P, 10), all RCTs predominantly of 4-8 weeks duration using olive or fish oil); 3 studies Level III-2 (Quality rating: 2P, 10) (cohort: 2 studies adult European 5573 & 20343; 1 study of 93 children aged 10 yrs).
Consistency	Good	All studies looked at short term effect of fat/oil supplementation. RCT; 5 No effect, 1 protective and no effect. Two cohort in adults; 1 increased/no effect and 1 protective. One cohort in children increase / no effect.
Clinical impact	Poor	Slight as mostly non significant results for systolic and diastolic BP.
Generalisability	Satisfactory	Generalisable to the Australian adult and child (>10y) population.
Applicability	Good	Applicable to the Australian population.

The evidence concerning fats and oils and the risk of hypertension is consistent. Although there is a range of ages and populations in the studies, the evidence is applicable to the Australian setting. There are six RCTs (Quality rating: 5 P 1 O; 5/6 no risk) and three Cohort studies (2 P 1 O; 1/3 no risk) that inform the body of evidence statement. The evidence indicates that, in the short term (predominantly 4 – 18 weeks), fats and oils are neutral in the development of hypertension.

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Table 12.4 Studies used to make evidence statement for fats and oils and the risk of hypertension

Reference [1]	Ulbak et al. 2004 [3643]	Raitakari et al. 2005 [4034]	Sanders et al. 2006 [4413]	Perona et al. 2003 [463]
Type of study [2]	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Fish oil vs. olive oil supplementation during the first 4 months of lactation. Impact on BP of children at 2.5 years of age.	Dietary advice provided twice a year since 7 months of age to minimise exposure to known environmental atherosclerosis risk factors; recommended intake of 30% energy from fat,<=10% from saturated fat vs those who received basic health education given at the Finnish well-baby clinics - 11 year follow-up.	4 g DHA oil/day vs. placebo for 4 weeks.	4 weeks of a diet enriched in either VOO1 or VOO2 (virgin olive oils of the same variety with a similar composition of minor components and fatty acids except for oleic and linoleic).
N [5]	Fish oil: 30/ olive oil: 22	179/190	DHA: 40; placebo:39	29 (crossover)
Population/study information [6]	Mothers with low fish intakes were randomly assigned to receive supplementation with 4.5g fish oil or olive oil/day during the first 4 months of lactation. BP of the children was then assessed at 2.5 years of age; 73 children from the 150 invited to	11 year old followup from STRIP study (dietary intervention to lower CVD risk factors from 7 months of age).	Staff from 3 London Colleges; age: DHA: female 31.6(13.2), male 29.8(11.5); placebo: female 35.2(14.5), male 33.4(14.7); BMI 18-35; chol <7.8, fasting TAG <3.0, sys BP <140, diastolic BP <90.	Men and women 65+ years; free living residents of home for at least 5 years; average age 84.9(6.4); BMI 28.0(4.8); follow-up: 4 weeks monitoring, 4 weeks intervention 1, 4 weeks washout, 4 weeks intervention 2.

	participate consented and had full datasets.			
Quality [7]	Neutral - not representive of study population as participants taken from previous study where only low fish eaters where chosen. Those completing this study had better compliance in previous study. Group characteristics not provided; no ITT.	Positive (blinding not possible for participants, unclear if those conducting tests were blinded).	Positive - only staff from colleges were included, therefore not representive of the adult population. However still positive as other questions in this factor were met, double blinding used.	Positive - double blind, residents from elderly home, however this is probably quite representive of the very elderly population. Unsure if withdrawals.
Results [8]	Diastolic ns; systolic ns	Diastolic ns; systolic ns	Diastolic ns; systolic ns	Diastolic ns; systolic ns between groups
Clinical importance [9]	3	2	3	3
Clinical relevance [10]	2	2	2	2
Effect of risk (increase/none/protect)	none	none	none	none
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 12.4 Studies used to make evidence statement for fats and oils and the risk of hypertension (cont.)

Reference [1]	Bondia-Pons et al. 2007 [178]	Damsgaard et al. 2008 [4160]	Alonso & Martinez-Gonzalez 2004 [344]	Psaltopoulou et al. 2004 [4885]	Schack-Nielsen et al. 2005 [3278]
Type of study [2]	RCT	RCT	Cohort	Cohort	Cohort
Level of evidence [3]	II	II	III-2	III-2	III-2
Intervention/ comparator [4]	Main study is 25ml olive oil per day for 3 x 3weeks differing only in phenolic concentrations; however analysis relevant to this is comparision between northern Europe(NE), Central Europe (CE) and Southern Europe (SE) which differ in habitual olive oil intake.	5ml per day fish oil vs. olive oil for 8 weeks. Within each group also alocated to use fats with a high LA content (S/B - sunflower and Becal) or low - LA content (R/K - rapeseed oil, rapeseed oil enriched butter spread).	HT incidence according to energy adjusted olive oil intake (Q1 vs Q5 = 4.8 vs 34.6 g per day).	Relationship between olive oil intake and arterial BP / hypertension. Mean olive oil intake in g per day (M / W): 83.7 ± 24.0 / Women 76.6 ± 21.8.	Relationship between arterial stiffness (pulse wave velocity - PWV) and dietary fat intake. Mean total fat intake as % daily energy intake (girls / boys): 35.2 ± 3.7% / 35.7 ± 4.3%
N [5]	155 crossover (50 northern Europe (NE); 60 Central Europe (CE); 45 Southern Europe (SE)).	OO: S/B (16) R/K (17); FO S/B (17) R/K (14).	5573 (3384 women 2189 men).	20343 (8685 men 11658 women).	93 (32 girls 44 boys).
Population/study information [6]	Healthy men from 6 centres in 5 European countries; age 33.3(11.1);	Danish males 18-40 years.	Olive oil (and other food intake) assessed using validated 136 item	Olive oil intake assessed using validated 150 FFQ in general Greek	Dietary intake assessed using 7 day food record (household

	NE/CE have lower usual olive oil intakes than SE; 13 weeks - 3 x 3 week intervention periods; 2 x 2 week washout periods.		FFQ in Spanish university graduates. Median FU time 28.5 months. Part of the SUN study.	adult population Part of the EPIC study - Greek arm.	measures) in Danish children aged 10 years. Part of Copenhagen Cohort Study on Infant Nutrition and Growth.
Quality [7]	Positive - nutritional analysis software different in each country, numbers indicate 5 dropouts, but not discussed, wording suggest double blind but not very clear; no ITT.	Postive - double blinding, good description but no ITT.	Neutral	Positive	Positive
Results [8]	Diastolic ns; systolic $p<0.05$ for 2 groups not regularly consuming olive oil at baseline, ns for group regularly consuming olive oil, significnat difference at baseline between group regularly consuming OO and those not.	Fish oil and fat interventions did not significantly affect fasting or postpriandial BP or HR.	Whole sample: Multivariate OR (95% CI) for Q1 vs Q5: 0.63 (0.36-1.07, p for trend 0.13) Men: Multivariate OR (95% CI) for Q1 vs Q5: 0.46 (0.23-0.94, p for trend 0.02) Women: Multivariate OR (95% CI) for Q1 vs Q5: 0.97 (0.4-2.36, p for trend 0.74).	Multiple regression - β Coefficient (95% CI): Systolic BP (M / W): -0.8 (-1.1- -0.6) / -0.8 (-1.1- -0.5) Diastolic BP (M / W) -0.4 (-0.5- -0.2) / -0.3 (-0.4- -0.1).	Multiple regression - β Coefficient (95% CI); partial r (for total fat intake as % E): PWV (aortal-radial): 3.1 (0.9-5.2); 0.31, $p<0.01$ PWV (aortal-femoral): 1.8 (0.2-3.2); 0.27, $p<0.05$

Clinical importance [9]	2	3	2	1	4
Clinical relevance [10]	2	2	2	2	3
Effect of risk (increase/none/protect)	protect or none	none	increase - none	protective	increase - none
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

12.5 FATS AND OILS and ALL CAUSE CANCER INCIDENCE and MORTALITY

Does a particular intake of fats and oils affect the risk of all cause cancer?		
Evidence statement		Consumption of long chain PUFA is not associated with total all-cause cancer incidence or mortality.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	2 systematic reviews (1st RCTs , 2nd cohort/ Case control) (2P, both no effect).
Consistency	Good	2 systematic reviews of RCT and cohort and case control studies, large number of studies included in both systematic reviews both gave no consistent data to show omega 3 fatty acids had any effect on either all cause cancer incidence or mortality.
Clinical impact	Poor	Omega 3 no effect on all-cause cancer incidence (1 SR: prospective cohort (n=38), P) or All-cause cancer mortality [1SR: RCT (n=48) meta analysis RR = 1.07 (95%CI; 0.88 to 1.30, heterogeneity 0.91]; meta anlysis of cohort (n= 41) data RR = 1.02 (95% CI; 0.87 to 1.19, heterogeneity 0.27), regardless of dose.
Generalisability	Good	Wide range of review populations, all adult.
Applicability	Satisfactory	Applicable to the Australian health setting, but most data from America and Europe where dietary fat intake is quite different and often culturally or ethnically based, therefore specifically applicable to only equivalent populations sub categories in Australia.

The body of evidence statement concerning fats and oils and the risk of all cause cancer incidence and mortality is supported by two systematic reviews (one RCT, two cohort/case control). The evidence supports a neutral affect of omega-3 fatty acids on all-cause cancer incidence (one SR: prospective cohort (n=38), P) or all-cause cancer mortality (1SR: RCT (n=48) meta analysis RR = 1.07 (95%CI 0.88 - 1.30, heterogeneity 0.91); meta analysis of cohort (n= 41) data RR = 1.02 (95% CI 0.87 - 1.19, heterogeneity 0.27) regardless of dose (up to 7 g per day). No data was available from studies of greater than 7 g per day omega 3 fatty acids. The systematic review on incidence of cancer was primarily a narrative review and could provide no relative risk statistics, but demonstrated a trend of no affect of omega-3 fatty acids on the incidence of all cause cancer.

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Table 12.5 Studies used to make evidence statement for fats and oils and the risk of all cause cancer incidence and mortality

Reference [1]	**MacLean et al. 2006 [4903]**	**Hooper et al. 2004 [5608]**
Type of study [2]	Systematic review of cohort studies. No case control studies used.	Systematic Review of RCT.
Level of evidence [3]	III-2	I
Intervention/ comparator [4]	Omega 3 fatty acids and risk of cancer (all types).	Dietary supplementation, provided diet or dietary advise to increase n-3 PUFA. Product used must have had 10% n-3 content of total fat vs vvegetable oil predominantly olive oil.
N [5]	5145 initial search, after exclusion criteria and quality check 38 met inclusion criteria.	48 RCT (111 papers), 41 cohort (42 papers).
Population/study information [6]	Not provided. 20 large Cohort studies (n= from 6000 – 121,000) person years of observation (n= from 9000 - 1.5 million). Adults.	36, 913 Overall 563,218 individuals + Umea and Janus studies where cohort was not described.
Quality [7]	Positive	Positive
Results [8] - Systematic Reviews - RCT	Not reported	No significant effects of n-3PUFA on cancer, RR1.07 (95% CI 0.88 - 1.30, heterogeneity 0.91). Senisitivity analysis to remove bias left 7 events and no further subgrouping possible.
Results [8] - Systematic Review - cohort	Omega-3 FA intake has little or no effect on the risk of developing Ca (whether that be an increased or decreased risk). The effect is unlikely to be representative of sample size as all cohorts were relativley large. For the largest studies with smallest variance, the RR was the closest to the null value; for those studies that showed an association (+ve or -ve) had smaller sample size and large variance. Intake of omega-3 FA varied accross cohorts, but as there is little evidence to suggest an association between	Of the 3 studies not included, two showed no effect of high dose n-3 PUFA, in one study high dose n-3 PUFA increased risk of breast cancer (not confirmed in other breast cancer analysis).

	omega-3 FA intake and risk of cancer, the large association variation in intake may support the lack of association.	
Clinical importance [9]	3	3
Clinical relevance [10]	2	2
Effect of risk (increase/none/protect)	none	none
Generalisability	y	y
Applicability	y	y
Comment		Death from other causes were listed, and showed no effect of n-3 PUFA intake. In RCT and Cohort studies. One study (Maclure, 91) showed RR of 2.39 (95% CI 1.33 - 4.30) of n-3 PUFA intake and early onset menarch (defined as <12.5 yo). This has been associated with increased risk of breast cancer.
		Unlikely to be seeing long enough follow-up in these trials to pick up build up of body toxins, followed by ca initiation, development and fatality.

12.6 FATS AND OILS and BREAST CANCER

Does a particular intake of fats and oils affect the risk of breast cancer?		
Evidence statement		Consumption of total fat across a range of intakes is not associated with breast cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	3 cohort (Quality rating: 3 P), 3 Case-control (Quality rating: 3 N). Effect not consistent in all studies with different fatty acids having different effects.
Consistency	Poor	3 cohort (not consistent) and 3 case control (not consistent) and not consistent collectively.
Clinical impact	Poor	No good evidence of specific fatty acids and any cancer type, trends for increasing risk of breast cancer and total fat, SFA/Animal fat and MUFA and PUFA in particular studies but no consistent data, the most consistent of these is for increased intake of SFA/Animal fats and increased risk of developing cancer in case control studies.
Generalisability	Satisfactory	Wide range of review populations- all adults.
Applicability	Satisfactory	Most data from America and Europe where dietary fat intake is quite different and often culturally or ethnically based, therefore specifically applicable to only equivalent populations sub categories in Australia.

The body of evidence statement concerning fats and oils and the risk of developing breast cancer is supported by three cohort (Quality rating: P) and three case control (Quality rating: N) studies. Statements about specific fatty acids cannot be made.The literature shows no good evidence of specific fatty acids and breast cancer, however there was a trend for increasing risk of breast cancer and total fat, SFA/Animal fat and MUFA and PUFA in particular studies but it must be stressed that the data is not consistent and the grade of recommendation is D.

References

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Table 12.6 Studies used to make evidence statement for fats and oils and the risk of breast cancer

Reference [1]	**Kalianpur et al. 2008**	**Garcia-Segovia 2006**	**Wang et al. 2008**	**Thiebaut et al. 2009**	**Voorrips et al. 2002**
Type of study [2]	Case control	Case control	Case control	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	111-2	111-2
Intervention/ comparator [4]	Case: newly diagnosed primary breast cancer in the region - identified by cancer register. Conrol: randomly seleced from resident register, age 5 yr interval, sex and residential address matched - no breast cancer diagnosis.	Case: histologically confirmed breast cancer. Conrol Selected from the Canary Islands Nutrition Survey.	Case: first primary invasive breast cancer diagnosed between 1995-1999 Control: random didgit dialing, frequency matched to cases by ethnicity and 5yr range age.	HR of breast cancer by quintile of estimated dietary fat intake (various types of PUFA and sources of PUFA).	RR of breast cancer by quintile of energy intake and fat intake (g/day of various types of fat and fat sources).
N [5]	1455/1556	291/464	1703/2045	56, 007/77,613	1598/1812
Population/study information [6]	Shanghai, population based.	Canary Islands, population based.	F 35-79 years, White, African American and Latinas selected.	F 40-65years, Members of the National Education Scheme, France.	Postmenopausal Women aged 55-69yrs, Netherlands.
Quality [7]	Neutral	Neutal	Neutral	P large sample size, population possible not representative due to being members of the national education scheme.	P - Comparison of cases vs. subcohort members, not quintiles; large sample size.
Results [8]	Total fat intake NS; high daily intake of animal fat significantly increased risk of breast cancer in all women, particularly	PUFA and SFA and breast cancer NS. MUFA at highest intake (>47g/day) OR=0.52 (95% CI 030-0.92) significant, but	Dietary intake of Total fat positively associated with risk of breast cancer, adjusted for age, ethnicity, and total energy intake	HR Omega-6 lowest quintile (3.41%EI/d) 1.00 vs. highest quintile (8.97%EI/d) 0.93 (0.80-1.09, p=0.30); HR for Total Omega 3	RR Total fat lowest quintile (61g/d) 1.0 vs. highest quintile (86g/d) RR 1.05 (0.82-1.34, p 0.66); Monounsaturated fat

	postmenopausal OR=1.57 (95%CI 1.2-2.02, ptrend<0.01). Hgh intake of plant fat protective OR=0.70 (95% CI 0.60-0.83, ptrend<0.01).MUFA increased risk OR=1.32 (95% CI 1.2-1.56, ptrend<0.01).SFA increased risk in all women OR=1.20 (95% CI 1.01-1.42, ptrend=0.05). PUFA NS.	lost when adjusted for other fatty acids. Oive oil significantly inversely associated with breast cancer OR=0.27(95% CI 0.17-0.42, p<0.001).	(quartile (Q4) v Q1 OR 1.48 (95%CI 1.22-1.8, p trend<0.01). Oleic acid associated with breast cancer risk OR 4 v Q1= 1.43 (95% CI 1.17-1.76, p trend<0.0001) than linoleic acid OR4vQ1= 1.27 (95% CI 1.04-1.54, p trend<0.04) Saturated fat NS. Cooking fat: cooking with olive/canola oil compared to vegetable/corn oil, 30% increased risk of breast cancer OR=1.30 (95% CI 1.06-1.58); hydrogenated fats higher OR=1.58 (95% CI 1.2-2.10).	lowest quintile (0.44%EI/d) 1.00 vs. highest quintile (0.90%EI/d) HR 0.99 (0.84, 1.15) p0.69.	(18g/d) 1.00, vs. highest quintile (27g/d) RR 0.89 (0.65, 1.15) p 0.06; Trans fat lowest quintile (1.5 1g/d).1.00 vs. highest quintile (3.6g/d) 1.20 (0.90, 1.58) p=0.04.
Clinical importance [9]	2	2	2	1 A clinically important benefit for the full range of plausible estimates. The confidence limit closest to the measure of no effect (the 'null') rules out a clinically unimportant effect of the intervention.	1 A clinically important benefit for the full range of plausible estimates. The confidence limit closest to the measure of no effect (the 'null') rules out a clinically unimportant effect of the intervention.
Clinical relevance [10]	1	1	1	1 Evidence of an effect	1 Evidence of an effect

				on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.
Effect of risk (increase/none/protect)	Total fat and PUFA none, animal fat MUFA and SFA increased.	MUFA (Olive Oil) protective. Other fatty acids and total fat none.	Dietary fat: Total fat increased; oleic acid increased, linoleic increased, SFA none. Cooking fat, olive/canola none, vegetable/corn oil increased, hydrogenated fat increased.	none	No effect for total fat intake; Protective for Monounsaturated fat, cis unsaturated fat, oleic acid and linolenic acid. Increased risk for trans unsaturated fat, CLA, Trans Vaccenic Acid.
Generalisability	y	y	y	y - although French population.	y - although Dutch population.
Applicability	n	n	y	y - although French population.	y - although Dutch population.

12.7 FATS AND OILS and ENDOMETRIAL CANCER

Does a particular intake of fats and oils affect the risk of endometrial cancer?		
Evidence statement		Consumption of monounsaturated fatty acids (amount not specified) is not associated with risk of endometrial cancer.
Grade		D
Evidence statement		A high intake of total and / or saturated fat and / or animal fat (amount not specified) is associated with increased risk of endometrial cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Poor	1 systematic review (3 cohort studies and 9 case control studies) (Quality rating: P); The effect was increased risk for SFA/ animal fat and total fat, MUFA protective.
Consistency	Poor	Case control data and cohort data not consistent. However within each study type the results are consistent. In some cases meta-analysis was not able to be performed.
Clinical impact	Excellent	Total Fat: Case control studies indicate role of total fat in risk of endometrial Ca, ORs 1.2-3.9. Meta analysis of 7 case control studies: 1.72 (95% CI: 1.28, 2.32) mod heterogeneity (I2: 48.8%, p=0.07). Saturated Fatty Acids: 5 pop based case control studies - elevated risk associated with higher SFA intake, meta analysis: of high vs low intake suggested a 50% increased risk associated with higher intake of SFA. Animal fat meta analysis: 68% increased risk associated with high animal intake, no heterogeneity. 17 - 35% ↑risk endometrial Ca per 10g.1000kcal animal fat intake from case control data. MUFA: 5 case control studies MUFA and risk of endometrial Ca + 2 on oleic acid, OR 0.76 - 2.5. No meta analysis due to inconsistent data. PUFA inconsistent results in all studies, no meta analysis performed.
Generalisability	Satisfactory	Wide range of review populations- all adult women. Small sample size.
Applicability	Poor	Small case control and cohort studies, difficult to generalise to adult women in Australia.

The body of evidence statement concerning fats and oils and the risk of developing endometrial cancer is supported by one systematic review (three cohort studies and nine case control studies) (P). Total Fat:

Case control studies indicate role of total fat in risk of endometrial cancer, ORs 1.2-3.9. Meta-analysis of seven case control studies: 1.72 (95% CI 1.28-2.32, mod heterogeneity I2: 48.8%, p=0.07). SFA: five population based case control studies - elevated risk associated with higher SFA intake, meta analysis: of high vs. low intake suggested a 50% increased risk associated with higher intake of SFA. Animal fat meta-analysis: 68% increased risk associated with high animal intake, no heterogeneity. 17 - 35% ↑risk endometrial cancer per 10 g.1000kcal animal fat intake from case control data. MUFA: five case control studies MUFA and risk of endometrial cancer, plus two on oleic acid, OR 0.76 - 2.5. No meta analysis due to inconsistent data. PUFA inconsistent results in all studies, no meta analysis performed.

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Table 12.7 Studies used to make evidence statement for fats and oils and the risk of endometrial cancer

Reference [1]	**Bandera et al. 2007**
Type of study [2]	Systematic review of case-control and cohort studies.
Level of evidence [3]	III-2
Intervention/ comparator [4]	Role of dietary lipids on endrometrail cancer risk.
N [5]	285 identified, through subsequent searches to add and using exclusion criteria, 13 papers were included - 3 cohort studies and 9 case control studies (2 papers from one study used where appropriate).
Population/study information [6]	Adults, female. Numbers not included.
Quality [7]	Positive.
Results [8] - Systematic Reviews - RCT	Not reported.
Results [8] - Systematic Review - cohort	Total Fat: Case control studies indicate role of total fat in risk of endometrial Ca, ORs 1.2-3.9. Meta analysis of 7 case control studies: 1.72 (95% CI 1.28-2.32, mod heterogeneity I2: 48.8%, p=0.07). After adjustment for quality and excluding the cohort studies (insufficient in number to do a meta analysis on) 49% increased risk for the highest category of consumption compared to the lowest - no heterogeneity.SFA: 5 population based case control studies - elevated risk associated with higher SFA intake.
	SFA: 5 population based case control studies - elevated risk associated with higher SFA intake. Meta analysis: of high v low intake suggested a 50% increased risk associated with higher intake of SFA.
	MUFA: 5 case control studies MUFA and risk of endometrial cancer and 2 on oleic acid, OR 0.76 - 2.5. No meta analysis due to inconsistent data.
	Animal fat meta analysis: 68% increased risk associated with high animal intake, no heterogeneity. 17 - 35% ↑risk endometrial Ca per 10g.1000kcal animal fat intake from case control data.
Clinical importance [9]	2
Clinical relevance [10]	2
Effect of risk (increase/none/protect)	MUFA: none. Total fat and SFA/Animal fat: increased risk for endometrial Ca.

Generalisability	No - case control and cohort data only, and they are not consistent.
Applicability	To equivalent study populations and with caution.
Comment	The data is inconclusive as it is based on cohort and case control data only and in most of the fatty acid groups the data is different for cohort vs case control. Although the within study type data is more consistent.
	Author concludes that there is an increased endometrial cancer risk with increased total fat, saturated fat and animal fat intakes. Limited numbers of studies, small study populations and case-control and cohort studies not in agreeance make strong comments on the data difficult. Limitation of studies is that while mostly women with hysterectomy were excluded at baseline (Furberg et al. did not) there was no update of the hysterectomy status at follow-up.

12.8 FATS AND OILS and MENTAL HEALTH

Does a particular intake of fats and oils affect the risk to Mental Health?		
Evidence statement		Consumption of higher omega 3 LCPUFA fat (intakes amount not specified) is associated with a reduced risk of dementia.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Poor	1 systematic review of RCTs (P) which found no papers to include in the SR. 2 x RCTs (2P), 1 in young children (no effect) and one elderly (no effect); 5 x cohort (3P, 2O); N-3 PUFA, 4 Protective, 1 No effect; n-6 PUFA, 1 protective, 2 increased risk; MUFA, 2 protective,1 no effect; SFA, 2 no effect, 1 increased.
Consistency	Satisfactory	Many populations, wide variety of dose, wide variety of fatty acids considered large effect range.
Clinical impact	Satisfactory	Omega 3 fatty acids protective (4/5 cohort): regular consumption of omega-3 fatty acids had a 60% lower risk of dementia (0.41 (0.17-0.995, p=0.049); RCT (2) data showed no effect of omega 3 fatty acids on cognitive function.
Generalisability	Satisfactory	Wide range of review populations.
Applicability	Poor	Mostly overseas populations with different fatty acid profiles of their total diet.

The body of evidence statement concerning fats and oils and Mental Health is supported by two RCTs of relevance (P). Statements about total fat and other specific fatty acids cannot be made.

One study on a young child population showed no affect of fats and oils on measures of cognitive development. One study on an elderly population showed no affect on cognitive function. The body of evidence statement is also supported by five cohort studies (3P, 2O); N-3 PUFA: four protective one none; N-6 PUFA, one protective, two increased; MUFA, two protective, one none; SFA, two none, one increased.

A systematic review on fats and oils and mental health was not included in the body of evidence statement as it found no RCT studies that met the inclusion criteria.

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Table 12.8 Studies used to make evidence statement for fats and oils and the risk to Mental Health

Reference [1]	**Lim et al. 2006 [4888]**	**Ryan et al. 2008 [3292]**	**van de Rest et al. 2008 [3921]**	**Mamalakis et al. 2004 [1450]**
Type of study [2]	Systematic review RCT	RCT	RCT	Cohort
Level of evidence [3]	I	II	II	III-2
Intervention/ comparator [4]	Any omega-3 intervention, alone or in combination included (if omega-3 effect can be demonstrated).	400mg DHA/ placebo high oleic sunflower same delivery system.	Low dose FO containing 400mg (226 ± 3mg EPA; 176 ± 4mg DHA) or high dose FO containing 1800mg (1,093 ± 17mg EPA; 847 ± 23mg DHA) EPA-DHA and placebo high oleic acid sunflower oil in similar delivery system.	
N [5]	Nil	77/86	Low dose n=100, high dose n= 96, placebo n= 106.	150; 78 gave adipose tissue samples; 124 the depression assessment (GDS-15). Compete data on 63.
Population/study information [6]	60 yrs and over with no evidence of dementia at study onset. Studies need to demonstrate adequate screening techniques.	Healthy girls and boys ages 4 yrs 0 months to 4yrs 8 months. Normal developmental milestones achieved, able to understand instructions provided in cognitive testing, 10th - 95th çentile height and weight. No family hx of ADHD, not premature,	>65y, population based near Wageningen University: excuded if >16 on Centre for Epidemiologic Studies Depression Scale (CES-D); <21 on Mini Mental State Examination (MMSE); current or recent use of fish oil supplements or of	Elderly men, from the seven countries study, 80-96 years (mean age 84), in the year 2000.

		consumed <3 oz of fish no more than 2 times per week, not supplemented with n-3 FA, no inborn error of metabolism or other medical conditions that precluded involvement, no medication for seizures or anxiety, depression, bipolar or psychosis.	>800mg EPA-DHA equivalent from fish per day; medications for depression or dementia; > 4 glasses of alcohol/day. Compliance >80% during study.	
Quality [7]	Positive	Positive	Positive	Negative
Results [8] - Systematic Reviews - RCT	Nil, no papers found to match the inclusion criteria.	NS, in ITT population better result in one test (PVVT) and DHA levels in capillary blood R2=0.21, p=0.008).	NS for any cognitive function test and either dose EPA-DHA.	Depressed individuals had lower adipose tissue LNA ($p<0.02$) and higher total adipose n-6/n-3 ratio ($p<0.03$); depression correlated inversely with LNA ($r= -0.32$, $p>0.009$) and LA ($r= -0.24$, $p<0.05$); Stepwise multiple linear regression showed that 7% of variablity in depression was accounted for by LNA ($F=6.02$, $p<0.02$) - increasing long term intake of LNA with decreased depression.
Results [8] - Systematic Review - cohort		3	3	Stepwise multiple linear regression showed that 7% of variability in

				depression was accounted for by LNA (F=6.02, p<0.02) - increasing long term intake of LNA with decreased depression.
Clinical importance [9]		3	1	1
Clinical relevance [10]		none to improved	none	1
Effect of risk (increase/none/protect)		y young white children	y - older adults	LNA protective
Generaliseablity		yes similar population to Australia	y - similar population, low intake of omega 3 in diet	y-older greek men
Applicability				n - different dietary patterns to Australia

Table 12.8 Studies used to make evidence statement for fats and oils and the risk to mental health

Reference [1]	**Morris et al. 2003 [2678]**	**Laitinen et al. 2006 [2643]**	**Barberger-Gateau et al. 2007 [2634]**	**Kyrozis et al. 2009 [795]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]				
N [5]	8501 initial, 6158 participated in survey; of these 1056 randomly selected and 729 evaluated for prevalent Alzheimers disease. 3 year follow up interview	2293 randomly selected; 1449 subjects participated in re-examination.	9294, 8085 at least one follow-up examination.	1225 eligible, 816 agreed to participate, missing data in 71, 745 subjects included in medical assessment of these 610 involved in study.

	n=4320 again 1249 randomly sampled and 842 evaluated for Alzheimers.			
Population/study information [6]	65 yrs and older; 62% black, 38% white and 61% female, mean education 11.8y.	900 women and 549 men; mean age 50.4(6.0) at midlife examination and 71.3(4.0) at follow-up.	>65 y; not institutionalised.	Greek, part of EPIC study, >60 yr age.
Quality [7]	neutral	positive	positive	positive
Results [8] - Systematic Reviews - RCT	Total intake of n-3 FA inversely and linearly associated with risk of incident Alzheimers disease in age and multivariate analysis(p trend = 0.01), top quintile had a 70% significant reduction in risk compared to the lowest quintile. Linear protective association with DHA (60 - 80% significant risk reduction).	Total fat intake: moderate fat intake (2nd quartile) at midlife decreased risk of dementia and Alzheimers compared to little or none and high intake. Moderate PUFA and MUFA intake (2nd quartile) associated with decreased risk of dementia. Moderate intake of SFA increased risk.	Regular consumption of omega-3 fatty acids had a 60% lower risk of dementia 0.41(0.17-0.995, p=0.049); adjusted for age, gender, education, city, income, and marital status, significance did not continue when adjusted for apoE genotype and BMI and diabetes status. NS for any other dietary fat intake, omega-3 FA HR 0.43 (95%CI 0.18 - 1.05, p=0.06) regular consumption of omega-6 fats is associated with increased risk of dementia HR 1.12, (95% CI 1.30-3.46, p=0.003) only for non ApoE4 carriers.	MUFA, particularly olive oil significantly negatively associated with GDS score: βcoefficient -0.55 (95% CI -1.04 - -0.06, p=0.029) and βcoefficient -0.37 (95% CI -0.65 - -0.01, p=0.042) respectively. PUFA, particularly seed oils significantly positively associated with GDS scores βcoefficient 0.30 (95% CI0.03 - 0.6, p=0.032g) and β coefficient 0.27 (95% CI 0.05 - 0.50, p=0.017). NS all other fats.

Results [8] - Systematic Review - cohort	Consumption of n-3 FA and fish was associated with decreased risk of incident Alzheimers disease in a large prospective cohort study. Persons who consumed at least 1 fish meal per week were associated with decreased risk (60%) of incident alzheimers disease. Of the n-3 PUFA only DHA was protective.	Midlife moderate fat intake compared to little /none and high intake may be protective of risk of dementia and Alzheimer's disease. Moderate use of PUFA and MUFA were protective, SFA intake increased risk of dementia and Alzheimers.	A diet high in fruits and vegetables, fish and omega-3 fatty acids could be protective of developing dementia and Alzheimers disease. Consumption of omega-6 could have detrimental effects if not countered by omega-3 intake, especially in ApoE non carriers.	A diet high in MUFA and low in seed oils is likely to be negatively associated with evidence of depression, when controlling for other dietary medical, anthropometric and lifestyle factors.
Clinical importance [9]	1	1	1	1
Clinical relevance [10]	1	1	1	1
Effect of risk (increase/none/protect)	DHA protective.	Moderate intake of total, PUFA and MUFA protective, SFA increased.	Omega-3 protective, omega-6 increased; all other fatty acids and fats none.	Omega-3, total lipids, and SFA none; PUFA seed oils increased, MUFA and olive oil protective.
Generalisablity	y	y	y	y
Applicability	y	y	y	y

Summary of studies not included (i.e. no body of evidence statement)

Statement related to other studies eligible for Inclusion

The Fats and Oils systematic review had 450 studies coded "I", included in this reference list. However, unlike the other systematic review topics, the Fats and Oils review did reach the upper limit of 10 systematic reviews on the one disease outcome for a number of outcomes. Therefore, this limited the number of studies that were extracted. This is consistent with the process outlined in the decision tree in the Process manual. For example the Fats and Oils in Cardiovascular disease had 10 systematic reviews, so only those 10 systematic reviews were used to inform the evidence statement. The attached reference list includes all studies relevant to the search strategy and the keywords.

Fats and Oils and the risk of bone disease

Two cohort studies (2 O); one study increased risk of bone disease with increasing omega-6: omega-3, one study omega-3 protective. Small number of cohort studies, no statement can be made on role of fat in the risk of bone disease. One systematic review excluded as it was not considered an appropriate intervention (i.e. classified as Exclude not a study (NS)).

Fats and Oils and the risk of Stroke

Three cohort studies (3 P); one study no effect for fat, one study omega-3 protective and saturated fat no effect, one study animal fat protective, no effect for all other fats. Given the small number of cohort studies, no statement can be made on the role of fat in the risk of stroke.

Fats and Oils and the risk of Cancer

Nine case control studies (cancer of the stomach (two); lung (one); maternal diet and brain tumor (one); laryngeal/oral/oesophagus (one each); prostate (one) ovarian (one) and one cohort study (prostate) not included in body of evidence statement. Overall, no good evidence of specific fatty acids and any cancer type, therefore no statement can be made on the role of fat in the risk of stomach, lung, brain, laryngeal/oral/oesophageal, prostate, and ovarian cancers.

Margarine Specific Studies

All papers that included margarine as a key word were about phytosterol margarine, not studies eligible for the review. There were no RCTS specifically testing non-phytosterol margarines.

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13. SODIUM AND SALT (SI.1)

Evidence Statements

13. SODIUM AND SALT (S1.1)

Search Results

The initial search of the databases included 906 references for sodium and the specified disease outcomes. The detailed searches are included in a separate document on searches. One hundred and ninety four references were retrieved for detailed review and 52 references were included as eligible for data extraction. Data from 11 cross sectional studies were not extracted, leaving 41 papers for review. Six other studies were not used because too few papers related to a particular outcome, or they were already summarised in reviews. Thirty-five papers were finally used to form the body of evidence statements for sodium. Sufficient evidence was found to make statements for sodium and blood pressure (adults and adolescents/children), bone health (pre- and postmenopausal women), cardiovascular disease (adults) and cancer (adults). There was inadequate evidence to make statements for any other disease states or other age or sex groups, including pregnancy.

Despite many studies on cardiovascular disease, cerebrovascular disease (stroke) was only identified as a specific outcome in two studies (one Level II and one Level III-2) therefore a body of evidence statement was not constructed. The Level II study had a low risk of bias but intervention was potassium-enriched salt substitute rather than Na restriction alone. In that study of veteran Taiwanese men living in hostel accommodation, a 50 % reduction for stroke was demonstrated over 31 months of intervention. Replacement of sodium chloride salt with a potassium-enriched salt substitute may decrease risk of stroke.

Regarding outcomes in pregnancy, one Level I Cochrane systematic review (meta-analysis of 2 original studies) was retrieved that found no benefit of sodium restriction on pre-eclampsia and associated outcomes (not included in body of evidence).

The body of evidence refers to dietary sodium because many of the studies used to form the body of evidence statement measured total sodium (Na) intake or urinary Na excretion. None of the reviewed studies examined the effects of Na from sodium chloride (NaCl) as compared to Na from other sources such as sodium bicarbonate, sodium aspartame or inherent sodium naturally present in milk and other foods. Therefore, in the absence of any other information, it is concluded that total dietary Na impacts on blood pressure and other outcomes.

13.1 SODIUM and BLOOD PRESSURE: Adults

Does a particular intake of salt or sodium affect blood pressure in adults?	
Evidence Statement	Decreaseing consumption of sodium decreased blood pressure (BP) in hypertensive adults; a reduction of 1800mg reduces systolic BP by about 5mmHg and diastolic by about 3mmHg
Grade	A
Evidence Statement	Decreasing consumption of sodium decreases blood pressure (BP) in normotensice adults; a reduction of 1800mg reduces systolic BP by about 2mmHg and diastolic BP by about 1mmHg
Grade	A

Component	**Rating**	**Notes**
Evidence Base	Excellent	5 Level I meta analyses with low risk of bias; 7 Level II studies (RCTs) with low risk of bias, and 2 Level II and 2 Level IV studies (non-systematic reviews) with moderate to high risk of bias (negative quality rating).
Consistency	Excellent	All Level I studies consistently showing BP reduction with Na reduction.
Clinical impact	Good	BP reduction higher in hypertensives (about 5mmHg drop in systolic BP) than in normotensives (about 1 - 2 mmHg drop in systolic BP), and higher in certain ethnic groups (blacks/Japanese/Chinese).
Generalisability	Excellent	Population studies in body of evidence include Australian populations and others are similar to the target population for the guideline.
Applicability	Excellent	Directly applicable to Australian healthcare context.

The studies used to make the body of evidence statement are listed below and summarised in Table 13.1.

All studies included in the body of evidence statement showed consistent positive associations between sodium intake and blood pressure in adults. It is not possible to conclude a definitive threshold level for sodium intake from the studies included in this review since the level of salt restriction ranged widely. A Cochrane meta-analysis Level I study of 20 trials in individuals with elevated blood pressure and 11 trials in normotensive individuals demonstrated that a median urinary sodium reduction of 78 mmol/24h resulted in a mean reduction in blood pressure of -5.06 mmHg (95% CI-5.81 - -4.31) for systolic and -2.70 mmHg (95% CI-3.16 - -2.24) for diastolic. In normotensives, a median reduction in urinary sodium of 74 mmol/24h lowered blood pressure by a mean of -2.03 mmHg (95% CI -2.56 - -1.50) for systolic and -0.99 mmHg (-1.40 - -0.57) for

diastolic. The sodium goals of included trials varied between <80 mmol/24hr and < 100 mmol/24hr of urinary sodium excretion. This magnitude of BP reduction was remarkably consistent with that shown in another meta-analysis (Geleijnse et al. 2003) in which a median urinary sodium reduction of 77 mmol/24h resulted in BP reductions of -5.24/ -3.69 mmHg in hypertensives and -1.26/-1.14 mmHg in normotensives. Another Cochrane meta-analysis (Jurgens 2004) found smaller, but still significant, reductions in diastolic BP in normotensives. Some ethnic groups, such as USA blacks and Japanese, have greater BP reductions in response to Na restriction than Caucasians.

A modest reduction in sodium intake for a duration of 4 or more weeks has a significant and, from a population viewpoint, important effect on blood pressure in both individuals with normal and elevated blood pressure. The meta-analysis of He & MacGregor (2004) demonstrates a correlation between the magnitude of salt reduction and the magnitude of blood pressure reduction. Within the daily intake range of 3 – 12 g salt (equivalent of 1200 - 4800 mg Na/day), the lower the sodium intake achieved, the lower the blood pressure. However, another Cochrane review that included longer-term studies of at least 26 weeks follow-up did not find a dose-response effect for sodium reduction (Hooper, 2004).

Only one study (Level I meta-analysis) was identified in pregnancy in which prevention of pre-eclampsia with salt restriction was not demonstrated. There is insufficient evidence to make separate recommendations in this group at present.

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13.2 SODIUM and BLOOD PRESSURE: Children and Adolescents

Does a particular intake of salt or sodium affect blood pressure in children and adolescents?		
Evidence Statement		Consuming a diet low in sodium reduces blood pressure in children up to 18 years of age
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	1 Level I meta-analysis with low risk of bias, and 1 Level II study (review), 2 Level IV studies (non-systematic reviews) with high risk of bias (negative quality rating).
Consistency	Excellent	BP reduction with Na reduction demonstrated in a Cochrane review.
Clinical impact	Good	Reductions of BP of the magnitude: systolic: -1.17 mm Hg; diastolic: - 1.29 mm Hg in children and adolescents. Insufficient evidence for infants.
Generalisability	Good	Population studies in body of evidence similar to the target population for the guideline.
Applicability	Excellent	Directly applicable to Australian healthcare context.

The studies used to make the body of evidence statement are listed below and summarised in Table 13.1. A Level I meta-analysis of 10 trials in children and adolescents (N = 966) found that Na restriction over a median intervention of 4 weeks resulted in significant reductions in blood pressure (systolic: -1.17 mm Hg; diastolic: - 1.29 mm Hg). In the same meta-analysis, three trials of infants (N = 551) with a median duration of 20 weeks found a significant reduction in systolic blood pressure of -2.47 mm Hg. Further long-term studies are needed to assess whether Na restriction in early childhood result in beneficial BP reductions later in life but at the present time there is enough evidence to warrant a body of evidence statement in this age group.

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Table 13.1 Studies used to make evidence statement for sodium and blood pressure

Reference [1]	**Hooper 2004 [1036]**	**He 2004 [1023]**	**Jurgens 2004 [1040]**	**Geleijnse 2004 [609]**
Type of study [2]	Meta-analysis (Cochrane review) [11 RCTs]	Meta-analysis (Cochrane review) [31 RCTs; 20 in hypertensives and 11 in normotensives]	Meta-analysis (Cochrane review) [115 RCTs; 58 in hypertensives and 57 in normotensives]	Meta-analysis [40 RCTs on sodium; 253 total trials included in lifestyle analysis]
Level of evidence [3]	I	I	I	I
Intervention/ comparator [4]	Dietary advice to reduce Na intake/ Blood Pressure & CVD.	Modest reduction in salt intake and duration of 4 + wks / Blood Pressure.	Low Na diet vs high/normal Na diet / Blood Pressure.	Dietary and lifestyle interventions, incl Na reduction / Blood Pressure.
N [5]	3514 (n = 2326 normotensives; n = 387 untreated HTs; n = 801 treated HTs).	11 trials in individuals with normal BP (n=2220) and 20 trials in individuals with elevated BP (n=802).	10,079	40 trials; N not given.
Population/study information [6]	All RCTS. Normotensives, untreated and treated HTs, from Australia, New Zealand, Italy, UK, USA. Follow-up of 6 to 60 mths.	Normotensives and hypertensives; Median age = 50 yrs (range 24 -73 yrs) Follow-up of 4 weeks to 1 year.	Normotensive and hypertensives, mostly Caucasian. Some data on USA blacks/Japanese. Follow-up of 4 days to 1 year (median = 28 days).	18 +yrs, from Finland, Italy, UK, USA, Netherlands.
Quality [7]	P	P	P	P
Results [8]	The two studies on mortality suggests no significant difference in cardiovascular morbidity between low sodium and control groups relative risk 0.82 (95% CI 0.56 - 1.21). Systolic BP reduced on a low Na diet at both intermediate (6-12mths)	NTs: median urinary Na reduction of 74 mmol/24h assoc. with BP reduction of -2.03 mmHg (95% CI -2.56 - -1.50) for systolic and -0.99 mmHg (-1.40 - -0.57) for diastolic. HTs: median reduction in urinary Na of 78 mmol/24hr associated with BP reduction of -5.06	NT: low Na intake reduced SBP by -1.27 mm Hg (CI -1.76 - -0.77, p<0.0001) and DBP by -0.54 mm Hg (CI -0.94 - -0.14, p = 0.009). HT: reduced SBP by -4.18 mmHg (CI -5.08- - 3.27, p < 0.0001) and DBP by -1.98 mm Hg (CI -2.46 - -	A median urinary Na reduction of 77 mmol/24h resulted in BP reductions of 1.26/-1.14 mmHg in normotensives and -5.24/ -3.69 mmHg in hypertensives.

	-2.5 mm Hg (95% CI -3.8 - -1.2) and late (13-60 mths) follow up -1.1 mmHg (95% CI -1.8 - -0.4).Diastolic BP also reduced at intermediate follow up - 1.2 mmHg (95% CI -1.8 - -0.6), less so later (by 0.6 mmHg, -1.5 to 0.3).	mmHg (95%CI -5.81 - -4.31) for systolic; -2.70 mmHg (95% CI-3.16 - - 2.24) for diastolic. Weighted linear regression showed significant relationship between reduction in urinary Na and reduction in BP (dose response).	1.32, $p < 0.0001$).Higher magnitude of BP reduction in black and Japanese.	
Clinical importance [9]	1. A clinically important benefit for the full range of plausible estimates (for BP). 2. No effect on CVD mortality/ events).	1. A clinically important benefit for the full range of plausible estimates.	1. The confidence interval does not include any clinically important effects (for NT). 2. A clinically important benefit for the full range of plausible estimates (for HT).	1. A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	1. Evidence of an effect on patient-relevant outcomes, including benefits.	1. Evidence of an effect on patient-relevant outcomes, including benefits.	1. Evidence of an effect on patient-relevant outcomes, including benefits.	1. Evidence of an effect on patient-relevant outcomes, including benefits.
Generalisability	y	y	y	y
Applicability	y	y	y	y
Comments	Long-term reduction of Na intake is difficult to maintain using dietary advice strategies alone.	Dose response relationship shown with Na reduction. BP benefits of an reduction greatest in those with raised BP.	Most studies short in duration (mean = 8 days in NT trials).	

Table 13.1 Studies used to make evidence statement for sodium and blood pressure (cont.)

Reference [1]	**He 2006 [151]**	**Kawano 2007 [1053]**	**Dickinson 2007 [1000]**	**Robertson 2003 [1116]**
Type of study [2]	Meta-analysis (13 RCTs; 10 in children/adolescents; 3 in infants).	Non-systematic review (6 RCTs).	Non-systematic review (6 meta analyses plus others).	Non-systematic review (2 non-systematic reviews; 1 cohort, 2 RCTs; 5 cross section).
Level of evidence [3]	I	II	II	IV
Intervention/ comparator [4]	Low Na diet vs. high/normal Na diet / Blood Pressure.	Low Na diet vs. high/normal Na salt diet / Blood Pressure.	Low sodium diet vs. high/normal Na diet (Mean = 78 - 118mmol Na/day reduction) / Blood Pressure.	Na reduction / Blood Pressure.
N [5]	Children/adolescents: N = 966. Infants: N = 551.	Not stated, healthy adults.	13,993	Not stated; 5 meta analyses cited.
Population/study information [6]	Children ≤18y incl newborn and infants. Follow-up: Children/adolescents: 2wks to 3 years (median = 4 weeks). Infants: 8 weeks to 6 months (median = 20 wks).	Uses data from US studies and one Japanese study to set Japanese guidelines.	Adults, adolescents, children.	Neonates, children, adults, elderly; NT and HTs.
Quality [7]	P	N	N	N
Results [8]	Children: For sodium intake reductions of 42% (IQR = 7 to 58%), BP reductions of systolic: 1.17 mm Hg (95% CI 1.78 - 0.56 mm Hg, p	Systolic BP reduction of 1mm Hg with every decrease in salt intake of 1 g/day (400 mg Na).	A 520mg/d lower lifetime Na intake translates into approx 5mm Hg smaller rise in systolic BP as individuals advance from 25 to 55 years of age.	Na reduction lowers BP, more so in hypertensives than normotensives (no numerical values given).

	0.001); diastolic: 1.29 mm Hg (95% CI 1.94 - 0.65 mm Hg, p 0.0001). Infants: reduction in systolic BP = 2.47 mm Hg (95% CI 4.00 - 0.94 mm Hg, p 0.01).			
Clinical importance [9]	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates (HT only).	1. A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	1. Evidence of an effect on patient-relevant outcomes, including benefits.	1. Evidence of an effect on patient-relevant outcomes, including benefits.	1. Evidence of an effect on patient-relevant outcomes, including benefits (HT only).	Evidence of an effect on patient-relevant outcomes, including benefits.
Generalisability	y	y	y	y
Applicability	y	y	y	y
Comments	First meta-analysis of RCTs in children and infants. Relatively small BP reductions, but clinically significant if preventive of BP increases with age into adulthood.	Non-systematic review. Current guidelines for treatment of hypertension, including Japanese, recommend dietary salt reduction to 6g/day or less in hypertensives.	Non-systematic review. Modest Na reduction over lifetime estimated to save 150 000 lives annually.	Non-systematic review. Na reduction lowers BP (No estimate of effect given). No trials cited showed increases in BP with a restriction.

Table 13.1 Studies used to make evidence statement for sodium and blood pressure (cont)

Reference [1]	**Geleijnse, 2002 [1012]**	**China Salt Subs Gp, 2007 [991]**	**Takahashi, 2006 [1133]**	**Melander, 2007 [1088]**
Type of study [2]	Non-systematic review [6 RCTs, 1 cohort, 1 cross section]	RCT	RCT (community-based trial)	RCT (cross-over)

Level of evidence [3]	IV	II	II	II
Intervention/ comparator [4]	Reduced Na in infancy and childhood / Blood Pressure.	High K salt substitute/normal salt (Anticipated decrease in Na = 45mmol (1035mg)/24 h (17% reduction)/ Blood Pressure.	dietary advice to reduce salt / Blood Pressure.	Low Na (50 mmol/day)/High Na (150mmol/day) / Blood Pressure.
N [5]	Not stated	302 intervention 306 control	274 intervention 276 control	46
Population/study information [6]	Infants and children < 18yrs.	High risk of future vascular disease; 12 mth follow-up.	rural Japanese 40 - 69y.	Healthy normotensive Swedish men and women (mean age 53 (11) yrs).
Quality [7]	N	P	P	P
Results [8]	Inconclusive	3.7 mmHg reduction in sys BP; no difference for diastolic BP. Max effect seen at 12 mth visit (5.4 mmHg; 2.3 - 8.5).	-3.1 (-5.4 to -0.9) for systolic BP; -5.2 (-9.9 to -0.4) in hypertensives; No diastolic effect. Between-group difference in urinary Na = 39 mmol/24hr (95% CI 56 - 21mmol/24hr, p < 0.001).	5.8 (3.4 to 8.2) mmHg reduction in ambulatory 24hr BP with low Na diet (urinary Na = 51 mmol vs 140 mmol/24hr on each diet; cross-over design).
Clinical importance [9]	No measure of effect provided.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	3. No clinically important effects.	1. Evidence of an effect on patient-relevant outcomes, including benefits.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.

Generalisability	y	y	n	y
Applicability	y	n	y	y
Comments	Not systematic review, but due to limited studies in infants and children was included. Further studies needed to assess whether Na restriction in early childhood result in beneficial BP reductions later in life.			

Table 13.1 Studies used to make evidence statement for sodium and blood pressure (cont.)

Reference [1]	**Nowson, 2009 [1102]**	**Dickinson, 2009 [1001]**	**Chen, 2009 [990]**	**Charlton, 2008 [989]**
Type of study [2]	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Low Na, low acid load, DASH-type diet/higher acid reference healthy diet / Blood Pressure.	Low Na (50 mmol/day) vs usual Na (150 mmol/day) / Blood Pressure (flow mediated dilatation).	Low Na (51 mmol/day) for 7 days followed by high Na diet (308 mmol/day) for additional 7 days/ Blood Pressure (Salt sensitivity protocol).	Na-reduced, K-increased food based intervention/usual Na products / Blood Pressure.
N [5]	46 intervention 49 control	29 (crossover)	1853	80
Population/study information [6]	Postmenopausal hypertensive women.	Australian overweight and obese normotensive men and women.	Chinese non-diabetic adults 16+y.	black, treated hypertensive South Africans.
Quality [7]	P	P	P	P
Results [8]	5.6 (intervention) vs. 2.7 (control) reduction in systolic BP.	Net effect of 1.52 % increase in flow mediated dilatation with low Na diet (relative increase of 30 %).	High salt sensitivity defined as >5mmHg drop in MAP on low Na or >5mmHg in MAP on high Na. Multivariable-adjusted mean changes in BP significantly > in those with metabolic syndrome than those without on both low-Na and high-Na diets ($p<0{\cdot}0001$ for all comparisons). Risk of salt sensitivity rose with	Net reduction of systolic BP (-6.2 mmHg (0.9 - 11.4) in intervention compared to control group.

			increasing numbers of risk factors for metabolic syndrome. Compared with no risk factors, those with 4 – 5 risk factors had a 3·54-fold increased odds (95% CI 2·05–6·11) of high salt-sensitivity during the low-Na and a 3·13-fold increased odds (1·80–5·43) of high salt-sensitivity during the high-Na intervention.	
Clinical importance [9]	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	1. Evidence of an effect on patient-relevant outcomes, including benefits.	2. Evidence of an effect of a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	2. Evidence of an effect of a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	1. Evidence of an effect on patient-relevant outcomes, including benefits.
Generalisability	y	y	y	y
Applicability	y	y	y	y
Comments				

13.3 SODIUM and BONE HEALTH

Is a particular intake of salt or sodium beneficial or detrimental with respect to bone health in adults?		
Evidence statement		Consuming a low sodium diet is associated with improved markers of bone health in postmenopausal women D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Six Level II studies (5 RCTs with low risk of bias) plus 1 Level III-1 (sys rev of cohort studies), but outcomes were biomarkers of bone health such as cross-linked telopeptides (bone resorption marker) and BMD rather than osteoporosis, fracture risk etc.
Consistency	Satisfactory	Most studies (all those in postmenopausal women) consistent with increased bone turnover or bone resorption with higher salt intakes; RCT in young Finnish adults found no effect over 7 wks.
Clinical impact	Poor	Not possible to indicate clinical impact from biomarker information; longer term studies required with endpoints such as osteoporosis and fracture rates.
Generalisability	Good	Populations studied in the BOE are similar to the target population in the case of postmenopausal women.
Applicability	Satisfactory	Probably applicable to Australian healthcare context with some caveats. Effect of Na intake on bone likely to be dependent on habitual calcium intake.

The studies used to make the body of evidence statement are listed below and summarised in Table 13.2. A systematic review on diet and the prevention of osteoporosis (three RCTs and one cohort study related to Na intake) that was prepared as the background paper for the Joint WHO/FAO Expert Consultation on diet, nutrition and prevention of chronic diseases (Prentice, 2004) identified sodium to be negatively associated with fracture as an outcome with the level of evidence rated as 'possible'.

Most of the studies examined only surrogate outcomes of bone health and most were conducted only in postmenopausal women.

It appears that sodium restriction may be a more effective measure in those on habitually low calcium intakes.

References

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women and its interaction with vitamin D receptor genotype", *British Journal of Nutrition*, vol. 91, no. 1, pp. 41-51.

Massey, L. K. 2005, "Effect of dietary salt intake on circadian calcium metabolism, bone turnover, and calcium oxalate kidney stone risk in postmenopausal women", *Nutrition Research*, vol. 25, no. 10, pp. 891-903.

Natri, A. M., Karkkainen, M. U., Ruusunen, M., Puolanne, E., Lamberg-Allardt, C. & Karkkainen, M. U. M. 2005, "A 7-week reduction in salt intake does not contribute to markers of bone metabolism in young healthy subjects", *European Journal of Clinical Nutrition*, vol. 59, no. 3, pp. 311-7.

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Thierry-Palmer, M., Henderson, V. M., Hammali, R. E., Cephas, S., Palacios, C., Martin, B. R. & Weaver, C. M. 2008, "Black and white female adolescents lose vitamin D metabolites into urine", *American Journal of the Medical Sciences*, vol. 335, no. 4, pp. 278-83.

Table 13.2 Studies used to make evidence statement for sodium and bone health

Reference [1]	**Prentice 2004 [1112]**	**Teucher 2003 [1142]**	**Harrington 2004 [1019]**
Type of study [2]	Non-systematic review (3 RCTs; 1 cohort study). Paper prepared as background for Joint WHO/FAO Expert Consultation on diet , nutrition and prevention of chronic diseases (2002).	Non-systematic review (9 RCTs).	RCT.
Level of evidence [3]	III-2	II	II
Intervention/ comparator [4]	High Na intake/ Bone turnover.	Salt loading / Bone markers.	High protein + high Na diet/Normal protein +low Na diet/ NTx (bone resorption marker).
N [5]	Not stated	211	24
Population/study information [6]	Pre and postmenopausal women.	All women.	Healthy post menopausal women in Ireland (50 – 67 yrs).
Quality [7]	N	N	P
Results [8]	Na intake has adverse effect on calcium homeostasis and bone turnover in post-menopausal women; weak but significant association with BMD and age-related bone loss.	Results inconsistent but increases in crosslinked telopeptide or deoxyproline up to 23 % and 21 %, respectively seen on high salt diet. Salt restriction may be a more effective measure in those on low Ca intakes, for reduction in loss of BMD.	Calciuric diet increased mean NTx (bone resorption marker) by 19 % over 4 weeks.
Clinical importance [9]	No measure of effect provided.	A clinically important benefit for the full range of plausible estimates.	A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	Evidence of an effect on a proven surrogate outcome but for a different intervention.	Evidence of an effect of a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	Evidence of an effect of a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.
Generalisability	y	y	y

Applicability	y	y	n
Comments	Non systematic review of all dietary components associated with bone health, not just Na. Data limited to a small number of studies.	Only 2 RCTs had BMD as outcomes (9 and 24 mths follow-up); both in postmenopausal women. Benefits for bone health with Na restriction likely to be shown at earlier ages over the lifecourse, ie. at achievement of Peak Bone Mass. Likely to be different Na-associated effects on bone with differing Ca intakes. Biomarkers studies short duration and small N.	

Table 13.2 Studies used to make evidence statement for sodium and bone health (cont.)

Reference [1]	**Natri 2005 [1099]**	**Teucher 2008 [1141]**	**Massey 2005 [1078]**	**Thierry-Palmer 2008 [1144]**
Type of study [2]	RCT	RCT	RCT (metabolic study)	RCT (metabolic study)
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	low salt (Na 80mmol/d Na) . usual salt (Na 127 mmol/d) / Bone metabolism.	High salt (3.9 g) vs. low salt (11.2 g) on either high Ca (1284 mg/d) or low Ca (518 mg/d) diets / Bone turnover.	50 mmol Na/day (low Na) vs. 220 mmol/day (high Na) / various Bone markers.	56 mmol Na/day (low Na) vs. 168 mmol/day (high Na) / urinary 25_OHD binding proteins.
N [5]	29	11 (crossover)	10 (crossover)	21 (crossover)
Population/study information [6]	Finnish 21 - 39y adults with high Ca intake.	Post menopausal UK women.	Postmenopausal women.	Black and white US adolescents.
Quality [7]	P	P	P	P
Results [8]	No change in markers of bone metabolism over 7 week intervention.	Higher salt intakes resulted in change in bone calcium balance (positive to negative) when consumed as part of a high calcium diet,	No effect of sodium intake on calcitriol, ionized calcium, PTH, and bone alk phos. Urinary deoxypyridinoline and N-telopeptide concentrations	Higher sodium intakes may increase urinary losses of 25-OHD binding proteins, lowering vit D status.

		but with a low calcium diet, the bone calcium balance was negative on both high and low salt diets.	(/mmol creatinine), osteocalcin and urinary calcium higher on high-salt diet.	
Clinical importance [9]	3. The confidence interval does not include any clinically important effects.	2. The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	3. The confidence interval does not include any clinically important effects.	2. The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.
Clinical relevance [10]	3. Evidence of no effect on a proven surrogate outcome but for a different intervention.	2. Evidence of an effect of a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	2. Evidence of no effect of a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.	3. Evidence of an effect on a proven surrogate outcome but for a different intervention.
Generalisability	n	y	y	y
Applicability	y	y	n	n

13.4 SODIUM and CARDIOVASCULAR DISEASE

Does a particular intake of salt or sodium affect the risk of cardiovascular disease in adults?		
Evidence statement		Reducing sodium intake by about 1000mg/day is associated with reduced risk of cardiovascular events
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	One Level I meta-analysis (11 RCTs) with low risk of bias; 1 Level II study (RCT) with low risk of bias and 5 Level III-2 studies (2 reviews and 3 cohort studies - 2 with low bias and 1 moderate bias).
Consistency	Satisfactory	Some inconsistency reflecting genuine uncertainty around clinical question (CVD end points and CVD mortality), although long term follow up (10 - 15yr) of the two Trials of Hypertension Prevention RCTs demonstrated a 25% reduction in CVD events with Na reduction.
Clinical impact	Satisfactory	RR reduction of up to 30 % shown in some studies but magnitude of effect not consistent.
Generalisability	Good	Populations studies in the body of evidence are similar to the target population for the guideline.
Applicability	Good	Applicable to Australian healthcare context with few caveats.

The studies used to make the body of evidence statements are listed below and summarised in Table 13.3. The best evidence for the impact of sodium reduction on cardiovascular disease outcomes is provided by the long term follow up of the two Trials of Hypertension Prevention (TOHP I and II) RCTs conducted in adults aged 30 – 54 years with untreated pre-hypertension (diastolic = 80 – 89 mmHg and systolic < 140 mmHg). Sodium reduction was achieved by intensive counselling with or without weight loss. Sodium reduction was associated with a drop of 25 % in CVD outcomes after an average 19 years of follow-up.

References

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Cook, N. R., Cutler, J. A., Obarzanek, E., Buring, J. E., Rexrode, K. M., Kumanyika, S. K., Appel, L. J. & Whelton, P. K. 2007, "Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP)", *BMJ: British Medical Journal*, vol. 334, no. 7599, pp. 885-888.

Cook, N. R., Obarzanek, E., Cutler, J. A., Buring, J. E., Rexrode, K. M., Kumanyika, S. K., Appel, L. J. & Whelton, P. K. 2009, "Joint effects of sodium and potassium intake on subsequent cardiovascular disease: the Trials of Hypertension Prevention follow-up study", *Archives of Internal Medicine*, vol. 169, no. 1, pp. 32-40.

He, J., Ogden, L. G., Bazzano, L. A., Vupputuri, S., Loria, C. & Whelton, P. K. 2002, "Dietary sodium intake and incidence of congestive heart failure in overweight US men and women: first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study", *Archives of Internal Medicine*, vol. 162, no. 14, pp. 1619-1624.

Hooper, L., Bartlett, C., Davey, S. G., Ebrahim, S. & Davey, S. G. 2004, "Advice to reduce dietary salt for prevention of cardiovascular disease.[update of Cochrane Database Syst Rev. 2003;(3):CD003656; PMID: 12917977]", *Cochrane Database of Systematic Reviews*, vol., no. 1, pp. CD003656.

Reddy, K. S. & Katan, M. B. 2004, "Diet, nutrition and the prevention of hypertension and cardiovascular diseases. Diet, Nutrition and the Prevention of Chronic Diseases: scientific background papers of the Joint WHO/FAO Expert Consultation (Geneva, 28 January-1 February 2002)", *Public Health Nutrition*, vol. 7, no. 1A, pp. 167-186.

Table 13.3 Studies used to make evidence statement for sodium and cardiovascular disease

Reference [1]	**Hooper 2004 [1036]**	**Beevers 2002 [981]**	**Reddy 2004 [1114]**
Type of study [2]	Meta-analysis (Cochrane review) (11 RCTs).	Non-systematic review of epidemiological studies (5 cohort).	Non systematic review (1 meta analysis; 1 cohort study, 1 RCT (DASH-Sodium)and 3 community-based quasi-experimental trials). Paper prepared as background for Joint WHO/FAO Expert Consultation on diet , nutrition and prevention of chronic diseases (2002).
Level of evidence [3]	I	III-2	III-2
Intervention/ comparator [4]	Dietary advice to reduce Na intake/ CVD.	High Na intake / CVD.	70 - 80 mmol Na reduction (meta-analysis) / CVD.
N [5]	3514 (n = 2326 normotensives; n = 387 untreated HTs; n = 801 treated HTs).	>26,000	1 meta analysis; 1 cohort study, 1 RCT (DASH-Sodium)and 3 community-based quasi-experimental trials.
Population/study information [6]	All RCTS. Normotensives, untreated and treated HTs, from Australia, New Zealand, Italy, UK, USA. Follow-up of 6 to 60 mths.	HT, NT, adults, elderly, infants.	Hypertensive, normotensive adults, infancy, elderly.
Quality [7]	P	N	N
Results [8]	The two studies on mortality suggests no significant difference in cardiovascular morbidity between low sodium and control groups relative risk 0.82 (95% CI 0.56 -.21).	Hazard ratios for CHD, CVD and all cause mortality, associated with a 100 mmol increase in 24 h Na = 1.51 (95% CI 1.14–2.00), 1.45 (1.14–1.84) and 1.26 (1.06–1.50), respectively, in both men and women. Frequency of acute coronary events, but not acute stroke events, rose significantly with increasing Na excretion.	Overall association of increasing Na excretion with CVD and all cause mortality.

Clinical importance [9]	. 3. Does not include clinically important effects for CVD mortality/ events.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	3. The confidence interval does not include any clinically important effects.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.
Generalisable	y	y	y
Applicable	y	y	y
Comments	Long-term reduction of Na intake is difficult to maintain using dietary advice strategies alone.	Non systematic review of all dietary components associated with bone health, not just Na. Data limited to a small number of studies.	

Table 13.3 Studies used to make evidence statement for sodium and cardiovascular disease (cont.)

Reference [1]	**Chang 2006 [referred to in 965]**	**Cook 2009 [994]**	**He 2002 [1027]**	**Cook 2007 [993]**
Type of study [2]	RCT	Cohort (follow-up of controls from TOHPI AND II).	Cohort	Cohort (follow-up of intervention groups from two RCTs TOHP1 and II).
Level of evidence [3]	II	III-2	III-2	III-2
Intervention/ comparator [4]	K-enriched low Na salt/regular salt / CVD & Stroke.	Extreme quartiles (Q1 - Q4) of 24 hr urinary Na : difference in median of 122 mmol/24h (men) and 95 mmol/24h (women) over 1-3 yrs measurement / CVD.	Quartiles of Na intake at baseline (0 - 50.2; >50 - 76.2; >76.2 - 113.6; >113.6 mmol Na/day) / Congestive heart failure.	Na reduction by intensive counselling/usual care or weight loss / CVD.
N [5]	768 intervention/1213 control.	2275	5233 (non-overweight) and 5129 overweight ; N = 10,362.	3126
Population/study information [6]	Elderly Taiwanese men living in veteran retirement homes.	Pre-hypertensive adults followed for 10 - 15 yrs.	Men and women (25 - 74y) without history of CHF, followed for 19 yrs.	Adults aged 30-54 years with prehypertension.
Quality [7]	P	P	P	P
Results [8]	-38.8 % relative risk reduction in CVD mortality; 70 % RR reduction in heart failure and 50 % reduction for cerebrovascular disease.	Non-significant trend in CVD risk across sex-specific quartiles of urinary Na excretion (rate ratio [RR] from lowest to highest, 1.00, 0.99, 1.16, and 1.20; P=0.38 for trend), but a significant trend across quartiles of the Na to K excretion ratio (RR, 1.00, 0.84, 1.18, and 1.50; P=0.04 for	RR for Congestive Heart Failure (CHF) in overweight people = 1.43 (1.07 - 1.91) after adjustment for known risk factors.	Risk of CVD event was 25% lower among those in intervention group RR = 0.75 (95% CI 0.57 - 0.99, p=0.04), adjusted for trial, clinic, age, race, and sex, and 30% lower after further adjustment for baseline sodium excretion and weight (0.70; 0.53 - 0.94).

		trend). Models containing both Na and K, linear effects were: RR 1.42 (95% CI 0.99 - 2.04 per 100 mmol/24 hr of urinary sodium excretion, p = .05).		
Clinical importance [9]	1. A clinically important benefit for the full range of plausible estimates.	2. The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	1. A clinically important benefit for the full range of plausible estimates.	1. A clinically important benefit for the full range of plausible estimates.
Clinical relevance [10]	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.	1. Evidence of an effect on patient-relevant outcomes, including benefits and harms, and quality of life and survival.
Generalisability	y	y	y	y
Applicability	n	y	y	y
Comments				

Summary of studies not included in Body of Evidence statements
The following diet-health relationships had too few studies to develop a body of evidence statement.

Salt and stroke
There were two studies with stroke as an outcome. One Level II (RCT) study with low risk of bias but intervention was potassium-enriched salt substitute rather than sodium restriction alone (Chang, 2006). The study population was Taiwanese elderly men therefore it is hard to judge whether it is sensible to generalise to target population. One case control study in which hypertensives from the Gaza Strip who had been on treatment for at least one year were found to have a 16 fold increased risk of stroke associated with high salt intake but only in people who had a low level of stress (Baune 2005).

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Baune, B. T., Aljeesh, Y., Bender, R. & Baune, B. T. 2005, "Factors of non-compliance with the therapeutic regimen among hypertensive men and women: a case-control study to investigate risk factors of stroke", *European Journal of Epidemiology*, vol. 20, no. 5, pp. 411-9. **<5 studies**

Chang, H.Y., Hu, Y.W., Yue, C.S.J., Wen YW., Yeh, W.T., Hsu, L.S., Tsai,S.Y., Pan, W.H. 2006. "Effect of potassium-enriched salt on cardiovascular mortality and medical expenses of elderly men." *American Journal of Clinical Nutrition*. Vol.;83,. pp. 1289 –1296. **< 5 studies**

Cook, N. R. 2008, "Salt intake, blood pressure and clinical outcomes", *Current Opinion in Nephrology & Hypertension*, vol. 17, no. 3, pp. 310-4. **Included in review**

Duley, L., Henderson-Smart, D. & Meher, S. 2005, "Altered dietary salt for preventing pre-eclampsia, and its complications", *Cochrane Database of Systematic Reviews*, vol., no. 4, pp. CD005548. **<5 studies**

Godoy, R., Goodman, E., Gravlee, C., Levins, R., Seyfried, C., Caram, M. & Jha, N. 2007, "Blood pressure and hypertension in an American colony (Puerto Rico) and on the USA mainland compared, 1886-1930", *Economics & Human Biology*, vol. 5, no. 2, pp. 255-79. **XS**

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Obarzanek, E., Proschan, M. A., Vollmer, W. M., Moore, T. J., Sacks, F. M., Appel, L. J., Svetkey, L. P., Most-Windhauser, M. M. & Cutler, J. A. 2003, "Individual blood pressure responses to changes in salt intake: results from the DASH-Sodium trial.[see comment]", *Hypertension*, vol. 42, no. 4, pp. 459-67. **Included in review**

Schrader, H., Schmelz, E. & Marrugat, J. 2002, "Relationship between diet and blood pressure in a representative Mediterranean population", *European Journal of Nutrition*, vol. 41, no. 4, pp. 161-167. **XS**

Xu, C., Sun, Z., Zheng, L., Zhang, D., Li, J., Zhang, X., Liu, S., Zhao, F., Hu, D. & Sun, Y. 2008, "Prevalence of and risk factors for isolated systolic hypertension in the rural adult population of Liaoning Province, China", *Journal of International Medical Research*, vol. 36, no. 2, pp. 353-6. **XS**

Yin, R., Li, H., Wu, J., Lin, W., Yang, D., Pan, S., Huang, J. & Long, X. 2007, "Effects of alcohol consumption and other lifestyle behaviors on blood pressure for the middle-aged and elderly in the Guangxi Hei Yi Zhuang and Han populations", *Alcohol*, vol. 41, no. 8, pp. 541-50. **XS**

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14. SUGARS (S1.1)

Evidence Statements

14. SUGARS (S1.1)

Search results

The initial search of the data bases included 4,226 references for sugars and the specified disease outcomes. The detailed search is included in a separate document on searches. In all, 126 references concerning sugars had data extracted and 22 papers were used to form the body of evidence statements for sugars. Sufficient evidence was found to make statements for sugars and obesity, dental caries, cardiovascular disease, type 2 diabetes and cancer (including pancreatic, colorectal, breast, and bladder cancer).

14.1 SUGARS and CANCER

Does a particular intake of sugars effect the risk of cancer?		
Evidence Statement		Consumption of sucrose is not associated with the risk of cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Poor	4 level 111-2 prospective cohort studies and one level 111-2 case-control study with low risk of bias (Quality ratings; 5P).
Consistency	Good	4 out of 5 studies showed no significant increase in risk of cancer with increasing sucrose consumption. The case-control study that found a significant association was on sugar-sweetened beverages.
Clinical impact	Poor	In the cohort studies, the RRs were 0.88 – 1.30 but all 95% CI's included 1.0 except for the case-control study that had an OR of 3.27 (95% CI 1.96 - 5.45).
Generalisabilty	Satisfactory	A wide range of adult populations studied: US, Canada and Uruguay. Age range 30 – 89 years and both genders covered.
Applicability	Satisfactory	Probably applicable to Australian healthcare context with some caveats

The four cohort studies and the one case control studies contributing to the body of evidence are in Table 14.2. Two studies were of pancreatic cancer (Michaud et al. 2002; Nothlings et al. 2007), and the remainder was of colo-rectal (Michaud et al. 2005), and breast cancer (Silvera et al. 2005). The case-

control study was of bladder cancer (De Stefani et al. 2008). The studies were all from the Americas, and included both genders and a relatively broad age range. Overall, there was no evidence for an effect of sucrose-based sweeteners on risk of a variety of common cancers. Total sweetened beverages (predominantly sucrose-based) were strongly related to bladder cancers in the case-control study (De Stefani et al. 2008). However, three of the cohort studies (Michaud et al. 2002; Michaud et al. 2005; Nothlings et al. 2007) showed positive associations with fructose and pancreatic and colo-rectal cancer but overall, there were insufficient studies to include a separate body of evidence statement for fructose and cancer risk. The World Cancer Research Fund stated there was no convincing or probable evidence of increased risk of cancer with sugar intake but there was some limited suggestive data for an association of sugar with colorectal cancer and high sugar intake.

References

De Stefani, E., Boffetta, P. et al. 2008, "Dietary patterns and risk of bladder cancer: a factor analysis in Uruguay." *Cancer Causes & Control,* vol. 19, no. 10, pp. 1243-9.

Michaud, D. S., Fuchs, C. S. et al. 2005, "Dietary glycemic load, carbohydrate, sugar, and colorectal cancer risk in men and women." *Cancer Epidemiology, Biomarkers & Prevention,* vol. 14, no.1, pp. 138-47.

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Nothlings, U., Murphy, S. P. et al. 2007, "Dietary glycemic load, added sugars, and carbohydrates as risk factors for pancreatic cancer: the Multiethnic Cohort Study." *American Journal of Clinical Nutrition*, vol. 86, no. 5, pp. 1495-501.

Silvera, S. A., Jain, M. et al. 2005, "Dietary carbohydrates and breast cancer risk: a prospective study of the roles of overall glycemic index and glycemic load." *International Journal of Cancer,* vol. 114, no. 4, pp. 653-8.

Table 14.1 Studies used to make evidence statements for sugars and cancer

Reference [1]	**Michaud et al. 2002 [4926]**	**Nothlings et al. 2007 [3689]**	**Michaud et al. 2005 [4413]**	**Silvera et al. 2005 [4407]**	**De Stefani et al. 2008 [2240]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Case-control
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Quintiles of sucrose and fructose intake	Quartiles of sucrose and fructose intake	Quintiles of sucrose and fructose intake	Quintiles of sucrose intake	3 dietary patterns 1) Sweet beverages; 2) Western diet, and; 3) Prudent diet
N [5]	180 cases of pancreatic cancer out of 88,802 women	434 incident pancreatic cancers in 162,150 women and men	1809 incident colorectal cancers in 121,700 women and 51,529 men	1461 incident breast cancers in 49,613 women	255 cases badder cancer; 597 controls
Population/ study information [6]	US Nurses Health Study. Median age 46.8 years; BMI = 23.7; Calories = 1586; Carbohydrate = 39.1% of energy	The Multiethnic Cohort Study in Hawaii and Los Angeles, USA. Median age 60 years; BMI = 25.5; Calories = 2014; Carbohydrate = 53.2 % of energy; 33% Japanese American, 30% white, 28.5% Hawaiian, 14% African American; and 19% Latino	US Nurses Health Study (1) and Health Professionals Follow-up Study. Women median age 47 years; BMI = 24; Calories = 1583; Carbohydrate = 156 g/d; Men median age 54 years; BMI = 26; Calories = 2024; Carbohydrate = 235 g/d	Canadian National Breast Screening Study. Mean age 48.5 years (range 40-59)	Uruguay. Male Public Hospitals. Median age = 60-69 yrs; BMI = 22.9-25.1; 88.2%
Quality [7]	P	P	P	P	P
Results [8]	Sucrose consumption and pancreatic cancer risk RR 1.26 (95% CI 0.63 - 2.51, P=0.98) Fructose consumption and pancreatic cancer risk RR = 1.99 (0.94 - 4.22, P=0.12)	Sucrose consumption and pancreatic cancer risk RR 1.23 (95% CI 0.91- 1.65, P=0.21) Total sugar consumption and pancreatic cancer risk RR =1.28 (0.95-1.73, P= 0.09) Fructose consumption and pancreatic cancer	Sucrose consumption and colo-rectal cancer risk in men RR 1.30 (95% CI 0.99-1.69, P=0.03) Sucrose consumption and colo-rectal cancer risk in women RR = 0.89 (0.72-1.11, P= 0.10) Fructose consumption	Total sugar consumption and risk of breast cancer HR 0.88 (95% CI 0.70–1.12, P=0.38)	Sweet beverages and bladder cancer OR 3.27 ((95% CI 1.96–5.45, P<0.0001)

		risk RR 1.35 (1.02-1.80, P=0.046)	and colo-rectal cancer risk in women RR 0.92 (0.59-1.44, P=0.47)		
Effect on risk (Increase/None/Protect)	None	None	None	None	Increase
Clinical importance[9]	3	3	3	3	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	n
Applicability	y	y	y	y	y

14.2 SUGARS and DENTAL DISEASE

Does a particular intake of sugars effect the risk of dental disease?		
Evidence Statement		High or frequent consumption of added sugars, particularly for infants and young children, is associated with increased risk of dental caries.
Grade		C .
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 level 1V systematic review (low risk bias) and 4 level 111-2 prospective cohort studies (low to medium risk bias)
Consistency	Good	For frequency of intake of added sugars, 19 of 31 studies from the systematic review and 1 of 4 cohort studies showed positive associations with dental caries. For intake of added sugars 6 of 15 studies from the systematic review and 4 of 4 cohort studies showed associations with caries.
Clinical impact	Good	A summary statistic is not reported in the systematic review. For sugar intake two cohort studies reported OR of 1.4 to 3.04.
Generalisabilty	Good	Males and females less than 35 years of age in North America and Europe with a broad range of sugars consumption.
Applicability	Good	Applicable to Australian healthcare context with few caveats

The systematic review (Anderson et al. 2009) and four cohort studies (Levy et al. 2003, Ruottinen et al. 2004, Marshall et al. 2007 and Warren et al. 2009) contributing to the body of evidence are in Table 14.4. The systematic review (Anderson et al. 2009) is of people living in Asia, Europe and North America, who are aged 1 – 35 years. The cohort studies (Levy et al. 2003, Ruottinen et al. 2004, Marshall et al. 2007 and Warren et al. 2009) were of North American and European children (infants to 11 years of age), and were relatively small for this type of study. While the evidence suggests that a frequent intake of foods and beverages high in added sugars increases the risk of dental caries there is insufficient evidence provided in the searched published literature between 2002 and 2009 to determine a dose-response. However, it should be noted that there have been a number of key references published prior to 2002 that could be used to guide decision making.

References

Anderson, C. A., Curzon, M. E. et al. 2009, "Sucrose and dental caries: a review of the evidence." *Obesity Reviews,* vol. 10, Suppl 1, pp. 41-54.

Levy, S. M., Warren, J. J. et al. 2003. "Fluoride, beverages and dental caries in the primary dentition." *Caries Research,* vol. 37, no. 3, pp. 157-65.

Marshall, T. A., Eichenberger-Gilmore, et al. J. M. 2007, "Comparison of the intakes of sugars by young children with and without dental caries experience." *Journal of the American Dental Association,* vol. 138, no. 1, pp. 39-46.

Ruottinen, S., Karjalainen, S. et al. 2004, "Sucrose intake since infancy and dental health in 10-year-old children." *Caries Research,* vol. 38, no. 2, pp. 142-8.

Warren, J. J., Weber-Gasparoni, K. et al. 2009, "A longitudinal study of dental caries risk among very young low SES children." *Community Dentistry & Oral Epidemiology,* vol. 37, no. 2, pp. 116-22.

Table 14.2 Studies used to make evidence statements for sugars and dental disease

Reference [1]	**Anderson et al. 2009 [2050]**	**Levy et al. 2003 [5207]**	**Marshall et al. 2007 [6175]**	**Ruottinen et al. 2004 [5179]**	**Warren et al. 2009 [1988]**
Type of study [2]	Systematic Review (majority cross-sectional)	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	1V	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	15 papers graded B1, reporting a total quantity of sucrose as measured in g/d, one paper stated g of sucrose consumed per 1000 kcal consumed, and one paper stated quantities of sucrose as large, moderate and small amounts. All other manuscripts did not assess total sugar consumption. Frequencies were variously reported as: between meal consumption (snack frequency); total frequency of eating episodes throughout the day; at and between meals intakes of sucrose (total frequency throughout the day); weekly frequency of total sugars; weekly	Dietary intake was partitioned into eleven broad categories: water, formula, breast milk, cow's milk, juices and juice drinks, non-juice beverages as purchased, beverages made from frozen concentrates, beverages made from powdered concentrates, ready-to-feed baby food, infant cereal made from powder, and other foods made with water (Jell-O®, soup, etc.).	Iowa Fluoride Study. 3 day diaries yearly from age 1-5y and dental caries between age 4.5 to 6.9 years. Foods and beverages coded as containing non-milk extrinsic (NME) or intrinsic/milk sugars (IMS). NMES= highly processed e.g. 100% juice or with added sugars e.g. fruit pie, ice cream, jam, breakfast cereals, juice drinks, yogurts with added sugars. IMS=minimally processed e.g. fresh, frozen, dried fruit, of dairy origin e.g. milk with no added sugars.	Mean±SD in high sucrose group 52.6± 13.1 g/d range 25.7-82.8 g/d; Low sucrose group 32.5± 18.5 g/d range 5.3-81.6 g/d	Dietary intake was partitioned into eleven broad categories: water, formula, breast milk, cow's milk, juices and juice drinks, non-juice beverages as purchased, beverages made from frozen concentrates, beverages made from powdered concentrates, ready-to-feed baby food, infant cereal made from powder, and other foods made with water (Jell-O®, soup, etc.).

	frequency of snack and sweet intakes; other variables relating to specific food groups.				
N [5]	Total not stated. Sample sizes varied from 69 to 139.	291 children	children, n=600, n= 447 at age 3 yrs	66 children	128 infants
Population/ study information [6]	M and F Global, 1 to <35 years of age,	US Children 6 weeks - 4 years old, mean age 5.17 years at dental exam; 53.3% female; 99% white	US Children aged 1-5y and dental caries between age 4.5 to 6.9 years, 52% female (n = 329) and 43% firstborn (n = 271).	Finnish children mean age 10 years (range 8-11)	Us infants age range 6-24 months; mean age 12.6 months; 58% male; 75% Caucasian
Quality [7]	P	O	P	O	O
Results [8]	The analysis showed that there is no reliable relationship of quantity of sugar used to dental caries. A significant relationship of frequency of use of sugar(s) to dental caries was reported in 19 out of the 31 papers considered.	Intake of SSB/non-formula milk(incl flav.) at age 6wks-12mo and caries (1.70 p<0.0005), non-formula milk (incl flav.) at age 24-36 mo (0.69 =0.05). SSB intake at age 12-24 mo (1.42 p=0.05), but NS after controlling for SSB/non-formula milk (incl.flav.) at age 6wks-12 mo.	Subjects' total, NME, food NME and intrinsic/milk sugars intakes at ages studied did not differ between subjects with and without caries experience. In logistic regression models, after adjustment for age at dental examination and fluoride intake, beverage NME sugar intake at 3 years predicted caries (p<0.05). Median (IQR) of beverage NME for caries free subjects: 27 (16, 40) vs caries	Decayed, missing and filled teeth in high vs. low sucrose intake group - mean±SD 3.9±3.9 in high sucrose and 1.9±2.5 in low sucrose, P=0.032; Frequency of sucrose intake and caries risk - in high sucrose consumers r=0.376; p =0.031; in low r =0.033, p =0.854	Sugar sweetened beverage consumption and caries OR 3.04 (95% CI 1.07–8.64, P= 0.04)

			present 34 (19, 48) p=0.035		
Effect on risk (Increase/None /Protect)	None	Increase, indicates importance of early dietary intake	Increase	Increase	Increase
Clinical importance[9]	1	1	1	1	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	Yes	Yes	Yes	Yes	Yes
Applicability	Yes	Yes	Yes	Yes	Yes

14.3 SUGARS and OBESITY

Does a particular intake of sugars affect measures of body weight and/or body fat?		
Evidence statement		A reduction in sugar consumption prevents increases in measures of body weight and/or body fat.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Poor	1 systematic review of 11 intervention studies, 4 prospective studies, and 1 cross-sectional study (high risk bias). In addition, 3 randomised controlled trials (low to medium risk bias) and 1 retrospective cohort study (medium risk bias).
Consistency	Satisfactory	Studies were inconsistent, but the inconsistency may be explained by varied energy intakes when comparing groups (see narrative below). 3 studies (2 RCT, 1 cohort) reported a protective effect and 1 SR reported no effect with reduced sugar intake. 1 RCT reported increased risk with increased sugar intake.
Clinical impact	Satisfactory	It is difficult to separate changes in total energy consumption from changes in sugar consumption. In the one study that compared groups with statistically equivalent total energy consumption, weight loss was -0.27 kg (SE 0.3, $P<0.02$) over 24 days with a low GI diet compared to a high sucrose diet.
Generalisability	Excellent	Western populations, including UK, France, USA, and Canada.
Applicability	Excellent	Directly applicable.

In this section, measures of weight status include body weight, BMI, BMI z-score, waist and hip circumference, fat mass, percent body fat, and skinfold thicknesses. However, not every study included all of these measures. Studies examining added sugar in foods only or foods and beverages were included, while studies examining added sugars in beverages only were excluded due to overlap with another question (see Chapter 15 - Beverages). Only studies examining sugars added to a product were included, while studies examining sugars naturally occurring in a product were excluded. Overall, one randomised controlled trial examined sucrose (Brynes 2003) and one systematic review (Vermunt 2003), two randomised controlled trials (Paineau 2008, Rodearmel 2007), and one retrospective cohort (Drapeau 2004) examined dietary sugar.

Large, long-term studies are lacking in this area. The studies included in this report are generally industry-funded, small, short-term randomised controlled trials and intervention studies. No studies were retrieved that measured the long-term development of overweight or obesity specifically related to sugar consumption. Four (Vermunt 2003, Brynes 2003, Paineau 2008, Rodearmel 2007) of the

five included studies were supported or partially supported by industry groups; two of these four (Paineau 2008, Rodearmel 2007) were conducted by independent research organizations. Affiliations were taken into consideration when determining study quality.

The systematic review (Vermunt 2003) was of poor quality, but reported that replacing sucrose with low-energy sweeteners does not result in weight loss but may support weight maintenance in children and adults. In studies with energy restriction in this systematic review, consumption of sugar compared to complex carbohydrate had no effect on weight change. In studies with an ad libitum diet, the review reported that there may be greater weight loss with consumption of complex carbohydrates compared to sugars and other simple carbohydrates, but the authors suggest this is likely due to differences in total energy intake.

Two randomised controlled trials (Paineau 2008, Rodearmel 2007) and one retrospective cohort study (Drapeau 2004) examined the effect of reducing sugar intake on measures of weight status in adults. In one randomised controlled trial (Paineau 2008), after 10 months, an intervention group to reduce fat and sugar consumption and increase complex carbohydrate consumption had significantly reduced BMI, reduced fat mass, and a lower increase in hip circumference compared to the control group ($P<0.05$ for all). However, the reduction in energy intake ($P<0.05$), fat intake ($P<0.01$), and sugar intake ($P<0.01$) during the 10 months were also significantly greater in the intervention group compared to the control group. Thus, it is likely the improved measures of weight status were due to reduced total energy intake rather than specifically sugar. In addition, the reduction in fat intake confounds the effect of the reduction in sugar intake. A second randomised controlled trial (Rodearmel 2007) examined adults in an intervention group to increase physical activity and reduce dietary sugar by substituting sugar with sucralose, compared to adults in a control group. After six months, there were no significant differences in changes of measures of weight status (BMI, percent body fat, waist circumference) between the intervention and control groups. Energy intake was at least 420kJ (100kcal)/day lower in the intervention group compared to the control group 77% of the days in the 6 month period, and physical activity was significantly higher in the intervention group compared to the control group ($P<0.05$), therefore confounding the effect of the sugar reduction. In the retrospective cohort study (Drapeau 2004), when adults considered their diet changes over the past five years, those who reported consuming less sugar and sweet foods had a lower increase in the sum of skinfold thicknesses and a lower increase in waist circumference than subjects consuming more or the same amount of sugar and sweet foods during the past five years ($P<0.05$). Changes in energy intakes were not reported, and the change in sugar and sweet food consumption was not quantified. This retrospective study provides only low level evidence, and does not contribute greatly to the body of evidence statement.

One randomised controlled trial (Brynes 2003) in moderately overweight men compared (1) a high carbohydrate and high GI diet, providing 46 g sucrose; (2) a high sucrose diet, providing 132g sucrose; (3) a high carbohydrate and low GI diet, providing 45g sucrose; and (4) a low carbohydrate and high fat diet, providing 51 g sucrose. After 24 days and with no significant difference in total energy intake, the authors reported a significant difference in weight change in the group consuming the high carbohydrate/low GI diet (-0.27 kg, SE 0.3) compared to the group consuming the high sucrose diet (+0.84 kg, SE 0.3, $P<0.02$ between groups). No other measures of weight status were reported. However, it must be noted that while the total energy intake was not statistically

significant, the mean daily intake for the high carbohydrate/low GI diet group was 2080 kJ lower than the mean daily intake for the high sucrose group, which over the 24 d period could contribute to the change in weight. The primary outcome of this study was to determine insulin, glucose, and fatty acid profiles, not change in weight.

Two randomised controlled trials examined the effect of reducing sugar intake on measures of weight status in children. Therefore, there is not sufficient evidence to develop a separate body of evidence statement in children. In one randomised controlled trial (Paineau 2008), after 10 months there were no differences in any measures of weight status in children in an intervention group to reduce fat and sugar and increase complex carbohydrates, compared to children in a control group. Measures of weight status included weight, BMI, BMI z-score, fat mass, fat-free mass, waist circumference, and hip circumference. The intervention group had significantly greater reductions in total energy intake ($P<0.01$), fat intake ($P<0.01$), and sugar intake ($P<0.01$) compared to the control group. A second randomised controlled trial (Rodearmel 2007) examined children in an intervention group to increase physical activity and reduce dietary sugar by substituting sugar with sucralose, compared to children in a control group. After 6 months, there were no significant differences in change in BMI z-score ($P=0.282$), percent body fat ($P=0.611$), or waist circumference ($P=0.462$) between these two groups. However, the intervention group more frequently maintained or reduced BMI-for-age ($P<0.05$) and less frequently increased BMI-for-age than in the control group ($P<0.05$) over a period of 6 months. Children in the intervention group had significantly more steps/day ($P<0.05$) and consumed fewer sugar-sweetened foods and less table sugar ($P<0.001$) than the control group. Energy intake was at least 420kJ (100kcal)/day lower in the intervention group compared to the control group 77% of the days in the 6-month period. It cannot be determined if the reduced sugar intake or the increased physical activity played a larger role, but it is likely that the significant effects were due to a combination of reduced total energy intake and increased physical activity rather than specifically sugar.

Overall, if a reduction in sugar intake results in a lower total energy intake then weight gain is arrested. However if there are specific effects of reducing sugar compared with reducing another macronutrient or carbohydrate type then it is essential that total energy intake be tightly controlled to investigate this. The methods of the above studies are quite different from one another and are confounded by other factors, making it difficult to develop a body of evidence statement. Further evidence of a higher quality is required and analysis of long standing cohorts to determine if habitual consumers of added sugars have higher body weight than those who do not would be helpful to build the evidence base.

References

Brynes, A. E., Edwards, C. M., Ghatei, M. A., Dornhorst, A., Morgan, L. M., Bloom, S. R. & Frost, G. S. 2003, "A randomised four-intervention crossover study investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men", *British Journal of Nutrition*, vol. 89, no. 2, pp. 207-218.

Drapeau, V., Despres, J., Bouchard, C., Allard, L., Fournier, G., Leblanc, C. & Tremblay, A. 2004, "Modifications in food-group consumption are related to long-term body-weight changes", *American Journal of Clinical Nutrition*, vol. 80, no. 1, pp. 29-37.

Paineau, D. L., Beaufils, F., Boulier, A., Cassuto, D. A., Chwalow, J., Combris, P., Couet, C., Jouret, B., Lafay, L., Laville, M., Mahe, S., Ricour, C., Romon, M., Simon, C., Tauber, M., Valensi, P., Chapalain, V., Zourabichvili, O. & Bornet, F. 2008, "Family dietary coaching to improve nutritional intakes and body weight control: a randomized controlled trial", *Archives of Pediatrics & Adolescent Medicine*, vol. 162, no. 1, pp. 34-43.

Rodearmel, S. J., Wyatt, H. R., Stroebele, N., Smith, S. M., Ogden, L. G. & Hill, J. O. 2007, "Small changes in dietary sugar and physical activity as an approach to preventing excessive weight gain: the America on the Move family study", *Pediatrics*, vol. 120, no. 4, pp. e869-79.

Vermunt, S. H., Pasman, W. J., Schaafsma, G., & Kardinaal, A. F. 2003, "Effects of sugar intake on body weight: a review", *Obesity Reviews*, vol. 4, no. 2, pp. 91-9.

Table 14.3 Studies used to make evidence statement for consumption of sugars and obesity

Reference [1]	**Vermunt (2003) [5206]**	**Brynes (2003) (6022)**	**Rodearmel (2007) (6672)**
Type of study [2]	Systematic review of 11 intervention studies, 4 prospective studies, and 1 cross-sectional study	RCT	RCT
Level of evidence	I	II	II
Intervention/ comparator [4]	Effect of dietary sugar relative to (1) low-energy sweeteners, (2) complex carbohydrates, and (3) fat on body weight	Investigate acute and medium-term effects of (1) high carbohydrate and high GI diet, (2) high sucrose diet, (3) high carbohydrate and low GI diet, and (4) low carbohydrate and high fat diet	Increase physical activity by 2000 steps per day and reduce energy intake by 420 kJ/day, primarily by replacing dietary sugar with sucralose VERSUS control (no dietary or physical activity advice)
N [5]	Low energy sweeteners: 4 intervention studies, 4 prospective studies, 1 cross-sectional study; complex carbohydrates: 5 intervention studies; fat: 2 intervention studies. Number of subjects not always given.	17	Children: 95; Parents: 109
Population/study information	Healthy-weight, overweight, and obese children and adults. Study duration 14 days - 6 months.	Moderately overweight, middle-aged, currently healthy men with one or more cardiac risk factors. UK. Crossover study with 1 week run-in period, then 24 days of treatment, then minimum of 3 week washout before next treatment, then 24 days of next treatment, etc.	Overweight children, aged 7-14 yrs (mean age 11 yrs), ~48% male, ~50% white, mean BMI ~25, mean BMI z-score ~1.7. Parents of overweight children. USA. 6-month intervention.
Quality [7]	N	0	P
Results [8]	Low energy sweeteners vs sugar: results are not consistent. Difficult to trust cohort studies because subjects concerned about weight might be using low-energy sweeteners. Low energy sweeteners replacing sugar does not seem to result in	Small but significant weight loss in the "low GI" group (-0.27 kg, SE 0.3) compared to the "high sucrose" group (+0.84 kg, SE 0.3, P<0.02). Energy intake was not significantly different between these 2 groups.	No difference in change in BMI z-score, percent body fat, or waist circumference between groups in children or adults. More children in intervention group maintained or reduced BMI-for-age and fewer increased BMI-for-age than in the control

	weight loss, but could aid in weight maintenance. Complex CHOs vs sugar: with energy restriction, CHO source is not important. With ad libitum, may be greater weight loss with complex CHO vs simple CHO, but a bit inconsistent, and difference may be due to differences in energy intake. Fat vs sugar: change in body weight is not different with sucrose vs fat diets. No statistics given.		group (P<0.05). Cannot determine if sugar reduction or increased physical activity was the cause.
Effect on risk	None	High sugar: increase	Reduce sugar: protect
Clinical importance	3	1	2
Clinical relevance	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

Table 14.3 Studies used to make evidence statement for consumption of sugars and obesity (cont.)

Reference [1]	**Paineau 2008 (6311)**	**Drapeau 2004 (6515)**
Type of study [2]	RCT	Retrospective cohort
Level of evidence	II	III
Intervention/ comparator [4]	Intervention to (1) reduce fat and increase complex carbohydrates, (2) reduce fat AND sugar and increase complex carbohydrates, and (3) no dietary advice	Using a 3d diet record and food questionnaire on perceived changes in consumption over past 5 years, identify dietary pattern modifications associated, including intake of sugar and sweet foods, with body weight and adiposity changes
N [5]	Group 1: 280 children and 280 parents (fat only); Group 2: 275 children and 274 parents (fat and sugar); Group 3: 394 children and 393 parents (control)	248
Population/study information [6]	Children: mean age 7.7y, mean BMI ~16.6, mean BMI z-score 0.65, ~52% girls, 18% overweight; Parents mean age 40.5y, mean BMI ~24.2, ~82% women, 33% overweight. France. 10-month intervention.	Parents and offspring (age >18y) in Quebec Family Study. 45% men. Ages 18-65y (mean 40y). Mean BMI at baseline 25.3. 6 year follow-up. Canada.
Quality [7]	P	P
Results [8]	There were no changes between groups in the children. In parents, the group that reduced both fat and sugar and increased complex carbohydrate had a reduction in BMI, reduction in fat mass, and a lower increase in hip circumference that were significantly different compared to the control group ($P<0.05$). Energy intake was significantly less in this group ($P<0.01$). There were no significant differences for change in weight, fat free mass, or waist circumference. There were no	Subjects consuming less sugar and sweet foods had a lower increase in the sum of skinfold thicknesses than subjects consuming more or the same amount of sugar and sweet foods during the past 5 years ($P<0.05$). Subjects consuming less sugar and sweet foods had a lower increase in waist circumference than subjects consuming the same amount of sugar and sweet foods during the past 5 years

	significant differences in the group that reduced fat only and increased complex carbohydrate.	(P<0.05). Energy intakes were not reported.
Effect on risk	Reduce sugar: protect	Reduce sugar: protect
Clinical importance	2	2
Clinical relevance	1	1
Generalisability	y	y
Applicability	y	y

INCLUDED STUDIES not in BOE < 5 studies

Sugars, other than pure fructose, and cardiovascular disease

One CT (Quality rating positive) and one cohort study (Quality rating positive) were not included in the fructose and CVD risk body of evidence because they were not about fructose *per se*: the CT by Brynes et al. (2003) was about sucrose; and the cohort study by Fung et al. (2009) was about sugar-sweetened beverages (based on high fructose corn syrups (HFCS 55% fructose) in the USA). There were insufficient studies (< 5) to form a body of evidence for sucrose and CVD risk or HFCS 55% and CVD risk.

References

Brynes, A. E., C. M. Edwards, et al. (2003). "A randomised four-intervention crossover study investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men." British Journal of Nutrition 89(2): 207-218.

Fung, T. T., V. Malik, et al. (2009). "Sweetened beverage consumption and risk of coronary heart disease in women." American Journal of Clinical Nutrition 89(4): 1037-42.

Sugars and bone health

1 cross-sectional study (Quality rating P) by Tucker et al. (2006) was not included in the sugars and bone health BOE because there were not enough studies to form a body of evidence statement.

References

Tucker, K. L., K. Morita, et al. (2006). "Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: the Framingham Osteoporosis Study." American Journal of Clinical Nutrition 84(4): 936-942.

Fructose and cancer

Three cohort studies (Quality ratings 3P) were not included in the fructose and cancer risk BOE because there were not enough studies to form a body of evidence statement. Data from these three studies was included in the sugars and cancer body of evidence, however.

References

Michaud, D. S., Fuchs, C. S. et al. 2005, "Dietary glycemic load, carbohydrate, sugar, and colorectal cancer risk in men and women." *Cancer Epidemiology, Biomarkers & Prevention,* vol. 14, no.1, pp. 138-47.

Michaud, D. S., Liu, S. et al. 2002, "Dietary sugar, glycemic load, and pancreatic cancer risk in a prospective study." *Journal of the National Cancer Institute,* vol. 94, no. 17, pp. 1293-300.

Nothlings, U., Murphy, S. P. et al. 2007, "Dietary glycemic load, added sugars, and carbohydrates as risk factors for pancreatic cancer: the Multiethnic Cohort Study." *American Journal of Clinical Nutrition*, vol. 86, no. 5, pp. 1495-501.

Sugars and hypertension

One RCT (Quality rating O) by Swarbrick et al. (2006) was not included in a sugars and hypertension body of evidence because there were not enough studies to form a body of evidence statement.

References

Swarbrick, M. M., K. L. Stanhope, et al. 2008, "Consumption of fructose-sweetened beverages for 10 weeks increases postprandial triacylglycerol and apolipoprotein-B concentrations in overweight and obese women." *British Journal of Nutrition* vol. 100 no. 5, pp. 947-952.

Type 2 diabetes

One systematic review (Laville and Nazare 2009) and one cohort study (Palmer et al. 2008) were used to consider sugars and type 2 diabetes. The search strategy and study selection criteria were not adequately described in the systematic review (Laville and Nazare. 2009), and a meta-analysis was not performed making it difficult to determine clinical impact. The cohort study (Palmer et al. 2008) was well designed and described, but was in a group of African-American women with a median age of 38 years (range 21 - 69 years), and median BMI of 28 kg/m^2. It is worth noting that 34% of participants in this cohort study had a family history of diabetes.

References

Laville, M and Nazare J. A. 2009, "Diabetes, insulin resistance and sugars." *Obesity Reviews,* vol. 10 Suppl 1, pp. 24-33.

Palmer, J. R. Boggs D. A et al. 2008, "Sugar-sweetened beverages and incidence of type 2 diabetes mellitus in African American women." *Archives of Internal Medicine,* vol. 168, no. 14, pp. 1487-92.

15. BEVERAGES (S1.1)

Evidence Statements

15. BEVERAGES (S1.1)

Search results

The initial search generated two databases Sugar Sweetened Beverages (SSB) with 578 references and Beverages with 2935 references which were combined. Duplicates (191) were manually removed resulting in a combined database of 3322 references for beverages and the specified disease outcomes. The detailed search is included in a separate document on searches. In all 88 papers were used to form 22 body of evidence statements for beverages and cardiovascular disease, weight and obesity, type 2 diabetes, dental and bone health; and a range of cancers including gastric, colorectal, liver, bladder, breast, ovarian and endometrial.

15.1 SUGAR SWEETENED BEVERAGES (SSB) and OBESITY

Does a particular intake of sugar sweetened beverages affect the risk of weight gain and obesity?		
Evidence statement		Consumption of sugar sweetened beverages is associated with increased risk of weight gain in adults and children.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	Level III and IV evidence from 2 meta analyses, 3 systematic reviews; 2 clinical trials, 4 cohorts.
Consistency	Good	2 meta analyses, 3 systematic reviews, 2 clinical trials and 5 cohort studies.
Clinical impact	satisfactory	Clinical impact appears small but significant, especially for those with high levels of consumption. Effect size estimation from meta-analysis of clinical trials r= 0.2-0.3 p<0.001.
Generalisability	good	Many of the studies are from North America and may not be fully applicable to Australian conditions.
Applicability	good	Applicable to groups with high consumption.

The studies used to make the body of evidence statements are shown in Table 15.1. Differences in study designs were noted. Concerns about case control and cohort studies not providing good evidence (changes in drinking behaviours of overweight individuals) and limited number of RCTs of large size or duration are raised. Evidence from one meta-analysis indicated that industry funded studies provided results of smaller effect size. One industry funded meta-analysis was required to slightly adjust their results due to concerns raised by other scientists. However, RCTs showed more consistency with 6/7 RCTs reported in meta analyses, systematic reviews or independently showing significant association in at least 1 subgroup. More good quality RCTs of adequate duration are

needed to improve the evidence base. Many of the significant associations were found in sub groups of cohort studies and RCTs so may be more significant for some populations. Effect seen is small but significant.

An additional longitudinal study published after search dates, provides additional evidence to support above recommendation (Fioritio et al. 2009).

Specific evidence in children was provided by one meta analysis that found effect size of SSB intakes on BMI to be medium in children (0.29 CI 0.22-0.35), and 4 cohort studies all providing evidence of an effect with higher BMI associated with intakes of SSB.

S1.7 Is there a dose response relationship of sugar sweetened beverages on body weight indices over the long term (≥ 1 year)?

Evidence from two meta analyses provide effect size but limited information is provided on dose response. The first meta analysis analysed 13 Level 111 and IV studies and determined effect size by study design, gender, age, type of beverage and self report or measured intakes. Data from Level 11 and 111 experimental studies found that effect sizes for body weight were different for each sex with effect size large for females (0.49 CI 0.17-0.72) and medium for males (0.17 CI 0.01-0.32); effect size was found to be medium for children (0.29 CI 0.22-0.35) and adults (0.15 CI 0.05-0.24); and was stronger when other sugared beverages were included with a medium effect size for mixed beverage intake (0.27 CI 0.21-0.34) compared to a smaller effect size for sugared soda drinks only (0.15 CI 0.04-0.25). Longitudinal studies were found to have smaller effect size (0.04 CI 0.01-0.07) compared to studies of experimental design (0.24 CI 0.18-0.30). Level IV evidence of all study designs found that reported soda drink intakes provided a smaller effect size (0.07 CI 0.07-0.08) than when intakes were measured (0.16 CI 0.08-0.23).

The second meta analysis of nine studies (7 cohort and 2 experimental) had eight studies in common with the first meta analysis, and combined the studies of different designs for analysis. As described above, effect sizes from longitudinal studies were smaller than that seen in experimental trials, and may have acted to dilute the effect size.

References

Dubois, L., Farmer, A., Girard, M. & Peterson, K. 2007, "Regular sugar-sweetened beverage consumption between meals increases risk of overweight among preschool-aged children.[see comment]", *Journal of the American Dietetic Association*, vol. 107, no. 6, pp. 924-34; discussion 934-5.

Faith, M. S., Dennison, B. A., Edmunds, L. S. & Stratton, H. H. 2006, "Fruit juice intake predicts increased adiposity gain in children from low-income families: weight status-by-environment interaction", *Pediatrics*, vol. 118, no. 5, pp. 2066-75.

Forshee, R. A., Anderson, P. A. & Storey, M. L. 2008, "Sugar-sweetened beverages and body mass index in children and adolescents: a meta-analysis.[see comment][erratum appears in Am J Clin Nutr. 2009 Jan;89(1):441-2]", *American Journal of Clinical Nutrition*, vol. 87, no. 6, pp. 1662-71.

Gibson, S. 2008, "Sugar-sweetened soft drinks and obesity: a systematic review of the evidence from observational studies and interventions", *Nutrition Research Reviews*, vol. 21, no. 2, pp. 134-147.

Malik, V. S., Schulze, M. B. & Hu, F. B. 2006, "Intake of sugar-sweetened beverages and weight gain: a systematic review", *American Journal of Clinical Nutrition*, vol. 84, no. 2, pp. 274-288.

Phillips, S. M., Bandini, L. G., Naumova, E. N., Cyr, H., Colclough, S., Dietz, W. H., Must, A. 2004, "Energy-dense snack food intake in adolescence: longitudinal relationship to weight and fatness", *Obesity Research*, vol. 12, no. 3, pp. 461-72.

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Tam, C., Garnett, S., Cowell, C., Campbell, K., Cabrera, G. & Baur, L. 2006, "Soft drink consumption and excess weight gain in Australian school students: Results from the Nepean study", *International Journal of Obesity*, vol. 30, no. 7, pp. 1091-1093.

Taylor, R. W., McAuley, K. A., Barbezat, W., Strong, A., Williams, S. M. & Mann, J. I. 2007, "APPLE Project: 2-y findings of a community-based obesity prevention program in primary school age children", *American Journal of Clinical Nutrition*, vol. 86, no. 3, pp. 735-742.

Vartanian, L. R., Schwartz, M. B. & Brownell, K. D. 2007, "Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis", *American Journal of Public Health*, vol. 97, no. 4, pp. 667-675.

Wolff, E., Dansinger, M. L. 2008, "Soft drinks and weight gain: how strong is the link?" *Medscape journal of medicine*, vol. 10, no. 8, pp. 189.

Table 15.1 Studies used to make evidence statement for sugar sweetened beverages, obesity and weight gain

Reference [1]	**Forshee et al. 2008 [1332]**	**Vartanian et al. 2007 [3345]**	**Gibson et al. 2008 [1426]**	**Malik et al. 2006 [2202]**	**Wolff et al. 2008 [14]**
Type of study [2]	Meta analysis	Meta analysis	systematic review	systematic review	systematic review
Level of evidence [3]	111-1	IV	IV	IV	IV
Intervention/ comparator [4]	BMI, intake of sugar sweetened beverages	SSB consumption, energy intake and BMI.	SSB intake and BMI, adiposity, weight change	SSB intakes, BMI, BMI z score, weight, adiposity, weight gain,	SSB intakes, BMI, BMI z score, weight, adiposity, weight gain,
N [5]	14,609	no population data.	115,988	136,772	116,699
Population/study information [6]	12 studies;10 longitudinal, 2 RCT children and adolescents age range 6-19yrs.	Soft drink & energy intake: 21 studies: 12 cross-sectional, 5 prospective, 16 CTs. SD and BMI: 27 studies 11 Cross sectional, 11 prospective, 5 CTs M and F children and adults	44 studies: 23 cross-sectional, 17 prospective, 4 CT, adults and children. M and F aged 2-65 years	30 studies (15 cross-sectional, 10 prospective, and 5 CTs) M and F aged 2 - 99 yrs	30 studies (15 cross-sectional, 10 prospective, and 5 CTs) M and F adults and children, aged 2-44 yrs
Quality [7]	O	O	O	O	O
Results [8]	SSB and BMI association near zero. Effect size increased after error in weighting corrected: random effects: 0.03 (-0.01 - 0.07)	Soft drink & energy intake: Longitudinal studies: r=0.24 p<0.001; clinical trials (short): r=0.21 P<.001. (significant heterogeneity) clinical trials (long): r=0.30 P<.001, no significant heterogeneity SD and BMI: Crosssectional :r=0.05	Small effect on BMI/wt/wt gain/adiposity in susceptible individuals or with high intakes of SSB Cross-sectional=23 (12 +ve, 11 NS or null) Longitudinal studies=17 (8 +ve, 9 non significant); clinical trials=4 (all +ve for at least some sub-groups).	Increased intake of SSB is associated with increased BMI. Cross-sectional studies=15 (9+ve, 5NS, 1 -ve); Prospective studies=10 (6 +ve,4NS); clinical trials=5 (all +ve)	6/15 cross-sectional studies showed +ve association, 6/10 cohorts +ve, 5/5 CTs +ve association with SSB and BMI in at least variable/group.

		p<.001 Longitudinal: r=0.09 p<.001 CT: r=0.24 p<0.001 (all +ve)			
Effect on risk Increase/None/Protect	None	increase	increase	increase	increase
Clinical importance[9]	2	1	2	1	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 15.1 Studies used to make evidence statement for sugar sweetened beverages, obesity and weight gain (cont)

Reference [1]	**Stookey et al. 2007 [3112]**	**Phillips et al. 2004 [2648]**	**Dubois et al. 2007 [1230]**	**Faith et al. 2006 [1279]**	**Tam et al. 2006 [3180]**
Type of study [2]	cohort	cohort	cohort	cohort	cohort
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	replacement of SSB with H2O and Energy Intake	Energy dense snack food and soft drink intake and BMI z score	consumption of SSB and risk of overweight	consumption of fruit juice (not specified) and BMI	consumption of cordials and soft drinks and BMI over 5 yrs
N [5]	118	196	1944	1797	268
Population/ study information [6]	overweight dieting females aged 25-50 yrs	non obese girls aged 9-10 yrs	Longitudinal Study of Child Development in Québec Canadian children aged 4.5 yrs	Women, Infants, Children Supplemental Nutrition Program. US Children 1-5 yrs monitored over 4 yrs	Australian school children aged 7.7 yrs over 5 yrs
Quality [7]	p	P	P	P	P
Results [8]	Controlling total	only soft drink intake	regular SSB	In children at risk of	Median CHO intake

	beverage vol, food composition, and energy expenditure, each 1 unit of soft drinks replaced by water associated with a 9 (2) kcal/d lower energy intake P<0.05, If all SSBs were replaced by water would result in predicted reduction of 200kcal/day	associated with BMI z score. Q3 and Q4 of % kJ from soft drink had BMI z scores 0.17 higher than Q1 p<0.001	consumption between meals OR of o/wt in consumers vs non consumers OR 2.4 (CI 1.105-5.054, p ≤ 0.05)	o/wt or o/wt, increased FJ associated with increased adiposity gain. 1 serve FJ/day associated with ß=0.009 p<0.01.	from soft drink/cordial 10g/d higher (P=0.002) in children who were overweight/obese at follow-up vs acceptable BMI at both baseline and follow-up, and 23g/d higher (P=0.019) vs those overweight/obese at baseline but with acceptable BMI at follow-up. No associations with fruit juice/drink or milk.
Effect on risk Increase/None/ Protect	Increase (reduced intake-protect)	increase	increase	increase for fruit juice (Type not specified)	Increase for soft drink/cordial None- fruit juice
Clinical importance[9]	1	1	1	1	1
Clinical relevance [10]	2	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 15.1 Studies used to make evidence statement for sugar sweetened beverages, obesity and weight gain (cont.)

Reference [1]	**Taylor et al. 2007 [3213]**	**Sichieri et al. 2009 [6]**
Type of study [2]	Cluster CT	RCT
Level of evidence [3]	111-1	11
Intervention/ comparator [4]	height, weight, waist circumference, blood pressure, diet (validated food questionnaire), physical activity at baseline,1 and 2 yrs.	Reduced intake of Sugar sweetened carbonated beverages
N [5]	730	435 controls 608 intervention
Population/ study information [6]	APPLE Project NZ Children, 4 intervention and 3 control schools. Intervention n=250 M 138, age 7.7 (1.8) Control n=219 M 108, age 7.7 (1.6)	Intervention group: BMI= 18.3(3.6); Male: 46.9%; Overweight: 15.8%; Age: 10.9 (0.81) years. Comparator group: BMI= 18.2 (3.2) (P=0.69); Male: 47.4% (P=0.90); Overweight: 14.3% (P=0.70); Age= 10.9 (0.75) years (P=0.30)
Quality [7]	P	P
Results [8]	Intervention vs control: lower BMI z score mean 0.09 (0.01- 0.18) after 1 yr, 0.26 (0.21- 0.32) at 2 yrs. Decrease in waist circumference -1.0 (-2.0 - 0.0) and systolic blood pressure -2.9 (-5.2- -0.6). Intervention used less soft drinks (67% of control P =0.04) and fruit juice/drinks(70%; P=0.03) and more fruit P= 0.01.	significant decrease in daily intake of carbonated drinks in the intervention vs. control (mean difference -56 ml (95% CI -119- -7 ml) and NS overall reduction in BMI, P=0.33. However, in students overweight at baseline, the intervention group showed greater BMI reduction (-0.4kg/m2 vs -0.2kg/m2 control group but NS (P=0.11)), but was significant in girls (regression co-efficient -0.01, P=0.009).
Effect on risk Increase/None/Protect	Increase (reduced intake-protect)	Increased (reduced intake protect in overweight girls only)
Clinical importance[9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

15.2 FRUIT JUICE and OVERWEIGHT and OBESITY

Does a particular intake of fruit juice affect the risk of weight gain and obesity?		
Evidence statement		Consumption of fruit juice is not associated with increased risk of weight gain in children.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level III evidence from 1 clinical trial (children) and 7 cohort studies (6 in children, 1 in adults).
Consistency	Poor	1 clinical trial and 3 cohort studies found negative associations, but 4 cohorts found no association.
Clinical impact	Poor	Unable to estimate clinical impact as the 4/8 studies showing weight status change use 4 different statistical measures.
Generalisability	Good	Studies are from North America, Australia, UK, Italy and Germany.
Applicability	Good	Applicable to Australia.

The studies used to make the body of evidence statement are shown in Table 15.2. There were eight studies in total, seven studies in children (six cohort and one clinical trial) and one cohort study in adults. Overall, 4/8 studies found increased risk of weight gain. Four of seven studies in children found no association whilst two cohorts and one clinical trial found increased risk of weight gain in children. The single cohort study in adults found increased risk of weight gain. Intervention studies that reduce sugar sweetened beverages intake and of RCT design were more likely than cohort studies to show increased risk of weight gain. There was only one such trial in children and it demonstrated that reduction in intake was protective of weight gain. The evidence statement can only be made for children as there is insufficient data in adults. It received a D grading because the consistency is poor and further evidence is required to be confident in the evidence statement.

References

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Johnson, L., Mander, A. P., Jones, L. R., Emmett, P. M. & Jebb, S. A. 2007, "Is sugar-sweetened beverage consumption associated with increased fatness in children?" Nutrition, vol. 23, no. 7-8, pp. 557-563

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Tam, C., Garnett, S., Cowell, C., Campbell, K., Cabrera, G. & Baur, L. 2006, "Soft drink consumption and excess weight gain in Australian school students: Results from the Nepean study", International Journal of Obesity, vol. 30, no. 7, pp. 1091-1093

Taylor, R. W., McAuley, K. A., Barbezat, W., Strong, A., Williams, S. M. & Mann, J. I. 2007, "APPLE Project: 2-y findings of a community-based obesity prevention program in primary school age children", American Journal of Clinical Nutrition, vol. 86, no. 3, pp. 735-74

Table 15.2 Studies used to make evidence statement for fruit juice, obesity and weight gain

Reference [1]	**Faith et al. 2006 [1279]**	**Tam et al. 2006 [3180]**	**Taylor et al. 2007 [3213]**
Type of study [2]	cohort	cohort	Cluster CT
Level of evidence [3]	111-2	111-2	111-1
Intervention/ comparator [4]	Serves/day of fruit juice and adiposity gain (defined as Δ in age and gender standardised BMI/month i.e. BMI z score slope)	Grams CHO/day consumed from fruit juice and fruit juice drinks and BMI z-score change over 5 yrs	2 yr controlled school intervention targeting reductions in sweetened drinks and increased fruit and vegetable intake and activity. Assessed dietary fruit juice, BMI z-score, waist circumference at 1 and 2 yrs.
N [5]	2801	268	730
Population/ study information [6]	Women, Infants, Children Supplemental Nutrition Program. US Children 1-4 yrs monitored over 4 yrs	Australian school children aged 7.7 yrs over 5 years	APPLE Project NZ Children, 4 intervention and 3 control schools. Intervention n=250 M 138, age 7.7 (1.8) Control n=219 M 108, age 7.7 (1.6)
Quality [7]	P	P	P
Results [8]	Each additional serve of FJ was associated with increased adiposity gain: 1 serve FJ/day associated with ß=0.009 p<0.01 (in children with ≥ 85th percentile BMI z-score) and for all children ß=0.005 p<0.01.	No associations with fruit juice/drink Those with acceptable BMI consumed similar amounts of fruit juice/drink 14 (0-48) g/day compared to BMI gainers/losers/or those overweight or obese [8.6 (0–59) 13 (0–41.4) 14 (0–44) 0.734g/day respectively] p=0.734	Intervention used less soft drinks (67% of control P =0.04), fruit juice/drinks (70% of control; P=0.03) and more fruit P=0.01. Intervention vs. control: lower BMI z score mean 0.09 (0.01- 0.18) after 1 yr, 0.26 (0.21- 0.32) at 2 yrs. Decrease in waist circumference -1.0 (-2.0- -0.0cm) and systolic blood pressure -2.9 (-5.2 - -0.6mmHg). An interaction existed between intervention group and overweight status (P = 0.029), mean BMI z score reduced in normal-weight -0.29 (-0.38- -0.21) but not o/wt -0.02 (-0.16 - 0.12) intervention children vs.

			controls.
Effect on risk Increase/None/ Protect	Increase in all children but greater in those with BMI z-score ≥ 85th percentile.	None	Increase (reduced intake-protect)
Clinical importance[9]	1	2	1
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

Table 15.2 Studies used to make evidence statement for fruit juice, obesity and weight gain (cont.)

Reference [1]	**Newby et al. 2004 [2490]**	**Libuda et al. 2008 [2087]**	**Johnson et al. 2007 [227]**
Type of study [2]	cohort	cohort	cohort
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	consumption of beverages including fruit juice and annual weight change	consumption of beverages including fruit juice and BMI standard deviation score	SSB consumption, including fruit juices at ages 5 yrs and 7 yrs and body fatness (dual-energy x-ray absorptiometry) at age 9 yrs in British children
N [5]	1345	244 subjects between 9 and 18	n = 521 at age 5yrs n = 682 at age 7yrs
Population/ study information [6]	children age 2 to 5 years participating in the North Dakota Special Supplemental Nutrition Program for Women, Infants, and Children (WIC)	Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) study	Avon Longitudinal Study of Parents and Children

Quality [7]	P	P	P
Results [8]	regression adjusted for age, sex, energy intake, change in height, and additional sociodemographic variables, weight change was not significantly related to intakes (per ounce) of fruit juice (ß=0.01 lb/year: -0.01 to 0.20, P=.28), fruit drinks (ß=-0.03 lb/year, -0.07 to 0.01, P=.28),	BMI standard deviation scores (BMI SDS) increased with increased fruit juice consumption (+0·096 SDS/MJ increase in fruit juice intake P=0·01) in girls	Change in fat mass at 9 yrs/serve FJ at 5 yrs -0.11 (-0.61,-0.38)kg, p= 0.66; Change in fat mass at 9 yrs/serve FJ at 7 yrs 0.25(-0.08, 0.58)kg, p= 0.14
Effect on risk Increase/None/Protect	none	Increase in girls	None
Clinical importance[9]	2	1	2
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	**y**	y	y

Table 15.2 Studies used to make evidence statement for fruit juice, obesity and weight gain

Reference [1]	**Striegel-Moore 2008 [3121]**	**Bes-Rastrollo 2006 [805]**
Type of study [2]	cohort	cohort
Level of evidence [3]	111-2	111-2
Intervention/ comparator [4]	Beverages including fruit juice and BMI	consumption of foods and beverages including fruit juices and weight gain in a Mediterranean population
N [5]	2371 girls (1210 black, 1161 white)	7194 men and women
Population/ study information [6]	USA 9 or 10 years until age 19 years	mean age of 41 years who were followed-up for a median of 28.5 months with mailed questionnaires
Quality [7]	P	P
Results [8]	Estimates of the predicted change in BMI for each additional 100 g/day FJ ß=0.005 (SE 0.007) NS and FJ drink ß=0.009 (SE 0.007) NS.	Adjusted OR for any wt gain ≥1 kg for Q1 vs Q5 of sweetened fruit juice intake are Q1= 1.00 (ref.) Q2=0.99 (0.84 - 1.17) Q3=1.08 (0.91-1.28) Q4=1.08 (0.92 - 1.27) Q5=1.16 (0.99 - 1.36, p trend =0.039)
Effect on risk Increase/None/ Protect	None	Increase for sweetened FJ
Clinical importance[9]	2	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

15.3 SUGAR SWEETENED BEVERAGES and BONE HEALTH

Does a particular intake of sugar sweetened beverages affect bone health?		
Evidence statement		Consumption of soft drinks is associated with increased risk of reduced bone strength.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	satisfactory	1 meta-analysis (1 cohort, 2 case control and 2 cross sectional), 1 clinical trial, 1 case control, 2 cohorts.
Consistency	good	Four of the 6 studies showed negative association of soft drink intake and BMD; and meta- analysis of 4 studies and 1 case control found negative association with fracture risk.
Clinical impact	satisfactory	Meta-analysis found effect size for soft drink and BMD r = - 0.3 and fracture risk r = 0.06.
Generalisability	good	Studies in younger and 1 older population, similar to Australian populations
Applicability	good	Applicable to Australian conditions.

The studies used to make the body of evidence statements are shown in Table 15.3. The included studies report associations with variables of bone health including BMD, bone remodelling indices and fracture risk. There were six studies assessing SSB and BMD, with 4/6 reporting negative associations (2/4 studies from the meta-analysis, one CT and one cohort study showing effect in females for cola drinks only, including diet). Increased risk of fracture was associated with soft drink intake (meta analysis of four studies and one independent case control study). Three studies (one meta analysis, 1 case control and 1 cohort) found negative associations of soft drink and milk intake. Meta analysis found industry funded studies had reduced effect size, suggesting bias.

References

Kristensen, M., Jensen, M., Kudsk, J., Henriksen, M. & Molgaard, C. 2005, "Short-term effects on bone turnover of replacing milk with cola beverages: a 10-day interventional study in young men", *Osteoporosis International*, vol. 16, no. 12, pp. 1803-8.

Libuda, L., Alexy, U., Remer, T., Stehle, P., Schoenau, E. & Kersting, M. 2008, "Association between long-term consumption of soft drinks and variables of bone modeling and remodeling in a sample of healthy German children and adolescents", *American Journal of Clinical Nutrition*, vol. 88, no. 6, pp. 1670-1677.

Manias, K., McCabe, D. & Bishop, N. 2006, "Fractures and recurrent fractures in children; varying effects of environmental factors as well as bone size and mass", *Bone*, vol. 39, no. 3, pp. 652-657.

Tucker, K. L., Morita, K., Qiao, N., Hannan, M. T., Cupples, L. A. & Kiel, D. P. 2006, "Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: the Framingham Osteoporosis Study", *American Journal of Clinical Nutrition*, vol. 84, no. 4, pp. 936-942.

Vartanian, L. R., Schwartz, M. B. & Brownell, K. D. 2007, "Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis", *American Journal of Public Health*, vol. 97, no. 4, pp. 667-675.

Table 15.3 Studies used to make evidence statement for sugar sweetened beverages and bone

Reference [1]	**Vartanian 2007 [3345]**	**Kristensen et al. 2005 [83]**	**Manias et al. 2006 [2215]**	**Libuda et al. 2008 [2086]**	**Tucker et al. 2006 [3284]**
Type of study [2]	Meta analysis	Controlled trial	case control	cohort	cohort
Level of evidence [3]	111-2	111-1	111-2	111-2	111-2
Intervention/ comparator [4]	serum calcium levels, BMD, fracture risk and soft drink (SD) consumption	BMD and soft drink intake/cross over design: low Ca^{2+}diet + 2.5 L cola or milk	recurrent fractures vs. first fracture vs fracture free controls	BMC (bone mineral content), polar strength strain index and soft drink (SD) intakes	BMD and soft drink intake
N [5]	For BMD: 2 cross sectional, 1 cohort, 1 case control For fracture: 1 case control, 2 cross sectional and 1 not defined	11	150 (50 in each group)	228	2538
Population/study information [6]	longitudinal	Denmark Males aged 22-29 yrs	UK M and F aged 4-16 yrs	Germany healthy children aged 6-18yrs	US Framingham Offspring Cohort n=2538
Quality [7]	O	P	P	P	P
Results [8]	SD intake and BMD, 2/4 studies negative association between SD intake and BMD and 2 NS, average r= -0.3. Fracture risk and SD: SD intake and fracture risk: r=0.06 (no p values reported).	Serum phosphate (P<0.001), 1,25(OH)2D (P<0.001), PTH (P=0.046) and osteocalcin (P<0.001) increased in cola vs milk period. Bone resorption markers	Carbonated drink consumption was higher in all fractures vs controls (p=0.016), one fracture vs control, (p=0.0716), recurrent fractures vs control (p=0.0182) and recurrent fractures	Long-term intake of SD (inc non-caffeine): -ve association with BMC P < 0.05 & bone modelling indicies P<0.05 Long-term intake of caffeinated SD -ve and milk intake positive	Cola intake associated with lower BMD at each hip site, but not spine, in women not men P <.001. Mean BMD of daily cola drinkers 3.7% lower at femoral neck and 5.4% lower at

	Definition of effect size; ≤0.10 small, 0.25 medium and ≥0.40 large.Effect sizes of Industry funded studies less than non industry funded.	increased after cola vs milk period p<0.001.	vs. 1 fracture (p=0.0359). Milk intake was lower in recurrent fractures vs. controls (p=0.0097) and recurrent fractures vs. one fracture (p=0.0162)	association with bone remodelling indices p < 0.05. All SD intake - ve association with total protein and milk intake, but not with potential renal acid load.	Ward's area vs. those with <1 serving cola/mo. Similar results for diet cola and decaff cola P<- 0.05. No significant relations with non-cola carbonated beverages.
Effect on risk Increase/None/Protect	increase	increase	increase	increase	increase for cola only in females
Clinical importance[9]	2	1	1	1	2
Clinical relevance [10]	1	2	1	2	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

15.4 SUGAR SWEETENED BEVERAGES and DENTAL HEALTH

Does a particular intake of soft drink affect dental health?		
Evidence statement		Consumption of soft drink is associated with increased risk of dental caries in children.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 systematic review (4 studies, design not given) and 3 cohort studies.
Consistency	Excellent	Studies showed positive association of soft drink consumption with increased caries rates. Meta-analysis found Industry Funded studies had reduced effect size, suggesting bias.
Clinical impact	Good	OR of 1.45 to 3.0 with highest intakes of soft drink consumption.
Generalisability	Satisfactory	All studies in children, most studies in the US.
Applicability	Satisfactory	Applicable to Australian conditions.

The studies used to make the body of evidence statements are shown in 15.4. The included studies report associations with variables of dental health, presence of caries and dental erosions. The majority of studies were from the USA. There were no studies in adults; all studies were performed in children, concentrating on the primary dentition. The review study investigated soft drinks only and not all sugar sweetened beverages such as fruit juices or cordials. The 3 additional cohort studies all showed increased caries risk with SSB intake.Study subjects were often from low SES demographic groups and exposure to fluoridated water varied.

Three additional cohort studies received from the NHMRC add support to this recommendation. One study found that children who changed from low to high consumption of soft drinks had 1.75 times higher mean number of new decayed, missing and filled tooth surfaces vs. low consumers (Lim et al. 2008). The second study found higher exposures to 100% juice at snacks (at age 2 years) and soda pop at meals (at 2 years and 1-5 years) increased caries risk ($P < 0.05$) (Marshall et al. 2005), and the third study found low SES children had greater consumption of soft drinks and powder based beverages and had higher mean number of decayed and filled surfaces (Hamasha et al. 2006).

References

Levy, S. M., Warren, J. J., Broffitt, B., Hillis, S. L. & Kanellis, M. J. 2003, "Fluoride, beverages and dental caries in the primary dentition", *Caries Research*, vol. 37, no. 3, pp. 157-165.

Marshall, T. A., Eichenberger-Gilmore, J. M., Broffitt, B. A., Warren, J. J. & Levy, S. M. 2007, "Dental caries and childhood obesity: roles of diet and socioeconomic status", *Community Dentistry & Oral Epidemiology*, vol. 35, no. 6, pp. 449-458.

Vartanian, L. R., Schwartz, M. B. & Brownell, K. D. 2007, "Effects of soft drink consumption on nutrition and health: a systematic review and meta-analysis", *American Journal of Public Health*, vol. 97, no. 4, pp. 667-675.

Warren, J. J., Weber-Gasparoni, K., Marshall, T. A., Drake, D. R., Dehkordi-Vakil, F., Dawson, D. V., Tharp, K. M. 2009, "A longitudinal study of dental caries risk among very young low SES children", *Community Dentistry & Oral Epidemiology*, vol. 37, no. 2, pp. 116-22.

Table 15.4 Studies used to make evidence statement for sugar sweetened beverages and dental health

Reference [1]	**Vartanian 2007 [3345]**	**Marshall 2007 [2230]**	**Warren 2009 [3418]**	**Levy et al. 2003 [2071]**
Type of study [2]	Systematic literature review	cohort	cohort	cohort
Level of evidence [3]	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Soft drink intake and dental caries	Grams soda pop/day and number of caries	Grams and number of serves of sugar sweetened beverages/day and number of caries	Grams and number of serves of sugar sweetened beverages/day and number of caries
N [5]	not given	427	128	291
Population/study information [6]	All studies in children. 4 studies -designs not given from USA(3) and Iceland (1).	US children from the Iowa Fluoride Study, dental assessment in children aged 4.5-6.9 yrs	US toddlers age 6-24 months from low SES receiving nutritional support	US Iowa Fluoride Study, aged 6 wks to 4 yrs, 6.7% male, 53.3% female
Quality [7]	O	P	P	P
Results [8]	4 studies found small +ve association between soft drink consumption and dental caries (r = 0.03). No effect in diet drinks. Effect sizes explanation (0.10 small, 0.25 medium,>0.40 large).	Children with caries had higher soda pop intakes P < 0.05: at 2 y: 16 g vs. 0 g; 3 years: 32 g vs. 0 g; 1–5 years: 44 g vs. 28 g; all P < 0.01). Regression for caries prediction: soda-pop intakes displaced by mother's education, leaving 'at risk' of overweight and mother's education as significant predictors.	sugar sweetened beverage linked to increased caries risk OR 3.0 (CI 1.1-8.6)	Intake of SSB/non-formula milk(incl flav.) at age 6wks-12mo and caries (1.70 p<0.0005), non-formula milk (incl flav.) at age 24-36 mo (0.69 =0.05). SSB intake at age 12-24 mo (1.42 p=0.05), but NS after controlling for SSB/non-formula milk (incl.flav.) at age 6wks-12 mo.
Effect on risk Increase/None/Protect	increase	increase	increase	Increase, indicates importance of early dietary intake.
Clinical importance[9]	1	2	1	1

Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

15.5 COFFEE and GASTRIC CANCER

Does a particular intake of coffee affect the risk of gastric cancer?		
Evidence statement		Consuming more than 4 cups of coffee a day is associated with increased risk of gastric cancer
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from one meta analyses of 23 studies (16 case control, 7 cohort studies) and 1 cohort study.
Consistency	Good	Meta analysis by study design shows no significant effect. Only 1 cohort not included in the meta-analysis showed increased risk.
Clinical impact	Poor	No clinical impact.
Generalisability	Good	Studies from USA (5), Europe (8), Japan (6), Other Asia (2), S America (2)
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in 15.5. The meta analysis analysed 23 studies with 16 case control (10 hospital based and 5 population based, one not given) and 7 cohort studies. No studies showed significant associations. When risk was calculated by cohort, case control and hospital case control, all found non-significant effect. The risk estimates were found to differ by country of origin, and substantial methodological differences were noted between studies. The single cohort study showed increased risk with increasing coffee consumption.

References

Botelho, F., Lunet, N. & Barros, H. 2006, "Coffee and gastric cancer: systematic review and meta-analysis", *Cadernos de Saude Publica*, vol. 22, no. 5, pp. 889-900.

Larsson, S. C., Giovannucci, E. & Wolk, A. 2006, "Coffee consumption and stomach cancer risk in a cohort of Swedish women", *International Journal of Cancer*, vol. 119, no. 9, pp. 2186-9.

Table 15.5 Studies used to make evidence statement for coffee and gastric cancer

Reference [1]	**Botelho et al. 2006 [72]**	**Larsson et al. 2006 [2022]**
Type of study [2]	Meta-analysis of 23 studies (10 hospital case control, 5 population case control, 1 case control, 7 cohort studies)	cohort
Level of evidence [3]	Level 111-2	111-2
Intervention/ comparator [4]	Coffee consumption and risk of gastric Cancer	coffee and gastric cancer
N [5]	229,608	61,433
Population/study information [6]	Europe (8), USA (5), Japan (5), other Asia (3), South America(2) M and F Black, White	Adult Swedish women
Quality [7]	O	P
Results [8]	23 studies Overall highest vs lowest intake OR=0.97 (0.76-1.37) Cohort studies OR=1.02 (0.76-1.37) Case control population based OR=0.90 (0.70-1.15) Case control hospital based OR= 0.97 (1.02-1.57) No beneficial or adverse effect of coffee on gastric cancer	HR 1.49 (CI 0.97–2.27) for women who drank 2–3 cups /d and HR1.86 (CI 1.07–3.25) for ≥ 4 cups/d vs ≤ 1 cup/day (p for trend= 0.01). An increase of 1 cup of coffee per day was associated with a statistically significant 22% increased risk of stomach cancer HR1.22 (CI 5 1.05–1.42).
Effect on risk Increase/None/Protect	none	increase
Clinical importance[9]	2	2
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

15.6 COFFEE and HEPATOCELLULAR CANCER

Does a particular intake of coffee affect the risk of hepatocellular cancer?		
Evidence statement		Consumption of coffee is associated with reduced risk of hepatocellular cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	satisfactory	Level 111 evidence from two meta analyses of 10 studies, including 6 case-control (5 in common), 4 cohort (all in common).
Consistency	satisfactory	Two meta analyses consistent but included same studies (except for 1 additional case control study).
Clinical impact	Good	Coffee protective for liver cancer in liver disease and in healthy subjects with 30-50% risk reduction in consumers compared to non-consumers.
Generalisability	satisfactory	Studies for Japan (5), Italy (3), Greece (1)
Applicability	satisfactory	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.6. The two meta analyses had studies in common, but conclusions consistent. The meta-analysis by Larsson et al. found all studies had negative association with liver cancer with 6/11 significant.

Differences in types of coffee (boiled, decaffeinated, filter, instant) used in different countries make comparisons difficult with studies not usually identifying coffee type. Brewed coffee is commonly consumed in US, while filtered coffee is common in European countries and Japan. Instant coffee is not as commonly consumed except perhaps in Australia and the UK.

References

Bravi, F., Bosetti, C., Tavani, A., Bagnardi, V., Gallus, S., Negri, E., Franceschi, S., La Vecchia, C. 2007, "Coffee drinking and hepatocellular carcinoma risk: a meta-analysis", *Hepatology*, vol. 46, no. 2, pp. 430-5.

Larsson, S. C. & Wolk, A. 2007, "Coffee consumption and risk of liver cancer: a meta-analysis.[see comment]", *Gastroenterology*, vol. 132, no. 5, pp. 1740-5.

Table 15.6 Studies used to make evidence statement for coffee and hepatocellular cancer

Reference [1]	**Bravi et al. 2007 [43]**	**Larsson et al. 2007 [49]**
Type of study [2]	meta analysis of 6 case control and 5 cohort studies	meta analysis
Level of evidence [3]	Level 111-2	Level 111-2
Intervention/ comparator [4]	Cups/day of coffee consumption and risk of Hepatocellular Cancer	Cups/day of coffee consumption and risk of Hepatocellular Cancer
N [5]	>235,525	241,406
Population/study information [6]	Italy (3), Japan (7), Greece (1) male and female adults	Japan (6) and Southern Europe (3- Italy and Greece) male and female adults
Quality [7]	O	O
Results [8]	RR for coffee vs non-drinkers 0.54 (0.38-0.76) for case control studies and 0.64 (0.56-0.74) for cohort studies	RR for increments of 2 cups coffee/day 0.69 (0.55– 0.87) for persons without a history of liver disease and 0.56 (0.35– 0.91) for those with a history of liver disease.
Effect on risk Increase/None/Protect	protect	protect
Clinical importance[9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

15.7 COFFEE and BREAST CANCER

Does a particular intake of coffee affect the risk of breast cancer?		
Evidence statement		Consumption of coffee is not associated with risk of breast cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from one meta analyses of 18 studies (9 case-control and 9 cohort studies).
Consistency	Satisfactory	Eleven of 18 studies (cohort and case control) showed a small reduced risk but the pooled estimated risk is not significant.
Clinical impact	Poor	No significant impact.
Generalisability	Satisfactory	Studies from USA (7), Europe (8), Japan (2), Israel (1)
Applicability	Satisfactory	applicable to Australian conditions.

The study used to make the body of evidence statement is shown in Table 15.7. One meta-analysis of 18 studies from the USA, Europe, Japan and Israel found a small non significant reduction in risk in highest vs lowest or non coffee drinkers: RR 0.95 (0.90-1.00). No statistically significant heterogeneity was found among individual studies, although for Asian studies the I^2 % was high (58.6).

References

Tang, N., Zhou, B., Wang, B. & Yu, R. 2009, "Coffee consumption and risk of breast cancer: a metaanalysis", *American Journal of Obstetrics and Gynecology*, vol. 200, no. 3, pp. 290.e1-290.e9.

Table 15.7 Studies used to make evidence statement for coffee and breast cancer

Reference [1]	**Tang et al. 2009 [3194]**
Type of study [2]	meta analysis of 9 cohort and 9 case control studies.
Level of evidence [3]	Level 111-2
Intervention/ comparator [4]	coffee and breast cancer
N [5]	25,250
Population/study information [6]	Adults,: Europe (8), USA (7), Asia (2), Israel (1)
Quality [7]	O
Results [8]	Cohort studies: 5/9 reduced risk and overall RR 0.95 (0.88-1.02) Case control: 6/9 reduced RR and overall RR 0.95 (0.87-1.04) Overall: small reduced risk of breast cancer with highest vs non/lowest coffee intake RR 0.95 (0.90-1.00). Studies for Asia NS
Effect on risk Increase/None/Protect	none
Clinical importance[9]	2
Clinical relevance [10]	1
Generalisability	y
Applicability	y

15.8 COFFEE and ENDOMETRIAL CANCER

Does a particular intake of coffee affect the risk of endometrial cancer?		
Evidence statement		Consumption of coffee is associated with reduced risk of endometrial cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level 111 evidence from 1 meta-analysis of 9 studies (2 cohort, 7 case control)
Consistency	Poor	5/9 studies show significant negative association; Significant heterogeneity.
Clinical impact	Satisfactory	7% reduction for each additional cup per day.
Generalisability	Satisfactory	Studies from Europe (5), Asia (2), Canada (1)
Applicability	Satisfactory	Applicable to Australian conditions.

The study used to make the body of evidence statement is shown in Table 15.8. One meta analysis provided analysis of nine studies from Europe, Asia and Canada. Of the studies five showed significant reduction, two non- significant reduction and two non-significant increased risk. However, significant heterogeneity was found between the studies with the data from low to moderate drinking groups showing least (p=0.107) and therefore may be more reliable. Differences in types of coffee (boiled, decaffeinated, filter, instant) used in different countries make comparisons difficult with studies not usually identifying coffee type. Brewed coffee is commonly consumed in US, while filtered coffee is common in European countries and Japan. Instant coffee is not as commonly consumed except perhaps in Australia and the UK.

References

Bravi, F., Scotti, L., Bosetti, C., Gallus, S., Negri, E., La Vecchia, C. & Tavani, A. 2009, "Coffee drinking and endometrial cancer risk: a metaanalysis of observational studies", *American Journal of Obstetrics and Gynecology*, vol. 200, no. 2, pp. 130-135.

Table 15.8 Studies used to make evidence statement for coffee and endometrial cancer.

Reference [1]	**Bravi et al. 2009 [185]**
Type of study [2]	meta analysis
Level of evidence [3]	Level 111-2
Intervention/ comparator [4]	Coffee consumption and risk of endometrial Cancer Low-moderate (>2 to<4 cups/d), heavy drinkers (≥3 cups/d)
N [5]	21,775
Population/study information [6]	9 studies (2 cohort, 7 case control) from Europe (5), Asia (2), Canada (1)
Quality [7]	O
Results [8]	Coffee drinkers vs non-drinkers: RR=0.80 (0.68-0.94), but significant heterogeneity found between studies. Low-moderate drinkers (>2 to <4 cups/day) vs non drinkers RR= 0.87 (0.78-0.97); heavy drinkers vs non drinkers RR= 0.64 (0.48-0.86); increase of 1 cup/d RR= 0.93 (0.89-0.97). Inverse relation between coffee and endometrial cancer. Data of low-mod drinkers showed least heterogeneity and may be more reliable. 2 studies NS increase RR, 2 studies NS reduced RR and 5 studies significant reduced RR.
Effect on risk Increase/None/Protect	protect
Clinical importance[9]	1
Clinical relevance [10]	1
Generalisability	y
Applicability	y

15.9 COFFEE and COLORECTAL CANCER

Does a particular intake of coffee affect the risk of colorectal cancer?		
Evidence statement		Consumption of coffee is not associated with risk of colorectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 1 Systematic review (18 studies, 15 case control and 3 cohort) and 3 cohort studies.
Consistency	Satisfactory	11/15 case control studies no significant effect and 6/6 cohort studies no significant effect.
Clinical impact	Poor	No significant protection noted.
Generalisability	Satisfactory	Studies from Europe (10), Nth America (6), Asia (4), Sth America (1).
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement is shown in Table 15.9. One systematic review provided analysis of 18 studies from Europe, Asia and the Americas and found no association. Two of the three additional cohort studies showed sub-group analysis of protection in women but NS overall.

References

Lee, K. J., Inoue, M., Otani, T., Iwasaki, M., Sasazuki, S., Tsugane, S., Group, J. S. 2007, "Coffee consumption and risk of colorectal cancer in a population-based prospective cohort of Japanese men and women", *International Journal of Cancer*, vol. 121, no. 6, pp. 1312-8.

Michels, K. B., Willett, W. C., Fuchs, C. S. & Giovannucci, E. 2005, "Coffee, tea, and caffeine consumption and incidence of colon and rectal cancer", *JNCI: Journal of the National Cancer Institute*, vol. 97, no. 4, pp. 282-292.

Oba, S., Shimizu, N., Nagata, C., Shimizu, H., Kametani, M., Takeyama, N., Ohnuma, T., Matsushita, S. 2006, "The relationship between the consumption of meat, fat, and coffee and the risk of colon cancer: a prospective study in Japan", *Cancer Letters*, vol. 244, no. 2, pp. 260-7.

Tavani, A., La Vecchia, C. 2004, "Coffee, decaffeinated coffee, tea and cancer of the colon and rectum: a review of epidemiological studies, 1990-2003", *Cancer Causes & Control*, vol. 15, no. 8, pp. 743-57.

Table 15.9 Studies used to make evidence statement for coffee and colorectal cancer

Reference [1]	**Tavani et al. 2004 [3207]**	**Lee et at 2007[2054]**	**Michels et al. 2005 [2325]**	**Oba et al. 2006 [2521]**
Type of study [2]	systematic review	cohort	cohort	cohort
Level of evidence [3]	Level 111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Coffee cups/day, caffeine mg/day and colon cancer	Cups/day of coffee and colorectal cancer	coffee, tea, caffeine and colorectal cancer	coffee, tea, caffeine and colorectal cancer
N [5]	>494,745	96,162	131,193	30,221
Population/study information [6]	18 studies, 15 case control and 3 cohort; males and females from Europe, Asia, North and South America	Japanese males (mean 51.9 yrs) and females (mean 52.3 yrs).	USA NHS and HPFS males (age 40-75) and females (age 30-55yrs)	Japan 13,894 Males and 16,327 females aged 35 yrs or older
Quality [7]	O	P	P	p
Results [8]	Case control studies: 4/15 studies significant (1 increased, 3 reduced risk), 9/15 non-significant; Cohort studies: non-significant. Rectal cancer: non-significant. Meta-analysis (1998 Giovannucci-5 cohort and 12 case-control studies, reported RR= 0.76 signif) Decaff coffee non-significant.	Compared with lowest consumers of coffee, women with ≥ 3 cups/d RR 0.44 (0.19–1.04; p for trend =0.04). NS for rectal cancer in women. Men, NS in any colorectal cancer.	No association b/w coffee and colorectal cancer. Regular consumers of de-caff coffee ≥ 2/d had a 52% (CI 19% to 71%) lower incidence of rectal cancer vs those never consuming decaffeinated coffee.	Women: daily coffee (caffeinated) intake: RR 0.43 (0.22–0.85, P for trend<0.01) vs. women who never consumed coffee or did so < once a month, no effect in males.
Effect on risk Increase/None/Protect	none	Protect in women only	None (protect for decaffeinated coffee)	Protect in women only.
Clinical importance[9]	3	2	2	2
Clinical relevance [10]	1	1	1	1

Generalisability	y	y	y	y
Applicability	y	y	y	y

15.10 COFFEE and BLADDER CANCER

Does a particular intake of coffee affect the risk of bladder cancer?		
Evidence statement		Consumption of coffee is associated with increased risk of bladder cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 2 Systematic reviews and 1 meta-analysis (18 cohort and 23 case control studies)
Consistency	Satisfactory	All reviews found small to moderate increased risk but within reviews some inconsistencies ranging from protection to increased risk.
Clinical impact	Good	Up to 20% increased risk
Generalisability	Good	US, Europe, Japan.
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.10. One meta-analysis of case control studies found increased risk. One SLR found mixed results: case control studies showed increased risk with 8/17 studies with other studies NS; but cohort studies showed only small increased risk for males. The second SLR had mixed results. The residual confounding by smoking, a significant risk factor for bladder cancer, has been raised as a factor in the results. There is some evidence that the water used to prepare the coffee impacts on bladder cancer risk. The consumption of coffee made from tap water containing chlorination by-products may increase the risk of bladder cancer. Differences in types of coffee (boiled, decaffeinated, filter, instant) used in different countries also make comparisons difficult with studies not usually identifying coffee type. Brewed coffee is commonly consumed in US, while filtered coffee is common in European countries and Japan. Instant coffee is not as commonly consumed except perhaps in Australia and the UK.

References

Pelucchi, C., La Vecchia, C. 2009, "Alcohol, coffee, and bladder cancer risk: a review of epidemiological studies", *European Journal of Cancer Prevention*, vol. 18, no. 1, pp. 62-8.

Villanueva, C. M., Cantor, K. P., King, W. D., Jaakkola, J. J., Cordier, S., Lynch, C. F., Porru, S., Kogevinas, M. 2006, "Total and specific fluid consumption as determinants of bladder cancer risk", *International Journal of Cancer*, vol. 118, no. 8, pp. 2040-7.

Zeegers, M. P., Kellen, E., Buntinx, F., van den Brandt, P. A. 2004, "The association between smoking, beverage consumption, diet and bladder cancer: a systematic literature review", *World Journal of Urology*, vol. 21, no. 6, pp. 392-401.

Table 15.10 Studies used to make evidence statement for coffee and bladder cancer

Reference [1]	**Pelucchi 2009 [2615]**	**Zeegers et al. 2004 [3571]**	**Villanueva et al. 2006 [3374]**
Type of study [2]	Systematic review of 21 studies	Systematic review	Meta-analysis
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	Cups/day of coffee and bladder	coffee and bladder	coffee and bladder
N [5]	224,564	nil data	2729 cases 5150 controls.
Population/study information [6]	4 cohort (USA 2, Netherlands, Norway) , 17 case control (9 hospital)-N America 6, Europe 8, Serbia 1, Japan 1, Uruguay 1.	14 epidemiological studies (mainly case control) for coffee.	6 case control studies (3 Europe, 3 Nth America). Heterogeneity NS
Quality [7]	O	O	O
Results [8]	2/4 cohort studies showed NS association and 1/4 showed increased RR in men RR 3.52(1.02-12.2) for 2-4 cups/wk vs non drinkers and 1/4 showed reduced RR in women RR 0.44 (0.22-0.86) for 4-<5 cups per day vs non drinkers and NS association in men. Case control studies 8/17 showed significant increase OR and 9/17 showed no significant association for coffee consumption and bladder cancer risk.	Coffee consumption probably not associated with bladder cancer. Coffee after adjustment for age, smoking and sex RR 1.2 (1.0-1.4).	for coffee consumption > 5 cups/day vs. 0-5 cups/day OR 1.26 (1.10-1.44); Males OR 1.23 (1.05-1.44) and Females OR 1.31 (0.99-1.74). After adjustment for quartiles of cigarette pack years OR=1.24 (1.08-1.43). Tap water intake (known to contain carcinogens) associated with increased risk 1.10 (CI 1.04-1.17) and results above adjusted for non-tap but not tap water intake.
Effect on risk Increase/None/Protect	None to increased	small increase	Increase (but did not adjust for tap water intake)
Clinical importance[9]	2	2	1
Clinical relevance [10]	2	2	1

Generalisability	y	y	y
Applicability	y	y	y

15.11 COFFEE and OVARIAN CANCER

Does a particular intake of coffee affect the risk of ovarian cancer?		
Evidence statement		Consumption of coffee is not associated with risk of ovarian cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 1 meta-analysis (15 studies), 1 cohort and 1 case control study.
Consistency	Satisfactory	9/12 case control studies no significant effect and 5/5 cohort studies no significant effect.
Clinical impact	Poor	No significant effect noted
Generalisability	good	One study from Canada and the USA plus others not specified.
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.11. The cohort studies showed consistency in outcome with none showing significant effect. The meta-analysis of 15 studies showed no significant heterogeneity for the cohort studies, but significant heterogeneity for the case control and for the studies overall.

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Table 15.11 Studies used to make evidence statement for coffee and ovarian cancer.

Reference [1]	**Steevens et al. 2007 [36]**	**Silvera et al. 2007[3018]**	**Song et al. 2008 [3071]**
Type of study [2]	Meta analysis (15 studies-11 case control and 4 cohort)	cohort	case control
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	coffee (cups/day) and risk of ovarian cancer	coffee (cups/day) and ovarian cancer	Coffee (cups/day) and ovarian cancer
N [5]	15 studies	49,613	781 cases and 1263 controls
Population/study information [6]	No study information provided	Canadian women National Breast Screening Study	USA
Quality [7]	O	P	p
Results [8]	coffee intake highest (≥5 c/d) vs lowest (0-<1c/d) RR=1.18 (CI 0.97,1.44) Coffee increment 1 cup/day RR= 1.04 (CI 0.97, 1.12) non- significant.	Borderline positive association observed in women who drank >4 cups coffee/day compared to non drinkers HR = 1.62 (CI = 0.95–2.75, P trend = 0.06).	No association of coffee with ovarian cancer risk, p trend =0.27.
Effect on risk Increase/None/Protect	None	None	none
Clinical importance[9]	3	3	3
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

15.12 COFFEE and LUNG CANCER

Does a particular intake of coffee affect the risk of lung cancer?		
Evidence statement		Consumption of coffee is associated with increased risk of lung cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 1 meta-analysis (13 studies-5 cohort, 8 case control studies (3 population,5 hospital)
Consistency	Poor	5/13 positive association and 8/13 studies no significant effect. Cohort studies significant increase but case-control no association.
Clinical impact	Satisfactory	Significant 14% increase in risk with 2 cups/day
Generalisability	Good	Norway (2), Japan (4), Sweden (2), USA (2), Canada (1), Uruguay (1), Czech (1).
Applicability	Good	Applicable to Australian conditions.

One meta analysis of 13 studies shows positive association between highest coffee intake and lung cancer, but studies showed significant heterogeneity and two studies did not adjust for smoking. Increase of two cups/day associated with 14% increased risk of lung cancer. In stratified analyses, prospective studies showed increased risk while other designs were not significant. Eight studies from America and Japan showed increased risk but five studies from Europe were not significant. When analysed by smoking status three studies in non smokers showed borderline reduced risk and non significant increased risk in smokers. Two studies assessing decaffeinated coffee intake showed reduced risk. The meta analysis authors note “residual confounding effects of smoking or other factors may still exist; these results should be interpreted with caution”. Differences in types of coffee (boiled, decaffeinated, filter, instant) used in different countries also make comparisons difficult with studies not usually identifying coffee type. Brewed coffee is commonly consumed in US, while filtered coffee is common in European countries and Japan. Instant coffee is not as commonly consumed except perhaps in Australia and the UK.

Reference:

Tang, N., Wu, Y., Ma, J., Wang, B. & Yu, R. 2009, "Coffee consumption and risk of lung cancer: A meta-analysis", *Lung Cancer*, vol. In Press, Corrected Proof, no.

Table 15.12 Studies used to make evidence statement for coffee and lung cancer

Reference [1]	**Tang et al. 2009 [3193]**
Type of study [2]	Meta analysis (5 cohort and 8 case control studies- 3 population,5 hospital-based controls)
Level of evidence [3]	111-2
Intervention/ comparator [4]	Coffee intakes and lung cancer
N [5]	5347 lung cancer cases and 104,911 non-cases.
Population/study information [6]	Norway (2), Japan (4), Sweden (2), USA (2), Canada (1), Uruguay (1), Czech (1).
Quality [7]	O
Results [8]	Positive association between highest coffee intake and lung cancer RR = 1.27 (1.04–1.54). Significant heterogeneity p=0.004. 2 studies not adjusted for smoking. Increase of 2 cups/day associated with 14% increased risk of lung cancer (RR = 1.14:1.04–1.26). Stratified analyses: prospective studies (RR=1.57:1.15-2.14) while other designs were NS. Studies from America and Japan (8 studies) increased risk but studies from Europe (5 studies) were NS. When analysed by smoking status 3 studies in non smokers showed borderline reduced risk (RR=0.78:0.60-1.0) and in smokers (2 studies) RR=1.28 (0.87–1.88). Decaffeinated coffee (2 studies) RR=0.66 (0.54–0.81). Authors note: " residual confounding effects of smoking or other factors may still exist, these results should be interpreted with caution"
Effect on risk Increase/None/Protect	Increase but residual confounding of smoking and other factors may be evident.
Clinical importance[9]	1
Clinical relevance [10]	1
Generalisability	y
Applicability	y

15.13 COFFEE and CARDIOVASCULAR DISEASE

Does a particular intake of coffee affect the risk of cardiovascular disease?		
Evidence statement		Consumption of coffee is not associated with risk of coronary heart disease.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 1 meta analysis (13 case control studies and 10 cohort studies) and 3 cohort and 1 case control study.
Consistency	Poor	Meta-analysis found no association with pooled analysis, but increased risk with case control but not cohort studies. The 3 cohort studies showed no significant association between coffee and CHD. The one case control showed a positive association for first non fatal infarct.
Clinical impact	Poor	Little effect on rates of CHD.
Generalisability	Satisfactory	Impact seen in smokers. Studies from USA (14), Italy (4), Greece (2), Scotland (2), Portugal (1), Sweden (2) and Denmark (1).
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.13. One meta analysis showed no association. No major publication bias was found in the meta-analysis. The 13 case control studies analysed by the meta-analysis found increased risk but the 10 cohort studies showed no association. Of the additional studies, three cohort studies were non-significant overall, with one finding increased risk in previous or current smokers, but no association in 'never smokers'; and another showing protection for subjects with normal to low BP, but increased risk in hypertensive subjects. One population-based case-control study found positive associations with filtered and boiled coffee for intakes greater than 700ml/day. Differences in the types of coffee used in different countries make study comparisons difficult with studies not usually identifying coffee type. Brewed coffee is commonly consumed in US, while filtered coffee is common in European countries and Japan. Instant coffee is not as commonly consumed except perhaps in Australia and the UK.

References

Greenberg, J. A., Chow, G. & Ziegelstein, R. C. 2008, "Caffeinated Coffee Consumption, Cardiovascular Disease, and Heart Valve Disease in the Elderly (from the Framingham Study)", *The American Journal of Cardiology*, vol. 102, no. 11, pp. 1502-1508.

Hammar, N., Andersson, T., Alfredsson, L., Reuterwall, C., Nilsson, T., Hallqvist, J., Knutsson, A., Ahlbom, A., Sheep & the, V. s. 2003, "Association of boiled and filtered coffee with incidence of first nonfatal myocardial infarction: the SHEEP and the VHEEP study", *Journal of Internal Medicine*, vol. 253, no. 6, pp. 653-9.

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Table 15.13 Studies used to make evidence statement for coffee and coronary heart disease

Reference [1]	**Sofi et al. 2007 [55]**	**Rosner et al. [2811]**	**Klatsky et al. 2008 [1930]**
Type of study [2]	Meta analysis (13 case control and 10 cohort studies)	cohort	cohort
Level of evidence [3]	Level 111-2	111-2	111-2
Intervention/ comparator [4]	Coffee consumption (cups/day) and risk of CHD	coffee consumption and MI	coffee and risk of CAD
N [5]	440,865	32,650	127,212
Population/study information [6]	USA (13 studies), Italy (4), Greece (2), Portugal (1), Denmark (1), Scotland (2). Male and Female Black, White	Swedish women, aged 40–74 years	USA study mean age 40.7 yrs, 44.2% Male
Quality [7]	O	P	P
Results [8]	Pooled-no association. Case-control studies: >4 c/d, OR 1.83 (1.49-2.24), highest (3-4 cups/day), OR 1.33 (1.04-1.71), but no association low daily (≤2 cups/day), OR 1.03 (0.87-1.21). Cohort studies: no association, RR=1.16 (0.95-1.41) for the highest category, and 1.05 (0.90-1.22) and 1.04 (0.90-1.19) for the 2nd and 3rd highest categories, respectively.	RR of MI with drinking 5 cups/ week vs 0–4 cups/week was 0.68 (CI 0.43, 1.07). NS trend toward lower risk with higher consumption levels.	For ever smokers drinking 4 cups/d RR 1.3 (1.1 to 1.6) for Females, RR 1.2 (1.0 to 1.29) Males; No effect in never smokers. Time effect noted: For ever smokers: 4 cups/d baseline CAD RR 1.2 (1.0-1.3), whereas at 10 years, RR 1.3(1.2-1.5) Suggests residual confounding by incomplete control for smoking.
Effect on risk Increase/None/Protect	None	None	Increased in ever smokers. None in never smokers.
Clinical importance[9]	3	3	2
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

Table 15.13 Studies used to make evidence statement for coffee and coronary heart disease

Reference [1]	**Hammar et al. 2003 [1541]**	**Greenberg et al. 2008 [199]**
Type of study [2]	Population-based case-control study	cohort
Level of evidence [3]	111-2	111-2
Intervention/ comparator [4]	Coffee (dL/day) and first nonfatal myocardial infarction	Coffee (cups/day) and CHD
N [5]	1943 cases and 1943 matched controls	1,354
Population/study information [6]	Sweden, adults aged 45-65/70 years.	US Framingham subjects aged 65.4 to 96.6 years
Quality [7]	P	P
Results [8]	Men: intakes of 7-9 dL filtered coffee/ day vs intake of ≤ 3 dL/day: RR= 1.32 (1.03-1.70). Intake of at least 10 dL/day RR=1.93 (1.42-2.63) for filtered and RR= 2.20 (1.17-4.15) for boiled coffee. Women: Intakes of 7-9 dL filtered coffee/ day vs intake of ≤ 3 dL/day RR= 0.89 (0.61–1.31) Boiled coffee vs filtered coffee showed increased risk in men (RR= 1.41: 1.07-1.80) and women (RR= 1.63: 1.04-2.56)	For CHD mortality or event: ≥1 cup/day vs 0 HR=0.69 (0.47–1.00) p=0.02 linear trend. BP categories:<140/90 HR=0.45 (0.24-0.84); BP 140-160/90-100 HR=0.69 (0.47-1.0); BP <160/100 HR=0.57 (0.36-0.91) BP ≥160/100 HR=0.87 (0.44-1.72)
Effect on risk Increase/None/Protect	Increase for filter and boiled coffee in males at high intake >700ml Increase for women for boiled coffee	Protect for subjects with normal to low BP. increase in hypertensive subjects
Clinical importance[9]	2	2
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

15.14 COFFEE and HYPERTENSION

Does a particular intake of coffee affect the risk of hypertension?		
Evidence statement		Consumption of coffee increases systolic blood pressure.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level 111 studies of 1 meta-analysis (11 trials- 2 RCTs), 3 additional clinical trials and 3 cohorts.
Consistency	Poor	Meta-analysis for short term effect shows increased BP; cohort studies and clinical trials show mixed results.
Clinical impact	Satisfactory	Small increase in systolic BP of 0.5-2 mmHg, with differences in coffee types noted.
Generalisability	Poor	Only limited number of RCTs and different effects seen with race, coffee type and age.
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.14. The meta analysis found the pooled data for coffee trials showed significant increase in systolic but not diastolic BP. Stratification found the effect was significant for boiled and filtered coffee but not instant, in younger not older subjects; effect on systolic BP was found in those with usual intakes <400mg/day and on both systolic and diastolic BP in those with usual intakes ≥ 400mg/day. The three cohort studies (two in US health professionals and one from the Netherlands) found mixed results. One cohort from the US found inverse U shaped curve of risk vs consumption, one no effect and one protection in women >6 cups/day and reduced SBP in those aged >39years. The three CT also showed mixed results with an increase in BP in male coffee drinkers who smoked, protection in regular alcohol consumers and no effect in BP except in caffeine naive subjects. Differences in types of coffee (boiled, decaffeinated, filter, instant) used in different countries make comparisons between other studies difficult as coffee type is often not identified. Brewed coffee is commonly consumed in US, while filtered coffee is common in European countries and Japan. Instant coffee is not as commonly consumed except perhaps in Australia and the UK.

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Winkelmayer, W. C., Stampfer, M. J., Willett, W. C. & Curhan, G. C. 2005, "Habitual Caffeine Intake and the Risk of Hypertension in Women", *JAMA: Journal of the American Medical Association*, vol. 294, no. 18, pp. 2330-2335.

Table 15.14 Studies used to make evidence statement for coffee and hypertension

Reference [1]	**Noordzij et al. 2005**	**Winkelmayer et al. 2005 [3486]**	**Papadelis et al. 2003 [2592]**
Type of study [2]	meta analysis (11 trials- 2 RCT, 7 cross over, 2 parallel)	cohort	clinical trial
Level of evidence [3]	Level 111-1	111-2	111-2
Intervention/comparator [4]	Coffee consumption and blood pressure	HT and quintiles of coffee intake	the effect of coffee and stress on BP
N [5]	1,010	155 594	16
Population/study information [6]	No country information given. Adults 23-77 yrs M+F Trials using instant (8), filtered (7), boiled (3).	2 cohorts: NHS1 and NHS11, US female nurses	Greece, healthy males
Quality [7]	O	P	P
Results [8]	BP elevations for coffee systolic: 1.22 mmHg (0.52–1.92) Diastolic: 0.49mmHg (-0.06–1.04)]. Stratified data: For coffee type: boiled coffee systolic: 4.75 mmHg (2.33–7.17), diastolic: NS. Filtered coffee: systolic:2.07 mmHg (0.95–3.18), diastolic NS. Instant coffee systolic and diastolic NS. For age < 40 years, systolic 2.41 (1.43, 3.38), diastolic 0.73 (0.01, 1.44) but >40 y NS effect.	Habitual coffee consumption not associated with HT. No linear association: NHS1 P trend=0.29 NHS11 p trend=0.53. Q3 vs Q1 had 13% (CI 8%-18% NHS1) and 12% (CI 6%-18% NHS 11) increased risk of HT showing inverse U shaped curve of risk vs consumption.	non coffee drinkers: signif rise in BP after 3 but not 1 cup coffee (mean 124 vs 122 mmHg p<0.05); smoking coffee drinkers: rise in BP with both 1 and 3 cups coffee for 3 cups vs none 140 vs 126 mmHg p<0.05), non smoking coffee drinkers -NS. Coffee caused increase in BP in non coffee drinkers and coffee drinking smokers, but not habitual coffee drinking non-smokers placed under stress.
Effect on risk Increase/None/Protect	Increase for systolic, none for diastolic (except for high coffee intakes).	None	increase in male coffee drinkers who smoke
Clinical importance[9]	2	2	2
Clinical relevance [10]	1	1	1

Generalisability		y	y
Applicability		y	y

Table 15.14 Studies used to make evidence statement for coffee and hypertension (cont.)

Reference [1]	**Funatsu et al. 2005 [86]**	**Kennedy et al. 2008 [1877]**	**Klag et al. 2002 [1928]**	**Uiterwaal et al. 2007 [3299]**
Type of study [2]	Randomised cross over clinical trial	clinical trial	cohort	cohort
Level of evidence [3]	111-1	111-2	111-2	111-2
Intervention/ comparator [4]	Group A: 4 wks of ≥ 3 cups filtered coffee daily then nil for 4 wks. Group B: 4 wks no coffee drinking then 4 wks ≥ 3 cups/day. Usual alcohol intakes of> 60ml per day. Weekly BP.	BP before coffee, 50 minutes after and immediately after a 9-min mental stress task. Coffee vol = 350mL	coffee (cups/day) and risk of HT	coffee (cups/day)and risk of HT
N [5]	42	20	1017	2985 men and 3383 women
Population/study information [6]	Japan, 42 hypertensive or pre-hypertensive Males aged 30-65 yrs who consumed alcohol and coffee daily	Canada 10 caffeine-naïve (23 ± 5.0 years) and 10 caffeine-habituated (25 ± 6 years) females	US white male former medical students	Netherlands
Quality [7]	P	P	P	P
Results [8]	Group A: coffee drinking caused a decrease in BP (SBP - 10mmHg SBP p=0.0015 and DBP	systolic blood pressure increased in the caffeine-naïve participants only (10.3 mm Hg p<0.05)	1 cup/day increased systolic and diastolic BP by 0.19 (0.02-0.35) and 0.27 (0.15-0.39). Based on baseline	Coffee abstainers at baseline had a lower risk of hypertension than did those with a coffee intake of >0-3

	- 7mmHg DBP p<0.001) and no coffee drinking caused an increase in BP (SBP +8mmHg p=0.003 and DBP of+ 5mmHg p=0.0014) Group B: no change in BP with coffee cessation or reintroduction. Between groups: Coffee drinking vs non coffee drinking caused reduced BP for systolic 1st half p<0.05 and 2nd half p<0.001 and diastolic 1st half p<0.05 and 2nd half p<0.01.		coffee intake HT RR=1.07 (0.67-1.69) and on most recent intake RR=1.43 (0.94-2.18).	cups/d OR= 0.54(0.31, 0.92). Women with >6 cups/d vs >0-3 cups/d had OR= 0.67 (0.46, 0.98). Subjects aged ≥ 39 y at baseline had 0.35 mm Hg (-0.59, -0.11 mm Hg) lower SBP per cup intake/d but NS for DBP.
Effect on risk Increase/None/Protect	Protect in regular alcohol consumers	None Increase in caffeine naive subjects	None	Increase Protect in women >6 cups/day. Protect for SBP for those over 39 years.
Clinical importance[9]	2	1	2	2
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

15.15 COFFEE and TYPE 2 DIABETES.

Does a particular intake of coffee affect the risk of Type 2 diabetes?		
Evidence statement		Consumption of coffee of 4 or more cups per day is associated with reduced risk of Type 2 Diabetes.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111-2 and IV evidence from 1 meta-analysis (9 cohort and 7 cross sectional studies) and 8 additional cohort studies.
Consistency	Good	The majority of studies show protection. Meta-analysis - 5/8 cohort studies show protection for ≥ 6 cups/day and 4/8 for ≥4 cups/day and 4/7 of additional cohort studies with adequate data show protection for ≥3 cups/day.
Clinical impact	Good	Meta-analysis reports a RR of 0.65 for ≥ 6 cups/day and a RR of 0.72 for 4-6 cups/day.
Generalisability	Good	Studies from US, Japan, Europe, UK.
Applicability	Excellent	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.15. One meta analysis of nine cohort and seven cross sectional studies found habitual coffee consumption associated with lower type 2 diabetes with greater reduction for higher intakes. Five of the additional eight cohort studies show protection overall and 2/8 significant in subgroup analysis e.g. males not females, <60 years and with weight loss; one study from the UK not significant except when combined with tea. Differences in types of coffee (boiled, decaffeinated, filter, instant) are apparent in studies and coffee type is not always identified. The findings from the meta-analysis suggest that reduced risk is most likely associated with consumption of drip filtered coffee.

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Table 15.15 Studies used to make evidence statement for coffee and type 2 diabetes

Reference [1]	**van Dam and Hu 2005[92]**	**van Dam et al. 2006 [573]**	**Paynter et al. 2006 [429]**	**Greenberg 2005[649]**	**Hamer et al. 2008 [121]**
Type of study [2]	systematic review 9 cohort and 7 cross sectional studies	cohort	cohort	cohort	cohort
Level of evidence [3]	Level IV	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Coffee consumption and risk of type 2 diabetes	coffee (cups/day) consumption groups and type 2 diabetes	coffee (cups/day)consumption and type 2 diabetes	consumption of coffee (cups/day) and type 2 diabetes	consumption of coffee, tea and type 2 diabetes
N [5]	201,867	88,259	15,792	7006	5823
Population/study information [6]	M and F Studies of Asians, Europeans, Americans and Pima Indians	US Nurses Health Study 11 aged 26-46 yrs	Data from the ARIC Study (Atherosclerosis Risk in Communities) adult US 54 yrs Blacks and Whites	NHANES 11 Epidemiology Follow up Study US adults aged 32-88 yrs	Whitehall 11 British Civil Servants Study aged 35-55 yrs
Quality [7]	O	P	P	P	P
Results [8]	Habitual coffee consumption associated with lower type 2 diabetes. For cohort studies: Compared to lowest intakes of 0-2 cups/day For ≥6 cups/d RR 0.65 (0.54-0.78) For 4-6 c/d RR 0.72 (0.62-0.83). For 1-4 cups/d RR 0.94 (0.88-1.01**).** For cross sectional	RR of type 2 diabetes p trend P<0.0001. For 1 cup/day RR 0.87(0.73-1.03); For 2-3 cups/d RR 0.58(CI 0.49-0.68) For ≥4 cups/d RR 0.53 (CI 0.41-0.68) vs non-drinkers	Increased coffee intake significantly associated with decreased risk of type 2 diabetes in Males not Females. For ≥ 4cups/d HR= 0.77 p trend = 0.02, women HR = 0.89 p trend = 0.32.	Reduced HR for a 2 cups/day increment in intake of ground-caffeinated or decaff. but only applied to those <60 yrs who had lost weight.	For coffee intakes HR 0·80 (0·54- 1·18) NS. Tea and coffee combined (2 or > cups per day of both beverage) and DM HR 0·68 (CI 0·46- 0·99, P<0·05) after full adjustment.

	studies: OR 0.48 (0.28-0.82) for ≥5 cups/d and OR 0.60 (0.42-0.85) for 3-4 cups/d compared to <1-2 cups/day.				
Effect on risk Increase/None/Protect	Protect	Protect	Protect in men	Protect in < 60yrs who had lost weight	None for coffee alone, protect combined with tea
Clinical importance[9]	1	1	2	2	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 15.15 Studies used to make evidence statement for coffee and Type 2 diabetes (cont.)

Reference [1]	**Iso 2006]527]**	**Hu et al. 2006**	**Odegaard et al. 2008**	**Smith et al. 2006**
Type of study [2]	cohort	cohort	cohort	cohort
Level of evidence [3]	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Consumption of coffee (cups/day) and type 2 diabetes	consumption of coffee (cups/day) and type 2 diabetes incidence	consumption of coffee (cups/day) and type 2 diabetes incidence	consumption of coffee (cups/day) and type 2 diabetes
N [5]	17,413	21,385	36,908	36,908
Population/study information [6]	Cohort from the Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC Study)	10,188 Finnish men and 11,197 women aged 35-74 yrs	Singaporean Chinese Health Study M and F aged 45-74 yrs	US participants aged 45-74 yrs in 1993-1998
Quality [7]	P	P	P	P

Results [8]	Coffee consumption associated with reduced risk of type 2 diabetes. For ≥ 3 c coffee/d OR 0.58 (CI 0.37 - 0.90), vs those who drank <1 c/wk.	Consumption of 0–2, 3–6 and >7 cups of coffee/day had HR of 1.00, 0.77 and 0.66 (P=0.022 for trend) in men, 1.00, 0.71 and 0.52 (P=0.001 for trend) in women, and 1.00, 0.75 and 0.61 (P<0.001 for trend) in men and women combined. In obese/inactive people, coffee drinking of ≥7 cups/d reduced the risk of type 2 diabetes to half.	4 cups coffee/d vs non daily consumption RR 0.70(0.53, 0.93)	Past and current coffee drinkers vs never drinkers OR 0.38 (0.17– 0.87) and 0.36 (0.19–0.68) 317 participants with baseline IGT who were past or current coffee drinkers vs non drinkers OR 0.31 (0.11– 0.87) and 0.36 (0.16–0.83)
Effect on risk Increase/None/Protect	Protect	Protect	Protect	Protect
Clinical importance[9]	1	1	1	1
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

15.16 TEA and BREAST CANCER.

Does a particular intake of tea affect the risk of breast cancer?		
Evidence statement		Consumption of green and black tea is not associated with risk of breast cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory (Green tea) Poor (Black tea)	Level 111 evidence from studies with low to medium risk bias. For green tea, 1 meta analysis (3 cohort, 2 case control and 2 case control studies of early recurrence) plus 3 additional case control studies. For black tea 3 cohorts and 1 case control (included green tea).
Consistency	Poor	For green tea, meta-analysis shows protection, but only for early recurrence (2 studies). Three (3) case controls show protection. For black tea, 3 cohort and 1 case control show no effect.
Clinical impact	Good	Green tea reduced risk of early recurrence by 45%. No effect for black tea.
Generalisability	Poor	Green tea studies completed in Asian populations. Black tea studies from USA, Europe and Singapore.
Applicability	Poor	Green tea not widely consumed in Australia but growing in popularity.

The studies used to make the body of evidence statement are shown in Table 15.16. For green tea consumption, one meta-analysis of three cohort and two case control studies found a non significant trend to reduced risk of breast cancer. Two additional case control studies in the meta-analysis assessed early recurrence of breast cancer and found significant reduced recurrence in early stage I and II cancers. Of the additional three case control studies in green tea all showed significant reduced risk. Genotype and race differences noted, and may suggest reduced risk in some sub-groups. Black tea studies were from US (1), Europe (2) and Singapore (1). For black tea there were three cohort studies and one case control (also included green tea) and all found no significant association of black tea and with breast cancer risk.

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Table 15.16 Studies used to make evidence statement for tea and breast cancer

Reference [1]	**Seely et al. 2005 [172]**	**Ganmaa et al. 2008[191]**	**Michels et al. 2002[3013]**	**Hiroven et al. 2006 [1628]**
Type of study [2]	meta analysis	cohort	cohort	cohort
Level of evidence [3]	Level 111-2	111-2	111-2	111-2
Intervention/ comparator [4]	green tea intakes (cups/day) and risk of breast cancer and breast cancer recurrence	black tea (cups/day) and breast cancer risk	black tea (cups/day) and breast cancer risk	Black tea (mls/day) and breast cancer risk
N [5]	7 Studies (3 Cohort, 2 Case control, 2 of breast cancer recurrence). All subjects of Asian origin.	85,987	59,036	4396
Population/study information [6]	Mainly females, 1 study included males	US Nurse's Health Study	Swedish Mammography Screening Cohort females aged 40-76 yrs	France- SUpple´mentation en VItamines et Mine´raux AntioXydants (SU.VI.MAX) Study
Quality [7]	O	P	P	P
Results [8]	NS trend to reduced risk of breast cancer. Two studies assessing cancer recurrence found reduction for early stage 1 and 2 cancers RR 0.56 (0.38-0.83) I^2 0%.	Tea consumption ≥4 cups/day vs < 1cup/month RR 0.94 (0.77-1.14)	Consumption of tea was not associated with breast cancer incidence. (data stratified for age 50 but not by menopause status)	Black tea not associated with risk (>350ml/d) RR 0.75 (0.45-1.28)
Effect on risk Increase/None/Protect	none/ protect early recurrence for green tea	None for black tea	None for black tea	None for black tea
Clinical importance[9]	2	3	3	3
Clinical relevance [10]	1	1	1	1
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 15.16 Studies used to make evidence statement for tea and breast cancer (cont.)

Reference [1]	**Shrubsole et al. 2009 [3002]**	**Yuan et al. 2005 [3559]**	**Zhang et la 2007 [3582]**
Type of study [2]	case control	case control	case control
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	green tea (grams/month) and breast cancer risk	green tea (cups/day),breast cancer risk and ACE gene polymorphism	green tea (cups/day) and breast cancer risk
N [5]	6928 (cases=3454 controls=3474)	962 (cases=297 controls=665)	2018 (cases=1009, controls=1009)
Population/study information [6]	Shanghai Breast Cancer Study, females aged 20-74 yrs	Singapore Chinese Health Study	SE China, females aged 20-87 yrs
Quality [7]	P	P	P
Results [8]	green tea drinkers vs non drinkers OR 0.88 (0.79-0.98); in premenopausal women p trend=0.02 for yrs of drinking and dose/month p trend=0.046	All and low ACE genotype NS; High ACE genotype women had reduced risk (p trend =0.039) monthly drinking OR 0.33 (0.13-0.82) and weekly drinking OR 0.29 (0.10-0.79) vs no drinking. Black tea NS.	Reduced risk vs non drinkers. For lowest intake: OR 0.87 (0.73-1.04) to highest intake OR 0.61 (0.48-0.78) p trend<0.001; duration, number cups/day and new batches/day p trend <0.001
Effect on risk Increase/None/Protect	Protect for green tea	Protect for green tea in high ACE genotype subjects. None for black tea.	Protect for green tea
Clinical importance[9]	1	2	1
Clinical relevance [10]	1	2	1
Generalisability	y	y	y
Applicability	y	y	y

15.17 TEA and GASTRIC CANCER.

Does a particular intake of tea affect the risk of gastric cancer?		
Evidence statement		Consumption of green tea is not associated with risk of gastric cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Level 111 evidence from 2 meta-analysis (17 case control and 9 cohort studies, 10 in common) and 1 cohort study.
Consistency	Poor	Cohort studies no effect in both meta analyses; but pooled data for one meta overall and pooled data from 1 set of population case control studies show protection. Other hospital case control study shows no effect.
Clinical impact	Poor	No consistent significant impact.
Generalisability	Poor	Many studies from Japan and China.
Applicability	Poor	All studies from Asia

The studies used to make the body of evidence statement are shown in Table 15.17. The two meta analyses had 10 studies in common; however their results are not consistent, with one showing protection and one no effect. The difference in result may be explained by the inclusion of studies with different effects. In the meta analysis showing protection, one study with increased risk was excluded without explanation and studies not in common were NS, whilst the meta analysis showing no effect included one additional study showing increased risk. The single cohort study was not significant. Both meta analyses found significant heterogeneity between studies.

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Table 15.17 Studies used to make evidence statement for tea and gastric cancer.

Reference [1]	**Myung at al 2009 [110]**	**Zhou et al. 2008 [24]**	**Koizuma et al. 2003 [1946]**
Type of study [2]	Meta analysis of 8 case control and 5 cohort studies.	Meta analysis of 9 case control and 4 cohort studies.	cohort
Level of evidence [3]	Level 111-2	Level 111-2	Level 111-2
Intervention/ comparator [4]	green tea intakes (cups/day) and gastric cancer incidence	green tea intakes (cups/day) and gastric cancer incidence	green tea intakes (cups/day) and gastric cancer incidence
N [5]	257,390	140,129	65,915
Population/study information [6]	Cases and hospital/population controls. Studies from China (5), Japan (6), Japanese in Hawaii (1), Taiwan (1).	Case control (hospital and population based) and cohort studies from Japan (8) and China (6).	Japan, 2 cohort studies pooled; aged > 40yrs
Quality [7]	O	O	P
Results [8]	Pooled RR 0.82 (0.7-0.96); Pooled case control RR 0.73 (0.64-0.83); Pooled cohort study RR 1.04 (0.93-1.17). Significant heterogeneity found.	No reduced risk of gastric cancer with green tea intake. Pooled OR 0.98 (0.77-1.24). Pooled case control hospital: 1.12 (0.7-1.77) population: 0.67 (0.49-0.92) Cohort studies: 1.56 (0.93-2.60). Significant heterogeneity found.	Compared to 1 cup/day >5 cups/day had RR 1.06 (0.86-1.30) and was NS for all intake groups.
Effect on risk Increase/None/Protect	Protect	None	None
Clinical importance[9]	1	2	3
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

15.18 TEA and OVARIAN CANCER.

Does a particular intake of tea affect the risk of ovarian cancer?		
Evidence statement		Consumption of green or black tea is not associated with risk of ovarian cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 2 meta analyses (9 cohort and 6 case control studies, 8 in common), 2 cohorts and 1 case control study.
Consistency	Good	Both meta analyses of pooled data indicate no reduction.
Clinical impact	Poor	No effect on cancer rates noted.
Generalisability	Good	Studies from Nth America (6), Europe (4), Australia (1), China (1) plus other studies from meta not identified.
Applicability	Good	applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.18. The two meta analysis show non-significant reduction in risk with significant heterogeneity between the studies. The meta analyses had eight studies in common, with the meta-analysis showing marginal protection having three additional cohorts and one case control compared to the meta showing no effect having one additional case control study. Most studies from were from western countries, and were likely to include black tea. One study from China showed protection for green tea. The additional studies of two for black and one for black and green showed protection for green tea. However, as there were only two studies showing protection for green tea, no evidence statement has been made.

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Table 15.18 Studies used to make evidence statement for tea and ovarian cancer

Reference [1]	**Zhou et al. 2007[33]**	**Steevens et al. 2007 [36]**	**Larsson et al. 2005 [609]**	**Silvera et al. 2007 [314]**	**Song et al. 2008 [3071]**
Type of study [2]	Meta analysis of 2 cohort and 7 case control studies.	Meta analysis of 5 cohort and 7 case control studies.	cohort	cohort	case control
Level of evidence [3]	Level 111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	tea intakes (cups/day, type not specified) and risk of ovarian cancer	tea (cup/day, type not specified) and risk of ovarian cancer	Black tea (cups/day) and ovarian cancer	tea (cups/day, type not specified) and ovarian cancer	tea (cups/day)consumption and ovarian cancer
N [5]	39,503	n/a	61,057	49,613	
Population/study information [6]	studies from western countries (4 USA, 3 Europe, 1 Aust, 1 China), nil other information	12 studies, no country information given.	Sweden Adult women aged 40-76 yrs	Canadian women National Breast Screening Study	USA 781 cases and 1263 controls
Quality [7]	O	O	P	P	p
Results [8]	Tea consumption not associated with reduced risk of ovarian cancer. Pooled RR 0.84(0.66-1.07). Significant heterogeneity p<0.001. All 8 western studies excluding 1 China study pooled RR 1.01 (0.91-1.12). 1 China study RR 0.39 (0.27-0.57) for ≥1cup/day vs none.	Tea highest (≥5 c/d) vs lowest (0-<1c/d) RR 0.85(CI 0.71-1.01) 1 cup/d increment RR 0.94 (CI 0.89 - 1.00). Significant heterogeneity p<0.05.	For ≥2 cups tea/d HR 0.54 (CI 0.31-0.91) vs. < 1/month. Each additional cup of tea/ day associated with 18% lower risk of ovarian cancer HR 0.82 (0.68-0.99).	No association with tea p trend =0.77	Black tea ≥1cup/day vs. none OR 0.91 (0.65-1.27) Green tea ≥1cup/day vs none OR 0.82 (0.26-0.84)
Effect on risk Increase/None/Protect	None for pooled Protect in 1 Chinese	None	Protect	None	None for black tea Protect for green tea

	study (probably green tea)				
Clinical importance[9]	3	3	1	3	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

15.19 TEA and COLORECTAL CANCER.

Does a particular intake of tea affect the risk of colorectal cancer?		
Evidence statement		Consumption of green or black tea is not associated with risk of colorectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from studies with low to medium risk bias: 1 meta analysis (8 cohort and 11 case control studies), 3 cohorts and 1 case control studies
Consistency	Satisfactory	Most show no effect; meta-analysis and 2 cohorts no effect; 1 case control and 1 cohort study show gender specific protection.
Clinical impact	Poor	No effect overall.
Generalisability	Good	Broad range of populations included (6 Europe, 5 Nth America, 4 Asia, 4 other)
Applicability	Good	Applicable to Australian conditions.

The study used to make the body of evidence statement is shown in Table 15.19. The results from the meta analysis of eight cohort and 11 case control studies show no significant increased or decreased risk for colorectal cancer. Of the additional three cohort and one case control studies, one cohort and one case control, show gender specific (one male, one female) protection and two are not significant.

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Table 15.19 Studies used to make evidence statement for tea and colorectal cancer

Reference [1]	**Tavani et al. 2004 [3207]**	**Lee et at 2007[297]**	**Michels et al. 2005 [724]**	**Su et al. [1133]**	**Dora et al. [1218]**
Type of study [2]	systematic review of 19 studies (7 cohort, 12 case control; 7 population and 5 hospital)	cohort	cohort	cohort	case control
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Tea and colon cancer	Green tea (cups/day) and colorectal cancer	Tea (cups/day) and colorectal cancer	Tea (cups/day)and colorectal cancer	Tea (cups/day) and rectal cancer
N [5]	12,202 cases	96,162	131,193	24,627	986 (663 cases, 323 controls)
Population/study information [6]	M and F from Europe, Asia, Nth and South America	Japanese males (mean 51.9 yrs) and females (mean 52.3 yrs)	NHS and HPFS US males (age 40-75) and females (age 30-55yrs)	NHANES 1 Epidemiological Follow up Study- adult males and females aged 25-74 yrs	Moscow residents (funded by Unilever)
Quality [7]	O	P	P	P	P
Results [8]	6/7 Cohort studies NS, 1 study found ≥ 1 cup/day RR 2.09 (1.34-3.26) for colon cancer. 4/7 population case control NS, 3 studies (2 from China- probably green tea) show reduction in colon cancer in women only; 3/5 hospital case control	NS association of green tea and colorectal cancer in men or women.	No association of tea and colorectal cancer.	RR of colon cancer 0.57 (0.42 - 0.78) for ≤1.5 cups, 0.59 (0.35-1.00) for >1.5 c/d vs non tea drinkers in Cohort II. No effect in women. RR of colon cancer 0.41 (0.25-0.66) for men ≤1.5 c/d and 0.30 (0.09-0.98) >1.5 c/d (P trend=0.01).	High vs low intake for: Dry tea: women: OR 0.40 (0.23-0.70), men: OR 0.77 (0.42-1.43). Zavarka (tea concentrate): women: OR 0.47 (0.26-0.83); men: OR 0.99 (0.52-1.96); beverage volume: women: OR 0.68 (0.39-1.19); in men:

	studies NS with 1 increased (Italy) and one decreased (Russia) RR. Overall 13/19 studies NS.			NS results in Cohort I.	OR 1.03(0.53-2.09).
Effect on risk Increase/None/Protect	None	None	None	Protect in males	Protect in women for dry tea and tea concentrate
Clinical importance[9]	2	3	3	2	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

15.20 TEA and STROKE.

Does a particular intake of tea affect the risk of stroke?		
Evidence statement		Consumption of green and black tea is associated with reduced risk of stroke.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from studies with low to medium risk bias: 1 meta analysis (8 cohort, 2 case control and 1 cross sectional studies), 1 systematic review (4 cohort, 1 case control and 1 cross sectional) and an additional 2 cohorts and 1 case control study.
Consistency	Satisfactory	Most studies showed reduced risk for green tea. Black tea showed effect in meta-analysis, but not individual studies.
Clinical impact	Satisfactory	Risk reduction ranges from 20-60%.
Generalisability	Satisfactory	Asia (8), USA (4), Northern Europe (5).
Applicability	Satisfactory	Black tea commonly consumed; green tea less commonly consumed, but is growing in popularity.

The studies used to make the body of evidence statement are shown in Table 15.20. The meta analysis of 11 studies (eight cohort, two case control and one cross sectional) assessed green and black tea intakes and found reduced risk. Six of the nine studies found reduced risk with black tea and three with green tea. In the systematic review of six studies (four cohort, one case control and one cross sectional), two studies from Asia (green tea) show protection, but of the four western studies only one show protection. The three additional studies found green, but not black tea protective.

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Table 15.20 Studies used to make evidence statement for tea and stroke

Reference [1]	**Arab et al. 2008 [673]**	**Fraser et al. 2007 [160]**	**Kuriyama et al. 2008[1993]**	**Okamoto 2006 [2543]**	**Tanabe et al. 2008 [3188]**
Type of study [2]	meta analysis of 10 studies (8 cohort, 2 case control and 1 cross sectional)	systematic review of 6 studies (4 cohort, 1 case control and 1 cross sectional)	cohort	case control	cohort
Level of evidence [3]	IV	IV	111-2	111-2	111-2
Intervention/ comparator [4]	tea intakes (not separately identified) and risk of stroke	tea intakes and risk of stroke	green tea (cups/day) consumption and stroke	Green tea (cups/day) and stroke (subarachnoid haemorrhage SAH)	Green and black tea (cups/day) and stroke
N [5]	194,965	65,118	40,530	603 (201 cases)	6358
Population/study information [6]	USA (3), Northern Europe (3), Japan (2), China (1) M and F adults	Northern Europe (2), USA (1), Australia (1) Asia (2) M and F aged 30-69 yrs. 5 studies (1 cross sectional and 4 cohort) in common with meta-analysis by Arab.	Japan, M and F aged 40-79 yrs	Japan, 77 M, 124 F	Japan Tokamachi–Nakasato cohort study
Quality [7]	O	O	P	p	P
Results [8]	Regardless of country of origin type of tea, individuals	2 Asian studies (green tea) show protection, 4 Western studies	Men : stroke for ≥ 5 cups vs never HR 0.65 (0.45-0.93). Females: CVD 3-4	Subjects consuming TEA <1, and >or=1 time per day had adjusted OR= 0.74	low intake HR, 0.43 (CI, 0.25-0.74),high green tea intake groups HR 0.41

	consuming ≥3 cups of tea/d had a 21% lower risk of stroke vs. <1 cup per day Pooled RR 0.79 (0.72– 0.86) Black tea (6 studies) RR 0.76 (0.64–0.89) Green tea (3 studies) RR 0.78 (0.69–0.88)	show no effect.	cups HR 0.69 (0.52-0.93) and ≥ 5 cups HR 0.69 (0.53-0.90), stroke 3-4 cups/day HR 0.61(0.41-0.90) and ≥ 5 cups HR 0.58 (0.41-0.84) and Cerebral Infarction for 3-4 cups/day HR 0.47 (0.24-0.84) and ≥ 5 cups/day HR 0.38 (0.21-0.69).	(CI 0.34-1.58), and 0.56 (CI 0.32-0.98) in comparison with non daily green tea drinkers, respectively (p-trend <0.001)	(CI 0.24-0.70) Inverse association remained when cerebral infarction and cerebral haemorrhage analysed separately. The consumption of roasted tea (black)- no association.
Effect on risk Increase/None/Protect	Protect for green Protect for black tea	Protect for green. None for black.	Protect for green	Protect for SAH for green tea	Protect for green None for black tea
Clinical importance[9]	1	2	1	1	2
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

15.21 TEA and CARDIOVASCULAR DISEASE.

Does a particular intake of tea affect the risk of cardiovascular disease?		
Evidence statement		Consumption of black tea is not associated with risk of cardiovascular disease.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	1 Systematic review of 13 studies (9 cohort and 4 case control), 3 cohort studies and 1 hospital case control studies.
Consistency	Satisfactory	Eight of 13 studies in the systematic review were non-significant, 4 studies show risk reduction and 1 study shows increased risk. Of the additional 4 studies all were non-significant.
Clinical impact	Poor	No effect overall.
Generalisability	Satisfactory	Studies from Europe (7), USA (5), UK (2), other (3)
Applicability	Good	Applicable to Australian conditions.

The studies used to make the body of evidence statement are shown in Table 15.21. The review by Gardner included 13 prospective studies with eight non significant, four showing risk reduction and one showing increased risk. Of the four additional studies (three cohorts and one case control) all showed no effect.

References

Gardner, E. J., Ruxton, C. H., Leeds, A. R. & Ruxton, C. H. S. 2007, "Black tea--helpful or harmful? A review of the evidence", *European Journal of Clinical Nutrition*, vol. 61, no. 1, pp. 3-18.

Greenberg, J. A., Chow, G. & Ziegelstein, R. C. 2008, "Caffeinated Coffee Consumption, Cardiovascular Disease, and Heart Valve Disease in the Elderly (from the Framingham Study)", *The American Journal of Cardiology*, vol. 102, no. 11, pp. 1502-1508.

Kuriyama, S. 2008, "The relation between green tea consumption and cardiovascular disease as evidenced by epidemiological studies", *Journal of Nutrition*, vol. 138, no. 8, pp. 1548S-1553S.

Lagiou, P., Samoli, E., Lagiou, A., Tzonou, A., Kalandidi, A., Peterson, J., Dwyer, J. & Trichopoulos, D. 2004, "Intake of specific flavonoid classes and coronary heart disease--a case-control study in Greece", *European Journal of Clinical Nutrition*, vol. 58, no. 12, pp. 1643-8.

Sesso, H. D., Paffenbarger, R. S., Jr., Oguma, Y., Lee, I. M. 2003, "Lack of association between tea and cardiovascular disease in college alumni.", *International Journal of Epidemiology*, vol. 32, no. 4, pp. 527-33.

Table 15.21 Studies used to make evidence statement for tea and cardiovascular disease.

Reference [1]	Gardner et al. 2007 [60]	Lagiou et al. 2004 [2005]	Greenberg et al. 2008 [199]	Kuriyama et al. 2008 [1993]	Sesso et al. 2003 [2965]
Type of study [2]	systematic review of 13 studies (9 cohort and 4 case control studies)	Hospital-based case-control study	cohort	population-based prospective cohort study (Ohsaki Study)	Cohort study College Alumni Health Study
Level of evidence [3]	Level 111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	black tea intakes and risk of coronary heart disease	SD increase in flavan-3-ols and CHD	Tea(cups/day) and CHD	Tea (cups/day) and CHD	Tea (cups/day) and CHD
N [5]	340,330	329 cases and 570 controls	1354	19,060 men and 21,470 women	17,228 subjects
Population/study information [6]	Europe (6), USA (3), UK (2), other (2) Males and Females	Greece	US Framingham subjects aged 65.4 to 96.6 years	Japan aged 40-79 years	USA mean age 59.5 years
Quality [7]	O	P	P	P	P
Results [8]	Cohort studies- 6 NS, 2 reduced risk and 1 increased risk. Case control studies- 2 reduced risk and 2 NS.	1 SD increase in flavan-3-ols OR 0.76(0.59-0.97). Inverse association found to be associated with wine and tea, controlling for wine OR 0.81(0.61-1.07)	For CHD mortality or event: ≥1 cup/day vs 0 HR 1.35 (0.92-1.97)	NS effect of tea and CHD men p trend=0.66, females p trend=0.31	No significant effect p trend=0.25
Effect on risk Increase/None/Protect	None	None	None	None	None
Clinical importance[9]	2	3	3	3	3
Clinical relevance	1	1	1	1	1

[10]					
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

15.22 TEA and LUNG CANCER

Does a particular intake of tea affect the risk of lung cancer?		
Evidence statement		Consumption of green and black tea is not associated with risk of lung cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	Level 111 evidence from 1 Systematic review of 19 studies (6 cohort and 13 case control).
Consistency	Poor	13 of 19 studies in the systematic review were non-significant, 4 studies show risk reduction and 2 studies showed increased risk. In never smokers 4/7 studies showed reduced risk.
Clinical impact	Poor	No effect overall.
Generalisability	Satisfactory	Studies from Northern Europe (2), UK (1), USA and Canada (5), Japan (4), China (4), Uruguay (1) and Czech Republic (2)
Applicability	Satisfactory	Applicable to Australian conditions.

The study used to make the body of evidence statement is shown in Table 15.22. The one systematic review comprised 19 studies (six cohort and 13 case control) from northern Europe (two), UK (one), USA and Canada (five), Japan (four), China (four), Uruguay (one) and Czech Republic (two). The majority of the studies found no reduction in risk of lung cancer; 4 /19 studies (1/6 cohorts and 3/13 case control studies) reported significantly reduced risks with highest vs lowest intakes. Two older studies found increased risk ratios (from UK and China). Findings were similar for green and black tea. In never or former smokers four of seven studies (four Czech Republic, two China and one Canada) reported significant protective associations. Indicates a small beneficial association, particularly among never-smokers. The World Cancer Research Fund comments that there is limited evidence suggesting tea protects against lung cancer (WCRF Expert Report section 4.2.7. pg 114).

Reference

Arts, I. C. 2008, "A review of the epidemiological evidence on tea, flavonoids, and lung cancer", Journal of Nutrition, vol. 138, no. 8, pp. 1561S-1566s

Table 15.22 Studies used to make evidence statement for tea and lung cancer

Reference [1]	**Arts 2008**
Type of study [2]	Systematic review of 19 studies of green and black tea
Level of evidence [3]	111-2
Intervention/ comparator [4]	Highest vs lowest intakes of green and black tea and lung cancer
N [5]	272256
Population/study information [6]	Males and females from northern Europe (2), UK (1), USA and Canada (5), Japan (4), China (4), Uruguay (1) and Czech Republic (2)
Quality [7]	N
Results [8]	4 /19 studies (1/6 cohorts and 4/13 case control studies) reported significantly reduced risks with highest vs lowest intakes. One older UK study found increased risk ratios. Findings similar for green and black tea but became more significant when only methodologically sounder cohort studies included. In never or former smokers 4 of 7 studies (4 Czech Republic, 2 China and 1 Canada) reported significant protective associations. Indicates a small beneficial association, particularly among never-smokers
Effect on risk Increase/None/Protect	Protect in never smokers
Clinical importance[9]	1
Clinical relevance [10]	1
Generalisability	y
Applicability	y

STUDIES NOT INCLUDED IN BOE as < 5 Studies

Sugar sweetened beverages and oesophageal cancer

Three population case control studies of 2991 controls and 1403 cases showed no associations with oesophageal cancer (Ibiebele at al, 2008, Lagergren et al. 2006, Mayne et al. 2006)

Sugar sweetened beverages and CHD risk factors

Fung et al. 2009 in the Nurses' Health Study found increased risk for CHD after adjustment for standard and dietary risk factors. RRs (95% CIs) of CHD according to categories of cumulative average of SSB consumption (<1/mo, 1-4/mo, 2-6/wk, 1/d, and ≥2 servings/d) were 1.0, 0.96 (0.87, 1.06), 1.04 (0.95, 1.14), 1.23 (1.06, 1.43), and 1.35 (1.07, 1.69) (P for trend < 0.001).

A clinical trial by Schoppen et al. 2004 found one litre of sodium rich carbonated water intake decreased total cholesterol and LDL-cholesterol levels by 6.8% (P = 0.001) and 14.8% (P < 0.0001), respectively, whereas HDL-cholesterol concentration increased by 8.7% (P = 0.018), compared to the control period. Fasting serum glucose concentration decreased by 6.7% (P < 0.0001).

Fruit juice and type 2 diabetes

One study by Bazzano et al. 2008 found an increase of 1 serving/day of fruit juice was associated with an increased risk of diabetes HR1.18 (1.10-1.26). The cohort study was undertaken with 71,346 females from the Nurses Health study**.**

Coffee and Bone

One cohort study found high coffee consumption significantly increased fracture risk (p for trend 0.002), but no association was found with tea. The increased risk of fracture with high coffee consumption was confined to women with a low calcium intake (<700 mg/day): HR 1.33 (95% CI 1.07-1.65) with ≥4 cups (600 ml)/day of coffee compared to <1 cup (150 ml)/day The same comparison but risk estimated for women with a high propensity for fractures ≥2 fracture types) revealed a HR 1.88 (CI 1.17-3.00) (Hallstrom et al. 2006). A second study in older women found coffee intake ≥ 5 cups/day RR 1.7 (1.1-2.7) was associated with lower calcaneal and radial bone density (Korpelainen et al. 2003).

Coffee and CVD risk factors

Two cohort studies investigated coffee consumption and risk of metabolic syndrome. One found reduced HDL cholesterol in females (with >2 cups/day) but not males and one found no associations after fully adjusting for confounders.(Balk et al. 2009 and Driessen et al. 2009)

Coffee and cognition

One systematic review of 4 studies of the association between coffee intakes and Alzheimer's Disease found reduced risk estimate 0.73 (CI 0.58-0.92) but high heterogeneity (Barranco et al. 2007).

One study investigating cognitive decline women (but not men) consuming >3 cups/day vs < 1 cup/day showed less decline in verbal retrieval OR 0.67 (CI 0.53-0.85),over 4 years. There was no reduction in risk of dementia (Ritchie et al. 2007). Another study in men showed a 10-year cognitive decline of 1.2 points (4%) for coffee consumers vs an additional decline of 1.4 points (P<0.001) for non coffee consumers (van Gelder et al. 2007).

Coffee (caffeine) and glaucoma

One study found that consuming five or more cups of caffeinated coffee daily increased the risk of open angle glaucoma (POAG), RR 1.61 (CI 1.00-2.59, P for trend = 0.02); tea or caffeinated cola intake were not associated with risk. Greater caffeine intake was more adversely associated with POAG among those reporting a family history of glaucoma particularly in relation to POAG with elevated IOP (P for trend = 0.0009; P interaction = 0.04) (Kang et al. 2008)

Coffee and GDM

Adeney et al. 2007 investigated coffee consumption in 1744 non-diabetic pregnant women during early gestation and found that those reporting moderate pre-pregnancy caffeinated coffee intake had a significantly reduced risk of GDM adjusted RR 0.50 (CI 0.29-0.85) compared with non-consumers. No risk reduction was associated with decaffeinated coffee intake.

Coffee and oral cancer

One cohort study found an inverse association between coffee consumption and the risk of oral, pharyngeal, and esophageal cancers in 38,679 subjects aged 40-64 years in Japan. Coffee consumption of ≥1 cup coffee/day compared with no consumption showed HR 0.51 (0.33-0.77) (Naganuma et al. 2008)

Another study on oral/pharyngeal and esophageal cancer found the OR for >3 cups/day of coffee compared with ≤ 1 were 0.6 (CI 0.5-0.9) for oral/pharyngeal, and 0.6 (CI 0.4-0.9) for esophageal cancer (Tavani et al. 2003), and in a separate analysis of a young sample from the same cohort high consumption of coffee was related to reduced risk of oral and pharyngeal cancer in young adults (OR 0.25) (Rodriguez et al. 2004).

Coffee and melanoma

Naldi et al. 2004 found no association between coffee or tea drinking and risk of cutaneous malignant melanoma (CMM).

Coffee and tea and weight gain

One cohort study found an increase in coffee and tea consumption was associated with less weight gain in women, the association was stronger in those with BMI ≥25, who were less physically active, or who were current smokers (P for interaction < 0.001) (Lopez-Garcia 2006)

Coffee and prostate cancer

One case control study found increased risk of prostate cancer with tertile 3 vs tertile 1 of coffee intake after multivariate adjustment OR1.9 (1.2-3.0) (Gallus et al. 2007).

Coffee and tea and renal cancer

One cohort study found no association between coffee intake (mostly espresso and mocha) and RCC risk, with an OR of 1.02 (CI 0.73-1.43) in drinkers of ≥ 4 cups/day vs < 1 cup/day or with tea intake (OR 0.78 (0.59-1.05) for drinkers of ≥ 1 cup/day vs nondrinkers (Montella et al. 2009).

Coffee and stroke

One cohort study (Nurses' Health Study) found coffee consumption (RRs) of stroke across categories of coffee consumption (<1 cup/month, 1/ month to 4/week, 5-7/week, 2-3/day, and ≥4/day) were 1, 0.98 (0.84 -1.15), 0.88 (0.77 -1.02), 0.81 (0.70- 0.95), and 0.80 (0.64 - 0.98) (P for trend=0.003). After further adjustment for high blood pressure, hypercholesterolemia, type 2 diabetes, the inverse association remained significant. The association was stronger among never and past smokers (RR for ≥4 cups a day versus <1 cup a month, 0.57 (95% CI 0.39 - 0.84) than among current smokers (RR for ≥4 cups a day versus <1 cup a month, 0.97 (CI 0.63 - 1.48). Other drinks containing caffeine such as tea and caffeinated soft drinks were not associated with stroke. Decaffeinated coffee was associated with a trend toward lower risk of stroke after adjustment for caffeinated coffee consumption (RR for ≥2 cups a day versus <1 cup a month, 0.89 (95% CI 0.73 -1.08, P for trend=0.05) (Lopez-Garcia et al. 2009).

Tea and Bone disease

Tea was not found to be related to increased risk of osteoporotic fracture in two cohort studies (Hallstrom et al. 2006 and Chen et al. 2003). However, the study by Chen et al. did find increased BMD ($p<0.05$) in postmenopausal women in the Women's Health Initiative Observational Study cohort with increased tea consumption.

Tea and CVD risk factors.

One clinical trial by de Santana et al. 2008 found no significant difference in LDL, HDL and TG levels in tea drinkers. However, a significant difference in total cholesterol was found in the group receiving green tea and soy combined. Groups given green tea showed increased total plasma antioxidant potential

Tea and oral, pharyngeal and oesophageal cancer

One cohort study from Japan found that compared with men who had never drunk green tea OR for oral cancer was increased for men who were drinking ≥ 5 cups green tea/day OR 1.67 (0.89-3.16, P for trend=0.04) (Ishikawa et al. 2006). One cohort study from China found green tea drinking was protective in women OR 0.257 (0.070-0.941) (Wang et al. 2007), whilst another cohort study from

China found that ever drinking green tea increased risk in two counties, one a high risk count and the other low risk county OR 1.2 (CI 0.9-1.5); OR 1.9 (CI 1.4-2.4, respectively), and drinking tea at high temperature was also found to increase cancer risk OR 1.9 (CI 1.2-2.9); OR 3.1 (CI 2.2-4.3), respectively). However, after adjustment for tea temperature, ever drinking tea was no longer related to cancer. Monthly consumption of tea (p for trend = 0.067) and tea concentration (p for trend = 0.006) after adjustment for tea temperature (Wu et al. 2009).Another cohort study by Tavani et al. 2003 showed no relationship between black tea intakes and oral, pharyngeal and esophageal cancer

INCLUDED STUDIES NOT CONTRIBUTING TO BOE

Adeney, K. L., Williams, M. A., Schiff, M. A., Qiu, C. & Sorensen, T. K. 2007, "Coffee consumption and the risk of gestational diabetes mellitus.[see comment]", *Acta Obstetricia et Gynecologica Scandinavica*, vol. 86, no. 2, pp. 161-6.**Excluded: <5 studies**

Balk, L., Hoekstra, T. & Twisk, J. 2009, "Relationship between long-term coffee consumption and components of the metabolic syndrome: the Amsterdam Growth and Health Longitudinal Study", *European Journal of Epidemiology*, vol. 24, no. 4, pp. 203-9.**Excluded: < 5 studies**

., Barranco Quintana, J. L., Allam, M. F., Serrano Del Castillo, A. & Fernandez-Crehuet Navajas, R. 2007, "Alzheimer's disease and coffee: a quantitative review", *Neurological Research*, vol. 29, no. 1, pp. 91-5.**Excluded: < 5 studies**

Bazzano, L. A., Li, T. Y., Joshipura, K. J. & Hu, F. B. 2008, "Intake of fruit, vegetables, and fruit juices and risk of diabetes in women", *Diabetes Care*, vol. 31, no. 7, pp. 1311-7.**Excluded: <5 studies**

Chen, Z., Pettinger, M. B., Ritenbaugh, C., LaCroix, A. Z., Robbins, J., Caan, B. J., Barad, D. H. & Hakim, I. A. 2003, "Habitual tea consumption and risk of osteoporosis: a prospective study in the women's health initiative observational cohort", *American Journal of Epidemiology*, vol. 158, no. 8, pp. 772-81.**Excluded: <5 studies**

de Santana, M. B., Mandarino, M. G., Cardoso, J. R., Dichi, I., Dichi, J. B., Camargo, A. E. I., Fabris, B. A., Rodrigues, R. J., Fatel, E. C. S., Nixdorf, S. L., Simao, A. N. C., Cecchini, R. & Barbosa, D. S. 2008, "Association between soy and green tea (Camellia sinensis) diminishes hypercholesterolemia and increases total plasma antioxidant potential in dyslipidemic subjects", *Nutrition*, vol. 24, no. 6, pp. 562-568.**Excluded: <5 studies**

Dhingra, R., Sullivan, L., Jacques, P. F., Wang, T. J., Fox, C. S., Meigs, J. B., D'Agostino, R. B., Gaziano, J. M., Vasan, R. S.2007, "Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community.[erratum appears in Circulation. 2007 Dec 4;116(23):e557]", *Circulation*, vol. 116, no. 5, pp. 480-8.**Excluded: <5 studies**

Driessen, M. T., Koppes, L. L., Veldhuis, L., Samoocha, D., Twisk, J. W., Koppes, L. L. J. & Twisk, J. W. R. 2009, "Coffee consumption is not related to the metabolic syndrome at the age of 36 years: the Amsterdam Growth and Health Longitudinal Study", *European Journal of Clinical Nutrition*, vol. 63, no. 4, pp. 536-42.**Excluded: < 5 studies**

Fung, T. T., Malik, V., Rexrode, K. M., Manson, J. E., Willett, W. C., Hu, F. B., Fung, T. T. 2009, "Sweetened beverage consumption and risk of coronary heart disease in women", *American Journal of Clinical Nutrition*, vol. 89, no. 4, pp. 1037-42.**Excluded: <5 studies**

Gallus, S., Foschi, R., Talamini, R., Altieri, A., Negri, E., Franceschi, S., Montella, M., Dal Maso, L., Ramazzotti, V. & La Vecchia, C. 2007, "Risk Factors for Prostate Cancer in Men Aged Less Than 60 Years: A Case-Control Study from Italy", *Urology*, vol. 70, no. 6, pp. 1121-1126.**Excluded: < 5 studies**

Hallstrom, H., Wolk, A., Glynn, A. & Michaelsson, K. 2006, "Coffee, tea and caffeine consumption in relation to osteoporotic fracture risk in a cohort of Swedish women", *Osteoporosis International*, vol. 17, no. 7, pp. 1055-64.**Excluded: < 5 studies**

Ibiebele, T. I., Hughes, M. C., O'Rourke, P., Webb, P. M. & Whiteman, D. C. 2008, "Cancers of the esophagus and carbonated beverage consumption: a population-based case-control study", *Cancer Causes & Control*, vol. 19, no. 6, pp. 577-584.**Excluded: <5 studies**

Ishikawa, A., Kuriyama, S., Tsubono, Y., Fukao, A., Takahashi, H., Tachiya, H., Tsuji, I. 2006, "Smoking, alcohol drinking, green tea consumption and the risk of esophageal cancer in Japanese men", *Journal of Epidemiology*, vol. 16, no. 5, pp. 185-92.**Excluded: <5 studies**

Jian, L., Lee, A. H., Binns, C. W. 2007, "Tea and lycopene protect against prostate cancer", *Asia Pacific Journal of Clinical Nutrition*, vol. 16 Suppl 1, no., pp. 453-.**Excluded: <5 studies**

Jian, L., Xie, L. P., Lee, A. H., Binns, C. W. 2004, "Protective effect of green tea against prostate cancer: a case-control study in southeast China", *International Journal of Cancer*, vol. 108, no. 1, pp. 130-5.**Excluded: <5 studies**

, J. H., Willett, W. C., Rosner, B. A., Hankinson, S. E. & Pasquale, L. R. 2008, "Caffeine consumption and the risk of primary open-angle glaucoma: a prospective cohort study", *Investigative Ophthalmology & Visual Science*, vol. 49, no. 5, pp. 1924-31.**Excluded: < 5 studies**

Kikuchi, N., Ohmori, K., Shimazu, T., Nakaya, N., Kuriyama, S., Nishino, Y., Tsubono, Y. & Tsuji, I. 2006, "No association between green tea and prostate cancer risk in Japanese men: the Ohsaki Cohort Study", *British Journal of Cancer*, vol. 95, no. 3, pp. 371-3.**Excluded: <5 studies**

Korpelainen, R., Korpelainen, J., Heikkinen, J., Vaananen, K. & Keinanen-Kiukaanniemi, S. 2003, "Lifestyle factors are associated with osteoporosis in lean women but not in normal and overweight women: a population-based cohort study of 1222 women", *Osteoporosis International*, vol. 14, no. 1, pp. 34-43.**Excluded: < 5 studies**

Kurahashi, N., Sasazuki, S., Iwasaki, M., Inoue, M., Tsugane, S., Group, J. S., Kurahashi, N. 2008, "Green tea consumption and prostate cancer risk in Japanese men: a prospective study.[see comment]", *American Journal of Epidemiology*, vol. 167, no. 1, pp. 71-7.**Excluded: <5 studies**

Lagergren, J., Viklund, P. & Jansson, C. 2006, "Carbonated soft drinks and risk of esophageal adenocarcinoma: a population-based case-control study", *JNCI: Journal of the National Cancer Institute*, vol. 98, no. 16, pp. 1158-1161.**Excluded: <5 studies**

Lopez-Garcia, E., Rodriguez-Artalejo, F., Rexrode, K. M., Logroscino, G., Hu, F. B. & van Dam, R. M. 2009, "Coffee consumption and risk of stroke in women", *Circulation*, vol. 119, no. 8, pp. 1116-1123.**Excluded: < 5 studies**

Lopez-Garcia, E., van Dam, R. M., Rajpathak, S., Willett, W. C., Manson, J. E., Hu, F. B.2006, "Changes in caffeine intake and long-term weight change in men and women", *American Journal of Clinical Nutrition*, vol. 83, no. 3, pp. 674-80.**Excluded: <5 studies**

Mayne, S. T., Risch, H. A., Dubrow, R., Chow, W. H., Gammon, M. D., Vaughan, T. L., Borchardt, L., Schoenberg, J. B., Stanford, J. L., West, A. B., Rotterdam, H., Blot, W. J. & Fraumeni, J. F., Jr. 2006, "Carbonated soft drink consumption and risk of esophageal adenocarcinoma", *Journal of the National Cancer Institute*, vol. 98, no. 1, pp. 72-75.**Excluded: <5 studies**

Meunier, P. J., Jenvrin, C., Munoz, F., de la Gueronniere, V., Garnero, P., Menz, M. 2005, "Consumption of a high calcium mineral water lowers biochemical indices of bone remodeling in postmenopausal women with low calcium intake", *Osteoporosis International*, vol. 16, no. 10, pp. 1203-9.**Excluded: < 5 studies**

Montella, M., Tramacere, I., Tavani, A., Gallus, S., Crispo, A., Talamini, R., Dal Maso, L., Ramazzotti, V., Galeone, C., Franceschi, S. & La Vecchia, C. 2009, "Coffee, decaffeinated coffee, tea intake, and risk of renal cell cancer [corrected] [published erratum appears in NUTR CANCER 2009 Mar-Apr;61(2):284]", *Nutrition & Cancer*, vol. 61, no. 1, pp. 76-80.**Excluded: < 5 studies**

Naganuma, T., Kuriyama, S., Kakizaki, M., Sone, T., Nakaya, N., Ohmori-Matsuda, K., Nishino, Y., Fukao, A., Tsuji, I., Naganuma, T., Kuriyama, S., Kakizaki, M., Sone, T., Nakaya, N., Ohmori-Matsuda, K., Nishino, Y., Fukao, A. & Tsuji, I. 2008, "Coffee consumption and the risk of oral, pharyngeal, and esophageal cancers in Japan: the Miyagi Cohort Study", *American Journal of Epidemiology*, vol. 168, no. 12, pp. 1425-32.**Excluded: < 5 studies**

Naldi, L., Gallus, S., Tavani, A., Imberti, G. L., La Vecchia, C. & Oncology Study Group of the Italian Group for Epidemiologic Research in, D. 2004, "Risk of melanoma and vitamin A, coffee and alcohol: a case-control study from Italy", *European Journal of Cancer Prevention*, vol. 13, no. 6, pp. 503-8.**Excluded: < 5 studies**

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16. ALCOHOL (S1.1)

Evidence Statements

16. ALCOHOL (S1.1)

Search results

The initial search of the databases revealed 1363 articles for alcohol and the specified disease outcomes. The detailed search is included in a separate document on searches. In all, 70 references concerning alcohol had data extracted (included) and 53 of these papers were used to form the BOE statements for alcohol. Sufficient evidence was found to make BOE statements for alcohol and cardiovascular disease, type 2 diabetes, mental health and a range of cancers including breast, colorectal, oesophageal, oral and nasopharyngeal, renal, liver, ovarian, pancreatic and Non Hodgkins lymphoma.

Alcohol intake can be reported as number of alcoholic drinks (with or without specification of grams of alcohol/drink), or total alcohol intake in grams. Only studies that provided the latter measure, or enabled its calculation, were included in this review. Other measures were frequently collected, including alcohol type, drinking history and frequency of drinking episodes. These proved not to have significant results and are not reported here. Type of alcoholic beverage is mentioned only for the few studies that found a significant result for this measure and only for interest- the evidence is not such that any recommendations about beverage type can be made.

Note about other systematic reviews of the literature on alcohol and health outcomes.

Two other major umbrella reviews (one by the NHMRC (2009), the other by the World Cancer Research Fund/American Cancer Institute for Research (2007)) have been conducted that included alcohol and health outcomes. Comparability of these reviews with the present review depends on the time period of the search as well as the specified measures of alcohol and health. The key findings are discussed below.

1. NHMRC*, NHMRC Guidelines to Reduce Health Risks from Drinking Alcohol,* Commonwealth of Australia, 2009.

This was a revision of previous guidelines, based on a systematic review conducted by the former NHMRC Health Advisory Committee under the guidance of an Expert Working Committee. The search included EMBASE and Cochrane databases from 2000 to early 2007 for studies relating to alcohol consumption in humans. Papers published in 2000 were subsequently excluded. Only negative risks of alcohol were considered due to the lack of certainty in the evidence about potential health benefits. Levels of evidence were not ascribed due to "the analytic approach taken in their development" (p10).

In terms of the overlap with the current systematic review for revision of the Dietary Guidelines, only a small part of the NHMRC alcohol review focused on alcohol-related disease, forming one section of Guideline 1: Reducing the risk of alcohol-related harm over a lifetime. Five major systematic review or

meta analyses were found that informed this aspect of guideline 1, two of which were published prior to the limit of the current systematic review, for revision of the Dietary Guidelines. Of the three articles remaining (Corrao et al. 2004 (neoplasms), Di Castelnuovo et al., 2002 (vascular risk), and Fillmore et al., 2006 (CHD)), only the Di Castelnuovo et al. (2002) review was included in the CVD section of the current systematic review for revision of the Dietary Guidelines.

In the paper by Rehm et al. (2008), the authors show how they used meta analyses of epidemiological evidence, predominantly the data of Corrao et al. (1999), to:

1. Identify causal links between alcohol and cancer of the lip, oral cavity, pharynx, oesophagus, liver, breast; and hypertension, IHD, ischaemic and haemmorhagic stroke and cirrhosis of the liver; and
2. Develop a model to calculate risk (see Rehm et al. 2008).

In terms of overall risk of death from chronic disease, risk increased by 10% with each standard drink (Rehm et al. 2008).

They concluded that "for both men and women, the lifetime risk of death from alcohol related disease or injury remains below 1 in 100 if no more than two standard drinks are consumed in each drinking occasion…every drink above this level continues to increase the lifetime risk of both disease and injury" (p2, NHMRC, 2009).

The conclusions of the former NHMRC review and the body of evidence for the current review are consistent for: cancer of the breast, oesophagus, oral cavity, pharynx and larynx, and liver. Conclusions were found to be inconsistent for heart disease and renal cancer, as the former NHMRC review did not include studies on the positive effects of alcohol, and the current review found alcohol had a positive effect on both these disease outcomes. Non-Hodgkins lymphoma, colorectal and pancreatic cancer were not listed as having increased risk with alcohol consumption in the former NHMRC review.

References from NHMRC, 2009, that were not part of the Endnote library for this review:

Corrao et al., (1999) "Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol –related conditions: a meta-analysis", *Addiction*, vol. 94, pp. 1551-73.

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2. WCRF/ACIR, *Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective",* American Institute for Cancer Research, 2007.

The WCRF review, while it did not actually come up on the initial search, was included as a review document in the body of evidence for the relevant cancer outcomes. This review was published in 2007, and included studies published up to and including 2005.

The current systematic review for revision of the Dietary Guidelines had a lower limit of 2002 and upper limit of 2009. There was little overlap of included studies, and any that did occur were removed.

The WCRF data contributes strongly to our review for specific cancers.

16.1 ALCOHOL and CARDIOVASCULAR DISEASE

Does a particular intake of alcohol affect the risk of cardiovascular disease in adults?		
Evidence statement		Consumption of alcohol regularly at an intake of 1 standard drink per day for women and 1.5-2 per day for men increases HDL cholesterol.
Grade		B
Evidence statement		Consumption of alcohol regularly at an intake of 1 standard drink per day for women and 1.5-2 per day for men is associated with a reduced risk of CVD morbidity and mortality.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	8 Level II studies with positive quality ratings with low risk of bias, 10 Level III studies (8 with positive quality ratings) with low levels of bias plus one systematic review of case control and prospective studies (19 included studies).
Consistency	Satisfactory	All Level II studies administered 30-40g alcohol (2.3-3.0 standard drinks or 250-300mls wine or equivalent beverage) of periods of 4 hours to 30 days (mean 17days), Greater intakes were for men (40g) and women (30g). The large majority of Level III studies (mean follow up 10 yrs range 4-24yrs) are favourable at alcohol intakes of greater than or equal to 1 standard drink (13g Alcohol per day) for increased levels of HDL cholesterol and lower risk of CHD morbidity and mortality.
Clinical impact	Good	Alcohol intake increased HDL levels from between 4-18% over the short (<30days) intervention time periods. Protective mean ORs and HR's 0.22-0.63 for non fatal coronary heart disease events. Red wine showed a trend of having bigger impact on HDL levels and morbidity and mortality from CHD than other types of alcoholic beverages (beer and spirits).
Generalisability	Good	For all Level II and III studies populations in body of evidence differ, all were free living general adult (non pregnant) populations >18 yrs of age, which included both males and females and free of medical conditions, it is sensible to apply this evidence to the target population.

Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol are similar.

No systematic reviews were identified that had conducted a meta analysis.

Eight RCTs, one review of case control and prospective studies (16 included studies all published prior to 2001) and 10 cohort studies were used to make the body of evidence statements for alcohol and cardiovascular disease. All included studies were conducted in general (non pregnant) adult populations (>18years) and showed low risk of bias with only three studies ranking 'neutral' quality.

The included RCTs used small sample sizes (<70 participants) and administered alcohol intakes between 30-40g, with greater intakes for men (40g) than women (30g). 7/8 RCTs showed significant effects of increasing alcohol intake on increasing HDL levels, one study showed increase but not to the level of significance. No recommendation could be made about beverage type as included studies used different forms of alcohol (wine, beer and spirits).

Cohort studies showed favourable effects for increased HDL lipoprotein cholesterol levels and overall lower CHD mortality, with ORs ranging between 0.22-0.63. The comparator / reference group varied across studies, and mainly comprised non drinkers or alcohol abstainers. Definitions of this reference group also varied, and could be considered anyone having consumed from 1-5 drinks in the previous year.

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Table 16.1 Studies used to make evidence statements for alcohol and cardiovascular disease

Reference [1]	**Tsang 2005 [765]**	**Tousoulis 2008 [867]**	**Sierksma 2002 [406]**	**Hansen 2005 [257]**	**Beulens 2008 [856]**
Type of study [2]	RCT	RCT	RCT	RCT	RCT
Level of evidence [3]	II	II	II	II	II
Intervention/ comparator [4]	Subjects were randomly allocated to either red wine (RW) group or control (C). RW 375ml red wine, 12% alcohol each day for 2 weeks. Volunteers were advised to avoid all alcohol and foods and beverages rich in polyphenols and to limit fruit and vegetables over the study period. Blood samples were obtained weekly	Red wine 264ml White wine 264ml Beer 633ml Whisky 79ml, control 250ml Water	Randomised crossover trial for 3 weeks, 5 men and 5 women were allocated to beer sequence (5 vol% alcohol) followed by no alcohol beer <0.1vol% alcohol. A one week washout period.The other half consumed no beer followed by the beer. During the beer period alcohol = 40 and 30g per day for men and women. Total diet was supplied 17% energy protein, 39% fat and 44% CHO. Body weight determined every 3-4 days.	Participants were randomly divided into four groups after stratification by gender. Particiapnts conusmed daily during 4 weeks either: red wine (males 300mls, females 200mls) water and red grape extract (wine equivalent dose of total polyphenol, anthocyanin or half dose) or water and placebo tablets. The daily alcohol intake was 38.3g for male and 25.5g for women. A week before and during the intervention no other sources of alcohol or anthocyanins were allowed. Subjects were given a list of these foods	The randomised crossover trial consisted of two treatment periods of 3 weeks, each preced by a one week washout period where participants were instructed to consume no alcohol. Randomised to consume sequence beer (5%vol ethanol) followed by alachol free beer (<0.1% alcohol) or the other way around. Participants consumed 3 cans of the beer or alcohol free beer daily with thier evening meal equalling 40g ethanol / day during treatment. In the last 10 days of each treatment diet was controlled All food and drink was supplied by TNO and particiapnts were not

					allowed to eat anything except that which was provided except tea, coffee and water. The diet was 37% fat, 15% protein and 48% CHO, excluding energy from alcohol.
N [5]	Total n= 20 RW 12 Control 8 M and F	n=67 M and F	n=19 M	n = 69	n = 20 M
Population/study information [6]	non smokers 23-50 yrs not taking medication or supplements	Healthy subjects with no history of heart disease, dibates, HT dyslipidemia, obesity, they were not receiving any regular medications or antioxidant substances	Men 45-64yrs, weight 79.2 ± 9.2TG mmol/ l 1.2 ±0.4 chol 6.2 ±1.1 HDL 1.5 ±0.4 Women 49-62 weight 74 ±7.3 TG 0.9 ±0.4 Cholsterol6.9 ±1.3 HDL 2.0 ± 0.4. All were non smoking. Eligible if consumption of <28 alchol containing beverages per week for men and <21 for women BMi between 21-31 and no family history of alcoholism	Participants needed to be aged 38-75yrs not on lipid lowering medication, antihypertensives or antioxidant supplements, no alcoholism or have any uncommon dietary habits (vegtariansm). NS differences between groups	Men aged 18-25yrs
Quality [7]	P	P	P	P	P
Results [8]	Moderate consumption of red wine (375mls) rich in gallic acid, flavanols and anthocyanins over a 2 week period	No signifcant effect on HDLD or cholesterol levels. red wine and beer may signifncantly improve endothelial function and decrease	Moderate alcohol consumption (30-40g) sig increased HDL levels (by 11%) and sig reduced CRP and fibrinogen levels	Daily intake of 200-300ml red wine increased HDL (0.07mmol/ L) and lowered fibrinogen relative to drinking	In this population of healthy young men profound effects of moderate alcohol consumption (40g per day for 3 weeks) on

	significantly increased concentrations of total phonelics in the plasma. There was also significant modest increase (0.1mmol / L) in HDL in intervention group	Van Willebond (thrombosis and fibinolysis) levels 4 hours after consumption		water with or without fermented garpe extract. The effect or red wine seems to be caused by the alcohol content.	HDL (increase 18%) and LDL cholesterol (-7.8%). Possible that overweight patients may respond less favourbaly to alcohol consumption than lean subjects
Clinical importance [9]	1	2	1	2	2
Clinical relevance [10]	1	2	1	2	2
Generalisability	y	y	y	y	y
Applicability	M and F	M and F	M only	M and F	M only

TNO=the Netherlands Organization for Applied Scientific Research

Table 16.1 Studies used to make evidence statements for alcohol and cardiovascular disease (cont.)

Reference [1]	**Badia 2004 [316]**	**Avellone 2006 [185]**	**Addolorato 2008 [906]**	**Di Casteluovo 2002 [646]**	**Snow 2009 [1327]**
Type of study [2]	RCT	RCT	RCT	Review of case control and prospective studies	Cohort
Level of evidence [3]	II	II	II	III-2	III-2
Intervention/ comparator [4]	The study was an open, prospective randomized crossover clinical trial. During the first 2 weeks of the study the subjects did not drink any alcoholic beverages. During the following four weeks the subjects all received 30g ethanol / day as red wine (2 glasses of 160ml each per day with dinner at 12.5°) and 30 g ethanol per as an alocoholic beverage with low phenolic content (100ml gin / day with dinner) in a random cross over design.	Participants were randomly subdivided into two groups and were assigned to either receive with a crossover design one of two types of sicilian wine either Nero d'Avola-Rallo or Etna Torrepalino. Group A n= 24 whose diet was supplemented for 4 weeks with 250ml / day of red wine 12 with Nero d'avola and 12 with Etna Torrepalino) during meals and the follwing 4 weeks when they returned to their usual wine intake and Group B n=24 who for 4 weeks maintained their usual wine intake (no drink only occasiobally) and whose diet for the	After two weeks abstinece from alcohol (T0) subjects were randomly divided into four groups. Group A consumed 40g ethanol per day in a lager type beer (1000ml 4% ethanol) for 30 days. Group B 40g ethano each day in red wine (400ml, 11% ethanol) for 30 days. Group C 40g ethanol per day in spirit (120ml of disillate 40% volume) for 30 days. Group D maintained abstinece from alcohol during the study period and served as the control group. The amount of alcoholic beverages was fractioned into two administrations on any day of the study and was consumed by	Alcohol consumption and vascular risk	Alcohol g/ day

		follwing 4 weeks was supplemented with 250nl per day 12 with Nero and 12 woth Etna during meals.	subjects with the amin daily meals consisting of a normal mediterranean diet.		
N [5]	n = 8 M and F	n= 48 M and F	n = 40	Wine analysis: 201308 persons Beer: 208096	1154 M and F
Population/study information [6]	Healthy men aged 30-50yrs who worked at the University of Barcelona	aged 35-65	young men mean age 28±6	Nondrinkers (non or <1drink per month) and drinkers (various categories)	aged 18-64
Quality [7]	P	P	P	0	P
Results [8]	30g of alcohol from either gin (100ml) and red wine (320mls) showed signifncat improvement in HDL concentrations (increased by (7%). Moderate alcohol consumption (30g per day) may reduce monocyte adhesion which may be benficial for athersclerosis.	250mls for 4 weeks Red wine significantly increased HDL (increased 4 %) and improved the HDL and LDL ratio it also sig reduced fibrinogen	All subjects exposed to ethanol increased their HDL (increased 8%) and not the control. Cholesterol increased in the beer and wine groups only	Reduction in vascular risk associated with alcohol consumption	Number of CHD events n=103) 68 in men 35 in women. Men who consumed > 1.39 standard drinks per day had sig decreased risk of CHD for older men 50-64yrs at baseline). Heavy episodic drinking (> 8 standrad drinks per session) was associated with increased CHD risk and hyeprtension trend (P0.054)
Clinical importance [9]	1	1	1	1	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	y	y	y
Applicability	M and F	M and F	M and F	Yes	M and F

Table 16.1 Studies used to make evidence statements for alcohol and cardiovascular disease (cont.)

Reference [1]	**Gigleux 2006 [161]**	**Harriss 2007 [1257]**	**Mukamel 2006 [201]**	**Mukamel 2003 [395]**	**Nielsen 2004 [1092]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Alcohol g/ day	Alcohol g/ day	Alcohol intake, weekly number of drinks	Alcohol intake g/ day	Alcohol intake, number of drinks
N [5]	1966 M Quebec Cardiovascular study	38 200 M and F	4410 M and F	38077 M Health Professionals Follow up study	13977 M and F
Population/study information [6]	(age 46-76yrs)	aged 27-75yrs	aged 65 and over.	40-75yrs	aged 20yrs and older
Quality [7]	P	P	P	P	P
Results [8]	1 or more standard drinks per day had significant cardioprotective effects with increased HDL and decreased CRP when compared to non drinkers (<1.3g/d). Men who consumed >15.2g / day (1.16 standard drinks) alcohol had 39% decreased RR of IHD	Usual daily alcohol intake (>20g/ day or 1.5 SD) was assoc with reduced CVD and CHD mortiality for women but not men. Drinking frequency was assoc inversly with CVD and CHD death for men but not for women.	675 cases of myocardial infarction. There was an inverse association between alcohol intake and realtive risk of CHD. Consumption of 14 or more drinks per week (2 per day) was associated with the lowest risk of CHD 0.58(0.39-0.83).	1418 cases of MI during follow up. As compared with men who consumed alcohol less than once per week , men who consumed alcohol 3-4 or 5-7 times per week had decreased risk of MI 0.68 (0.55-0.84 and 0.63 (0.54-74). The risk was simialr among men who consumed less than 10g alochol per day and those who consumed >30g. No single type of beverage conferred additional benefit noe	The apparent protective effect of moderate alcohol intake (1-2 drinks per day) on coronary heart disease attenuated during prolonged follow up.

				consumption with meals. A 12.5g increase in alcohol consmption over a 4 yr follow up was assoc with a RR of 0.78(0.62-0.99)	
Clinical importance [9]	1	2	1	1	2
Clinical relevance [10]	2	2	1	1	2
Generalisability	y	y	y	y	y
Applicability	M only	M and F	M and F	M only	M and F

Table 16.1 Studies used to make evidence statements for alcohol and cardiovascular disease (cont.)

Reference [1]	**Marques-Vidal 2004 [307]**	**Moraes 2003 [1165]**	**Koppes 2005 [207]**	**Ambler 2003 [394]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Alcohol intake ml / alcohol per week	Alcohol intake g /day	Alcohol, units of intake	Alcohol intake grams of alcohol per week
N [5]	9750 M	1091 M and F	317 M and F Amsterdam Growth and Health Longitudinal study	7749 M and F
Population/study information [6]	aged 50-59yrs	Mean age 42.8±16.9	mean age 32.4	35-65yrs
Quality [7]	P	0	0	P
Results [8]	During follow up there were 106 cornery deaths or MI and 94 angina pectoris. for people in france subjects in the hhighest quartile (>441 ml / week) of intake had significant lower RR of developing AP than non drinkers 0.38 (0.15-0.96) The amount of alcohol consumption rather than the type is realated to both angina pectoris and MI in france but not ireland.	A total of 52 people presented a cardio event.The consumption of alcohol was independently assoc with a higher incidence of CVD HR 1.001(1.00-1.003)	A 10 g / day (0.75 standard drink) difference in alcohol consumption was positvly associated with with a 0.05mmol/L (1.9mg(dl) difference in HDL cholesterol in both corss sectional (P0.004) and longitudinal (P<0.001) analyses. The relationship did not differ for men or women or for the consumption of beer, wine or distilled spirits. realtionships with changes in total cholesterol, A significant non linerar relationship was found with sys BP in which drinkers of 30g alchol / day 2.3 stadnard drinks) had the lowest values.	Higher alcohol consumption (>7 glasses per week) is assoicated with more favourable/ higher levels of HDL and fibrinogen. In contrast higher levels of beer and spirits is assoicated iwith less favourable systolic BP

Clinical importance [9]	1	2	2	2
Clinical relevance [10]	1	2	2	2
Generalisability	y	y	y	y
Applicability	M only	M and F	M and F	M and F

16.2 ALCOHOL and TYPE 2 DIABETES MELLITUS

Does a particular intake of alcohol affect the risk of diabetes in adults?		
Evidence statement		Alcohol intake of 1-3 standard drinks per day is not associated with risk of type 2 diabetes.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Three Level II studies (with mean follow up of 25 days consuming from 1-3 standard drinks per day 125mls - 500mls), Two Level III studies (mean follow up 4.6 range 3-6.yrs) and one systematic review of cohort studies (Level III) (total 15 studies included) with high risk of bias due to sponsorship which included industry members. 3 cross sectional studies retrieved but not yet extracted.
Consistency	Poor	2 out of 3 Level II studies showed no improvement in insulin sensitivity at follow time periods regardless of alcohol intake, Level III studies showed inconsistencies in decreased risk of type 2 diabetes with increasing alcohol intake (HR 0.78) and the other increasing alcohol intake associated with higher fasting glucose levels.
Clinical impact	Poor	The review of cohort studies shows reduced risk of type 2 diabetes associated with moderate (with lowest RR for consumption of 12-24g/ days 0.66 (0.59-0.75)) however overall, not enough evidence from other Level II and III studies to suggest clinically important benefits from alcohol intake of type 2 diabetes parameters (fasting glucose and insulin).
Generalisability	Good	For all Level II and III studies populations in body of evidence differ, all were free living adult populations > 18 yrs of age, which included both males and females and free of medical conditions.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol are similar.

The studies used to make the BOE statements are shown in Table 16.2. Three RCTs, one review of cohort studies (15 included studies published prior to 2003), and two cohort studies were used to make the body of evidence statements shown in Table 16.2. The literature showed inconsistencies of the effect of alcohol intake and various parameters of type 2 diabetes (fasting glucose, insulin and in one review RR of type 2 diabetes) which varied for all studies making comparisons across studies difficult. The included RCTs used small sample sizes (<50 participants), with two of the three showing no effect on insulin sensitivity. The review showed reduced risk of type 2 diabetes (RR 0.66) at intakes between 12-24g of alcohol per day. One cohort study showed a decreased HR with increasing alcohol intake; the

lowest HR indicated at the intake range of 70-140 g alcohol per week. Results were independent of alcohol type.

References

Banini, A. E., L. C. Boyd, et al. 2006, "Muscadine grape products intake, diet and blood constituents of non-diabetic and type 2 diabetic subjects", *Nutrition*, vol. 22, no. 11-12, pp. 1137-45.

Beulens, J. W., E. C. de Zoete, et al. 2008, "Effect of moderate alcohol consumption on adipokines and insulin sensitivity in lean and overweight men: a diet intervention study", *European Journal of Clinical Nutrition*, vol. 62, no. 9, pp. 1098-1105.

Beulens, J. W. J., R. P. Stolk, et al. 2005, "Alcohol consumption and risk of type 2 diabetes among older women", *Diabetes Care*, vol. 28, no. 12, pp. 2933-8.

Koppes, L. L. J., J. M. Dekkeer, et al. 2005, "Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies", *Diabetes Care*, vol. 28, no. 3, pp. 719-725.

Vernay, M., B. Balkau, et al. 2004, "Alcohol consumption and insulin resistance syndrome parameters: associations and evolutions in a longitudinal analysis of the French DESIR cohort", *Annals of Epidemiology*, vol. 14, no. 3, pp. 209-214.

Zilkens, R. R., V. Burke, et al. 2003, "The effect of alcohol intake on insulin sensitivity in men: a randomized controlled trial", *Diabetes Care*, vol. 26, no. 3, pp. 608-12.

Table 16.2 Studies used to make evidence statements for alcohol and type 2 diabetes mellitus

Reference [1]	**Beulens et al. 2005 [213]**	**Vernay et al. 2004 [1134]**	**Koppes et al. 2005 [651]**	**Banini et al. 2006 [988]**	**Beulens et al. 2008 [568]**	**Zilkens et al. 2003 [385]**
Type of study [2]	Cohort	Cohort	Systematic Review of Cohort	Randomised trial case control	Randomised cross over trial	Randomised cross over trial
Level of evidence [3]	III-2	III-2	III-2	II	II	II
Intervention/ comparator [4]	Alcohol intake (g) / week.	Alcohol intake g/ day.	Alcohol intake and incidence of type II diabetes.	Subjects with type 2 diabetes were assigned to take one of three supplements Muscadine juice (MJ) muscadine wine (MW) and dealcoholised muscadine wine (DzW). Non diabetic patients were randomly assigned to the MJ group and the control group without supplementation. Each subject was asked to drink 150mL of the assigned supplement (except the control group	The crossover trial consisted of two treatment periods of 3 weeks, each preceded by a one week washout period where participants were instructed to consume no alcohol. Randomised to consume sequence beer (5%vol ethanol) followed by alcohol free beer (<0.1% alcohol) or the other way around. Participants consumed 3 cans of the beer or alcohol free beer daily with their	Participants entered a 4 week baseline period in which a consistent pattern of alcohol intake was established aided by weekly provision of 12 x 375ml cans of beer 4.9% alcohol. For the first study period subjects were randomised using a random numbers generated with Excel to either continue their usual alcohol intake or to reduce their alcohol intake by substituting a low alcohol beer 0.9% alcohol also

				which did not receive supplementation) after dinner for 28 days.	evening meal equaling 40g ethanol / day during treatment. In the last 10 days of each treatment diet was controlled All food and drink was supplied by TNO and participants were not allowed to eat anything except that which was provided except tea, coffee and water. The diet was 37% fat, 15% protein and 48% CHO, excluding energy from alcohol.	supplied. During the second study period subjects switched over. Participants were encouraged to limit all other non beer alcohol.
N [5]	16,330 F	3385 M and F	11,959 incident cases of type 2 diabetes 369,862 individuals	n= 52 M and F	n= 20 M	total n= 16
Population/study information [6]	aged 45-70yrs, Dutch Prospect EPIC Study	aged 34- 64yrs		n= 25 controls n= 29 type 2 diabetes aged 45- 65 yrs	aged 18-25 yrs	aged 20-65 yrs
Quality [7]	P	P	Negative - sponsored by the	P	P	P

			Alcohol Task Force of Europe which included industry members.			
Results [8]	760 incident cases. HR decreased with increasing alcohol consumption P<0.05 with the lowest HR for 70-139.9g alcohol per week (0.78(0.56-1.08). The effect was independent of type of alcohol.	In men fasting glucose was associated with alcohol intake; a 20g higher intake of alcohol was associated with higher fasting values of glucose (0.7mmol / L). Alcohol intake had little effect on insulin resistance syndrome.	Considerable reduced risk of type 2 diabetes associated with moderate (with lowest RR for consumption of 12-24g/ days 0.66 (0.59-0.75)) but not heavy alcohol consumption in men and women with low and high BMI.			
Clinical importance [9]	1	3	Yes	Daily intake of 150ml of wine with meals improved fasting insulin levels in people with Type 2 diabetes only.	Moderate alcohol consumption did not affect insulin sensitivity within 3 weeks of moderate alcohol consumption.	A daily reduction in alcohol intake from 7 to one standard drink per day over 4 weeks did not alter the insulin sensitivity in non diabetic men
Clinical relevance [10]	1	3	Yes males and females	2		
Generalisability	y	y	y	y	y	y
Applicability	F only	M and F	M and F	M and F	M only	M and F

TNO=the Netherlands Organization for Applied Scientific Research

16.3 ALCOHOL and MENTAL HEALTH

Does a particular intake of alcohol affect the risk of mental health in adults?		
Evidence statement		Consumption of alcohol at the level of 1 standard drink per day for women and 1.5-2 per day for men, with a maximum intake of 4 standard drinks per day, is associated with reduced risk of dementia in older adults.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Six Level III studies with low to moderate risks of bias. 1 case control study retrieved but not yet extracted.
Consistency	Good	Level III studies had a mean follow up of 4.25yrs (range 2-8yrs). All Level III studies demonstrate a favourable effect for reduced risk of dementia (all types) with increasing alcohol intake at an intake of between 1-4 standard drinks per day (125mls-500mls).
Clinical impact	Good	Alcohol intake decreased risk for dementia (all types) with OR of 0.58-0.71. The most common type of dementia diagnosed in populations was vascular dementia. One study demonstrated a protective effect of alcohol for decline in cognitive functioning. Inconsistent findings between studies of the effect heavy drinking episodes (>21 drinks per week) and increased risk of dementia (1 no effect 1 pronounced effect).
Generalisability	Good	For all Level III studies. Populations in body of evidence differ. The majority were free living adult populations, all were aged > 55yrs of age, which included both males and females , it is sensible to apply this evidence to the target population.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types are similar.

Six cohort studies were used to make the body of evidence. The length of follow-up of included studies varied from two to eight years, with all studies carried out in populations >55 years of age and sample sizes ranging from n= 1445 to 11 102. All studies demonstrated a favourable effect of reduced risk of dementia with increasing alcohol intake at levels between one to four standard drinks (125-500ml) per day. This effect extended across all types of dementia, with vascular dementia and Alzheimers disease

predominantly noted in included studies. Studies showed inconsistent findings on the effects of heavy drinking (>21 drinks per week) and the associated risk of dementia. Deng et al. (2006) showed heavy drinking to be associated with high risk of dementia, while Stampfer et al. (2005) showed no effect for both men and women.

References

Deng, J., D. H. D. Zhou, et al. 2006, "A 2-year follow-up study of alcohol consumption and risk of dementia", *Clinical Neurology and Neurosurgery*, vol. 108, no. 4, pp. 378-383.

Larrieu, S., L. Letenneur, et al. 2004, "Nutritional Factors and Risk of Incident Dementia in the PAQUID Longitudinal Cohort", *Journal of Nutrition, Health & Aging*, vol. 8, no. 3, pp. 150-154.

Luchsinger, J. A., M.-X. Tang, et al. 2004, "Alcohol Intake and Risk of Dementia", *Journal of the American Geriatrics Society*, vol. 52, no. 4, pp. 540-546.

Ruitenberg, A., J. C. van Swieten, et al. 2002, "Alcohol consumption and risk of dementia: the Rotterdam Study", *The Lancet*, vol. 359, no. 9303, pp. 281-286.

Solfrizzi, V., A. D'Introno, et al. 2007, "Alcohol consumption, mild cognitive impairment, and progression to dementia", *Neurology*, vol. 68, no. 21, pp. 1790-1799.

Stampfer, M. J., J. H. Kang, et al. 2005, "Effects of moderate alcohol consumption on cognitive function in women.[see comment]", *New England Journal of Medicine*, vol. 352, no. 3, pp. 245-53.

Table 16.3 Studies used to make evidences statements for alcohol and mental health

Reference [1]	**Deng et al. 2006 [1004]**	**Luchsinger et al. 2004 [1283]**	**Stampfer et al. 2005 [260]**	**Larrieu et al. 2004 [1281]**	**Ruitenberg et al. 2002 [1234]**	**Solfrizzi et al. [121]**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	III-2	III-2	III-2	III-2	III-2	III-2
Intervention/ comparator [4]	Alcohol intake, units per week.	Alcohol intake, frequency of consumption.	Alcohol intake, g / day.	Alcohol intake ml per day.	Alcoho intake, frequency of consumption.	Alcohol intake number of drinks per day.
N [5]	2632 M and F	980 M and F	11,102 M and F	2950 M and F	5395 M and F	n=1445 M =F
Population/study information [6]	Aged 60 yrs and over. Comparisons made to non drinkers.	Aged 65 yrs and older. Comparisons made to non drinkers.	Aged 70 yrs and over.	Aged 65 yrs and over.	The Rotterdam study, particpants were aged 55 yrs and over which included some particianots from institutions.	Participants were aged 65-84yrs participating in the Italian Longitudinal Study independent or instituionalised.
Quality [7]	P	P	P	P	P	P

Results [8]	Light to moderate drinking (1-21 units per week) (1 -2.6 standard drinks) was associated with a significantly lower risk (0.52(0.32-0.85)) of dementia (in particular vascular dementia) compared with non drinking, effect more pronounced in men. Excessive drinking was associated with higher risk of dementia. For wine a significantly lower risk of dementia existed for light to moderate drinkers. no association with spirits. Light to moderate drinking was associated with a significantly lower risk of dementia compared to non drinkers.	light to moderate (1 serving a month to 3 servings a day) intake of wine was associated with a decreased risk of dementia and Alzheimers disease (0.59(0.38-0.91)). Similar intakes of beer, spirits or total alcohol were not related to Alzheimers disease.	Moderate drinkers had (those who consumed less than 15g of alchol per day (1.1 standard drinks) had better mean cognitive scores than non drinkers, particularly in women. Among moderate drinkers the risk of impairment 0.77 (0.67-0.88). No significant associations with higher levels of drinking (1530g per day) and the risk of cognitive decline.	Moderate consumption (250-500ml per day) of wine is associated with a decreased 0.56 (0.36-0.92) risk of dementia and 0.53(0.30-0.95) risk of Alzheimers disease.	Increasing alcohol intake was associated with decreased risk of dementia up to <4 drinks per day. With the lowest risk for those who consumed 1-3 drinks per day (0.58(0.38-0.90)). The same trend was noted for dementia sub type.	Patients who had minor cognitive impairment but who consumed less than 1 drink per day (approx 15g alcohol) had a lower rate of progression to dementia than abstainers (HR 0.15(0.03-0.78). There was no association between higher levels of drinking (>1 drink per day) and rate of progression to dementia. No effects by type of alcohol.
Clinical importance [9]	2	2	2	2	2	2
Clinical relevance [10]	2	2	2	2	2	2
Generalisability	y	y	y	y	y	y
Applicability	M and F	M and F	M and F	M and F	Men and women, however some	M and F

					particpants were institutionalized.	

16.4 ALCOHOL and BREAST CANCER

Does a particular intake of alcohol affect the risk of breast cancer in adults?		
Evidence statement		Consumption of alcohol, even from low (10-15 g/d), is associated with increased risk of breast cancer.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	The evidence base is at Level 3, with a meta-analysis of cohort studies conducted as part of the World Cancer Research Fund review in 2004, and subsequent evidence from 3 large cohort studies and 4 case-control studies.
Consistency	Good	Studies showed excellent consistency in the association between increased risk of breast cancer (in the order of 10-12%) and alcohol consumption, mostly in terms of current intake. However, there was not good consistency around whether the relationship is linear, or has a threshold with category of alcohol intake. There was also a lack of consistency around sub-analyses for menopause status, with one Danish cohort study finding alcohol only increased risk at high levels of intake in for premenopausal women while a US case-control study found that risk only increased for moderate to high levels of alcohol consumption in post-menopausal women, and other studies did not do these analyses. There is no clear evidence that type of alcoholic beverage makes a difference (excepting the findings about wine from one French and one US case-control study) rather the effect appears to come from the amount of ethanol.
Clinical impact	Good	For those that had statistically significant results, confidence intervals ranged between 1.0 and 1.2.
Generalisability	Good	Populations in the studies varied, however may be generalised to the female adult population of Australia, having been conducted in the USA, UK and Europe.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

One meta analysis of a cohort study, three cohort studies and four case control studies were used to make the body of evidence statements for alcohol and breast cancer (see Table 16.4). The WCRF meta-analysis showed a slight but clear linear increase in risk for increasing levels of alcohol consumption.

The evidence published since that review provided further evidence that alcohol increases the risk of breast cancer. The UK Million Women Study found evidence of a linear trend while other studies found evidence of a threshold effect, where risk only increased for the highest levels of drinking, not for light or moderate levels. The Million Women Study in the UK consisted of women with relatively low total alcohol consumption. Bessasoud and Daures (2008), in France, found a threshold at 1.5 drinks (15 g ethanol per day); Li et al. (2009) found a linear effect, after a threshold of 1-2 drinks/day (g not specified). Other studies, including cohort studies by Petri et al. (2004) and case control studies by Terry et al. (2006) and Newcomb et al. (2009), also found an increased risk but no significant linear trend.

Only two studies, both case-controls, found an effect of alcohol type; both the US and French studies found wine, specifically, to be protective. While the French study did not evaluate the effects of red and white wines, the US study found neither red nor white wine to be associated with increased breast cancer risk.

The reference ranges for frequency/quantity of alcohol consumption varied between studies due to different definitions of the amount of ethanol/drink (some specified 10 g, others 12 g per drink), while one study failed to specify the amount in one drink.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Bessaoud, F. and J. P. Daurès 2008, "Patterns of Alcohol (Especially Wine) Consumption and Breast Cancer Risk: A Case-Control Study among a Population in Southern France", *Annals of Epidemiology*, vol. 18, no. 6, pp. 467-475.

Deandrea, S., R. Talamini, et al. 2008, "Alcohol and breast cancer risk defined by estrogen and progesterone receptor status: a case-control study", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 17, no. 8, pp. 2025-8.

Li, Y., D. Baer, et al. 2009, "Wine, liquor, beer and risk of breast cancer in a large population", *European Journal of Cancer*, vol. 45, no. 5, pp. 843-50.

Newcomb, P. A., H. B. Nichols, et al. 2009, "No difference between red wine or white wine consumption and breast cancer risk", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 18, no. 3, pp. 1007-10.

Petri, A. L., A. Tjonneland, et al. 2004, "Alcohol Intake, Type of Beverage, and Risk of Breast Cancer in Pre- and Postmenopausal Women", *Alcoholism: Clinical and Experimental Research*, vol. 28, no. 7, pp. 1084-1090.

Terry, M. B., F. F. Zhang, et al. 2006, "Lifetime Alcohol Intake and Breast Cancer Risk", *Annals of Epidemiology*, vol. 16, no. 3, pp. 230-240.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research***.**

Table 16.4 Studies used to make evidence summary for alcohol and breast cancer

Reference [1]	**WCRF 2007 [1401]**	**Allen et al. 2009 [1]**	**Li et al. 2009 [1318]**	**Petri et al. 2004 [1279]**	**Terry et al. 2006 [1027]**	**Deandrea 2008 [1381]**	**Bessaoud 2008 [876]**
Type of study [2]	Meta-Analysis of Cohort	Cohort	Cohort	Cohort	Case-Control	Case-Control	Case-Control
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption (g) and Breast Cancer	current alcohol consumption in g	current alcohol consumption: frequency and type	Current alcohol consumption: frequency and type	Lifetime and current alcohol consumption: frequency	Alcohol consumption and Breast Cancer	Alcohol consumption and Breast Cancer
N [5]	Not specified (9 studies included)	n=1,280,296 (n=68775)	2829 cases, 70,033 cohort controls	13,074 472 incident cases breast Ca	1508 cases 1556 controls	989 cases 1350 controls	437 cases 922 controls
Population/study information [6]	Women (pre and post menopausal) participating in large cohort studies	UK, Million Women Study	Females, 40.6 yrs (mean);	Females >20-91yrs, Danish; stratified by pre or post menopause	Women participating in the Long Island Breast Cancer Study Project, USA	Italian women (over 56% post-menopausal)	Women aged 25-85 yrs living in the south of France
Quality [7]	P	p	p	P	**P**	P	P
Results [8]	A 10% (6-14%) increased risk, with no threshold, for every increase of 10g/day of current	Increasing current alcohol consumption was associated with a 12% (9-14%) increased risk	Increased risk of Breast Ca with a threshold at 1-2 drinks/day of current alcohol intake, increasing	Increased risk with high current ethanol consumption (>27 drinks/wk (324g ethanol) for pre-menopausal women 3.49	No association between current alcohol intake and breast cancer risk. Women with a BMI <25	Increased risk of 13% (7-20%) for every 10g EtOH increase per day, but only in women with an ER+	Current alcohol consumption of 10 to 15 g of alcohol/day associated with decreased

	ethanol intake. In 7 of the 9 studies the risk was increased. Linear trend significant.	of breast cancer for every 10g ethanol/day, in a linear relationship ($p<0.001$).	linearly to 3 or more drinks/day. Results not stated in g ethanol. No relation to alcohol type. No risk in less than one drink per day.	(1.36-8.99) but not post-menopausal women. Total alcohol intake above 27 drinks/wk) increased RR of breast cancer among pre-menopausal women, but no association for post menopausal women. Linear effect absent. No effect of type of alcohol.	and moderate lifetime consumption of alcohol (15-30 g Ethanol /day) had higher risk of breast cancer. Risk decreased for higher intakes, and no linear trend. OR were slightly higher for pre than post-menopausal women. No associated between alcohol and breast cancer for lighter or heavier intake. No effect of type of alcohol.	tumour. Alcohol is related to ER+ breast tumours but not ER-. Current alcohol intake is more strongly related to ER+ breast tumours than ER-. Confirmed general relationship of alcohol and breast cancer also.	risk of breast cancer OR= 0.58, (CI 0.34-0.97) in unadjusted analyses and OR=0.21, (CI 0.10-0.91) in adjusted analyses. Above 15g ethanol/day risk increased risk, (threshold) so no significant trend overall (see Table 3); No relationship with pattern of alcohol consumption (see Table 4); no relationship between frequency of beverage type and breast cancer risk in adjusted

							analyses (Table not shown); however sporadic (defined as between 10-12g wine/day) pattern of wine consumption associated with a significant decrease in breast cancer risk in adjusted analyses OR= 0.51 (0.30-0.91) compared with non wine drinkers (see Fig 1).
Effect on risk (Increase/None/Protect)	Increase	increase	Increase	Increase	Current intake: none. Lifetime intake: Increase	Increase	Increase
Clinical importance [9]	1	1	1	1	1	1	4

Clinical relevance [10]	1	1	1	1	1	1	1
Generalisability	For women	For women	For women	For women	For women	For women	For women
Applicability	y	For women	y	For premenopausal women	For women	For women	For women

16.5 ALCOHOL and COLORECTAL CANCER

Does a particular intake of alcohol affect the risk of colorectal cancer in adults?		
Evidence statement		Consumption of alcohol, even at low levels (10g/day) of consumption, is associated with an increased risk of colon cancer and rectal cancer.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	All Level III-2 evidence; 1 meta-analysis of cohort studies on colon cancer and 1 meta-analysis on rectal cancer) (3 cohort studies - 2 colorectal and 1 colon-only), all with minimal bias.
Consistency	Satisfactory	Colon cancer: the meta-analysis and one cohort study showed an increased risk, but the 2 other cohort studies, showed no relationship. Rectal cancer: the meta-analysis showed an increased risk, as did one of the cohort studies, but not the other. There is no clear evidence that type of alcoholic beverage makes a difference to risk.
Clinical impact	Good	For those that had statistically significant results, confidence intervals ranged mostly between 0.1-0.18. Potentially greater clinical impact in those with a family history of colorectal disease (evidence from 1 cohort study.
Generalisability	Good	Populations in the studies varied however may be generalised to the male or female adult population of Australia. The two largest cohort studies only included women. The results may be particularly important in those with a family history of colorectal cancer.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

One meta-analysis of cohort studies on colon cancer and one on rectal cancer were conducted by the WCRF (2007). These were used, together with three cohort studies, to make the body of evidence statements for alcohol and colorectal cancer (see Table 16.5). There were no case-control studies for this outcome. Results were slightly different for colon cancer and rectal cancer so they are treated separately in the recommendation. Regarding colon cancer, the WCRF (2007) meta analysis and one cohort study showed an increased risk, but the two other cohort studies (Allen 2009, Bongaerts et al. 2006) showed no relationship. Regarding rectal cancer, the WCRF (2007) meta analysis showed an increased risk, as did one of the cohort studies (Allen 2009). However, the Bongaerts et al. (2006) cohort study did not show such evidence of increased risk. Slightly stronger evidence exists of a relationship between rectal cancer and alcohol than for colon cancer.

There is no clear evidence that type of alcoholic beverage makes a difference to risk.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Bongaerts, B. W. C., A. F. P. M. de Goeij, et al. 2006, "Alcohol and the risk of colon and rectal cancer with mutations in the K-ras gene", *Alcohol*, vol. 38, no. 3, pp. 147-154.

Fuchs, C. S., W. C. Willett, et al. 2002, "The influence of folate and multivitamin use on the familial risk of colon cancer in women", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 11, no. 3, pp. 227-34.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*

Table 16.5 Studies used to make evidence statements for alcohol and colorectal cancer

Reference [1]	**WCRF 2007 [1401]**	**WCRF 2007 [1401]**	**Allen et al. 2009 [1]**	**Bongaerts et al. 2006 [1021]**	**Fuchs et al. 2002 [441]**
Type of study [2]	Meta analysis of cohort	Meta analysis of cohort	Cohort	Cohort	Cohort
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption and colorectal (1 study) and colon cancer (8 studies)	Alcohol consumption and rectal cancer	Alcohol consumption and colon and rectal cancer	Alcohol consumption and colon cancer and rectal cancer	Alcohol consumption and colon cancer
N [5]	Not stated	Not stated	n=1,280,296 F	n=815 case, n=5000 sub-cohort	n=88758 F
Population/study information [6]	Men and Women from major international cohort studies	Men and Women from major international cohort studies	UK, Million Women Study	Dutch older adults (55-69y)	USA: Nurses Health Study 30-55yrs
Quality [7]	N	N	p	p	0
Results [8]	9% (3-14%) increased risk of colon cancer per 10g ethanol/day.	6% (1-12%) increased risk of rectal cancer per 10g/day, with a larger effect for men than for women.	10% (2-18%) increased risk of rectal cancer for every 10g ethanol/day, in a linear relationship (p=0.02) in this female cohort of predominantly light to moderate drinkers. There was no relationship between alcohol consumption and	No linear trend for alcohol consumption and risk of colon and rectal tumors. Intakes at or above a threshold of 30g ethanol/day were associated with a higher risk of CRC when compared with abstainers, RR 1.24 (0.7-2.3) but the CI crossed zero.	Relative risk of colon cancer is largely influenced by family history (family history non-drinker RR= 1.91 (1.32-2.78)) however consumption of alcohol at a rate 30g or greater per day increased chances of colon cancer in those with family history

			risk of colon cancer (p=0.8).		to RR of 3.80 (2.13-6.76)(alcohol with no family history RR= 0.88(0.56-1.39).
Effect on risk (Increase/None/Protect)	Increase colon (men and probably women)	Increase rectal (men and probably women)	Increase (rectal) none (colon)	? Increase colon and rectal	Increased (colon cancer) for women with a first degree relative with colorectal cancer
Clinical importance [9]	1	1	1	4	1
Clinical relevance [10]	1	1	1	1	1
Generalisability	y	y	For women	y	For women
Applicability	y	y	For women	For older adults	For women

16.6 ALCOHOL and OESOPHAGEAL CANCER

Does a particular intake of alcohol affect the risk of oesophageal cancer in adults?		
Evidence statement		Consumption of alcohol is associated with increased risk of cancer of the oesophagus.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	A systematic review (8 chort studies, 56 case-control studies) with a meta-analysis of a cohort and 20 case-control studies, all from the WCRF; and 1 cohort and 1 case-control study of Level III-2 evidence.
Consistency	Good	All showed increased risk, although the 2009 Australian study showed risk only increased for squamous cell type.
Clinical impact	Good	For those that had statistically significant results, confidence intervals ranged mostly between 1.02-1.44.
Generalisability	Good	Populations in the studies varied however may be generalised to the adult population of Australia.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

The WCRF (2007) meta analysis of the cohort and 20 case-control studies, the Allen (2009) cohort study and one case-control study (Pandeya et al. 2009), were used to make the body of evidence statements for alcohol and oesophageal cancer (see Table 16.6). The cohort included in the WCRF meta analysis was large and population based, but all male with 10,900 Norwegian men. The meta analysis of the 20 case-control studies demonstrated a dose-response relationship. The high heterogeneity of the studies was explained by the reviewers as being partly due to variation in measurements of alcohol, or cancer, or failure to adequately adjust for smoking.

Unfortunately, the WCRF reported in terms of total alcoholic drinks, rather than alcohol intake in g (unlike other outcomes in the same report); they stated that they converted to number of drinks from the quantitative amounts wherever possible, but did not state what conversion factor was used. The data was still included here because of the seminal nature of that report.

The large cohort study was only performed on women; the case-control study was from the Australian population and included both men and women. Interestingly, they separated the oesophageal cancer cases into type (squamous cell or adenomatous) and found the adenomatous type had no relationship with alcohol. Future studies may get clearer results should the same distinction be made.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Pandeya, N., G. Williams, et al. 2009, "Alcohol Consumption and the Risks of Adenocarcinoma and Squamous Cell Carcinoma of the Esophagus", *Gastroenterology*, vol. 136, no. 4, pp. 1215-1224.e2.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*.

Table 16.6 Studies used to make evidence statements for alcohol and oesophageal cancer

Reference [1]	**WCRF 2007 [1401]**	**Allen et al. 2009 [1]**	**Pandeya et al. 2009 [810]**
Type of study [2]	Meta-Analysis of Cohort	Cohort	Case-Control
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption (g) and Breast Cancer	Alcohol consumption and cancer including renal cell carcinoma	Alcohol consumption and oesophageal cancer type
N [5]	Not specified (studies included)	n=1,280,296 (n=68775)	Cases: EAC n= 365; EGJAC n= 426; ESCC n= 303; controls= 1580
Population/study information [6]	Women (pre and post menopausal) participating in large cohort studies	UK, Million Women Study	Australian, national study
Quality [7]	P	p	P
Results [8]	Increasing alcohol consumption was associated with a 26% (10-44%) increased risk of oesophageal cancer per drink consumed in the meta-analysis with no threshold.	Increasing alcohol consumption was associated with a 22% (8-38%) increased risk of oesophageal cancer for every 10g ethanol/day, in a linear relationship (p=0.002).	Current consumption above a threshold of 170g alcohol/wk (24g/day) was associated with 3% (2-5%) increased risk of SCC type oesophageal cancer, for every extra 10g of alcohol consumed; lifetime consumption of above 60g/day was associated with more than 4 fold increase in risk in those with SCC type cancers; no association between alcohol and increased risk in adenomatous type.
Effect on risk (Increase/None/Protect)	Increase	Increased risk, no threshold	Increase after threshold (but only in squalors cell type)
Clinical importance [9]	1	1	1
Clinical relevance [10]	1	1	1
Generalisability	For men	For women	Australian study
Applicability	y	y	y

16.7 ALCOHOL and CANCER OF THE ORAL CAVITY, PHARYNX and LARYNX

Does a particular intake of alcohol affect the risk of cancers of the oral cavity, pharynx and larynx in adults?		
Evidence statement		Consumption of alcohol is associated with an increased risk of cancer of the oral cavity, pharynx and larynx.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	All Level III-2 evidence ; 1 meta-analysis of cohort studies, 1 pooled analysis of case-control studies and 1 cohort study. The meta-analysis of case-control studies had high heterogeneity.
Consistency	Excellent	All studies showed increased risk associated with increasing levels of alcohol consumption (estimated to be between 24 and 29% per 10g ethanol/day).
Clinical impact	Good	For those studies that had statistically significant results, confidence intervals ranged mostly between 1.45 and 1.8.
Generalisability	Good	Populations in the studies varied however may be generalised to the adult population of Australia.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

One meta analysis of two cohort studies (WCRF), one meta analysis of 15 case-control studies (Purdue 2009) and one cohort study, were used to make the body of evidence statements for alcohol and cancer of theoral cavity, pharynx and larynx (see Table 16.7). The cohorts included in the WCRF were both large and population based: the first a large cohort of Norwegian men, the second the EPIC study cohort of 10 European countries (both men and women). Unfortunately, the WCRF reported in terms of total alcoholic drinks, rather than alcohol intake in g (unlike other outcomes in the same report); they stated that they converted to number of drinks from the quantitative amounts wherever possible, but did not state what conversion factor was used. The data was still included here because of the seminal nature of that report. A separately published study (Chen et al., 2009), as part of the WCRF, conducted a meta analysis of 14 case-control studies. However, this was not included in the evidence base because only one of the 14 studies had defined the quantification of one alcoholic drink, thereby making it impossible for the pooled analysis to report these results. Some of the studies included in the Purdue (2009) pooled analysis were also included in the WCRF (2007) meta-analysis of case-control studies, but the recommendation was not based on the latter figure.

Alcohol is known to have a potentiating effect on tobacco smoke in the development of these cancers, but the studies included controlled for the effect of smoking, and alcohol appears to be an independent risk factor.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Purdue, M. P., M. Hashibe, et al. 2009, "Type of alcoholic beverage and risk of head and neck cancer--a pooled analysis within the INHANCE Consortium", *American Journal of Epidemiology*, vol. 169, no. 2, pp. 132-42.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*.

Table 16.7 Studies used to make evidence statements for alcohol and cancer of the oral cavity, pharynx and larynx

Reference [1]	**WCRF 2007 [1401]**	**Purdue et al. 2009 [1339]**	**Allen et al. 2009 [1]**
Type of study [2]	Meta-Analysis of Cohort	Systematic Review of Cohort	Cohort
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption (g) and Breast Cancer	Alcohol consumption (g) and Head and Neck Cancer	Alcohol consumption and cancer of oral cavity, pharynx and larynx
N [5]	Not specified (studies included)	9107 cases HNC 14,219 controls	n=1,280,296 (n=68,775)
Population/study information [6]	Women (pre and post menopausal) participating in large cohort studies	Participants from all studies were 15-80 yrs, all studies were registered with International HNC Consortium	UK, Million Women Study
Quality [7]	0	0	P
Results [8]	24% (18-30%) increased risk of cancer of the mouth, pharynx and larynx with every additional 1 drink/day in a continuous curvilinear relationship ($p<0.00005$) with no threshold.	HNC risk increased significantly with level of total alcohol intake for beer only and spirits only drinkers at all levels of consumption, but only at higher levels of consumption in wine-only drinkers, compared to never drinkers, however significant heterogeneity shown.	Increasing alcohol consumption was associated with a 29% (14-45%) increased risk of cancer of the oral cavity and pharynx for every 10g ethanol/day, in a linear relationship ($p<0.001$). Increasing alcohol consumption was associated with a 44% (10-88%) increased risk of cancer of the larynx for every 10g ethanol/day, in a linear relationship ($p=0.008$).
Effect on risk (Increase/None/Protect)	Increased	Increased	Increased risk in a linear relationship with no threshold.
Clinical importance [9]	1	2	1
Clinical relevance [10]	1	1	1
Generalisability	y	y	For women
Applicablility	y	y	y

16.8 ALCOHOL and RENAL CANCER

Does a particular intake of alcohol affect the risk of renal cancer in adults?		
Evidence statement		Consumption of alcohol is associated with a reduced risk of developing renal cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Poor	All Level III-2 evidence; 1 meta-analysis of 2 cohort studies, 1 meta-analysis of 2 case-control studies, 1 cohort studies and 1 case-control studies.
Consistency	Good	Results all showed a protective effect of alcohol consumption on renal cancer, with a linear trend. The highest levels of consumption conferred the most protection.
Clinical impact	Good	For those that had statistically significant results, confidence intervals ranged mostly between 0.5-2.0.
Generalisability	Satisfactory	Populations in the studies varied (some drank more heavily for female populations) however broadly generalisable to the adult population of Australia.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

The evidence base for this outcome is limited to data from a total of six studies. The WCRF review (2007) conducted a meta analysis of two unadjusted cohort studies, both of which were on women (Sweden, Iowa), and a meta-analysis of two unadjusted case-control studies that included men and women (one Iowa study of 261 male and 145 female cases published in 2002; one San-Francisco study of 1204 non-Asian residents published in 1998). Both reviews showed no heterogeneity. In addition to these was the UK Million Women Study cohort evidence (Allen et al. 2009), which appeared to represent a low drinking population, and the Italian case-control study (Pelucchi et al. 2008) that had a much higher rate of drinking in women and wine drinking, generally compared to the Australian population. Despite these differences, there was a consistent decrease in risk observed with increasing levels of alcohol consumption, even at the highest levels, which would be consistent with the definition of alcohol abuse. At levels of consumption consistent with current NHMRC recommendations, the effect size ranged from 0.87 (4 drinks or less day, Pelucchi et al. 2008), 0.93 (1-2 drinks/day, Allen et al. 2009), to 0.48 -0.90 for one drink (10g ethanol) in the WCRF (2007) cohort and case-study meta analyses, respectively. There was no evidence of an effect of alcohol type, and the decrease in risk appears to come from ethanol per se, although there is no agreed upon mechanism by which this may occur.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Pelucchi, C., C. Galeone, et al. 2008, "Alcohol consumption and renal cell cancer risk in two Italian case-control studies", *Annals of Oncology*, vol. 19, no. 5, pp. 1003-8.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*.

Table 16.8 Studies used to make evidence statements for alcohol and renal cancer

Reference [1]	**WCRF 2007 [1401]**	**Allen et al. 2009 [1]**	**Pelucchi et al. 2008 [53]**
Type of study [2]	Meta-Analysis of Cohort and Case-Control	Cohort	Case-Control
Level of evidence [3]	111-2	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption (g) and renal cancer	Alcohol consumption and cancer including renal cell carcinoma	Alcohol consumption and renal cell cancer
N [5]	Not specified (studies included)	n=1,280,296 (n=68775)	1115 incident cases 2582 controls
Population/study information [6]	Women (pre and post menopausal) participating in large cohort studies	UK, Million Women Study	Hospitalised Italian men and women
Quality [7]	P	p	P
Results [8]	RR= 0.48 (95% CI 0.26-0.90) decreased risk of renal cancer per 10 g of Ethanol /day, with no heterogeneity from cohort study meta-analysis; RR= 0.90 (95% CI 0.77-1.05) decreased risk per 10 g EtOH/day for case-control meta-analysis.	12% decreased risk (CI -22 - -1%) of renal cell carcinoma with every 10g/day increase in ethanol.	3% decreased risk (CI-5% - 0) of renal cell carcinoma for each 10g of ethanol consumed/day (p=0.10). Risk of renal cell carcinoma decreased throughout the range of alcohol consumption.
Effect on risk (Increase/None/Protect)	Protect	Protect	Protect
Clinical importance [9]	2	1	2
Clinical relevance [10]	1	1	1
Generalisability	For women	For women	y
Applicability	For women	For women	y

16.9 ALCOHOL and LIVER CANCER

Does a particular intake of alcohol affect the risk of liver cancer in adults?		
Evidence statement		Consumption of alcohol, even at low levels (10 g/d) is associated with increased risk of liver cancer in some populations.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	1 meta-analysis of 6 cohort studies, 1 cohort study.
Consistency	Good	Both sources showed increase risk.
Clinical impact	Good	For the 2 sources, confidence intervals ranged mostly between 1.2 and 1.51.
Generalisability	Poor	The meta-analysis consisted mainly of men from Japan or China, compromising generalisability. The findings from the UK million women study are more generalisable to our population.
Applicability	Poor	The Japanese and Chinese studies in the meta-analysis mainly consisted of male, diseased populations. The UK study is applicable only to women.

The WCRF conducted a meta analysis of six cohort studies and while two of the included studies had relative risks <1, the effect estimate was 1.10 (95% CI 1.02- 1.17) per 10g EtOH /day, with no heterogeneity across studies. The studies were either conducted in Japan or China, and while some were population based, most were on special groups (e.g. men with cirrhotic liver or hepatitis) rather than the general population. This limits the generalisability of results. The WCRF also conducted a meta analysis of case control studies which gave an effect estimate of 1.17 (95% CI 1.09-.25) per 10g EtOH/day with high heterogeneity (possibly due to including studies with alcoholic behaviour).

Despite the limitations in these reviews, the WCRF recommendation was strongly worded: 'ample, generally consistent evidence from both cohort and case control studies. A dose-response relationship is apparent. No threshold was identified." p 170. [1401].

Alcohol causes liver cancer through the precursor of cirrhosis. The International Agency for Research on Cancer has classified alcohol as a Class 1 carcinogen for liver cancer (WCRF).

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

WCRF, W. C. R. F. A. I. f. C. R. 2007, "Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective", *American Institute for Cancer Research*.

Table 16.9 Studies used to make evidence statements for alcohol and liver cancer

Reference [1]	**WCRF 2007 [1401]**	**Allen et al. 2009 [1]**
Type of study [2]	Meta-Analysis of Cohort	Cohort
Level of evidence [3]	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption (g) and breast cancer	Alcohol consumption and cancer
N [5]	Not specified (6 cohort studies included)	n=1,280,296 (n=68775)
Population/study information [6]	Mostly men participating in special cohort studies of liver disease (e.g. cirrhosis and hepatitis); predominantly Japanese, some Chinese	UK, Million Women Study
Quality [7]	N	p
Results [8]	Increasing alcohol consumption was associated with a 10% (2-17%) increase in risk per 10g EtOH /day, with no heterogeneity in the meta-analysis	Increasing alcohol consumption was associated with a 24% (2-51%) increased risk of liver cancer for every 10g ethanol/day, in a linear relationship (p=0.03)
Effect on risk (Increase/None/Protect)	Increase	Increase
Clinical importance [9]	1	1
Clinical relevance [10]	1	1
Generalisability	n	y
Applicability	n	y

16.10 ALCOHOL and PANCREATIC CANCER

Does a particular intake of alcohol affect the risk of pancreatic cancer in adults?		
Evidence statement		Consumption of high intakes of alcohol is associated with an increased risk of pancreatic cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	1 pooled analysis of 14 cohort studies, and 1 cohort study- all studies with minimal bias.
Consistency	Poor	The pooled analysis found increased risk with high levels of alcohol consumption the cohort study found no relationship.
Clinical impact	Varied	For those that had statistically significant results, confidence intervals were broad (1.03-1.45 for males and females together).
Generalisability	Good	Populations in the studies varied however may be generalised to the male or female adult population of Australia. Pooled data included an Australian study.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

The evidence base for the relationship between alcohol intake and pancreatic cancer came from one meta analysis (Genkinge et al. 2009) and one cohort study (Allen et al. 2009). The meta analysis (Genkinge et al. 2009) included data from 14 cohort studies (where separate data from men and women from the same cohort was counted as two studies). None of these individual studies found an association, but the pooled data showed a weak positive association for pancreatic cancer risk in those consuming 30g or more (three or more standard drinks) alcohol/day, compared to non-drinkers. The relationship was significant for the total group (men and women), and women only, but not men only. The UK Million Women cohort study (Allen et al. 2009**)** found no association. There is not sufficient evidence on which to base a clear recommendation.

The WCRF (2007) made no recommendation about pancreatic cancer and alcohol due to lack of evidence of a relationship.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Genkinger, J. M., D. Spiegelman, et al. 2009, "Alcohol intake and pancreatic cancer risk: a pooled analysis of fourteen cohort studies", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 18, no. 3, pp. 765-76.

Table 16.10 Studies used to make evidence statements for alcohol and pancreatic cancer

Reference [1]	**Genkinge et al. 2009 [1312]**	**Allen et al. 2009 [1]**
Type of study [2]	Meta analysis of cohort studies	Cohort
Level of evidence [3]	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption and pancreatic cancer	Alcohol consumption and cancer
N [5]	n=319,716 men and 542,948 women (2,187 incident cases pancreatic cancer	n=1,280,296 (n=68775)
Population/study information [6]	14 prospective cohort studies (the pooling project of prospective studies of diet and cancer)	UK, Million Women Study
Quality [7]	0	p
Results [8]	Weak positive association observed for pancreatic cancer risk in those consuming 30g or more (3 or more standard drinks) alcohol/day, 1.22 (1.03-1.45) for all, and 1.41 (1.07-1.85) in women, compared to non-drinkers, (not sig in men).	No statistically significant association between pancreatic cancer and alcohol intake.
Effect on risk (Increase/None/Protect)	Increase	None
Clinical importance [9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	yes - for women
Applicability	y	yes - for women

16.11 ALCOHOL and NON-HODGKINS LYMPHOMA

Does a particular intake of alcohol affect the risk of non-Hodgkins lymphoma in adults?		
Evidence statement		Consumption of alcohol is associated with reduced risk of Non Hodgkins lymphoma.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	2 Level III-2 studies; 1 pooled analysis of 9 case-control studies and 1 very large cohort study, both with minimal bias
Consistency	Satisfactory	Both sources showed a decrease in risk, although the meta-analysis found no effect for current amount of alcohol intake in g/day.
Clinical impact	Satisfactory	For the cohort study with statistically significant results, confidence intervals ranged between (0.62- 0.94).
Generalisability	Good	Populations in the studies varied however may be generalised to the male or female adult population of Australia.
Applicability	Good	The studies are applicable to the Australian population as Alcohol intakes and types of alcohol used are similar.

The body of evidence statements, shown in Table 16.11, were based on two evidence sources. The first was a pooled analysis of nine case-control studies, and the other the UK Million Women cohort study. The pooled analysis, which contained data from both men and women, found no relationship with current intake, but a significant decrease when never drinkers were compared with ever drinkers. The cohort study, comprising UK women who tended to be relatively light drinkers, found that risk decreased in a linear relationship.
The WCRF (2007) made no recommendation about Non-Hodgkins lymphoma and alcohol due to lack of evidence of a relationship.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Morton, L. M., T. Zheng, et al. 2005, "Alcohol consumption and risk of non-Hodgkin lymphoma: a pooled analysis", *The Lancet Oncology*, vol. 6, no. 7, pp. 469-476.

Table 16.11 Studies used to make evidence statements for alcohol and non-Hodgkin's Lymphoma

Reference [1]	**Morton et al. 2005 [1074]**	**Allen et al. 2009 [1]**
Type of study [2]	Meta-analysis	Cohort
Level of evidence [3]	111-2	111-2
Intervention/ comparator [4]	Alcohol and non-Hodgkin lymphoma	Alcohol consumption and cancer
N [5]	15175 6492 cases 8683 controls	n=1,280,296 (n=68775)
Population/study information [6]	7864 M and 7311 F 95% of white ethnic origin mean age 58 (17-86)yrs; Interlymph register 9 case-control studies	UK Million Women Study
Quality [7]	n	p
Results [8]	Ever drinkers had a lower risk of NHL than never drinkers, OR= 0.83 (0.76-0.89) but no relationship with current drinking in terms of total alcohol consumption in g/day.	Increasing alcohol consumption was associated with a decreased risk of Non Hodgkin lymphoma, in a linear relationship (p=0.001) RR of 0.77 (0.62- 0.94) for 15 drinks or more /wk compared with non-drinkers.
Effect on risk (Increase/None/Protect)	None/Protective	Protective
Clinical importance [9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	yes - for women
Applicability	y	yes - for women

16.12 ALCOHOL and OVARIAN CANCER

Does a particular intake of alcohol affect the risk of ovarian cancer in adults?		
Evidence statement		Consumption of alcohol is not associated with risk of ovarian cancer.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	All (2 systematic review of cohort studies, 2 cohort studies and 1 case-control) Level III-2 studies with low risk of bias.
Consistency	Satisfactory	Most studies showed no association between alcohol risk and ovarian cancer with a couple of exceptions (one study that pooled data from population-based case-control studies showed a decreased risk, and one case-control that separated mucinous from non-mucinous ovarian cancer showed an increased risk). Inconsistent evidence about beverage type. Webb found risk decreased with wine while Chang et al. found risk increased.
Clinical impact	Satisfactory	For some studies, confidence intervals ranged across 1.0.
Generalisability	Good	Populations in the studies varied however may be generalised to the female adult population of Australia-some Australian data included in the review.
Applicability	Good	The studies are applicable to the Australian population as alcohol intakes and types of alcohol used are similar.

One meta analysis of 10 cohort studies (Genkinger et al. 2006), one pooled analysis of 14 case-control studies (Webb et al. 2004), two cohort studies (Chang et al. 2007), and one case control study (Modugno F et al. 2003) were used to make the body of evidence statements for alcohol and breast cancer (see Table 16.4).

Most studies showed no evidence of a relationship between ovarian cancer and alcohol intake; however there were some discrepant results. One study that pooled data from population-based case-control studies (Webb et al. 2004) showed a decreased risk, and one case-control that separated mucinous from non-mucinous ovarian cancer (Modugno F et al. 2003) showed an increased risk but only in the mucinous type. These authors noted the importance of further studies separating my type to investigate this effect. There was inconsistent evidence about beverage type with Webb et al. (2004) finding risk decreased with wine, while Chang et al. 2007 found risk increased.

The WCRF (2007) made no recommendation about pancreatic cancer and alcohol due to lack of evidence of a relationship.

References

Allen, N. E., V. Beral, et al. 2009, "Moderate alcohol intake and cancer incidence in women.[see comment]", *Journal of the National Cancer Institute*, vol. 101, no. 5, pp. 296-305.

Chang, E. T., A. J. Canchola, et al. 2007, "Wine and other alcohol consumption and risk of ovarian cancer in the California Teachers Study cohort", *Cancer Causes & Control*, vol. 18, no. 1, pp. 91-103.

Genkinger, J. M., D. J. Hunter, et al. 2006, "Alcohol intake and ovarian cancer risk: a pooled analysis of 10 cohort studies", *British Journal of Cancer*, vol. 94, no. 5, pp. 757-62.

Modugno, F., R. B. Ness, et al. 2003, "Alcohol consumption and the risk of mucinous and nonmucinous epithelial ovarian cancer", *Obstetrics & Gynecology*, vol. 102, no. 6, pp. 1336-1343.

Webb, P. M., D. M. Purdie, et al. 2004, "Alcohol, wine, and risk of epithelial ovarian cancer.[see comment]", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 13, no. 4, pp. 592-9.

Table 16.12 Studies used to make evidence statements for alcohol and ovarian cancer

Reference [1]	**Genkinger et al. 2006 [193]**	**Webb et al. 2004 [323]**	**Allen et al. 2009 [1]**	**Chang ET et al. 2007 [150]**	**Modugno F et al. 2003 [1148]**
Type of study [2]	Systematic Review of Cohort	Systematic Review	Cohort	Cohort	Case-Control
Level of evidence [3]	111-2	111-2	111-2	111-2	111-2
Intervention/ comparator [4]	Alcohol consumption and ovarian cancer	Alcohol consumption and ovarian cancer	Alcohol consumption and cancer	Alcohol and ovarian cancer	Alcohol and mucinous and non-mucinous ovarian cancer
N [5]	529 638 women (2001 ovarian cancer cases)	Not stated	1,280,296 (n=68775)	90371 (253 incident cases)	761 cases/ 1352 controls
Population/study information [6]	Participants 27-93yrs, 10 cohorts pooled.	7 hospital and 7 population studies pooled (separately).	UK, Million Women Study.	Adult women <=85yrs (median 50yrs) active and retired schoolteachers in California Teachers Study.	Delaware, USA, population-based.
Quality [7]	0	0	p	P	0
Results [8]	No association between alcohol intake (or type of alcoholic beverage) and ovarian cancer risk.	The results of the population-based studies of 0.72 (0.54-0.97) suggest that, compared with non-drinkers, women who consume alcohol have a reduced risk of ovarian cancer (number of standard drinks not reported). However the pooled estimate of risk in the	No statistically significant association between ovarian cancer and alcohol intake.	Total alcohol intake did not affect risk of ovarian cancer. Found evidence of increased risk associated with wine independent of alcohol content for mid-age women.	Overall, no association between ovarian cancer and alcohol, but the heaviest levels of drinking (≥24 drinks/wk or ~>46g ethanol/day) were associated with increased risk of mucinous cancers OR= 1.93 (1.02-

		hospital based studies showed no increased risk 1.10 (0.83-1.44). Found some evidence of a reduced risk for wine drinkers.			3.65).
Effect on risk (Increase/None/Protect)	None	None/ Protective	None	None	None overall/increase for mucinous ovarian cancer.
Clinical importance [9]	1	1	4	1	1
Clinical relevance [10]	1	1	1	1	2
Generalisability	y - for women	yes-for women, not the hospital studies	y - for women	y - for women	y - for women
Applicability	y - for women	yes-for women, not the hospital studies	y - for women	y - for women	y - for women

Summary of studies that were included but did not contribute to an Evidence Statement

12 papers were not included in a body of evidence because insufficient studies prevented preparation for that outcome (i.e. less than 5 studies).

Cancer-lung

Chao, C., Slezak, J. M., Caan, B. J., Quinn, V. P., Chao, C., Slezak, J. M., et al. (2008). Alcoholic beverage intake and risk of lung cancer: the California Men's Health Study. *Cancer Epidemiology, Biomarkers & Prevention, 17*(10), 2692-2699.

Multiethnic cohort of positive quality (84,170 men, 45-69 years who were members of the Kaiser Permanente California health plans). Incident lung cancer cases up to December 2006 (n = 210). A significant linear decrease in risk of lung cancer associated with consumption of red wine among those who had ever smoked: hazard ratio (HR), 0.98 (95% CI 0.96-1.00) for increase of 1 drink per month. Consumption of ≥1 drink of red wine per day associated with an approximately 60% reduced lung cancer risk in those who had ever smoked: HR 0.39 (95% CI 0.14-1.08). No clear associations with lung cancer were seen for intake of white wine, beer, or liquor. Adjustments for age, race/ethnicity, education, income, body mass index, history of chronic obstructive pulmonary disease/ emphysema, and smoking history. (Results should not be extrapolated to heavy alcohol consumption).

Rachtan, J. (2002). Alcoholic beverages consumption and lung cancer cell types among women in Poland. *Lung Cancer, 35*(2), 119-127.

Case-control study; 242 cases with diagnosis of lung cancer, 352 female healthy controls. The multivariate analysis (adjusted for smoking exposure and other variables), showed that usual past vodka-drinking women demonstrated significantly higher risk than non-drinking women. Significant dose–response relationships were observed for each histologic type separately. Usual past vodka drinking (at least ≥100 g) significantly increased the risk in all histologic subgroups separately, but the highest risk was observed for small cell carcinoma. For adenocarcinoma, vodka drinking significantly increased risk at the lower (<100 g) and the higher (≥100 g) levels of drinking. Results confirmed synergistic influence of vodka drinking and cigarette smoking on risk of lung cancer, and significant influence of usual past vodka drinking on lung cancer risk for lifelong non-smokers.

Cancer- prostate

Crispo, A., Talamini, R., Gallus, S., Negri, E., Gallo, A., Bosetti, C., et al. (2004). Alcohol and the risk of prostate cancer and benign prostatic hyperplasia. *Urology, 64*(4), 717-722.

Hospital-based case-control study in Italy between 1991 and 2002. 2663 men <75 years had incident, histologically confirmed prostate carcinoma (1294 cases) or symptomatic obstructive benign prostatic hyperplasia (1369 cases). Alcohol consumption showed no consistent association with prostate cancer risk, but a statistically significant inverse trend in risk for benign prostatic hyperplasia. Compared with abstainers, <3 drinks per day (OR 0.88) 3-4 drinks (OR 0.71), 5-6 drinks (OR 0.79) ≥7 drinks (OR 0.65). No difference with type of alcoholic beverage. Researchers concluded drinking alcohol is unrelated to prostate cancer risk.

Schoonen, W. M., Salinas, C. A., et al. (2005). Alcohol consumption and risk of prostate cancer in middle-aged men.[see comment]. [Research Support, U.S. Gov't, P.H.S.]. *International Journal of Cancer, 113*(1), 133-140.

Population-based case-control study in King County, WA, USA; 753 newly diagnosed prostate cancer cases, 40-64 years of age; 703 control subjects, frequency matched to cases by age, were selected through random digit dialling. No clear association with prostate cancer risk was seen for overall alcohol consumption. Each additional glass of red wine consumed per week showed a statistically significant 6% decrease in relative risk (OR = 0.94; 95% CI = 0.90-0.98). Evidence for a decline in risk estimates across increasing categories of red wine intake (trend p=0.02). No clear associations were seen for consumption of beer or liquor.

Sutcliffe, S., Giovannucci, E., Leitzmann, M. F., Rimm, E. B., Stampfer, M. J., Willett, W. C., et al. (2007). A prospective cohort study of red wine consumption and risk of prostate cancer. [Comparative Study Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. *International Journal of Cancer, 120*(7), 1529-1535.

Cohort (Health Professionals Follow-up Study). Between 1986 and 2002, 3,348 cases of prostate cancer diagnosed among 45,433 eligible participants. Compared to men who did not consume red wine, no linear trend was observed between red wine consumption and prostate cancer in the full analytic cohort (p-trend = 0.57). Among men with unchanged alcohol consumption in the prior 10 years, and those additionally <65 years of age, slightly lower risks were observed for men who consumed ≤4 glasses of red wine/week, whereas null or slight increased risks were observed for men who consumed >4 glasses/week, resulting in a lack of linear trend.

Cancer- Hodgkins Lymphoma

Gorini, G., Stagnaro, E., Fontana, V., Miligi, L., Ramazzotti, V., Amadori, D., et al. (2007). Alcohol consumption and risk of Hodgkin's lymphoma and multiple myeloma: a multicentre case-control study.[see comment]. [Comparative Study Multicenter Study Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. *Annals of Oncology, 18*(1), 143-148.

A multicentre population-based case-control study of 363 Hodgkin's lymphoma (HL), 270 multiple myeloma (MM) cases, and 1771 controls. For HL, considering nonsmokers only, ever drinkers had a significantly decreased risk than never drinkers (OR=0.46). Significantly lower risks in all levels of total alcohol intake were also detected. In the analysis for ever-smoking HL cases and controls, ever drinkers had the same risk as never drinkers. For MM, ever drinkers had a non-significantly decreased risk than non-drinkers (OR=0.74), and ORs in almost all consumption levels were not significant. For HL and MM, the beverage type did not affect the risk significantly, and no consistent dose-response relationships were found, considering intensity or duration of alcohol consumption.

Health and Well-being

Baglietto, L., English, D. R., Hopper, J. L., Powles, J., & Giles, G. G. (2006). Average volume of alcohol consumed, type of beverage, drinking pattern and the risk of death from all causes. [Research Support, Non-U.S. Gov't]. *Alcohol & Alcoholism, 41*(6), 664-671.

A Cohort of positive quality (Melbourne Collaborative Cohort Study) with 36,984 participants, 1971 deaths in the average of 10.5 years of follow-up. For both men and women, mortality curves were J-shaped (nadir at 9-12 g/day of alcohol consumption; upper protective dose of 42-76 g/day). Wine consumption was associated with lower mortality (for men, minimum hazard ratio (HR) at 20-39

g/day of wine consumption: 0.69 (95% CI 0.54-0.87) for women, minimum HR at 1-19 g/day: 0.82 (95% CI 0.70-0.98). Beer associated with an increased risk for men (P for trend = 0.05), but not for women. After adjustment for total amount of alcohol consumed, the number of drinking-days was inversely associated with the risk of dying in men (P-trend = 0.04).

Eigenbrodt, M. L., Fuchs, F. D., Couper, D. J., Goff, D. C., Jr., Sanford, C. P., Hutchinson, R. G., et al. (2006). Changing drinking pattern does not influence health perception: A longitudinal study of the atherosclerosis risk in communities study. *Journal of Epidemiology & Community Health, 60*(4), 345-350.

A postive quality study that investigated 12,332 middle aged men and women from the atherosclerosis risk in communities study 1987 to 1995). Covariates included age, sex, race, income, smoking status, educational level, and obesity. Health for persons who stopped or started drinking, or continued to abstain was more likely to decline than was health for persons who continued to drink even after adjustment and restrictions (drinking cessation: OR = 1.6 (95% CI 1.1- 2.3); started drinking; OR = 1.4 (95% CI 0.9- 2.2) continued abstaining from alcohol: OR = 1.5 (95% CI 1.3 - 1.9). Among participants with poor perceived health, starting, stopping, or continuing to abstain from alcohol did not improve health in relation to participants that continued to drink.

Leon, D. A., Saburova, L., Tomkins, S., Andreev, E., Kiryanov, N., McKee, M., et al. (2007). Hazardous alcohol drinking and premature mortality in Russia: a population based case-control study.[see comment]. [Research Support, Non-U.S. Gov't]. *Lancet, 369*(9578), 2001-2009**.**

Case-control study (Cases - all deaths in men aged 25-54 years living in Izhevsk occurring between Oct 20, 2003, to Oct 3, 2005; controls - selected at random from the city population and were frequency matched to deaths by age). 751 (51%) cases were classed as problem drinkers or drank non-beverage alcohol, compared with 192 (13%) controls. The mortality OR for hazardous drinkers vs abstained/non-problematic beverage drinkers, was 6.0 (95% CI 5.0-7.3) after adjustment for smoking and education. The mortality ORs for drinking non-beverage alcohol in the past year (yes vs no) was 9.2 (7.2-11.7) after adjustment for age. A strong direct gradient with mortality was seen for frequency of non-beverage alcohol drinking independent of volume of beverage ethanol consumed. 43% of mortality was attributable to hazardous drinking adjusted for smoking and education.

Obesity and weight gain

Halkjaer, J., Sorensen, T. I. A., Tjonneland, A., Togo, P., Holst, C. & Heitmann, B. L. 2004, "Food and drinking patterns as predictors of 6-year BMI-adjusted changes in waist circumference", *British Journal of Nutrition*, vol. 92, no. 4, pp. 735-48.

A positive quality longitudinal study with 2300 middle-aged men and women with repeated measurements of dietary intake, BMI and WC from 1982 to 1993 (three time point measurements). Among women, but not men, high intakes of beer and spirits were associated with gain in Waist circumference (WC). For men, drinking one to three servings of beers per week compared with not drinking beer was associated with a borderline significant increase (P=0·10) in WC; a moderate intake of wine compared with no intake was associated with a decrease in WC. However associations for males were weakened considerably after adjustment for concurrent changes in BMI.

Vadstrup, E. S., Petersen, L., Sorensen, T. I., Gronbaek, M. & Sorensen, T. I. A. 2003, "Waist circumference in relation to history of amount and type of alcohol: results from the Copenhagen City Heart Study", *International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, vol. 27, no. 2, pp. 238-46.

Prospective population study (neutral quality) with 2916 men and 3970 women aged 20-83 years from Copenhagen City Heart Study, Denmark. OR of having a high waist circumference after 10 y showed a linear increase in both men and women, and they were 1.65 (95% CI 1.07-2.55) in men and 2.16 (0.86-5.14) in women who drank more than 28 beverages per week of total alcohol compared to those who drank one to six beverages per week. Men drinking more than 21 beers per week had OR of having a large waist circumference after 10 y of 1.63 (0.99-2.67) and women drinking more than 14 beers per week had odds ratio of 2.53 (0.92-6.34), compared to men and women who drank no beer. Also for spirits, there was an increase in both men and women. No linear trend was found for wine in either men or women.

Wannamethee, S. G., Field, A. E., Colditz, G. A. & Rimm, E. B. 2004, "Alcohol intake and 8-year weight gain in women: a prospective study", *Obesity Research*, vol. 12, no. 9, pp. 1386-96.

A prospective study (positive quality) of 49,324 women 27-44 years old. Significant inverse relationship between alcohol and BMI even after adjustment for dietary factors and a wide range of confounders (cross-sectional analyses). Non-linear relationship was seen between alcohol and weight gain (≥5 kg) in all women (multivariate prospective analyses). Compared with non-drinkers, the adjusted relative odds (95% CI) of weight gain according to grams per day were 0.94 (0.89-0.99) for those consuming 0.1 - 4.9 g/d, 0.92 (0.85-0.99) for 5 to 14.9 g/d, 0.86 (0.76- 0.78) for 15 to 29.9 g/d, and 1.07 (0.89-1.28) for those consuming 30+ g/d ($p < 0.0001$ for quadratic trend). Heavy drinkers (30+ g/d) had increased odds of weight gain, most marked in the younger women (<35 years) (odds ratio 1.64; (95% CI 1.03- 2.61). In African-American women, light drinking was associated with increased odds of weight gain compared with non-drinkers (odds ratio = 2.43; 95% CI 1.22 - 4.82).

7 Studies not included in a BOE for various reasons (eg already covered in a review, not able to calculate alcohol amount, lower level of evidence)

CVD: Case control studies not included in BOE given adequate higher level evidence available

Athyros, V. G., Liberopoulos, E. N., Mikhailidis, D. P., Papageorgiou, A. A., Ganotakis, E. S., Tziomalos, K., et al. (2007). Association of drinking pattern and alcohol beverage type with the prevalence of metabolic syndrome, diabetes, coronary heart disease, stroke, and peripheral arterial disease in a Mediterranean cohort. *Angiology, 58*(6), 689-697.

Cross-sectional analysis of a representative sample of Greek adults (n = 4,153) classified as never, occasional, mild, moderate, or heavy drinkers. Cases with overt coronary heart disease (CHD), stroke, or peripheral arterial disease (PAD) were recorded. In our population, 17% were never, 23% occasional, 27% mild, 24% moderate, and 9% heavy drinkers. Moderate alcohol consumption was associated with a lower trend for the prevalence of the metabolic syndrome (MetS) (P = .0001), DM (P < .0001), CHD (P = .0002), PAD (P = .005), and overall CVD (P = .001) but not stroke compared with no alcohol use. Heavy drinking was associated with an increase in the prevalence of all of these disease states. Wine consumption was associated with a slightly better effect than beer or spirits consumption on the prevalence of total CVD, and beer consumption was associated with a better

effect than spirits consumption. Alcohol intake was positively related with body weight, high-density lipoprotein cholesterol levels, and hypertension.

de Lange, D. W., Van Golden, P. H., Scholman, W. L. G., Kraaijenhagen, R. J., Akkerman, J. W. N., & Van de Wiel, A. (2003). Red wine and red wine polyphenolic compounds but not alcohol inhibit ADP-induced platelet aggregation. *European Journal of Internal Medicine, 14*(6), 361-366.

Unfractionated red wine, a red wine polyphenolic extract, and alcohol were added in different concentrations to a standardized quantity of blood platelets 2 min before aggregation was induced by different concentrations of ADP.
Alcohol in concentrations up to 0.24 percent did not inhibit platelet aggregation in vitro initiated with ADP. Red wine only inhibited platelet aggregation at very high concentrations (≈0.24 and 0.48 alcohol%).

Romeo, J., González-Gross, M., Wärnberg, J., Díaz, L. E., & Marcos, A. (2008). Effects of moderate beer consumption on blood lipid profile in healthy Spanish adults. *Nutrition, Metabolism and Cardiovascular Diseases, 18*(5), 365-372.

Case-control study where 57 healthy Spanish adults were their own control with a previous wash-out phase (30-day alcohol abstinence period, followed by a moderate intake of beer for 30 days). HDL-cholesterol, erythrocytes, haematocrit and MCV levels increased significantly ($p<0.05$) after moderate beer consumption in women. In men, a decrease in HDL-cholesterol levels was observed after alcohol abstention. Haematocrit and MCV counts also increased significantly ($p<0.05$) in men after moderate beer consumption.

Ventura, P., Bini, A., Panini, R., Marri, L., Tomasi, A., Salvioli, G., et al. (2004). Red wine consumption prevents vascular oxidative stress induced by a high-fat meal in healthy volunteers. [Comparative Study]. *International Journal for Vitamin & Nutrition Research, 74*(2), 137-143.

15 healthy volunteers given a high-fat meal with 250 mL of water; 3 days later received same meal with 250 mL of red wine. During the meal without wine, plasma lipid parameters increased significantly, whereas plasma total plasma antioxidant levels decreased, and a trend toward reduction wine; no significant difference in individual lipid parameter trends after a meal with and without wine was observed. Wine ingestion induced higher total plasma antioxidant levels and uric acid. Plasma D-ROM was significantly increased postprandially, but significantly lowered post wine ingestion.

Mental health

Truelsen, T., Thudium, D. & Gronbaek, M. 2002, "Amount and type of alcohol and risk of dementia: the Copenhagen City Heart Study.[see comment]", *Neurology*, vol. 59, no. 9, pp. 1313-9
Case-control nested in a cohort study of participants in the third Copenhagen City Heart Study (1991 to 1994), ≥65 years, who were screened using the Mini-Mental State Examination and subsequently examined for dementia (positive quality). There were 83 subjects diagnosed with dementia and the remaining 1,626 non-demented subjects were included as controls. Average weekly total alcohol intake had no significant effect on risk of dementia. Monthly and weekly intake of wine was significantly associated with a lower risk of dementia. For beer and spirits, only a monthly intake of beer was significantly associated with an increased risk of dementia. The effect of alcohol on risk of dementia did not differ between men and women.

Obesity

Berkey, C. S., Rockett, H. R. H., & Colditz, G. A. (2008). Weight Gain in Older Adolescent Females: The Internet, Sleep, Coffee, and Alcohol. *The Journal of Pediatrics, 153*(5), 635-639.e631.

A Cohort of neutral quality (Growing Up Today Study- children of NHSII) study of 5036 predominantly white girls aged 14-21 years in 2001 (4427 girls in analysis after excluding smokers and pregnant). Girls who consumed two or more serves of alcohol each week gained significantly more wt (+.114 BMI points (SE 0.47)) over 12 months than those who consumed 0-3 serves per month (0 BMI gain) after adjusting for age, menarche, ht growth and baseline BMI, as well as internet use, sleep and coffee. Not included in body of evidence because outcome (standard drink) was not stated in terms of grams of alcohol, nor could the results for children be separated from the results for adults.

Cancer- oropharyngeal

Chen, L., Gallicchio, L., Boyd-Lindsley, K., Tao, X. G., Robinson, K. A., Lam, T. K., et al. (2009). Alcohol consumption and the risk of nasopharyngeal carcinoma: a systematic review. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. *Nutrition & Cancer, 61*(1), 1-15.

Systematic review of influence of alcohol drinking on the risk of nasopharyngeal carcinoma (NPC). protocol by the World Cancer Research Fund, 15 bibliographic databases searched. 14 case-control studies from five countries. For total alcohol intake, the pooled ORs of the highest vs. lowest category = 1.33 (95% CI1.09-1.62) (11 studies). Data from six studies indicated a J-shape dose-response trend, with NPC risk decreasing with up to 15 drinks/wk and increasing with higher intake. Inadequate data to assess associations between NPC and intake of beer, wine, and spirits. Not included in the body of evidence because covered in WCRF.

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Control, vol. 18, no. 1, pp. 91-103.

Chao, C., Slezak, J. M., Caan, B. J. & Quinn, V. P. 2008, "Alcoholic beverage intake and risk of lung cancer: the California Men's Health Study", *Cancer Epidemiology, Biomarkers & Prevention*, vol. 17, no. 10, pp. 2692-9.

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Crispo, A., Talamini, R., Gallus, S., Negri, E., Gallo, A., Bosetti, C., La Vecchia, C., Dal Maso, L. & Montella, M. 2004, "Alcohol and the risk of prostate cancer and benign prostatic hyperplasia", *Urology*, vol. 64, no. 4, pp. 717-722.

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Rachtan, J. 2002, "Alcoholic beverages consumption and lung cancer cell types among women in Poland", *Lung Cancer*, vol. 35, no. 2, pp. 119-127.

Romeo, J., González-Gross, M., Wärnberg, J., Díaz, L. E. & Marcos, A. 2008, "Effects of moderate beer consumption on blood lipid profile in healthy Spanish adults", *Nutrition, Metabolism and Cardiovascular Diseases*, vol. 18, no. 5, pp. 365-372.

Schoonen, W. M., Salinas, C. A., Kiemeney, L. A. L. M. & Stanford, J. L. 2005, "Alcohol consumption and risk of prostate cancer in middle-aged men.[see comment]", *International Journal of Cancer*, vol. 113, no. 1, pp. 133-40.

Sutcliffe, S., Giovannucci, E., Leitzmann, M. F., Rimm, E. B., Stampfer, M. J., Willett, W. C. & Platz, E. A. 2007, "A prospective cohort study of red wine consumption and risk of prostate cancer", *International Journal of Cancer*, vol. 120, no. 7, pp. 1529-35.

Ventura, P., Bini, A., Panini, R., Marri, L., Tomasi, A. & Salvioli, G. 2004, "Red wine consumption prevents vascular oxidative stress induced by a high-fat meal in healthy volunteers", *International Journal for Vitamin & Nutrition Research*, vol. 74, no. 2, pp. 137-43.

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17. LIFE COURSE (S1.3)

Evidence Statements

17. LIFE COURSE (S1.3)

Search results

The initial search of the databases included 4138 references for factors that lead to children adopting appropriate life course food consumption and dietary patterns. The detailed search is included in a separate document on searches. Data was extracted from 123 references, and 48 publications were used to form the final body of evidence statements. While there was no evidence to develop statements on outcomes related to life course consumption, the development of overweight was used as a surrogate outcome for poor dietary choices throughout the life course. Sufficient evidence was found to make statements for the relationships between the development of overweight and birth weight, breastfeeding, television watching, rapid growth during childhood, maternal smoking during pregnancy, maternal employment, parental overweight status, parental education, socioeconomic status, social class, school-based interventions, and behavioural interventions. Evidence was found on the association between the following factors during childhood and the development of overweight, but was not strong enough to develop a body of evidence statement: self-reported dieting (four cohort studies), type of childhood schooling (two cohort studies), fruit and vegetable intake (three cohort studies), consumption of take away food and low quality snacks (four cohort studies), consumption of breakfast (three cohort studies), sleeping patterns (four cohort studies), child smoking (two cohort studies), urban versus rural residence (three cohort studies), food insecurity (three cohort studies), use of food stamps (one cohort study), food prices (two cohort studies), small for gestational age (one cohort study), size during adolescence (one cohort study), parental skills training (one RCT), cognitive ability (one cohort study), low self esteem/depression (three cohort studies), locus of control (two cohort studies), stressful family life (two cohort studies), migration status (two cohort studies), ousehold instability (one cohort study), centre-based child care attendance (two cohort studies), and dietary pattern (two cohort studies). Additionally, evidence existed but was not strong enough for a body of evidence statement for factors during childhood associated with use of alcohol as an adult (four cohort studies), the development of unhealthy weight control behaviours (body dissatisfaction: one very poor systematic review and two cohort studies; media influence: two cohort studies; dieting or frequent self-weighing: two cohort studies, maternal smoking during pregnancy: one cohort study), and adult dietary pattern (three cohort studies). Finally, four cohort studies examined the influence of child dietary pattern on diet quality, but again evidence was not strong enough to develop a body of evidence statement.

17.1 LIFE COURSE FOOD CONSUMPTION and BIRTH WEIGHT

Is birth weight associated with children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Increased birth weight, especially above 4000g, is associated with increased risk of overweight or obesity in childhood, adolescence, and later in life.
Grade		A
Component	**Rating**	**Notes**
Evidence Base	Excellent	13 cohort studies (11 P, 2 0).
Consistency	Good	10 of the 13 cohort studies found a significant association between birth weight and increased incidence of overweight or obesity later in life.
Clinical impact	Good	Odds ratios for increased overweight/obesity associated with increased birth weight ranged from 1.0 to 2.3.
Generalisability	Excellent	Western populations, such as Australia, Germany, USA, and UK.
Applicability	Excellent	Directly applicable.

As shown in the Process Manual, cohort studies are Level II evidence, making this an excellent evidence base. Ten of the 13 cohort studies found a significant association between high birth weight and increased BMI, waist circumference, skinfold thickness, or incidence of overweight or obesity either in childhood, adolescence, or later in life. Two additional cohorts reported an inverse association only in males, not females. However, the evidence is consistent and strong enough to guide practice.

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Goldani, M., Haeffner, L., Agranonik, M., Barbieri, M., Bettiol, H. & Silva, A. 2007, "Do early life factors influence body mass index in adolescents?", *Brazilian Journal of Medical and Biological Research*, vol. 40, no. 9, pp. 1231-1236.

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Table 17.1 Studies used to make evidence statement for life course food consumption and birth weight

Reference [1]	**Sturm 2008 (310)**	**Yang 2008 (728)**	**Goldani 2007 (1021)**	**Mamun 2005 (2131)**	**Salsberry 2007 (1188)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II	II
Intervention/ comparator [4]	Effect of birth weight (regressor variable) on change in BMI in children.	Association between birth weight (per 100 g) and prevalence of overweight and obesity in early adulthood (ages 18-26 yrs).	Association of birth weight (<2500 g, 2500-2999 g, 3000-3499 g, 3500-3999 g, >4000 g) on mean BMI at age 17yrs.	Association between birth weight (continuous variable) and development of overweight at ages of 5-14yrs.	Effect of birth weight on development of early adolescent overweight (age 12yrs).
N [5]	6918 at 3yrs, 4557 at 5yrs.	20 745 at baseline, 9542 at follow-up.	3468 at baseline, 1189 at follow-up.	7223 at baseline, 2934 for analysis.	7207 at baseline, 3368 for analysis.
Population/study information [6]	Children starting kindergarten in 1998-9 school year in over 1000 US schools (Early Childhood Longitudinal Study - Kindergarten Class). 5 year follow up.	Adolescents 12-18yrs followed from 1995 till 2001-2002 (18-26 yrs old), from the National Longitudinal Study of Adolescent Health, United States.	Males born in Ribeirao Preto, Brazil (most developed economic area of Brazil) in 1978-79, and who enlisted in army in 1997-98; data taken at birth and at age 17yrs.	Children born 1981-1984 at one of two major obstetric hospitals in Brisbane. (Mater-University of Queensland Study of Pregnancy - MUSP). Followed for 14yrs.	Children born between 1980-1990 in USA of mother's in the National Longitudinal Study of Youth. 46% white, 32% black, 22% Hispanic. Mean age 13.0yrs. 12yrs follow-up.
Quality [7]	P	P	0	P	P
Results [8]	Using data adjusted for confounders, birth weight was not associated with a significant change in BMI from	For males, birth weight (each 100 g increase) is associated with an increased prevalence of	BMI at age 17yrs was higher with birth weight >4000 g 1.37 kg/m^2 (95% CI 0.22-2.53)	Increased birth weight adj RR 2.10 (95% CI 1.50-2.94) had an increased risk of a child	Higher birth weight (birth weight categories not defined) was

	either kindergarten to third grade (-0.039 kg/m^2, SE 0.021m, P=0.-63) or kindergarten to fifth grade (-0.041 kg/m^2, SE 0.030, P=0.177).	overweight adj OR 1.03, (95% CI 1.00-1.07) in early adulthood. There was no association in females.	P<0.05 compared to birth weight of <2500g. Not adjusted for many confounding variables.	being overweight/obese at age 5 and 14 yrs.	associated with greater risk of adolescent overweight (adj OR 1.01 (95% CI 1.00-1.01).
Effect on risk	None	Increase for males, none for females	Increase	Increase	Increase
Clinical importance	1	1	1	1	1
Clinical relevance	2	2	2	2	2
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 17.1 Studies used to make evidence statement for life course food consumption and birth weight (cont.)

Reference [1]	**Dubois 2006 (1624)**	**Dubois 2006 (1771)**	**Classen 2005 (2043)**	**Reilly 2005 (2072)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Relationship between birth weight (<2500 g, 2500-4000 g, >4000 g) and development of overweight in pre-school children.	Effect of birth weight (<2500 g, 2500-2999 g, 3000-4000 g, >4000 g) on weight for stature >95th percentile at age 5 mo and BMI >95th percentile at age 4.5 yrs.	Relationship between birth weight (75 ounces or less vs. 150 ounces or more) on development of overweight or obesity in children over the age of 8 yrs.	Relationship between birth weight (continuous: 100 g units) and development of obesity at age 7 yrs.
N [5]	1514	2103 at baseline, 1944 at year 5.	4980	13 971 at baseline, 5493 at age 7 yrs.
Population/study information [6]	Children born in Quebec, Canada in 1998 (Longitudinal Study of Child Development in Quebec). 4-5 yr follow-up.	Random sample of children born in Quebec, Canada in 1998. 48.9% female. 5yr follow-up.	Children aged 2-18yrs in US (NLSY79), 50% male, 30% black, 20% Hispanic. 18yr follow-up.	Children in the UK followed from birth (Avon longitudinal study of parents and children - ALSPAC) at age 7y.
Quality [7]	P	P	P	P
Results [8]	Children with a birth weight <2500 g were at increased risk of obesity using Cole criteria adj OR 3.14 (95% CI 1.16-8.53) but were not at increased risk of being overweight (BMI >95th percentile). Children with a birth weight >4000 g were at increased risk of overweight adj OR 2.30 (95% CI 1.41-3.74) but were not at increased risk of obesity.	Birth weight of >4000 g was associated with an increased risk of having a weight-for-stature >95th percentile at age 5 mo unadj OR 1.6 (95% CI 1.0-2.5) and BMI >95th percentile at age 4.5 yrs unadj OR 2.3 (95% CI 1.4-3.7). Adjusted OR was not reported.	Birth weight >95th percentile is related to a 5% increase in overweight or obese youth (adj marginal effect probit estimate = 0.057 (SE 0.025), P<0.05).	100 g increase in birth weight was independently associated with the risk of obesity adj OR 1.05 (95% CI 1.03-1.07) at age 7 yrs.

Effect on risk	Increase for both high and low birth weight.	Increase	Increase	Increase
Clinical importance	1	1	1	1
Clinical relevance [10]	2	2	2	2
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 17.1 Studies used to make evidence statement for life course food consumption and birth weight (cont.)

Reference [1]	**Burke 2005 (2224)**	**Kuh (2002) 3127**	**Hawkins (2009) 3148**	**Araujo 2009 (3150)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Effect of birth weight (continuous variable) with change in BMI to age 8yrs.	Relationship of birth weight (continuous variable) to waist:hip ratio and waist circumference in adults.	Relationship between birth weight z-score and development of childhood overweight at age 3yrs.	Effect of birth weight (<2.850, 2.850-3.180, 3.180-3.500, >3.500g) and ponderal index at birth (<2.53, 2.53-2.70, 2.71-2.89, >2.89g/cm^3) on prevalence of obesity, mean triceps measure (mm), mean subscapular measure (mm), and BMI at age 11 yrs.
N [5]	1430	5362 at baseline, 3266 at follow-up, 3174 for analysis.	18 296 at baseline, 14 630 at follow-up, 13 188 for analysis.	5249
Population/study information [6]	Children in Australia aged 16 wks of gestation to age 8 yrs (Western Australia Pregnancy Cohort Study). Surveyed at age 1, 3, 6, and 8yrs.	Children born in England, Scotland and Wales, from the Medical Research Council's National Survey of Health and Development, followed from birth until age 43 yrs.	Children born between 2000 and 2002, from the Millennium Cohort Study. Followed from birth till age 3 yrs. Parents were residents in England, Wales, Scotland, and Northern Ireland. The study over-represented children living in disadvantaged areas and from ethnic minority groups.	Infants born at a hospital in Pelotas, Brazil in 1993. Mean birth weight 3156 g. 11 yr follow-up.
Quality [7]	P	0	P	P

Results [8]	Change in BMI at the age of 8 yrs was positively associated with birth weight 0.573 kg/m^2 (95% CI 0.259-0.886) P=0.001, adjusted.	In men, birth weight (adj) was significantly and positively associated with waist circumference 1.00cm (95% CI 0.48-1.52), P<0.001. There was no association in women.	In the fully adjusted model, birth weight z-score was associated with early childhood overweight adjusted OR 1.36 (95% CI 1.30-1.42).	Birth weight and ponderal index were all positively related to BMI, incidence of obesity, and skin fold measurements at age 11 yrs. Birth weight was the strongest predictor, with a BMI increase (adj) at age 11 yrs of 0.46 kg/m^2 for each z-score increase in birth weight. Prevalence of obesity trended upwards with each increase in quartile of birth weight (P trend < 0.001).
Effect on risk	Increase	Increase in men, none in women.	Increase	Increase
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisability	y	y	y	n
Applicability	y	y	y	y

17.2 LIFE COURSE FOOD CONSUMPTION and BREASTFEEDING

Is breastfeeding associated with children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Compared to infants who are formula fed, being breastfed is associated with reduced risk of becoming obese in childhood, adolescence, and early adulthood.
Grade		A
Component	**Rating**	**Notes**
Evidence Base	Excellent	1 meta-analysis (neutral quality) of 4 historical cohort, 13 prospective cohort, 2 case-control, and 10 cross-sectional studies, involving over 600,000 subjects.
Consistency	Excellent	All 29 individual studies reported some protective effect, but not all were significant.
Clinical impact	Excellent	Odds ratio for developing obesity was 0.87 (95% CI 0.85-0.89) in breast-fed subjects compared to formula-fed subjects.
Generalisability	Excellent	Includes both western and developing countries.
Applicability	Excellent	Directly applicable.

All 29 individual studies in the meta analysis found some protective effect, although not all were significant. Most of the studies were in children and adolescents, and only two extended into early adulthood. The pooled meta analysis statistic showed a significant association between being breastfed and the development of obesity later in life in both the crude analysis and with adjustment for paternal BMI, maternal SES, and maternal smoking. However, with the adjusted analysis, only six individual studies could be included. One additional meta analysis examining body mass index was not included in the body of evidence statement; this second meta analysis included 16 of the same studies as included in the first meta-analysis, and only examined mean BMI without distinguishing between those who were overweight compared to obese.

References

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Table 17.2 Studies used to make evidence statement for life course food consumption and breastfeeding.

Reference [1]	**Owen 2005 (3865)**	**Owen 2005 (4265)**
Type of study [2]	Meta analysis of 4 historical cohort, 13 prospective cohort, 2 case-control, 10 cross-sectional studies.	Meta-analysis of 17 prospective cohort, 2 historical cohort, 13 cross-sectional studies.
Level of evidence [3]	I	I
Intervention/ comparator [4]	Association between infant feeding and development of obesity later in life.	Association between infant feeding and mean BMI (absolute) later in life.
N [5]	672 161	Not provided
Population/study information [6]	Children born 1946-1996, most followed through childhood or adolescence, with 2 studies following through early adulthood (age 33 yrs maximum); Canada, UK, Germany, Sweden, Czech Republic, China, Turkey, Australia, New Zealand, Italy, Slovak Republic, USA.	6-week-old infants followed minimum of 1 yr, maximum of 70yrs; USA, The Netherlands, Italy, UK, Germany, Denmark, Australia, New Zealand, China, Czech Republic, Brazil.
Quality [7]	0	0
Results [8]	Breastfed subjects were less likely to be defined as obese than were formula-fed infants OR 0.87 (95% CI 0.85-0.89). All individual studies reported some protective effect of breastfeeding, but not all were significant. Definition of obesity varied among studies.	This study found lower mean BMIs in subjects who had been breastfed in infancy than in those who had been formula-fed in the crude analysis (difference in BMI -0.04 (95% CI -0.05 to -0.02). This small effect was halved by adjustment for maternal BMI in early life and became non-significant with meta-analysis of 11 studies that simultaneously adjusted for maternal BMI, maternal SES, and maternal smoking.
Effect on risk (Increase/None/Protect)	Protect	None
Clinical importance [9]	1	2
Clinical relevance [10]	2	2
Generalisability	y	y
Applicability	y	*y*

17.3 LIFE COURSE FOOD CONSUMPTION and TELEVISION WATCHING

Is time spent watching television associated with children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Hours spent watching television by children is associated with increased risk of development of overweight or obesity.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 systematic review (neutral quality) (within review, outcome of body weight: 3 cross-sectional studies; outcome of body fatness: 17 cross-sectional studies, 6 longitudinal studies; outcome of between-meal snacking: 7 cross-sectional studies; outcome of dietary fat intake: 2 cross-sectional studies; outcome of "other" diet-related: 8 cross-sectional studies, 1 RCT), 1 randomised controlled trial (1 P), 9 cohort studies (8 P, 1 N).
Consistency	Satisfactory	Of the Level II data in the systematic review; 8 out of 9 cohort studies found a positive association with BMI or development of overweight/obesity; the RCT found a significant effect on BMI z-score after 12 mo but not 24 mo; 5 of 6 longitudinal studies examining body fatness found no relation with television viewing.
Clinical impact	Good	Impact and measure of television watching varied across studies.
Generalisability	Excellent	Western populations including New Zealand, UK, USA, and Canada.
Applicability	Excellent	Directly applicable.

The systematic review did not include a meta analysis and consisted primarily of cross-sectional data with only a few longitudinal studies; therefore few conclusions could be drawn from the review due to the low level of evidence. However, six longitudinal studies identified in the review examined the outcome of body fatness, with five of the six reporting no relation between television viewing and body fat. In the additional randomised controlled trial retrieved, an intervention to reduce television viewing and computer use resulted in a greater reduction in BMI z-score in the intervention group at 12 months, but this was not sustained at 24 months. Finally, eight of the nine additional cohort studies reported a direct relationship between hours spent watching television and change in BMI or development of overweight or obesity. Therefore, although the cohort data is fairly consistent, due to inconsistencies in the systematic review and randomised controlled trial, there is only some support for this body of evidence statement.

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Table 17.3 Studies used to make evidence statement for life course food consumption and television viewing

Reference [1]	**Gorely 2004 (2399)**	**Epstein 2008 (706)**	**Danner 2008 (130)**	**Landhuis 2008 (529)**
Type of study [2]	Systematic review (Outcome of body weight: 3 cross-sectional studies; outcome of body fatness: 17 cross-sectional studies, 6 longitudinal studies; outcome of between-meal snacking: 7 cross-sectional studies; outcome of dietary fat intake: 2 cross-sectional studies; outcome of "other" diet-related: 8 cross-sectional studies, 1 RCT)	RCT	Cohort	Cohort
Level of evidence [3]	I	II	II	II
Intervention/ comparator [4]	Correlates of television watching.	Intervention to reduce time spent watching television and using computer by 50%, compared to no intervention. Measured this by using TV Allowance, an automated device that controls and monitors the use of televisions and computer monitors.	Association between hours of TV viewing (continuous variable) and change in BMI from K through grade 5.	Effect of television viewing as a child (mean viewing hours per weekday between ages 5-15 yrs) on BMI at age 32 yrs.
N [5]	Ranged from 22 to 20 766, with a median of 444/study.	35 in intervention group, 32 in control group.	14 369 at baseline, 7334 at follow-up.	972
Population/study information [6]	Aged 2-18 yrs. North America, Europe, Asia.	Children aged 4-7yrs and >75th percentile BMI for age and sex with at least 14 hours television viewing or computer use per week. 2 year follow-up.	Children from Early Childhood Longitudinal Study (ECLS-K), United States, followed from kindergarten to Grade 5.	Subjects born in New Zealand in 1972-73, followed through age 32 yrs.
Quality [7]	0	P	P	P

Results [8]	There was no association between body fatness and TV viewing (39.5% of all studies had a positive association). Of only the longitudinal studies, only 1 of the 6 samples found a positive correlation between television viewing and body fatness, while the other 5 found no association. 3 of the 4 cross-sectional samples found a positive relation between body weight and TV viewing. TV watching seemed associated with between-meal snacking, but not related to caloric intake, total energy intake, or food variety. Relation to dietary fat could not be estimated.	Intervention to reduce television viewing and computer use successfully reduced viewing/use. Reduction in zBMI was significantly greater in the intervention group at 12 mo (P=0.03), but not at 24 mo (-0.24 SE 0.32 for intervention group, -0.13 SE 0.37 for control group). Energy intake was significantly less in the intervention group at 18 and 24 mo. Physical activity was not different between groups.	There was a significant ($p<.001$) TV by time squared interaction after controlling for confounders, which suggests that hours of TV watching was significantly and positively associated with increased BMI acceleration. It was estimated that watching 4 hrs of TV per day would result in the average child reaching or exceeding the 85th BMI percentile by Grade 5.	Childhood television viewing was positively associated with increased BMI at age 32 yrs 0.55 kg/m^2 (95% CI 0.16-0.94) P=0.006, adj. For each hour of television watching as a child, odds for adult obesity increased was 1.25 (95% CI 1.01-1.53), even when controlling for adult viewing.
Effect on risk	Increase for body weight, none for body fatness	Protect at 12 mo, none at 24 mo	Increase	Increase
Clinical importance	NA	1	1	1
Clinical relevance	1	2	2	2
Generalisability	y	y	y	y
Applicability	y	y	y	y

Table 17.3 Studies used to make evidence statement for life course food consumption and television viewing (cont.)

Reference [1]	**Bhargava 2008 (473)**	**Henderson 2007 (825)**	**Viner 2005 (1861)**
Type of study [2]	Cohort	Cohort	Cohort
Level of evidence	II	II	II
Intervention/ comparator [4]	Association between time (minutes) spent watching television and change in BMI and BMI z-score from K to grade 5.	Relationship between television viewing (hrs per week) on change in BMI during adolescence.	Relationship between early childhood TV watching (hrs per day and no. of days of TV watching during week at age 5 yrs, hrs per day and no. of days of TV watching on weekend at age 5 yrs, frequency (often compared with sometimes or never) of TV viewing at age 10 yrs), parental attitudes of TV watching, BMI z-score at age 10 yrs, and BMI z-score and incidence of obesity (BMI >30) at age 30 yrs.
N [5]	19 684 at baseline 11 479 at follow up 7635 for analysis.	2379 girls at baseline. No. at follow-up not provided.	8158
Population/study information [6]	Children from the Early Childhood Longitudinal Study-Kindergarten (ECLS-K) in USA followed from K to 5th grade.	Girls from the National Heart, Lung, and Blood Institute Growth and Health Study, US, followed from age 9-10 yrs until age 15-19 yrs.	Children born in UK in 1970. Followed up at age 5, 10, 16, 26, and 29-30 yrs.
Quality [7]	P	P	P

Results [8]	Time spent watching television was positively and significantly associated with children's BMI and Z-scores of BMI. ln (watch television) (min per day) was associated with maximum likelihood estimate from dynamic random effects models of: ln (weight) 0.004 kg SE 0.001, ln (BMI) 0.004 kg/m^2 SE 0.001, BMI z-score 0.032 SE 0.006.	For white girls, baseline level of TV viewing was positively associated with change in BMI from ages 11 to 14 yrs: every additional hour of TV viewed per day at baseline was associated with an increase in BMI of 0.03, (SE 0.01, p<.01). For black girls, baseline TV viewing was not associated with change in BMI. However, for neither white nor black girls did TV viewing at wave 5 (when girls were age 14 yrs, on average) predict change in BMI for the remainder of adolescence, from the ages of 15 to 19 yrs.	BMI z-score at age 10 yrs was not associated with weekday TV viewing zBMI -0.01 (95% CI -0.03 to 0.01) P=0.4 at age 5 yrs, but was associated with weekend television viewing zBMI 0.02 (95% CI 0.002 to 0.02) P=0.04 and maternal belief that TV is harmful to young children zBMI -0.02 (95% CI -0.04 to -0.001) P=0.04 at age 5 yrs (all adjusted). BMI z-score at age 30 yrs was not associated with weekday TV viewing zBMI -0.01 (95% CI -0.03 to 0.02, P=0.7 at age 5 yrs, maternal belief that TV is harmful to young children zBMI -0.01 (95% CI -0.03 to 0.05) P=0.5 at age 5 yrs, frequency of TV watching at 10 yrs (often compared with sometimes or never, zBMI 0.02 (95% -0.4 to 0.08) P=0.5, or viewing after 6pm at age 5 yrs, but was associated with weekend TV viewing at age 5 yrs zBMI 0.03 (95% CI 0.01-0.05) P=0.01 (all adjusted). Each hour of weekend TV watched at age 5 yrs was associated with an additional 7% increase in risk of adult obesity and 0.03 SD (approximately 0.13 kg/m^2) increment in BMI in adult life.
Effect on risk	Increase	Increase for white girls aged 11-14 yrs. None for white girls aged 15-19 yrs. None for black girls.	Increase for weekend, none for weekday.
Clinical importance	1	1	1
Clinical relevance	2	2	2

Generalisability	y, but low SES and participants in Food Stamp program.	y	y
Applicability	y	y	y

Table 17.3 Studies used to make evidence statement for life course food consumption and television viewing (cont.)

Reference [1]	**Sturm 2005 (1921)**	**Reilly 2005 (2072)**	**Burke 2005 (2224)**	**Baker (2009) 3155**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Relationship between hours/day kindergarten child watches television and BMI change and development of overweight through 3rd grade.	Relationship between television viewing (≤ 4, 4.1-8, >8 hours per week) at age 38 mo and development of obesity (BMI ≥ 95th percentile).	Relationship between hours spent watching TV at age 6 yrs on child overweight/obesity at age 8 yrs.	Relationship between hours per week of television viewing and child overweight among Hispanic children of immigrants and children of natives.
N [5]	13 282	13 971 at baseline, 5493 at age 7 yrs.	1430	Number at baseline not provided, 10 966 at follow-up, 6430 for analysis.
Population/study information [6]	Children in the US in kindergarten. Followed through 3rd grade (4 years).	Children in the UK followed from birth (Avon longitudinal study of parents and children - ALSPAC). 7 year follow-up.	Children in Australia aged 16 weeks of gestation to age 8 yrs (Western Australia Pregnancy Cohort Study). Surveyed at age 1, 3, 6, and 8 yrs.	Children from Early Childhood Longitudinal Study (ECLS-K), United States, followed from kindergarten to Grade 5. 1,121 Hispanic children of immigrants, 496 Hispanic children of natives, and 4,813 non-Hispanic white children.
Quality [7]	P	P	P	N
Results [8]	Hours of television watching per day in kindergarten was associated with a BMI change from K to 3rd grade of 0.067 kg/m^2 (SE	Television viewing of 4-8hrs per wk and >8hrs per wk at age 3 was associated with increased risk of obesity at age 7 yrs, compared to ≤ 4 hrs per wk (4-8 hrs: adj OR 1.37 (95%	Child overweight/obesity at age 8 yrs was positively associated with hours spent in watching television as age 6 yrs adj OR 1.53 (95% CI 1.16-2.02) P=0.002. Each hour per day of	Hours/week of television viewing was significantly, positively associated with BMI percentile (adj regression coef. = 0.023, P<0.01).

	0.021, P=0.001) and from K to 1st grade of 0.025 kg/m^2 (SE 0.011, P=0.019).	CI 1.02-1.83) >8h: adj OR 1.55 (95% CI 1.13-2.12). Chi2 test for linear trend = 26.7.	television watching at age 6 yrs was associated with a 40% increase in risk of obesity at age 8 yrs.	
Effect on risk (Increase/None/Protect)	Increase	Increase	Increase	Increase
Clinical importance [9]	1	1	1	1
Clinical relevance [10]	2	2	2	2
Generalisable	y	y	y	y
Applicability	y	y	y	y

17.4 LIFE COURSE FOOD CONSUMPTION and EXCESS WEIGHT GAIN DURING CHILDHOOD

Is excess weight gain relative to height associated with children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Excessive weight gain relative to height during childhood is associated with an increased risk of overweight later in life.
Grade		A
Component	**Rating**	**Notes**
Evidence Base	Excellent	1 systematic review (of 14 cohort studies and 1 cross-sectional study) (1 P), 3 cohort studies (3 P).
Consistency	Good	16/18 cohort studies were consistent.
Clinical impact	Excellent	Relative risks ranged from 1-4.
Generalisability	Excellent	Western populations, including Australia, and USA.
Applicability	Excellent	Directly applicable.

The systematic review included 15 cohort studies and one cross-sectional study, involving over 325 000 participants. The cross-sectional data was not included in developing the body of evidence statement due to the low level of evidence. All but two of the 15 cohort studies included in the review reported a positive association between rapid growth and development of overweight, obesity, or other anthropometric measures, regardless of their definitions. The three additional cohort studies retrieved, one conducted in Australia, support this conclusion. These additional cohort studies were considered Level II evidence as randomised controlled trials are not feasible due to the life course nature of the question. Although the effect of catch up growth is rarely differentiated in the studies and needs to be studied further, the evidence base is strong and consistent, and this statement can be used to guide practice.

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Table 17.4 Studies used to make evidence statement for life course food consumption and rapid growth during childhood

Reference [1]	**Monteiro 2005 (2126)**	**Mamun 2005 (2131)**	**Nader 2006 (3977)**	**Dubois 2006 (1771)**
Type of study [2]	Systematic review of 14 cohort studies and 1 cross-sectional study.	Cohort	Cohort	Cohort
Level of evidence	I	II	II	II
Intervention/ comparator [4]	Effect of rapid weight gain in infancy and childhood on obesity later in life. Measurements of growth included: weight gain from birth to age 4 mo-1 yr, variations in BMI z-score from birth to age 12-15 yrs, variations or increase in >0.67 standard deviation in weight-for-age z-score from birth to age 4 mo-15 yrs, variations or increase in >0.67 standard deviation in height-for-age z-score from age 20 mo to age 15 yrs, increase in >0.67 standard deviation in weight-for-height z-scores from age 20 mo to age 43 mo, change in length-for-age z-score from age 15 d to age 3 yrs, weight gain greater than 90th or 97th percentile of standard population from birth to age 6 mo-1 yr, percent of final adult height acquired by age 7 yrs, and being small for gestational age and being above 2 standard deviations in height at age 18-25 yrs.	Relationship between rate of weight gain (nearest gram per day) during the first 6 mo of life and overweight and obese status at ages 5 yrs and 14 yrs (overweight = BMI >17.42 for a boy and 17.15 for a girl at age 5 yrs, >22.62 for a boy and >23.34 for a girl at age 14 yrs; obese = BMI >19.30 for a boy and >19.17 for a girl at age 5 yrs, >27.63 for a boy and >28.57 for a girl at age 14 yrs).	Relationship between BMI percentile (<50%, <75%, <85%, and <95%) at a young age (age 24 mo, 36 mo, 54 mo, 7 yrs, and 9 yrs) and development of overweight and obesity by age 12 yrs.	Relationship between monthly weight gain from 0-5 mo (in quintiles) on development of child's overweight (BMI >95th percentile) by age 4.5yrs.
N [5]	325,412	7223 at baseline, 2934 for analysis.	1,042	2103 at baseline, 1944 at year 5.
Population/study	Infants and children	Children born 1981-1984 at	Healthy children born	Random sample of

information [6]		one of two major obstetric hospitals in Brisbane. (Mater-University of Queensland Study of Pregnancy). Followed for 14 yrs.	at 10 locations in USA. 24% ethnic. 51.7% male. 12 yr follow up.	children born in Quebec, Canada in 1998. 48.9% female. 5 yr follow-up.
Quality [7]	P	P	P	P
Results [8]	All but 2 studies reported a positive association between rapid growth – regardless of definition – and occurrence of overweight, obesity, or greater adiposity measures, regardless of age at which measured. No summary statistic is reported. Examples of individual data: for every 100 g of monthly weight gain in first 4 mo of life, there was a 38% increase (P<0.001) in risk of overweight at age 7 yrs; subjects with ≥ 1 increase in standard deviation in weight-for-age z-score between birth to 4 mo had a 5.2-fold risk of developing obesity (P=0.008) and 6.2-fold risk of developing overweight (P=0.003); growth rates of height, weight, and BMI above mean values at age 7 yrs (+0.3 to 0.4 z-scores) were associated with obesity at age 64-75 yrs.	Rate of weight gain was positively associated with the transition from overweight or obese to normal as well as to the continuity of overweight or obesity. 1 g per day of weight gain in first 6 mo of life was associated with an increased risk of a child moving from normal weight status to overweight or obese adj RR 1.02 (95% CI 1.00-1.05), moving from overweight or obese to normal weight status adj RR 1.07 (95% CI 1.04-1.09), and being overweight/ obese at both age 5 and 14 yrs adj RR 1.06 (95% CI 1.04-	No. of times >85th percentile for BMI during age 25-54 mo is associated with increased odds of being >85th percentile BMI at age 12 yrs (≥ 1 time OR 5.9 (95% CI 3.9-8.8). Number of times >85th percentile for BMI during age 7-11 yrs is associated with increased odds of being >85th percentile BMI at age 12y (≥ 1 time OR 106.9, 95% CI 55.7-205.4). The longer a child remained in the lower range of normal BMI,	Weight gain in the 4th and 5th quintiles during the first 5mo of life was associated with increased risk of childhood overweight (BMI >95th percentile) at age 4.5 yrs: 4th quintile adj OR 1.8 (95% CI 1.0-3.5), 5th quintile adj OR 3.9 (95% IC 1.9-7.9).

		1.08).	the less likelihood there was that the child would become overweight by early adolescence. Any time a child reaches the 85th percentile for BMI may be an appropriate time for intervention.	
Effect on risk	Increase	Mixed	Increase	Increase
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisability	y	y	y	y
Applicability	y	y	y	y

17.5 LIFE COURSE FOOD CONSUMPTION and MATERNAL SMOKING DURING PREGNANCY

Is maternal smoking during pregnancy associated with children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Babies born to mothers who smoke during pregnancy are at an increased risk of development of overweight or obesity in adolescence and adulthood.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	6 cohort studies (6 P).
Consistency	Excellent	All studies were consistent.
Clinical impact	Excellent	Odds ratios for childhood or adolescent overweight or obesity ranged from 1.3 to 1.8.
Generalisability	Excellent	Western populations, including Australia, USA, Canada, UK.
Applicability	Excellent	Directly applicable.

Maternal smoking during pregnancy is included in the life course question as a marker of influence of environment. All six cohort studies, including over 30 000 participants, reported a positive relationship between maternal smoking during pregnancy and childhood or adolescent overweight. All included studies are of high quality and all were adjusted for potential confounders. Cohorts were sampled from Australian, USA, and UK populations, making the results generalisable to the Australian population. Therefore, this statement should be used to guide practice.

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Table 17.5 Studies used to make evidence statement for life course food consumption and maternal smoking during pregnancy

Reference [1]	**Salsberry 2007 (1188)**	**Al Mamun 2006 (1621)**	**Dubois 2006 (1771)**	**Reilly 2005 (2072)**	**Power 2003 (2666)**	**Hawkins (2009) 3148**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II	II	II
Intervention/ comparator [4]	Relationship between maternal smoking during pregnancy (yes/no) and adolescent overweight (≥ 95th percentile BMI).	Association between maternal smoking during pregnancy (never smoked, smoked throughout pregnancy, and smoked before and/or after pregnancy but not during pregnancy) and overweight and obesity at age 14 yrs.	Relationship between maternal smoking during pregnancy (yes/no) and development of childhood overweight (weight-for-stature ≥ 95th percentile at 5 months and BMI ≥ 95th percentile at 4.5 yrs).	Relationship between maternal smoking during pregnancy (0, 1-9, 10-19, ≥ 20 cigarettes/d at 28-32 wks gestation) and development of child obesity (BMI ≥ 95th percentile).	Relationship between maternal smoking during pregnancy (yes/no) and development of high risk adults (defined as combination of low birth weight and high BMI at age 33 yrs).	Relationship between maternal smoking during pregnancy (0, 1-9, 10-19, ≥ 20 cigarettes/d at 28-32 wks gestation) and development of childhood overweight.
N [5]	7207 at baseline, 3368 for analysis.	3,253	2103 at baseline, 1944 at year 5.	13971 at baseline, 5493 at age 7.	7017	18 296 at baseline, 14 630 at follow-up, 13188 for analysis.
Population/study information [6]	Children born between 1980-1990 in USA of mother's in the National Longitudinal Study of Youth. 46% white, 32% black,	Mater-University Study of Pregnancy and Its Outcomes; Brisbane, Australia; 52% male; Followed for 14 yrs.	Random sample of children born in Quebec, Canada in 1998. 48.9% female. 5yr follow-up.	Children in the UK followed from birth (Avon longitudinal study of parents and children - ALSPAC). 7 yr follow-up.	Single births in England, Scotland, and Wales (Prenatal Mortality Survey). 49% male. 33 yr follow-up.	Children born between 2000 and 2002, from the Millennium Cohort Study. Followed from birth till age 3 yrs. Parents were

	22% Hispanic. Mean age 13.0yrs. 12 yr follow-up.					residents of UK.
Quality [7]	P	P	P	P	P	P
Results [8]	Smoking during pregnancy adj OR 1.41 (95% CI 1.08-1.84) was significantly associated with adolescent's overweight (mean age 12yrs).	Adolescent offspring of mothers who reported having smoked during pregnancy were more likely to be overweight and obese than those whose mothers did not smoke during pregnancy. Smoked during pregnancy: adj OR for overweight 1.30 (95% CI 1.05-1.60), adj OR for obese 1.40 (95% CI 1.01-1.94), compared to mothers who never smoked. Smoked before or after pregnancy, but not during pregnancy: adj OR for overweight 1.14 (0.85-1.53), adj OR for obese 0.90 (0.53-1.53).	Maternal smoking during pregnancy OR 1.8 (95% CI 1.2-2.8) had a significant effect on childhood overweight (BMI >95th percentile) at age 4.5 yrs, compared to no maternal smoking during pregnancy.	Smoking during pregnancy (compared to none, 1-9 cigarettes per day, adj OR 1.76 (95% CI 1.21-2.52); 10-19 cigarettes per day adj OR 1.59 (95% CI 1.08-2.34) ; ≥ 20 cigarettes per day, adj OR 1.80 (95% CI 1.01-1.39) was associated with the risk of obesity at age 7 yrs. Chi^2 test for linear trend = 27.17.	Smoking in pregnancy was a predictor of high risk status (combination low birth weight and high BMI at age 33 yrs): adj OR 1.79 (95% CI 1.37-2.29) in men and adj OR 2.27 (95% CI 1.79-2.86) in women.	Smoking during pregnancy (1–9 cigarettes per day adj OR 1.34 (95% CI 1.17-1.54); 10–19 cigarettes per day adj OR 1.49 (95% CI 1.26-1.75); 20+ cigarettes per day adj OR 1.34 (95% CI 1.05-1.70) was associated with early childhood overweight (age 3 yrs).
Effect on risk	Increase	Increase	Increase	Increase	Increase	Increase
Clinical	1	1	1	1	1	1

importance						
Clinical relevance	2	2	2	2	2	2
Generalisability	y	y	y	y	y	y
Applicability	y	y	y	y	y	y

17.6 LIFE COURSE FOOD CONSUMPTION and MATERNAL EMPLOYMENT

Is maternal employment associated with children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Children of mothers who work, especially those of higher incomes, have increased risk of childhood obesity.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	8 cohort studies (6 P, 1 0, 1 N).
Consistency	Satisfactory	7 studies found a positive association, 1 study found no association and was conducted in Australia.
Clinical impact	Satisfactory	The odds of early childhood overweight were increased with: any maternal employment (OR 1.14, 95% CI 1.00-1.29); every 10h/wk of maternal employment (OR 1.10, 95% CI 1.04-1.17); maternal employment of greater than 21h/wk (1.23, 95% CI 1.10-1.37).
Generalisability	Poor	Studies in the US and UK found an association, but over-represented children living in disadvantaged areas and from ethnic minority groups. The one study in an Australian population found no association.
Applicability	Poor	Due to the poor generalisability, this is not applicable to the Australian population.

Seven of the eight cohort studies reported children were at increased risk of development of overweight if their mother was employed. Of these, three reported a stronger association among children of higher income families, while one reported a stronger association in children in families just above the poverty line. These seven studies included four different cohorts in the US and UK, with children followed from birth to age 3 -16 years. Three of these cohorts over-represented children living in disadvantaged areas and from ethnic minority groups, thus the association may not be generalisable to the general Australian population. In contrast to the above studies, the one study that was conducted in an Australian population reported no association between maternal or paternal employment and the change in BMI z-score. This was a relatively small cohort of only 1373 at follow-up (age 8-13 yrs) and did not analyse income, but was of high quality. Therefore, the body of evidence provides some support for a recommendation, but caution should be taken when generalising the recommendation to the entire Australian population, especially given the Australian study found no association. Given the poor "generalisability" rating this body of evidence statement could not be graded higher than a D.

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Table 17.6 Studies used to make evidence statement for life course food consumption and maternal employment

Reference [1]	**Hesketh 2009 (40)**	**von Hinke Kessler Scholder 2008 (311)**	**Hawkins 2008 (360)**	**Miller 2008 (466)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Relationship between maternal employment (no paid employment, part-time, full-time) and paternal employment (no paid employment or part-time versus full-time) and change in child BMI z-score.	Relationship between maternal employment (full-time or part-time) at child's age 7 yrs on development of childhood overweight at age 16 yrs.	Relationship between maternal and partner employment (none vs any, working atypical hours (yes/no), do not spend enough time with child because of work (yes/no), hours worked/week (10h increments)) and development of overweight in children aged 3 yrs.	Association between maternal nonstandard work schedules (number of years worked nonstandard shift by the time the child was 13-14 yrs) and adolescent overweight ($\geq 85^{th}$ percentile BMI).
N [5]	1943 at baseline, 1373 at follow-up.	3350	18296 at baseline, 13113 at follow-up.	Number at baseline not provided, 2353 mother-child pairs at follow-up.
Population/study information [6]	Primary school children from Victoria, Australia. Children from the 1997 Health of Young Victorians Study (HOYVS) aged 5-10 yrs at baseline and 8-13 yrs at follow-up.	Children born in UK in 1958 (National Child Development Study - British birth cohort). 16 yr follow-up.	Singleton children in the Millennium Cohort Study, born between 2000 and 2002 in the United Kingdom, followed up from 9 mo until age 3 yrs of age. Over-represented children living in disadvantaged areas and from ethnic minority groups.	2353 mother-child pairs from the National Longitudinal Survey of Youth (1979-2004), United States. Children are followed from birth until age 13-14 yrs. Approximately half non-Hispanic white, half combination of Hispanic and African American.
Quality [7]	P	0	P	P

Results [8]	Maternal or paternal employment status was not associated with change in BMI z-score: mother employed part time β=0.01 (95% CI -0.06-0.07), mother employed full time β=0.05 (95% CI -0.03-0.13), father employed full-time β=-0.01 (95% CI -0.10-0.09).	Maternal full time work during mid childhood (age 7 yrs) was associated with increased probability of child becoming overweight, suggesting that both intensity and timing play a role. Mother working full time at age 7 yrs was associated with increased probability of becoming overweight by age 16 yrs (+5.5%, SE 2.7%, P<0.05, adjusted data). There was no evidence that part-time or full-time employment at earlier or later ages of childhood influences probability of becoming overweight.	Any maternal employment after the child's birth was associated with early childhood overweight adj OR 1.14 (95% CI 1.00-1.29). Children were more likely to be overweight for every 10 hour a mother worked per week adj OR 1.10 (95% CI 1.04-1.17). An interaction with household income revealed that this relationship was only significant for children from households with an annual income of >$57,750. These relationships were also evident among mothers in employment.	The no. of years the mother worked nonstandard schedules was associated with adolescent BMI unadj β 0.526 (95% CI 0.023-1.028) and adolescent overweight unadj β 1.341 (95% CI 1.0071-1.679). Results were driven by those families with predicted incomes in the 2nd quartile (family incomes near but above the poverty line), with a few or many years of nonstandard work schedules also associated with increased risk of adolescent overweight in 2-parent families.
Effect on risk	None	Increase	Increase	Increase
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisable	y	y	y	y
Applicability	y	y	y	y

Table 17.6 Studies used to make evidence statement for life course food consumption and maternal employment (cont.)

Reference [1]	**Classen 2005 (2043)**	**Anderson 2003 (2845)**	**Hawkins (2009) 3148**	**Baker (2009) 3155**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Relationship between mother's employment status (does not work vs. works 35 or more hr per wk) when child is under age of 8 yrs and development of overweight or obesity when child is over age of 8 yrs.	Relationship between maternal employment (hours worked per week; never worked, worked <35 hrs per wk since birth, worked ≥ 35 hrs per wk since birth) and likelihood of child being overweight.	Relationship between maternal employment (never worked, 1-20 hrs per wk, 21+ hrs per wk) and development of childhood overweight.	Association between maternal employment (<35hrs per wk vs. ≥ 35 hrs per wk) and development of child overweight (percentile BMI) among Hispanic children of immigrants and children of natives.
N [5]	4980	6283 women at baseline, number of subsequent children not provided.	18296 at baseline, 14630 at follow-up, 13188 for analysis.	Number at baseline not provided, 10966 at follow-up, 6430 for analysis.
Population/study information [6]	Children aged 2-18 yrs in US (National Longitudinal Survey of Youth 79), 50% male, 30% black, 20% Hispanic. 18 yr follow-up.	Overweight children aged 3-11 yrs and mothers in the US (National Longitudinal Survey of Youth). 37.8% Hispanic, 35.2% black, 25.1% white. 6y follow-up.	Children born between 2000 and 2002 in UK (Millennium Cohort Study). Over-represented children living in disadvantaged areas and from ethnic minority groups. Followed from birth to age 3y.	Children from Early Childhood Longitudinal Study (ECLS-K) in US, followed from K to 5th grade. 1,121 Hispanic children of immigrants, 496 Hispanic children of natives, and 4,813 non-Hispanic white children. 6 yr follow-up.
Quality [7]	P	P	P	N
Results [8]	Maternal employment status was related to child obesity, but not overweight. Marginal	The intensity of mother's work over the child's lifetime has a positive effect on a child's likelihood of being overweight if	In the fully adjusted model, maternal employment of > 21 hours/week (compared with never worked) was associated with early	Effect of maternal employment on BMI percentile varies significantly by family income, Hispanic

	effects probit estimates for obesity, 0.026, SE 0.011, P<0.05; for overweight, 0.023, SE 0.014.	the child is in a high income family, with a well-educated, or white mother. For these subgroups, a 10 hr increase in average hrs worked per wk over a child's life is estimated to increase the likelihood that the child is overweight by 1-4%, depending on the specification. Thus, a mother of this type moving from part-time (20 hours per week) work to full-time work (40 hours per week) is expected to increase the probability that her child is overweight by 2-8%.	childhood overweight adj OR 1.23 (95% CI 1.10-1.37). Working 1-20 hours per week was not associated with childhood overweight adj OR 1.10 (95% CI 0.99-1.23).	ethnicity, and nativity status (all P < 0.05). Among Hispanic children of immigrants, maternal employment seems to protect children from weight gain rather than promote it. However, this relationship is only marginally significant among high income children (P=0.08). The relationship between maternal employment and income differs significantly for Hispanic children of natives compared to Hispanic children of immigrants (P = 0.02). For non-Hispanic whites, the effect of maternal employment on percentile BMI is only significant for high-income children.
Effect on risk	Increase for obesity, none for overweight.	Increase	Increase	Increase for high income whites. None for income levels below high income.
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisability	y	y	y	y
Applicability	y	y	y	y

17.7 LIFE COURSE FOOD CONSUMPTION and PARENTAL OVERWEIGHT

Does parental overweight lead to children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Parental overweight or obesity is associated with increased risk of child overweight or obesity. The risk is greater when both rather than one parent is overweight or obese.
Grade		A
Component	**Rating**	**Notes**
Evidence Base	Excellent	14 cohort studies (13 P, 1 0).
Consistency	Good	All cohort studies were consistent, except one was not significant for paternal weight, one was not significant for maternal weight, and one was not significant in males.
Clinical impact	Excellent	Odds ratios for child being overweight/obese range from 1.0 to 3.4 for one parent and 1.9 to 10.4 for both parents being overweight/obese.
Generalisability	Excellent	Western populations, including Australia, USA, Canada, and UK.
Applicability	Excellent	Directly applicable.

All of the 14 cohort studies are in agreement that an overweight or obese parent increases the risk of the child being overweight or obese. One study in the UK found the association significant for only paternal BMI, not maternal BMI. In the National Longitudinal Study of Adolescent Health in the US, the association was only significant in females, not males. In the Health of Young Victorians Study in Australia, after adjusting for child's BMI at baseline, the association was significant only with maternal obesity, not maternal overweight or paternal overweight or obesity. Four studies were in an Australian population, and the remaining ten studies were in US, UK or Canadian populations, making this association very generalisable to the Australian population. Therefore, there is sufficient body of evidence for this statement to guide practice.

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Table 17.7 Studies used to make evidence statement for life course food consumption and parental overweight

Reference [1]	**Hesketh 2009 (40)**	**Li 2009 (212)**	**Yang 2008 (728)**	**Salsberry 2007 (1188)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Association between maternal and paternal BMI and change in child BMI z-score.	Association between 1-SD increase in maternal and paternal BMI z-scores at different life stages (at age 7, 11, 16, 23, and 33 yrs) on change in BMI z-score of their children (at age 4-8 yrs and age ≥ 9 yrs).	Association between parental obesity (at least one parent obese vs no parent obese) and development of overweight and obesity in early adulthood (at age 18-26 yrs).	Effect of maternal pre-pregnancy weight status (normal weight, overweight, or obese based on BMI) and mother's weight status when child is age 12 yrs on child's development of overweight at age 12 yrs.
N [5]	1943 at baseline, 1,373 at follow-up.	2027 cohort families, 3076 children.	20 745 at baseline, 9542 at follow-up.	7207 at baseline, 3368 for analysis.
Population/study information [6]	Primary school children from Victoria, Australia. Children from the 1997 Health of Young Victorians Study (HOYVS) aged 5-10 yrs at baseline and 8-13 yrs at follow-up.	Parents born in UK in 1958 who had children over the age of 4 yrs by 1991 (mean age of child 8.7yrs). 31 year follow up of parents.	Adolescents aged 12-18 yrs followed from 1995 until 2001-2002 (aged 18-26 yrs), from the National Longitudinal Study of Adolescent Health, United States.	Children born between 1980-1990 in USA of mothers in the National Longitudinal Study of Youth. 46% white, 32% black, 22% Hispanic. Mean age 13.0 yrs. 12 yr follow-up.
Quality [7]	P	P	P	P

Results [8]	Maternal adiposity was associated with change in BMI z-score adj β=0.02 (95% CI 0.01-0.02) P<0.001).	Increased parental BMI in both childhood and adulthood and a high BMI gain in both childhood and adulthood were associated with a higher BMI and an increased risk of overweight/obesity in the offspring. The association was independent of adult parental BMI. For example, for mother with 1-SD increase in BMI z-score at age 11 yrs, adj OR for overweight/obesity in offspring at age >9y is 1.57 (95% CI 1.13-2.17); with 1-SD increase in BMI z-score at age 16 yrs, adj OR for overweight/obesity in offspring at age >9 yrs is 1.40 (95% CI 1.01-1.94). Associations are significant at most mother's and father's ages (7, 11, 16, 23, and 33y), and at most offspring ages (4-8 yrs and ≥ 9 yrs).	Having at least one obese parent also significantly increased the odds of overweight adj OR 1.98 (95% CI 1.12-3.49) and obesity adj OR 3.43 (95% CI 1.88-6.27) in females in early adulthood. There was no association in males: overweight adj OR 0.91 (95% CI 0.51-1.63), obesity adj OR 1.59 (95% CI 0.82-3.06).	Mother's weight status was significantly associated with adolescent's overweight: Pre-pregnancy overweight adj OR 2.18 (95% CI 1.51-3.13), pre-pregnancy obesity adj OR 4.28 (95% CI 2.69-6.83), mother overweight when child is age 12 yrs adj OR 1.55 (95% 1.11-2.14), mother obese when child is age 12 yrs adj OR 2.53 (95% CI 1.64-3.92). Mother's weight gain until child is age 12 yrs was not associated with development of child overweight by age 12 yrs adj OR 1.02 (95% CI 0.98-1.05).
Effect on risk	Increase	Increase	Increase for females, none for males.	Increase
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisability	y	y, but mothers were a bit younger than the normal population.	y	y
Applicability	y	y	y	y

Table 17.7 Studies used to make evidence statement for life course food consumption and parental overweight (cont.)

Reference [1]	**Dubois 2006 (1624)**	**Dubois 2006 (1771)**	**Classen 2005 (2043)**	**Reilly 2005 (2072)**	**Mamun 2005 (2131)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II	II
Intervention/ comparator [4]	Relationship between mother's BMI (<25 vs ≥ 25) and number of parents with BMI ≥ 25 (none, 1, or 2) with development of overweight in pre-school children.	Relationship between mother's BMI and father's BMI (<18.5, 18.5-24.9, 25.0-29.9, ≥ 30), and number of parents overweight or obese when child is age 18 mo and development of child's overweight (BMI >95th percentile) by age 4.5 yrs.	Relationship between mother's BMI (<18.5, >25 and <30 (overweight), >30 and <40 (obese), and >40 (morbidly obese)) and development of overweight or obesity in children over age 8 yrs.	Relationship between parental BMI (before pregnancy: neither parent obese, father only obese, mother only obese, both obese) and development of child obesity (BMI ≥ 95th percentile) at age 7 yrs.	Relationship between parental BMI (father normal, father overweight or obese, mother normal, mother overweight or obese, both normal, normal mother and overweight or obese father, normal father and overweight or obese mother, both overweight or obese) and child development of overweight status between ages of 5-14 yrs.
N [5]	1514	2103 at baseline, 1944 at year 5.	4980	13 971 at baseline, 5493 at age 7.	7223 at baseline, 2934 for analysis.
Population/study information [6]	Children born in Quebec, Canada in 1998 (Longitudinal Study of Child Development in Quebec). 4-5 yr follow-up.	Random sample of children born in Quebec, Canada in 1998. 48.9% female. 5 yr follow-up.	Children aged 2-18y in US (NLSY79), 50% male, 30% black, 20% Hispanic. 18 yr follow-up.	Children in the UK followed from birth (Avon longitudinal study of parents and children - ALSPAC). 7 year follow-up.	Children born 1981-1984 at one of two major obstetric hospitals in Brisbane. (Mater-University of Queensland Study of

					Pregnancy). 14y follow-up.
Quality [7]	P	P	P	P	P
Results [8]	Having overweight/obese parents increased the odds for obesity as defined by the Cole criteria adj OR 2.5 (95% CI 1.2–5.4) for one overweight/obese parent; adj OR 5.2 (95% CI 2.3–11.9) for two overweight/obese parents) and overweight as defined by BMI ≥ 95th percentile for age adj OR 2.1 (95% CI 1.3-3.3) for one overweight/obese parent; adj OR 3.8 (95% CI 2.2–6.6) for two overweight/obese parents).	Parental overweight or obesity adj OR for 1 parent, 2.1 (95% CI 1.3-3.6), adj OR for 2 parents, 3.2 (95% CI 1.7-5.8) had a significant effect on childhood overweight (BMI >95th percentile) at age 4.5 yrs. Parent's BMI was associated with child BMI >95th percentile at age 4.5y: mother BMI 25.0-29.9 = unadj OR 2.0 (95% CI 1.3-3.1); mother's BMI ≥ 30 = unadj OR 3.4 (95% CI 2.1-5.7); father BMI 25.0-29.9 = unadj OR 1.7 (95% CI 1.0-2.6), father BMI ≥ 30 = unadj OR 3.0 (95% CI 1.7-5.3).	Mother's overweight status increased the risk of child becoming overweight. Compared to mother with BMI 18.5-25, mother with BMI >40 is 32% more likely to have an overweight/obese child, and mother with BMI 30-40 is 23% more likely to have an overweight/obese child.	Parental obesity was independently associated with child's development of obesity. Compared to neither parent obese: father only obese, adj OR 2.54 (95% CI 1.72-3.75); mother only obese, adj OR 4.25 (95% CI 2.86-6.32), both obese, adj OR 10.44 (95% CI 5.11-21.32), P<0.001.	Parental overweight status is an important determinant of whether a child is overweight at either stage or changes from not being overweight at 5 yrs to becoming overweight at 14 yrs (compared to normal weight mother and father, mother overweight or obese/normal father: RR 3.02 (95% CI 1.86-4.91); father overweight or obese/normal mother RR 2.14 (95% CI 1.49-3.07); both overweight or obese RR 7.44 (95% CI 4.60-12.02).
Effect on risk	Increase	Increase	Increase	Increase	Increase
Clinical importance	1	1	1	1	1
Clinical relevance	2	2	2	2	2
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 17.7 Studies used to make evidence statement for life course food consumption and parental overweight (cont.)

Reference [1]	**Burke 2005 (2224)**	**Field 2004 (2436)**	**Power 2003 (2666)**	**Hawkins (2009) 3148**	**Hesketh 2004 (4238)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II	II
Intervention/ comparator [4]	Relationship between mothers' and fathers' BMI (continuous variable) and mother or father being overweight or obese (yes/no) and BMI in children at age 8 yrs.	Relationship between mother's BMI (overweight status – yes/no) on change in child's BMI z-score.	Relationship between parental BMI and development of high risk adults (combination of low birth weight and high BMI at age 33 yrs).	Relationship between parental overweight (measured BMI when child was age 9 mo: both <25, mother only ≥ 25, father only ≥ 25, both ≥ 25) and mother pre-pregnancy overweight (BMI <25 or ≥ 25) and development of childhood overweight (includes obesity) by age 3 yrs.	Effect of mother and father BMI (underweight, healthy weight, overweight, or obese) and number of overweight or obese parents at baseline on change in child BMI z-score.
N [5]	1430	8203 G 6774 B	7017	18 296 at baseline, 14 630 at follow-up, 13 188 for analysis.	1438
Population/study information [6]	Children in Australia aged 16 weeks of gestation to age 8y (Western Australia Pregnancy Cohort Study). Surveyed at age 1, 3, 6, and 8y.	Children aged 9-14 yrs in USA (Growing Up Today Study). Children of women in Nurses' Health Study II. 3 yr follow-up.	Single births in England, Scotland, and Wales (Prenatal Mortality Survey). 49% male. 33 yr follow-up.	Children born in UK between 2000 and 2002, from the Millennium Cohort Study. The study over-represented children living in disadvantaged areas and from ethnic minority groups. Followed from birth till age 3 yrs.	Children aged 5-10 yrs in Victoria, Australia (Health of Young Victorians Study). 3.2y (mean) follow-up.
Quality [7]	P	0	P	P	P
Results [8]	Insufficient data on father's BMI and weight status. BMI at age 8 yrs was associated with mother's BMI adj coefficient 0.12 kg/m^2 (95% CI 0.094-0.15)	There is an association between mother being overweight and increase in BMI z-score (combined boys and girls): adj	Paternal BMI was a predictor of high risk status of combination low birth weight and high BMI at age 33 yrs: adj OR 1.07 (95% CI 1.01-1.10) in men, adj OR 1.07 (95% CI	Compared to neither parent being overweight, parental overweight (both: adj OR 1.89 (95% CI 1.63-2.19); father only: adj OR 1.45 (95% CI 1.28-1.63); mother only: adj OR 1.37 (95% CI 1.18-1.58) and mother's pre-pregnancy	Parental BMI influenced change in BMI z-score from baseline to follow-up; relationships were stronger for maternal than paternal BMI, and stronger for girls than boys. The association lost some significance when

	P<0.001). Development of overweight or obesity by age 8 yrs is associated with mother being overweight or obese adj OR 2.6 (95% CI 1.8-3.6) P<0.001.	change in BMI z-score = 0.059 (95% CI 0.036-0.082).	1.03-1.11) in women. There was no association with maternal BMI.	overweight (adj OR 1.28 (95% CI 1.14-1.45) were associated with development of child overweight or obesity by age 3 yrs.	the child's baseline BMI was adjusted for, but remained significant for mother's obesity. Compared to a healthy weight, association of child overweight/obesity with mother overweight adj OR 1.3 (95% CI 0.8-2.0), mother obese adj OR 1.8 (95% CI 1.1-3.1), father overweight adj OR 1.4 (95% CI 0.9-2.0), father obese adj OR 1.0 (95% CI 0.6-1.9).
Effect on risk	Increase	Increase	Increase for paternal BMI, none for maternal BMI.	Increase	Increase for maternal obesity, none for paternal overweight or obesity.
Clinical importance	1	1	1	1	1
Clinical relevance	2	2	2	2	2
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

17.8 LIFE COURSE FOOD CONSUMPTION and PARENTAL EDUCATION

Is parental education related to children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Higher parental education, particularly the mother's, is associated with reduced risk of their children becoming overweight.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	8 cohort studies (7 P, 1 0), with some risk of bias.
Consistency	Poor	4 studies found a negative association, 4 studies found no association.
Clinical impact	Good	Bhargava 2008 reported that a higher parental education was related to a lower BMI z-score of 0.12 +/- 0.002. Classen 2005 reported that children of college-educated mothers have an 8% lower risk of becoming overweight or obese.
Generalisability	Excellent	Populations from Australia, USA, and Canada.
Applicability	Excellent	Directly applicable.

The results were inconsistent, but were suggestive of an inverse association between parental education and child development of overweight. Of the eight cohort studies, four studies involving approximately 27,000 participants reported an inverse association, and four studies involving 8000 participants reported no association. Both groups were comprised of cohorts in Australia and North America. Most (three) of the studies reporting an inverse association measured tertiary education of the mother, while the fourth measured grade one through nine only, and all four of the studies reporting no association measured tertiary education. Due to the large sample sizes of the studies reporting an association compared to those reporting no association, it seems there is likely a relationship, but care should be taken when making a recommendation based on this body of evidence.

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Table 17.8 Studies used to make evidence statement for life course food consumption and parental education.

Reference [1]	**Bhargava 2008 (473)**	**Sturm 2005 (1921)**	**Classen 2005 (2043)**	**Burke 2005 (2224)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence [3]	II	II	II	II
Intervention/ comparator [4]	Association between parental education (1-9) and child BMI and BMI z-score.	Relationship of mother's education level (less than high school diploma, high school diploma or equivalent, some college, Bachelor's degree or higher) on risk of child becoming overweight and change in child's BMI.	Relationship between mother's education (high school only, some college, graduated college) and development of overweight or obesity in children over the age of 8y.	Relationship between mother's education (secondary, technical qualification or diploma, tertiary) and BMI in children.
N [5]	19 684 at baseline, 11 479 at follow up, 7635 for analysis.	13 282	4980	1430
Population/study information [6]	Children from the Early Childhood Longitudinal Study-Kindergarten (ECLS-K) in USA followed from kindergarten till Grade 5.	Children in the US in kindergarten. Followed through 3rd grade (4 yrs).	Children aged 2-18y in US (NLSY79), 50% male, 30% black, 20% Hispanic. 18yr follow-up.	Children in Australia aged 16 weeks of gestation to age 8y (Western Australia Pregnancy Cohort Study). Surveyed at age 1, 3, 6, and 8 yrs.
Quality [7]	P	P	P	P

Results [8]	BMI z-score was significantly negatively associated with higher parental education: natural log of parental education level (1-9) is associated with BMI z-score reduction of -0.159 (SE 0.017).	Compared to children of mothers with less than a high school diploma, children whose mother had completed college gained less weight (change in BMI = -0.262, SE 0.098, P=0.007) between kindergarten and third grade. There was no association for the lower levels of education.	College educated mothers have a lower risk (8% overall) of having a child that becomes overweight or obese. White females with college-educated mothers are 10% less likely to become overweight or obese compared to white females with less than high school-educated mothers.	Child BMI at 6 yrs was negatively associated in mothers with tertiary education (RANOVA P=0.001). No further quantitative data reported.
Effect on risk	Protect	Protect	Protect	Protect
Clinical importance [9]	1	1	1	1
Clinical relevance [10]	2	2	2	2
Generalisability	y, but low SES and participants of Food Stamp program	y	y	y
Applicability	y	y	y	y

Table 17.8 Studies used to make evidence statement for life course food consumption and maternal employment (cont.)

Reference [1]	**Hesketh 2009 (40)**	**Mamun 2005 (2131)**	**Oliver 2008 (646)**	**Dubois 2006 (1771)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Relationship between mother's and father's education level (≤ year 10, year 11-12, trade apprenticeship or diploma, tertiary) and change in child BMI z-score.	Relationship between maternal education (did not complete secondary school, completed secondary school, completed further/higher education) and change in weight status (becoming overweight/obese or becoming a healthy weight) between age of 5-14yrs.	Relationship between parental education (less than high school, high school/some post secondary, and post secondary degree/diploma) and BMI from childhood to adolescence.	Relationship between mother's education level (no high school diploma, high school diploma, college diploma, university diploma) and child BMI >95th percentile.
N [5]	1943 at baseline, 1373 at follow-up.	7223 at baseline, 2934 for analysis.	2152	2103 at baseline 1944 at yr 5
Population/study information [6]	Primary school children from Victoria, Australia. Children from the 1997 Health of Young Victorians Study (HOYVS) aged 5-10yrs at baseline and 8-13yrs at follow-up.	Children born 1981-1984 at one of two major obstetric hospitals in Brisbane. (Mater-University of Queensland Study of Pregnancy - MUSP). Followed for 14yrs.	Children in Canada aged 2-3yrs at baseline. 50.4% male. 68% urban. 49% overweight. 15% high income adequacy, 64% middle/middle-high income adequacy, 20% low/low-middle income adequacy. 8 yr follow-up.	Random sample of children born in Quebec, Canada in 1998. 48.9% female. 5yr follow-up.
Quality [7]	P	P	0	P
Results [8]	Maternal or paternal education level did not have an association with change in BMI z-score. Compared to ≤ year 10, mother's tertiary	There was no association with maternal education and change in weight status between age 5yrs and 14yrs (P=0.585). Compared to children of mothers who did no complete secondary school, children of mothers who completed higher education	Education level had no effect on change in BMI percentile. Compared to high school/some post secondary school, parents having no high school	Mother's education level had no association with BMI at or above the 95th percentile at age 4.5yrs. Compared to university degree:

	education β = -0.02 (95% CI -0.10 to 0.06) P=0.39; father's tertiary education β = -0.05 (95% CI -0.14 to 0.03) P=0.27. All unadjusted.	were not associated with a change from normal to overweight/obese adj RR 1.51 (95% CI 0.96-2.38) a change from overweight/obese to normal adj RR 1.57 (95% CI 0.77-3.18) or maintaining overweight/obese adj RR 1.23 (95% CI 0.74-2.06).	certificate was not associated with child's BMI percentile adj β=1.38 (95% -3.21 to 5.97). Parents having a postsecondary degree was not associated with child's BMI percentile adj β=-1.45 (95% -4.45 to 1.56).	college degree adj OR 1.5 (95% CI 0.9-2.5) high school diploma adj OR 1.2 (95% CI 0.7-2.1) no high school diploma adj OR 1.4 (95% CI 0.8-2.4).
Effect on risk	None	None	None	None
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisability	y	y	y	y
Applicability	y	y	y	y

17.9 LIFE COURSE FOOD CONSUMPTION and SOCIOECONOMIC STATUS

Is socioeconomic status or family income related to children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		In developed countries, a low family income or socioeconomic status is associated with increased risk of overweight or obesity during childhood, adolescence, and young adulthood.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	9 cohort studies (8 P, 1 0), with some risk of bias due to variable confounding factors.
Consistency	Satisfactory	6 studies found a significant effect, 3 studies found no effect.
Clinical impact	Excellent	Odds ratios for increased BMI or childhood overweight range from 1.95-2.5 for low socioeconomic status.
Generalisability	Excellent	Western populations, including Australia, New Zealand, UK, USA, and Canada.
Applicability	Excellent	Directly applicable.

Most studies in developed countries (data from Australia, New Zealand, UK, USA, and Canada), reported an inverse association between socioeconomic status or family income and risk of obesity. Three studies examined the same cohort (Early Childhood Longitudinal Study), but only two of the studies reported a significant relationship. One possible reason for the inconsistency is that the study that found no significant association only followed the subjects through the third grade, while the other two followed through the fifth grade. The second study that did not find a significant association measured socioeconomic status using the Socio-Economic Index for Areas Index of Relative Socioeconomic Disadvantage, which estimates socioeconomic status of subjects by the area they live in, rather than by individual or household income. Therefore, the independent variable in this study is slightly different to those of the other eight studies. The third study that did not report significant results was also of poorer quality due to possible measurement bias; the transition from parental report of child's weight to child report of weight can lead to the appearance of declining BMI values over time. Lack of control for parental BMI is also a potential confounder. Because the inconsistencies of the results can be explained, this evidence statement can be trusted to guide practice.

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Table 17.9 Studies used to make evidence statement for life course food consumption and socioeconomic status

Reference [1]	**Matijasevich 2009 (22)**	**Hesketh 2009 (40)**	**Sturm 2005 (1921)**	**Danner 2008 (130)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Effect of socioeconomic position (measured by family income quintiles and maternal education tertiles (0-4yrs, 5-8yrs, ≥ 9yrs)) on development of overweight (BMI-for-age > +1 SD) and obesity ((BMI-for-age > +2 SD).	Relationship between SES (measured with SEIFA Index of Relative Socioeconomic Disadvantage) and change in child BMI z-score.	Relationship between family income (6 groups, from <$15,000 to >$75,000) on risk of developing child overweight and BMI change.	Relationship between SES (low (quintile 1), middle (quintile 3), high (quintile 5)) and change in BMI.
N [5]	Avon: 6751; Pelotas: 1982 study - 3147; 1993 study - 4441	1943 at baseline 1373 at follow-up.	13 282	14 369 at baseline 7334 at follow-up.
Population/study information [6]	Children born to mothers attending health clinics in Avon, UK and Pelotas, Brazil. Children in UK were followed from birth until age 11yrs; 1982 study - children in Brazil were followed from birth until 18yrs; 1993 study - children in Brazil were followed from birth until 11yrs.	Primary school children from Victoria, Australia. Children from the 1997 Health of Young Victorians Study (HOYVS) aged 5-10yrs at baseline and 8-13yrs at follow-up.	Children in the US (Early Childhood Longitudinal Study-K). Followed from kindergarten to 3rd grade (4 yrs).	Children from Early Childhood Longitudinal Study (ECLS-K), United States, followed from kindergarten to Grade 5.
Quality [7]	P	P	P	P
Results [8]	In the ALSPAC (Avon) study, no association was found between overweight and family income in boys. In the same study, a higher prevalence of overweight was found in the poorest (for girls only) and both boys and girls of women with the lowest educational achievement.	SES did not have an association with change in BMI z-score (adjusted for baseline BMI z-score). β=0.004 (95% CI -0.00-0.01) P=0.06.	Family income was not associated to change in BMI between K and 3rd grade. Real family income in $1000 (slope): BMI change is not associated with <25th percentile (adj β=-0.010 kg/m^2, SE 0.007,	SES is significantly inversely related to BMI. For SES quintile: kindergarten BMI adj β=-0.16 kg/m^2, SE 0.020, P<0.001; change in BMI adj β=-0.030 kg/m^2, SE 0.0051, P<0.001.

			P=0.133), 25th-50th percentile (adj β=0.008 kg/m^2, SE 0.005, P=0.132), 50th-75th percentile (adj β=-0.004 kg/m^2, SE 0.003, P=0.200), >75th percentile (adj β=-0.001 kg/m^2, SE 0.001, P=0.241).	
Effect on risk	Increase in UK girls, None for UK boys, Protect in Brazil 1993 boys and girls, Protect in Brazil 1993 men, Increase in Brazil 1993 women.	None	None	Increase
Clinical importance	1	1	1	1
Clinical relevance	2	2	2	2
Generalisability	y for UK cohort, n for Brazil cohorts.	y	y	y
Applicability	y	y	y	y

Table 17.9 Studies used to make evidence statement for life course food consumption and socioeconomic status (cont.)

Reference [1]	**Bhargava 2008 (473)**	**Oliver 2008 (646)**	**Dubois 2006 (1771)**	**Burke 2005 (2224)**	**Poulton 2002 (2934)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II	II
Intervention/ comparator [4]	Association between socio-economic (analysed 13 household income categories, from <$5,000 to >$200,000) and child BMI and BMI z-score.	Relationship between income adequacy (low/low middle vs middle/middle high vs high) on BMI percentile from childhood to adolescence.	Relationship between household income at time of pregnancy and at child's age 4.5yrs (<$20,000, $20,000-39,999, $40,000-59,999, and ≥ $60,000) and BMI >95th percentile at age 4.5yrs.	Relationship between family income (≤ $40,000 or > $40,000) on child BMI.	Effect of child's SES (as measured by parental occupational status – categorised into low, medium, and high) on BMI and waist:hip ratio as an adult.
N [5]	19 684 at baseline, 11 479 at follow up, 7 635 for analysis.	2152	2103 at baseline, 1944 at year 5.	1430	980
Population/study information [6]	Children from the Early Childhood Longitudinal Study-Kindergarten (ECLS-K) in USA followed from kindergarten to Grade 5.	Children in Canada aged 2-3yrs at baseline. 50.4% male. 68% urban. 49% overweight. 15% high income adequacy, 64% middle/middle-high income adequacy, 20% low/low-middle income adequacy. 8 year follow-up.	Random sample of children born in Quebec, Canada in 1998. 48.9% female. 5yr follow-up.	Children in Australia aged 16 wks of gestation to 8 yrs (Western Australia Pregnancy Cohort Study). Surveyed at age 1, 3, 6, and 8yrs.	Children in Dunedin, New Zealand, followed from birth (Dunedin Multidisciplinary Health and Development Study). Baseline sample at 3yrs and followed through age 26yrs.
Quality [7]	P	0	P	P	P
Results [8]	BMI z-score was	Adjusting for both family and	Compared to	Increased BMI at	Low SES as a child was

	significantly negatively associated with higher household incomes (adj zBMI -0.013, SE 0.002, P<0.05).	neighbourhood characteristics, compared to middle/middle high income adequacy, BMI percentile was not associated with low/low middle (adj β=0.5 (95% CI -3.58 to 4.59) or high adj β=1.68 (95% CI -2.6 to 5.97) income adequacy.	income >$60,000, household income <$20,000 at time of pregnancy was associated with BMI >95th percentile at age 4.5yrs unadj OR 2.2 (95% CI 1.3-3.6) P=0.0013. Household income at 4.5yrs was associated with BMI >95th percentile at 4.5yrs (compared to income >$60,000, <$20,000 household income = adj OR 2.5 (95% CI 1.3-4.8) $20,000-40,000 = adj OR 1.6 (95% CI 1.0-2.7).	the age of 6yrs and 8yrs was associated with lower income (RANOVA P=0.004).	significantly related to higher BMI and higher waist:hip ratio. OR for BMI in low vs high socioeconomic status = 1.95 (SE 0.49), P<0.0001. OR for waist:hip ratio for low vs high SES = 1.57 (SE 0.51), P=0.002. No significant differences when comparing medium vs high SES.
Effect on risk	Increase	None	Increase	Increase	Increase
Clinical importance	1	1	1	1	1
Clinical relevance	2	2	2	2	2
Generalisability	y, but low SES and participants in Food Stamp program.	y	y	y	y
Applicability	y	y	y	y	y

17.10 LIFE COURSE FOOD CONSUMPTION and SOCIAL CLASS

Is low social class related to children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Low social class is associated with an increased risk of overweight or obesity.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	7 cohort studies (5 P, 2 0).
Consistency	Satisfactory	4 studies found an inverse association, 2 studies found an inverse association in one gender only and no association in the other gender, 1 study found no association.
Clinical impact	Satisfactory	Low/unskilled social class was associated with an increase in adolescent BMI of a range of 1.2-1.7 units. Odds ratio for adolescent or adult overweight for being in the low/manual social class ranged from 1.49-2.47.
Generalisability	Satisfactory	Studies are able to be generalised to the Australian population and include USA, UK and Brasil.
Applicability	Satisfactory	Limited applicable to the Australian population.

Results of the cohort studies were slightly mixed, but overall there is likely an association between low social class and increased risk of overweight or obesity. All studies followed subjects through adulthood (age 17-53 yrs) except for the one study reporting no association (followed only through age 9 yrs), suggesting risk of overweight is not increased until a person of low social class reaches adulthood. One cohort reported an association between social class as a child (age 4 yrs) and measures of overweight in both men and women at age 53 yrs, but the association was significant in women only when examining overweight and social class as a young adult (age 26 yrs). No other study made this comparison. Most studies were conducted in the US or UK and none in Australia.

References

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Wright, C. M. & Parker, L. 2004, "Forty years on: the effect of deprivation on growth in two Newcastle birth cohorts", *International Journal of Epidemiology*, vol. 33, no. 1, pp. 147-52.

Yang, S., Lynch, J., Schulenberg, J., Roux, A. V. D. & Raghunathan, T. 2008, "Emergence of socioeconomic inequalities in smoking and overweight and obesity in early adulthood: the national longitudinal study of adolescent health", *American Journal of Public Health*, vol. 98, no. 3, pp. 468-77.

Table 17.10 Studies used to make evidence statement for life course food consumption and social class

Reference [1]	**Yang 2008 (728)**	**Goldani 2007 (1021)**	**Power 2007 (1091)**
Type of study [2]	Cohort	Cohort	Cohort
Level of evidence [3]	II	II	II
Intervention/ comparator [4]	Association between family socioeconomic position (measured by combination of occupation of head of household, household income, and maternal education, and categorised into low, middle, and high) during adolescence and overweight and obesity in early adulthood.	Relationship between social class at birth (high vs intermediate vs low) on BMI at age 17yrs.	Effect of childhood social class (measured by father's occupation – professional (I), managerial/technical (II), other non-manual (IIInm), skilled manual (IIIm), partly skilled (IV), unskilled manual or no male head of household (V)) on BMI as an adult.
N [5]	20 745 at baseline 9542 at follow-up.	3468 at baseline 1189 at follow-up	9377
Population/study information [6]	Adolescents aged 12-18 yrs followed from 1995 till 2001-2002 (aged 18-26 yrs), from the National Longitudinal Study of Adolescent Health, United States.	Males born in Ribeirao Preto, Brazil (most developed economic area of Brazil) in 1978-79, and who enlisted in army in 1997-98. 17 yr follow-up.	Subjects in the UK from childhood to age 44-45 yrs (Perinatal Mortality Survey).
Quality [7]	P	0	P
Results [8]	Family SEP during adolescence was significantly related to obesity of females aged 18-26 yrs. Compared to high SEP: middle SEP, OR for obesity = 4.21 (95% CI 2.11-8.42); middle SEP, OR for overweight = 2.01 (95% CI 1.16-3.48); low SEP, OR for obesity = 2.47 (95% CI 1.18-5.18); low SEP, OR for overweight = 1.04 (95% CI	Compared to high social class at birth, low social class was associated with increased BMI at age 17-18 yrs adj β=1.21 kg/m^2 (95% CI 0.49-1.93) P<0.05).	Childhood social class was directly associated with BMI (age 44-45yrs) (I professional, II managerial/technical, III other non-manual, IV unskilled manual, V no male head of household): adj BMI increase of 0.41 kg/m^2 (95% CI 0.32-0.49) for each increase in social class (as social class becomes

	0.53-2.02). There was no association in males.		lower). Adj SD score=0.080 (95% CI 0.064-0.097).
Effect on risk (Increase/None/Protect)	Increase for females; none for males.	Increase	Increase
Clinical importance [9]	1	1	1
Clinical relevance [10]	2	2	2
Generalisability	y	y (bc most developed area)	y
Applicability	y	y	y

Table 17.10 Studies used to make evidence statement for life course food consumption and social class (cont.)

Reference [1]	**Power 2003 (2666)**	**Langenberg 2003 (2704)**	**Kuh (2002) 3127**	**Wright 2004 (2540)**
Type of study [2]	Cohort	Cohort	Cohort	Cohort
Level of evidence	II	II	II	II
Intervention/ comparator [4]	Relationship between social class of origin (based on father's occupation in 1958 – manual vs non-manual) and development of high risk adults (defined as combination of low birth weight and high BMI) at age 33 yrs.	Effect of childhood social class (based on father's occupation – professional (I), intermediate (II), skilled non-manual (III), skilled manual (III), semi-skilled (IV), unskilled (V)) on waist: hip ratio (%), waist: height ratio (%), waist circumference (cm), and BMI (kg/m^2) at age 53 yrs.	Relationship between father's social class (manual vs non-manual) and waist: hip ratio, waist circumference, and hip circumference at age 43yrs.	Effect of child social class (classified with Townsend scores, divided into 4 percentile groupings, and labelled affluent, intermediate, deprived, and very deprived) on child BMI at age 9 yrs.
N [5]	7017	1472 M and 1563 F	5362 at baseline, 3266 at follow-up, 3174 for analysis.	2174
Population/study information [6]	Single births in England, Scotland, and Wales (Prenatal Mortality Survey). 49% male. 33 yr follow-up.	Subjects born in UK and followed for 53yrs	Children born in England, Scotland and Wales, from the Medical Research Council's National Survey of Health and Development, followed from birth until age 43 yrs.	Children born in UK, followed to age 9 yrs.
Quality [7]	P	P	0	P

Results [8]	Compared to non-manual social class, manual social class was a predictor of high risk status (=combined low birth weight and high BMI at age 33 yrs): adj OR 1.61 (95% CI 1.16-2.21) in men, adj OR 1.49 (95% CI 1.11-2.02) in women.	Father's social class at age 4 yrs was inversely associated with waist: hip ratio (P=0.002), waist: height ratio (P=0.002), and BMI in men (compared to professional, adj difference in mean BMI = +0.6 kg/m^2 for intermediate, +0.8 for skilled non-manual, +1.7 for skilled manual, +1.1 for semi-skilled, +1.7 for unskilled, P=0.002), but not waist circumference. Father's social class at age 4 yrs was inversely associated with waist: height ratio (P<0.001), waist circumference (P=0.001), and mean BMI in women (compared to professional, adj difference in mean BMI = 0.0 kg/m^2 for intermediate, -0.7 for skilled non-manual, +1.1 for skilled manual, +1.5 for semi-skilled, +0.6 for unskilled, P<0.001), but not waist:hip ratio.	Compared to men from a non-manual social class, men from a manual social class are associated with greater adj WHR +0.56 (95% CI 0.02-1.10) and a greater adj waist circumference +0.84 (95% CI 0.13-1.54). There was no association in women (P=0.056 for WHR, P=0.299 for WC).	There was no significant difference in BMI between "deprivation" gradients (affluent, intermediate, deprived, very deprived) at age 4 yrs (P=0.31) or 9 yrs (P=0.16).
Effect on risk	Increase	Increase	Increase in men, none in women	None
Clinical importance	1	1	1	3
Clinical relevance	2	2	2	2

Generalisability	y	y	y	y
Applicability	y	y	y	y

17.11 LIFE COURSE FOOD CONSUMPTION and SCHOOL-BASED INTERVENTIONS

Do school-based nutrition intervention programs lead to children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Interventions delivered in the school environment that are focused on eating and physical activity improve weight outcomes in children.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Good	2 systematic reviews (1 P, 1 N), one of 25 intervention studies, the other of 10 intervention studies.
Consistency	Satisfactory	Doak 2006 reported that 68% of interventions were effective.
Clinical impact	N/A	No summary statistics reported in either review.
Generalisability	Excellent	Western populations.
Applicability	Excellent	Directly applicable.

The two systematic reviews are in agreement that a school-based intervention can improve child weight outcomes. The first review (Doak 2006) examined 25 school-based intervention studies involving over 53 000 subjects, and found that 68% of interventions were successful. This review was of high quality and had well described inclusion and exclusion criteria. However, the second review (Cole 2006) only included studies that had statistically significant results, thus eliminating many of applicable publications on the topic. Regardless, the review included ten school-based interventions involving 4300 subjects; five of these studies were also included in the first systematic review. Results from this second review were not used to formulate the body of evidence statement due to bias introduced by selecting only studies with significant results. Therefore, due to the mixed results reported in the first review, care should be taken when using this evidence statement to guide practice and school curriculum.

References

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Doak, C. M., Visscher, T. L., Renders, C. M., & Seidell, J. C. 2006, "The prevention of overweight and obesity in children and adolescents: a review of interventions and programmes", *Obesity Reviews*, vol. 7, no. 1, pp. 111-36.

Table 17.11 Studies used to make evidence statement for life course food consumption and school-based interventions

Reference [1]	**Doak 2006 (1834)**	**Cole 2006 (1684)**
Type of study [2]	Systematic review of 25 intervention studies	Systematic review of 10 interventions studies
Level of evidence [3]	I	I
Intervention/ comparator [4]	Success of childhood overweight prevention programs	Effect of school-based interventions using healthy lifestyle education, dietary habits, and physical activity interventions on BMI reduction in children
N [5]	53 118	4309
Population/study information [6]	Children aged 6-19yrs	Children aged 4-14yrs
Quality [7]	P	N
Results [8]	68% of interventions were effective (statistically significant difference in either BMI or skinfold thickness measures between intervention and control groups). Non-effective studies had a (nonsignificant) higher mean participation rate than effective studies. Effective studies had a larger mean sample size, lower number of participating schools, and shorter mean duration than non-effective studies (statistical significance not provided). All 3 interventions attempting to reduce TV watching were successful. 5 studies showed different results for each gender. Also a trend for ethnic differences.	Social learning is useful when designing interventions for preventing and treating childhood overweight. Results not meta-analysed but all tabulated studies reported effective intervention components with 3 effective in girls but not boys.
Effect on risk (Increase/None/Protect)	Protect	Protect
Clinical importance [9]	NA	3
Clinical relevance [10]	2	1
Generalisability	y	y
Applicability	n	y

17.12 LIFE COURSE FOOD CONSUMPTION and BEHAVIOURAL INTERVENTIONS

Do behavioural intervention programs lead to children adopting appropriate life course consumption and dietary patterns?		
Evidence statement		Behavioural interventions including diet and exercise reduce the risk of overweight or obesity in overweight children. These interventions are more effective when they are family-based.
Grade		A
Component	**Rating**	**Notes**
Evidence Base	Excellent	2 meta analyses (1 P, 1 0), one of 6 intervention studies and one of 16 intervention studies, and 2 systematic reviews (1 P, 1 N), one of 13 intervention studies and one of 16 studies.
Consistency	Excellent	All reviews were consistent.
Clinical impact	Excellent	Meta-analysis reported in Young 2007: mean effect size of family-based intervention of -0.62 (95% CI -0.80 to -0.44) for percent overweight.
Generalisability	Excellent	Western populations.
Applicability	Excellent	Directly applicable.

The two meta analyses (one of six intervention studies and one of 16 intervention studies) and two systematic reviews (one of 13 intervention studies and one of 16 intervention studies) were in agreement. Gilles (2008) included three studies examining behavioural interventions and three separate studies with parental involvement, but did not report the number of subjects. The other three reviews were all relatively small (total number of subjects ranging from 601 to 1025), but taken together the four reviews all indicate behavioural interventions are effective in improving weight outcomes in overweight children. Three of the reviews also examined the effect of family involvement, finding that involvement may improve effectiveness. Due to the strong evidence base and consistency, this recommendation should be used to guide practice.

References

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Gilles, A., Cassano, M., Shepherd, E. J., Higgins, D., Hecker, J. E. & Nangle, D. W. 2008, "Comparing active pediatric obesity treatments using meta-analysis", *Journal of Clinical Child & Adolescent Psychology*, vol. 37, no. 4, pp. 886-92.

Kelly, S. A. & Mazurek, B. M. 2008, “Systematic review of multicomponent interventions with overweight middle adolescents: implications for clinical practice and research”, *World Views on Evidence-Based Nursing*, vol. 5, no. 3, pp. 113-35.

Young, K. M., Northern, J. J., Lister, K. M., Drummond, J. A. & O'Brien, W. H. 2007, "A meta-analysis of family-behavioral weight-loss treatments for children", *Clinical Psychology Review*, vol. 27, no. 2, pp. 240-9.

Table 17.12 Studies used to make evidence statement for life course food consumption and behavioural interventions

Reference [1]	**Gilles 2008 (174)**	**Young 2007 (1374)**	**Berry 2004 (5211)**	**Kelly 2008 (5217)**
Type of study [2]	Meta analysis of 6 intervention studies.	Meta analysis of 16 intervention studies.	Systematic review of 13 intervention studies.	Systematic review of 16 intervention studies.
Level of evidence [3]	I	I	I	I
Intervention/ comparator [4]	Effectiveness of active treatments (behavioural, cognitive therapy, parental involvement, medication) on paediatric obesity.	Effect of family-behavioural treatments on BMI and % overweight.	Effect of nutrition education, exercise education, behavioural therapy, and problem solving on weight outcomes in children.	Effect of physical activity, nutrition and behaviour modification interventions in improving weight in overweight adolescents.
N [5]	11 studies total number of subjects not provided.	Family behavioural treatment – 522, other treatment – 57, control condition - 87.	601	1025
Population/study information [6]	Children younger than age 18 yrs. Countries not provided.	Children ages 5-12 yrs.	Children ages 5-17 yrs.	Adolescents ages 12-20 yrs.
Quality [7]	0	P	N	P
Results [8]	Behavioural interventions (d=0.21, P<0.001), parental involvement (d=1.75, P<0.01), and medication (sibutramine) (d=0.65, P<0.001) significantly improved obesity outcome, while cognitive therapy did	The results of this meta analysis indicate family-behavioral treatments produce large and reliable effects that appear to be maintained across follow-up intervals spanning several months. The other treatments and control conditions analysed	Behavioural modification (exercise, diet) targeted at children and parents together or separately report weight loss in both parents and children. Behavioural therapy targeting children and parents together or parents separately improve weight outcomes.	Structured programs addressing nutrition, physical activity and behavioural skills appear to reduce weight and CVD risk factors in overweight adolescents. Dose of

	not have a significant effect.	did not yield large and statistically reliable outcomes. Thus, family-behavioral treatments appear to be an effective strategy for weight-loss in children.	Problem solving interventions targeting parents of overweight children showed outcomes for the children but when parent and children were targeted together weight outcomes did not change.	intervention was associated with success.
Effect on risk (Increase/None/Protect)	Protect	Protect for family-behavioural interventions.	Protect	Protect
Clinical importance [9]	1	1	3	1
Clinical relevance [10]	2	2	5	2
Generalisability	y	y	y	y
Applicability	y	y	y	y

Life Course (S1.3)

Summary of studies not included in body of evidence statements

Factors during childhood associated with the development of overweight: self-reported dieting

Four cohort studies investigated the association between self-reported dieting and development of overweight or obesity. Three reported a positive association between dieting and increase in BMI z-score or development of overweight, and one reported an inverse association:

- The first study (n=14,972, positive quality) of children in US aged 9-14 yrs (Growing Up Today Study) reported that among the girls, frequent dieters and infrequent dieters gained more than non-dieters (0.058 and 0.042 BMI z-scores, respectively) after a 3 yr follow-up, but there was no difference between dieters and non-dieters in boys (Field 2003).
- The second study (n=4461, positive quality) of children in UK (1970 British Birth Cohort) reported that increase in BMI z-score between age 16 and 30 yrs was predicted by a history of dieting to lose weight B=0.09 (95% CI 0.01-0.18) (Viner 2006);
- The third study (n=825, positive quality) of females in sixth to ninth grades in the US reported that on average, girls who reported "never" dieting were most likely to have an increased BMI z-score after one year than those who reported at least "a little" dieting, and those who reported "always" dieting were more likely to have a decreased BMI z-score than those who reported "never", "a little", or "sometimes" dieting. The same pattern was true for the Dieting Behavior Scale (Senf 2006);
- The fourth study (n=1728, positive quality) of seventh-grade students in the US (Teens Eating for Energy and Nutrition at Schools) reported that in both girls and boys, trying to lose weight at baseline was associated with the student transitioning from a healthy weight status to overweight status (adj odds ratio 2.61, 95% CI 1.73-3.95) during the eighth grade (Klein 2008).

Type of Childhood Schooling

One cohort study (n= 1189, neutral quality) of males born in Mexico reported there was no association between low, intermediate, or high conscript schooling and increased BMI at age 17 yrs (Goldani 2007).

One cohort study (n= 5380, positive quality) of children in the USA followed from beginning of kindergarten to end of first grade (Early Childhood Longitudinal Study, Kindergarten Cohort) reported that the average BMI gain was twice as fast during summer vacation (0.076 kg/m^2, 95% CI 0.054-0.099 kg/m^2) compared to either during kindergarten (0.020 kg/m^2, 95% CI 0.012-0.028 kg/m^2) or first grade (0.033 kg/m^2, 95% CI 0.024-0.041 kg/m^2), P<0.01 (von Hippel 2007).

Fruit and Vegetable Intake

Three cohort studies examined the association between fruit and/or vegetable intake and change in BMI z-score, change in BMI percentile, or development of obesity, all reporting no association:

- The first study (n=14 918, positive quality) of children aged 9-14 yrs in the US (Growing Up Today Study) reported that among the girls, intake of fruits, fruit juice, or vegetable (alone or combined) is significantly and positively related to three year changes in BMI z-score after adjusting for caloric intake. There were no significant associations among the boys (Field 2003).
- The second study (n=790, positive quality) of 4th graders in Canada (Quebec Heart Health Demonstration Project) followed through 9th grade reported that neither obesity nor dietary restraint were associated with fruit and vegetable consumption (Bisset 2007).
- The third study (n=6430, negative quality) of kindergarten children in the US (Early Childhood Longitudinal Study – Kindergarten Cohort) reported that vegetable intake was not associated with change in BMI percentile from kindergarten to grade 5 (Baker 2009).

Consumption of Take Away Food and Low Quality Snacks

Four cohort studies examined the relationship between consumption of take away foods/low quality snacks and change in BMI, change in BMI z-score, or development of overweight or obesity. Two reported a positive association, while one reported an inverse association:

- The first study (n=14 355, positive quality) of children aged 9-14 years in the US (Growing Up Today Study) reported that children who increased their consumption of take away fried food from "never or once per week" to "4-7 per week" increased their BMI 0.21 kg/m^2 (95% CI 0.03-0.39) over 3 years. The association was stronger in girls aged 9-12 years compared to those older than 13 yrs at baseline, and was stronger in boys older than 13y compared to boys aged 9-12y at baseline (Taveras 2005);
- The second study (n=4461, positive quality) of children born in the UK (1970 British Birth Cohort) reported that an increase in BMI z-score (β=0.21, 95% CI 0.05-0.38) between age 16 and 30 years was predicted by eating takeaway meals twice or more per week (Viner 2006);
- The third study (n=790, positive quality) of students in Canada followed from 4th to 9th grade (Quebec Heart Health Demonstration Project) reported that continued, stable low quality snacking, a higher baseline take away food consumption, and a greater decline in take away food consumption over time were all associated with the development of obesity (Bisset 2007);
- The fourth study (n=7356, positive quality) of children born in Sweden reported that those who rarely consumed fried potatoes/French fries at age 2.5 yrs have a higher risk of being overweight/obese at age 5 yrs than those who consumed these foods 1–2 times/week. However, these results need to be interpreted with caution as it is unlikely that fried potatoes/French fries protect against overweight/obesity (Huus 2009).

Consumption of Breakfast

Three cohort studies examined the association between frequency of breakfast consumption and change in BMI, and reported conflicting results:

- The first study (n=14 586, positive quality) of children aged 9-14 yrs in the USA (Growing up Today Study) reported that overweight children who never ate breakfast lost BMI over the following year compared to overweight children who ate breakfast nearly every day (P=0.01 for both boys and girls). In contrast, normal weight children who never ate breakfast gained BMI relative to peers who ate breakfast nearly everyday (Berkey 2003);
- The second study (n=1896, positive quality) of girls aged 9-10 years in the USA (National Heart, Lung, and Blood Institute Growth and Health Study) reported that in girls of healthy weight at baseline, frequency of breakfast consumption had no effect on BMI at 10 yr follow-up. In girls who were overweight at baseline, frequent breakfast consumption was associated with a lower BMI-for-age at 10 yr follow-up (Albertson 2007);
- The third study (n=2216, positive quality) of middle and high school students in the US (Project EAT) reported that the frequency of eating breakfast was inversely associated with 5-year change in BMI (P<0.05). This remained significant after adjusting for confounding and dietary factors, but lost significance after adjusting for psychosocial variables (Timlin 2008).

Sleeping Patterns

Four cohort studies examined the association between infant and child sleep time and BMI or development of overweight or obesity, with all four studies reporting an inverse association:

- The first study (n=972, positive quality) of children born in New Zealand reported that shorter childhood sleep times (a mean of up to 11 hours in bed between ages 5 and 11 years) were significantly associated with higher adult BMI values at age 32 years -0.93 kg/m^2 (95% CI -1.54 to -0.31) P=0.003. Longer sleep time during childhood was associated with lower odds of obesity at age 32 years adjOR= 0.65 (95% CI 0.43-0.97) P=0.034) (Landhuis 2008);
- The second study (n=915, positive quality) of children born in the USA reported that infant sleep < 12 hrs/day was associated with a higher BMI z-score +0.16 (95% CI 0.02-0.29), higher skinfold thicknesses (+0.79 mm, 95% CI 0.18-1.40), and increased odds of overweight (adjOR2.04, 95% CI 1.07-3.91) at age 3 yrs. Mean weight-for-length z-score increased by 0.02 (adj), 95% CI 0.003-0.05, for each 1 hour/day decrease in sleep duration (Taveras 2008);
- The third study (n= 2001, neutral quality) of children born in Brisbane (Mater-University Study of Pregnancy and Its Outcomes) reported that children whose mothers reported the child often experienced irregular sleeping at ages 2-4 yrs have significantly higher BMI mean difference = 0.79 kg/m^2 (95% CI 0.08-1.50) and increased odds of being obese at age 21yrs adj odds ratio 1.67 (95% CI 1.07-2.63) compared to those who reported rarely/never experienced irregular sleeping (Al Mamun 2007);
- The fourth study (n= 5493, positive quality) of children born in the UK (Avon Longitudinal Study of Parents and Children) reported that shorter child sleep duration (<10.5 hrs versus >12 hrs) was associated with increased odds of obesity adjOR1.45 (95% CI 1.10-1.89) at age 21 years (Reilly 2005).

Child Smoking

Two cohort studies examined the association between childhood smoking and BMI or abdominal obesity, reporting conflicting results:

- The first study (n=2701, positive quality) of 7th grade students in South London reported that adjusting for baseline BMI and other potential confounders, students who smoked regularly in the 11th grade (>6 cigarettes/week) had significantly lower BMI (P=0.002) than all other groups (Fidler 2007);
- The second study (n=5771, positive quality) of children born in Finland reported that with univariate analysis, females who regularly smoked at age 14 yrs were less frequently abdominally obese at age 31 yrs (P=0.043) than females who did not smoke. Multivariate analysis was not reported, and it is assumed that the association became insignificant. No association was seen in males (Laitinen 2004).

Urban versus Rural Residence

Two cohort studies examined the association between urban versus rural residence and change in BMI over time, reporting conflicting results:

- Jokela (2009) examined adolescents aged 12-18 yrs in Finland (n=1300, positive quality, Cardiovascular Risk in Young Finns Study), and reported that living in a rural area predicted a greater increase of BMI from adolescence to adulthood (21 year follow-up) than living in an urban area (P=0.01). On average, BMI of participants in the most rural group was 0.9 kg/m^2 higher than BMI of those in the most urban group. However, the association between rural/urban residence and BMI increase in adulthood was not significant after adjusting for all relevant confounders (P=0.06);
- Hesketh (2009) studied children aged 5-10 years in Victoria (n=1373, positive quality, Health of Young Victorians Study) and reported that compared to urban residence, rural residence is significantly associated BMI z-score reduction -0.06 kg/m^2 adj, 95% CI -0.12 to -0.002) after an 8-13 yr follow-up (Hesketh 2009).

One cohort study (n=6677, positive quality) of youth (mean age 14.9y) in the US reported there was no association found between urban sprawl and change in BMI (Ewing 2006).

Food Insecurity

Three cohort studies examined the relationship between food insecurity and change in weight or development of overweight. Two studies reported a positive association, while one study reported no association:

- The first study (n=11 400, positive quality) of children in the US followed from kindergarten to the third grade (Early Child Longitudinal Study - Kindergarten Cohort) reported that food insecurity in kindergarten significantly effected change in BMI and change in weight from kindergarten to third grade in girls. Girls from persistently food insecure households had a

0.552 kg/m^2 greater gain (P=0.021) in BMI compared to girls from persistently food secure households. Becoming food insecure resulted in 0.430 kg/m^2 greater BMI gain (P=0.059) in boys compared to boys who did not become food insecure (Jyoti 2005);
- The second study (n=1514, positive quality) of children born in Canada (Longitudinal Study of Child Development in Quebec) reported that odds for both overweight (adj odds ratio (2.0, 95% CI 1.1–3.6) and obesity (adj odds ratio 3.4, 95% CI 1.5–7.6) increased in preschool children with food insufficiency during the preschool years (Dubois 2006);
- The third study (n= 7635, positive quality) of children followed from kindergarten to the fifth grade (Early Childhood Longitudinal Study-Kindergarten) reported that household food insecurity score was not a significant predictor of child BMI or BMI z-score (P<0.05) (Bhargava 2008).

Use of Food Stamps

One cohort study (n=7843, neutral quality) of children of mothers enrolled in the National Longitudinal Survey of Youth in the USA reported that compared with girls and boys whose families did not participate in the food stamp program during the previous five yrs, food stamp program participants during all five yrs was associated with a 42.8% increase for young girls and a 28.8% decrease for young boys in the predicted probability of overweight. Long-term food stamp program participation was not associated with overweight in older children. However, these models were not controlled for food insecurity or SES (Gibson 2004).

Food Prices

Two cohort studies using the same cohort of kindergarten children in the US (Early Childhood Longitudinal Study – Kindergarten Cohort) examined the association between food prices and weight change or development of overweight, and reported similar results:

- The first study (n=6918, positive quality) followed the children to third grade and reported that increasing fruit and vegetable prices by one standard deviation raised BMI by 0.054 kg/m^2 (SE 0.022, P=0.016) by first grade and 0.114 kg/m^2 (SE 0.033, P<0.001) by third grade (Sturm 2005);
- The second study (n=4557, positive quality) followed the children to fifth grade and reported that a one standard deviation increase in price of fruits and vegetables was associated with an increase in BMI of 0.094 kg/m^2 (SE 0.031, P=0.002) by third grade and 0.20 kg/m^2 (SE 0.045, P<0.001) by fifth grade (Sturm 2008).

Small for Gestational Age

One cohort study (n=5771, positive quality) of children born in Finland reported that smallness for gestational age tended to increase the risk of abdominal obesity at age 31 yrs, but only among men who had had normal body weight at age 14 yrs. There was no association among women (Laitinen 2004).

Size during Adolescence

One cohort study (n=5771, positive quality) of children born in Finland reported that males who were overweight at age 14 yrs had greater odds of being abdominally obese at age 31 yrs adjOR 3.89 (95% CI 2.84-5.29) not controlling for BMI at age 31 yrs adjOR1.79 (95% CI 1.07-2.99) controlling for BMI at age 31 yrs). The same trend occurred in women (adjOR 3.34 (95% CI 2.48-4.51) not controlling for BMI at age 31 yrs), but the association was no longer significant after controlling for BMI at age 31 yrs (Laitinen 2004).

Parental Skills Training

One RCT (n=91, positive quality) of overweight children in Adelaide reported that after 1 yr follow-up, there were no differences in BMI z-score between children of parents who received standardized parenting skills training plus additional intensive lifestyle education sessions, children of parents who received standardized parenting skills training only, and children of parents who received no training. Waist circumference z-score was significantly reduced in the intervention groups but not the control group (P=0.03) (Golley 2007).

Cognitive Ability

One cohort study (n=17,414, positive quality) of children born in the UK (National Child Development 1958 Study) reported that after adjusting for confounding factors, there was no association between childhood IQ score and development of obesity by age 42 yrs (Chandola 2006).

Low Self Esteem/Depression

Three cohort studies examined the association between low self esteem or depression and weight change or development of overweight, all reporting positive association in at least a portion of the cohort:

- The first study (n=9374, neutral quality) of school children in grades 7-12 in the USA (National Longitudinal Study of Adolescent Health) reported that depressed mood at baseline was associated with development of obesity after 1 year in those not obese at baseline adjOR 2.05 (95% CI 1.04-4.06) and worsened obesity in those obese at baseline (Goodman 2002);
- The second study (n=1157, positive quality) of elementary school children in Victoria (Health of Young Victorians Study) reported that of non-overweight children only, children with low baseline self esteem scores were more likely to develop overweight/obesity by three year follow-up than children with higher baseline self-esteem scores adjOR 2.1 (95% CI 1.2-3.6). Baseline self-esteem score did not predict which overweight/obese children would move into the non-overweight category during the study (Hesketh 2004).

- The third study (n=1728, positive quality) of seventh grade students in the USA (Teens Eating for Energy and Nutrition at Schools) reported that in boys, symptoms of depression were associated with transitioning from healthy weight status to overweight status adjOR 1.04 (95% CI 1.02-1.07). No association was found in girls (Klein 2008).

Locus of Control

Two cohort studies investigated the association between childhood locus of control and change in BMI z-score or development of obesity, both reporting an inverse association:

- The first study (n=7551, positive quality) of children born in the UK reported a 1 standard deviation increase in locus of control score at age 10 years was associated with a reduced risk of obesity adj odds ratio 0.86 (95% CI 0.78-0.95) and overweight adj odds ratio 0.87 (95% CI 0.82-0.93) at age 30 yrs. Locus of control was also significantly correlated with BMI as a continuous variable: r=-0.06, P<0.001 (Gale 2008);
- The second cohort study (n= 917, positive quality) of children aged 3-12 yrs in the US (Early Child Care and Youth Development study) reported that children who were low in self-regulation had the most rapid gains in BMI z score from age 3 to 12 years (P< 0.05) (Francis 2009).

Stressful Family Life

Two cohort studies examined the influence of a stressful family life on development of obesity, both reporting a positive association:

- The first study (n= 9377, positive quality) of children born in the UK (Perinatal Mortality Study) reported that stressful emotional experiences in childhood are associated with an increased risk of obesity as an adult (45 yr follow-up). Retrospectively, adjusting for all childhood and adult confounders, BMI was associated with verbal 0.47 kg/m^2 (95% CI 0.10-0.86) and physical 0.64 kg/m^2 magazine (95% CI 0.22-1.10) abuse, mother depression -0.31 kg/m^2 (95% CI -0.53 to -0.07), strict upbringing 0.26 kg/m^2 (95% CI 0.04-0.5), and central obesity was associated with physical abuse adjOR1.33 (95% CI 1.11-1.60), physical neglect adjOR 1.32 (95% CI 1.01-1.73), strict upbringing adjOR 1.13 (95% CI 1.02-1.25), physical punishment adjOR 1.24 (95% CI 1.05-1.47), and witnessed abuse adjOR 1.23 (95% CI 1.02-1.48) (Thomas 2007);
- The second study (n= 7443, positive quality) of children born in Sweden reported that children from families that reported stress in at least two of the four psychological domains assessed had significantly higher odds for obesity (at age 2yr: adjOR 2.6 (95% CI 1.3-5.4) P<.01; at age 5y: adjOR 2.1 (95% CI 1.3-3.5 P<.01) (Koch 2008).

Migration Status

One cohort study (n=74 541, positive quality) of kindergarten children in the USA born of natives, the 1.0 generation, or the 1.5 generation (Early Longitudinal Survey - Kindergarten Cohort) reported that among children of the 1.0 generation, children of immigrants from higher-income countries have greater BMI increases than children from lower-income countries with five year follow-up. Also

among children of 1.0 generation, the relationship between family SES and BMI increase is significantly more positive among children of immigrants from lower-income countries than those from higher-income countries. BMI increase is positively associated with generation in lower SES children from low-income countries, while BMI increase is negatively associated with generation for higher SES children from low-income countries (Van Hook 2007).

One cohort study (n=1786, positive quality) of children born in Vienna reported being an immigrant did not significantly increase the odds of being overweight or obese at 15 yrs of age when compared with local Austrian children and adolescents. Nevertheless, Yugoslavian girls have increased odds of being overweight or obese at age 6 yrs when compared with their Austrian counterparts (unadj OR 1.556, 95% CI 1.040-2.38) while Yugoslavian boys have increased odds of being overweight or obese at age 10 when compared with their Austrian counterparts unadjOR1.551 (95% CI 1.066-2.257) (Kirchengast 2006).

Household Instability

One cohort study (n=1449, neutral quality) of children born in the USA reported that the level of household instability was not associated with an increase in child BMI percentile or development of overweight at age three years in either low or high poverty areas (Chambers 2009).

Centre-Based Child Care Attendance

Two cohort studies examined the association between child care and BMI percentile or development of overweight:

- One cohort study (positive quality) of 1224 children followed for 3-7 yrs in the USA reported that compared to no child care attendance, limited child care attendance of 0-15 hrs per week in children aged 3-5 yrs was associated with a decreased risk of the child being overweight at age 6-12 yrs adjOR 0.56 (95% CI 0.34-0.93). There was no significant association between extensive child care attendance of >15 hrs per wk and risk of overweight (Lumeng 2005);
- One cohort study (n= 6430, negative quality) of children in the USA followed from kindergarten to grade 5 (Early Childhood Longitudinal Study, Kindergarten Cohort) reported that there was no association between child care arrangements and BMI percentile (Baker 2009).

Dietary Pattern

Two cohort studies examined the association between dietary pattern as a child and BMI:

- One cohort study (n=1037, positive quality) of children and adolescents in Finland (Cardiovascular Risk in Young Finns Study) reported that neither dietary pattern was associated with adult BMI (21 yr follow-up) (Mikkila 2007);
- One cohort study (n=1430, positive quality) of children in Australia (Western Australia Pregnancy Cohort Study) reported that BMI at age eight years was negatively associated with the "cereals" dietary pattern (bread, cereals, and spreads such as jam), but no association with the "takeaways" (takeaway foods, processed meats, and desserts), "fruitveg" (fruit, vegetables, and dairy foods), "meats" (chicken, meat dishes, eggs, and fish), or "sweets" (snacks, confectionary, cakes and sweet beverages) dietary patterns (Burke 2005).

Factors during Childhood Associated with Use of Alcohol as an Adult:

Four cohort studies examined the association between alcohol use as an adult and potential contributing factors during childhood:

- One cohort study (positive quality) following 6292 males in Denmark for 36 yrs reported males with fathers from the higher social classes more often became wine drinkers adjOR = 0.80 (95% CI 0.70-0.90) than men with working class fathers. However, father's social class was not associated with abstention, heavy alcohol consumption, or daily fruit and vegetable intake (Osler 2008);
- One small cohort study (n=972, positive quality) followed children in New Zealand from birth to age 32 yrs. Childhood socioeconomic status was not significantly associated with risk of alcohol/drug dependence: with intermediate socioeconomic status, adj relative risk of alcohol/drug dependence = 1.42 (95% CI 0.80-2.50); with low socioeconomic status, adj relative risk of alcohol/drug dependence = 1.47 (95% CI 0.78-2.78) (Melchior 2007);
- One small cohort study (n=1303, positive quality) followed children born in Brisbane from birth to age 21 yrs. No association was found between either birth factors (birth weight, gestation, intensive care, Apgar score at 1 minute and 5 minutes, early behaviour) or childhood factors (parenting style, physical punishment, internalising behaviour, maternal anxiety) and the development of alcohol-related disorders by age 21 in either males or females. Externalising symptoms (males: adjOR 2.12 (95% CI 1.37-3.30); females: adjOR 2.04 (95% CI 1.13-3.68) at age 14 yrs were significantly associated with alcohol problems. For youth aged 14 yrs, maternal alcohol consumption of ≥ 1 drink/day greatly increased risk of developing an alcohol-related disorder (males: adjOR 1.93 (95% CI 1.10-3.37) P=0.046; females: adjOR 1.79 (95% CI 0.92-3.46) P=0.014) (Alati 2005);
- One cohort study (n= 11,419, positive quality) of men and women in the UK followed from birth to age 42 yrs reported poorer cognition in early childhood was associated with non-drinking over two decades in early adulthood in both men and women. Decreasing ability rank across childhood was associated with raised odds of binge drinking at 23 and 33 years in men and 42 years in women. Women with lower ability had decreased odds of binge drinking in their 20s, but increased odds in their 40s (Jefferis 2008).

Factors during Childhood Associated with Development of Unhealthy Weight Control Behaviours:

Body Dissatisfaction

One systematic review and two cohort studies examined the association between body dissatisfaction and the development of unhealthy weight control behaviours, each reporting a positive association:

- One poor quality (unusable) systematic review examined the association between body dissatisfaction and the development of eating disorders. The authors concluded that sociocultural processes foster body dissatisfaction, which increases the risk for bulimic pathology, suggesting that prevention and treatment interventions might be enhanced by focusing greater attention on body image disturbances (Stice 2002);
- One small cohort (positive quality) of 2516 junior and senior high school students in the USA reported that lower levels of body satisfaction are associated with unhealthy weight control behaviours and binge eating after five years (relative risks not reported) (Neumark-Sztainer 2006);
- One cohort (n= 1103, positive quality) of female students in the USA followed for four years reported that thin body preoccupation and social pressure ($P<0.0001$) was identified as a risk factor for development of an eating disorder (McKnight 2003).

Media Influence

Two cohort studies examined the association between media influence and the development of unhealthy weight control behaviours, reporting similar results:

- One cohort study (1130 males, 1386 females, positive quality) of school children (mean age 12.8 yrs in younger cohort and mean age 15.8 yrs in older cohort) in the USA reported that the frequency of magazine reading was positively associated with healthy (adjOR ranges from 1.63-2.39 for “hardly ever” and “sometimes” reading magazines, not associated with "often"), unhealthy (adjOR ranges from 1.61-2.04 for “hardly ever”, “sometimes”, and “often” reading magazines), and extreme (adjOR ranges from 2.26-3.16 for “hardly ever”, “sometimes”, and “often” reading magazines) weight-control behaviours in females, but not males, after five years (van den Berg 2007);
- One cohort study (n= 11,087, positive quality) in children aged 9-15 yrs in the USA reported that with a seven year follow up, trying to look like females in the media was associated with an increased risk of binge eating (adjOR 2.2, 95% CI 1.4-3.4) and an increased risk of purging (adjOR 1.5, 95% CI 1.1-2.2) in females, but there was no association in males (Field 2008).

Dieting or Frequent Self-Weighing

Two cohort studies examined the association between frequent self-weight or dieting and the development of unhealthy weight control behaviours, reporting similar results:

- One cohort study (n=2516, positive quality) of students in US middle and high schools followed for five years reported that frequent self weighing was associated with an increase in unhealthy weight control behaviours and binge eating in middle and high school girls, and unhealthy weight control behaviours in middle school boys (Neumark-Sztainer 2006);

- One cohort study (n= 11 087, positive quality) of children aged 9-15 yrs in the USA followed for seven years reported that frequent dieting was associated with an increased risk of binge eating (adjOR 2.2 (95% CI 1.4-3.7)), an increased risk of purging (adjOR 3.1 (95% CI 1.9-5.2)), and an increased risk of both binge eating and purging (adjOR 7.4 (95% CI 2.2-25.0)) in females (Field 2008).

Maternal Smoking during Pregnancy

One cohort study (n=4046, positive quality) of girls born in the UK and followed for 30 years reported women whose mothers smoked during pregnancy were significantly more likely to have bulimia at age 30 years (adjOR 2.64 (95% CI 1.47-4.74)) than women whose mothers did not smoke during pregnancy. Women whose mothers gave up smoking prior to pregnancy were not at increased risk (Montgomery 2005).

Factors During Childhood Associated with Adult Dietary Pattern

One cohort study (n=3187, positive quality) of children born in the UK (1946 British Birth Cohort) reported that people who remained in the non-manual social class consumed significantly higher amounts of food items correlated with the "health aware" dietary pattern (including high-fibre breakfast cereals, wholemeal breads, apples and bananas) than those who remained in the manual social class. Those who made the transition from manual social class in childhood to non-manual social class by age 43 years partly adopted the distinctive dietary patterns of the non-manual social classes. Consumption of items in the “refined” dietary patterns (including whole-fat milk, white bread, sugar and butter) and “sandwich” (including tomatoes, lettuce, onions, bacon and ham) did not differ by social class or regional mobility (Mishra 2004).

One cohort study (n=8282, positive quality) of children born in the UK (1970 British Cohort Study) reported that after adjusting for confounding factors, children with higher verbal mental ability were significantly more likely to have a frequent consumption of fresh fruit, vegetables, fish, and foods fried in vegetable oil in adulthood, and more unlikely to frequently consume chips (Batty 2007).

One cohort study (n=790, positive quality) of students in Canada followed from 4th grade to 9th grade (Quebec Heart Health Demonstration Project) reported that low dietary restraint was associated with a greater frequency of both take away food consumption and low quality snacking over time. Subjects with low dietary restraint maintained a stable consumption of take away food over time whereas the rest of the sample decreased consumption of take away food (Bisset 2007).

Influence of Child Dietary Pattern on Diet Quality:

Four cohort studies examined the association between dietary pattern as a child and diet quality over time:

- Two cohort studies (n=2379, both positive quality) involved girls aged 9-10 years in the US (National Heart, Lung, and Blood Institute Growth and Health Study, 10 year follow-up). The first reported that frequency of take away food consumption increases with age, and is associated with higher levels of energy, total fat, saturated fat, and sodium intakes ($P<0.001$) (Schmidt 2005). The second reported that frequency of breakfast consumption decreases with increasing age, frequency of breakfast consumption is lower in African-American girls than white girls, and high frequency of breakfast consumption is associated with higher calcium and fibre intake (Affenito 2005);
- One cohort study (n=1037, positive quality) of children and adolescents in Finland (Cardiovascular Risk in Young Finns Study) reported that there were two distinct dietary patterns: "traditional" (rye, milk, coffee, potatoes, sausages, and butter) and "health-conscious" (tea, vegetables, fish, cheese, and other dairy products). Subjects with "health-conscious" pattern had higher intakes of vitamin C and fibre and lower intake of sucrose at age 21 years. Differences in fat (total and specific) intakes between the two patterns at 21 years were less pronounced. Correlation between dietary pattern at baseline and at 21 years was 0.32 for "traditional" and 0.38 for "health-conscious." The correlation was stronger among subjects aged 15-18 yrs at baseline and among subjects in the upper quintile of the dietary pattern (Mikkila 2005);
- One cohort study (n=1710) of adolescents in the USA (Project EAT) reported that family meal patterns during adolescence predicted diet quality and meal patterns during early young adulthood (5 yr follow-up). Among females, intakes of vegetables, magnesium, potassium, and fibre were still directly associated and soft drinks inversely associated with Time 1 family meals. Among males, intakes of fruit, vegetables, dark-green and orange vegetables, and potassium were still directly associated with Time 1 family meals (Larson 2007).

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18. BARRIERS (S1.4)

Evidence Statements

18. BARRIERS (S1.4)

Search results

The initial search of the data bases included 623 references relating to economic, physical and psycho-social barriers and the enablers to adults achieving diets consistent with dietary guidelines. The detailed search is included in a separate document on searches. In all, 39 articles were retrieved that had information pertaining to the relevant outcomes, and 20 references concerning barriers had data extracted and 20 papers were used to form the body of evidence statements for barriers. Due to the nature of the research question and search terms, only cross sectional studies were identified.

18.1 ECONOMIC, PHYSICAL AND SOCIAL BARRIERS TO DIETS CONSISTENT WITH DIETARY GUIDELINES

What are the economic, physical and psycho-social barriers and the enablers to adults achieving diets consistent with dietary guidelines?		
Evidence statement		Barriers associated with achieving diets consistent with dietary guidelines include lower socioeconomic status and lower educational attainment. Lower socioeconomic groups perceive cost as a barrier to healthy food purchase.
Grade		D
Evidence statement		Enablers associated with achieving dietary guidelines include being female, older age, higher socioeconomic status, higher education and nutrition knowledge.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Poor	Level IV evidence from cross-sectional studies (n=20 studies).
Consistency	Good	Fairly consistent evidence that compliance with dietary recommendations is better among women, better educated adults and those with higher socioeconomic position.
Clinical impact	Satisfactory	Some show statistically significant results but factors and statistical assessment have too much variation to summarise point estimates of impact.
Generalisability	Good	Populations in body of evidence relevant to all adult age groups, older adults and women, and pregnant/postpartum women. Results from Australian studies are consistent with overseas studies.
Applicability	Good	Applicability to the populations above.

The studies used to make the body of evidence statements are shown in Table 18.1. This particular research question can currently only be addressed by examining cross sectional analyses of the various factors that influence compliance with dietary guideline recommendations. There were no

RCTs, cohort or case control studies identified in the literature review. The consistency of the study results means that the evidence base can be trusted to guide the evidence statement with some caveats.

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Table 18.1 Studies used to make evidence statement for barriers and enablers to achieving diets consistent with dietary guidelines

Reference [1]	**Atlantis et al. 2008 [78]**	**Baker et al. 2006 [170]**	**Ball et al. 2004 [288]**	**Bodnar et al. 2002 [344]**	**Cassady et al. 2007 [96]**
Type of study [2]	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cross sectional
Level of evidence [3]	IV	IV	IV	IV	IV
Intervention/ comparator [4]	NA	NA	NA	NA	NA
N [5]	16 314 adults	81 supermarkets	10 561 women	2063 pregnant women	25 supermarkets
Population/study information [6]	Adult participants of Aust National Health Survey	Missouri, USA Audit of supermarkets	Women aged 50-55 yrs in Australian Longitudinal Study on Women's Health	Pregnant women who attended public prenatal clinics in USA	California supermarkets
Quality [7]	Neutral	Neutral	Neutral	Neutral	Neutral
Results [8]	Poor compliance in meeting dietary guidelines. Less than 5% of adults met guidelines for physical activity and diet guidelines. Overweight was associated with increased odds (11%) OR 1.11 (95% CI 1.0- 1.24) p=0047 of consuming ≥2 serves of fruit/day for women but not for men. NS for vegetables for men	Some communities have less access to fruit and veg, which can affect them being able to meet the Dietary Guidelines. Mixed race or white high-poverty areas were less likely than predominately white higher income communities to have access to foods that enable individuals to make healthy choices.	Only about one-third of women complied with >50% of the dietary recommendations. Women working in lower SES occupations OR=0.5 (95% CI 0.4-0.6), women living alone OR= 0.9 (95% CI 0.8-1.2) or living with other than a partner or children OR=0.7 (95% CI: 0.5-1.0) were at significantly increased risk of not meeting the guidelines. No difference in dietary compliance between	Pregnant women who were> 30 years old (58.3% p<0.05), from higher income groups (59.8% p<0.05), high school graduates (58.5% p<0.05) had significantly higher diet quality index scores.	Cost of fruit and veg can be a barrier for low income groups. To comply with 2005 US Dietary Guidelines, a low income family would need to devote 43% to 70% of their food budget to fruit and veg.

	and women.		women living in urban, regional OR=1.0 (95% CI: 0.9-1.1) or rural areas OR=0.9 (95% CI:0.8-1.2).		
Effect on risk Increase/None/Protect	None for weight status and vegetable intake, protect for fruit intake in overweight in females only.	Increase	Increase for lower socioeconomic occupations, living with others (not partner, children). None for area of residence.	Protect for older pregnant women , higher socioeconomic groups, high school graduate.	Increase for low income.
Clinical importance[9]	2	NA	2	1	NA
Clinical relevance [10]	5	5	5	5	5
Generalisability	y	y	y	y	n
Applicability	y	y	y	y	n

Table 18.1 Studies used to make evidence statement for barriers and enablers to achieving diets consistent with dietary guidelines (cont.)

Reference [1]	**Giskes et al. 2007 [411]**	**Giskes et al. 2006 [190]**	**Kolodinsky et al. 2007 [120]**	**Inglis et al. 2005 [199]**	**McNaughton et al. 2008 [83]**
Type of study [2]	Cross sectional	Cross sectional	Cross sectional	Qualitative study	Cross sectional
Level of evidence [3]	IV	IV	IV	IV	IV
Intervention/ comparator [4]	NA	NA	NA	NA	NA
N [5]	812 Brisbane residents	1339	200 college students	56	8220 adults
Population/study information [6]	Adult participants of Brisbane Food Study	Dutch adults aged 25-79 yrs	University of Vermont	Female focus group members held in Melbourne	Adult participants of the Australian National Nutrition Survey
Quality [7]	Neutral	Neutral	Neutral	Neutral	Neutral
Results [8]	Lower SES groups less likely to make food purchasing choices consistent with dietary guidelines, despite there being consistent availability of recommended foods in the supermarkets (e.g. OR of purchasing wholemeal bread for lowest income group compared with highest income group was 0.46 (CI:0.27-	Adults from disadvantaged backgrounds less likely to comply with dietary recommendation. For lowest vs highest quartile of household income: Unhealthy grocery choice OR=1.54 (1.02-2.32), low fruit intake OR=1.99 (1.3-3.07). For area most deprived OR for skipping breakfast =1.6(1.0- 2.56); fat	Increase dietary knowledge associated with increased likelihood of meeting dietary guidelines. Significant difference between knowledge scores of those who always made the healthful choice compared with those who rarely made the healthful choice $p<0.05$.	Women in low socioeconomic groups perceive the cost of healthy eating to be higher and cite lack of time as a barrier to healthy eating.	Compliance with Dietary Guidelines is generally poor in Australian adults. Women have more favourable diets than men (Dietary Guidelines Index 99.6 vs 91 $p<0.05$). Older adults (regression coefficient -3.14 (95% CI -5.07- -1.20) $p<0.0001$ for the youngest age group compared oldest group), adults with higher income (regression coefficient -4.00 (95% CI -5.87- -2.13) $p<0.0001$ for the lowest income group), living in the least socio-economically disadvantaged areas (regression coefficient -2.69 (95% CI -

	0.78); low fat dairy milk OR=0.32 (CI:0.20-0.51).	and saturated fat intake NS by household income or area most deprived.			4.55- -0.82) p<0.04 for the lowest SEIFA score), non-smokers (regression coefficient -8.76 (95% CI -10.30- -7.22) p<0.0001), and those with moderate.vigorous physical activity levels (regression coefficient 7.20 (95% CI 5.70-8.70) p<0.0001) were more compliant with Dietary Guidelines.
Effect on risk Increase/None/Protect	Increase for low income.	Increase for disadvantaged background and household income.	Protect for dietary knowledge.	Increase for low socio economic status.	Protect for females, older adults, living in least socioeconomic disadvantaged area, non smokers and moderate exercise levels.
Clinical importance[9]	1	1	1	NA	1
Clinical relevance [10]	5	5	5	5	5
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

Table 18.1 Studies used to make evidence statement for barriers and enablers to achieving diets consistent with dietary guidelines (cont.)

Reference [1]	**Nelson et al. 2002 [342]**	**Sanchez et al. 2007 [413]**	**Story et al. 2002 [373]**	**Turrell et al. 2003 [335]**	**Turrell et al. 2004 [298]**
Type of study [2]	Cross sectional	Cross sectional	Conceptual framework	Cross sectional	Cross sectional
Level of evidence [3]	IV	IV	IV	IV	IV
Intervention/ comparator [4]	NA	NA	NA	NA	NA
N [5]	349 adults in low income households in London	878 adolescents aged 11-15 yrs	NA	1003 Brisbane residents	1003 Brisbane residents
Population/study information [6]	Low Income Diet Methods Study commissioned by Food Standards Agency	Adolescents in California were recruited through primary care clinics	US paper	Brisbane Food Study	Brisbane Food Study
Quality [7]	Neutral	Neutral	Neutral	Neutral	Neutral
Results [8]	Income is an important predictor of dietary adequacy, with lower income groups having poorer diets.	Majority of adolescents did not meet dietary guidelines. Being older ($p = 0.01$ for boys and $p =<0.001$ for girls) and being overweight ($p = 0.04$ for boys and $p= 0.007$ for girls) were associated with poor dietary compliance in boys and girls. In girls, having a parent who	Four levels of influences operate on adolescent eating behaviours - individual or intrapersonal influences (eg psychosocial, biological); social environmental or interpersonal (eg family or peers); physical environmental or community settings (eg	Food purchasing behaviours of socioeconomically disadvantaged groups were least in accord with dietary guidelines recommendations.	Living in a socio-economically advantaged area was associated with a slight tendency to purchase healthier food (based on the Dietary Guidelines). Increasing the area SES measure was associated with a 2.01 unit increase on fruit

		smoked (p<0.01) and having a parents who did not meet fruit and vegetables recommendations (p= 0.007), was associated with poorer dietary compliance.	school, fast food outlets, convenience stores); and macrosystem or societal (eg mass media, marketing and advertising, social and cultural norms).		purchasing index (95% CI -0.49 to 4.50); a 0.60 increase on vegetable purchasing index (95% CI-1.36 2.56); and 0.94 increase on the grocery food index (95% CI -1.35 to 3.23).
Effect on risk Increase/None/Protect	Increase for lower income	Increase for overweight and younger adolescents. Increase for girls with parent who smoked and who did not meet recommended vegetable intakes.	NA	Increase for socioeconomically disadvantaged.	Protect for socio economically advantaged and vegetable purchasing.
Clinical importance[9]	NA	1	NA	NA	2
Clinical relevance [10]	5	5	NA	5	5
Generalisability	n	y	na	n	y
Applicability	y	y	na	y	y

Table 18.1 Studies used to make evidence statement for barriers and enablers to achieving diets consistent with dietary guidelines (cont.)

Reference [1]	**Turrell et al. 2006 [[173]**	**Collins et al. 2008 [53]**	**Dynesen et al. 2003 [316]**	**Hearty et al. 2007 [414]**	**Kettings et al. 2009**
Type of study [2]	Cross sectional	Cross sectional	Cross sectional	Cross sectional	Economic modeling and quantitative analysis
Level of evidence [3]	IV	IV	IV	IV	IV
Intervention/ comparator [4]	NA	NA	NA	NA	NA
N [5]	1003 Brisbane residents	9895 women	995 adults	1256 adults	Seven day meal plan developed (based on Australian Dietary Guidelines) for two typical welfare dependant families, and costed on Australian food prices (online supermarket and a metropolitan retail outlet in Melbourne).
Population/study information [6]	Brisbane Food Study	Women aged 50-55 in Australian Longitudinal Study on Women's Health	Danish population survey	Irish cross sectional survey	Australian food prices
Quality [7]	Neutral	Neutral	Neutral	Neutral	Neutral
Results [8]	Food shoppers with low levels of education ß coefficient = -1.75 (95% CI -2.24 -1.27) for no post school	Women from higher socioeconomic areas had better compliance with dietary recommendations. 46%	Compliance with dietary recommendations was more common in women OR=6.07 (95% CI 3.91-9.43), older	Females OR=0.46 (95% CI 0.35-0.62), increasing age OR=0.95 (95% CI 0.94-0.97), higher	In Australia, the cost of a modeled meal plan based on the Australian Dietary Guidelines uses 44% of the disposable

	education compared with bachelors degree), and those residing in low income households ß coefficient = -11.05 (95% CI -12.48 -5.90) for lowest income quartile compared with highest income quartile), were least likely to purchase foods that supported the Dietary Guidelines. Socio-economic differences in dietary knowledge impacts on compliance with dietary recommendations. Low levels of education and those residing in low income households, were least likely to purchase foods that supported the Dietary Guidelines.	of those in the most well educated quintile vs 29% in the lowest educated quintile (p <0.0001) had an Australian Recommended Food Score.	adults OR= 9.72 (95% CI 3.02-31.31), those from higher SES areas, those with higher education levels OR= 3.69 (95% CI 1.53-8.92)and multi person households OR= 4.6 (95% CI 2.47-8.80).	social class (p=0.001), tertiary education OR=0.57 (95% CI 0.37-0.87), and increased recreational activity OR=0.97 (95% CI 0.94-0.99) are associated with a lower odds ratio for having a negative attitude towards healthy eating behaviour.	income of welfare dependant families, and 18% of the disposable income for families on an average income. Substituting generic brands for market brands reduced weekly food costs by 13%. In a modeled diet based on the Australian Dietary Guidelines, Australian Guide to Healthy Eating, and Nutrient Reference Values, vegetables cost the most of all food groups. The cost of fruit and vegetables was 44% of the total cost of food, reflecting the public health recommendation of "eat most" fruit and vegetables.
Effect on risk Increase/None/Protect	Increase for lower education and low income household.	Protect for higher education.	Protect in females, older adults, higher education levels, multi person households.	Protect for females, older age, higher social class, tertiary education and high recreational activity levels.	None.
Clinical	1	1	1	1	1

importance[9]					
Clinical relevance [10]	5	5	5	5	5
Generalisability	y	y	y	y	y
Applicability	y	y	y	y	y

19. AGE OF INTRODUCTION OF SOLID FOODS (S1.5)

Evidence Statements

19. AGE OF INTRODUCTION OF SOLID FOODS (S1.5)

S1.5 SOLID FOODS

Search results

The initial search of the databases included 862 references on the age of introduction of solid foods. The detailed search is included in a separate document on searches. Data was extracted from 11 references, and 10 publications were used to form the final body of evidence statements. Sufficient evidence was found to make statements on the relationships between age of introduction of solid foods and development of overweight and development of allergic symptoms. Additional evidence was found on the relationship between introduction of solid foods and diarrheal disease (one cohort study), but the evidence was not strong enough to develop a body of evidence statement.

19.1 AGE OF INTRODUCTION OF SOLID FOODS and OVERWEIGHT

Is the age of solid food introduction in children associated with the development of overweight later in life?		
Evidence statement		Age of introduction of solid foods is associated with risk of overweight in children younger than the age of 7 years.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Good	1 systematic review (of 1 systematic review and 3 cohort studies - 1N), 2 cohort studies (2P).
Consistency	Poor	The systematic review was of poor quality; one cohort study found no effect, the larger cohort study found a positive effect.
Clinical impact	Poor	There was unclear association
Generalisability	Excellent	USA and UK populations.
Applicability	Excellent	Directly applicable.

The systematic review included one systematic review and three cohort studies in its analysis, all finding no relationship between the age of weaning and development of infant or child overweight. However, the review was of poor quality and did not critically analyse the included studies. Weaning was defined as the introduction of solid foods in this publication, but in the individual studies this may have been slightly different than our objective to examine the introduction of solid foods. The two cohort studies contributing to the body of evidence statement were both of high quality and were both conducted in the UK. One reported that age of introduction of complementary feeding was not associated with obesity at seven years, while the other reported that introduction of

solid foods before age four months was associated with increased risk of overweight at three years. Complementary feeding was not defined in the publication, but it is commonly known as the transition from infant formula or breast milk to solid foods. Overall, it appears that age of introduction of solid foods has no effect on the risk of overweight in children, but due to the inconsistencies care must be taken when using this statement to guide practice.

References

Hawkins, S. S., Cole, T. J., Law, C. & Millennium Cohort Study Child Health, G. 2009, "An ecological systems approach to examining risk factors for early childhood overweight: findings from the UK Millennium Cohort Study", *Journal of Epidemiology & Community Health*, vol. 63, no. 2, pp. 147-55.

Hawkins, S. S. & Law, C. 2006, "A review of risk factors for overweight in preschool children: a policy perspective", *International Journal of Pediatric Obesity*, vol. 1, no. 4, pp. 195-209.

Reilly, J. J., Armstrong, J., Dorosty, A. R., Emmett, P. M., Steer, C., Sherriff, A. & Avon Longitudinal Study of Parents and Children Study Team. 2005, "Early life risk factors for obesity in childhood: cohort study", *BMJ*, vol. 330, no. 7504, pp. 1357.

Table 19.1 Studies used to make evidence statement for age of introduction of solid foods and overweight.

Reference [1]	**Reilly 2005 [395]**	**Hawkins 2009 [685]**	**Hawkins 2006 [249]**
Type of study [2]	Cohort	Cohort	Systematic review of 4 studies (1 systematic review, 3 cohort studies)
Level of evidence [3]	II	II	I
Intervention/ comparator [4]	Early life risk factors for development childhood obesity at age 7 yrs, including age at which complementary feeding is begun (<1, 1-2, 2-3, 3-4, or 4-6 mo). Complementary feeding was not defined in the publication.	Risk factors at various levels (individual, family, community and area) for development of childhood overweight. Included introduction of solid foods at < 4 mo compared to ≥ 4 mo.	Relationship between breastfeeding and weaning on development of overweight in preschool children. Weaning is defined as the introduction of solid foods in this publication.
N [5]	13 971 at baseline, 8234 at follow-up, 5493 for analysis.	18 296 at baseline, 14 630 at follow-up, 13 188 for analysis.	Number of subjects not provided. Breastfeeding: 15 studies; Weaning: 4 studies.
Population/study information [6]	Children born in 1991-92, from the Avon longitudinal study of parents and children (ALSPAC), followed from birth till age 7 yrs. Mothers lived in 3 health districts centred in Bristol, UK. Mainly white and singleton.	Children born 2000-02, from the Millennium Cohort Study. Followed from birth until age 3 yrs. Parents were residents in England, Wales, Scotland, and Northern Ireland. The study over-represented children living in disadvantaged areas and from ethnic minority groups.	Preschool children in US and UK.
Quality [7]	P	P	N
Results [8]	Following adjustment for confounding factors, breastfeeding (p=0.464) and timing of introduction of complementary feeding (p=0.296) were not significantly related to the risk of obesity at age 7 yrs.	In the fully adjusted model, introduction to solid foods < 4 mo adj OR 1.12 (95% CI: 1.02-1.23) was associated with a increased risk of early childhood overweight; while breastfeeding > 4 months (0.86, 0.76 to 0.97) (compared with none) was associated with a	There may be an inverse relationship between breastfeeding (unclear if duration or ever) and later overweight (no difference between preschool children, older children, or adults). There is no relationship between time of weaning and overweight during

		decreased risk of early childhood overweight.	infancy or in children younger than age 7 yrs. However, there was no quantitative data reported.
Effect on risk (Increase/None/Protect)	None	Increase for solid introduction at < 4 months.	None.
Clinical importance [9]	3	1	N/A
Clinical relevance [10]	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

19.2 AGE OF INTRODUCTION OF SOLID FOODS and ALLERGIC SYNDROMES

Is the age of solid food introduction in children associated with the development of allergic syndromes?		
Evidence statement		Delay in the introduction of solid foods until after the age of 6 months is associated with increased risk of developing allergic syndromes.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 poor quality systematic review of 11 prospective studies (1N), 2 randomised controlled trials (2P), 4 cohort studies (4P).
Consistency	Poor	Studies examined different foods and different allergies. Overall, 3 cohort studies and 1 RCT reported an increase in any allergy with the introduction of solids after age 4-7 months. 1 cohort study reported a reduction in food allergy with the introduction of solids before age 4 months. These associations become inconsistent when dividing into food allergy and other allergies. 2 cohort studies reported an increase in food allergy with the introduction of solids after age 4-6 months, 1 cohort found no association between food allergy and introduction of solids after age 7 months, and 1 cohort reported a reduction in food allergy with the introduction of solids before age 4 months. 1 cohort study reported an increase in other allergies with the introduction of solids after age 7 months, 1 RCT reported an increase in other allergies only with introduction of meat after age 6 months and only in high risk subjects, 1 cohort reported no association between development of other allergies and introduction of solid foods after age 4-6 months, and 1 cohort reported no association between development of other allergies and introduction of solids before age 4 months. The final cohort study reported a reduction in development of both food and other allergies with the introduction of fish at age 3-8 months compared to 9 months or older.
Clinical impact	Poor	Introduction of solids after age 4-6 months: Food allergy OR range from 1.85 to 7.85; Other allergy OR range from 0.44 to 20.86. Introduction of solids before age 4 months: Food allergy OR range from 0.39 to 0.49 with CI not crossing 1; Other allergy OR range 0.32 to 1.45.

Generalisability	Excellent	USA and UK populations.
Applicability	Excellent	Directly applicable.

The systematic review was of very poor quality. The review authors used a systematic method to retrieve studies, but the included studies were not listed, quality was not assessed, eligibility criteria were not identified, and data abstraction was not discussed. The authors of the review concluded that the evidence relating the age of introduction of solid foods to the development of atopy is lacking, inconclusive, and inconsistent, but also recommended the exclusion of supplemental foods during the first 6 months of life due to the risk of the development of allergic symptoms. The systematic review did not contribute to the body of evidence statement. One of the RCTs measured age of introduction of solid foods, but did not report any results on this. This study also did not contribute to the body of evidence statement. Therefore, only one RCT and four cohort studies were used to develop the statement. The other RCT reported no association between either age at introduction of solid foods in general, specific type of solid food introduced, or diversity of foods and the development of eczema. However, increased risk was reported with delay of the introduction of meat until after six months, but only in subjects with a family history of allergy. Two cohort studies examined the late introduction of solids in general, and reported conflicting results. One cohort study (Snijders 2008) reported no association with food allergies but an increased risk of other allergies with the introduction of solids after age seven months, while the other cohort study (Zutavern 2008) reported an increased risk of food allergies, but no association with other allergies with the introductions of solids at 4-6 months or after 6 months. The latter cohort study also reported a reduced risk of food allergy with early diversity of foods (both one to two, and three to eight, food groups before age four months), but reported no association between age at introduction of solids and allergic sensitisation to cow's milk, peanut, or hen's egg. A third cohort study (Poole 2006) reported that delaying the initial exposure to cereal grains until after age six months significantly increased the risk of developing wheat allergy during childhood, suggesting that early introduction of cereal grains is protective. Age of introduction of rice cereal had no association. The final cohort study (Kull 2006) reported that children who were introduced to fish between age three-eight months had fewer allergies (asthma, eczema, and allergic rhinitis) compared to children introduced to fish at age nine months or older, suggesting that early introduction of fish is protective. Therefore, although the data appear to suggest that delaying the introduction of solid foods until after age six months may increase the risk of certain allergies, the data are somewhat conflicting and may only occur in subjects with a family history of allergy, and there are not enough studies on either solid foods in general or specific types of solid foods to use this to guide practice. As three of the five studies reported introduction of solids after six months, the timeframe of six months rather than four months is used in the body of evidence statement.

References

Becker, A., Watson, W., Ferguson, A., Dimich-Ward, H. & Chan-Yeung, M. 2004, "The Canadian asthma primary prevention study: outcomes at 2 years of age", *Journal of Allergy & Clinical Immunology*, vol. 113, no. 4, pp. 650-6.

Filipiak, B., Zutavern, A., Koletzko, S., von Berg, A., Brockow, I., Grubl, A., Berdel, D., Reinhardt, D., Bauer, C. P., Wichmann, H. E., Heinrich, J. & Gini Group. 2007, "Solid food introduction in relation to eczema: results from a four-year prospective birth cohort study", *Journal of Pediatrics*, vol. 151, no. 4, pp. 352-8.

Fiocchi, A., Assa'ad, A., Bahna, S. & Adverse Reactions to Foods Committee of the American College of Allergy Asthma and Immunology. 2006, "Food allergy and the introduction of solid foods to infants: a consensus document. Adverse Reactions to Foods Committee, American College of Allergy, Asthma and Immunology", *Annals of Allergy, Asthma, & Immunology*, vol. 97, no. 1, pp. 10-20.

Kull, I., Bergstrom, A., Lilja, G., Pershagen, G. & Wickman, M. 2006, "Fish consumption during the first year of life and development of allergic diseases during childhood", *Allergy*, vol. 61, no. 8, pp. 1009-15.

Poole, J. A., Barriga, K., Leung, D. Y. M., Hoffman, M., Eisenbarth, G. S., Rewers, M. & Norris, J. M. 2006, "Timing of initial exposure to cereal grains and the risk of wheat allergy", *Pediatrics*, vol. 117, no. 6, pp. 2175-82.

Snijders, B. E. P., Thijs, C., van Ree, R. & van den Brandt, P. A. 2008, "Age at first introduction of cow milk products and other food products in relation to infant atopic manifestations in the first 2 years of life: the KOALA Birth Cohort Study", *Pediatrics*, vol. 122, no. 1, pp. e115-22.

Zutavern, A., Brockow, I., Schaaf, B., von Berg, A., Diez, U., Borte, M., Kraemer, U., Herbarth, O., Behrendt, H., Wichmann, H. E., Heinrich, J. & Lisa Study Group. 2008, "Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA", *Pediatrics*, vol. 121, no. 1, pp. e44-52.

Table 19.2 Studies used to make evidence statement for age of introduction of solid foods and allergic syndromes

Reference [1]	**Snijders 2008 (87)**	**Zutavern 2008 (142)**	**Filipiak 2007 (175)**
Type of study [2]	Cohort	Cohort	RCT
Level of evidence	II	II	II
Intervention/ comparator [4]	Effect of duration of breast feeding, age at introduction of cow's milk and age at introduction of solids on development of eczema, atopic dermatitis, recurrent wheeze and sensitisation at age 2 yrs.	Effect of delayed introduction of solids until after 4 mo or introduction of a diversity of foods at 4 mo on development of allergy.	Effect of delayed introduction of solids on development of eczema in a high risk group.
N [5]	2558 infants	2073 children	Intervention group 2,252 Control group 3739.
Population/study information [6]	KOALA birth cohort Study, The Netherlands. Healthy infants.	From L I S A birth cohort study, Germany. Examined both total cohort, and subset of cohort with no skin or allergic symptoms.	Birth cohort Germany. Examined both entire cohort and subset of cohort with a family history of allergy.
Quality [7]	P	P	P
Results [8]	Introduction of solids after 7 mo increases the risk of eczema at age 2 yrs OR 2.10 (1.17-3.76), recurrent wheeze OR 3.52 (1.42-8.73), atopic dermatitis OR 9.46 (2.05-43.61), any sensitisation OR 4.31 (1.14-16.22), and the risk of sensitisation to one or more inhaled allergens OR 20.86 (2.17- 200.75). Introduction of solids after 7 mo was not associated with sensitisation to cow's milk OR 1.85 (0.35-9.37), peanut OR 7.85 (0.58-106.55), or hen's egg OR 5.88	1. Delay in introducing solid foods until 4-6 mo (OR range from 0.60-1.35) or > 6 mo (OR range from 0.44-1.45) has no effect on the diagnosis or symptoms of eczema, asthma, or allergic rhinitis. 2. Delay in introducing solid foods until 4-6 mo or > 6 mo appears to increase the odds of sensitisation to food allergens: Introduced 4-6 mo, OR 2.15 (1.28-3.62); Introduced > 6mo, OR 1.88 (0.98-3.58). 3. Relative to infants not introduced to solids in the first 4 mo, introduction of a diversity of food groups by 4 mo has no effect on diagnosis or symptoms of eczema, asthma, or allergic rhinitis or on the development of sensitisation to inhaled allergens	1. No association between the time of introduction of solids and the development of doctor diagnosed or symptomatic eczema. 2. No association between diversity of solid foods at 4 months and the development of doctor diagnosed or symptomatic eczema. 3. With family history of allergy, delaying the introduction of solids until after 6 mo had no effect on development of doctor diagnosed or symptomatic eczema. 4. With family history of allergy

	(0.45-76.85).	(OR range from 0.32-1.45). 4. Relative to infants not introduced to solids in the first four mo, the introduction of a diversity of foods protects against sensitisation to foods: Introduced 1-2 food groups, OR 0.38 (0.19-0.73); Introduced 3-8 food groups, OR 0.49 (0.24-0.98).	the introduction of meat and meat products after the age of 6 mo increased the risk of doctor-diagnosed eczema OR 1.42 (1.11-1.81). 5. With family history of allergy the introduction of dairy products, vegetables, fruit, cereal or egg after the age of 6 mo had no effect on the risk of doctor-diagnosed or symptomatic eczema.
Effect on risk	Late solids: increase for eczema, atopic dermatitis, recurrent wheeze, inhaled allergens; None for food sensitisations.	Late solids: None for eczema, asthma, or rhinitis. Increase for food allergen sensitisation. Early solids: None for eczema, asthma, or rhinitis. Protect for food allergen sensitisation for early food diversity.	Increase for late meat in high risk subjects. None for other foods in high risk subjects. None for regular subjects.
Clinical importance	1	1	3
Clinical relevance	1	1	1
Generalisability	y	y	y
Applicability	y	y	y

Table 19.2 Studies used to make evidence statement for age of introduction of solid foods and allergic syndromes (cont.)

Reference [1]	**Kull 2006 (295)**	**Poole 2006 (303)**	**Becker 2004 (504)**	**Fiocchi 2006 (290)**
Type of study [2]	Cohort	Cohort	RCT	Systematic review of 11 prospective studies.
Level of evidence	II	II	II	I
Intervention/ comparator [4]	Association between fish consumption during the first year of life and development of allergic diseases by age 4yrs.	Association between cereal-grain exposures (wheat, barley, rye, oats) in the infant diet and development of wheat allergy.	Avoidance of house dust mite, pet al.lergen and tobacco smoke plus breastfeeding, and delayed introduction of solid foods with control (nothing). Dependent variable is development of asthma or atopy.	Relationship between introduction of solids and development of allergy.
N [5]	4089 at baseline, 3670 at follow-up, 2614 for analysis.	1819 at baseline, 1612 at follow-up and for analysis.	Intervention= 278 but data only obtained for 246. Control=267 but data only obtained for 230.	Number of subjects not provided; 11 studies examining allergic risk with timing of intro of solid foods.
Population/study information [6]	Children born in 1994-96 in Stockholm, Sweden, from the Children, Allergy, Milieu, Stockholm, Epidemiological survey [BAMSE], followed from birth until age 4 yrs. Healthy infants only - those with eczema or recurrent wheeze during the first year of life were excluded.	US Children born in 1993–2004, from the Diabetes Autoimmunity Study in the Young [DAISY]. Identified by either newborn screening for HLA genotype at St Joseph's Hospital in Denver, Colorado, US (n = 1111), or first-degree relatives of individuals with type 1 diabetes mellitus from the Denver metropolitan area (n = 501). 70% non-Hispanic white, 23%	Children born with high risk of developing asthma based on immediate family history. Canada.	Not provided, but assume it includes western populations. Healthy vs high risk population not reported in study.

		Hispanic. Followed from birth till mean age of 4.7 yrs.		
Quality [7]	P	P	P	N
Results [8]	An inverse association was observed in analyses based on age at introduction of fish. Children introduced to fish between 3-8 mo of age had a reduced risk for asthma OR 0.73 (95% CI 0.55–0.97), eczema (OR 0.77, 0.64–0.92), allergic rhinitis (OR 0.77, 0.60–0.97), and sensitization to food and airborne allergens (OR 0.78, 0.64–0.95) at age 4 yrs compared with children introduced to fish at 9 mo or older. Fish consumption of 2-3 times per month at age 12 mo is associated with reduced risk of allergy at age 4 yrs: Asthma OR 0.82 (0.54-1.29), eczema OR 0.71 (0.53-0.95), allergic rhinitis OR 0.51 (0.35-0.73), at least one allergic disease OR 0.58 (0.45-0.76).	Delaying initial exposure to cereal grains until after 6 mo significantly increase the risk of developing wheat allergy at mean age of 4.7yrs (OR: 3.8, 95% CI (1.18-12.28)), after adjusting for breastfeeding duration, introduction of rice cereal, family history of allergy, and history of food allergy before 6 mo of age. The timing of rice-cereal introduction was not significantly associated with wheat allergy after adjustment for cereal-grain exposure, breastfeeding duration, and family history of allergy.	No specific data was reported on association with delayed introduction of solids and risk of asthma or atopy.	Evidence of a link between the early introduction of solid foods in general and the onset of atopy is conflicting and inconsistent. Evidence as to an optimal time for the introduction of any individual solid food in the infant's diet is lacking. The introduction of solid foods is not an ideal research end point because its full benefit depends on the duration of breastfeeding. But, authors recommend: (1) Exclusion of supplemental foods is indicated during the first 6 months of life because if has a preventative effect against the onset of allergic symptoms. (2) The introduction of supplemental foods during the first 4 months of life has been associated with a higher risk of allergic disease up to the age of 10 yrs. Data was not quantified.
Effect on risk	Protect for fish.	Increase: late grains; none: late rice.	N/A	Increase for early intro.
Clinical importance	1	1	N/A	N/A
Clinical	1	1	1	1

relevance				
Generalisability	y	y	y	y
Applicability	y	y	y	y

20. DIETARY PATTERNS (UI.1)

Evidence Statements

20. DIETARY PATTERNS (U1.1)

What dietary patterns, food groups (not nutrients) are associated with health and disease outcomes in the general population and vulnerable groups including low socio economic status, Aboriginal and Torres Strait Islanders and culturally and linguistically diverse groups, and those living in rural and remote areas, without serious disease?

The emphasis of this umbrella review is on whole dietary patterns, not single foods as S1.1, or nutrients. As an "umbrella" review, it only examined published review papers.

Search results

The initial search of the data bases included 1094 references for dietary patterns and the specified disease outcomes. The detailed search is included in a separate document on searches. In all 150 references concerning dietary patterns were retrieved and 34 had data extracted and eight systematic reviews were used to form the body of evidence statements. Sufficient evidence was found to make body of evidence statements for dietary patterns relating to the Mediterranean Pattern, patterns based on diet quality scoring systems and patterns that include Breakfast Consumption across the outcomes related to nutrient intakes, body weight, CHD and mortality, as detailed below.

There were two systematic reviews where body of evidence statements could not be made that were on the impact of dietary interventions relative to social disadvantage (Oldroyd 2008 [804]) and determinants of healthy eating for those with low income (Power 2005 [723]). These reviews suggested that nutrition interventions have greater impacts in higher SES and non-ethnic groups but do not have a detrimental impact in low SES groups and highlight that economic and cultural influences impact on consumption of specific foods or food groups.

The majority of studies were excluded because they were not reviews. The abstract of non-systematic reviews that were recent have been included as an appendix and gives an overview of reviews that were retrieved, but were not systematic, were rated as of negative quality, but still provide some insights to the current state of the literature in specific areas and /or are the best available summaries of these topics. The dietary patterns reviews were dominated by those relating to the Mediterranean Diet. For this dietary pattern, the papers reviewing the health outcomes of prostate cancer, longevity, cardiovascular disease and metabolic syndrome have been summarised. Other reviews describing dietary patterns more generally have focussed on the health outcomes related to cardiovascular disease, metabolic syndrome, hypertension, obesity and cancer. These have been summarised by dietary pattern approach and grouped under each specific heading.

Given that limited studies reporting diet patterns and health related outcomes for indigenous Australian were detected with the initial search strategy, an additional broad search was conducted in December 2009 to retrieve records relating to diet or nutrition or food in relation to the term

"Australian aboriginals". The search strategy is included in an appendix and the ENDNOTE library has been added to the review materials.

This search yielded 179 references, of which there were no reviews on dietary patterns amongst Indigenous Australians. While 59 abstracts provided some details of health related outcomes, only 14 reported any details related to dietary intake. Of these 14, two were very recent and the full papers were not able to be received prior to completion of the review. Of the remaining 12 articles there was an editorial [21] and a small pre-post study [46] by R. Jones reporting the results on hearing status and ear infections in a small group (n ≈12) of primary school children in a remote Aboriginal community showing improvement and reduced antibiotic use and improved plasma biomarkers after the provision of fruit at school.

[176] McDermott et al. (2009) conducted a cross-sectional survey of nutrition and health status in ASTI women of child-bearing age in rural and remote communities if far North Queensland (n=656), with follow-up of a small group (n=132) seven years later. The only dietary data reported was fruit and vegetable intakes, with means of 0.9 and 1.5 serves per day respectively. They found regular consumption of harmful levels of alcohol was common. Mean red cell folate level were low with 16-33% having levels below the reference range.

[8] Brimblecombe et al. (2009) explored the relationship between dietary quality and energy density of foods (MJ/kg) and energy cost ($/MJ) over a 3-month period in 2005, for an Aboriginal population living in a remote region of northern Australia. They found that the dietary intakes were high in refined carbohydrates and low in fresh fruit and vegetables and that foods with high energy density were associated with lower costs, contributing disproportionately to energy availability. They concluded that the this energy-cost differential influences the capacity of Australian Aboriginal people living in remote communities to attain a healthy diet and needed to be factored when developing nutrition policy and strategies in Aboriginal communities given that poor nutrition is a major determinant of preventable chronic disease.

[66] Clough et al. (2004) examined kava use and markers of dietary quality in Arnhem Land (n= 98). They found that Total and LDL cholesterol were elevated in kava using groups but users had higher HDLs. However, the key important nutrition related finding was that kava users had plasma carotenoid levels (indicative of fruit and vegetable consumption) that were very low, but that this was not different from all community members in this region.

[27] Chan et al. (2007) examined the short-term efficacy of a culturally appropriate lifestyle intervention on risk factors for cardiovascular disease in overweight urban Indigenous Australians in Queensland, both with or without type 2 diabetes (n=100). After six months they found reduction is waist circumference and improved diastolic blood pressure. They also reported an improvement in "Diet Score" but no methods were given for the assessment of diet and no other dietary intake results were reported.

[89] Gilchrist et al. (2004) reported smoking and infant feeding practices in a cohort of Indigenous mother who delivered infants (n=425) at Perth hospital from 2000-2001. While they found high rates of maternal smoking they did not find any relationship with lower rates of breastfeeding initiation or

duration at 24 weeks post-partum. They note the relationship between maternal smoking and low infant birth weight.

[93] Mackerras (2006) This editorial discussed the implications of a study by Binns et al. in 2006 in the same journal issue and whether the higher rates of breastfeeding in the Indigenous population described are confounded or not by virtue of using a sample of indigenous women delivering in a publica hospital in Perth.

[92] Binns (2006) The study documented the breastfeeding initiation and duration rates of Aboriginal mothers (n=425) delivering in six public hospitals and followed them up for six months. At discharge 89.4% (CI 86.6-92.1) of mothers were breastfeeding, declining to 58.8% (CI 53.5-64.1) at six months. These rates were higher when compared with non-Aboriginal mothers, but lower than the highest socioeconomic group. The thought that less than one-third of Aboriginal mothers achieved the World Health Organization recommendation exclusive breastfeeding until the infant is six months.

References

Oldroyd, J., C. Burns, et al. 2008, "The effectiveness of nutrition interventions on dietary outcomes by relative social disadvantage: a systematic review", *Journal of Epidemiology & Community Health*, vol. 62, no. 7, pp. 573-579.

Power, E. M. 2005, "Determinants of healthy eating among low-income Canadians", *Canadian Journal of Public Health*, vol. 96, no., pp. S37-42.

References - Indigenous Australians

Binns, C. W., Gilchrist, D., Woods, B., Gracey, M., Scott, J., Smith, H., Zhang, M. & Roberman, B. 2006, "Breastfeeding by Aboriginal mothers in Perth", *Nutrition & Dietetics*, vol. 63, no. 1, pp. 8-14.

Brimblecombe, J. K., O'Dea, K., Brimblecombe, J. K. & O'Dea, K. 2009, "The role of energy cost in food choices for an Aboriginal population in northern Australia.[see comment]", *Medical Journal of Australia*, vol. 190, no. 10, pp. 549-51.

Chan, L. C. K., Ware, R. S., Kesting, J., Marczak, M., Good, D. & Shaw, J. T. E. 2007, "Association between anthropometric measures of obesity and cardiovascular risk markers in a self-selected group of indigenous Australians", *European Journal of Cardiovascular Prevention & Rehabilitation*, vol. 14, no. 4, pp. 515-7.

Clough, A. R., Rowley, K. & O'Dea, K. 2004, "Kava use, dyslipidaemia and biomarkers of dietary quality in Aboriginal people in Arnhem Land in the Northern Territory (NT), Australia", *European Journal of Clinical Nutrition*, vol. 58, no. 7, pp. 1090-3.

Gilchrist, D., Woods, B., Binns, C. W., Scott, J. A., Gracey, M. & Smith, H. 2004, "Aboriginal mothers, breastfeeding and smoking", *Australian & New Zealand Journal of Public Health*, vol. 28,

no. 3, pp. 225-228.

Kruger, E., Dyson, K. & Tennant, M. 2005, "Pre-school child oral health in rural Western Australia", *Australian Dental Journal*, vol. 50, no. 4, pp. 258-62.

Mackerras, D. 2006, "Breastfeeding in Indigenous Australians... OS pg 8", *Nutrition & Dietetics*, vol. 63, no. 1, pp. 5-7.

McDermott, R., Campbell, S., Li, M. & McCulloch, B. 2009, "The health and nutrition of young indigenous women in north Queensland - intergenerational implications of poor food quality, obesity, diabetes, tobacco smoking and alcohol use", *Public Health Nutrition*, vol. 12, no. 11, pp. 2143-9.

B. A., McDonald, E. L., Bailie, R. S., Rumbold, A. R., Morris, P. S. & Paterson, B. A. 2008, "Preventing growth faltering among Australian Indigenous children: implications for policy and practice", *Medical Journal of Australia*, vol. 188, no. 8 Suppl, pp. S84-6.

20.1 DIETARY PATTERNS, THE MEDITERRANEAN DIET AND HEALTH OUTCOMES

What dietary patterns or food groups are associated with health, well-being or disease outcomes?		
Evidence statement		Consumption of a Mediterranean dietary pattern is associated with a reduced total mortality.
Grade		B
Evidence statement		Interventions promoting a Mediterranean dietary pattern reduce dyslipaemia, weight gain and total mortality.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	3 systematic reviews (3 P) of predominantly cohort studies for Mediterranean Diet patterns with 36, 21, and 43 included studies.
Consistency	Good	Consistent for cohorts and intervention studies for mortality and improved health outcomes. Consistent within interventions for plasma lipids, weight and mortality.
Clinical impact	Excellent	When ORs or Hazard Ratios were significant, they were in the range from 0.25 to 0.7. The risk reduction for total mortality ranged from 17 to >30%
Generalisability	Good	Populations in body of evidence can be contextualised to mainly Australian adults (>190y)
Applicability	Good	Applicable to adults consuming or able to adopt this eating pattern

The studies included in the body of evidence statement are shown in Table 20.1.

References

Buckland, G., A. Bach, et al. 2008, "Obesity and the Mediterranean diet: a systematic review of observational and intervention studies", *Obesity Reviews*, vol. 9, no. 6, pp. 582-93.

Roman, B., L. Carta, et al. 2008, "Effectiveness of the Mediterranean diet in the elderly", *Clinical Interventions In Aging*, vol. 3, no. 1, pp. 97-109.

Serra-Majem, L., B. Roman, et al. 2006, "Scientific evidence of interventions using the Mediterranean diet: a systematic review (Structured abstract)", *Nutrition Reviews*, vol., no. 2 Supplement, pp. S27-s47.

Table 20.1 Studies used to make evidence statements for Mediterranean Dietary Pattern

Reference [1]	**Roman et al. 2008 [28]**	**Buckland 2008 [531]**	**Serra-Majem 2006 [7]**
Type of study [2]	Systematic Review	Systematic Review	Systematic Review
Level of evidence [3]	II	III-2	II
Intervention/ comparator [4]	Adherence to Mediterranean diet in elderly (>65yrs) / morbidity and mortality	Adherence to Mediterranean diet by score / Weight status association or after intervention	Mediterranean Diet interventions / CVD risk factors and mortality
N [5]	>165 000	>75 000	> 17 000
Population/study information [6]	M19, 31, 51, 65; F 19, 31, 51, 65	B14 G14 M19,31,51,65; F19, 31, 51, 65	Age not reported
Quality [7]	P	P	P
Results [8]	greater adherence association with a reduction in mortality from 17 to >30% and may be greater for those >55yrs	Inconsistent association with weight and MD in cohorts. Interventions using MD associated with small, but significantly greater weight reduction.	Clinical trial show adherence to MD associated with improved lipids and secondary prevention trial a reduction in mortality (OR range 0.25-0.7) range. One study showed a 60% reduction in cancer risk and another significant improvement in arthritis pain
Effect on risk (Increase/None/Protect)	Protect	Protect	Protect
Clinical importance [9]	1	2	1
Clinical relevance [10]	1	2	1

Generalisability	n	y	y
Applicability	y	y	y

20.2 DIETARY PATTERNS, BREAKFAST CONSUMPTION AND HEALTH OUTCOMES

What dietary patterns or food groups are associated with health, well-being or disease outcomes?		
Evidence statement		Consumption of breakfast is associated with improved nutrient intakes.
Grade		C
Evidence statement		Consumption of breakfast is associated with reduced risk of overweight and obesity.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	2 systematic reviews (111-2, 2P); 1 on association between consumption and family characteristics (24 cross-sectional studies) and 1 on nutrient intakes (47 studies, both cross-sectional or intervention (number not specified in the review)).
Consistency	Good	Breakfast consumption associated with better nutrient profiles in children/ adolescents in 8 studies and only not significant in one, after adjustment for confounders. Some inconsistency for body weight but 13 studies were protective from overweight and 5 had no association. Breakfast consumption associated with 12 family socio-cultural, demographic characteristics and 4 that decrease consumption.
Clinical impact	Excellent	OR for o'wt/ obesity for breakfast skipper 1.95-2.0; OR for o'wt/ obesity for breakfast consumer 0.68-0.72. Higher nutrient intakes in breakfast consumer. More likely to consume breakfast if parents consume it, in a 2-parent family and not socio-economically deprived.
Generalisability	Good	Populations in body of evidence can be contextualised to Australian children and adolescents.
Applicability	Excellent	Highly applicable to children and adolescents.

The studies included in the body of evidence statement are shown in Table 20.2.

References

Pearson, N., S. J. Biddle, et al. 2009, "Family correlates of breakfast consumption among children and adolescents. A systematic review", *Appetite*, vol. 52, no. 1, pp. 1-7.

Rampersaud, G. C., M. A. Pereira, et al. 2005, "Breakfast habits, nutritional status, body weight, and academic performance in children and adolescents", *Journal of the American Dietetic Association*, vol. 105, no. 5, pp. 743-762.

Table 20.2 Studies used to make evidence statements for Breakfast Consumption

Reference [1]	**Pearson 2009 [751]**	**Rampersaud 2005 [707]**
Type of study [2]	Systematic Review	Systematic Review
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Breakfast consumption / family characteristics.	Breakfast consumption / nutrient intakes and body weight.
N [5]	357-18 177	> 95 000
Population/study information [6]	C1,4; B9, 14; G9, 14	C1, C4; B 9, 14; G 9, 14; M 19, F 19
Quality [7]	P	P
Results [8]	Breakfast consumption association with 12 family socio-cultural, demographic characteristics and 4 that decrease consumption. More likely to consume breakfast if parents consume it, in a 2-parent family and not socio-economically deprived.	Breakfast consumption associated with better nutrient profiles in children/ adolescents in 8 studies and not significant in one after adjustment for confounders. Improved body weight profile in 13 studies with no association in 5; ORs only reported in 3 studies and for breakfast skipper the OR for o'wt/obesity varied from 1.95 to 2.0 while for breakfast consumers the OR for o'wt/obesity varied from 0.68 to 0.72. Results for academic performance and cognition are variable and highly confounded.
Effect on risk (Increase/None/Protect)	Not Applicable	Protect
Clinical importance [9]	1	1
Clinical relevance [10]	1	1
Generalisability	y	y
Applicability	y	y

20.3 DIETARY PATTERNS RANKED USING DIET QUALITY SCORES AND HEALTH OUTCOMES

What dietary patterns or food groups are associated with health, well-being or disease outcomes?		
Evidence statement		Consumption of a dietary intake pattern aligned with National Dietary Guidelines or recommendations is associated with reduced morbidity and mortality.
Grade		C
Evidence statement		Consumption of a dietary intake pattern aligned with National Dietary Guidelines or recommendations is not associated with risk of overweight or obesity.
Grade		D
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	2 systematic reviews (2 Level II, 6 Level III-2 studies, 1 narrative synthesis) of predominantly cohort studies for a range of eating patterns (7P, 1N, 1O) with moderate to high risk of bias.
Consistency	Satisfactory	1. Consistent reduction in morbidity in association with high diet quality and usually greater for men and less for women. 2. Inconsistent associations with body weight (30 studies, 11 no association, 10 positive, 9 negative).
Clinical impact	Good	Higher diet quality &/or variety commonly associated with reduction in morbidity in the range of 10-20%, usually greater for men and less for women. When ORs or Hazard Ratios are significant, they were in the range from 0.5 to 0.8. The effect size is usually attenuated by 10 to 20% by common confounders of age, education, SES.
Generalisability	Good	Populations in body of evidence can be contextualised to mainly Australian adults (>19y).
Applicability	Good	Varying applicability but encompasses adults with some studies in children and adolescents.

The studies included in the body of evidence statement are shown in Table 20.3.

References

Togo, P., M. Osler, et al. 2001, "Food intake patterns and body mass index in observational studies", *International Journal of Obesity & Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, vol. 25, no. 12, pp. 1741-51.

Wirt, A., and Collins, C.E. 2009, "Diet Quality - What is it and does it matter?" *Public Health Nutrition,* pp1-20.

Table 20.3 Studies used to make evidence statements for Diet Quality Scores

Reference [1]	**Wirt 2009 [1139]**	**Togo et al. 2001 [202]**
Type of study [2]	Systematic Review	Systematic Review
Level of evidence [3]	III-2	III-2
Intervention/ comparator [4]	Categories with Diet Quality or Variety Scores / Morbidity and Mortality data.	Diet quality and/or variety scores / Weight status.
N [5]	>20 000 000	> 300 000
Population/study information [6]	M and F; all age ranges excluding children and pregnant women.	C1, B14, G14; M 19, 31, 51, 65; F 19, 31, 51, 65.
Quality [7]	P	P
Results [8]	Higher diet quality &/or variety commonly associated with reduction in morbidity in the range of 10-20%, usually greater for men and less for women.	Inconsistent associations with body weight (Of 30 studies, 11 no association, 10 positive, 9 negative).
Effect on risk (Increase/None/Protect)	Protect	10 Increase/11 None/9 Protect
Clinical importance [9]	1	2
Clinical relevance [10]	1	1
Generalisability	Y	Y
Applicability	Y	Y

Dietary Patterns and Socio-Economic Status and Health Outcomes

These two reviews were not included in the body of evidence statement but are shown in Table 4.

References

Oldroyd, J., C. Burns, et al. 2008, "The effectiveness of nutrition interventions on dietary outcomes by relative social disadvantage: a systematic review", *Journal of Epidemiology & Community Health*, vol. 62, no. 7, pp. 573-579.

Power, E. M. 2005, "Determinants of healthy eating among low-income Canadians", *Canadian Journal of Public Health*, vol. 96, no., pp. S37-42.

Table 20.4 Studies used to make evidence statements for Socio-Economic Status

Reference [1]	**Oldroyd 2008 [804]**	**Power 2005 [723]**
Type of study [2]	Systematic Review	Systematic Review
Level of evidence [3]	II	Narrative review
Intervention/ comparator [4]	Impact of nutrition interventions / SES	Dietary intake / determinants of healthy eating in low income Canadians
N [5]	> 5500	Not reported
Population/study information [6]	C4, B9, G9, M19,31,52; W 19,31,51	Not reported
Quality [7]	P	N
Results [8]	Nutrition interventions had greater impacts in higher SES and non-ethnic groups but do not have a detrimental impact in low SES. After 1 year children from high SES had a great increase in fruit and veg (2.4 vs. 1.3 portions), $p<0.000$.	Economic and cultural influences impact on food consumption. Income affects food intake both directly and indirectly, with economic and cultural thresholds likely for specific foods and food groups.
Effect on risk (Increase/None/Protect)	Not Applicable	Not Applicable
Clinical importance [9]	2	2
Clinical relevance [10]	3	3
Generalisability	y	y
Applicability	y	y

U1.1 Summary of the studies *Included*, but not used in the Body of Evidence Statements.

The abstracts of the non-systematic reviews deemed relevant to this topic, but that did not contribute to a body of evidence statement ar eincluded in an appendix. The references however appear below.

References

Bautista, M. C. & Engler, M. M. 2005, "The Mediterranean diet: is it cardioprotective?", *Progress in Cardiovascular Nursing*, vol. 20, no. 2, pp. 70-76.

Bellisle, F. 2004, "Impact of the daily meal pattern on energy balance", *Scandinavian Journal of Nutrition*, vol. 48, no. 3, pp. 114-118.

Bullo, M., Casas-Agustench, P., Amigo-Correig, P., Aranceta, J. & Salas-Salvado, J. 2007, "Inflammation, obesity and comorbidities: the role of diet", *Public Health Nutrition*, vol. 10, no. 10A, pp. 1164-72.

Carlson, J. J. & Monti, V. 2003, "The role of inclusive dietary patterns for achieving secondary prevention cardiovascular nutrition guidelines and optimal cardiovascular health", *Journal of Cardiopulmonary Rehabilitation*, vol. 23, no. 5, pp. 322-333.

Chahoud, G., Aude, Y. W. & Mehta, J. L. 2004, "Dietary recommendations in the prevention and treatment of coronary heart disease: do we have the ideal diet yet?[see comment]", *American Journal of Cardiology*, vol. 94, no. 10, pp. 1260-7.

Couch, S. C. & Daniels, S. R. 2005, "Diet and blood pressure in children", *Current Opinion in Pediatrics*, vol. 17, no. 5, pp. 642-647.

de Lorgeril, M. & Salen, P. 2006, "The Mediterranean-style diet for the prevention of cardiovascular diseases", *Public Health Nutrition*, vol. 9, no. 1A, pp. 118-23.

de Lorgeril, M. & Salen, P. 2007, "Modified cretan Mediterranean diet in the prevention of coronary heart disease and cancer: An update", *World Review of Nutrition & Dietetics*, vol. 97, no., pp. 1-32.

Dontas, A. S., Zerefos, N. S., Panagiotakos, D. B., Vlachou, C. & Valis, D. A. 2007, "Mediterranean diet and prevention of coronary heart disease in the elderly.[erratum appears in Clin Interv Aging. 2008;3(2):397 Note: Vlachou, Cleo [added]]", *Clinical Interventions In Aging*, vol. 2, no. 1, pp. 109-15.

Esposito, K., Ciotola, M. & Giugliano, D. 2006, "Mediterranean diet, endothelial function and vascular inflammatory markers", *Public Health Nutrition*, vol. 9, no. 8A, pp. 1073-6.

Esposito, K., Ciotola, M. & Giugliano, D. 2007, "Mediterranean diet and the metabolic syndrome", *Molecular Nutrition & Food Research*, vol. 51, no. 10, pp. 1268-74.

Friberg, P. & Johansson, M. 2007, "Effects of an omega-3-enriched Mediterranean diet (modified diet of Crete) versus a Swedish diet", *World Review of Nutrition & Dietetics*, vol. 97, no., pp. 52-66.

Gerber, M. 2001, "The comprehensive approach to diet: a critical review", *Journal of Nutrition*, vol. 131, no. 11 Suppl, pp. 3051S-5S.

Giugliano, D., Ceriello, A. & Esposito, K. 2006, "The effects of diet on inflammation: emphasis on the metabolic syndrome", *Journal of the American College of Cardiology*, vol. 48, no. 4, pp. 677-85.

Giugliano, D. & Esposito, K. 2008, "Mediterranean diet and metabolic diseases", *Current Opinion in Lipidology*, vol. 19, no. 1, pp. 63-8.

Itsiopoulos, C., Hodge, A. & Kaimakamis, M. 2009, "Can the Mediterranean diet prevent prostate cancer?", *Molecular Nutrition & Food Research*, vol. 53, no. 2, pp. 227-39.

Lairon, D. 2007, "Intervention studies on Mediterranean diet and cardiovascular risk", *Molecular Nutrition & Food Research*, vol. 51, no. 10, pp. 1209-14.

McCarron, D. A. & Reusser, M. E. 2001, "Are low intakes of calcium and potassium important causes of cardiovascular disease?", *American Journal of Hypertension*, vol. 14, no. 6 Pt 2, pp. 206S-212S.

Panagiotakos, D. B. & Polychronopoulos, E. 2005, "The role of Mediterranean diet in the epidemiology of metabolic syndrome; converting epidemiology to clinical practice", *Lipids in Health & Disease*, vol. 4, no. 1, pp. 7.

Pineo, C. E. & Anderson, J. J. B. 2008, "Cardiovascular benefits of the Mediterranean diet", *Nutrition Today*, vol. 43, no. 3, pp. 114-122.

Srinath Reddy, K. & Katan, M. B. 2004, "Diet, nutrition and the prevention of hypertension and cardiovascular diseases", *Public Health Nutrition*, vol. 7, no. 1A, pp. 167-86.

St-Onge, M., Keller, K. L. & Heymsfield, S. B. 2003, "Changes in childhood food consumption patterns: a cause for concern in light of increasing body weights", *American Journal of Clinical Nutrition*, vol. 78, no. 6, pp. 1068-1073.

Taylor, E., Missik, E., Hurley, R., Hudak, S. & Logue, E. 2004, "Obesity treatment: broadening our perspective", *American Journal of Health Behavior*, vol. 28, no. 3, pp. 242-249.

Trichopoulou, A., Corella, D., Martínez-Gonzalez, M. A., Soriguer, F. & Ordovas, J. M. 2006, "The Mediterranean diet and cardiovascular epidemiology... Health effects of olive oil and the Mediterranean diet. Olive Oil and Health: First International Congress, October 21-23, 2004, Jaen, Spain", *Nutrition Reviews*, vol. 64, no. 10 Part 2, pp. S13-9.

Trichopoulou, A. 2004, "Traditional Mediterranean diet and longevity in the elderly: a review", *Public Health Nutrition*, vol. 7, no. 7, pp. 943-7.

Weih, M., Wiltfang, J. & Kornhuber, J. 2007, "Non-pharmacologic prevention of Alzheimer's Disease: nutritional and life-style risk factors", *Journal of Neural Transmission*, vol. 114, no. 9, pp. 1187-97.

Zarraga, I. G. E. & Schwarz, E. R. 2006, "Impact of dietary patterns and interventions on cardiovascular health.[erratum appears in Circulation. 2006 Nov 7; 114(19):e577]", *Circulation*, vol. 114, no. 9, pp. 961-73.

21. DIETARY INTAKE DATA (UI.3)

Evidence Statements

21. DIETARY INTAKE DATA (U1.3)

- ***What are the most recent data on dietary patterns and intakes of foods and food components (including nutrients) in Australia?***
- ***How does the data vary across age/sex groups in the general population and vulnerable groups including low socio economic status, Aboriginal and Torres Strait Islanders and culturally and linguistically diverse groups, and those living in rural and remote areas?***

Executive Summary

As this was an Umbrella Review, individual studies were not eligible for inclusion and this has limited the number of studies used to form body of evidence statements. Some of the important recent individual studies that were therefore not retrieved and have not been included are:

- National Health Surveys
- Indigenous Health Surveys
- Several State-based surveys
- Australian National Children's Nutrition and Physical Activity
- AusDiab
- Central Sydney Area study of children aged 2-5
- National Lead Survey of children aged 2-4, with anaemia results.

It appears that in the period of the search (1995-2009) there have been very few reviews of relevance to these questions. Of the 45 articles in the database, only three of the relevant eight publications were systematic and graded of positive quality. Most were non-systematic, with no description of the search methods or quality assessment processes. Most studies addressed very specific questions (e.g. about the effect of supplementation with a specific nutrient) rather undertaking a comprehensive review. Some individual studies with a specific focus on dietary patterns were included due to the limited numbers of review articles obtained. There was only sufficient evidence to make one body of evidence statement.

Summaries and relevant quotes from each study are given after the body of evidence statement, rather than attempt to present the very diverse studies in a standard tabulated format.

Dietary patterns and dietary intakes

No studies were retrieved related to adult dietary patterns or intakes. Feeding patterns of pre-term or low birth weight infants were the most common review topics with the remaining articles focusing on adolescents and young children. In relation to infant feeding schedules, no specific recommendations were provided. When addressing the use of formula or donor milk rather than mothers own breastmilk in pre-term infants, it was determined that serious gut problems may results with formula feeding despite

the rapid short term growth it creates. When then addressing formula and breastmilk on the development of pre-term infants, no further studies were identified.

For adolescents, breakfast quality was addressed using a cross-sectional study. This study found that a higher quality breakfast, composed of at least three different food groups, was consumed by a small proportion of adolescents, while most who ate breakfast consumed food from at least two different food groups. The total fat intake and in particular saturated fat intake is of particular concern for adolescents. Approximately one-eighth of adolescents were found to consume a higher proportion of energy from fat than carbohydrate. Adolescent girls were also more at risk of under-nutrition for energy, though beta-carotene and fibre intake was found to be low amongst both girls and boys. Low SES has an impact on energy and nutrients consumed by adolescent girls, with a greater risk of inadequate micronutrient intake.

Extra foods as defined by the Australian Guide to Healthy Eating comprise a large proportion of Australian children's diets (2-18years). Margarines, soft drinks, cordials, sugar and sweet biscuits are the top five food consumed by the majority of children in the 1995 NNS. In younger children (16-24 months) fats and oils and cereal based products (biscuits, cakes, pastries etc.) were consumed by 90% or more of the children followed by miscellaneous and non-milk sweetened beverages.

Given the paucity of data, it was not possible to summarise information on the normal range of intakes of other key food groups from the results of this search. No reviews on the amount of physical activity needed at each age group were retrieved.

Demographic influence

There were was only one review related to vulnerable groups within remote or rural areas of Australia. This review used a historical focus and again focussed on the dietary intakes of children, not adults. The Westernisation of the food intake and the implications on health outcomes such as impaired glucose tolerance and cardiovascular disease were discussed and the findings of the 1995 National Nutrition Survey children's fat intake data presented for comparison.

21.1 DIETARY PATTERNS AND INTAKES IN INFANTS

What are the most recent data on dietary patterns and intakes of foods and food components (including nutrients) in Australia for infants?		
Evidence Statement		Feeding maternal breastmilk to pre-term or low birthweight infants provides non-nutritive advantages compared to formula.
Grade of recommendation		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	Three Level I meta analyses (15 RCTs) focussed on different aspects of pre-term or low birthweight feeding.
Consistency	Satisfactory	There is agreement on findings for formula versus maternal milk in pre-term or low birthweight feeding, but no recommendation for feeding schedule. Further studies suggested though use of formula feeding of pre-term infants is discouraged.
Clinical impact	Good	Significantly higher incidence of necrotising enterocolitis in formula fed groups. RR 2.5 (CI 1.2-5.1).
Generalisability	Good	US, UK and European populations studied.
Applicability	Good	No reason to believe results not directly applicable in Australian context.

Included Studies:

Gracey, M. 2000, "Historical, cultural, political, and social influences on dietary patterns and nutrition in Australian Aboriginal children", *American Journal of Clinical Nutrition*, vol. 72, no. 5 Suppl, pp. 1361S-1367S.

Henderson, G., Anthony Mary, Y. & McGuire, W. 2007, "Formula milk versus maternal breast milk for feeding preterm or low birth weight infants", Cochrane Database of Systematic Reviews.

Milligan, R. A., Thompson, C., Vandongen, R., Beilin, L. J. & Burke, V. 1995, "Clustering of cardiovascular risk factors in Australian adolescents: association with dietary excesses and deficiencies", European Journal of Cardiovascular Risk, vol. 2, no. 6, pp. 515-23.

O'Sullivan, T. A., Robinson, M., Kendall, G. E., Miller, M., Jacoby, P., Silburn, S. R. & Oddy, W. H. 2009, "A good-quality breakfast is associated with better mental health in adolescence", Public Health Nutrition, vol. 12, no. 2, pp. 249-58.

Quigley, M., Henderson, G., Anthony Mary, Y. & McGuire, W. 2007, "Formula milk versus donor breast milk for feeding preterm or low birth weight infants", Cochrane Database of Systematic Reviews, vol., no. 4.

Tosh, K. & McGuire, W. 2006, "Ad libitum or demand/semi-demand feeding versus scheduled interval feeding for preterm infants", Cochrane Database of Systematic Reviews, vol., no. 3.

Additional NHMRC references

Rangan A M., Randall D, Hector, D.J., Webb, K.L. 2008, “Consumption of ‘extra’ foods by Australian children: types, quantities and contributions to energy and nutrient intakes”, European Journal of Clinical Nutrition, vol. 62, no. 3, pp. 356-364.

Webb K. L., Lahti-Koski, M., Rutishauser, I., Hector, D.J., Knezevic, N., Gill, T., Peat, J.K., Leeder, S.R. 2006, “Consumption of ‘extra’ foods (energy-dense, nutrient poor) among children aged 16-24 months for western Sydney, Australia”, Public Health Nutrition, vol. 9, no. 8, pp. 1035-1044.

1) DIETARY PATTERNS

Tosh, K. and W. McGuire (2006) "Ad libitum or demand/semi-demand feeding versus scheduled interval feeding for preterm infants." Cochrane Database of Systematic Reviews [17]

Quality Rating: Positive

Search Method: *Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2006), MEDLINE (1966 - March 2006), EMBASE (1980 – March 2006), CINAHL (1982 - March 2006), conference proceedings, and previous reviews. Randomised or quasi-randomised controlled trials (including cluster randomised trials) that compared a policy of feeding preterm infants on an ad libitum or demand/semi-demand basis versus feeding at scheduled intervals. (p3, Abstract)*

Summary:

Background

Feeding preterm infants in response to their hunger and satiation cues (ad libitum or demand/semi demand) rather than at scheduled intervals might help in the establishment of independent oral feeding, increase nutrient intake and growth rates, and allow earlier hospital discharge.

Objectives

To assess the effect of a policy of feeding preterm infants on an ad libitum or demand/semi-demand basis versus feeding prescribed volumes at scheduled intervals on growth rates and the time to hospital discharge.

Main results

We found seven randomised controlled trials that compared ad libitum or demand/semi-demand regimes with scheduled interval regimes in preterm infants in the transition phase from intragastric tube to oral feeding. The trials were generally small and of variable methodological quality. There is currently insufficient evidence to determine whether feeding preterm infants in response to their own hunger cues is better than feeding set volumes of milk at pre-defined intervals. We identified seven small trials that examined this issue, but in general these were methodologically (p3, Abstract)

Quigley, M., G. Henderson, et al. (2007) "Formula milk versus donor breast milk for feeding preterm or low birth weight infants." Cochrane Database of Systematic Reviews [27]

Quality Rating: Positive

Search Method: *The standard search strategy of the Cochrane Neonatal Review Group was used. This included electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 2, 2007), MEDLINE (1966 - May 2007), EMBASE (1980 - May 2007), CINAHL (1982 - May 2007), conference proceedings, and previous reviews. Randomised controlled trials comparing feeding with formula milk versus donor breast milk in preterm or low birth weight infants. (p5, Abstract)*

Summary:

Background

When sufficient maternal breast milk is not available, the alternative sources of enteral nutrition for preterm or low birth weight infants are donor breast milk or artificial formula milk. Feeding preterm or low birth weight infants with formula milk might increase nutrient input and growth rates. However, since feeding with formula milk may be associated with a higher incidence of feeding intolerance and necrotising enterocolitis, this may adversely affect growth and development.

Objectives

To determine the effect of formula milk compared with donor human breast milk on growth and development in preterm or low birth weight infants.

Data collection and analysis

Data were extracted using the standard methods of the Cochrane Neonatal Review Group, with separate evaluation of trial quality and data extraction by two reviewer authors, and synthesis of data using relative risk, risk difference and weighted mean difference.

Main results

Eight trials fulfilled the inclusion criteria. Only one trial used nutrient-fortified donor breast milk. Enteral feeding with formula milk compared with donor breast milk resulted in higher rates of growth in the short term. There was no evidence of an effect on long-term growth rates or neurodevelopmental outcomes. Meta analysis of data from five trials demonstrated a statistically significantly higher incidence of necrotising enterocolitis in the formula fed group: typical relative risk 2.5 (95% CI 1.2, 5.1); typical risk difference: 0.03 (95% CI 0.01, 0.06; number needed to harm: 33 (95% CI 17, 100). When a mother's own breast milk is not available for feeding her preterm or low birth weight infant, the alternatives are either formula milk or expressed breast milk from a donor mother ("donor breast milk"). Review of eight randomised controlled trials suggests that feeding with formula increases short-

term growth rates but is associated with a higher risk of developing the severe gut disorder "necrotising enterocolitis". There is no evidence of an effect on longer-term growth, or on development. Further trials that compare these two strategies are needed. These should probably compare formula milk adapted for preterm infants with donor breast milk supplemented with nutrients. (p5, Abstract)

Henderson, G., Y. Anthony Mary, et al. (2007) "Formula milk versus maternal breast milk for feeding preterm or low birth weight infants." Cochrane Database of Systematic Reviews [28]

Quality Rating: Positive

Search Method: *The standard search strategy of the Cochrane Neonatal Review Group was used. This included electronic searches of the Cochrane Central Register of Controlled Trials Register (CENTRAL, The Cochrane Library, Issue 3, 2007), MEDLINE (1966 - June 2007) and EMBASE (1980 - June 2007) and CINAHL (1982 to June 2007) (all accessed via OVID) and previous reviews including cross references. Randomised controlled trials comparing feeding with formula milk versus preterm human milk in preterm or low birth weight infants. (p3, Abstract)*

Summary:

Background

Maternal breast milk may contain less nutrients than artificial formula milk but may confer important non-nutrient advantages for preterm or low birth weight infants.

Objectives

To determine the effect of feeding with formula milk compared with maternal breast milk on rate of growth and developmental outcomes in preterm or low birth weight infants.

Data collection and analysis

The standard methods of the Cochrane Neonatal Review Group were used, with separate evaluation of trial quality and data extraction by two authors.

Main results

No eligible trials were identified. Formula milk may contain more nutrients than maternal breast milk but it lacks the antibodies and other substances present in breast milk that protect and develop the immature gut of preterm or low birth weight infants. No trials that compared feeding with formula milk rather than their own mother's breast milk were identified. However, since another Cochrane review has found that feeding with formula compared to donor breast milk increases the risk of serious gut

problems in preterm or low birth weight infants, it is unlikely that such a trial would be acceptable to mothers and caregivers. (p3, Abstract)

O'Sullivan, T. A., M. Robinson, et al. (2009). "A good-quality breakfast is associated with better mental health in adolescence." Public Health Nutrition 12(2): 249-58 [12]

Quality Rating: Neutral

Search Method: N/A (Cross-sectional population based study)

Quote:

The majority of adolescents (54.0%, n 452) consumed a breakfast consisting of food from two different food groups over the three days, while a high-quality breakfast consisting of three or more food groups was consumed by 11.4% (n 95). Milk, followed by fortified breakfast cereals and bread, were the food and beverage types most commonly consumed by the adolescents for breakfast. (p252)

When blood glucose concentrations fall below normal, hormones such as adrenalin and cortisol are released which are associated with feelings of agitation and irritability; symptoms such as difficulty concentrating and destructive outbursts can also occur. The breads and cereals food group is the most carbohydrate-dense of the food groups and incorporation of these foods into breakfast, in suitable portion sizes, may help to avoid low blood glucose concentrations. These behaviours of aggression and delinquency were encompassed into the externalizing mental health score, which showed a stronger association with breakfast quality in our study. (p254)

An increased intake of valuable vitamins and minerals at the start of the day, resulting from consumption of a breakfast with a variety of food groups, may partially explain the relationship with better mental health that was observed in our study. (p254)

Milligan, R. A., C. Thompson, et al. (1995). "Clustering of cardiovascular risk factors in Australian adolescents: association with dietary excesses and deficiencies." European Journal of Cardiovascular Risk 2(6): 515-23. [9]

Quality Rating: Neutral

Search Method: Cross-sectional study of 555 adolescents, mean age 15years.

Summary:

Table 2. Energy intake profile of girls and boys compared with target figures.

Source	Girls	Boys	Target†	% Above target‡	
Energy (MJ)*	7.5 (7.3, 7.8)	11.5 (11.1, 11.9)	8.6–9.8 (F) 10.5–11.8 (M)		
Carbohydrate (% energy)	46.8 (46.0, 47.6)	47.0 (46.3, 47.6)			
Protein (% energy)	15.4 (15.0, 15.8)	15.9 (15.5, 16.2)	10–15	51.1	59.5
Fat (% energy)	35.3 (34.5, 36.0)	34.8 (34.2, 35.4)	<33	66.9	65.7
Sugar (% energy)	20.8 (20.0, 21.6)	20.9 (20.3, 21.6)	<20	52.3	53.6
Fat composition					
Saturated (% energy)	15.4 (14.9, 15.8)	15.5 (15.1, 15.9)	10	94.0	94.8
Monounsaturated (% energy)	12.0 (11.7, 12.3)	11.8 (11.6, 12.1)	10	79.3	81.0
Polyunsaturated (% energy)*	5.3 (5.1, 5.6)	4.8 (4.6, 5.1)	10	2.6	1.7

Values for girls and boys are means with confidence intervals in parentheses. F, female, M, male. †Energy target is according to recommended dietary intakes [27]. Individual nutrient targets are from the Better Health Commission [10]. ‡Percentage of sample above the target figure supplied by the Better Health Commission [10]. *$P<0.05$, significant difference between sexes by t-test.

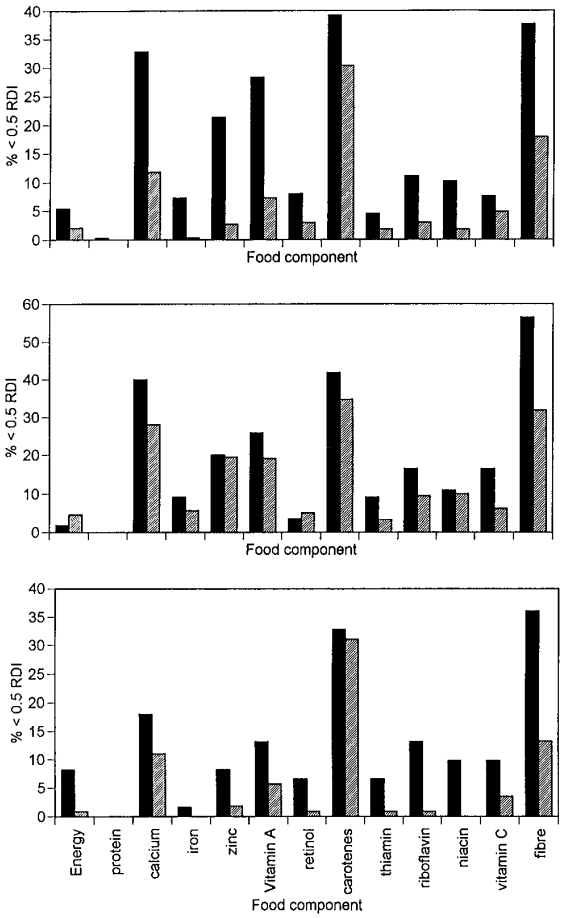

Fig. 1. Percentage of adolescents at risk of undernutrition (intake less than 50% of their recommended dietary intakes [24] or target guidelines [10]) for selected food components. (a) Girls (■) and boys (▨); (b) higher-risk (■) and lower-risk (▨) girls; (c) higher-risk (■) and lower-risk (▨) boys.

Table 3. Identification of higher-risk groups by cluster analysis.

	Girls		Boys	
Variable	Higher risk (n = 55)	Lower risk (n = 211)	Higher risk (n = 61)	Lower risk (n = 228)
Systolic blood pressure (mmHg)	120.7 (118.6, 122.8)*	114.0 (112.6, 115.4)	125.8 (122.0, 129.6)*	119.0 (117.4, 120.6)
Diastolic blood pressure (mmHg)	65.9 (64.1, 67.6)	65.3 (64.3, 66.2)	65.2 (63.2, 67.3)*	62.3 (61.4, 63.2)
Body fat (%)	28.3 (27.3, 29.3)*	20.0 (19.4, 20.6)	18.3 (16.6, 20.0)*	11.4 (10.9, 11.9)
Body mass index (kg/m²)	24.6 (23.8, 25.4)*	19.9 (19.7, 20.2)	23.1 (22.1, 24.1)†	20.1 (19.8, 20.4)
Fitness (laps)	33.6 (31.0, 36.3)*	53.9 (51.9, 55.9)	59.4 (54.5, 64.3)*	84.7 (82.4, 87.1)
Activity (/56)	17.4 (15.5, 19.3)	18.3 (17.2, 19.3)	20.5 (18.5, 22.5)*	24.4 (23.3, 25.5)
Energy intake (MJ)	7.1 (6.7, 7.6)	7.6 (7.3, 8.0)	9.2 (8.5, 9.9)*	12.1 (11.7, 12.5)
Fat intake (%)	37.9 (36.5, 39.3)*	34.6 (33.7, 35.4)	36.7 (35.3, 38.1)*	34.3 (33.6, 35.0)
Cholesterol (mg): energy adjusted‡	197.6 (170.4, 224.8)	191.2 (175.2, 207.2)	391.7 (350.2, 433.2)*	287.9 (267.3, 308.5)
Sodium (mg): energy adjusted‡	2590 (2357, 2823)*	2315 (2193, 2437)	3648 (3271, 4025)	3715 (3524, 3906)
Calcium (mg): energy adjusted‡	648 (567, 729)*	742 (692, 792)	1253 (1125, 1381)	1179 (1096, 1262)
Fibre (g): energy adjusted‡	15.9 (14.6, 17.2)*	18.1 (17.0, 19.2)	21.8 (19.8, 23.8)†	24.2 (22.8, 25.6)

Values are means, with confidence intervals in parentheses. *Variables used in cluster analysis for each sex (significantly different at $P<0.05$); †variables not used in cluster analysis but with significant differences at $P<0.05$; ‡nutrient means adjusted by analysis of variance using energy intake as the covariate.

Additional NHMRC references

Rangan A M et al. (2008) Consumption of 'extra' foods by Australian children: types, quantities and contributions to energy and nutrient intakes, European Journal of Clinical Nutrition: 62(3) 356-364

Quality Rating: Negative

Method: Reanalysis of 1995 NNS data for 2-18yr old children

Summary:

Table 1 Commonly consumed 'extra' foods among 3007 Australian children aged 2–18 years; percent consuming, mean intake per capita and per consumer, and percentage energy contribution, 1995 National Nutrition Survey

'Extra' food type	*Percent consuming*	*Test for trend by age group (P-value)*	*Mean intake per capita (g/day)*	*Mean intake per consumer (g/day)*	*Rank (% energy contribution)*
Margarine	61.8	↓ <0.0001	7.3	11.8	6 (2.5%)
Sugar-sweetened soft drinks	35.4	↑ <0.0001	180.7	511.1	2 (3.3%)
Cordials	35.4	↓ <0.0001	119.3	337.2	4 (2.7%)
Sugar	34.6	0.998	3.2	9.2	
Sweet biscuits	31.1	↓ <0.0001	10.4	33.2	7 (2.4%)
Ice cream/ice confection	30.0	0.762	41.3	137.6	3 (3.1%)
Chocolate/chocolate bars	26.8	0.560	10.6	39.7	9 (2.2%)
Fried potatoes	25.0	↑0.005	36.3	144.9	1 (4.2%)
Beverage flavourings	22.0	↓0.0002	1.5	6.7	
Lollies and confectionery	20.2	↓<0.0001	5.6	28.0	
Fruit drinks	18.9	↓0.0019	71.8	380.6	11 (1.4%)
Potato crisps	17.5	0.870	6.0	34.4	10 (1.5%)
Cakes and muffins	17.3	0.298	15.8	91.6	8 (2.3%)
Savoury biscuits – high fat	16.1	↓<0.0001	4.5	27.9	
Butter and dairy fats	15.9	0.155	7.3	10.6	
Muesli and fruit bars	14.4	↓ <0.0001	4.5	31.7	
Tea and coffee	14.1	↑<0.0001	50.9	361.0	
Jam and conserves	13.2	↓0.001	1.9	14.6	
Meat pies and savoury pastries	12.7	↑0.002	22.6	177.5	5 (2.6%)
Salad dressings	10.8	↑<0.0001	1.8	16.5	
Tomato and BBQ sauce	10.5	↑<0.0001	3.0	28.4	
Honey and sugar syrups	9.5	↓0.0004	1.6	16.7	
Ice blocks and sorbet	8.3	↓0.0003	9.2	110.4	
Extruded snacks	8.1	0.333	2.5	30.7	
Pizza	7.4	↑<0.0001	11.6	156.0	12 (1.3%)
Gravies	7.3	↑0.007	5.0	68.7	
Toppings	6.9	0.739	3.1	44.3	
Corn chips and popcorn	6.5	0.329	2.2	34.3	
Diet soft drinks	6.4	↑0.0002	24.4	378.9	
Hamburgers/chicken burgers	6.0	↑0.0002	10.0	165.4	
Sweet pies and pastries	5.9	↑<0.0001	6.9	117.2	
Chocolate spreads	5.6	↓<0.0001	0.8	14.0	
All 'extra' foods (including those consumed by <5% of 2–18 years olds)	99.8	0.331	725.3	726.9	40.9%

Webb K L et al. (2006) Consumption of 'extra' foods (energy-dense, nutrient poor) among children aged 16-24 months for western Sydney, Australia, Public Health Nutrition: 9(8) 1035-1044

Quality Rating: Neutral

Method: RCT; 429 children in Asthma Prevention Trial, using 3 day weighed food records.

Summary:

Table 1 'Extra' foods consumed, categorised by main food group, among 429 children aged 16–24 months

Food groups*	Percentage of consumers†	Mean per capita intake ($g\,day^{-1}$)‡	Percentage of total energy‡
Cereal-based products§	90	23.1	8.0
Sweetened non-milk beverages¶	70	87.1	4.7
Fats and oils	94	5.8	3.4
Confectionery	60	8.1	3.0
Fried potatoes‖	58	10.4	2.5
Snack foods	39	3.7	1.8
Sugar and products	63	6.7	1.1
Ice cream	26	5.4	1.0
Sauces and condiments	54	4.6	0.5
Miscellaneous	77	2.3	0.5
All 'extra' foods	99.9	157	26.5

*Foods were grouped as in the Australian 1995 National Nutrition Survey[34].
†A consumer was any child who consumed 'extra' foods at least once during the 3-day recording period.
‡Derived over all participants, rather than consumers only.
§Includes biscuits, cakes, pastries and other foods in which cereal is the major ingredient, such as pies, pasties, pizza and hamburgers.
¶Includes cordials, soft drinks and fruit drinks, but excludes fruit juice.
‖Fried potatoes include hot chips, wedges, hash browns, potato scallops and gems.

2) DEMOGRAPHIC INFLUENCE

Gracey, M. (2000). "Historical, cultural, political, and social influences on dietary patterns and nutrition in Australian Aboriginal children." American Journal of Clinical Nutrition 72(5 Suppl): 1361S-1367S. [2]

Quality Rating: Negative

Search Method: Not specified

Quote:

The contemporary diets of Australian Aborigines are energy rich and contain high amounts of fat, refined carbohydrates, and salt; they are also poor in fiber and certain nutrients, including folate, retinol, and vitamin E and other vitamins. (p1, Abstract)

Aboriginal food and diets before European settlement…

Animal foods that were hunted included mammals…, reptiles …, birds …, and fish in rivers and along the coast. The eggs of many of these creatures were important…Insects such as honey ants and wild bees provided honey that was and still is popular in remote areas—this was an important carbohydrate source. Witchetty grubs are high in fat and have a composition similar to that of olive oil— these grubs are eaten raw or are lightly cooked in the ashes of a small open fire. The fatty parts of animals such as goannas were traditionally very popular after being cooked whole on red hot coals on the ground and turned occasionally so that the skin could be cooked; in northern Australia, food may be steamed while wrapped in leaves (or, today, in metal foil). The seashore and river estuaries provided not only fish, sharks, stingrays, and dugongs, but also crabs, oysters, mussels, other shellfish, and snails. Inland waters were very important for fish, crustaceans, turtles, snakes, and birds and for plants such as water lilies. (p2)

Effects of European colonization…

Aborigines in remote areas tended to live in makeshift camps and were provided by religious missions or government agencies with bread, tea, milk or full-cream dried milk, refined flour, and refined white sugar. Their diets in these camps and in government "feeding stations" were lacking in fresh fruit and vegetables and were likely to be deficient in vitamin A, vitamin C, folate, and calcium (p2)

Aboriginal child health since the late 1960s…

The maintenance of a traditional lifestyle appears to be related to the prevalence of breast-feeding, but the determination of recent breast-feeding ranges is hampered by inadequate information… Traditionally, Aboriginal mothers breast-fed their babies frequently and exclusively for ≥6 months and continued to breast-feed for up to 4 years… Among 127 Aboriginal mothers studied in Perth in the early

1980s, 82% initiated breast-feeding but only 50% were still breast-feeding at 12 weeks, although 19% were still breast-feeding at 12 months, but only 6% were giving breast milk as the sole milk feed. (p3)

Aboriginal child nutrition and later health consequences?...

the development of impaired glucose tolerance, hyperlipidemia, and hyperinsulinemia can be rapid in previously traditional Aboriginal people. In a very remote community living on the Timor Sea coast in far northwest Australia, the change from a traditional diet (including plentiful seafood), supplemented by a mission fruit and vegetable garden up until the 1970s, then followed by the introduction of store-bought foods led to an increased prevalence of these health problems… Foods available in Aboriginal community food stores are usually limited and the diets are monotonous; they often lack fresh fruit and vegetables and include large amounts of refined flour, sugar, sliced white bread, sweetened soft drinks, confectionery, fried take-out food, and fatty cuts of meats, and cigarettes are popular purchases. (p4)

Intakes of energy, sugars, and fat were excessive, whereas the apparent intakes of dietary fiber and several nutrients including folate, calcium, retinol, carotene, riboflavin, and vitamin E were low. White sugar, flour, bread, and meat provided >50% of apparent dietary energy (38). Fried and heavily salted snack foods and take-out food like fried chicken (normally with the skin), French fries, meat pies, and crumbed sausages were very popular. Rates of consumption of sweetened carbonated beverages were very high and confectionery, chocolate, and ice pops or ice cream are usually consumed by children. (p4)

Some information about dietary fat intakes in other Australian children

The 1985 National Dietary Survey of Schoolchildren (aged 10–15 y) showed that the following were the major sources of dietary fats for Australian boys and girls: milk and milk products (26.2 g for boys, 23.8 g for girls), meat and meat products (23.7 and 22.2 g), fats (16.4 and 17.0 g), cereals and cereal products (14.2 and 15.2 g), vegetables (6.4 and 6.3 g), snack foods (3.8 and 4.9 g), confectionery (2.6 and 3.3 g), eggs (2.2 g and 2.3 g), nuts and seeds (1.8 and 2.0 g), condiments and soups (1.4 and 1.6 g), and all other foods (1.3 and 1.4 g). (p4)

U.1.4 What is the relationship between dietary intake and physical activity in promoting health and wellbeing?

Search Results

The initial search resulted in 4271 articles being retrieved. Of these 89 were duplicates, 99 were not studies, 1339 were not a relevant population and 2714 were not a relevant outcome. Thirty studies were retrieved and of these nine the body of evidence statements.

There were no review articles that addressed the general issue of the need for balance of dietary intake and physical activity for promotion of health and wellbeing. Sufficient evidence was found only to make evidence statements about the health promotion interventions combining diet and physical activity for preventing obesity in children and in adults, and for reducing the incidence of type II diabetes in adults. Systematic reviews were also obtained considering the relationship between diet and physical activity and reduction in weight after childbirth and also for the relationship between diet and physical activity in reducing cardiovascular risk factors, however the required number of studies (five) was not found in these reviews. There were no reviews evaluating DALY, QALY, muscle strength, growth and development in children, life expectancy or mortality. The small number of studies retrieved for consideration in this review reflects an overall health focus in the recent literature on treatment rather than prevention.

22. ENERGY BALANCE (UI.4)

Evidence Statements

22. ENERGY BALANCE (U1.4)

22.1 DIETARY INTAKE and PHYSICAL ACTIVITY in promoting health and wellbeing

What is the relationship between dietary intake and physical activity in promoting health and wellbeing?		
Evidence Statement		Combined diet and physical activity interventions is associated with reduced risk of overweight and obesity in children.
Grade of recommendation		C
Component	**Rating**	**Notes**
Evidence Base	Good	Two Level I meta analyses (34 and 22 RCTs) and Three Level II reviews (74 RCTs, 13 undefined), however intervention programs varied widely in content.
Consistency	Satisfactory	Some programs successful however evidence is inconsistent (2 Protect; 3 No effect).
Clinical impact	Satisfactory	Limited BMI reduction in some studies.
Generalisability	Good	Generally US or western populations. Impacts on infrastructure such as policy and schools may not be relevant.
Applicability	Good	Difference in schooling and healthcare systems may make some interventions in other country inapplicable.

The studies that make up the body of evidence are listed below and summarised in Table 22.1.

There is weak evidence that combined diet and physical activity interventions may prevent overweight and obesity in children however heterogeneity in studies makes direct clinical interpretation difficult. The number of reviews focussing on the area of preventing childhood obesity reflects the current health focus in this area. Programs vary significantly in their content and duration. Some are very broad educational programs implemented at a family or school level while others provide an individual approach. While there appears some evidence overall that a combination of diet and physical activity can have a positive impact on body mass index conclusions are clearly limited by the heterogeneity in study approaches.

References:

Bautista-Castana, I., Doreste, J. & Serra-Majem, L. 2004, "Effectiveness of interventions in the prevention of childhood obesity" *European Journal of Epidemiology*, vol. 7, pp. 617-622.

Campbell, K. & Hesketh, K. 2007, "Strategies which aim to positively impact on weight, physical activity, diet and sedentary behaviours in children from zero to five years. A systematic review of the literature", *Obesity Reviews*, vol. 8, no. 4, pp. 327-38.

Kamath, C., Vickers, K., Ehrlich, A., McGovern, L., Johnson, J., Singhal, V., et al. 2008, "Clinical review: behavioral interventions to prevent childhood obesity: a systematic review and metaanalyses of randomized trials", *Journal of Clinical Endocrinology & Metabolism,* vol 93, no. 12. pp. 4606-15.

Stice, E., Shaw, H. & Marti, C. N. 2006, "A meta-analytic review of obesity prevention programs for children and adolescents: the skinny on interventions that work", *Psychological Bulletin*, vol.5, pp. 667-691.

Summerbell C., Waters, E., Edmunds, L., Kelly, S., Brown, T. & Campbell K. 2005, "Interventions for preventing obesity in children", *Cochrane Database of Systematic Review*s, vol.3, no. 3.

22.2 DIET and PHYSICAL ACTIVITY and the prevention of adult obesity

What is the relationship between dietary intake and physical activity in promoting health and wellbeing?		
Evidence Statement		Combined diet and physical activity interventions is associated with reduced risk of overweight and obesity in adults.
Grade of recommendation		C
Component	**Rating**	**Notes**
Evidence Base	Good	There is only one level I review of 7 studies presenting conflicting results.
Consistency	Satisfactory	Only 3/7 studies showed a significant protective effect.
Clinical impact	Satisfactory	Of the studies showing positive effects, weight loss ranged from 0.9-1.8Kg over a 4.5m to 4 year interventions.
Generalisability	Good	Generalisable to Australian Adult population.
Applicability	Good	Studies are in relevant populations including Australia.

The studies that make up the body of evidence are listed below and summarised in Table 22.2.

There is conflicting evidence that combined diet and physical activity interventions may prevent overweight and obesity in children however heterogeneity in studies makes direct clinical interpretation difficult. As with the childhood studies, the programs considered in this review varied significantly in their approach with group, individual, or correspondence counselling on various dietary and activity approaches delivered at differing intervals for different periods of time. Authors comment they were surprised to find such a limited number of studies however suggest that there is currently a gap before more recently implemented prevention programmes will be published. To date the focus has been more on treatment which is not the purpose of this SLR.

Reference:

Lemmens, V., Oenema, A., Klepp, K, Henriksen, H., Brug, J. & Lemmens, V. 2008, "A systematic review of the evidence regarding efficacy of obesity prevention interventions among adults", *Obesity Reviews*, vol. 9, no. 5, pp. 446-55.

22.3 DIET and PHYSICAL ACTIVITY and the prevention of type 2 diabetes

What is the relationship between dietary intake and physical activity in promoting health and wellbeing?		
Evidence Statement		Lifestyle interventions combining diet and physical activity interventions are associated with reduced risk of developing type 2 diabetes in adults.
Grade of recommendation		B
Component	**Rating**	**Notes**
Evidence Base	Good	One Level I systematic review containing 8 RCT studies.
Consistency	Good	7 out of 8 studies showed protections. The one study suggesting a harmful effect also had CIs including 1.0.
Clinical impact	Good	Overall RR 0.63. 2 studies of the 8 had CI's including 1.0.
Generalisability	Good	Many subjects were already overweight, however results should be generalisable.
Applicability	Good	Applicable to the Australian healthcare setting with few caveats.

The studies that make up the body of evidence are listed below and summarised in Table 22.3.

As in the case of the obesity studies, clearly to date the focus has been on the treatment rather than the prevention of type 2 diabetes therefore only one review was retrieved for this body of evidence. This Level I systematic review containing eight studies combining diet and exercise to result in weight loss and prevent diabetes. The exercise approaches varied between trials with some giving only advice while others provided supervised training. Dietary interventions focused on caloric reduction. The similarity in these trials allowed combined analysis showing a favourable overall effect with six of eight studies having a significant point estimate and confidence interval.

Reference:

Orozco Leonardo, J., Buchleitner A., M., Gimenez-Perez, G., Roqué i Figuls, M., Richter, B. & Mauricio, D. 2008, "Exercise or exercise and diet for preventing type 2 diabetes mellitus", *Cochrane Database of Systematic Reviews*, vol., no. 3.

Table 22.1 Summary of studies on dietary intake/physical activity and overweight & obesity in children

Reference [1]	Kamath. 2008 [3193]	Summerbell 2005 [2263]	Campbell 2007 [206]	Bautista-Castano 2004 [2318]	Stice 2006 [2340]
Type of study [2]	Meta-analysis (34 RCTs)	Systematic Review (22 RCTs)	Systematic Review (9 RCTs)	Systematic Review (14 RCTs)	Meta-analysis (51 RCTs, 13 unspecified)
Level of evidence [3]	I	I	III-2	III-2	III-2
Intervention/ comparator [4]	"increased physical activity, increased healthy diet"	diet and/or physical activity in school, community or clinic-based setting	Family/home, group, preschool/childcare, primary care and mixed interventions	diet and PA in 9 studies, multiple approaches to nutritional education, behaviour change, including parental participation and school meal changes in some cases	parental involvement, psychoeducational content, dietary improvement, increased activity and reduced sedentary behaviour
N [5]	32,003	188	12595	3/14 had 50-100 subjects, 6/14 had between 100-500, 1/14 had between 500-1000 and 4/14 had >1000 subjects.	23,172
Population/study information [6]	M+F 2-18 years	M+F Children < 18	M+F, 0-5 years	M+F, 0-18 years	M+F, up to 22 years old
Quality [7]	positive	positive	Negative	Negative	Positive
Results [8]	BMI change -0.02 (-0.06,0.02kg/m2)	Of the 6/10 long term studies combining diet and physical activity interventions, 5 showed no effect. Of the 8/12 short term studies combining diet and physical activity interventions none showed a positive effect.	Few studies assessed relevant outcomes. "Most studies were able to show some level of effectiveness on some obesity-promoting behaviours in children".	9/14 used a diet and PA approach, outcome rated only as Effective (yes/no/girls only/boys only). 6/9 rated not effective, 1/9 rated as effective, 2/9 effective in girls only.	"The average effect size across all studies was very small (r=0.04), but was significantly larger than zero (z=2.94, p<0.01). The r's for effect sizes ranged from -0.24 to 0.50. Onl 13 of these interventions, or 21% of the 61 programs evaluated found sign
Effect on Risk (Increase/None/Protect)	None	None	Protect	None	Protect
Clinical importance [9]	4	4	4	4	4
Clinical relevance [10]	1	1	5	1	1
Generalisable	Uncertain	Yes	Uncertain	Yes	Yes
Applicable	Yes	Yes	Uncertain	Yes	Yes

Table 22.2 Summary of studies on dietary intake/physical activity and overweight & obesity in adults

Reference [1]	**Lemmens 2008 [44]**
Type of study [2]	Systematic Review (7RCTs)
Level of evidence [3]	I
Intervention/ comparator [4]	Diet and/or physical activity versus control of usual care, generic or no intervention. various dietary and physical activity interventions including individual and/or group counselling on diet and supervised or group physical activity programs, one study
N [5]	2,406
Population/study information [6]	M+F adults BMI<30; US, Netherlands, Australia, Sweden
Quality [7]	Negative
Results [8]	3/7 combined diet and exercise studies had a significantly protective (reduction in BMI 0.91-1.4kg/m2 over 4months to 3 years). Only 1/7 had a long-term follow-up (4.5 years)
Effect on Risk (Increase/None/Protect)	Protect
Clinical importance [9]	4
Clinical relevance [10]	1
Generalisable	Yes
Applicable	Yes

Table 22.3 Summary of studies on dietary intake/physical activity and Type 2 diabetes

Reference [1]	**2254 Orozoco 2008**
Type of study [2]	Systematic Review (8 RCTs)
Level of evidence [3]	I
Intervention/ comparator [4]	Exercise + diet compared with control
N [5]	2,241
Population/study information [6]	M+F adults in USA, Finalnd, UK, Italy, Japan, China and India
Quality [7]	Positive
Results [8]	RR of developing diabetes significantly reduced 0.63(0.49,0.70) OR also reduced 0.51(0.40,0.65)
Effect on Risk (Increase/None/Protect)	Protect
Clinical importance [9]	1
Clinical relevance [10]	1
Generalisable	Yes to people at high risk of diabetes
Applicable	Yes

Summary of studies not included in Body of Evidence statements

The following diet health relationships had too few studies to develop a body of evidence statement.

Diet and exercise for weight reduction in women after childbirth.

One systematic review examined the effects of diet or exercise or both for weight reduction after childbirth. Only four studies included both diet and exercise. Women who took part in a diet and exercise program n=169, WMD -2.89kg (95% CI -4.83, -0.95) lost significantly more weight than those in usual care (Amorin 2009).

Diet and exercise in reducing Cardiovascular risk

One systematic review examined the effects of 'lifestyle interventions' (in this review restricted to diet and/or exercise) on cardiovascular risk scores, blood pressure, lipid levels, weight or body mass index, and morbidity and mortality. Only four studies considered combined diet and exercise interventions. Two of the four studies showed small significant effects in reducing blood pressure, one of these studies also showed a small significant reduction in total cholesterol and BMI. The remaining two studies suggested only an improvement in diastolic blood pressure in men (Fleming 2008).

References

Amorim Adegboye Amanda, R., Linne Yvonne, M. & Lourenco Paulo Mauricio, C. 2007, "Diet or exercise, or both, for weight reduction in women after childbirth", Cochrane Database of Systematic Reviews, vol., no. 3.

M., Fleming, P. & Godwin, M. 2008, "Lifestyle interventions in primary care: systematic review of randomized controlled trials", Canadian Family Physician, vol. 54, no. 12, pp. 1706-13.

23. BREASTFEEDING (UI.5)

Evidence Statements

23. BREASTFEEDING (U1.5)

Search results

The initial search of the databases included 985 references for *U1.5 What are the benefits of breastfeeding (partial and exclusive) and the risks of not breastfeeding (any and exclusive), to infants and mothers, both in the short term and long term?* The detailed search is included in a separate document on searches. 292 reviews were retrieved and 101 were included, but only eight higher quality reviews were used to form the body of evidence statements. Some additional papers from the 1.7 Endnote were used.

Sufficient evidence was found to make body of evidence statements for breastfeeding benefits and risks for mothers and infants, as detailed below. There were no recent good quality reviews of supplements. The majority of studies were excluded because they were not reviews.

A summary of non-systematic reviews that were recent have been included as an appendix. There was some overlap between this question and the *s*earches for question: *U1.7 What nutritional factors are important in optimising breastfeeding outcoumes?*; and consequently some reviews from U1.7 have been used to inform the body of evidence statements in this review.

23.1 BREASTFEEDING and ADULT DISEASE OUTCOMES

What are the benefits of breastfeeding (partial and exclusive) and the risks of not breastfeeding (any and exclusive), to infants and mothers, both in the short term and long term?		
Evidence statement		Being breastfed initially, particularly exclusively breastfed is associated with lower total and LDL concentrations in adult life.
Grade		C
Evidence statement		Being breastfed in infancy is associated with lower systolic and diastolic blood pressure up to adolescence.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	2 Systematic reviews (2P) comparing adult chronic disease outcomes for infants who were breastfed versus formula fed, with both showing protection. The review on adult cholesterol levels included 13 cohort and 4 cross-sectional studies. The review on blood pressure included 2 RCTs, 9 cohorts and 4 cross-sectional studies.
Consistency	Good	Majority of studies consistent for both outcomes. In some

		studies the infant feeding group definitions of breastfeeding versus formula feedings were not completely exclusive.
Clinical impact	Good	Important at the population level. Meaningful reduction in plasma cholesterol level in adults after 17 to >50 years follow-up, of approx. 0.4mmol/L reduction for those breastfed, up to 0.15mmol/L reduction for those exclusively breastfed compared to those formula fed in infancy. From the meta-analysis, mean reduction was found in systolic (1.4 mmHg) and diastolic blood pressure (0.5 mmHg reduction) in breastfed versus bottle fed infants at up to 17 years.
Generalisability	Excellent	Breastfeeding definitions and rates are applicable to Australian women.
Applicability	Excellent	Studies conducted in Northern & Southern Europe, Eastern Europe, USA, South America, New Zealand, UK, South Africa and Australia and majority are directly applicable to Australia.

The studies included in the body of evidence statement are shown in Table 23.1.

References

Owen, C. G., Whincup, P. H., Kaye, S. J., Martin, R. M., Davey Smith, G., Cook, D. G., Bergstrom, E., Black, S., Wadsworth, M. E. J., Fall, C. H., Freudenheim, J. L., Nie, J., Huxley, R. R., Kolacek, S., Leeson, C. P., Pearce, M. S., Raitakari, O. T., Lisinen, I., Viikari, J. S., Ravelli, A. C., Rudnicka, A. R., Strachan, D. P., & Williams, S. M. 2008, "Does initial breastfeeding lead to lower blood cholesterol in adult life? A quantitative review of the evidence", *American Journal of Clinical Nutrition*, vol. 88, no. 2, pp. 305-14.

Table 23.1 Summary used to make evidence statements for breastfeeding and adult disease onset.

STUDY DETAILS (Review)	**Owen et al. 2008** [34]
Reference	
Affiliation/source of funds	University of London, University of Bristol, Umea University, Royal Free and University College Medical School, University of Southhampton, Southhampton General Hospital, State University of new York, The George Institute Sydney, Children's Hospital Zagreb, John Radcliffe Hospital Oxford, Turku University Central Hospital, University of Amsterdam, University of Otago; Supported by the British Heart Foundation Project.
Study design	Meta Analysis (4 cross sectional, 2 historical cohort, 10 prospective cohort, 1 retrospective cohort).
Level of evidence	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Date of search	1950 to 2007
Number of studies	17
Total number of participants	17 498 (12 890 breastfed, 4608 formula fed).
Population characteristics	Formula and breast fed infants followed up until 17 - 71 yrs; in 7 studies it was possible to compare groups of subjects who were exclusive breastfeeders and bottle feeders, in the remaining 10 studies the infant feeding groups were not completely exclusive Northern Europe, Eastern Europe, USA, South America, New Zealand.
Range of exposure	Initital infant feeding practices
Length of follow-up	16 to 71 years
Outcome(s) measured	PRIMARY: 1. Concentrations of total blood cholesterol in adult life.
INTERNAL VALIDITY	
Databases included in search	Medline, Embase, Web of Science.
Statistical analysis methods	Fixed effect models, mean difference, SE, chi-squared tests, meta-regression and sensitivity analysis.
Overall quality assessment	P

(Positive/Negative or Neutral) plus descriptive)	
RESULTS	
Outcome	10/17 studies related breastfeeding to a lower mean concentration of total cholesterol in later life than was associated with formula feeding. There was evidence of marked heterogeneity between studies (X^2=30, P=0.02). In a fixed effects model the breastfed subjects had marginally lower total cholesterol then did formula fed subjects mean diff: -0.04 mmol/L (95% CI 0.08-0.00 mmol/L). The pooled estimate from a random effects model was similar -0.05 mmol/L (95% CI -0.12-0.02 mmol/L). The mean difference was unaffected by exclusion of one study with nearly half of the statistical weight or after adjustment for age, current SEP, BMI, smoking status or all. The overall mean difference in total cholesterol from the 7 studies reporting data for exclusive breast and bottle feeding was stronger mean difference -0.15 mmol/L (95% CI: 0.23- -0.06 mmol/L) than that in the remaining 10 studies that did not report exclusive feeding. The mean differnce was little affected by adjustment on a within-study basis for age, current SEP, BMI, and smoking status.
EXTERNAL VALIDITY	
Generalisability	y
Applicability	y
Comments	
Conclusion	Initial breastfeeding (particularly when exclusive) may be associated with lower blood cholesterol concentrations in later life. Moves to reduce the cholesterol content of formula feeds below those of breast milk should be treated with caution.

23.2 BREASTFEEDING AND MATERNAL AND INFANT OUTCOMES

What are the benefits of breastfeeding (partial and exclusive) and the risks of not breastfeeding (any and exclusive), to infants and mothers, both in the short term and long term?		
Evidence statement		Infants who are exclusively breastfed for six months experience less morbidity from gastrointestinal infection than those who are mixed breastfed as of three or four months.
Grade		B
Evidence statement		Infants, from either developing or developed countries, who are exclusively breastfed for six months or longer do not have deficits in growth compared to those who are not exclusively breastfed.
Grade		B
Evidence statement		There are no apparent risks in a general recommendation for exclusive breastfeeding for the first six months of life, in both developing and developed-countries. However, infants should still be managed individually in order to achieve sufficient growth and minimise adverse outcomes.
Grade		B
Evidence statement		Exclusive breastfeeding for 6 months or more prolongs lactational amenorrhea for mothers.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Excellent	8 Systematic reviews [3 are Cochrane; 3 with meta-analysis (5P, 1O, 2N)]; 5 protective effect on breastfeeding success, 1 had no results and 1 found maternal perceived insufficient milk supply increased risk of lactation failure.
Consistency	Good	Definitions of breastfeeding (exclusive, partial, any) vary across studies. Consistent for support prolonging breastfeeding. Some of the same studies covered by the reviews.
Clinical impact	Good	For provision of support, the RR for ceasing breastfeeding was approx.0.65 to 0.9. When expressed as odds ratios for continued breastfeeding the ORs for support ranged from 1.9 to 5.2.
Generalisability	Excellent	Breastfeeding definitions and rates are applicable to Australian women.
Applicability	Good	While some reviews include studies conducted in developing countries, only those applicable to developed countries have been applied in developing the BOEs.

The studies included in the body of evidence statement are shown in Table 23.2.

References

Abdulwadud Omar, A., & Snow Mary, E. 2007, "Interventions in the workplace to support breastfeeding for women in employment", *Cochrane Database of Systematic Reviews*, vol., no. 3.

Baird, J., Cooper, C., Margetts, B. M., Barker, M., Inskip, H. M., & U. o. S. Food Choice Group 2009, "Changing health behaviour of young women from disadvantaged backgrounds: evidence from systematic reviews", *Proceedings of the Nutrition Society*, vol. 68, no. 2, pp. 195-204.

Bhutta, Z. A., Ahmed, T., Black, R. E., Cousens, S., Dewey, K., Giugliani, E., Haider, B. A., Kirkwood, B., Morris, S. S., Sachdev, H. P., Shekar, M., Maternal, G. Child Undernutrition Study, Bhutta, Z. A., Ahmed, T., Black, R. E., Cousens, S., Dewey, K., Giugliani, E., Haider, B. A., Kirkwood, B., Morris, S. S., Sachdev, H. P. S., & Shekar, M. 2008, "What works? Interventions for maternal and child undernutrition and survival.[see comment]", *Lancet*, vol. 371, no. 9610, pp. 417-40.

Britton, C., McCormick Felicia, M., Renfrew Mary, J., Wade, A., & King Sarah, E. 2007, "Support for breastfeeding mothers", *Cochrane Database of Systematic Reviews*, vol., no. 1.

de Oliveira, M. I., Camacho, L. A., & Tedstone, A. E. 2001, "Extending breastfeeding duration through primary care: a systematic review of prenatal and postnatal interventions (Structured abstract)", *Journal of Human Hypertension*, vol., no. 4, pp. 326-343.

Gatti, L. 2008, "Maternal perceptions of insufficient milk supply in breastfeeding", *Journal of Nursing Scholarship*, vol. 40, no. 4, pp. 355-363.

Kramer Michael, S. & Kakuma, R. 2002, "Optimal duration of exclusive breastfeeding", *Cochrane Database of Systematic Reviews*, vol., no. 1.

Szajewska, H., Horvath, A., Koletzko, B., & Kalisz, M. 2006, "Effects of brief exposure to water, breast-milk substitutes, or other liquids on the success and duration of breastfeeding: a systematic review", *Acta Paediatrica*, vol. 95, no. 2, pp. 145-52.

Table 23.2 Summary used to make evidence statement for breastfeeding and maternal and infant outcome

STUDY DETAILS (Review)	Szajewska et al. 2006 [151]	Kramer et al. 2002 [584]	Bhutta et al. 2008 [55]	Britton et l. 2007 [585]
Affiliation/source of funds	Medical University of Warsaw, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University of Munich.	McGill University, WHO Expert Committee on the optimal duration of exclusive breastfeeding.	Aga Khan University Bangladesh, Centre for Health and Population Research, Johns Hopkins Bloomberg School of Public Health USA, London School of Hygiene and Tropical Medicine, University of California, Federal University of Rio Grande de Sul Brazil, Sitaram Bhartia Institute of Science and Research India, World Bank Washington, Save the Children UK, Emergency Nutrition Network, International Food Policy Research Institute, Food for Education Programmes, Global Alliance against malnutrition, Bill and Melinda Gates Foundation, UNICEF Innocenti Research Centre.	University of York, UK.
Study design	Systematic Review	Meta-Analysis	Systematic Review	Meta Analysis
Level of evidence	III-1 Evidence obtained	III-2 Evidence obtained from	III-2 Evidence obtained from	III-2 Evidence obtained from

	from well-designed pseudorandomised controlled trials (alternate allocation or some other method).	comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.	comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.	comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Date of search	1966-2004	Prior to 1966 - 2000	NS	1966-2005
Number of studies	1	22 (11 from developing and 11 from developed countries).	34	34
Total number of participants	170 infants (experimental group = 83; control group = 87).	9998	NS	29 385 mother - infant pairs.
Population characteristics	OI	Lactating mothers and their healthy, term, singleton infants from developed and developing countries.	Breastfed and non breastfed infants from developing countries.	Pregnant women intending to breastfeed, postpartum women intending to breastfed and women breastfeeding their babies; Canada, USA, UK, Brazil, Bangladesh, Australia, India, Nigeria, Italy, Iran, Netherlands, Belarus, Mexico, Sweden.
Range of exposure	Experimental group received 5% glucose water from bottle, after breastfeeds, during the first 3 days of life.	To assess the effects of exclusive breastfeeding for 6 or more vs 3-4 mo with continued mixed breastfeeding until at least 6 mo.	Effect of promotion strategies on exclusive breastfeeding rates for infants younger then 6 mo and on continued breastfeeding up to 12 mo.	Intervention: Pregnant or lactating women intending to breastfed receiving contact with an individual or individuals (professional or volunteer) offering support which is supplementary to

				standard care with the purpose of facilitating continued breastfeeding Comparator: Mothers receiving usual postnatal care which varies between and within countries.
Length of follow-up	4 mo	NS	0-6 mo	Up to 9 mo post partum
Outcome(s) measured	Proportion of exclusively breastfed infants between birth and 6 mo, the proportion of infants receiving any breastmilk at fixed time points between birth and 6 mo, the proportion of infants still being breastfed at the end of their first year of life, breastfeeding duration, proportion of infants receiving infant formula between birth and 6 mo.	All infant and maternal health outcomes; infant outcomes especially growth (weight, length, head circumference, z scores, weight-for-age, length-for-age, weight for age, infections, morbidity, mortality, micronutrient status, neuromotor and cognitive development, asthma, atopic eczema, other allergic diseases, type 1 DM, blood pressure, adult chronic diseases. Maternal outcomes especially postpartum weight loss, duration of lactational amennorrhea, chronic diseases (osteoporosis, breast and ovarian cancer).	Mortality, breastfeeding duration, breastfeeding pattern (exclusive, partial, predominant).	PRIMARY: 1. Effect of the interventions on duration of any breastfeeding to specified points in time; 2. Stopping feeding before 4 to 6 wks and 2, 3, 4, 6, 9 and 12 mo SECONDARY: 1. Exclusive breastfeeding; 2. Measures of neonatal and infant morbidity; 3. Measures of maternal satisfaction with care or feeding method.
INTERNAL VALIDITY				
Databases	Medline, Embase, Cinahl,	Medline, Oldmedline, Cinahl,	Cochrane Library, ExtraMed,	Cochrane Pregnancy and

included in search	Cochrane.	EBM Reviews -Best Evidence, Sociofile, Cochrane, CAB Abstracts, EMBASE Psychology, EconLit, IMEMR, AIM, LILACS, Healthstar.	WHO Reproductive Health Library.	Childbirth Group's Trials Register, medline, Embase, MIDIRS.
Statistical analysis methods	Intention to treat analysis, p value.	Controlled clinical trials: Adequacy of randomization and concealment, losses to follow up analysis, measurement of outcome, 5 point Jadad scale Observational studies were assessed for control for confounding, losses to follow up, and assessment of outcomes as follows: for growth and morbidity outcomes, losses to follow up, assessment of outcome. All studies were stratified according to study design (controlled trials vs observational), provenance (developed vs developing), timing of feeding comparison (3 to 7 months vs prolonged (> 6 months)).	Multiplicative model, mortality RR, stunting OR.	RevMan 2003; Relative risks; random effects model; subgroup analyses.
Overall quality assessment (Positive/Negative	P	P	O	

or Neutral) plus descriptive)				
RESULTS				
Outcome		Indicators of child health (GIT infection, development of asthma, allergies, iron status), growth and development, and on maternal health (resumption of menses, postpartum weight loss). Comparison one: controlled trials of exclusive versus mixed breastfeeding for 4 - 6 mo, developing countries and Comparison two: observational studies of exclusive versus mixed breastfeeding for 3 -7 months, developing countries and Comparison three: observational studies of prolonged (more than 6 mo) exclusive versus mixed breastfeeding, developing countries are not relevant to Australia. Comparison 4 is relevant to the Australian population: Observational studies of exclusive versus mixed breastfeeding for 3-7mo in	Beginning breastfeeding within the first days after birth lowers mortality even in exclusively breastfed infants. One review showed that all forms of extra support increased the duration of 'any breastfeeding' with the RR for stopping any breastfeeding before 6 mo being 0.91 (95% CI 0.86-0.96). All forms of support affected the duration of exclusive breastfeeding more strongly than the likelihood of any breastfeeding RR 0.81 (0.74-0.89). Lay and professional support extended breastfeeding duration (RR before 4-6 wks 0.65 (0.51-0.82); RR before 2 months 0.74 (0.66-0.83).Further reviews reported that with individual counselling the OR of exclusive breastfeeding were increased in the neonatal period (15 studies; OR 3.45 (95% CI 2.2-5.42) $p<0.0001$;	There is a beneficial effect on the duration of any breastfeeding up to 6 mo with the implementation of any form of extra support RR 0.91 (95% CI 0.86- 0.96). Authors divided trials into 3 categories - high (> 80%), intermediate (60-80%) or low (<40%) initiation rates in the local area. Analysis of the trials conducted in settings with immediate initiation demonstrated all forms of support had a significant benefit on breastfeeding RR 0.92 (95% CI 0.85- 0.98), whereas there was no significant effect where there were high or low breastfeeding initiation rates RR 0.91 (95% CI 0.81- 1.01) and RR 0.88 (95% CI 0.69-1.12). The effect of any support on mothers exclusively breastfeeding is greater than on women continuing any form of

		developed countries. Studies were heterogeneous with a WMD of -12.45 (95% CI -23.46 to -1.44) g/mo & should be interpreted with caution, although even the lower 95% confidence limit is compatible with a lower weight gain in the EBF group. Given the large weight gains in both groups in the Belarussian study, the higher gain in the MBF group is not necessarily a beneficial outcome. Heinig 1993 and Kramer 2000a also reported on weight gain between 6 -9 mo (outcome two) (significant heterogeneity), (P = .04) and dominated by the larger size of the Belarussian study. The pooled WMD was -2.26 (95% CI -16.94 to +12.42) g/mo. Akeson 1996a, Heinig 1993, and Kramer 2000a reported on weight gain from 8 - 12 months (outcome three); the WMD was -1.82 (95% CI -16.72 to +13.08) g/mo, which excludes a reduced length gain in the EBF group of 5%	random effects) and at 6 mo (9 studies; OR 1.93 (95% CI 1.18-3.15) p<0.0001. Group counselling increased odds of exclusive breastfeeding in the neonatal period (6 studies; OR 3.88 (95% CI2.09-7.22) p<0.0001; random effects) and at 6 mo (5 studies; OR 5.19 (95% CI 1.9-14.15) p<0.00001; random effects). A study on a national mass media campaign in Honduras reported that it increased exclusive breastfeeding from 48-70% at 1 mo, from 24-31% at 4 mo, from 7-12% at 6 mo. The WHO growth reference study showed that infants exclusively breastfed were on average 360 g and 100 g heavier at 4 and 6 mo then predominantly non breastfed children on whom the US NCHS growth curves were based. Exclusive breastfeeding reduced HIV transmission compared with partial was reported in 1 study and a further study showed that HIV-free survival did not	breastfeeding RR 0.81 (95% CI 0.74- 0.89). Professional support vs usual care showed professional support to be effective at 4 mo only RR in 5 trials 0.78 (95% CI 0.67-0.91). The overall effect of extra support on stopping any breastfeeding did not reach statistical significance. Professional support resulted in a beneficial effect on exclusive breastfeeding RR in 16 trials 0.94 (95% CI 0.87 -1.01). Professional support showed to be beneficial on exclusive breastfeeding rates RR 0.91 (95% CI 0.84-0.98). Trials using lay people to conduct breastfeeding interventions demonstrated a significant decrease in breastfeeding cessation RR 0.86 (95% CI 0.76- 0.98). Combined lay and professional support vs usual care showed a significant reduction in cessation of any breastfeeding RR 0.84 (95% CI 0.77- 0.92) especially in

		of the mean and 10% of the SD for the Belarussian study. For length gain at 3 - 8 months (outcome four), the studies again show significant (P < .01) heterogeneity. Kramer 2000a found a slightly but significantly lower length gain in the EBF group at 4 - 8 months (difference -1.1 (95% CI -1.7 to - 0.5) mm/mo), whereas the pooled analysis yielded a WMD of - 0.4 (95% CI -0.7 to 0.0) mm/mo; the lower confidence limit is statistically compatible with a reduced length gain of less than 4% of the mean and 10% of the SD for the Belarussian study. Heinig 1993 and Kramer 2000a also reported on length gain at 6 - 9 months (WMD -0.4 (95% CI -1.0 to +0.1) mm/mo) (outcome five). For the 8 -12 moh period, the results show a slightly but significantly higher length gain in the EBF group (WMD+0.9 (95% CI +0.3 to +1.4)) mm/mo	differ in infants who were HIV-negative at 4 mo and were abruptly weaned or continued to be breastfed. Authors created a cohort model of child mortality and stunting by modelling the survival and linear growth status of the annual birth cohort of children from birth until 3 yrs in 36 countries with 90% of the global burden of stunted children. In children aged 6-23 mo the baseline breastfeeding category is breastfed (RR 1.0) vs non breastfed (RR 2.3). using this model, authors reported that mortality risk ratio for exclusive breastfeeding (age <1 mo) was 1.0 and 1.48 for predominant breastfeeding, 2.85 for partial breastfeeding and 14.4 for no breastfeeding. In the same model for ages 6-35.9 mo, the mortality risk ratio for predominant breastfeeding was 1.0 and 2.3 for no breastfeeding. Authors also reported on the effect of	the first 2 mo RR before 4 to 6 wks 0.65 f(95% CI 0.51-0.82); RR before 2 mo 0.74 (95% CI 0.66-0.83). 2 studies showed a significant reduction in cessation of exclusive breastfeeding RR 0.62 (95% CI 0.50- 0.77). Studies using face to face support showed a statistically significant benefit RR for giving up any breastfeeding 0.85 (95% CI 0.79 to 0.92). No significant effect was demonstrated when phone and face to face support were provided on breastfeeding continuation RR 1.00 (95% CI 0.91 -1.09). One study demonstrated a significant reduction in risk of 1 or more GI infections and atopic eczema in those receiving support from health professional trained in WHO/UNICEF Baby Friendly Initiative. A further study found no significant difference between peer peer and control group mean score on the Maternal

		(outcome six). Observational analyses from the Belarussian study (Kramer 2000a) also include data on weight-for-age, length-for-age, and weight for length z-scores at six, nine, and 12 mo. Means in both the EBF and MBF groups were well above (+0.5 to +0.6) the reference values at all three ages. Nonetheless, the weight-for-age z-score was slightly but significantly lower in the EBF group at all three ages: WMD -0.09 (95% CI -0.16 to -0.02) at 6 mo, -0.10 (95%CI -0.18 - -0.02) at 9 months, and -0.09 (95% CI -0.17 - -0.01) at 12 mo (outcomes seven to nine). Length-for-age z scores were very close to the reference (0) at 6 and 9 mo and slightly above the reference (0.15) at 12 mo. Again, the EBF group had slightly but significantly (except at 12 mo) lower values: WMD -0.12 (95% CI -0.20- -0.04) at 6 mo,-0.14 (95%CI -0.22 - -0.06) at 9 mo, and -0.02 (95%CI-0.10 -	nutrition-related interventions on mortality and stunting in 36 countries. A 99% coverage with breastfeeding promotion and support resulted in 11.6, 9.9 & 9.1% in proportional reduction in deaths before 12, 24 and 36 mo respectively. The % of DALYs averted at 36 mo was 21.9 million for 99% coverage with breastfeeding promotion and support.	Breastfeeding Evaluation Scale (mean scores 52.81 (SD 5.69) vs 52.98 (SD 5.94) p=0.26).

		+0.06) at 12 mo (outcomes 10 to 12). Mean weight for-length z-scores were high and rose (from about 0.65 to 0.80) from 6 -12 mo, with no significant differences between the EBF and MBF groups at any age: WMD +0.02 (95% CI -0.07- +0.11) at 6 mo, +0.03 (95% CI -0.06 - +0.12) at 9 mo, and -0.08 (95% CI -0.17 - +0.01) at 12 mo (outcomes 13 to 15). The prevalence of low (less than -2) z-scores did not differ significantly in the two Belarussian feeding groups for any of the three z-scores at any of the three ages, although the small number of infants with low z-scores provided low statistical power to detects such differences. RRs (and 95% CIs) for low weight-for-age were 0.92 (0.04 -19.04) at 6 mo, 1.52 (0.16-14.62) at 9 mo and 1.15 (0.13- 10.31) at 12 mo (outcomes 16 to18). For length-for-age, the corresponding figures were		

		1.53 (0.84 -.78) at 6 mo, 1.46 (0.80-2.64) at 9 mo, and 0.66 (0.23 -1.87) at 12 mo (outcomes 19 to 21). For weight -for-length, the figures were 0.31 (0.02- 5.34) at 6 mo, 1.14 (0.24- 5.37) at 9 mo, and 1.15 (0.13-10.31) at 12 mo (outcomes 22 to 24). The Belarussian study also provided data on head circumference. No significant differences were observed at 6 mo (difference -1.0 (95% CI -2.3 - +0.3) mm) (outcome 25) or 9 mo (+0.7 (95% CI -0.6 - +2.0) mm) (outcome 26), but the EBF group had a slightly but significantly larger circumference at 12 mo (outcome 27): difference = +1.9 (95% CI +0.6 - +3.2) mm. Heinig 1993 reported nearly identical sleeping time (729 versus 728 minutes/day) in the two groups (outcome 28). Akeson 1996a reported similar total amino acid and essential amino acid concentrations at 6 mo of age in the two feeding groups		

		(outcomes 29 and 30). Both Kramer 2000a and a cohort study from Finland (Kajosaari 1983) reported an atopic eczema at one yr (outcome 31). The two studies showed statistically significant (P= .03) heterogeneity, with Kajosaari 1983 reporting a significantly reduced risk RR 0.40 (95% CI 0.21 to 0.78), but the larger Belarussian study finding a much lower absolute risk in both feeding groups and no risk reduction with EBF RR 1.00 (95% CI 0.60 to 1.69). Although Kajosaari 1983 also reported a reduced risk of a history of food allergy (outcome 32), double food challenges showed no significant risk reduction RR 0.77 (95% CI 0.25 -2.41) (outcome 33). Neither Oddy 1999 nor Kramer 2000a found a significant reduction in risk of recurrent (2 or more episodes) wheezing in the EBF group pooled RR 0.79 (95% CI 0.49 -1.28) (outcome 34). In the		

		Kajosaari 1983 study, the reduction in risk of any atopy at five years (outcome 35) in the EBF group was nonsignificant RR 0.68 (95% CI 0.40 -.17), and no reduction in risk was observed for atopic eczema RR 0.97 (95% CI 0.50 - 1.89) (outcome 36). A reduction in risk of borderline significance was observed for pollen allergy at five years RR 0.53 (95% CI 0.28-1.01) (outcome 37). Both Kajosaari 1983 and Oddy 1999 reported on risk of asthma at 5 -6 yrs (outcome 38); the pooled RR was 0.91 (95% CI 0.61-1.36). Reduced risks of history of food allergy RR 0.61 (95% CI 0.12 - 3.19) (outcome 39) and allergy to animal dander RR 0.81 (95% CI 0.24 - 2.72) at five years (outcome 40) were far from achieving statistical significance. Oddy 1999 found no reduction in risk of a positive skin prick test at 6 yrs in the EBF group RR 0.99 (95% CI 0.73-1.35) (outcome		

		41). A small Italian study of hematologic outcomes at 12 mo by Pisacane in 1995 reported a statistically significantly higher hemoglobin concentration (117 versus 109 g/L (95% CI for the difference = +4.03 to +11.97 g/L)) (outcome 42), a nonsignificant reduction in anemia (hemoglobin less than 110 g/L) RR 0.12 (95% CI 0.01- 1.80) (outcome 43), a nonsignificantly higher ferritin concentration WMD+4.7 (95% CI -6.3 - +15.7mcg/L)(outcome 44), and a nonsignificant reduction in the risk of low (less than 10 mcg/L) ferritin concentration RR 0.42 (95% CI 0.12 - 1.54) (outcome 45) among infants in the EBF group. Of note in this study is that the exclusive and mixed breastfeeding continued in both groups until at least 12 mo (a criterion for selection into the Pisacane 1995 study).Kramer 2000a recorded only one and two deaths (outcome 46) among		

		the 621 and 2862 Belarussian infants in the EBF and MBF groups, respectively (RR 2.30 (95% CI 0.21- 25.37). The EBF had a significantly reduced risk of one or more episodes of gastrointestinal infection in the first 12 mo of life RR 0.67 (95% CI 0.46 - 0.97) (outcome 47), which was maintained in a multivariate mixed model controlling for geographic origin, urban vs rural location, maternal education, and number of siblings in the household adjusted OR 0.61 (95% CI 0.41- 0.93).No significant reduction in risk was observed for hospitalization for gastrointestinal infection, however RR 0.79 (95% CI 0.42-.49) (outcome 48). In the above-mentioned Australian cohort study, Oddy 1999 found no significant reduction of risk for one or more episodes of upper respiratory tract infection (outcome49) in the EBF group RR 1.07 (95%		

		CI 0.96- 1.20). Neither Oddy 1999 nor Kramer 2000a found a significantly reduced risk of two or more such episodes pooled RR 0.91 (95% CI 0.82 -1.02) (outcome 50). Nor did Oddy 1999 find a significant reduction in risk of 4 or more episodes of upper respiratory infectionRR 0.82 (95% CI 0.52 -1.29) (outcome 51) or of one or more episodes of lower respiratory tract infection (RR 1.07 (95%CI 0.86-1.33) (outcome 52). Kramer 2000a found a small and nonsignificant reduction in risk of 2 or more respiratory tract infections (upper and lower combined) RR 0.90 (95% CI 0.79 -1.03) (outcome 53). The combined crude results of Oddy 1999and Kramer 2000a show a substantial and statistically significant reduction in risk for hospitalization for respiratory tract infection pooled RR 0.75 (95% CI 0.60 -0.94), but the crude risk reduction in Kramer 2000a		

		was nearly abolished and became statistically nonsignificant in a multivariate mixed model controlling for geographic region, urban vs rural location, maternal education and cigarette smoking, and number of siblings in the household adjusted OR 0.96 (95% CI 0.71- 1.30) (outcome 54).In a study from Tucson, Arizona, (Duncan 1993) reported no difference in the average number of episodes of acute otitis media in the first 12 mo of life (outcome 55) in the exclusive vs MBF groups (1.48 vs. 1.52 episodes, respectively) (95% CI for the difference -0.49 to +0.41 episodes).Duncan 1993 and Kramer2000a both found a slightly elevated risk for one or more episodes of otitis media pooled RR 1.28 (95% CI 1.04 -1.57) (outcome56), but Duncan 1993 found a nonsignificant reduction in risk for frequent otitis media RR 0.81 (95% CI 0.43-1.52)		

		(outcome57).		
EXTERNAL VALIDITY				
Generalisability	y	y - for the results of the studies conducted in developed countries.	n	y - although some studies were conducted in developing countries.
Applicability	y	y	y	y
Comments	The unclear randomization and allocation concealment processes in the study suggest selection bias was possible. Furthermore the use of a telephone interview further suggests recall/reporting bias.	Definitions of exclusive breastfeeding varied across studies.	In the cohort model of child mortality and stunting, the protective effect of breastfeeding is assumed to cease when the child reaches 2. Although authors have considered a number of breastfeeding interventions and reviews, details of these interventions and reviews are not provided.	
Conclusion	There remains considerable uncertainty about the effect of brief exposure to water, breast-milk substitutes, or other liquids on the success and duration of breastfeeding.	Infants who are exclusively breastfed for 6 mo experience less morbidity from gastrointestinal infection than those who are mixed breastfed as of 3 or 4 mo, and no deficits have been demonstrated in growth among infants from either developing or developed countries who are exclusively breastfed for 6 mo or longer. Moreover, the mothers of	Proven nutrition-related interventions offer many possibilities for the reduction of the related burden of disease in both the short and the long term. The evidence for benefit from nutrition interventions is convincing.	Additional professional support was effective in prolonging any breastfeeding, but its effects on exclusive breastfeeding were less clear. WHO/UNICEF training courses appeared to be effective for professional training. Additional lay support was effective in prolonging exclusive breastfeeding, while its

		such infants have more prolonged lactational amenorrhea. Although infants should still be managed individually so that insufficient growth or other adverse outcomes are not ignored and appropriate interventions are provided, the available evidence demonstrates no apparent risks in recommending, as a general policy, exclusive breastfeeding for the first 6 mo of life in both developing and developed-country settings. Large randomized trials are recommended in both types of setting to rule out small effect son growth and to confirm the reported health benefits of exclusive breastfeeding for 6 mo or beyond.		effects on duration of any breastfeeding were uncertain. Effective support offered by professionals and lay people together was specific to breastfeeding and was offered to women who had decided to breastfeed. Further trials are required to assess the effectiveness (including cost-effectiveness) of both lay and professional support in different settings, particularly those with low rates of breastfeeding initiation, and for women who wish to breastfeed for longer than three months. Trials should consider timing and delivery of support interventions and relative effectiveness of intervention components, and should report women's views. Research into appropriate training for supporters (whether lay or professional) of breastfeeding mothers is also needed.

Table 23.2 Summary used to make evidence statement for breastfeeding and maternal and infant outcome (cont.)

STUDY DETAILS (Review)	Abdulwadud et al. 2007 [582]	Baird et al. 2009 [403]	Gatti. 2008 [491]	Ines Couto de Oliveira et al. 2001 [483]
Affiliation/source of funds	ASEBE TEFERI, Ethiopia; IMPART; BC Centre of Excellence for Women's Health, Canada.	University of Southhampton, South Hampton General Hospital UK, Medical Research Council.	Centre for Health Disparities Research, University of Pennsylvania, National Institute of Health Institutional Training Grant.	Brazilian Government Agency CAPES.
Study design	Meta Analysis.	Systematic Review of (3 systematic reviews).	Systematic review (15 prospective, longitudinal; 3 cross sectional, 3 secondary analysis of datasets).	Systematic review (33 experimental & 31 quasi-experimental studies).
Level of evidence	111-211	III-1 Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method).	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.	I
Date of search	1951 - 2006	1966-2008	1996-2007	1980-1999
Number of studies	0 trials have evaluated this	3	20	64
Total number of participants	N/A	NS	36 700	>3700
Population characteristics	NA	Breastfeeding mothers or pregnant women intending to	Healthy, full term breastfeeding dyads during	Pre-natal, and post-natal women

		breastfeed from disadvantaged backgrounds (in developed countries).	the first 6 mo of life.	
Range of exposure	Intervention: Any type of workplace strategy to encourage, assist and support breastfeeding for women returning to work after birth Comparator: Women receiving usual care.	Intervention: Reviews on interventions promoting and prolonging breastfeeding and providing support for mother who are breastfeeding. Interventions include breastfeeding literature, lay support, professional support, peer support and 1 on 1 counselling.	Examine reasons why women had low rates of duration and exclusivity of breastfeeding &/or associations between perceived milk supply and other maternal perceptions. 4 of the studies examined tools to predict insufficient milk supply. This was done through validated questionnaires, tools, Theory of planned behaviour, standard definitions, non validated tools, open ended questions, H & H Lactation Scale, The Perceived Insufficient Milk Tool.	Primary care interventions designed to extend breastfeeding duration (exclusive, full, or any kind of breastfeeding) during the prenatal and/or postnatal period. Interventions that took place during the delivery period only were excluded.
Length of follow-up	NA	NS	1 month to 24 months	Range from 2 to 12 mobut most to 6 mo
Outcome(s) measured	Primary: 1. Rate, duration and prevalence of exclusive breastfeeding. Secondary: 1. Employer-related; 2. Mother-related; 3. Infant-level outcomes.	Breastfeeding initiation, breastfeeding duration.	Breastfeeding levels, reasons for ceasing breastfeeding, supplementation and breastfeeding level, breastfeeding difficulties, breastfeeding self efficacy, breastfeeding satisfaction, prediction of breastfeeding at 12 wks, breastfeeding	Extension of breastfeeding (Full, partial or any kind of breastfeeding) at points in time varying from 4 wks to 6 mo. Main outcome measure was the proportion of mothers breastfeeding at or until a specified time point. Some studies reported

			support, perceptions of milk supply, coping strategies of PIM, risk factors for early cessation.	median or mean breastfeeding duration.
INTERNAL VALIDITY				
Databases included in search	Cochrane Pregnancy and Childbirth Group's Trials Register, Central, Medline, Cinahl, Lilacs, C2-Spectr.	Cochrane, Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Medline.	Cinahl, Medline, Pubmed.	Literature search used an earlier systematic infant-feeding review that focused on the developed world as the starting point. Additional databases searched (Medline, Popline, Health- Star, CAB-Health, Cochrane Library, CINAHL, and Lilacs) using the key words promotion, intervention, assessment, programme, community, education, effect, impact, and evaluation (linked to breastfeeding).
Statistical analysis methods	Intended to use RevMan 2003, fixed effect meta analysis, random effects model.	RR	Factor analysis, regression, survival analysis.	Present the interventions' maximum duration of effect that proved was statistically significant at a 90% level. The effects presented are the percentage of exclusive breast-feeding among intervention and control groups, and corresponding P value. The attributable

				fraction and 95% confidence intervals were constructed when data presented by the authors were conclusive or suggestive of effect. The attributable fraction (AF) was defined as the proportion of the outcome rate achieved in the intervention group that is due to the intervention, and is a measure of effectiveness. It is the difference between breastfeeding rates in the intervention (I) and control groups, expressed as a proportion of the rate in the intervention group: AF=(I - C)/I. or from the relative risk (RR). ; AF = (RR – 1)/RR.
Overall quality assessment (Positive/Negative or Neutral) plus descriptive)				P
RESULTS				
Outcome	No randomised controlled trials or quasi-randomised controlled trials were identified.	Interventions that use education and 1 on 1 support are effective in increasing breastfeeding initiation rates. Any form of additional support for mothers who are	Many women were found to discontinue breastfeeding during the 1st few weeks post partum as a result of Perceived Insufficient Milk (PIM) supply. Many women	Effect on duration with Prenatal Interventions: 6 of 8 studies effective (4 of 6 RCTs) with AF ranging from 19-78% for full BF at 6 mo to any BF at 4 wk.Effect on

		breastfeeding increases the duration of breastfeeding. Many of the studies reviewed were targeted at low income groups.	used infant satisfaction cues (e.g. crying, unsettled) as their primary indicators of milk supply. The H & H Lactation Scale and the Perceived Insufficient Milk Tool have been found useful to identify women at risk during early post-partum. Furthermore, PIM was associated with early weaning and / or decreased exclusivity in 10 studies. PIM was also associated with lower self efficacy or maternal confidence scores. Use of formula in hospital was associated with PIM in 3 studies and ceasing breastfeeding before leaving the hospital was related to PIM in 1 study.	duration with Postnatal Interventions:3 of 9 studies effective (2 of 8 RCTs) with AF ranging from 15-53% for any BF at 2 mo to full BF at 6 mo. Effect on duration with BOTH Pre- and Postnatal Interventions: 7 of 9 studies effective (3 of 4RCTs) with AF ranging from 20-92% for full BF at 4 mo in 2 studies; One study had an AF of 91% for full BF at 5 mo. Effect on duration with both Hospital and Postnatal Interventions: 4of 7 studies effective (3 of 6RCTs) with AF ranging from 24-88% for any BF at 4 mo to exclusive BF at 4 mo. Effect on duration with both Hospital and Pre- and Postnatal Interventions: All 4 studies effective (3 RCTs) with AF ranging from 20-100% for any BF at 1month to full BF at 6 mo.
EXTERNAL VALIDITY				
Generalisability	n/a	y	y	1
Applicability	N/A	y - note that the review focused on women from	y	1

		disadvantaged backgrounds but included studies on women generally.		
Comments	The lack of evidence resulting from this review emphasises the need for further research into breastfeeding education and support in the workplace post delivery.	The objectives of this review were focused on all interventions directed at changing health behaviours of young women from disadvantaged backgrounds and included smoking, physical activity and diet.	The majority of the studies reviewed identified IM as PIM. Both of the terms have different definitions.	

Conclusion	No trials have evaluated the effectiveness of workplace interventions in promoting breastfeeding among women returning to paid work after the birth of their child. The impact of such intervention on process outcomes is also unknown. Randomised controlled trials are required to establish the benefits of various types of workplace interventions to support, encourage and promote breastfeeding among working mothers.	Consistent evidence was found of intervention features associated with effective changes in a number of health behaviours. Interventions to change health behaviours of women of child-bearing age from disadvantaged backgrounds require: an educational approach delivered in person by professionals or peers; provide continued support after the initial intervention; some evidence to t that social support from peers and family involvement in the intervention maybe important. These findings are of relevance to the design of an intervention to improve diet in this group of women.	PIM is one of the most common and influential reasons for low rates of breastfeeding duration and exclusivity. Future research should be conducted to determine who is at high risk and to further validate screening tools; and whether PIM is a physiological or psychological issue. Perceived milk supply is considered modifiable and well-informed interventions to reduce the incidence of PIM might be a key element for improving rates of successful breastfeeding.	The primary health care units should inform, encourage, and support pregnant women in breastfeeding; the maternity hospitals should allow women to bond with their babies and help them to establish breastfeeding; and the primary health care units should be able to guide, reinforce, and support this practice continuously, completing the cycle. Although there is evidence supporting the effectiveness of primary care strategies in extending breastfeeding duration, there is a need for broad-based, well-designed studies testing the effect of the combination of the procedures referred above, preferably spanning the prenatal and postnatal periods, to encourage the development of evidence-based protocols concerning the promotion, protection, and support of breastfeeding in primary care.

23.3 BREASTFEEDING and ASTHMA and ATOPY

What are the benefits of breastfeeding (partial and exclusive) and the risks of not breastfeeding (any and exclusive), to infants and mothers, both in the short term and long term?		
Evidence statement		Breastfeeding is associated with a reduced risk of asthma and atopic disease.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Poor/satisfactory	1 Systematic review of cohort studies (Negative quality) and unclear the number of studies included but had 83 references cited.
Consistency	Good	ALL studies show increased risk of asthma and atopic disease when NOT breastfed.
Clinical impact	Satisfactory	Odds ratios in the range of 1.2 to 1.5 for increased risk of asthma and atopic disease.
Generalisability	Good	Can be contextualised to lactating Australian women and their infants.
Applicability	Good	Applicable to Australia.

The studies included in the body of evidence statement are shown in Table 23.3.

References

Oddy, W. H. 2009, "The long-term effects of breastfeeding on asthma and atopic disease", *Advances in Experimental Medicine & Biology*, vol. 639, no., pp. 237-51.

Table 23.3 Summary used to make evidence statements for breastfeeding and asthma and atopic disease

STUDY DETAILS (Review)	**Oddy 2009 [3]**
Affiliation/source of funds	
Study design	Systematic Review of Cohort studies.
Level of evidence	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Date of search	Not reported but most paper in the publication range of 1981 to 2002.
Number of studies	Not reported specifically, about 4 cohort studies, but 83 references cited. A table is given that specifies the inclusion criteria for assessing quality of the studies. Children had to be followed for at least 5 years.
Total number of participants	>4300
Population characteristics	Infants cohorts, both random population samples and cohorts of infants with a family history of asthma or atopy.
Range of exposure	Exposure criteria given: 1. Non-reliance on late maternal recall of breastfeeding; 2. Blind ascertainment of infant feeding history; 3. Sufficient duration of breastfeeding; 4. Sufficient exclusivity of breastfeeding.
Length of follow-up	5-17 yrs
Outcome(s) measured	Outcome criteria: 1. Strict diagnostic criteria; 2. Blind ascertainment of outcomes; 3. Consideration of severity of outcome; 4. Consideration of age of onset of outcome.
INTERNAL VALIDITY	
Databases included in search	Not reported.
Statistical analysis methods	Statistics: 1. Control for confounding factors; 2. Assessment of dose-response effects; 3. Assessment of effects in children at high risk of outcome; 4. Adequate statistical power.
Overall quality assessment	Negative but summarising previously published systematic review and giving a guide to interpretation of the studies.

(Positive/Negative or Neutral) plus descriptive)	
RESULTS	
Outcome	Odds ratios in the range of 1.2 to 1.5 for increased risk of asthma and atopic disease all show increased risk when not breastfed. Authors quote a previously published meta-analysis of 9 studies that showed that children breastfed for at least 3 months were significantly protected against development of asthma, OR= 0.80 and other meta analyses with a similar protective effect (26%-30%) for exclusive breastfeeding during the first 3 months from developing asthma, allergic rhinitis and atopic eczema.
EXTERNAL VALIDITY	
Generalisability	y
Applicability	y
Comments	
Conclusion	From the studies that met the strict criteria for breastfeeding and atopic disease, all demonstrated a protective effect of breast-milk feeding or conversely, a risk of formula feeding. However, the continuing protective effect of breastfeeding on asthma and atopy later in adolescence and adulthood has yet to be confirmed in larger longitudinal studies. Given the many benefits conferred by breast-milk, breastfeeding should continue to be promoted as the preferred infant feeding method for the first 6 months and up to two years, as recommended by WHO.

23.4 BREASTFEEDING and SUDDEN INFANT DEATH SYNDROME

What are the benefits of breastfeeding (partial and exclusive) and the risks of not breastfeeding (any and exclusive), to infants and mothers, both in the short term and long term?		
Evidence statement		Not breastfeeding is associated with an increased risk of Sudden Infant Death Syndrome.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 Systematic review (23 studies, 18 case-controls, 4 nested case-controls, 1 cohort) of excellent quality with meta-analysis with low risk of bias showing an increased risk of SIDs with "bottle" feeding.
Consistency	Good	19 studies had a protective effect for breastfeeding, 1 had no effect and 3 showed a negative effect. Sensitivity analysis conducted in the meta-analysis and similar ORs for bottle feeding shown for studies rated "good" (10 studies, OR range 0.56 to 5.95) or published in last 10 years.
Clinical impact	Excellent	Pooled OR for 23 studies was 2.11 (95%CI: 1.66 - 2.68). For higher quality studies only OR = 2.24 ("good" studies) and 2.32 (studies in last 10 years).
Generalisability	Excellent	Generalisable to Australian women and the review includes Australian data.
Applicability	Excellent	Directly applicable to Australia.

This body of evidence statement had to be stated as “not breastfeeding…” because breastfeeding could not be demonstrated to be protective, possibly due to confounding. *Not* breastfeeding, conversely, could be shown to increase the risk of sudden infant death syndrome.

The studies included in the body of evidence statement are shown in Table 23.4.

References

McVea, K. L. S., Turner, P. D., & Peppler, D. K. 2000, "The role of breastfeeding in sudden infant death syndrome", *Journal of Human Lactation*, vol. 16, no. 1, pp. 13-20.

Table 23.4 Studies used to make evidence statements for breastfeeding and sudden infant death syndrome (SIDS)

STUDY DETAILS (Review)	**McVea, K.L.S., P.D. Turner, and D.K. Peppler 2000 [1026]**
Reference	
Affiliation/source of funds	Olson centre for Women's Health, Nebraska.
Study design	Meta analysis of 23 studies (18 case-controls, 4 nested case -controls, 1 cohort)
Level of evidence	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Date of search	1966-1997
Number of studies	23
Total number of participants	>3100 cases 50 000 controls
Population characteristics	Infant populations from UK, Australia, NZ, Canada, USA, ScandInavia.
Range of exposure	Included studies if a minimal definition of SIDs was met and original data was presented to allow calculation of an OR for bottle feeding.
Length of follow-up	Not applicable.
Outcome(s) measured	Inclusive definition of SIDS as any sudden, unexplained death of a young child.
INTERNAL VALIDITY	
Databases included in search	MEDLINE and additional hand searches of the references lists and key papers included in the meta-analysis.
Statistical analysis methods	ORs and 95% CIs. Random effects model used in the meta-analysis due to heterogeneity of the studies with a pooled OR. Separate "pooled" OR for 2 groups of studies; those with "excellent" or "good" quality ratings published in last 10 years.
Overall quality assessment (Positive/Negative	P

or Neutral) plus descriptive)	
RESULTS	9 studies rated "good", 10 as "fair" and 4 as "poor". Better studies had higher risk for bottle feeding. OR for studies ranged from 0.56 to 5.95. 19 studies had a protective effect for breastfeeding, 1 had no effect and 3 showed a negative effect. Most of the studies were protective. The pooled OR for 23 studies was 2.11 (95% CI: 1.66 - 2.68). For higher quality studies only OR = 2.24 ("good" studies) and 2.32 (studies in last 10 years). 9 studies included data on partial breastfeeding and 7 had enough data to estimate SIDs risk; 4 showed a dose response for increasing use of formula feeding but none had sufficient power to demonstrate statistically significant difference for partial versus no breastfeeding.
Outcome	Death from SIDS
EXTERNAL VALIDITY	
Generalisability	Yes
Applicability	Yes
Comments	Data includes Australian studies. The meta-analysis suggested breastfeeding conveys a 50% reduced risk of SIDs.
Conclusion	Breastfeeding should be strongly encouraged, independent of SIDs and the evidence for SIDs protection is imperfect due to confounding.

U1.5 Summary of the studies *Included*, but not used in the Body of Evidence Statements.

A summary of the non-systematic reviews deemed relevant to this topic, but that did not contribute to a body of evidence statement are included in an appendix. The references however appear below.

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24. OPTIMISING BREASTFEEDING OUTCOMES (U1.7)

Evidence Statements

24. OPTIMISING BREASTFEEDING OUTCOMES (U1.7)

What nutritional factors are important in optimizing breastfeeding outcomes?

Search results

The initial search of the databases included 555 references for *U1.7 What nutritional factors are important in optimizing breastfeeding outcomes?* and the specified disease outcomes with 40 duplicates. The detailed search is included in a separate document on searches. In all, 87 references concerning nutritional factors and breastfeeding outcomes were retrieved, 18 had data extracted and 12 systematic reviews were used to form the body of evidence statements. Sufficient evidence was found to make BOE statements for nutritional factors relating to alcohol, selenium, support for breastfeeding and maternal perceived milk supply in relation to breastfeeding outcomes for mothers and infants, as detailed below. There were no recent good quality reviews of nutrients and breastfeeding, except for alcohol and selenium.

There were two systematic reviews on n-3 long chain polyunsaturated fatty acid (LCPUFA) supplementation and infant outcomes, but they reviewed those same RCTs [103] and [189]. Therefore no BOE statement was made. Collectively, these reviews suggest that there is no evidence supporting a beneficial effect in term infants on visual development as measured by electrophysiological tests, with supplementation of LCPUFAs. There is also suggestive, but inconclusive, evidence for a beneficial effect of maternal and supplementation during pregnancy and lactation on infant mental development and longer term cognition, but the evidence is inconclusive beyond age two years.

The majority of studies were excluded because they were not reviews. The abstract of non-systematic reviews that were recent have been included at the end of this section.

24.1 ALCOHOL, CAFFEINE and BREASTFEEDING OUTCOMES

What nutritional factors are important in optimizing breastfeeding outcomes?		
Evidence statement		Consumption of alcohol by lactating women in the range of 0.3-0.8g/ kg body weight is associated with increased risk of adverse infant outcomes.
Grade		B
Component	**Rating**	**Notes**
Evidence Base	Good	2 Systematic reviews; 1 (P) had 24 studies, with 14 in humans (6 Level III-1, 2 Level III-2, 2 Level II, 4 Level IV, 10 Level V (all animal) and 1 (N)) the number was not reported but had 33 references cited.
Consistency	Excellent	Decreased lactational performance with increasing alcohol consumption.
Clinical impact	Good	Maternal alcohol doses associated with adverse infant outcomes (development, feeding, sleeping) varied from 0.3g/kg to 0.8g/kg. Lactational performance reduced from maternal intakes of 0.5-1g/kg body weight.
Generalisability	Good	Human studies can be contextualised to lactating Australian women and their infants.
Applicability	Satisfactory	Only human data has been considered, but there is limited data in humans compared to the studies done in animal, mostly rats.

The studies included in the body of evidence statement are shown in Table 24.1.There were two systematic reviews that examined alcohol and breastfeeding outcomes. The positive quality review by Giglia & Binns (2006) is a comprehensive review of both human and animal studies and covers the literature on the effect of alcohol on breastfeeding physiology, lactogenesis and milk "let down", in detail. It addresses three questions in particular; the effect of alcohol on lactogenesis; the effect of maternal blood alcohol on breastmilk and infant blood alcohol and the effect of breastmilk alcohol on the infant. Evidence tables are provided to summarise studies for: 1) The effect of alcohol on the mother (1 review, 2 Level II, 4 Level III-1, 1 Level III-2, 2 Level IV studies); 2) The effect of alcohol on the infant (5 Level III-1, 1 Level III-2, 1 Level IV). The authors also synthesise advice for lactating women based on their evidence synthesis. This was that breastfeeding women should:-

1. Not consume alcohol in the first month of the infant life
2. After that, limit alcohol to 1-2 standard drink per day, consumed after breastfeeding
3. For occasions where more will be consumed then consider the option of expressing milk in advance and skipping one feed.

The second review by Haber & Allnutt (2005) was of negative quality and covered both alcohol and caffeine. This paper draws on similar literature but also encompasses studies on caffeine intake. There were only limited human studies on caffeine and not enough data to make a Body of Evidence Statement. Data was not extracted into summary tables within this review and it was only provided in a narrative style. While the authors' state their intention to provide guidance to lactating women on appropriate consumption of alcohol and caffeine, their statement are not explicit and there is not a clear link to their evidence synthesis.

References

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Table 24.1 Summary of studies to make evidence statements for alcohol, caffeine and breastfeeding outcomes

STUDY DETAILS (Review)	Giglia & Binns 2006	Haber et al. 2005
Affiliation/source of funds	Curtin University of Technology Australia, National Health and Medical Research Council.	Royal Hospital for Women, Australian Catholic University Sydney.
Study design	Systematic Review	Systematic Review
Level of evidence	III-1 Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method).	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Date of search	1990-2005	1966-2004
Number of studies	24 (14 human & 10 rat studies)	Not reported but 33 references cited
Total number of participants	NS	NS
Population characteristics	Lactating human and rat mothers, age not reported.	Lactating mothers; no other details provided.
Range of exposure	Maternal alcohol intake of <0.5 - >2 g / kg body weight (human studies only).	Not always reported but ranges from 1-3 standard drinks of wine (120 mL = I standard) to as much alcohol as the mothers could manage; whereas for caffeine ranges are from 36 to 750 mg.
Length of follow-up	NS	NS
Outcome(s) measured	Time taken for alcohol to reach human milk, effect of alcohol intake on milk ejection reflex, infant milk and alcohol consumption, oxytocin and prolactin levels, milk yield, breastfeeding initiation and duration, infant motor development.	Alcohol Studies: 1. Alcohol content of breastmilk; 2. Transfer of alcohol in breastmilk; 3. Alcohol infrared absorption and electrochemical reaction; 4. Oxytocin response; 5. Breastmilk production and consumption; 6. Infant feeding pattern; 7. Infant motor development; 8. Infants sleep-wake patterns; 9. Breastmilk flavour. Caffeine Studies: 1. Excretion of caffeine in breastmilk; 2. Iron concentrations in milk and infant iron status at 1 month of age; 3. Breastmilk composition.

INTERNAL VALIDITY		
Databases included in search	PubMed, Cinahl, Proquest, Science Direct, Web of Knowledge.	Cinahl, Medline, Cochrane, Psychinfo, ProQuest, University of Technology Health Source database.
Statistical analysis methods	Varies by study; not indicated for majority of studies.	NS
Overall quality assessment (Positive/Negative or Neutral) plus descriptive)	P	N
RESULTS		
Outcome		No tables provided.
EXTERNAL VALIDITY		
Generalisability	y	y
Applicability	n	n
Comments		The authors did not state any quantitative results for all studies including p value or confidence intervals.
Conclusion	Alcohol intake by lactating mothers in amounts recommended as 'safe' for nonlactating women may have a negative effect on infant development and behaviour. Clear guidelines for alcohol consumption are required for lactating women and health professionals to guide breastfeeding mothers to make educated choices regarding alcohol intake during this critical period of infant development.	The research reviewed in this paper suggests that maternal consumption of alcohol and caffeine prior to breastfeeding can have a detrimental effect on breastfed infants. The degree of risk seems to vary according to the drug in question. The negative effects of caffeine and alcohol for example when taken in moderation do not necessarily outweigh the benefits of breastfeeding to the infants. A cup of coffee or a glass of wine should cause no problem, especially if taken according to recommendations.

24.2 SELENIUM and BREASTFEEDING OUTCOMES

What nutritional factors are important in optimizing breastfeeding outcomes?		
Evidence statement		Breast-feeding is associated with higher infant selenium status compared to formula-feeding.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Satisfactory	1 Systematic review (O) with >190 references covering all aspects of selenium (Se) nutrition in relation to breastmilk and maternal factors impacting on this.
Consistency	Good	Internationally, there is a wide range of breast-milk Se concentrations, dependent on Se consumed in natural foods which is impacted by the Se content of the soils where foods are grown. Despite wide variation in median Se breastmilk concentration worldwide and that infants commonly do not achieve recommendations, Se status is greater in breast-fed than in formula-fed infants.
Clinical impact	Satisfactory	The Australian studies (1983-1997) reporting breastmilk Se concentrations, indicate they are comparable to the median concentrations reported internationally. Maternal Se status and most dietary intakes appear not sufficient to optimise breastfed infant's Se status, but are still associated with higher Se status compared to formula-fed infants.
Generalisability	Excellent	Breastmilk Se concentrations are generalisable to Australian women and the review includes Australian data.
Applicability	Excellent	Directly applicable to Australia. Australian soil Se concentrations will vary by region and therefore Se intake and breastmilk concentration.

The study included in the body of evidence statement is shown in Table 24.2. This is a major review that discusses selenium (Se) nutrition during breast-feeding, including environmental and maternal constitutional factors that affect breast-milk-Se metabolism and secretion. Papers in this review were located via a literature search of Medline and Web of Science on Se and breastmilk. The following headings are covered; Selenium species in breast milk; Maternal constitutional factors; Environmental factors; Selenium prophylaxis and breast-feeding; Selenium interactions and breast-feeding; Excess selenium in breast milk; Breast-feeding and the infant's selenium status.

The median Se concentration from studies worldwide are 26, 18, 15 and 17 ug/L in colostrum (0-5 days), transitional milk (6-21 days), mature milk (1-3 months) and late lactation (>5 months)

respectively. Se recommendations are not achieved by approx. 30% of the reported breastmilk Se Concentrations but Se status in breast-fed infants is greater than formula-fed infants. For reported Se breast milk concentrations in Australia the Se concentrations for fore and hind milk (10.8-13.9 ug/L) were comparable to mature milk (15ug/L).

References

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Table 24.2 Summary of studies used to make evidence statements for selenium and breastfeeding outcomes

STUDY DETAILS (Review)	**Dorea 2002**
Affiliation/source of funds	University of Brazil
Study design	Systematic review
Level of evidence	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Date of search	NS
Number of studies	not reported but > 190 references
Total number of participants	NS
Population characteristics	NS; Lactating women from > 10 countries (developed and developing).
Range of exposure	Not relevant but a Table of Se concentrations in breastmilk given from 16 studies by stage of lactation. Table also given for Se concentration for fore- and hind-milk.
Length of follow-up	
Outcome(s) measured	Selenium concentration in breast milk including fore and hind milk.
INTERNAL VALIDITY	
Databases included in search	Medline and Web of Science
Statistical analysis methods	
Overall quality assessment (Positive/Negative or Neutral) plus descriptive)	O

RESULTS	
Outcome	Tables given for: Se concentration in breastmilk and maternal plasma or serum concentrations (Table 26.3); Summary of studies comparing mean selenium concentrations in breast milk of term and preterm mothers (Table 26.4); Summary of mean breast-milk selenium concentrations in studies comparing countries or regions in the same country (Table 26.5); Summary of studies comparing breast-milk selenium concentrations in relation to natural-food selenium intake and dietary habits (Table 26.6); Summary of studies comparing breast-milk selenium concentrations and maternal dietary intake of selenium in natural foods (Table 26.7); Summary of breast-milk selenium concentrations compared with selenium prophylaxis studies (Table 26.8). Summary of studies that measured breast-milk selenium concentrations in breast milk from different parts of the world (Table 26.9). Australian data is reported in Tables 26.2, 26.3, 26.4 and 26.5. The median Se concentration from studies worldwide are 26, 18, 15 and 17 ug/L in colostrum (0-5d), transitional milk (6-21d), mature milk (1-3months) and late lactation (>5 months) respectively. Se recommendations are not achieved by approx. 30% of the reported breastmilk Se Concentrations but Se status in breast-fed infants is greater than formula-fed infants. For reported Se breast milk concentrations in Australia the Se concentrations for fore and hind milk (10.8-13.9) were comparable to mature milk (15ug/L).
EXTERNAL VALIDITY	
Generalisability	Y
Applicability	Y
Comments	
Conclusion	Maternal Se status reflects Se intake and modulates Se concentrations in human milk. Se bioavailability in natural foods (organic) or maternal supplements (organic and inorganic) has an important impact on breast-milk Se compounds. As a consequence, total Se in breast milk shows a wide variation, reflecting the content of natural foods grown in different soils. Se prophylaxis is effective in raising maternal Se status and increasing both breast-milk Se and milk GPX activity. The mammary gland secretes Se quite effectively as Se-containing amino acids in milk proteins and this chemical form protects the infant from excessive maternal Se. Current estimates of Se intakes of adults place most diets as sub-optimal in meeting daily Se requirements. Although maternal Se status under most diets may not be sufficient to provide optimal serum Se concentrations and full expression of GPX activity, breast-fed infants consistently show higher Se status than formula-fed infants.

24.3 FACTORS ASSOCIATED WITH ENHANCED BREASTFEEDING SUCCESS AND DURATION

What factors are important in optimizing breastfeeding outcomes?		
Evidence statement		Pre-natal and Perinatal support for breastfeeding can increase the proportion of women breastfeeding (both exclusive and non-exclusive) up to age 6 months.
Grade		A
Evidence statement		Breastfeeding support (any type) increases duration of both exclusive and non-exclusive breastfeeding both in the immediate post-natal period and at 6 months of age.
Grade		B
Evidence statement		Maternal perceived insufficient milk (PIM) supply is associated with increased risk of early cessation of lactation.
Grade		C
Component	**Rating**	**Notes**
Evidence Base	Excellent	8 Systematic reviews [3 are Cochrane; 3 with meta analysis (5P, 1O, 2N)]; 5 protective effect on breastfeeding success, 1 had no results and 1 found maternal perceived insufficient milk supply increased risk of lactation failure.
Consistency	Good	Definitions of breastfeeding (exclusive, partial, any) vary across studies. Consistent for support prolonging breastfeeding. Some of the same studies covered by the reviews.
Clinical impact	Good	For provision of support, the RR for ceasing breastfeeding was approx.0.65 to 0.9. When expressed as odds ratios for continued breastfeeding the ORs for support ranged from 1.9 to 5.2.
Generalisability	Excellent	Breastfeeding definitions and rates are applicable to Australian women.
Applicability	Good	While some reviews include studies conducted in developing countries, only those applicable to developed countries have been applied in developing the BOEs.

The studies included in the body of evidence statement are shown in Table 24.3.

References

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Table 24.3 Summary used to make evidence statement for breastfeeding and maternal and infant outcome

STUDY DETAILS (Review)	Szajewska et al. 2006 [151]	Kramer et al. 2002 [584]	Bhutta et al. 2008 [55]
Affiliation/source of funds	Medical University of Warsaw, Dr. von Hauner Children's Hospital, Ludwig-Maximilians-University of Munich.	McGill University, WHO Expert Committee on the optimal duration of exclusive breastfeeding.	Aga Khan University Bangladesh, Centre for Health and Population Research, Johns Hopkins Bloomberg School of Public Health USA, London School of Hygiene and Tropical Medicine, University of California, Federal University of Rio Grande de Sur Brazil, Sitaram Bhartia Institute of Science and Research India, World Bank Washington, Save the Children UK, Emergency Nutrition Network, International Food Policy Research Institute, Food for Education Programmes, Global Alliance against malnutrition, Bill and Melinda Gates Foundation, UNICEF Innocenti Research Centre.
Study design	Systematic Review	Meta Analysis	Systematic Review
Level of evidence	III-1 Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method).	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort

		studies, case-control studies, or interrupted time series with a control group.	studies, case-control studies, or interrupted time series with a control group.
Date of search	1966-2004	Prior to 1966 - 2000	NS
Number of studies	1	22 (11 from developing and 11 from developed countries)	34
Total number of participants	170 infants (experimental group = 83; control group = 87)	9998	NS
Population characteristics	OI	Lactating mothers and their healthy, term, singleton infants from developed and developing countries	Breastfed and non breastfed infants from developing countries
Range of exposure	Experimental group received 5% glucose water from bottle, after breastfeeds, during the first 3 days of life.	To assess the effects of exclusive breastfeeding (EBF) for 6 or more vs. 3-4 months with continued mixed breastfeeding (MBF) until at least 6 months.	Effect of promotion strategies on exclusive breastfeeding rates for infants younger than 6 months and on continued breastfeeding up to 12 months.
Length of follow-up	4 months	NS	0-6 months
Outcome(s) measured	Proportion of exclusively breastfed infants between birth and 6 months, the proportion of infants receiving any breastmilk at fixed time points between birth and 6 months, the proportion of infants still being breastfed at the end of their first yr of life, breastfeeding duration, proportion of infants receiving infant formula between birth and 6 months.	All infant and maternal health outcomes; infant outcomes especially growth (weight, length, head circumference, z scores, weight-for-age, length-for-age, weight for age, infections, morbidity, mortality, micronutrient status, neuromotor and cognitive development, asthma, atopic eczema, other allergic diseases, type 1 diabetes, blood pressure, adult chronic diseases. Maternal outcomes especially postpartum weight loss, duration of	Mortality, breastfeeding duration, breastfeeding pattern (exclusive, partial, predominant).

		lactational amennorrhea, chronic diseases (osteoporosis, breast and ovarian cancer).	
INTERNAL VALIDITY			
Databases included in search	Medline, Embase, Cinahl, Cochrane.	Medline, Oldmedline, Cinahl, EBM Reviews -Best Evidence, Sociofile, Cochrane, CAB Abstracts, EMBASE Psychology, EconLit, IMEMR, AIM, LILACS, Healthstar.	Cochrane Library, ExtraMed, WHO Reproductive Health Library.
Statistical analysis methods	Intention to treat analysis, p value.	Controlled clinical trials: Adequacy of randomization and concealment, losses to follow up analysis, measurement of outcome, 5 point Jadad scale Observational studies were assessed for control for confounding, losses to follow up, and assessment of outcomes as follows: for growth and morbidity outcomes, losses to follow up, assessment of outcome. All studies were stratified according to study design (controlled trials vs. observational), provenance (developed vs. developing), timing of feeding comparison (3 to 7 months vs. prolonged (> 6 months)).	Multiplicative model, mortality RR, stunting OR.
Overall quality assessment (Positive/Negative or Neutral) plus	P	P	O

descriptive)			
RESULTS			
Outcome		Indicators of child health (GIT infection, development of asthma, allergies, iron status), growth and development, and on maternal health (resumption of menses, postpartum weight loss).Comparison one: controlled trials of exclusive vs. mixed breastfeeding for 4-6 months, developing countries and Comparison two: observational studies of exclusive versus mixed breastfeeding for 3-7 months, developing countries and Comparison three: observational studies of prolonged (more than 6 months) exclusive versus mixed breastfeeding, developing countries are not relevant to Australia. Comparison 4 is relevant to the Australian population: Observational studies of exclusive versus mixed breastfeeding for 3-7 months in developed countries. Studies were heterogeneous with a WMD of -12.45 (95% CI -23.46 - -1.44) g per month & should be interpreted with caution, although even the lower 95% confidence limit is compatible with a lower weight gain in the EBF	Beginning breastfeeding within the first days after birth lowers mortality even in exclusively breastfed infants. One review showed that all forms of extra support increased the duration of 'any breastfeeding' with the RR for stopping any breastfeeding before 6 months being 0.91 (95% CI 0.86-0.96). All forms of support affected the duration of exclusive breastfeeding more strongly than the likelihood of any breastfeeding RR 0.81 (CI 0.74-0.89). Lay and professional support extended breastfeeding duration RR before 4-6 weeks 0.65 (CI 0.51-0.82); RR before 2 months 0.74 (CI 0.66-0.83). Further reviews reported that with individual counselling the OR of exclusive breastfeeding were increased in the neonatal period (15 studies; OR 3.45 (95% CI 2.2-5.42) p<0.0001; random effects) and at 6 months of age (9 studies; OR 1.93 (95% CI 1.18-3.15), p<0.0001). Group counselling increased odds of exclusive breastfeeding in the neonatal period (6 studies; OR 3.88 (95% CI2.09-7.22) p<0.0001;

		group. Given the large weight gains in both groups in the Belarussian study, the higher gain in the MBF group is not necessarily a beneficial outcome. Heinig 1993 and Kramer 2000a also reported on weight gain between six and nine months (outcome two) (significant heterogeneity), (P = .04) and dominated by the larger size of the Belarussian study. The pooled WMD was -2.26 (95% CI -16.94- 12.42) g per month. Akeson 1996a, Heinig 1993, and Kramer 2000a reported on weight gain from 8-12 months (outcome three); the WMD was -1.82 (95% CI -16.72-13.08) g per month, which excludes a reduced length gain in the EBF group of 5% of the mean and 10% of the SD for the Belarussian study. For length gain at three to eight months (outcome four), the studies again show significant (P < .01) heterogeneity. Kramer 2000a found a slightly but significantly lower length gain in the EBF group at four to eight months (difference -1.1 (95% CI -1.7- - 0.5) mm per month), whereas the pooled analysis yielded a WMD of - 0.4	random effects) and at 6 months (5 studies; OR 5.19 (95% CI 1.9-14.15) p<0.00001; random effects). A study on a national mass media campaign in Honduras reported that it increased exclusive breastfeeding from 48-70% at 1 month, from 24-31% at 4 months, from 7-12% at 6 months. The WHO growth reference study showed that infants exclusively breastfed were on average 360 g and 100g heavier at 4 and 6 months then predominantly non breastfed children on whom the US NCHS growth curves were based. Exclusive breastfeeding reduced HIV transmission compared with partial was reported in 1 study and a further study showed that HIV-free survival did not differ in infants who were HIV-negative at 4 months and were abruptly weaned or continued to be breastfed. Authors created a cohort model of child mortality and stunting by modelling the survival and linear growth status of the annual birth cohort of children from birth until 3 years in 36 countries with 90% of the global burden of stunted children. In children aged 6-23 months the baseline breastfeeding category is

		(95% CI -0.7 - 0.0) mm per month; the lower confidence limit is statistically compatible with a reduced length gain of less than 4% of the mean and 10% of the SD for the Belarussian study. Heinig 1993 and Kramer 2000a also reported on length gain at 6-9 months (WMD -0.4 (95% CI -1.0 - 0.1) mm per month) (outcome five). For the 8-12 month period, the results show a slightly but significantly higher length gain in the EBF group (WMD 0.9 (95% CI 0.3-1.4)) mm per month (outcome six). Observational analyses from the Belarussian study (Kramer 2000a) also include data on weight-for-age, length-for-age, and weight for-length z-scores at 6, 9, and 12 months. Means in both the EBF and MBF groups were well above (+0.5 to +0.6) the reference values at all three ages. Nonetheless, the weight-for-age z-score was slightly but significantly lower in the EBF group at all three ages: WMD -0.09 (95% CI -0.16 - -0.02) at six months, -0.10 (95% CI -0.18 - -0.02) at 9 months, and -0.09 (95% CI -0.17 to-0.01) at 12 months (outcomes seven to nine). Length-for-age z	breastfed (RR 1.0) vs. non breastfed (RR 2.3). Using this model, authors reported that mortality risk ratio for exclusive breastfeeding (age <1 month) was 1.0 and 1.48 for predominant breastfeeding, 2.85 for partial breastfeeding and 14.4 for no breastfeeding. In the same model for ages 6-35.9 months, the mortality risk ratio for predominant breastfeeding was 1.0 and 2.3 for no breastfeeding. Authors also reported on the effect of nutrition-related interventions on mortality and stunting in 36 countries. 99% coverage with breastfeeding promotion and support resulted in 11.6, 9.9 & 9.1% in proportional reduction in deaths before 12, 24 and 36 months respectively. The % of DALYs averted at 36 months was 21.9 million for 99% coverage with breastfeeding promotion and support.

		scores were very close to the reference (0) at 6 and 9 months and slightly above the reference (0.15) at 12 months. Again, the EBF group had slightly but significantly (except at 12 months) lower values: WMD -0.12 (95% CI -0.20 - -0.04) at 6 months,-0.14 (95% CI -0.22 to -0.06) at 9 months, and -0.02 (95% CI-0.10 - 0.06) at 12 months (outcomes 10 to 12). Mean weight for-length z-scores were high and rose (from about 0.65 to 0.80) from 6 to 12 months, with no significant differences between the EBF and MBF groups at any age: WMD 0.02 (95% CI -0.07- 0.11) at six months, 0.03 (95% CI -0.06 - 0.12) at 9 months, and -0.08 (95% CI -0.17- 0.01) at 12 months (outcomes 13 to 15). The prevalence of low (less than -2) z-scores did not differ significantly in the two Belarussian feeding groups for any of the three z scores at any of the three ages, although the small number of infants with low z-scores provided low statistical power to detect such differences. RRs (and 95% CIs) for low weight-for-age were 0.92 (0.04 - 19.04) at 6 months, 1.52 (0.16-14.62) at 9 months and 1.15 (0.13-10.31) at	

		12 months (outcomes 16 to18). For length-for-age, the corresponding figures were 1.53 (0.84-2.78) at six months, 1.46 (0.80-2.64) at 9 months, and 0.66 (0.23-1.87) at 12months (outcomes 19 to 21). For weight for- length, the figures were 0.31 (0.02- 5.34) at 6 months, 1.14 (0.24- 5.37) at 9 months, and 1.15 (0.13- 10.31) at 12 months (outcomes 22 to 24). The Belarussian study also provided data on head circumference. No significant differences were observed at six months (difference -1.0 (95% CI -2.3 - 0.3) mm) (outcome 25) or 9 months (+0.7 (95% CI -0.6 to +2.0) mm) (outcome 26), but the EBF group had a slightly but significantly larger circumference at 12 months (outcome 27): difference = +1.9 (95% CI 0.6 - 3.2) mm. Heinig 1993 reported nearly identical sleeping time (729 versus 728 minutes per day) in the two groups (outcome 28). Akeson 1996a reported similar total amino acid and essential amino acid concentrations at 6 months of age in the two feeding groups (outcomes 29 and 30). Both Kramer 2000a and a cohort study from Finland (Kajosaari	

		1983) reported an atopic eczema at one year (outcome 31). The two studies showed statistically significant (P= .03) heterogeneity, with Kajosaari 1983 reporting a significantly reduced risk (RR 0.40; 95% CI 0.21-0.78), but the larger Belarussian study finding a much lower absolute risk in both feeding groups and no risk reduction with EBF RR 1.00 (95% CI 0.60-1.69). Although Kajosaari 1983 also reported a reduced risk of a history of food allergy (outcome 32), double food challenges showed no significant risk reduction RR 0.77 (95% CI 0.25-.41) (outcome 33).Neither Oddy 1999 nor Kramer 2000a found a significant reduction in risk of recurrent (two or more episodes) wheezing in the EBF group pooled RR 0.79 (95% CI 0.49 -1.28) (outcome 34). In the Kajosaari 1983 study, the reduction in risk of any atopy at five years (outcome 35) in the EBF group was nonsignificant RR 0.68 (95% CI 0.40 -1.17), and no reduction in risk was observed for atopic eczema RR 0.97 (95% CI 0.50 -1.89) (outcome 36). A reduction in risk of borderline significance was	

		observed for pollen allergy at five years RR 0.53 (95% CI 0.28- 1.01) (outcome 37). Both Kajosaari 1983 and Oddy 1999 reported on risk of asthma at 5-6 years (outcome 38); the pooled RR was 0.91 (95% CI 0.61-1.36). Reduced risks of history of food allergy RR 0.61 (95% CI 0.12- 3.19) (outcome 39) and allergy to animal dander RR 0.81 (95% CI 0.24 - 2.72) at five years (outcome 40) were far from achieving statistical significance. Oddy 1999 found no reduction in risk of a positive skin prick test at 6 years in the EBF group RR 0.99 (95% CI 0.73- 1.35) (outcome 41). A small Italian study of hematologic outcomes at 12 months by Pisacane in 1995 reported a statistically significantly higher hemoglobin concentration (117 versus 109 g/L (95% CI for the difference = 4.03-11.97 g/L)) (outcome 42), a nonsignificant reduction in anemia (hemoglobin < 110 g/L) RR 0.12 (95% CI 0.01-1.80) (outcome 43), a nonsignificant higher ferritin concentration WMD+4.7 (95% CI -6.3 - 15.7mcg/L) (outcome 44), and a nonsignificant reduction in the risk	

		of low (less than 10 mcg/L) ferritin concentration RR 0.42 (95% CI 0.12 -1.54) (outcome 45) among infants in the EBF group. Of note in this study is that the exclusive and mixed breastfeeding continued in both groups until at least 12 months (a criterion for selection into the Pisacane 1995 study).Kramer 2000a recorded only one and two deaths (outcome 46) among the 621 and 2862 Belarussian infants in the EBF and MBF groups, respectively RR 2.30 (95% CI 0.21-25.37). The EBF had a significantly reduced risk of one or more episodes of gastrointestinal infection in the first 12 months of life (RR 0.67 (95% CI 0.46- 0.97) (outcome 47), which was maintained in a multivariate mixed model controlling for geographic origin, urban versus rural location, maternal education, and number of siblings in the household (adjusted OR 0.61 (95% CI 0.41 - 0.93).No significant reduction in risk was observed for hospitalization for gastrointestinal infection, however RR 0.79 (95% CI 0.42-1.49) (outcome 48). In the above-mentioned Australian cohort study,	

		Oddy 1999 found no significant reduction of risk for one or more episodes of upper respiratory tract infection (outcome49) in the EBF group RR 1.07 (95% CI 0.96-1.20). Neither Oddy 1999 nor Kramer 2000a found a significantly reduced risk of two or more such episodes pooled RR 0.91 (95% CI 0.82 -1.02) (outcome 50). Nor did Oddy 1999 find a significant reduction in risk of 4 or more episodes of upper respiratory infection RR 0.82 (95% CI 0.52 - 1.29) (outcome 51) or of one or more episodes of lower respiratory tract infection RR 1.07 (95%CI 0.86-1.33) (outcome 52). Kramer 2000a found a small and nonsignificant reduction in risk of two or more respiratory tract infections (upper and lower combined) RR 0.90 (95%CI 0.79 - 1.03) (outcome 53). The combined crude results of Oddy 1999and Kramer 2000a show a substantial and statistically significant reduction in risk for hospitalization for respiratory tract infection pooled RR 0.75 (95% CI 0.60-0.94), but the crude risk reduction in Kramer 2000a was nearly abolished and became	

		statistically nonsignificant in a multivariate mixed model controlling for geographic region, urban versus rural location, maternal education and cigarette smoking, and number of siblings in the household adjusted OR 0.96 (95% CI 0.71- 1.30) (outcome 54).In a study from Tucson, Arizona, (Duncan 1993) reported no difference in the average number of episodes of acute otitis median the first 12 months of life (outcome 55) in the exclusive versus MBF groups (1.48 vs. 1.52 episodes, respectively) (95%CI for the difference -0.49 -0.41 episodes). Duncan 1993 and Kramer2000a both found a slightly elevated risk for one or more episodes of otitis media pooled RR 1.28 (95% CI 1.04 -1.57) (outcome56), but Duncan 1993 found a nonsignificant reduction in risk for frequent titis media RR 0.81 (95% CI 0.43-1.52) (outcome57).	
EXTERNAL VALIDITY			
Generalisability	Y	Y - for the results of the studies conducted in developed countries	N
Applicability	Y	Y	Y

Comments	The unclear randomization and allocation concealment processes in the study suggest selection bias was possible. Furthermore the use of a telephone interview further suggests recall/reporting bias.	Definitions of exclusive breastfeeding varied across studies.	In the cohort model of child mortality and stunting, the protective effect of breastfeeding is assumed to cease when the child reaches 2. Although authors have considered a number of breastfeeding interventions and reviews, details of these interventions and reviews are not provided.	

Table 24.3 Summary used to make evidence statement for breastfeeding and maternal and infant outcome (cont.)

STUDY DETAILS (Review)	**Britton et al. 2007 [585]**	**Abdulwadud et al. 2007 [582]**	**Baird et al. 2009 [403]**	**Gatti. 2008 [491**	**Ines Couto de Oliveira et al. 2001 [483]**
Affiliation/source of funds	University of York, UK	ASEBE TEFERI, Ethiopia; IMPART; BC Centre of Excellence for Women's Health, Canada.	University of Southampton, South Hampton General Hospital UK, Medical Research Council.	Centre for Health Disparities Research, University of Pennsylvania, National Institute of Health Institutional Training Grant.	Brazilian Government Agency CAPES.
Study design	Meta Analysis	Meta Analysis	Systematic Review of (3 systematic reviews)	Systematic review (15 prospective, longitudinal; 3 cross sectional, 3	Systematic review (33 experimental & 31 quasi-experimental studies)

				secondary analysis of datasets)	
Level of evidence	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.	111-211	III-1 Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method).	III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.	I
Date of search	1966-2005	1951 - 2006	1966-2008	1996-2007	1980-1999
Number of studies	34	0 trials have evaluated this	3	20	64
Total number of participants	29385 mother - infant pairs	N/A	NS	36700	>3700
Population characteristics	Pregnant women intending to breastfeed, postpartum women intending to breastfed and women breastfeeding their babies; Canada, USA, UK, Brazil,	NA	Breastfeeding mothers or pregnant women intending to breastfeed from disadvantaged backgrounds (in developed countries),	Healthy, full term breastfeeding dyads during the first 6 months of life.	Pre-natal, and post-natal women.

	Bangladesh, Australia, India, Nigeria, Italy, Iran, Netherlands, Belarus, Mexico, Sweden.				
Range of exposure	Intervention: Pregnant or lactating women intending to breastfeed receiving contact with an individual or individuals (professional or volunteer) offering support which is supplementary to standard care with the purpose of facilitating continued breastfeeding Comparator: Mothers receiving usual postnatal care which varies between and within countries.	Intervention: Any type of workplace strategy to encourage, assist and support breastfeeding for women returning to work after birth Comparator: Women receiving usual care.	Intervention: Reviews on interventions promoting and prolonging breastfeeding and providing support for mother who are breastfeeding. Interventions include breastfeeding literature, lay support, professional support, peer support and 1 on 1 counselling.	Examine reasons why women had low rates of duration and exclusivity of breastfeeding &/or associations between perceived milk supply and other maternal perceptions. 4 of the studies examined tools to predict insufficient milk supply. This was done through validated questionnaires, tools, Theory of planned behaviour, standard definitions, non validated tools, open ended questions, H & H Lactation Scale, The Perceived Insufficient Milk (PIM) Tool.	Primary care interventions designed to extend breastfeeding duration (exclusive, full, or any kind of breastfeeding) during the prenatal and/or postnatal period interventions that took place during the delivery period only were excluded.

Length of follow-up	Up to 9 months post partum	NA	NS	1 month to 24 months	Range from 2 to 12 months but most to 6 months.
Outcome(s) measured	Primary: 1. Effect of the interventions on duration of any breastfeeding to specified points in time; 2. Stopping feeding before 4 to 6 weeks and 2, 3, 4, 6, 9 and 12 months. Secondary: 1. Exclusive breastfeeding; 2. Measures of neonatal and infant morbidity; 3. Measures of maternal satisfaction with care or feeding method.	Primary: 1. Rate, duration and prevalence of exclusive breastfeeding. Secondary: 1. Employer-related; 2. Mother-related; 3. Infant-level outcomes.	Breastfeeding initiation, breastfeeding duration.	Breastfeeding levels, reasons for ceasing breastfeeding, supplementation and breastfeeding level, breastfeeding difficulties, breastfeeding self efficacy, breastfeeding satisfaction, prediction of breastfeeding at 12 weeks, breastfeeding support, perceptions of milk supply, coping strategies of PIM, risk factors for early cessation.	Extension of breastfeeding (full, partial or any kind of breastfeeding) at points in time varying from 4 weeks to 6 months. Main outcome measure was the proportion of mothers breastfeeding at, or until, a specified time point. Some studies reported median or mean breastfeeding duration.
INTERNAL VALIDITY					
Databases included in search	Cochrane Pregnancy and Childbirth Group's Trials Register, Medline, Embase, MIDIRS.	Cochrane Pregnancy and Childbirth Group's Trials Register, Central, Medline, Cinahl, Lilacs, C2-Spectr.	Cochrane, Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Medline.	Cinahl, Medline, Pubmed.	Literature search used an earlier systematic infant-feeding review that focused on the developed world as the starting point.

					Additional databases searched (Medline, Popline, Health- Star, CAB-Health, Cochrane Library, CINAHL, and Lilacs) using the key words promotion, intervention, assessment, programme, community, education, effect, impact, and evaluation (linked to breastfeeding).
Statistical analysis methods	RevMan 2003; Relative risks; random effects model; subgroup analyses.	Intended to use RevMan 2003, fixed effect meta analysis, random effects model.	RR	Factor analysis, regression, survival analysis.	Present the interventions' maximum duration of effect that proved was statistically significant at a 90% level. The effects presented are the percentage of exclusive breast-feeding among intervention and control groups, and corresponding P value. The

					attributable fraction and 95% confidence intervals were constructed when data presented by the authors were conclusive or suggestive of effect. The attributable fraction (AF) was defined as the proportion of the outcome rate achieved in the intervention group that is due to the intervention, and is a measure of effectiveness. It is the difference between breastfeeding rates in the intervention (I) and control groups, expressed as a proportion of the rate in the intervention group: AF = (I - C)/I. or from the relative risk (RR). ; AF = (RR – 1)/RR.

Overall quality assessment (Positive/Negative or Neutral) plus descriptive)					P
RESULTS					
Outcome	There is a beneficial effect on the duration of any breastfeeding up to 6 months with the implementation of any form of extra support RR 0.91 (95% CI 0.86- 0.96). Authors divided trials into 3 categories - high (> 80%), intermediate (60-80%) or low (<40%) initiation rates in the local area. Analysis of the trials conducted in settings with immediate initiation demonstrated all forms of support had a significant benefit on breastfeeding RR 0.92 (95% CI 0.85-0.98), whereas there	No randomised controlled trials or quasi-randomised controlled trials were identified.	Interventions that use education and 1 on 1 support are effective in increasing breastfeeding initiation rates. Any form of additional support for mothers who are breastfeeding increases the duration of breastfeeding. Many of the studies reviewed were targeted at low income groups.	Many women were found to discontinue breastfeeding during the first few weeks post partum as a result of Perceived Insufficient Milk (PIM) supply. Many women used infant satisfaction cues (e.g. crying, unsettled) as their primary indicators of milk supply. The H & H Lactation Scale and the Perceived Insufficient Milk Tool have been found useful to identify women at risk during early post-partum. Furthermore, PIM was associated with early weaning and / or decreased	Effect on duration with Prenatal Interventions: 6 of 8 studies effective (4 / 6 RCTs) with AF ranging from 19-78% for full BF at 6mo to any BF at 4 weeks. Effect on duration with Postnatal Interventions: 3 / 9 studies effective (2 / 8 RCTs) with AF ranging from 15-53% for any BF at 2 months to full BF at 6 months. Effect on duration with BOTH Pre- and Postnatal Interventions: 7 / 9 studies effective (3 / 4 RCTs) with AF ranging from 20-92% for full BF at 4 months in 2 studies;

	was no significant effect where there were high or low breastfeeding initiation rates RR 0.91 (95% CI 0.81 - 1.01) and RR 0.88 (95% CI 0.69- 1.12). The effect of any support on mothers exclusively breastfeeding is greater than on women continuing any form of breastfeeding RR 0.81 (95% CI 0.74-0.89). Professional support vs. usual care showed professional support to be effective at 4 months only RR in 5 trials 0.78 (95% CI 0.67-0.91). The overall effect of extra support on stopping any breastfeeding did not reach statistical significance. Professional support			exclusivity in 10 studies. PIM was also associated with lower self efficacy or maternal confidence scores. Use of formula in hospital was associated with PIM in 3 studies and ceasing breastfeeding before leaving the hospital was related to PIM in 1 study.	One study had an AF of 91% for full BF at 5 months. Effect on duration with BOTH Hospital and Postnatal Interventions: 4 / 7 studies effective (3 / 6RCTs) with AF ranging from 24-88% for any BF at 4 months to exclusive BF at 4 months. Effect on duration with both Hospital and Pre- and Postnatal Interventions: All 4 studies effective (3 RCTs) with AF ranging from 20-100% for any BF at 1 month to full BF at 6 months.

	resulted in a beneficial effect on exclusive breastfeeding RR in 16 trials 0.94 (95% CI 0.87 - 1.01). Professional support showed to be beneficial on exclusive breastfeeding rates RR 0.91 (95% CI 0.84 -0.98). Trials using lay people to conduct breastfeeding interventions demonstrated a significant decrease in breastfeeding cessation RR 0.86 (95% CI 0.76 -0.98). Combined lay and professional support vs. usual care showed a significant reduction in cessation of any breastfeeding RR 0.84 (95% CI 0.77-0.92) especially in				

	the first 2 months RR before 4 to 6 weeks 0.65 (95% CI 0.51- 0.82); RR before 2 months 0.74 (95% CI 0.66- 0.83). 2 studies showed a significant reduction in cessation of exclusive breastfeeding RR 0.62 (95% CI 0.50- 0.77). Studies using face to face support showed a statistically significant benefit RR for giving up any breastfeeding 0.85 (95% CI 0.79- 0.92). No significant effect was demonstrated when phone and face to face support were provided on breastfeeding continuation RR 1.00 (95% CI 0.91- 1.09). One study demonstrated a significant reduction in risk of 1 or more				

	GI infections and atopic eczema in those receiving support from health professional trained in WHO/UNICEF Baby Friendly Initiative. A further study found no significant difference between peer peer and control group mean score on the Maternal Breastfeeding Evaluation Scale (mean scores 52.81 (SD 5.69) vs. 52.98 (SD 5.94) p=0.26).				
EXTERNAL VALIDITY					
Generalisability	y - although some studies were conducted in developing countries.	n/a	y	y	1
Applicability	y	n/a	y - Note that the review focused on women from disadvantaged backgrounds but included studies on	y	1

			women generally.		
Comments		The lack of evidence resulting from this review emphasises the need for further research into breastfeeding education and support in the workplace post delivery.	The objective's of this review were focused on all interventions directed at changing health behaviours of young women from disadvantaged backgrounds and included smoking, physical activity and diet.	The majority of the studies reviewed identified IM as PIM. Both of the terms have different definitions.	
Conclusion	Additional professional support was effective in prolonging any breastfeeding, but its effects on exclusive breastfeeding were less clear. WHO/UNICEF training courses appeared to be effective for professional training. Additional lay support was effective in prolonging exclusive breastfeeding, while its effects on duration	No trials have evaluated the effectiveness of workplace interventions in promoting breastfeeding among women returning to paid work after the birth of their child. The impact of such intervention on process outcomes is also unknown. Randomised controlled trials are required to establish the benefits of various types of	Consistent evidence was found of intervention features associated with effective changes in a number of health behaviours. Interventions to change health behaviours of women of child-bearing age from disadvantaged backgrounds require: an educational approach delivered in person by professionals or peers; provide continued support	PIM is one of the most common and influential reasons for low rates of breastfeeding duration and exclusivity. Future research should be conducted to determine who is at high risk and to further validate screening tools; and whether PIM is a physiological or psychological issue. Perceived milk supply is considered modifiable and well-	The primary health care units should inform, encourage, and support pregnant women in breastfeeding; the maternity hospitals should allow women to bond with their babies and help them to establish breastfeeding; and the primary health care units should be able to guide, reinforce, and support this practice continuously, completing the cycle.

	of any breastfeeding were uncertain. Effective support offered by professionals and lay people together was specific to breastfeeding and was offered to women who had decided to breastfeed. Further trials are required to assess the effectiveness (including cost-effectiveness) of both lay and professional support in different settings, particularly those with low rates of breastfeeding initiation, and for women who wish to breastfeed for longer than three months. Trials should consider timing and delivery of support interventions and relative effectiveness	workplace interventions to support, encourage and promote breastfeeding among working mothers.	after the initial intervention; some evidence to t that social support from peers and family involvement in the intervention maybe important. These findings are of relevance to the design of an intervention to improve diet in this group of women.	informed interventions to reduce the incidence of PIM might be a key element for improving rates of successful breastfeeding.	Although there is evidence supporting the effectiveness of primary care strategies in extending breastfeeding duration, there is a need for broad-based, well-designed studies testing the effect of the combination of the procedures referred above, preferably spanning the prenatal and postnatal periods, to encourage the development of evidence-based protocols concerning the promotion, protection, and support of breastfeeding in primary care.

	of intervention components, and should report women's views. Research into appropriate training for supporters (whether lay or professional) of breastfeeding mothers is also needed.				

U1.7 Summary of the studies *Included,* but not used in the Body of Evidence Statements.

The references of the non-systematic reviews deemed relevant to this topic, but that did not contribute to a body of evidence statement appear below.

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25. FOOD PROCESSING (UI.8)

Evidence Statements

25. FOOD PROCESSING (U1.8)

How does the processing, preparation and cooking of food, including:

- ***Frozen/ canned/ dried/ juice; and***
- ***Cooking methods, for example boiling, stir frying, roasting, microwaving, steaming etc***

change the bioavailability/nutritional value of the food, food safety and environmental impact?

Executive Summary

In the period of the search (2002-2009) there were very few reviews of relevance to this question. Only three of the 30 relevant reviews were systematic and graded of positive quality. Most were non-systematic, with no description of the search methods or quality assessment processes. Most addressed very specific questions (e.g. about the effect of processing on a particular nutrient or bioactive substance) rather than undertaking a comprehensive review. Thus the impact of processing on most essential nutrients was not addressed in these reviews. Almost all focus on industrial rather than domestic food processing. In general the authors conclude that new non-thermal methods of food preservation that are being developed (e.g. high pressure processing (HPP), pulsed electric fields (PEF), high intensity pulsed light, irradiation, ultrasound, and oscillating magnetic fields) offer the promise of better quality preserved foods with improved nutrient retention.

It was possible to produce four Evidence Statements only related to two topics: bioavailability/nutritional value and food safety.

In relation to food safety, there were three themes addressed:

1. The need for adequate cooking to ensure safety of meat products
2. Advice about methods of cooking meat to reduce the risk of production of mutagenic heterocyclic amines (HCAs) and polycyclic amine hydrocarbons (PAHs)
3. Summaries of the recently emerged problem of acrylamide in foods. This is still an active area of research and at this stage there is no advice that can be given to consumers to address this issue in relation to domestic food preparation.

There was only one review related to environmental impact and it was solely a summary of knowledge about the technical characteristics of various packaging materials used with food products, so it was not possible to develop an Evidence Statement. Glass may be a preferred material from an environmental point of view, but comprehensive life cycle analysis data is not available on which to base recommendations.

In most papers the authors did not describe a quantitative summary of results and often only a small part of the paper is relevant to the search questions. For this reason, structured summaries of the papers have not been developed; rather for each paper, a brief description of the search methods,

quality rating and summary of relevant conclusions are provided. Where very limited information was included, a full direct quote has been given, otherwise the key points have been summarised. The 2007 World Cancer Research Fund report concluded that there was Limited Suggestive evidence that grilled or barbecued animal food increases the risk of cancer. In the goals and recommendations the following summary is given (p385):

"While evidence suggesting that grilled (broiled) and barbecued (charbroiled) animal foods are a cause of stomach cancer is limited, there is evidence from experimental settings showing that carcinogens are formed when meats, animal foods, and some other foods are cooked at very high temperatures, and most of all when they are exposed to direct flames. While the epidemiological evidence that these are causes is limited, it is a wise precaution to avoid foods cooked this way. This effect is not found when foods are cooked by use of boiling water".

This is consistent with the fourth body of evidence statement below.

25.1 PROCESSING, PREPARATION and COOKING and NUTRITIONAL VALUE OF FOOD

How does the processing, preparation and cooking of food change the bioavailability/nutritional value of the food?		
Evidence Statement		New non-thermal methods of food processing may improve the nutritional quality of the food supply.
Grade of recommendation		D
Evidence Statement		Frying of foods is likely to affect the nutritional quality of foods adversely.
Grade of recommendation		D
Component	**Rating**	**Notes**
Evidence Base	Poor	13 non-systematic reviews (all negative quality). Many consider very limited and specific issues.
Consistency	Good	Most agree that new technologies have the capacity to improve nutritional bioavailability and that frying is undesirable.
Clinical impact	Poor	No quantitative assessment of impacts but likely effects slight.
Generalisability	Good	Most research based in US, UK and Europe.
Applicability	Good	No reason to believe results not applicable in Australian context.

25.2 PROCESSING, PREPARATION and COOKING and FOOD SAFETY

How does the processing, preparation and cooking of food change food safety?		
Draft Recommendation		Raw meat poses significant risks for foodborne illness and adequate cooking is essential to ensure food safety.
Grade of recommendation		B
Draft Recommendation		Production of mutagenic compounds during meat cooking can be minimised by using low temperature and water-based cooking methods.
Grade of recommendation		C
Component	**Rating**	**Notes**
Evidence Base	Good	15 reviews (3 positive quality; 1 neutral; 11 negative) - mostly non-systematic.
Consistency	Good	Consistent agreement on the importance of appropriate heat processing for food safety.
Clinical impact	Satisfactory	Only limited quantitative data on outcomes but likely to be moderate to substantial.
Generalisability	Good	Most research based in US, UK and Europe.
Applicability	Good	No reason to believe results not applicable in Australian context.

SUMMARIES OF INCLUDED ARTICLES

1) NUTRITION

Abbot MJ, Byrd-Brenner C. The State of the American Diet. How Can We Cope? *Topics in Clinical Nutrition* 2007; 22(3):202-233 [582]

Quality Rating: Negative.

Search Method: Medline and Google Scholar were used to search for articles on dietary intake and dietary surveys in the US from 1994-2006.

Quote:

"For those Americans who may have limited access to fresh food supply (eg. those living in inner city and remote rural areas) several options are available providing alternative sources of nutrient-rich food that have prolonged shelf lives. Advances in food preservation and processing have made the food supply nutrient-rich as well as safer than ever, while modern food processing methods preserve nutrient integrity, making the nutrient content of fresh, frozen, and canned foods highly comparable. The ability to stock and store frozen and canned food allows for those with more limited food availability access the option to stock a kitchen with shelf-stable (or longer life) nutrient-dense foods capable of meeting total nutrient needs. Furthermore, frozen and canned foods provide options for busy consumers looking for quick and easy ways to prepare meals" (p215).

Aherne SA, O'Brien NM. Dietary Flavonols: Chemistry, Food Content, and Metabolism. *Nutrition.* 2002; 18:75-81. [409]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"Although resistant to heat, oxygen, and moderate degrees of acidity, kitchen preparation will cause some flavonoid losses. Skins and leaves of most fruit and vegetables contain the greatest proportion of flavonols; hence preparation involving peeling, skinning, trimming and/or leaf selection may remove and reduce total flavonol content

Cooking tomatoes, broccoli and onions has been shown to reduce the level of quercetin in these foods. Boiling food results in the greatest reduction in quercetin content. This decrease is probably due to the leaching action of cooing water and/or chemical or thermal degradation. Microwave cooking also causes reduction in flavonol content of foods, whereas frying causes only a slight reduction in flavonol levels. However, an increase in frying time significantly reduces the levels of quercetin glucoside.

Flavonol content in processed foods (canned, glass jars, frozen) can be significantly lower (approximately 50%) than levels in fresh products. However processing of food products can increase flavonol levels in foods. The accumulation of quercetin or release of the aglycone form in processed foods can occur as a consequence of enzymatic hydrolysis of quercetin conjugates during pasteurisation, processing procedures and fermentation.

Intake of tea flavonoids can differ significantly depending on the type of tea or tea products consumed and method of preparation…. Particle size largely explains the differences seen in flavonoid yield between tea prepared from tea bags and loose teas. Tea produced from tea bags has higher flavonoid levels. Increase brewing time allows for a more efficient and improved extraction of flavonoids from black tea [28]" (p78).

Beekwilder J, Hall RD, RicDeVos CH. Identification and dietary relevance of antioxidants form raspberry. *BioFactors* 2005; 23:197-205. [290]

Quality Rating: Negative.

Search Method: Not stated.

Quote:

"When raspberries are snap frozen in liquid nitrogen, and subsequently stored at -20°C for a year, vitamin C content decreases by up to 50% . Other parameters such as the antioxidant capacity and anthocyanin content seem to be unaltered. A variety of short term treatments (3 days at room temperature, 4°C or -30°C) seem to have no detrimental effect greater than 20% on the antioxidant capacity, anthocyanin content or ellagitannin content…. In conclusion, freezing hardly affects the quality and quantity of raspberry antioxidants" (p202-3).

Boskou, D. Losses of Natural Antioxidants and Vitamin during Deep-Fat Frying. *Forum of Nutrition* 2003; 56:343-345 [358]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

Edible oils are important sources of liposoluble vitamins and natural antioxidants. When they are used for frying for prolonged periods they deteriorate … and important phytonutrients or other minor constituents are partially or wholly lost. Functional ingredients include:

- Tocopherols are present in all oils used for frying
- Phenolic acids such as sinapic, caffeic, ferulic, protocatechuic, and syringic are found in olive oil

- Lignon and related compounds (sesamol, sesaminol and sesamin) are strong antioxidants present in sesame oil
- Phytosterols are potent antipolymerization agents and provide frying oil with increased resistance upon heating at elevated temperatures
- Hydroxytyrosol is present in significant amounts in virgin olive oil and inhibits LDL oxidation
- Squalene is a free radical scavenger and is present in olive oil, wheat germ oil and bran oil.

These natural antioxidants have varying stabilities at frying temperatures….however this aspect of frying oils is only poorly studied and there are possible other minor constituents not yet identified which may contribute towards losses of functionality during heating.

Bruhn, C. Position of the American Dietetic Association: Agricultural and Food Biotechnology. *Journal of the American Dietetic Association* 2006; 106:285-293. [286]

Quality Rating: Negative.

Search Method: Updating the ADA 1995 position. Based on the Institute of Food Technologists expert panel report on Biotechnology and Foods (*Food Techol* 2005;54:124) and an ILSI task force comprehensive assessment of nutritional and safety issues associate with food produced with biotechnology (*Compr Rev Food Sci Technol* 2004;3:38-104).

Quote:

"It is the position of the American Dietetic Association that agricultural and food biotechnology techniques can enhance the quality, safety, nutritional value, and variety of food available for human consumption and increase the efficiency of food production, food processing, food distribution, and environmental and waste management. The American Dietetic Association encourages the government, food manufacturers, food commodity groups, and qualified food and nutrition professionals to work together to inform consumers about this new technology and encourage the availability of these products in the marketplace" (Abstract).

Camara F, Amaro MA. Nutritional aspects of zinc availability. *International Journal of Food Sciences & Nutrition* 2003;53:143-151. [375]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"Thermal treatments of food can impair zinc availability as a consequence of the formation of Maillard reaction products.

Processing of some vegetable foods, however, leads to hydrolysis of phytic acid to penta-, tetra- and tri-inositol phosphate with a low capacity for binding minerals…. Thus cooking of white beans reduced the inositol hexaphosphate content. Although zinc dialyzability from cooked beans was not higher than from raw beans, albumin deriving from cooked beans showed a significant increase in zinc dialyzability and that is due in part to the presence of inositols, mono- and diphosphates.

Fermentation of milk with S thermophilus and L bulagricus yielding yogurt increase zinc availability compared with raw milk justified by several possible reasons:

i) zinc is associated mainly with casein molecules which are thermoresistant;

ii) fermentation of milk by homo-fermentative bacterias produces lactic acid, which helps reduce the pH leading to coagulation of casein micelles" (p148).

Choe E, Min DB. Chemistry of deep-fat frying oils. *Journal of Food Science* 2007; 72(5):R77-R86. [241]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"Deep fat frying changes the flavour, stability and quality of the oil by hydrolysis, oxidation and polymerization. Tocopherols, essential amino acids, and fatty acids in foods are degraded during deep fat frying.

Frying time, food surface area, moisture content of food, types of breading or battering materials and frying oil influence the amount of oil absorbed to [ranging from 10-38%]" (pR77).

"Intermittent heating and cooling of oils causes higher deterioration than continuous heating, due to the oxygen solubility increase when the oil cools down from the frying temperature. 25% of the linoleic acid of sunflower oil was destroyed by intermittent frying whereas only 5% was destroyed in continuous frying" (pR82).

"A small surface-to-volume ratio of fryer for minimum contact of oil is recommended for deep-fat frying" (pR83).

Elvevoll EO, Østerud B. Impact of processing on nutritional quality of marine food items. *Forum of Nutrition* 2003;56:337-340. [359]

Quality Rating: Negative.

Search Method: Not stated (summary of studies from the author's research group in Norway).

Summary:

Marine oils for human consumption are normally subjected to significant refining procedures to remove pesticides and make an edible and stable product, including: degumming, deacidification, bleaching, deodorization. These processes remove number of components (proteins, peptides, amino acids, free fatty acids, phospholipids, pigments, sterols and metals) and may destroy potent antioxidants and remove components with potential beneficial effects.

At least one study comparing the effect of slightly processed (cold smoked) salmon or cod, versus refined oil "*indicate that there may be protective substances, relevant to the development on CHD, in seafood and marine oils whose effect disappears when the product is subject to rough processing conditions such as blanching, coking or refining"*

Esteve MJ, Frigola A. Refrigerated fruit juices: quality and safety issues. *Advances in Food and Nutrition Research* 2007; 52:103-139. [258]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

Newly developed non-thermal methods allow processing of foods below the temperatures used during pasteurisation, so flavours and essential nutrients undergo minimal or no changes. Foods can be non-thermally processed by irradiation, high hydrostatic pressure, antimicrobials, ultrasound, filtration, and electrical methods such as pulsed electric fields (PEFs), light pulses, and oscillating magnetic fields. Technological developments of high pressure and high intensity PEF processing have received increased attention during the last decade. PEF treated orange juice appears to retain a higher ascorbic acid content than heat-pasteurized orange juice stored at 4°C. High pressure treatment of orange juice can produce significant *increases* of 20-43% in the carotenoids content of fresh orange juice, and the levels are better retained during storage.

Henry CJK, Heppel N. Nutritional losses and gains during processing: future problems and issues. *Proceedings of the Nutrition Society* 2002; 61:145-148. [397]

Quality Rating: Negative

Search Method: Not stated.

Quotes:

"Heat is the most convenient way of extending the keeping quality of food. Heating food not only destroys microbes but also inactivates enzymes and toxins. Whilst the nutritional quality of foods (especially for some vitamins) may be reduced by heat processing, a judicious combination of high temperature and short time minimizes nutrient losses.

One example of the effect of change of process .... on the nutritional quality is thermal processing. The older in-container process is well established but gives a product that is measurably lower in the heat sensitive vitamins than that produced by an ultra-high temperature (aseptic processing) method. Recent work has concentrated on extending aseptic processing to viscous foodstuffs and foods containing solid particles, to the extent that a large range of sauces, soups and stews can be produced, even whole spaghetti. It is possible, using rapid heating, to produce sterile undercooked foodstuffs which, on heating by the consumer, will result in optimum quality on the plate" (p146).

Knorr D, Ade-Omowaye BIO, Heinz V. Nutritional improvement of plant foods by non-thermal processing. *Proceedings of the Nutrition Society* 2002; 61:311-318. [393]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

As a result of consumer demand for minimally-processed fresh-like food products with high sensory and nutritional qualities, there is a growing interest in several new non-thermal technologies, including high pressure processing (HPP), pulsed electric fields (PEF), high intensity pulsed light, irradiation, ultrasound and modified atmosphere packaging. Some of the quality advantages of these techniques (which subject the food to lower temperatures during processing) include: less reduction in ascorbic acid and higher retention of beta-carotene in juices, and whole vegetables like broccoli.

Nemeth K, Piskula MK. Food content, processing, absorption and metabolism of onion flavonoids. *Critical Reviews in Food Science and Nutrition.* 2007;47:397-409. [256]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

The onion is one of the richest and commonly consumed sources of dietary flavonoids, and quercetin accounts for a significant percentage of total daily flavonoid intake. The onion bulb contains a wide range of quercetin, isorhamnetin and kaempferol derivatives and the highest concentration of quercetin (expressed as aglycone) is found in onions (284-486mg/kg fresh edible part).

Flavonoids are generally found in higher concentrations in outer layers and skin of fruits and vegetables (where they provide ultraviolet protection) therefore peeling results in significant losses. After home-like peeling, red onions contained 79% of the original total content of quercetin glucoside and only 27% of the anthocyanins. Quercetin glucosides were not degraded when onion was cooked but transferred to the cooking water, turning onion soup into a good source of flavonoids. The total flavonoid content was also unaltered by frying in oil and butter.

Pokorn J, Panek J, Trojakova L. Effect of food component changes during frying on the nutrition value of fried food. *Forum of Nutrition* 2003; 56:348-350. [357]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

Most nutritional value generally decreases during deep frying as some nutrients are lost. Most losses occur in surface layers which are heated to temperatures close to that of the frying oil. The most significant nutritional effects of frying are:

- Lipid interchange between frying oil and fried food. If fresh oil is used, the content of essential fatty acids and tocopherol can increase. If the oil has been used several times the tocopherols will be almost completely lost.
- Changes of protein. Proteins are sensitive to heat and their digestibility decreases during frying. Tryptophan and lysine are two particularly heat sensitive amino acids.

Rungapamestry V, Duncan AJ, Fuller Z, Ratcliffe B. Effect of cooking brassica vegetables on the subsequent hydrolysis and metabolic fate of glucosinolates. *Proceedings of the Nutrition Society*. 2007; 66:69-81. [262]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"Cooking brassica vegetables affects the release of breakdown products of glucosinolates, which is the upper gastrointestinal tract following consumption of raw brassica containing active plant myrosinase. After consumption of cooked brassica devoid of plant myrosinases (because of inactivation during heating), glucosinolates are hydrolysed in the colon under the action of resident microflora. Feeding trials have show that hydrolysis of glucosinolates and absorption of isothiocyanates are greater following ingestion of raw brassica with active plant myrosinase than after consumption of the cooked plant.. These sources of variation may partly explain the weak epidemiological evidence relating consumption of brassicas to prevention of cancer" (Abstract).

SUMMARIES OF INCLUDED ARTICLES

2) FOOD SAFETY

Archer, DL. Freezing: an underutilized food safety technology*? International Journal of Food Microbiology* 2004; 90:127-138. [351]

Quality Rating: Negative.

Search Method: Not stated.

Quote:

"Freezing is an ancient technology for preserving foods. Freezing halts the activities of spoilage microorganisms in and on foods and can preserve some microorganisms for long periods of time. Frozen foods have an excellent overall safety record. The few outbreaks of food-borne illness associated with frozen foods indicate that some, but not all human pathogens are killed by commercial freezing processes. Freezing kills microorganisms by physical and chemical effects and possibly through induced genetic changes. Research is needed to better understand the physical and chemical interactions of various food matrices with the microbial cell during freezing and holding at frozen temperatures. The literature suggests that many pathogenic microorganisms may be sub-lethally injured by freezing, so research should be done to determine how to prevent injured cells from resuscitating and becoming infectious. Studies on the genetics of microbial stress suggest that the induction of resistance to specific stresses may be counteracted by, for example, simple chemicals. Research is needed to better understand how resistance to the lethal effect of freezing is induced in human pathogens and means by which it can be counteracted in specific foods. Through research, it seems possible that freezing may in the future be used to reliably reduce populations of food-borne pathogens as well as to preserve foods" (Abstract).

Butt AA, Aldridge KE, Sanders CV. Infections related to the ingestion of seafood. Part 11: parasitic infections and food safety. *The Lancet Infectious Diseases* 2004; 4:294-300. [341]

Quality Rating: Positive.

Search Method: Medline search of English language articles using the terms "seafood", "infection", "parasites" and specific organisms over the period 1980-2003.

Quotes

"Infections related to the ingestion of seafood are common. Fortunately most of these infections are mild and viral in origin and resolve without specific therapy. Consumers should take common precautions including obtaining seafood from reputable sources especially if the seafood is to be consumed uncooked. Adequate cooking of seafood is the safest way to prevent related infections" (Abstract).

"Heating is the most effective method of eliminating the risk of parasitic disease from seafood. The internal temperature of the thickest part of the product must reach a minimum of 65°C for 15s or longer. Heat smoking is also effective but cold smoking does not produce temperatures high enough for inactivation of the parasites. Freezing is also an acceptable method for parasitic inactivation, but is also temperature and time dependent: 15h at -35°C or 7 days at -20°C will be effective.

Individuals consuming a single serving of a raw shellfish from an approved harvesting site in the USA may have an estimated probability of one in 100 of becoming infected with a moderately infective enteric virus. To reduce the chance of infection from seafood it is recommended that such food be eaten fully cooked and that the catch should be harvested only from approved areas. People with certain medical conditions, especially liver disease, should take extra care to ensure that their seafood is cooked" (p299).

Dalton CB, Gregory J, Kirk MD, Stafford RJ *et al.* Foodborne disease outbreaks in Australia, 1995 to 2000. *Communicable Diseases Intelligence* 2004; 28(2):211-224. [333]

Quality Rating: Positive.

Search Method: Surveys of state and territory health departments for information on confirmed or suspected outbreaks from 1995-2000. Medline search plus state and territory health agency bulletins and the proceedings of the Australian Society of Microbiology, the Public Health Association and the Communicable Diseases Network Australia were reviewed to identify other foodborne outbreaks.

Summary:

From 1995 through 2000, 293 outbreaks were identified, with 214 being of foodborne origin. There were 20 deaths attributed to foodborne illness.

The most frequent aetiology of outbreaks was *Salmonella* in 35% of outbreaks, *Clostridium perfringens* in 14% and cigatera toxin in 11%. *Salmonellosis* and *Listeria monocytogenes* were each responsible for 40% of deaths. Restaurants and commercial caterers were associated with the highest number of outbreaks and cases.

The most frequently implicated vehicles in the outbreaks were meats (30%), fish (16%), seafood (6%), salad (6%), sandwiches (5%) and eggs (4%). Chicken was the most frequently implicated meat and was associated with 13% of outbreaks.

Dybing D, Farmer PB, Andersen M, Fennell TR *et al.* Human exposure and internal dose assessments of acrylamide in food. *Food and Chemical Toxicity* 2005;43:365-410. [314]

Quality Rating: Positive.

Search Method: Surveys questionnaire sent by ILSI Europe Expert Group on Acrylamide and ILSI North America to 31 individuals and institutions reporting on existing acrylamide dietary exposure assessment and databases. Detailed descriptions of use of best practice exposure assessment methods.

Summary:

The foods that contribute most to acrylamide exposure vary depending upon the population's eating habits and the way food is processed and prepared. Generally the most important categories of food appear to be: fried potato products such as French Fries and chills, ready-to-eat breakfast cereals, baked goods such as cookies, pies and cakes, brewed coffee and breads.

Little information is available on the acrylamide levels in food cooked at home and the overall contribution of home cooked foods to acrylamide exposure. Estimates of a 50% contribution to overall acrylamide intake have been made. Research on the formation of acrylamide during home cooking is underway in the US (NCFST) and the UK (FSA) but no quantitative results are available to date.

Options to reduce levels of acrylamide in food, either industrially processed or prepared at home, are very limited.

Friedman M, Levin CE. Review of methods of the reduction of dietary content and toxicity of acrylamide. *Journal of Agricultural and Food Chemistry.* 2009; 56(15):6113-6140. [217]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"Acrylamide is ubiquitous in the food supply and at this time public health measures for reducing acrylamide in the diet should focus on the highest potential foods, not on reducing the mean acrylamide intake…For the American diet based on ~ 2500 samples evaluated, the results show 100% of the population consumes some acrylamide as part of the diet with a mean intake of ~ 0.4-0.5 µg/kg bw/day" (p6114).

Summary

This paper summarises over 29 different potential agronomic, formulation and processing approaches in commercial food production to reduce acrylamide levels in high risk foods.

One Australian study showed that (a) the accumulation acrylamide in deep fried potato products in the range of 140-180°C, increased linearly with an inflection at 165°C, and (b) hot water blanching of raw potato chips resulted in a reduction, and that shallow frying induced significant increases in acrylamide levels versus deep frying. Microwave pre-cooking of potato chips prior to frying also resulted in significantly reduced acrylamide concentrations (36-60% less depending on frying temperature).

It may also be possible to reduce the adverse effects of dietary acrylamide by the co-ingestion of chemoprotective ingredients (eg, diallyl sulphide in garlic; ginseng extracts; l-arginine; taurine) but at the moment it is difficult to give clear advice to the public about how to mitigate undesirable effects of dietary acrylamide.

Humphrey T. Salmonella, stress response and food safety. *Nature Reviews Microbiology* 2004; 2(6):504-509. [339]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"Salmonella is an important foodborne pathogen and recent work indicates that the mortality rates of individuals who have been infected are three times those who have not been infected in the year after infection" (p504).

"The dose of Salmonella cells required to cause human infection is influenced by several factors including: degree of host resistance, content of the meal, physiological state of the cells. For example, Salmonella that has been pre-exposed to sub-lethal concentrations of acid (as found in mayonnaise) might be better able to withstand subsequent exposure to gastric acidity. It has long been believed that refrigeration and treatments that lower the pH or water activity are bacteriostatic for Salmonella, but this is not always the case. It is now apparent that these conditions can inhibit cell division but do not stop bacterial growth or replication" (p507).

"Outbreak investigations have revealed that the principal risk factors in domestic Salmonella outbreaks include undercooking, improper storage and cross-contamination. The last risk factor is of particular interest and is the subject of some controversy. The handling of high-risk foods like chicken will result in the spread of pathogenic bacteria…(and)…the plethora of kitchen hygiene products that are available suggest that a contaminated kitchen presents a significant challenge to human health. There is little unequivocal evidence to support this, although cross-contamination – such as direct contact between raw and cooked foods – is an important risk factor. It has yet to be established whether a Salmonella positive kitchen work surface poses a significantly increase risk of humans contracting Salmonella infection" (p508).

Humphrey T, O'Brien S, Madsen M. Campylobacters as zoonotic pathogens: A food production perspective. *International Journal of Food Microbiology* 2007; 117:237-257. [250]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

Consumption of poultry has been identified as a risk factor of Campylobacter infections in a number of studies and the frequency of contamination of red meat products at retail is lower than that seen in poultry. Campylobacters can survive for extended periods at low temperatures, but they are more sensitive to acid and drying than other food-borne pathogens. Several studies (including two in New Zealand) have also shown that consumption of chicken at home, rather than at restaurants, was protective.

Quotes

"Cross-contamination has been shown to be an important cause in approximately 30% of outbreaks. In both household and commercial catering it is essential that raw foods contaminated with campylobacters be cooked properly. After cooking the food must be protected from recontamination…..As with other zoonotic pathogens, contamination levels of campylobacters on kitchen surfaces can be effectively reduced by cleaning with detergents, hot water and disinfectants. However, consumers do not always know how to do this correctly and it is possible to isolate campylobacters from kitchen surfaces even after 'cleaning'. Proper hand washing is also very important and a recent review paper stated that this practice could reduce the risk of diarrhoea in a community by ~50%" (p253).

Kikugawa K. Prevention of mutagen formation in heated meats and model systems. *Mutagenesis* 2004;19(6):431-439. [327]

Quality Rating: Negative.

Search Method: Not stated.

Summary:

Heterocyclic amine (HCA) mutagens are produced in a wide variety of cooked and processed meats and fish and are known to be carcinogenic in rodents and considered to be probable human carcinogens. Possible means of preventing mutagen formation in cooked meats are described. One way is to control cooking temperature, time and method. Barbecued meat has high mutagenicity, while microwave cooking of meat is effective in reducing mutagenicity. Turning over beef patties repeatedly at lower temperatures reduces mutagenicity of cooked hamburgers compared to cooking for longer times on each side.

Another way is to increase water content and avoid loss of water in meats during cooking. Boiling meats does not induce mutagenicity and roasting or frying meats under conditions of lowered water loss can minimize mutagenicity. Addition of reducing sugars such as glucose and fructose to meat before cooking is also effective in inhibiting HCA formation, which may be due to suppression of generation of the pyrazine cation radical Maillard intermediate of heterocyclic amines.

Knize MG, Fenton JS. Formation and human risk of carcinogenic heterocyclic amines formed from natural precursors in meat. *Nutrition Reviews* 2005; 63(5):158-164. [304]

Quality Rating: Negative.

Search Method: Not stated.

Quote:

"The formation of heterocyclic amines is related to pan temperature when meat is cooked to the same final internal temperature. Surprisingly, the time needed to reach the 70°C internal temperature is about the same at 250°C (7min) as at 160°C (9min). This is due to the limit of the slow heat transfer through the meat, suggesting that simply using lower pan temperatures is a practical way to reduce heterocyclic amine formation without greatly increasing cooking time.

Flipping pan-fried beef patties over every minute, as opposed to turning the meat over once at 5 minutes, and cooking at a moderate pan temperature until the target internal temperature of 70°C is reached seems to be the most effective way to reduce heterocyclic amine content while avoiding undercooking" (p160-1).

LeJeune JT, Rajala-Schultz PJ. Unpasteurized milk: a continued public health threat. *Clinical Infectious Diseases.* 2009; 48(1):93-100. [211].

Quality Rating: Negative.

Search Method: Not stated.

Quote:

"Although milk and dairy products are important components of a healthy diet, if consumed unpasteurized, they can also present a health hazard due to possible contamination with pathogenic bacteria. These bacteria can originate even from clinically healthy animals from which milk is derived or from environmental contamination occurring during collection and storage of milk. The decrease frequency of bovine carriage of certain zoonotic pathogens and improved milking hygiene have contributed considerably to decreased contamination of milk but have not, and cannot, fully eliminate the risk of milkborne disease. Pasteurization is the most effective method of enhancing the microbiological safety of milk. The consumption of milk that is not pasteurized increases the risk of

contracting disease from a foodstuff that is otherwise very nutritious and healthy. Despite concerns to the contrary, pasteurization does not change the nutritional value of milk" (Abstract).

National Advisory Committee on Microbiological Criteria for Food. Responses to the questions posed by the Food Safety and Inspection Service regarding consumer guidelines for the safe cooking of poultry products. *Journal of Food Protection* 2009; 70(1):251-260. [264]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

- *"A single minimum internal temperature endpoint temperature of 165°F (=74°C) for cooking without time limitation should be recommended to ensure the microbiological safety of cooked poultry. This temperature will destroy Salmonella".*
- *"Guidance to the consumer should indicate that higher final temperatures may be needed for consumer acceptability and palatability [e.g. 170°F (=77°C) for whole muscle breast meat, 180°F (=82°C) for whole muscle thigh meat in order to eliminate the pink appearance and rubbery texture]".*
- *"Guidelines for the consumer should convey that a longer cooking time is needed if the product is frozen at the beginning of the cooking process".*
- *"The consumer should be advised that microwaving raw product from the frozen state is not advisable unless the package provides substantial further instructions for ascertaining that the product has achieved the recommended endpoint temperature".*

Redmond EC, Griffith CJ. Consumer food handling in the home: a review of food safety studies. Journal of Food Protection 2003; 66(1):130-161. [380]

Quality Rating: Neutral.

Search Method: Not fully described. Electronic database searches for studies from 1975 that assessed consumers' knowledge and behaviours about food safety, supplemented with information on unpublished studies from responses from Foodsafe listserv and personal communication at food safety conferences.

Summary:

88 studies identified (including two from Australia and four from New Zealand). Consumers have a high level of concern about food safety issues, largely incident-driven. The majority (80%) of consumers think themselves adequately informed regarding food safety, but levels of consumer knowledge determined in food safety surveys have differed; the majority has concluded that consumer knowledge is inadequate and needs improvement. Up to 95% of consumers do not know

the correct refrigeration temperatures and surveys of actual temperatures have reported up to 70% exceed recommended ranges.

Consumers' failure to associate home food-handling practices with foodborne illness is considered a serious impediment to convincing consumers to change inappropriate behaviours.

Analysis of results indicates that consumers food safety knowledge fails to correlate with self-reported behaviours, and intra-study comparisons conclude knowledge does not correlate with actual behaviour. (For example, in one study although nearly all respondents reported they washed their hands before preparing food, less than half actually did so).

Observational studies of consumers in Australia report:

- 75% fail to wash their hands or used an inadequate procedure for doing so
- 35% failed to wash utensils between preparation of raw and other foods
- 30% failed to clean the preparation surface before preparing ready-to-eat foods.

Consumers demonstrate judgements of optimistic bias, perceiving themselves to be less at risk from foodborne illness than others and continuing to consumer unsafe foods despite knowing the potential consequences of this behaviour.

Sinha R, Norat T. Meat cooking and cancer risk. <u>In</u> *Nutrition and Lifestyle: Opportunities for Cancer Prevention* E Riboli and R Lambert (Eds). IARC Scientific Publication, Lyon France. 2002; pp181-186. [348]

Quality Rating: Negative.

Search Method: Not stated. Reports results from 7 studies from 1995-1998 examining production of heterocyclic amines (HCAs) and polycyclic amines hydrocarbons (PAHs) when meat is cooked at high temperatures.

Summary:

High temperature cooking methods (pan-frying, oven broiling, and grilling/barbecuing) produce higher levels of mutagenic activity in meat samples. Degree of doneness of meat is a proxy for higher levels of meat-cooking carcinogens and is associated with increased risks for colorectal adenomas, lung, breast and stomach cancers.

Sugimura T, Wakabayashi K, Nakagama H, Nagao M. Heterocyclic amines; mutagens/carcinogens produced during cooking of meat and fish. *Cancer Science* 2004; 95(4):290-299. [348]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"More than ten kinds of HCAs actually produced by cooking or heating meat or fish have now been isolated and their structures determined. They are mutagenic in vivo and in vitro towards mammalian cells" (Abstract).

"Various easy and efficient ways to prevent the production of HCAs are available. Their generation mainly depends on an increase in temperature and heating time, and on dehydration of the meat. Therefore, prolonged cooked and broiling of meat and direct exposure to a naked flame should be avoided. Flipping hamburgers every minute for 7 minutes results in less than one tenth the level of HCA contained after flipping once with a cooking time of 8.9min. Usage of microwave ovens can be recommended. Avoid consuming charred parts produced on meat surfaces" (p296).

Woteki CE, Kineman BD. Challenges and approaches to reducing foodborne illness. *Annual Review of Nutrition* 2003; 23:315-344. [499]

Quality Rating: Negative.

Search Method: Not stated.

Quotes:

"The most effective measure used to defend the food supply against microbial contamination is heat" (p327).

"As consumer demands increase for more 'natural', fresh, ready-to-eat products, many new processing methods that rely on milder heat treatment of food products have been developed in recent years. Raw and minimally processed foods represent a new challenge to food safety for a number of reasons. Refrigeration temperatures are often not adequate in deterring microbial grown, and microwave heating, which is relied on heavily with such products, is not entirely effective in uniformly heating foods" (p329).

"Surveys indicate that the public has become more aware of food safety issues and has taken measures to improve in most areas. Nevertheless, consumer surveys and outbreak surveillance data suggest that education efforts should continue to focus in the areas of personal and kitchen hygiene, adequate cooking and avoiding cross-contamination" (p339).

SUMMARIES OF INCLUDED ARTICLES

3) ENVIRONMENT

Marsh K, Begusu B. Food packaging – roles, materials and environmental issues. Journal of Food Science. 2007; 72(3):R39-R55. [242]

Quality Rating: Negative.

Search Method: Not stated (This is a Scientific Status Summary from the Institute of Food Technologists).

Quote:

"The principal roles of food packaging are to protect food products from outside influences and damage, to contain the food, and to provide consumers with ingredient and nutritional information. Traceability, convenience and tamper indication are secondary functions of increasing importance. The goal of food packaging is to contain food in a cost-effective way that satisfies industry requirements and consumer desires, maintains food safety, and minimizes environmental impact" (pF39).

Summary

Food packaging accounts for almost two-thirds of total packaging waste by volume and food packaging is approximately 50% (by weight) of total packaging sales. The issue remains poorly understood, complicating efforts to address the environmental impacts.

Inadequate food protection and storage is a major cause of food waste, estimated by FAO to range from 25% for grains to 50% for fruit and vegetables world wide. Packaging may contribute to the reduction in total solid waste because the food waste from packaged food is significantly less than that from unpackaged food.

This paper summarises issues related to over 15 different types of packaging.

Summary of some common materials used with food

Packaging type	*Advantages/Disadvantages*	*Recyclable?*
Glass	Impermeable, transparent, rigid	Yes
Aluminium	Good barrier; light and strong; corrosion resistant	Yes
Tinplate	Good barrier; easy to coat; strong; low cost	Yes
Polyolefin plastics (eg margarine tub)	Flexible; light and strong; moisture resistant	No
Polyester plastics (eg drink PET bottle)	Transparent; light	Yes
Polyvinylidene chloride (eg cheese and meat packs)	High chlorine content present incineration problems	No
Polystyrene (eg egg cartons; drink cups)	Light and thermally insulating	Yes
Paper and board	Poor barrier qualities and not heat sealable	Not if dirty

Several approaches have been adopted to reduce environmental impact:

- Source reduction (e.g. product redesign)
- Lightweighting (thinner gauge materials)
- Reusable and refillable containers
- Recycling. In the US rates of recycling are approximately 90% for glass and 50% for aluminium.

As a comprehensive analysis of the material from production to disposal, life cycle analysis is important to determine the environmental impact of a package, incorporating a quantitative estimate of costs including material use, energy consumption and waste generation. From a product characteristic perspective the inertness and absolute barrier properties of glass make it the best choice material for most packaging applications, however the economic disadvantages of glass boost the use of alternatives such as plastic. Consumer desires drive product sales and although a bulk glass bottle might be the best material for a fruit juice or sports beverage, sales will be affected if competitors continue to use plastic to meet consumer desire for shatterproof, portable, single-serve containers

26. FOOD SELECTION GUIDES (NI.1, NI.2, NI.3)

Evidence Statements

26. FOOD SELECTION GUIDES (N1.1; N1.2; N1.3):

Narrative Review

N1.1 What current and past national food selection guides are used/have been used in Australia?

N1.2 What are the major national food selection guides currently used internationally?

N.1.3 What methods have been used to develop national food selection guides?

A single Endnote library search was conducted to address all three questions therefore the questions are considered under sub-headings in the following combined narrative review.

Contents

Introduction

Food guides are developed to assist consumers to visually translate scientific nutritional recommendations (dietary guidelines) into simple, practical advice on the types and quantities of various foods needed for optimum health. Foods are typically classified into basic groups according to similarity of nutrient composition (e.g. carbohydrate-rich), function (e.g. "energy" foods) or food type (e.g. grains and grain products) (Love 2002). The implication is that a balanced and adequate diet is probable if one or more items from each group are consumed daily (Gillespie 1990; Ahlström & Räsänen 1973). Thus, the main purpose of food guides is to assist the consumer in choosing a diet that is advocated by the dietary guidelines of that country (Davis et al. 2001).

In order for food guides to be effective in influencing food choices and dietary behaviours, they need to be country-specific, taking into consideration that country's public health concerns, dietary practices, cultural food habits and socio-economic circumstances (Gillespie 1990; Welsh 1996). In addition, food guides also need to acknowledge the way in which foods/drinks are commonly categorised by the population being targeted.

The aim of this review was to answer the following three questions:

- What current and past national food selection guides are used/have been used in Australia?
- What are the major national food selection guides currently used internationally?
- What methods have been used to develop national food selection guides?

The review aims to provide an overview of available national food guides in Australia and other countries around the world, as well as identify methods used to develop and test the effectiveness of these nutrition education tools.

Methods

A systematic search for articles was conducted in May 2009 of scientific literature available in English from 2002. The searches used combinations of the following terms: *food, guide, selection, national.* Searches of both original articles and reviews were conducted in the following databases: Cinahl, Medline, PreMedline, Psychinfo, Cochrane/DARE, and ERIC. 505 articles were discovered by the searches and, after review of titles and abstracts, 135 were retrieved for detailed review. Reasons for non retrieval were: not a study (30), not a relevant population (31), not a relevant outcome (252), or duplicated articles (57). After retrieval of the full articles, 88 more were excluded because the content was not a relevant outcome for this review or because the content had been better reviewed in another retrieved article. Many of the retrieved articles related to the development, validation or application of dietary indices such as the Healthy Eating Index (HEI). The HEI was created by researchers at the US Department of Agriculture (USDA) in 1995 to measure how well American diets conformed to the recommendations of the *Dietary Guidelines for Americans* and the original Food Guide Pyramid. These articles were excluded for the purpose of the current review since they were considered not to be a relevant outcome that would inform the review questions.

The remaining 47 articles were used as the basis of this narrative review and are indicated with asterisks in the reference list. Additional references and sources of information were retrieved from references cited in the bibliographies of the included articles. In addition, Google searches using the terms *food guides/Australia* and *MyPyramid* were conducted to identify potential sources of information on Australian food guides *per se* (N1.1) and the development and testing of food guides (N1.3), respectively. A PhD thesis (Love 2002; obtained from author) was also included as reference source in the review. 11 additional references were provided by the NHMRC for this review. Of those, one was outside of the time frame, three were already included in the Endnote library, five were excluded (not an outcome) and the remaining two were included (U.S. Department of Health and Human Services 2005; Rangan et al. 2008).

Results

N1.1 What current and past national food selection guides are used/have been used in Australia?

Current food guides

The Australian Guide to Healthy Eating (AGTHE) is the nationally adopted food guide for Australia. It is a circular shape and is based on the most recent dietary guidelines for Australian adults (NHMRC 2003). It is noteworthy that Australian's dietary guidelines include both food-based (e.g. Eat plenty of vegetables, legumes and fruits) and nutrient-based (e.g. Limit saturated fat and moderate total fat intake) recommendations, as shown in Table 26.1.

Table 26.1 Dietary guidelines for Australian adults and adolescents (NHMRC, 2003)

Enjoy a wide variety of nutritious foods	• Eat plenty of vegetables, legumes and fruits • Eat plenty of cereals (including breads, rice, pasta and noodles), preferably wholegrain • Include lean meat, fish, poultry and/or alternatives • Include milks, yoghurts, cheeses and/or alternatives. Reduced-fat varieties should be chosen, where possible • Drink plenty of water.
Take care to	• Limit saturated fat and moderate total fat intake • Choose foods low in salt • Limit your alcohol intake if you choose to drink • Consume only moderate amounts of sugars and foods containing added sugars.
Prevent weight gain: be physically active and eat according to your energy needs	
Care for your food: prepare and store it safely	
Encourage and support breastfeeding	

The Australian Guide to Healthy Eating is based on the NHMRC's 1995 Core Food Group analysis (NHMRC 1995), which translates nutrient requirements to food consumption recommendations. This, in turn, was based on both the 1991 Recommended Dietary Intakes (RDIs) (NHMRC 1991) and Australian 1989–1990 per capita food availability data (ABS 1992). The AGTHE also took into account the 1992 Dietary Guidelines for Australians (NHMRC 1992) and Children and Adolescents (NHMRC 1995).

Since the AGTHE was developed, a new set of Dietary Guidelines for various life stages (NHMRC 1995; 1999; 2003), and a new set of Nutrient Reference Values (NRVs) have been published with a wider range of nutrients and more values per nutrient (NHMRC 2006). The NRVs include both recommendations to ensure adequacy of nutrient intake and, for some nutrients, recommendations about levels that may reduce chronic disease risk, mainly cardiovascular disease and cancer (i.e. suggested dietary targets). These suggested dietary targets were made for the following nutrients: vitamin A, carotenes, vitamin C, vitamin E, folate, sodium and potassium, dietary fibre and long-

chain n-3 fats. In addition, acceptable macronutrient distribution ranges (AMDRs) are provided based on evidence surrounding cardiovascular disease, certain cancers, diabetes and risk of obesity and dietary modelling aimed at meeting the estimated average requirement or 83% of the adequate intake where appropriate (NHMRC 2006).

The approach taken in Australia to base its food guide on the core food groups (NHMRC 1995) does not provide clear guidance to consumers about many foods that are commonly eaten but that do not fit neatly into the core food group categorization. For example, a large proportion of energy is consumed from composite foods/meals which may include more than one food item from a food group depicted by a food guide. Another problem is that the 'extra' foods are generally not accounted for in pictorial representations despite being a major source of energy and nutrients. In children, the mean consumption of 'extra' foods by 16-24-month-olds from Western Sydney has been reported to be 150 g per day, contributing 25-30% of the total energy, fat, carbohydrate and sodium to the diets of the study children (Webb et al. 2006). 'Extra' foods also contributed around 20% of fibre, 10% of protein and zinc, and about 5% of calcium. Despite not differing in energy intake, children in the highest quintile of 'extra' foods intake had a higher percentage of energy provided by carbohydrate and sugars, and a lower intake of protein and saturated fat compared to those in the lowest quintile. Both nutrient density and intake of core foods was inversely associated with intake of foods from the 'extra' food group. Similar findings have been demonstrated for Australian adults, in whom 'extra' foods contributed 36% of total daily energy intake, as well as 16% of protein, 41% of total fat, 41% of saturated fat, 47% of sugar and approximately 20% of selected micronutrients to the diet (Rangan et al. 2009).

A current revision of the 1995 core food groups and the 2003 dietary guidelines necessitates the development of a new food guide. Baghurst (2007) recommends that the revised food guide adopt a more flexible approach to diet planning, as the US *MyPyramid* Guide has allowed through its web-based programme. A major benefit of the *MyPyramid* over previous food guides is its ability to account for personal food preferences. To reduce the danger of confusing the message, Baghurst (2007) suggests that an ‘average’ recommendation for paper/pencil/poster presentations of a food guide may be needed, but that if food choice flexibility is provided within this overall concept it may make the recommendations more widely acceptable.

26.1 The Australian Guide to Healthy Eating (Commonwealth Department of Health and Family Services 1998)

Baghurst (2007) raises the question of whether the food groupings need to be revisited. She highlights the issue of major differences in nutrient profiles between items currently included in the 'meats and alternatives' (i.e. vegetable protein and nuts) and discusses the possible need for a 'healthy fats' food group ('fats/oils/nuts/seeds') to direct the public to consume adequate intakes of nutrients such as omega-3 polyunsaturated fatty acids and vitamin E. Other concerns related to current food groupings in the vegetable and fruit major categories. The need to highlight the special attributes of certain types may require further subdivision of the vegetables and fruit group, as in the *MyPyramid*. If vegetables are left in one category, the question of whether potatoes and some other starchy tubers are excluded is raised. Indeed, many other countries place them elsewhere, such as in the 'bread and cereals' or 'starchy foods' groups. The current international recommendations for fruit and vegetable intake that propose a minimum of 400g/person/day, exclude potatoes and other starchy tubers from their classification (WHO/FAO 2003). The inclusion of legumes in both the meat and dairy food group, as well as in the vegetables food group, may be confusing to consumers. However, the concept of what constitutes an 'extra' food is probably the most challenging aspect of the core foods group revision. Further, emerging foods categories such as herbs and spices that are increasingly being shown to have health benefits related to their particularly high phytochemical content have not been incorporated in the dietary guidelines of many countries (Williams 2006) and therefore are not included in most food selection guides.

Undoubtedly, there are a number of issues to be addressed in updating the current AGTHE in order to ensure its usefulness in nutrition education activities and optimal uptake by Australian consumers. Translation of the NRVs into revised dietary guidelines and subsequently a new Australian food selection guide will need to be evidence-based. This will require valid information on national food consumption patterns and comprehensive food composition data (McNaughton 2007). Development of a new guide will also require a thorough understanding of the intrapersonal, social and environmental influences on eating.

Other food guides currently used in Australia

Some national initiatives have resulted in nutrition information being provided in various forms other than the AGTHE, including an indigenous version of the AGTHE and the Healthy Eating Pyramid developed by the Nutrition Foundation of Australia.

- *The Aboriginal and Torres Strait Islander Guide to Healthy Eating*

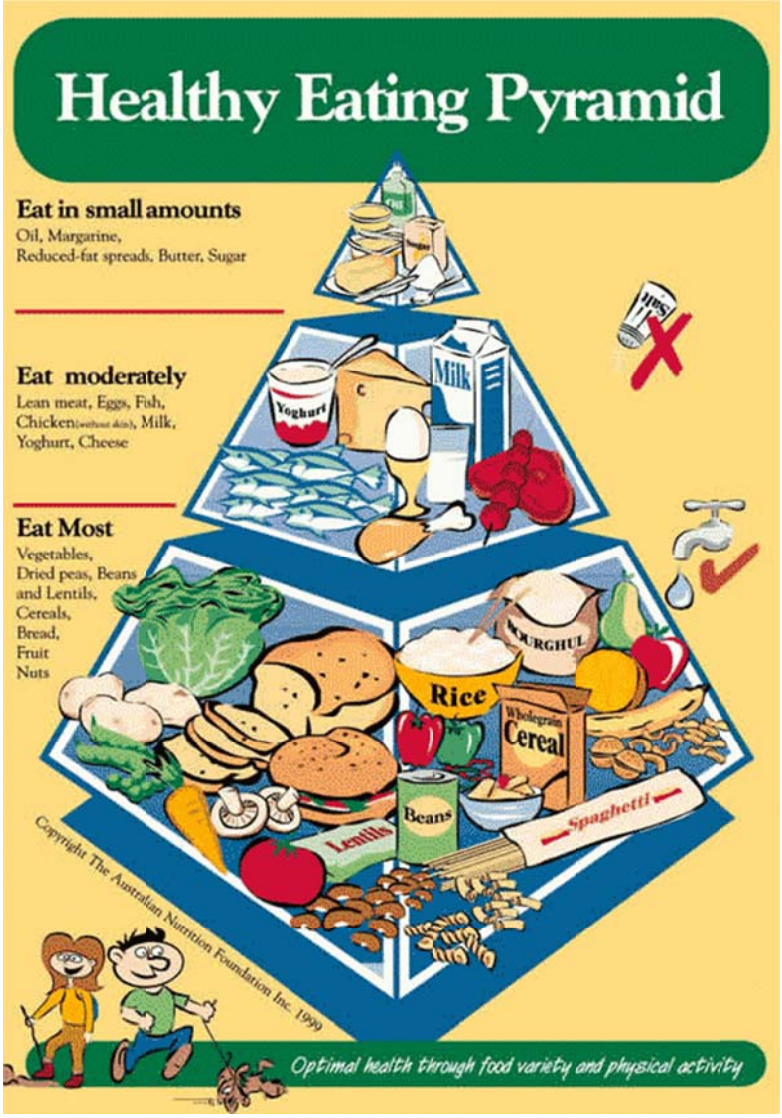
An indigenous foods version of the AGTHE was produced by various state governments.

Available at: http://www.your30.qld.gov.au/Portals/0/Your30/docs/eatwelltips_brochure_low.pdf (accessed 22/01/2010).

- *Healthy Eating Pyramid (Australian Nutrition Foundation, 1981)*

The Australian Nutrition Foundation Inc. developed the *Healthy Eating Pyramid* (formerly called Healthy Diet Pyramid) in 1981 and has since released various editions (Figure 26.2).

26.2 Healthy Eating Pyramid (Australian Nutrition Foundation, 1981)



Though not adopted as the national food guide, it has been used and distributed widely. The pyramid represents food from the core food groups, including a fats and oils group which appears at the apex of the pyramid together with sugar. The pyramid does not provide information on the 'extra' food group, nor on alcohol, but encourages water intake. Variety is encouraged through depiction of various food items within each food group, and the pyramid shape provides the consumer with information about recommended proportions from each of the food groups (food serve information is not provided) as well as the use of accompanying text that indicates which foods should be eaten in moderation. The Pyramid is a qualitative food guide that uses descriptive terms such as 'eat more', 'eat moderately' and 'eat less.' Physical activity messages are incorporated in the food guide with both text and pictorial representation.

The Healthy Eating Pyramid was based on the original Swedish triangle developed in the 1970s. Formal nutritional assessments of advice using the guide have not been undertaken, nor has research been conducted to determine consumer understanding of the guide.

Other approaches used in Australia to promote dietary guidelines

As well as the above food guides, other strategies to promote the Australian dietary guidelines have been undertaken, most notably the Go for 2 & 5® campaign. The Go for 2 & 5® campaign aimed to help Australians increase their daily consumption of fruit and vegetables (information obtained from Australian Government; Department of Health and Ageing website). The campaign was based on one originally developed by the Western Australian Department of Health and used social marketing techniques which included television advertising using animated cartoons, as well as written materials.

An evaluation of the campaign in Western Australia found that it had successfully reached the target audience and increased awareness of the recommended serves of fruit and vegetables. (Pollard et al. 2008). The population net increase in mean number of serves of fruit and vegetables per day over three years was 0.8 (0.2 serves of fruit and 0.6 serves vegetables) with the increase not being significant for fruit. Similarly, the national Go for 2&5® campaign has been successful in generating awareness, both amongst parents of 0 to 17 year olds and 9 to 12 year old children, and has increased knowledge in these groups (Elliot & Walker 2007). It has been estimated that in excess of $15 million will have been spent on the Go for 2&5® campaign at government level in the period through to June 2008, but this represents a small proportion of the total cost of the programme through monies raised in industry partnerships (Rowley 2006).

Past food guides used in Australia

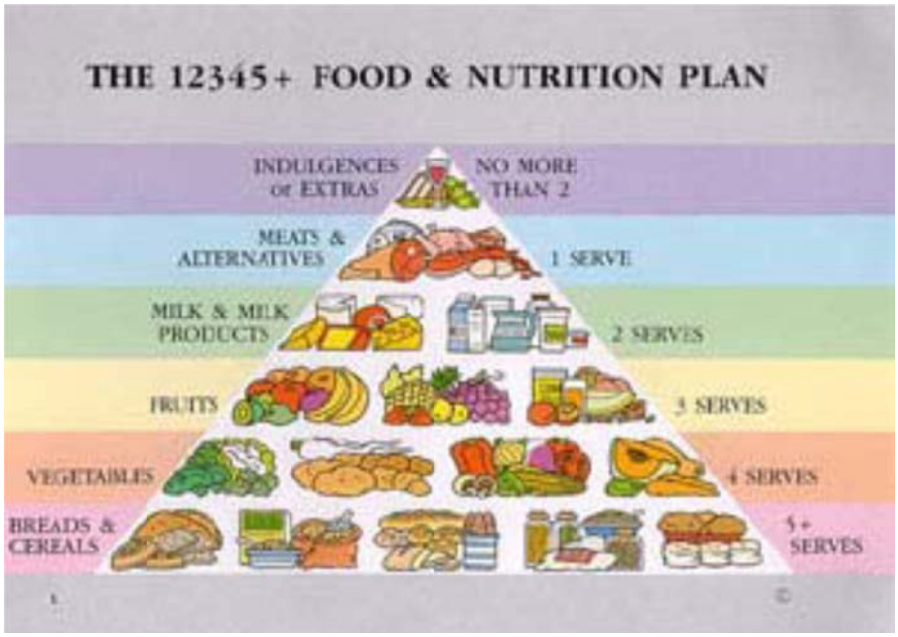
From the 1940s until the early 1990s, the five food groups were Australia's food selection guide (meat, fish, poultry, eggs, pulses; milk and milk products; fruit and vegetables; cereal products, including bread, flour, rice; butter or table margarine as recommended fats). Developed by the Australian Commonwealth Department of Health, the five food groups were mainly concerned with adequacy of the diet and prevention of deficiency states during times of war, famine, drought and economic hardship. They used a minimal requirement approach that was explained in terms of nutrient function. For example the meat and fish group provided iron and protein while the milk and milk products group provided calcium. The five food groups, being nutrient rather than food based, did not encourage dietary variety of foods that contained non-nutrient factors beneficial to health (e.g. phytochemicals, phytoestrogens etc.) nor did they accommodate the food habits of many cultural cuisines (Kouris-Blazos 2002). The five food groups approach is no longer used in Australia since it is considered unable to address the problems of excessive energy intake, particularly from fat sources. The five food groups were replaced by the development of the core food groups in 1995 (NHMRC 1995). The core food groups provide guidance about the minimal amounts of foods for good health. They were devised to provide at least 70 % of the RDIs for vitamins and minerals, 50 % of the RDI for protein, and 50 % of energy requirements (Cashel and Jeffreson 1995). It was acknowledged that the core food groups provided insufficient dietary fibre. Fats and oils were removed as a separate group since vegetables were considered to be a better source of vitamin A (through β-carotene). The core food groups did not model fats for their contribution of fatty acids but only for vitamin A content (Kouris-Blazos 2002).

Other past food guides used in Australia include the *Target on Healthy Eating* (Health Development Foundation/Victorian Food and Nutrition project), the *Jigsaw* (Queensland Nutrition project) and *12345+ Plan* of CSIRO (Baghurst et al. 1992) (Figure 26.3). The *Target on Healthy Eating* circle was unique in that it took into account more processed varieties of food in each food group. The target had sectors for food groups of different width (ie. narrow band for fats) but also an outer band of more processed products in each sector (group), with more fat, salt or sugar.

The CSIRO 12345+ Food and Nutrition Plan was a quantified and nutritionally assessed food guidance system aimed at achieving the dietary recommendations at the time. The main difference between this plan and the earlier five food group system used in Australia was that the 12345+ guide recommended less meat and increased recommendations for dairy, fruits, vegetables and cereals. Unlike the five foods guidance system, 12345+ did not have a specific fats and oils group, because an allowance for 6 grams of unsaturated fat was made for each slice of bread eaten (Kouris-Blazos 2002). The food plan allowed for up to two 'indulgences' a day (e.g. biscuits, buns, ice cream, chocolate, alcohol, processed meats, pies, pizza, alcohol etc.).

These earlier guides have been developed by state-based organizations or research groups, and were targeted to various audiences rather than at national level. All these guides had in common the need to be able to quantify foods in simple and meaningful ways for nutrition education purposes (NHMRC 2005).

26.3 CSIRO 12345+ Food and Nutrition Plan



http://www.nano.csiro.au/proprietaryDocuments/12345_Plan.pdf

N1.2 What are the major national food selection guides currently used internationally?

Introduction

Many countries have devised food guides as a means of translating dietary guidelines into consistent and consumer-friendly food-based messages. A food guide provides a conceptual framework for selecting the kinds and amounts of foods of various types which together provide people with a satisfactory diet (Welsh et al. 1992). In order to be effective, food guides need to incorporate the target population's food preferences, cultural practices and dietary patterns, as well as consider food availability (Painter et al. 2002). Food guides need to incorporate the unique dietary components of specific populations therefore universal dietary recommendations are not applicable (Simopoulos 1995). A comparison of international food guides was undertaken by Painter et al. in 2002 – this article has been extensively cited in this review. The national food guides of various countries were compared and summarised according to food categories and quantitative recommendations in each food group (see Tables 26.2 – 26.4). Official food guide pictorial representations for 16 countries were accessed from website searching.

Shapes of food guides

The international food guide illustrations adopt various different shapes, with the most common being the pyramid (US, Puerto Rico, Philippines), the food plate (United Kingdom, Mexico) and a circle (Australia, Portugal, Germany, Sweden). Other diverse shapes that have been used by various countries include the pagoda (China, Korea) and the rainbow (Canada). The food guide figure should be effective in conveying the message of both moderation and proportionality (Hunt et al. 1995; Nestle 1998). A consumer survey conducted by the USDA concluded that the pyramid was the preferred design for a national food guide illustration for the United States, due to its ease of understanding over other shapes such as a wheel, bowl, pie chart, and shopping cart (Nestle 1998). International food guides will be briefly discussed below, categorized by country, according to the shape of the guide.

Pyramids

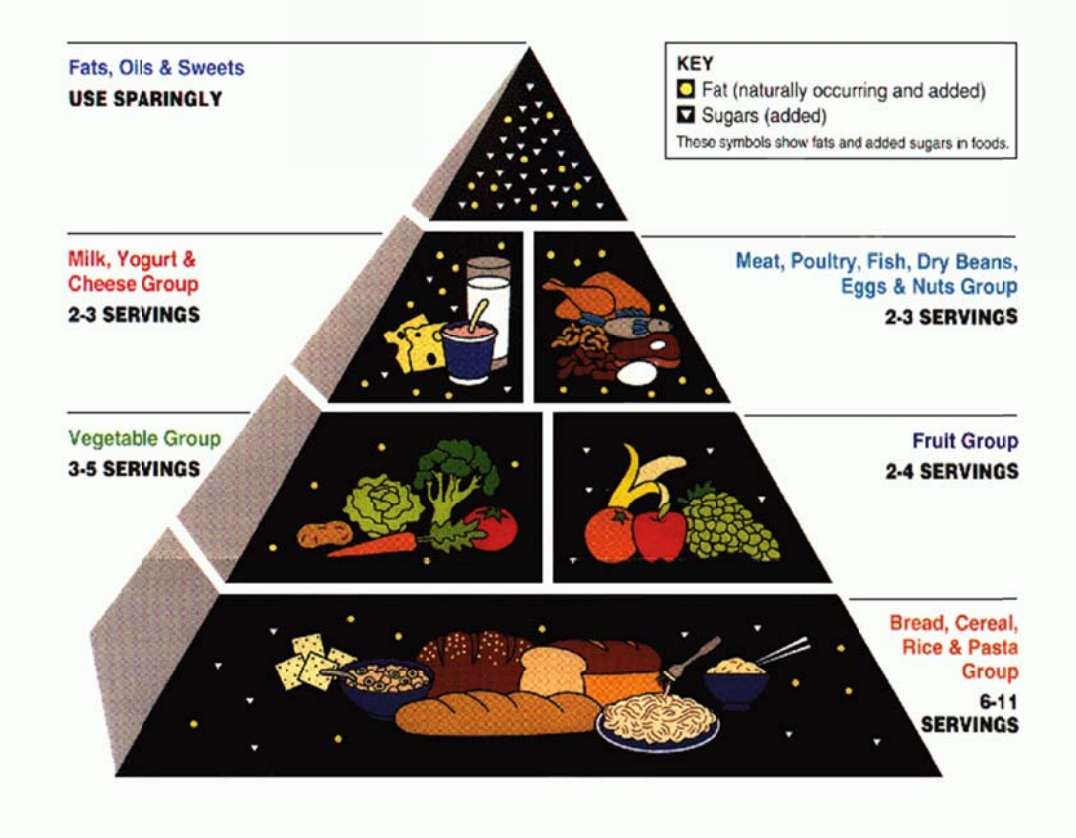
United States

The majority of articles in the Endnote search on food guides related to the latest version of the US Food Guide Pyramid (*MyPyramid*). Only comprehensive reviews related to the process of development and testing of that instrument were retrieved.

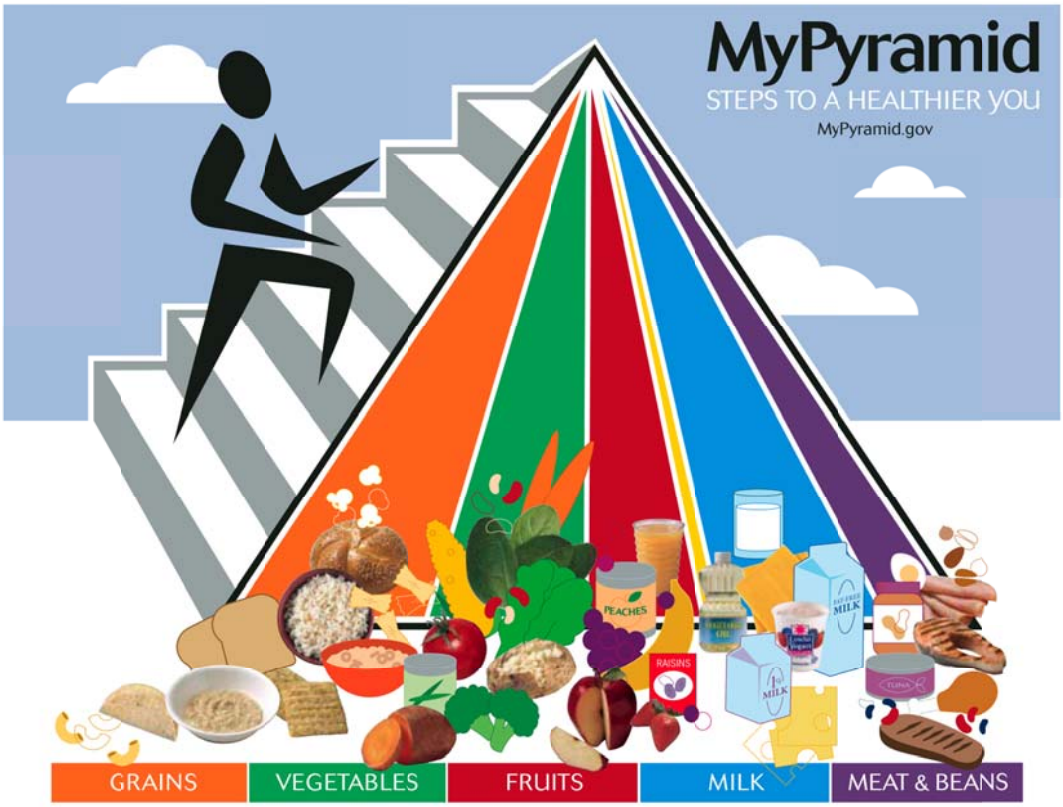
The United States has a long history of producing food guides according to evidence-based principles. Historically, the USDA (United States Department of Agriculture) published its first food guide in 1916, named "food for young children". In 1943 the seven guidelines was replaced by four food groups consisting of milk, meats, fruits, and vegetables. In the 1970s, a fifth food group was added - fats, sugars, and alcohol – and advice was provided to restrict these items. The first USDA food intake patterns that represented a "total diet" approach to food guides were developed in the mid-1980s through an extensive technical research process that has been well documented (Welsh 1992). These food intake patterns were first presented to consumers as a Food Wheel that was part of

a joint American Red Cross-USDA nutrition course in 1984. Later, the food intake patterns were presented in tabular form as "A Pattern for Daily Food Choices" in USDA publications that focused on how to use the Dietary Guidelines for Americans. Development of a new graphic approach to presenting these food intake patterns resulted in the original Food Guide Pyramid, released in 1992 (Figure 26.4). The *food guide pyramid* suggested optimal nutrition guidelines for each food category, per day, using a graphic of a pyramid with horizontal dividing lines to represent suggested percentages of the daily diet for each food group. In 2005, the USDA published *MyPyramid,* an Internet-based program capable of dispensing individualized dietary guidance based on sex, age, height, weight, and exercise habits (Figure 26.5). The US food guide is updated every five years, with the next revision due in 2010.

26.4 The original US Food Guide Pyramid (USDA, 1992)



26.5 MyPyramid (USDA, 2005)



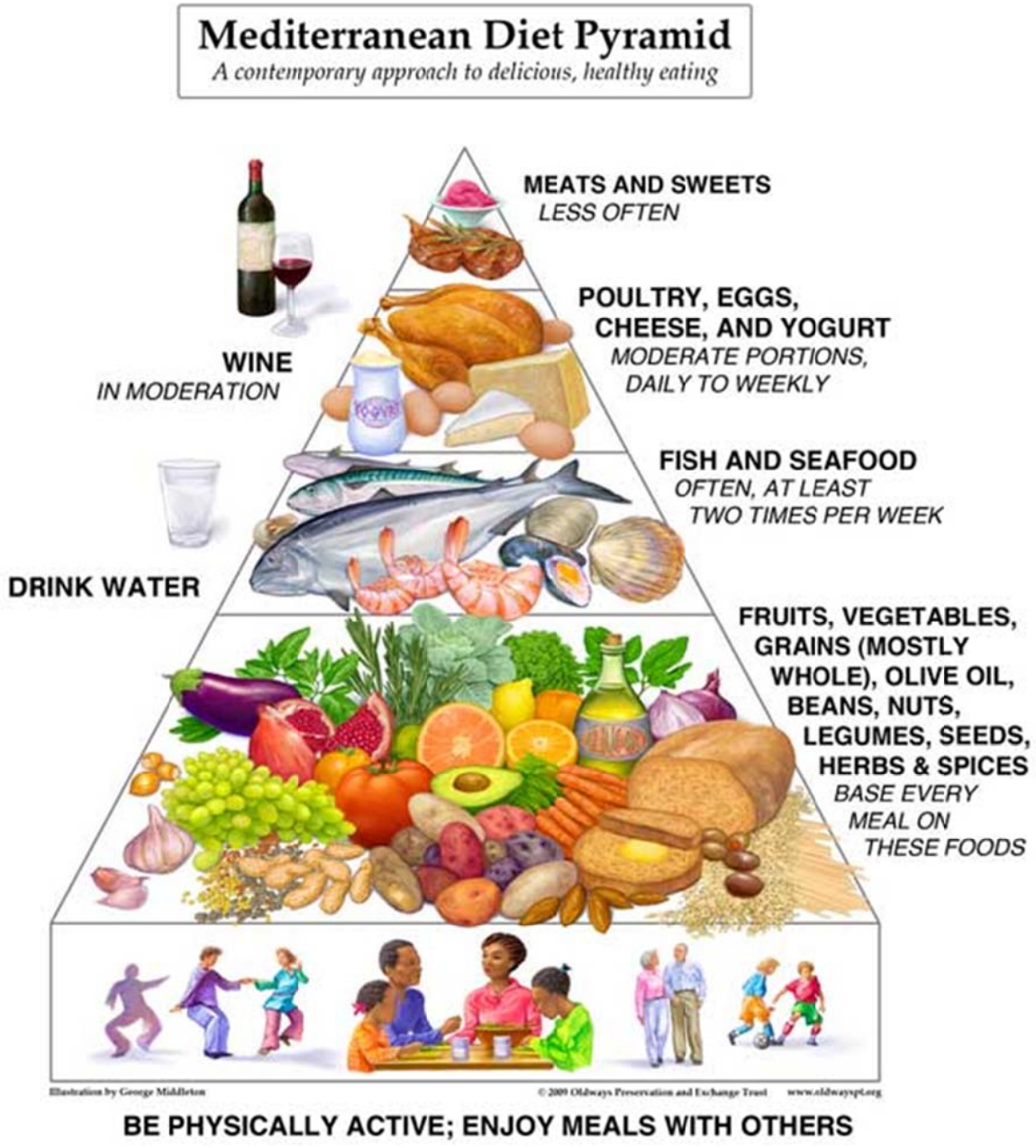
The original Pyramid's food patterns were designed to help Americans make daily food choices that were both *adequate* in meeting nutritional standards but also *moderate* in energy level and in food components often consumed in excess. The adequacy and moderation of these patterns were assessed by comparing nutrients in the patterns to nutritional goals from the 1980 Recommended Dietary Allowances (RDA), the 1980 Dietary Guidelines for Americans, and other standards that were current at the time. They were later assessed in comparison to the 1989 RDAs and the 1985 and 1990 Dietary Guidelines. They have also been re-evaluated based on updated food consumption information from national surveys.

The Mediterranean Diet Pyramid

Oldways, Harvard School of Public Health, and the World Health Organization introduced the classic Mediterranean Diet in 1993 at a conference in Cambridge, USA, along with a pyramid graphic to represent it visually. The pyramid continues to be a well-known guide to what is now universally recognized as an eating pattern that promotes longevity and good health and was recently redesigned to implement updates confirmed at the 15th Anniversary Mediterranean Diet Conference, November 2008 (Figure 26.6). The pyramid represents a traditional Mediterranean diet and was based on the dietary traditions of Crete, Greece and southern Italy around 1960 at a time when the rates of chronic disease among populations there were among the lowest in the world, while adult life expectancy was among the highest. The diet of the people of the southern Mediterranean consisted mainly of large amounts of fruits and vegetables, accompanied by beans and nuts, healthy grains, fish, olive oil, small amounts of dairy foods, and red wine. Other vital elements of the Mediterranean Diet Pyramid are daily exercise, sharing meals with others, and fostering an appreciation for the pleasure of eating.

Changes made to the revised Mediterranean Diet Pyramid include the combination of plant foods into a single group (fruits, vegetables, grains, nuts, legumes, seeds, olives and olive oil), inclusion of herbs and spices in the Pyramid, as well as highlighting the benefits of eating fish and shellfish at least twice per week.

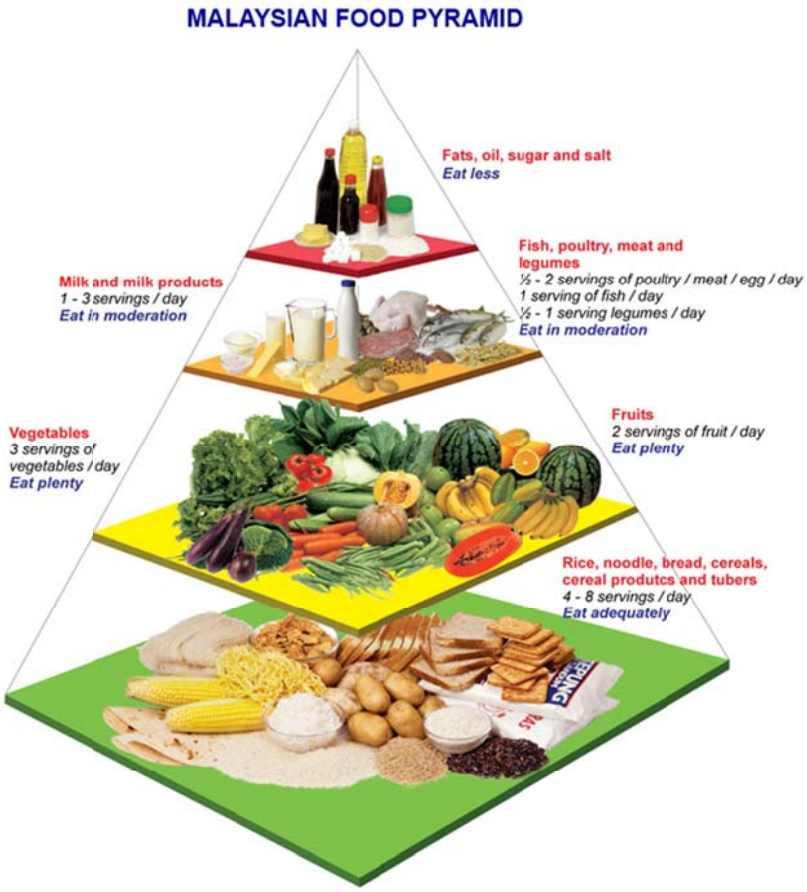
26.6 The Mediterranean Diet Pyramid



Malaysia

Malaysia published its food based dietary guidelines (FBDGs) and a food guide pyramid in 1999 (Figure 26.7).

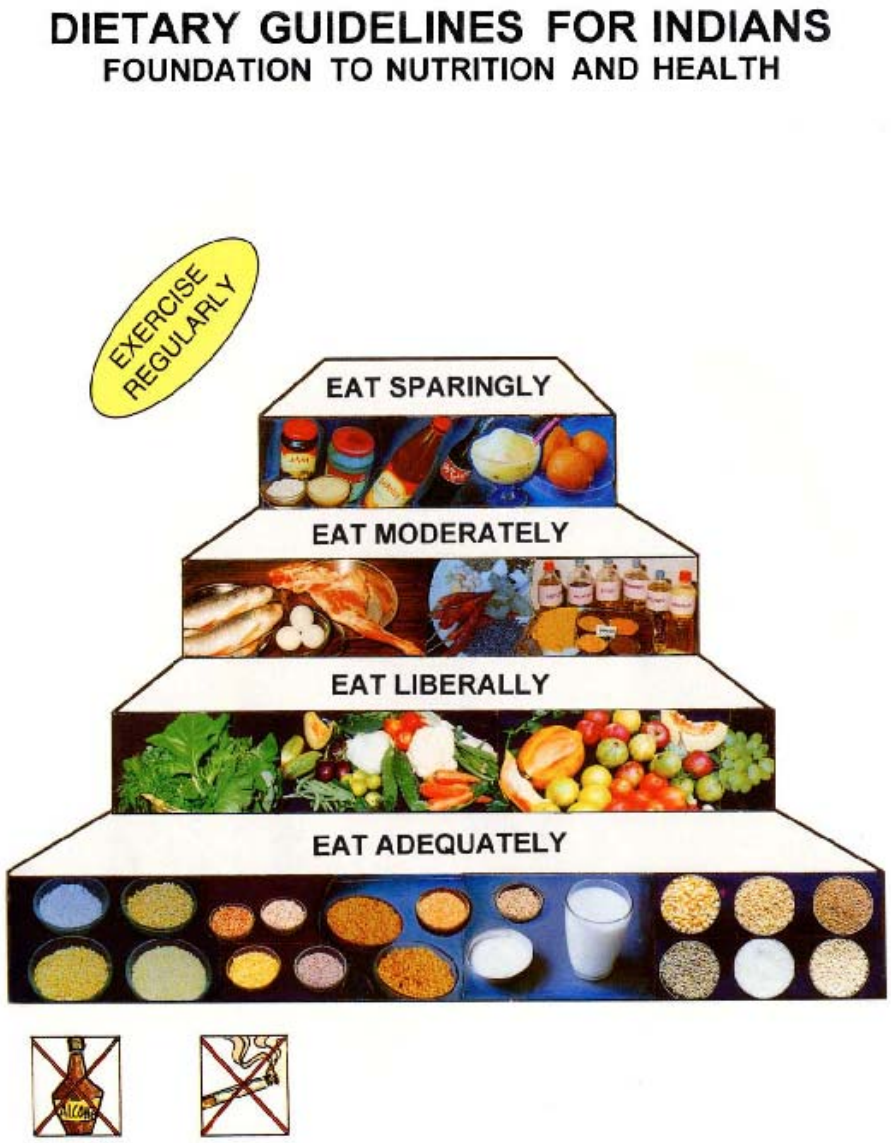
26.7 Malaysian Food Guide Pyramid



India

India has adopted a staircase-type pictorial guide, which is loosely based on a pyramid shape (Figure 26.8). Foods to be eaten least ('sparingly') are at the apex of the pyramid and those at the base (pulses and milk) should be eaten in 'adequate' amounts. Interestingly, the words 'Eat adequately' precede the 'Eat liberally' recommended food group (fruit and vegetables).

26.8 Food Guide for India



Philippines

The Filipino Pyramid Food Guide does not provide specific amounts and serving sizes recommended for items in each of the food groups, but rather suggests a proportionate approach (Figure 26.9). This is the only food guide that does not include a milk and dairy food group in their guide. Since milk is not a major component of the Filipino diet, it has been included in the major protein group.

26.9 Filipino Pyramid Food Guide

Puerto Rico

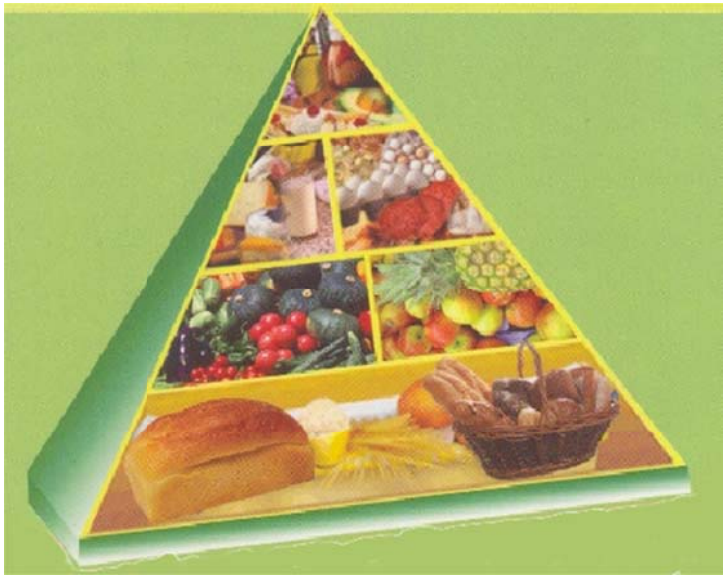
The food guide pyramid of Puerto Rico closely resembles that of the older original pyramid developed in the United States (Figure 26.10). Due to its tropical climate, Puerto Rico includes water in both its pictorial representation as well as in the written materials that accompany the guide (Painter et al. 2002).

26.10 Food Guide Pyramid of Puerto Rico

Albania

Some countries such as Albania have only recently established dietary guidelines. Their Food Based Dietary Guidelines published in December 2008 are accompanied by a food guide pyramid (Figure 26.11) that is based on a CINDI (Countrywide Integrated Non-communicable Diseases Intervention programme, WHO) pyramid and materials published by the World Health Organization.

26.11 The Food Guide Pyramid of Albania

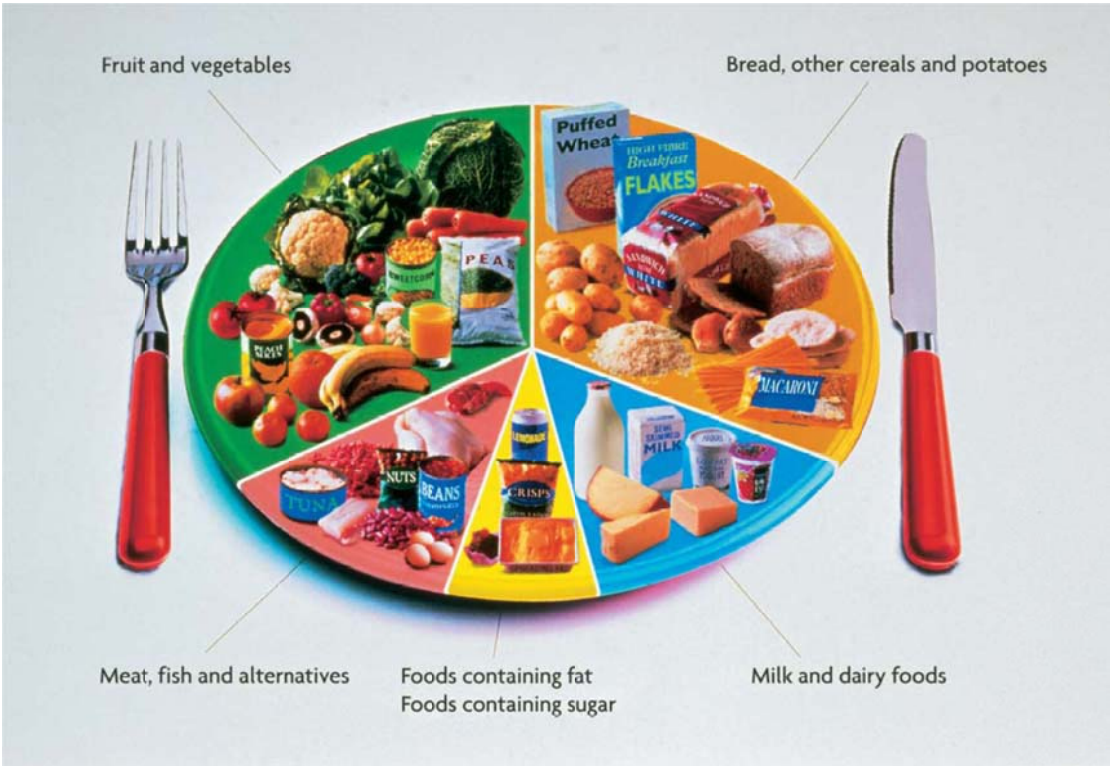


Food Plates

United Kingdom

The Balance of Good Health is a tilted plate model that is based on the Government's Eight Guidelines for a Healthy Diet (Figure 26.12). It is noteworthy that the UK food guide categorises potatoes into the bread and cereals group rather than in the fruit and vegetables food group. Other root crops such as turnips and parsnips are however included in the fruit and vegetables group.

26.12 The Balance of Good Health food guide (UK)



Balance of Good Health – United Kingdom (available at http://www.food.gov.uk/multimedia/pdfs/bghbooklet.pdf; accessed 27th November 3009)

Mexico

Mexico's food plate uses a colour-coded outer ring to indicate which food groups should be consumed liberally, moderately or sparingly (green, orange, red, respectively) (Figure 26.13). The fat and sugar food group is not included in this country's food guide.

26.13 Mexico's Plate of Good Eating

Circles

Whilst some circular food guides may represent a plate, if they have not been depicted with eating utensils, they have been classified as a circle rather than a plate model.

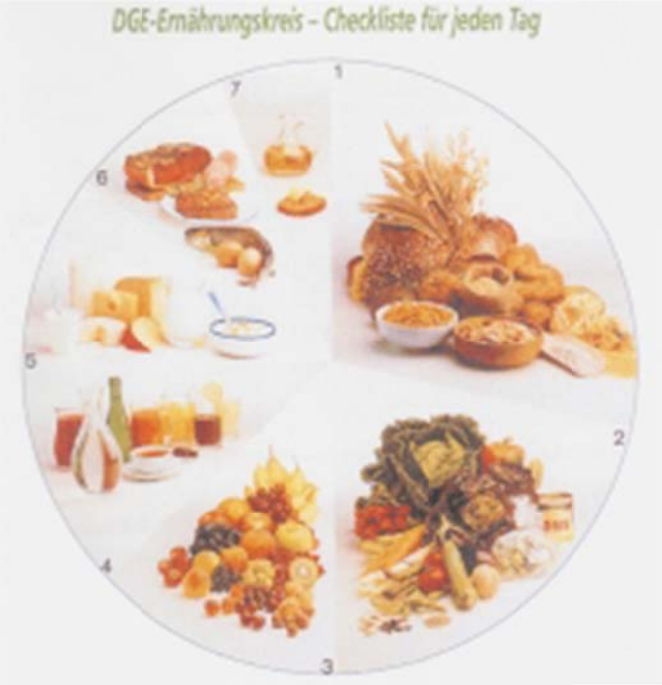
Australia

The Australian Guide to Healthy Eating has been described in section N1.1 above.

Germany

Germany's food guide includes seven different food groups, the recommended proportions from which are indicated in decreasing order, in a clockwise fashion (Figure 26.14). Germany is the only country to include a separate fluid group in its classification, in an attempt to encourage an adequate fluid intake.

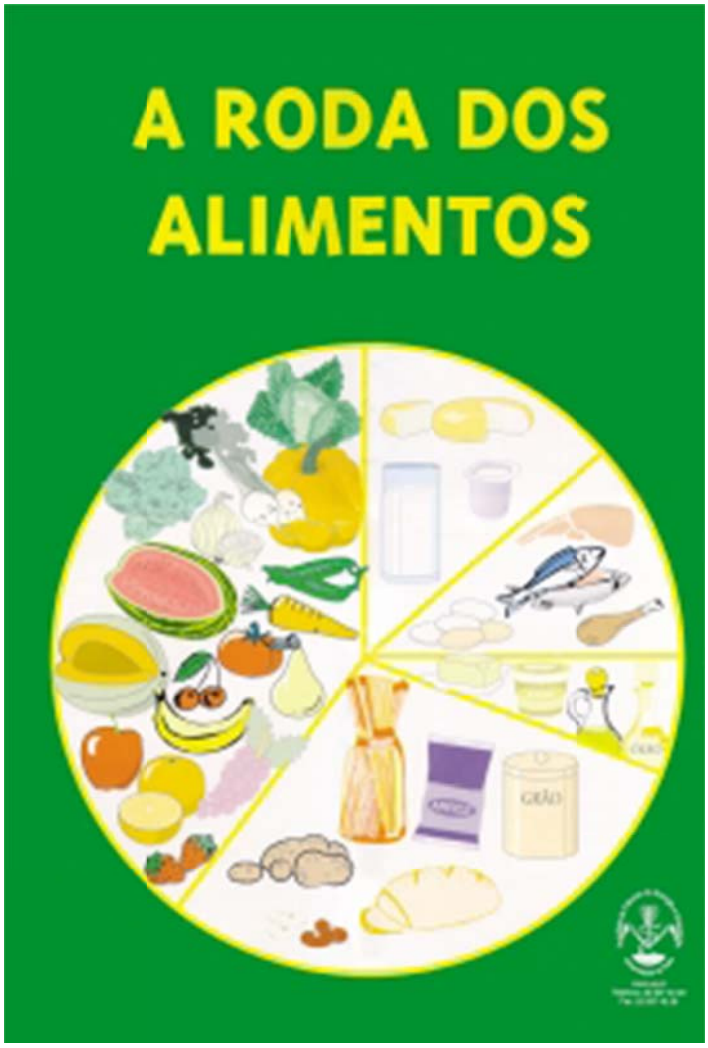
26.14 Germany's food guide circle



Portugal

Portugal, like the UK, Germany, Mexico and Koreas, groups potatoes in its bread and grains food group in its food guide circle (Figure 26.15).

26.15 Portugal's Food Guide circle



Sweden

Sweden's food circle shows seven different food groupings, with an additional food group comprising potatoes and root vegetables (Figure 26.16).

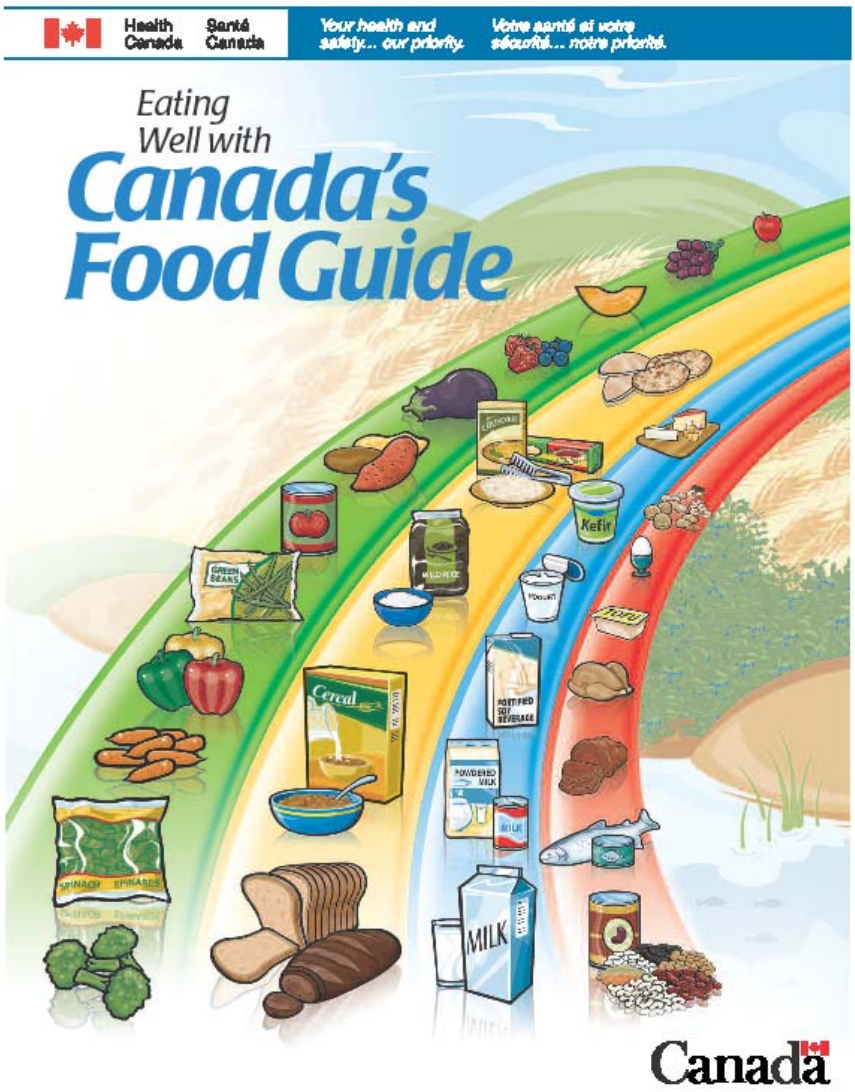
26.16 Sweden's food circle

Other shapes

Canada

Canada is the only country that uses a rainbow shape for its food guide. *The Eating Well with Canada's Food Guide* (2007) (Figure 26.17) replaces the previous version of the rainbow (*Canada's Food Guide to Healthy Eating*, 1992) and is presented as a 6-page fold-out booklet as well as being available as an interactive web-based tool. Food intake patterns are provided for nine age and sex groups, providing specific number of food servings from each food group for Canadians aged two years and older. Recommendations are also provided for each food group on quality of food choices, such as wholegrain products (grain products group), dark green and orange vegetables (vegetables and fruit group), lower fat alternatives (milk and alternatives group) and fish, vegetable protein and lean meat cut choices (meat and alternatives group).

26.17 The Eating Well with Canada's Food Guide (2007)



Korea

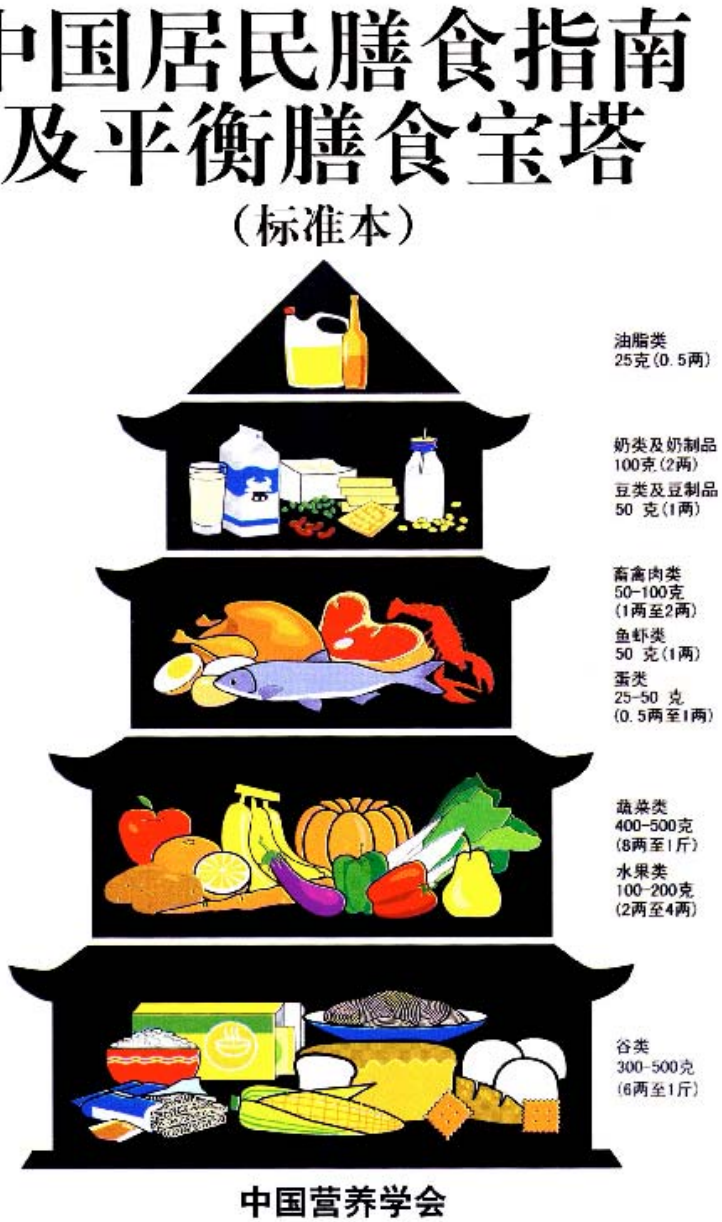
A pagoda shape depicts five food groups and conveys the message of quantities using this tiered pictorial that tapers upwards (Figure 26.18).

26.18 Korea's Food Guide

China

A pagoda shape is also used in China (Figure 26.19).

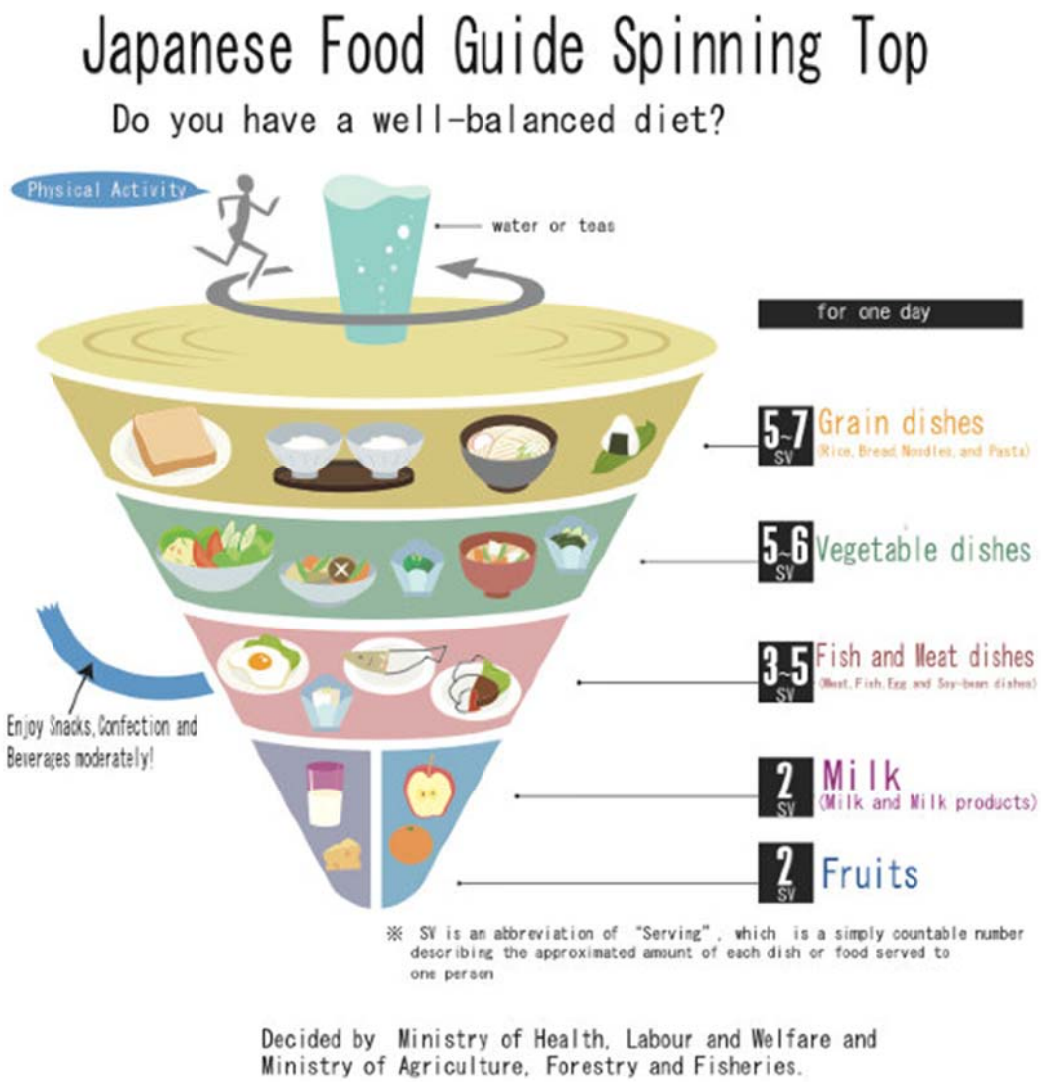
26.19 China's Food Guide



Japan

Japan is unique in that it is has developed a 'Food Guide Spinning Top' model that is conical in shape (Figure 26.20). Fluid (i.e. water or tea), together with physical activity (i.e. a figure running), is depicted at the top of the spinning top, to indicate their importance in a healthy diet. The Japanese guide specifies the number of dishes to correspond with the way that people typically consume foods at the table (Murphy & Barr 2007). Fruit and vegetables are classified as two different food groups and the recommendation regarding the different quantity of intake from each is clearly shown in the guide. Being dish- rather than individual food-based makes it easier to understand than the guides of the US, UK, Canada, Australia etc. that require consumers to think about how to combine individual food items into a healthy diet.

26.1 Japanese Food Guide Spinning Top



Thailand

In Thailand, the Nutrition Flag essentially depicts an upside-down pyramid (Figure 26.21). Rice and starchy food, including potatoes, make up the main food group. Serving sizes for the starchy food group, as well as the meat group and vegetables group are provided in terms of rice serving spoons.

26.2 Nutrition Flag: Healthy eating for Thais

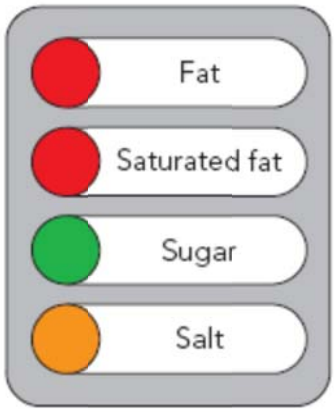
Food Labelling Food Guides

Various initiatives have recently been undertaken to help consumers differentiate between individual foods in an effort to assist total diet planning. These food labelling-based guides have not been formally adopted by regulatory authorities but rather remain industry-driven on a voluntary basis. The guides tend to be nutrient-based in their criteria, and in that regard cannot strictly considered to be food guides.

- ***Traffic light guides***

Front-of-pack nutrition labelling using signposting such as traffic light guides has gained momentum in some European countries, particularly in the United Kingdom. In that country, the Food Standards Agency (FSA) has set lower and upper boundaries for the dietary components of fat, saturated fat, sugar and salt (UK Food Standards Agency: Signposting; http://www.food.gov.uk/foodlabelling/signposting). Depending on the content of each of these components in 100 g or per 100 mL, a food would qualify for either a green (low), amber (moderate) or red (excessive) colour code (example provided in Figure 26.22). An individual food package would carry four colour codes, and the more green lights the food has, the better the choice. Red lights indicate nutrient excess which is associated with preventable chronic conditions, including obesity, heart disease, metabolic syndrome and diabetes. Shoppers can see at a glance a food's profile of compliance with the guidelines for each of the four areas where moderation is recommended.

26.3 Example of a traffic light label (taken from Beard et al. 2007)



Beard et al. (2007) argue that the traffic light guide could be useful if the approach allowed flexibility for each food. They provide the example of olive oil, that could be recommended oil in moderation (amber light) due to its healthy fatty acid composition, even though it happens to be 100% fat. Another example relates to the natural sugar content of fresh fruits – this is high enough to give many fruits an amber rating, but moderation is not the right message for fruit. Since Australian dietary guidelines refer only to added sugar, this potential misleading message could be avoided. Beard and colleagues (2007) also suggested that Australia might add a traffic-light label for energy

density (showing the same three colours based on kJ/100 g), and expand the saturated fat category to include trans fat, with very low thresholds triggering automatic red lights.

- ***Guideline Daily Amounts***

Another signposting initiative on food labelling is the Guideline Daily Amounts (GDA). This provides consumers with information on the approximate amount of energy (kJ or kcal), fat, saturated fat, carbohydrate, total sugars, protein, fibre, salt/sodium in the food serving. The figure is usually presented on food packaging as both an absolute amount and as a percentage of the guideline daily amount for that nutrient (Figure 26.23). The initiative is voluntary and largely driven by food and drink manufacturers, retailers and other industry organisations such as food and grocery councils. GDAs have been extensively implemented by food manufacturers and retailers across the UK, and their use is extending to other European countries (http://www.igd.com/index.asp?id=1&fid=5&sid=42&tid=62; accessed 14 December 2009). According to a survey carried out by the Confederation of Food and Drink Agencies of the EU (known as CIAA) in 2008 some 1,030 brands, including 80% of all soft drinks and branded breakfast cereals were using GDA labelling at that time. Of the 2,026 food and drink manufacturers surveyed across the EU, 44% were already labelling their products with GDAs.

26.4 Example of a GDA label on food packaging

http://www.bupa.co.uk/health_information/images/direct_news/diet_nutrition/img_food_labelling_gda.gif

Food Guides for Special Groups

Older adults

A Food Guide Pyramid for Older Adults was developed by Tufts University in 1999, and is still is widely used as an illustration in textbooks and manuals, is featured in newsletters for older Americans, and in informational material prepared by the Departments of Elder Affairs in a number of US states. It has recently been updated to correspond with the USDA (2005) *MyPyramid* to be computer-based (available at: http://nutrition.tufts.edu/1197972031385/Nutrition-Page-nl2w_1198058402614.html; accessed 27th November 2009).

The *Modified MyPyramid for Older Adults* (Figure 26.5) is aimed at people aged 70 years and older and emphasizes nutrient-dense food choices and the importance of fluid balance, but has added additional guidance about forms of foods that could best meet the unique needs of older adults and about the importance of regular physical activity (Lichtenstein et al. 2008). Since Lichtenstein and colleagues were concerned about computer use among older adults and the adaptability of *MyPyramid* to print form, the *Modified MyPyramid for Older Adults* is also available as a graphic print-out with icons representing foods in the following six food categories:

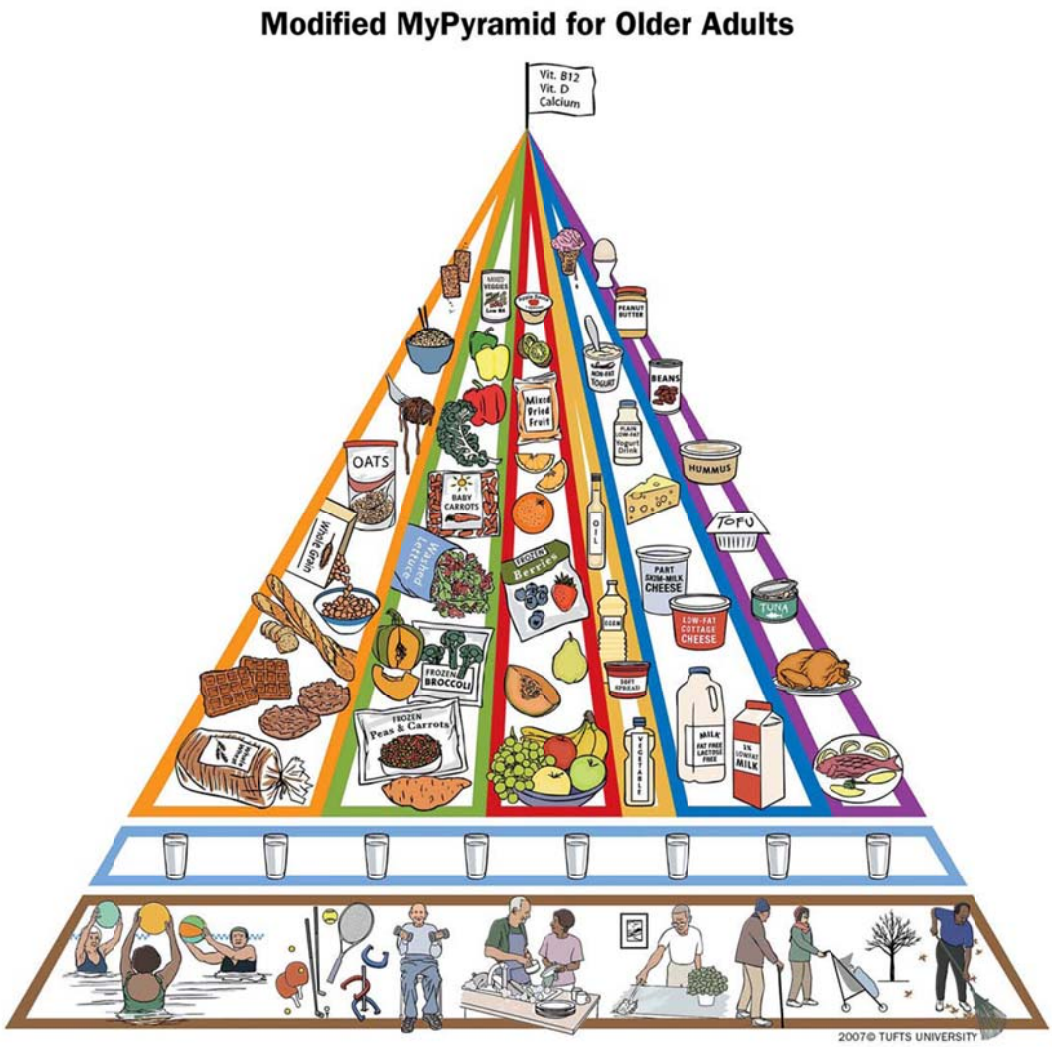
- Whole, enriched, and fortified grains and cereals such as brown rice and 100% whole wheat bread
- Bright-coloured vegetables such as carrots and broccoli
- Deep-coloured fruit such as berries and melon
- Low- and non-fat dairy products such as yogurt and low-lactose milk
- Dry beans and nuts, fish, poultry, lean meat and eggs
- Liquid vegetable oils and soft spreads low in saturated and *trans* fat
- Fluid intake.

Fluid and light-to-moderate physical activity, such as walking, house work, yard work and swimming, is emphasized.

Icons depicting packaged fruit and vegetables in addition to fresh example are suggested in the *Modified MyPyramid for Older Adults*. For example, bags of frozen pre-cut vegetables that can be resealed are shown or single-serve portions of canned fruit that may be easier to prepare as well as have a longer shelf life, thereby minimizing waste. The *Modified MyPyramid for Older Adults* stresses the importance of consuming fluids by having a row of glasses as its foundation. The authors note food and beverages with high water content, such as lettuce, vegetable juice and soups, are important contributors of fluid in an older person's diet.

Also included as an integral part of the *Modified MyPyramid for Older Adults* is a flag at the top suggesting that older adults may need certain supplemental nutrients, such as calcium, vitamin D and vitamin B12.

26.5 Modified MyPyramid for Older Adults



Preschoolers

The *Go, Grow, Glow* guide is a nutrition curriculum developed for preschool children in the US. Using a simplified version of *MyPyramid*, children learn the connection between foods and health. The guide is based on categorization of foods into three main groups:

- Grains are **Go** foods *(they help you run, jump and play all day)*
- Milk, meat and beans are **Grow** foods *(they help you to grow big and strong)*
- Fruits and vegetables are **Glow** foods *(they help you have shiny hair and sparkly eyes)*.

Available at: [http://www.google.com.au/imgres?imgurl=http://ceplacer.ucdavis.edu/files/43316.jpg&imgrefurl=http://ceplacer.ucdavis.edu/Custom_Program969/Go_Glow_Grow-Preschool.htm&h=161&w=125&sz=11&tbnid=MWpvuKeJispykM:&tbnh=98&tbnw=76&prev=/im

ages%3Fq%3DGo%2BGlow%2BGrow&hl=en&usg=__In8uPzvUbUQYUWkFM6xKfYdgX98=&ei=7ckqS_m5A5Lc7AP25dSMBg&sa=X&oi=image_result&resnum=1&ct=image&ved=0CAsQ9QEwAA]

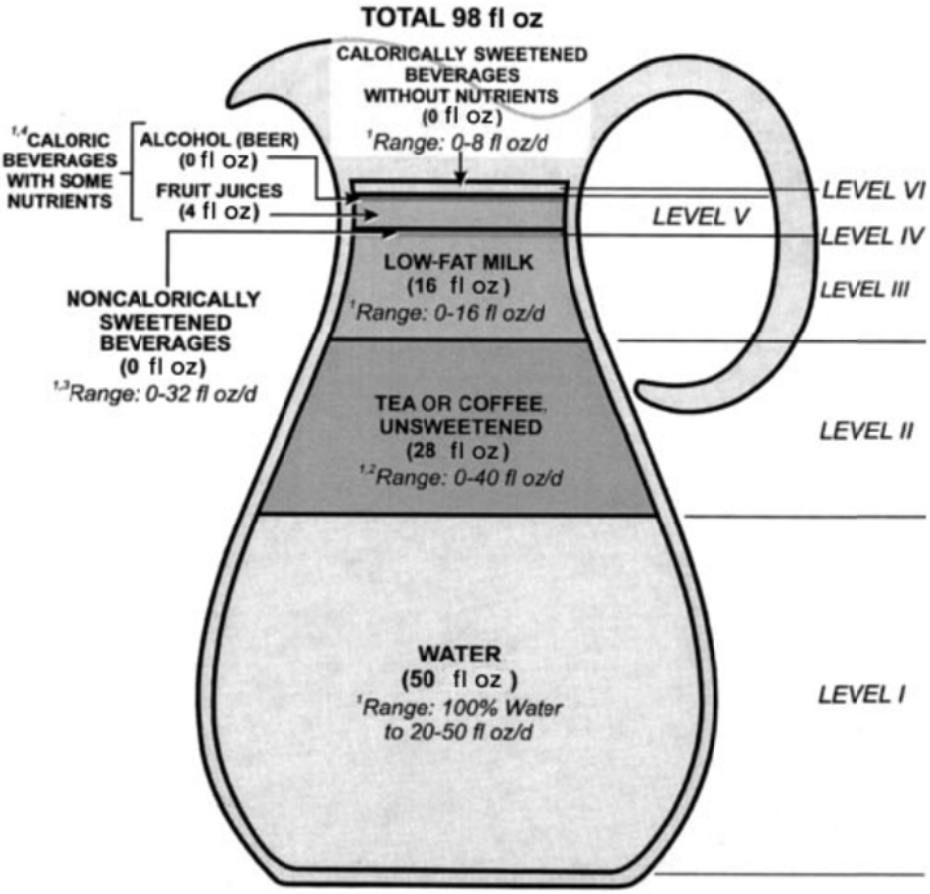
Vegetarians/vegans

A number of food guides have been adapted for use by vegetarians and vegans (Messina et al. 2003; Nakamoto et al. 2009; Venti & Johnston 2002).

Guides on Fluid Intake

A number of food guides have been developed to provide guidance on beverage intake patterns. Energy intake from beverages currently represents 21% of the total energy intake for Americans aged two years and above (Nielsen & Popkin 2004) and this is provided predominantly from calorically sweetened beverages. Given the large increase in unhealthy weight patterns in the United States over the past 20 years, beverage intake constitutes an important source of excess energy. Popkin and colleagues (2006) have proposed a guidance system for beverage consumption in the United States, which is depicted as a jug model. Figure 26.6 shows the suggested beverage consumption patterns (10% of energy from beverages) for a person with a 2200-kcal daily energy requirement. The actual volumes of each beverage type are shown for illustrative purposes only; however the total should sum to 98 fl oz.

26.6 Beverage Guidance System (Popkin et al. 2006)



The Beverage Guidance Panel's suggested range for each beverage:

1. Range: caffeine is a limiting factor up to 400 mg per day, or ~32 fl oz coffee/d (can replace water)
2. Can substitute for tea and coffee with the same limitations regarding caffeine. 100% fruit juices, 0–8 fl oz/d; alcoholic beverages, 0–1 drink/d for women and 0–2 drinks/d for men; whole milk, 0 fl oz/d. 1 fl oz = 29.57 mL

Another beverage guide was produced by Lipton tea (Figure 26.7) and is available on their website: http://www.liptont.com/tea_health/beverage_guide/registered_dietitians.aspx (accessed 13 December 2009).

26.7 Lipton Healthy Beverage Guide

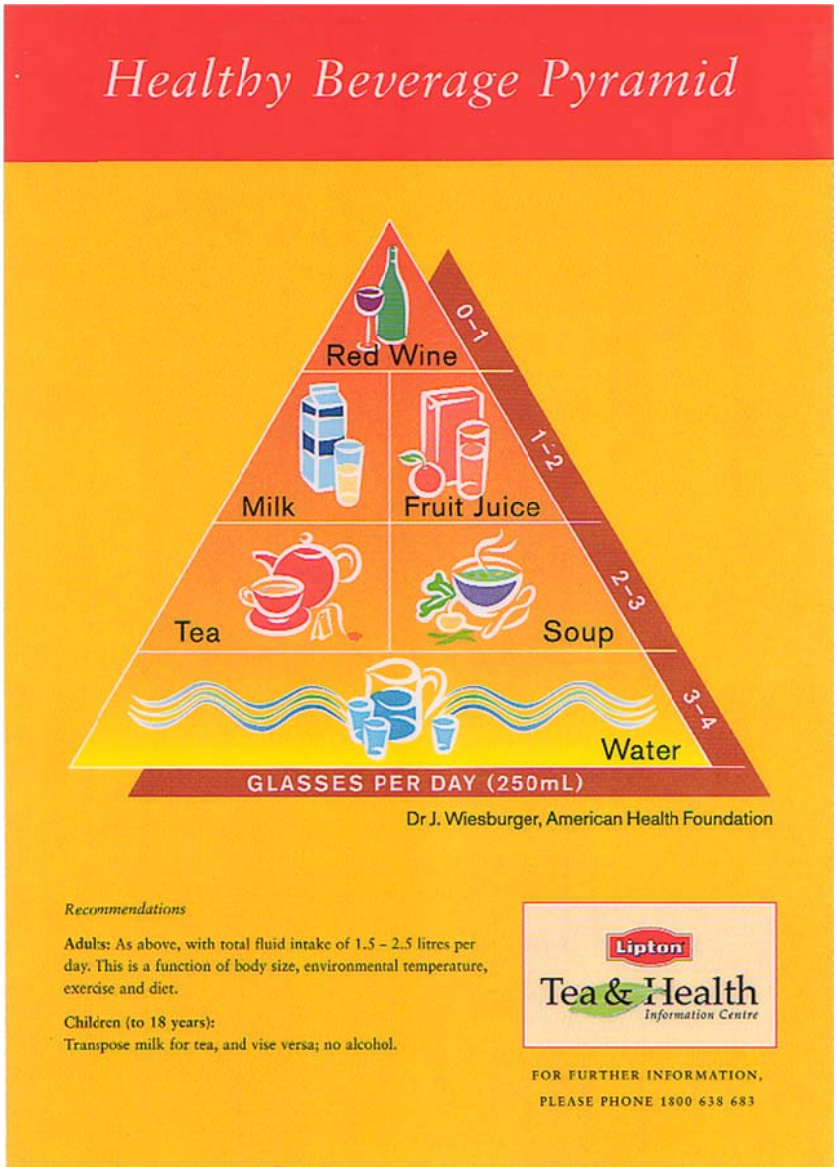


Table 26.2 Food guides of different countries – United Kingdom, The Netherlands, Australia and New Zealand

Adapted from Love 2002 (after The Children's Health Development Foundation, South Australia, and Deakin University, Victoria 1998; Hunt, Rayner & Gatenby 1995; BFNE 1993; Nutrition Task Force 1991).

UNITED KINGDOM	THE NETHERLANDS	AUSTRALIA	NEW ZEALAND
The Balance of Good Health	Voedingswijzer (The Food Guide)	The Australian Guide to Healthy Eating	No name
- tilted plate graphic - illustrates types and proportions of foods needed for a balanced and healthy diet	- tilted oval graphic - foods in each group are classified as "good", "better" or "best" choices as no foods are considered "unhealthy"	- circular graphic - illustrates foods most commonly eaten in Australia - foods grouped according to nutrient similarity	- no pictorial design
- 5 food groupings * bread, other cereals and potatoes * fruit and vegetables * milk and dairy foods * meat, fish and alternatives * foods containing fat and/or sugar	- 4 food groups, and fluids * carbohydrates (bread, potatoes, pastas, legumes, sweets, cookies) * vitamin C (vegetables, fruits, juices) * protein (milk and milk products, cheese, meat, poultry, eggs, fish, soya products, snacks) * fat (butter, margarine, oils, savoury sauces, nuts, crisps)	- 5 food groupings with water and other foods shown separately * breads, cereals, rice, pasta, noodles * vegetables, legumes * fruit * milk, yoghurt, cheese * meat, poultry, eggs, nuts, legumes - Water – 8 glasses/day	- 4 food groupings * vegetables and fruits * breads and cereals * milks and dairy products, especially low fat varieties * lean meats, poultry, fish, eggs, nuts and pulses

	* fluids (water, tea, coffee, soft drinks, alcohol)	- Other foods - to be eaten sometimes or in small amounts (biscuits, soft drinks, pies, chips, crisps, chocolate, ice-cream, oils, margarine)	

Table 26.3 Food guides of different countries – Indonesia, Philippines, Malaysia and Thailand

Reprinted with permission from Love 2000 (after Department of Health, Thailand 1999; Orbeta 1998; Ministry of Health, Malaysia 1997; Ministry of Health, Indonesia 1995).

INDONESIA	**PHILIPPINES**	**MALAYSIA**	**THAILAND**
No name	The Filipino Pyramid Food Guide	Food Pyramid	The Nutrition Flag
- triangular graphic - featuring 4 food groupings	- pyramid graphic - based on the United States Food Guide Pyramid - featuring 4 levels of consumption and 5 food groupings	- triangular (pyramid) graphic - featuring 4 levels of consumption and 5 food groupings	- upside-down triangular (pyramid) graphic
- 4 food groupings * base of triangle – staples/starchy foods (taro, rice, corn, potatoes, sweet potatoes, cassava, bread, sago, cooking banana, noodles) * middle tier – vegetables (tomatoes, cassava and paw-paw leaves, cabbage, spinach, fern shoots, yard-long bean, carrots) * middle tier – fruits (durian, oranges, pineapple, pears,	- 4 levels * level 1 (base of pyramid) – eat most (rice, root-crops, corn, noodles, breads, cereals) * level 2 – eat more (fruit, vegetables) * level 3 – eat some (fish, poultry, dry beans, nuts, egg, lean meats, low fat dairy) * level 4 (tip of pyramid) – eat a little (fats, oils, sugar)	- 4 levels * level 1 (base of pyramid) – eat most (cereals, cereal products, tubers) * level 2 – eat more (fruit, vegetables) * level 3 – eat moderately (fish, poultry, meat, legumes; and milk, dairy products) * level 4 (tip of pyramid) – eat least (fat, oil, sugar)	- 5 food groupings * rice, cereals, starchy foods * vegetables * milk * eggs, meat, legumes, sesame seeds * fruits * oils, sugar and salt

bananas, mango, paw-paw) * top tier – protein-rich foods (milk, legumes, soya, chicken, liver, meats, eggs, fish)			

Table 26.4 Food guides of different countries – Asian Region, Mediterranean, United States and Canada

Reprinted with permission from Love 2002 (after Oldways Website 1998; Hadjilouca 1997; Willet, Sacks, Trichopoulou, Drescher, Ferro-Luzzi, Helsing & Trichopoulos 1995; Health and Welfare Canada 1992; Welsh, Davis & Shaw 1992a).

ASIAN REGION	**MEDITERRANEAN (Crete, Greece, Italy)**	**UNITED STATES**	**CANADA**
Healthy Asian Diet Pyramid	Mediterranean Diet Pyramid	*MyPyramid*	*Eating Well with Canada's Food Guide*
- pyramid graphic - based on the United States Food Guide Pyramid - featuring 4 levels of consumption and 10 food groupings	- pyramid graphic - based on the United States Food Guide Pyramid - featuring 3 levels of consumption and 11 food groupings	- pyramid graphic to illustrate variety, balance (proportion) and moderation - range of servings is given for each food grouping - best choices within each food group given - interactive web-based program offers personalized eating plans and tools to plan and assess food choices - physical activity guidelines provided.	- rainbow graphic - featuring 4 food groupings with 6 directional statements
- 4 levels * level 1 - daily consumption (rice, rice products, noodles, breads, millet, corn, other grains; fruit; legumes, nuts, seeds; vegetables; vegetable oils) * level 2 – optional daily consumption (fish, shellfish; dairy)	- 3 levels * level 1 – daily consumption (breads, pasta, rice, couscous, polenta, bulgur, other grains, potatoes; fruits; beans, other legumes, nuts; vegetables; olive oil; cheese, yoghurt) * level 2 – a few times per week	- 7 major food groupings * grains * vegetables * fruits * milk * meat and beans * oils * discretionary calories	- 4 nutrient dense food groupings * vegetables and fruit * grain products * milk and alternatives * meat and alternatives Messages about quality of food choices within groups given. A Food guide serving is reference

ASIAN REGION	MEDITERRANEAN (Crete, Greece, Italy)	UNITED STATES	CANADA
* level 3 – weekly consumption (eggs, poultry; sweets) * level 4 – monthly consumption (red meat) * Additional advice - physical activity - moderate consumption of alcohol	(fish; poultry; eggs; sweets) * level 3 – a few times per month (red meat) * Additional advice - regular physical activity - wine in moderation		amount in each food group.

Table 26.5 Food guides of different countries – South Africa and "Lesser Developed" Countries

(From Love 2002; after Burns, Lovich, Maxwell & Shapiro 1997; Kuzwayo 1991; Wheat Board 1990; Fedfood (Pty) Ltd & Vandenburghs (Pty) Ltd 1985).

SOUTH AFRICA	**"LESSER DEVELOPED" COUNTRIES**
No name (presently under review)	Mixed Meal Guide (Multimix System)
No standard pictorial design - 3 food groupings often depicted as a 3-legged cooking pot - 5 food groupings commonly depicted as a circular graphic, a "food square" or an adaptation of the United States Food Guide Pyramid	"Main Foods" illustrated in the centre "Helper Foods" illustrated around the "Main Foods"
- 3 food groups * body building foods (meats, dairy, legumes) * energy foods (breads, cereals, fats) * protective foods (fruits, vegetables) - 5 food groups * grains and grain products * fruit and vegetables * meat and meat substitutes * milk and milk products * fats and oils	- Main foods * staples/carbohydrate-rich foods - Helper foods * beans * milk products * meat, eggs, fish * nuts * fats * sugars * fruits * vegetables * water

N1.2 Summary

Despite a wide spectrum of shapes that have been used to represent food guides in countries around the world, most guides provide consistent messages regarding what constitutes a healthy dietary pattern. Foods are generally grouped as grains, vegetables, fruits, meat, milk and dairy products, and fats and sugar. This fundamental classification of foods appears similar in all countries which have a national food guide.

Minor differences were evident in the fat and sugar group, the vegetable and fruit group and the milk and diary product group. Most countries combine fat and sugar in one group, with the exception of China, Sweden, Germany and Portugal. Sugar is not included at all in the Chinese pagoda, while the Mexican food guide does not include a group for either fat or sugar (Painter 2002). In Australia, the fat and sugar group is included in the corner of the guide as an 'extra' food group.

Fruits and vegetables are grouped together in the food groups for Canada, UK, China, Korea, Portugal and Mexico but are independent groups in other countries.

The only country lacking a milk and dairy food group was the Philippines, where milk is not commonly consumed. Instead, milk has been incorporated into the meat and major protein group for that country's food guide.

The placement of potatoes differed between countries, with most countries placing them in the vegetables group, but some (Korea, UK, Portugal, Germany, Mexico) grouping them into the grains (bread and cereals) group. In the case of Sweden, potatoes and root vegetables have been separated into a group that is apart from other vegetables.

Water and fluid appears in some of the pictorial food guides, and has been allocated its own beverage group in Germany's guide.

Beans and legumes are usually in the meat group due to their high protein content, but in Sweden, Germany and Australia these foods are placed into the vegetables group because of their high vitamin, mineral and fibre content. In the US MyPyramid food guide, dry beans and peas can be counted either as vegetables (dry beans and peas subgroup), or in the meat, poultry, fish, dry beans, eggs, and nuts (meat and beans) group. It is recommended that dry beans and peas would be counted in the vegetables group for individuals who regularly eat meat, poultry, or fish. For those who seldom consume meat, poultry, or fish (vegetarians), dry beans and peas could be counted in the meat and beans group.

Nuts are other foods that are classified in different ways. In countries including Australia, US and Puerto Rico, nuts are included in the meat group but in Korea they have been placed in the fats and olis group due to their high fat content.

Most food guides attempt to quantify recommended serving sizes from each of the food groupings, or at least represent quantities in terms of proportions of total food intake (as in the food plate, circle and pyramid models). An exception is the Filipino Pyramid which uses action words that imply proportion and frequency rather than specific food serve sizes.

Regardless of the shape of the pictorial food guide or the way in which foods have been grouped in the food guide, a core recommendation of all the food guides reviewed was consumption of large amounts of grains, vegetables and fruits with moderate intakes of meat, milk and dairy products.

N1.3 What methods have been used to develop national food selection guides?

In addressing the question of the methods used to develop food guides in countries around the world, it is important to first consider the characteristics and purpose of food guides. Food guides essentially have two components:

- a knowledge component – used to communicate basic nutrition concepts to the consumer i.e. food groupings/classification system based on similarity of nutrient content, function or food type;
- an behavioural component – used to translate the food groupings/classification system into concrete actions i.e. qualitative advice, and suggested minimum numbers of servings per food group per day (Axelson & Brinberg 1992, cited by Love 2000).

It is recommended that food guides be developed according to three criteria if they are to be effective and serve the purpose of translating dietary guidelines into practical recommendations on daily food intake (Cronin 1998; WHO 1998; Australian Nutrition Foundation 1996; Welsh 1996):

- The food guide should complement the dietary guidelines of that specific country;
- The food guide should acknowledge the foods/drinks commonly consumed by the people of that specific country, and the way(s) in which these foods are classified/categorised by the people of that specific country;
- Visual illustrations used to depict the food guide should be readily understood.

Food guides need to be updated to reflect the most current dietary guidelines of that country. An example of how guidelines change over time is given for the case of the United States between 1980 and 2000 (see Table 28.4). In the United States, every 5 years, an expert Dietary Guidelines Advisory Committee is appointed to make recommendations to the Secretaries concerning revision of *Dietary Guidelines for Americans*. The recommendations are to be targeted to the general public aged two years and older and based on the preponderance of scientific and medical knowledge that is current at the time of publication of the Committee's report. The most recent (2005) version of the guidelines makes a major departure from previous editions of *Dietary Guidelines for Americans* in that it does not include a message specifically directed toward sugars. The Committee provides a strong rationale for limiting one's intake of added sugars (i.e. sugars and syrups that are added to foods during processing or preparation or at the table) however this point is addressed under a new guideline "Choose Carbohydrates Wisely for Good Health" and also under the first and second topics, which address energy needs and controlling calorie intake, respectively. Such changes to the national dietary guidelines necessitate this to be clearly reflected in the accompanying national food guide, in order for the message to be communicated to consumers in an easy-to-understand way.

Dietary guidelines may be either nutrient-based, food-based (as in most developing countries) or a combination of both, as in the case of Australia. However food guides need to represent a healthy diet in terms of foods.

There are two main ways to evaluate the effectiveness of dietary guidelines and food guides. The first is to monitor implementation or uptake of the consumer instruments, such as monitoring the number and content of leaflets and booklets which are distributed or sold or requested over time; the

number and content of advertising campaigns and their impact; performing surveys on awareness and knowledge about dietary guidelines and nutrition messages. The other way is to monitor changes in outcomes including food sales and food purchases, food consumption patterns and indicators of health status.

Examples are provided below from specific countries regarding the methodology undertaken to develop and/or evaluate their national food selection guides. Since the majority of articles related to the development of the US *MyPyramid*, the process of its development is provided in detail. The experience of Canada and the United Kingdom is also reported, as these three countries represent the most comprehensively developed methodological techniques.

Australia – Australian Guide to Healthy Eating

The Australian Guide to Healthy Eating is the pictorial guide to translate the dietary guidelines into food and nutrition messages for the public. The first Dietary Guidelines for Australians were published in 1979 and later updated in 1992 to a set of 10 guidelines with the notable addition of two guidelines on calcium-rich and iron-rich foods for specific groups in the community (Baghurst 2003). In 1995, Dietary Guidelines for Children and Adolescents were developed and in 1999, a set of guidelines specially drafted to address the needs of older Australians, aged 65 years and older, was developed. The revised Dietary Guidelines for Adults, as well as those for Children and Adolescents which incorporate Infant Feeding Guidelines for Health Workers, were released in June 2003. The Dietary Guidelines in Australia are developed under the auspices of the National Health and Medical Research Council (NHMRC) using an evidence-based approach that involves extensive systematic reviews of the literature.

The development of the AGTHE is reported in two articles (Smith et al. 1999a; Smith et al. 1999b). Briefly, the AGTHE is based on the food grouping classification of the core food groups (NHMRC 1995). The core food groups differed from the previous five food groups classification in that the fruit and vegetable group was split into separate fruit and vegetable groups while the butter and margarine group was excluded as it was not required to meet the RDI level for any nutrient. The core food groups are: cereals; fruit; vegetables; meats and alternatives; and milk, cheese and yoghurt. Modelling was undertaken that involved composite food groups which were devised as reference portions, weighted to broadly reflect apparent mean intakes of foods consumed in Australia in 1989-90 (Smith et al. 1999a). For example, the reference 150 g fruit group portion was made up as 63 g of orange, 31 g of apple, 16 g of banana, 15 g of pineapple, 11 g of pear, 5 g of watermelon, 5 g of rockmelon and 4 g of apricot (Smith et al. 1999a). Modelling to calculate the amounts of food groups required to meet RDI levels for adults, children and pregnant and lactating women was undertaken. These calculations used the most recent food composition data available at the time.

Consultations were held in each state and territory of Australia with 27 government health, food, education and primary industries departments and nutrition-related units and projects. In conjunction with these, consultations were also held with professional groups and consumer groups in each state and territory to assess food guides currently in use in Australia and to determine current user expectations of a food guide. Postal surveys of health, food and nutrition professionals (n =571), and of randomly selected consumers (n =542) were also undertaken (Baghurst et al. 1994). Smaller focus

groups or workshops were held with schoolchildren, rural and urban Aboriginal people and selected migrant groups. It was found that professionals wanted explanatory materials outlining the rationale for the development of the guide, large posters, videos, small leaflets and booklets whereas consumers wanted recipe books, booklets and fridge magnets. The consumer survey showed that most people wanted specific serving size information, information about different foods contained within a designated food group and 'extra' foods (high fat, high sugar foods and drinks, and alcohol); information about nutrients including fat, salt, vitamins and alcohol; and. information about additives and pesticides. Most consumers preferred food photographs to food drawings. Health and nutrition professionals indicated that a total diet approach rather than depiction of a proportion of nutritional requirements was supported. Serving size information as part of the guide was strongly supported, but respondents stated that information could be qualitative or quantitative according to need.

A three-stage process was undertaken to develop the Australian Guide to Healthy Eating:

1. Concept development. Developing the scientific and communication rationale and the creative concept design process (Smith et al. 1999a);

2. Graphic design, evaluation and consultation - consisting of evaluation followed by revision (Smith et al. 1999b); and

3. Materials development and evaluation, followed by finalisation and approval of materials for publication (Smith et al. 1999b).

In order to ensure acceptability and relevance of the food guide, the AGTHE was evaluated by consumers, nutrition educators and users in many sectors, including a total of 21 focus groups, nine consultation workshops, four expert reference group workshops, a field testing trial involving 61 teachers, dietitians and other nutrition educators, and a survey of 750 consumers (Smith et al., 1999b). There was broad general agreement with the main scientific rationale of the guide from nutrition and health educators and user groups from other sectors. The consumer focus groups helped refine the graphic design work to ensure that the guide was interpreted appropriately by consumers.

United States – MyPyramid

Revisions of the food intake patterns for use in the development of the current *MyPyramid* were based on the same guiding principles that were used to develop the original Pyramid, namely to represent a total diet that is both *adequate* and *moderate*, as well as to reflect current food consumption choices in determining nutrient sources (Britten et al. 2006a).

Background to development of *MyPyramid*

(based on information retrieved from USDA MyPyramid.gov website: http://www.mypyramid.gov/professionals/MyPyramidDevelopment/MyPyramidDevelopment.html; accessed 26 October 2009):
The original Food Guide Pyramid, released in 1992, was updated, revised and released in 2005. Reasons for the revision were 1) to improve its effectiveness in motivating consumers to make healthier food choices and 2) to ensure that the U.S. Department of Agriculture's (USDA) food

guidance system reflected the latest nutritional science. The revision paralleled the development of the *2005 Dietary Guidelines for Americans*, which USDA and the U.S. Department of Health and Human Services (HHS) released in January 2005. The major modification with the *MyPyramid* compared to earlier versions of the Pyramid was to allow a more individualised approach for consumers to plan their diets, based on personal requirements and preferences. It was acknowledged that the previous Pyramid had not been effective in communicating nutrition information to the US population to result in behaviour change. The revised Pyramid includes focused messages and individualized educational tools, through multiple channels including print, internet and media. There are a number of variations of the *MyPyramid* for various audiences, including pregnant women, pre-schoolers, school-aged children and older people.

MyPyramid's daily food intake patterns identify amounts to consume from each food group and subgroup at a variety of energy levels. To ensure that these patterns reflect the latest science, they were updated to meet current nutrition standards through a standardised technical research process. The nutrition standards used as the basis for the *MyPyramid* were the Dietary Reference Intakes published by the National Academy of Sciences Institute of Medicine. During the dietary modelling phase, the new data released by the USDA's Agricultural Research Service on the nutritional content of foods and on food consumption patterns was used to update food intake patterns of the US population (as published in the *2005 Dietary Guidelines for Americans*). Prior to its release, the *MyPyramid* underwent various phases of development, validation and consumer testing to ensure that various patterns of food intake suggested by the food guide met the nutritional standards.
A multiple component research process was undertaken to revise the original Food Guide Pyramid to result in the *MyPyramid* Food Guidance System. This research has been published as a series of articles in a dedicated supplement to the *Journal of Nutrition Education and Behavior* (November/December 2006); these articles are summarised, according to the steps taken, below.

Table 26.6 Dietary Guidelines for Americans (1980-2000)
(after Kennedy & Davis 2000; DHHS/USDA 1995; http://www.health.gov/dietaryguidelines/dga2005/report/PDF/A_ExecSummary.pdf (accessed 30th Nov 2009)

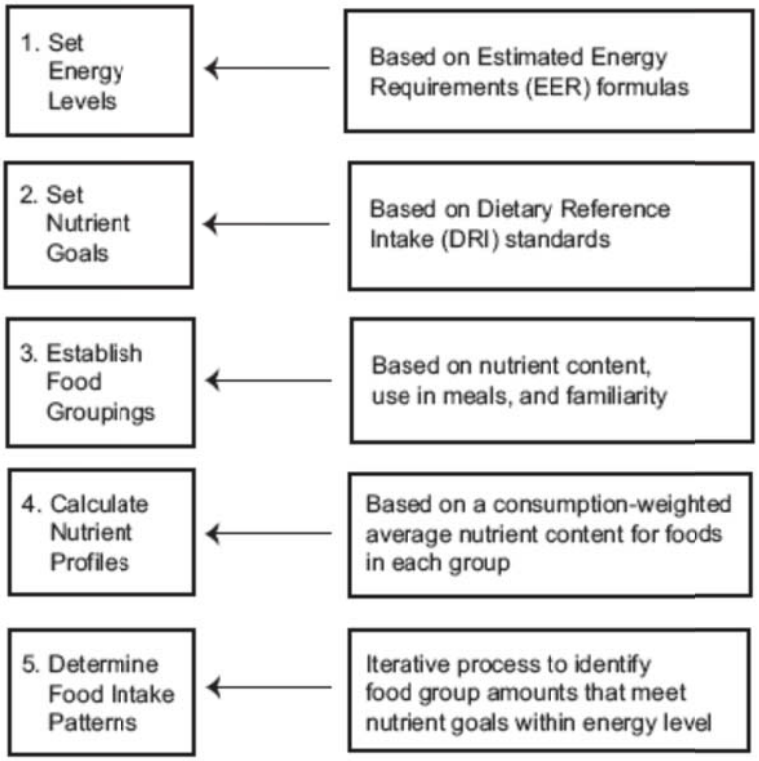
1980 (1st edition)	1985 (2nd edition)	1990 (3rd edition)	1995 (4th edition)	2000 (5th edition)	2005 (6th edition)
Eat a variety of foods.	Eat a variety of foods.	Eat a variety of foods.	Eat a variety of foods.	Let the pyramid guide your food choices.	Consume a variety of foods within and among the basic food groups while staying within energy needs.
Maintain ideal weight.	Maintain desirable weight.	Maintain healthy weight.	Balance the food you eat with physical activity – maintain or improve your weight.	Aim for a healthy weight.	Control calorie intake to manage body weight.
				Be physically active.	Be physically active every day.
Avoid too much fat, saturated fat and cholesterol.	Avoid too much fat, saturated fat and cholesterol.	Choose a diet low in fat, saturated fat and cholesterol.	Choose a diet with plenty of grain products, vegetables and fruits.	Choose a variety of grains daily, especially whole grains.	Increase daily intake of fruits and vegetables, whole grains, and nonfat or low-fat milk and milk products.
				Choose a variety of fruits and vegetables daily.	
				Keep food safe to eat.	Keep food safe to eat.
Eat foods with adequate starch and fibre.	Eat foods with adequate starch and fibre.	Choose a diet with plenty of vegetables, fruits and grain products.	Choose a diet low in fat, saturated fat and cholesterol.	Choose foods low in saturated fat and cholesterol and moderate in other fats.	Choose fats wisely for good health.
Avoid too much sugar.	Avoid too much	Use sugars only in	Choose a diet moderate	Choose beverages and	Choose carbohydrates

	sugar.	moderation.	in sugars.	foods to moderate your intake of sugars.	wisely for good health.
Avoid too much sodium.	Avoid too much sodium.	Use salt and sodium only in moderation.	Choose a diet moderate in salt and sodium.	Choose and prepare foods with less salt.	Choose and prepare foods with little salt.
If you drink alcohol, do so in moderation.	If you drink alcoholic beverages, do so in moderation	If you drink alcoholic beverages, do so in moderation.	If you drink alcoholic beverages, do so in moderation.	If you drink alcoholic beverages, do so in moderation.	If you drink alcoholic beverages, do so in moderation.

Step 1 Development of food intake patterns (Britten et al. 2006a).

The first step in the process was development of food intake patterns for Americans, according to the procedures outlined in Figure 26.27 (taken from Britten et al. 2006a).

26.8 Process used for development of food intake patterns



An analytic process was undertaken to identify appropriate amounts from each food group that together would meet nutritional goals for various age/gender groups. An important aspect of this step was the establishment of food groupings (ie. Box no. 3 in Figure 26.27). The food groups developed for the original Pyramid (i.e. fruits; vegetables; meat, poultry, fish, dry beans, eggs, and nuts; milk, yoghurt, and cheese; bread, cereal, rice, and pasta; and fats, oils, and sweets) were examined to identify where changes might be needed to help consumers select healthy diets that would reflect potential guidance from the 2005 Dietary Guidelines. Some subgroups that had been used in the development of food intake patterns for the original Pyramid, such as whole and enriched grains and the five vegetable subgroups (dark-green vegetables, orange vegetables, dry beans and peas, starchy vegetables, other vegetables) had not previously been translated into consumer guidance in a quantified manner and were also assessed in this analysis.

A need to distinguish between fats that are primarily sources of saturated fatty acids and those that are primarily sources of monounsaturated or polyunsaturated fatty acids ('healthy fats').was investigated by separating fats into subgroups of solid fats and oils and designating oils as an essential component of the food patterns. The potential for including subgroups for fish and nuts in the patterns, was explored as described in the dietary modelling process in Step 3 below (Britten et

al. 2006b). A new concept of 'discretionary calories' as calories that can be used flexibly once nutrient needs are fulfilled was also investigated in the modelling process. Discretionary calorie allowance was described as the difference between total energy requirements and the energy consumed to meet recommended nutrient needs.

Food intake patterns were established that met almost all nutrient goals within estimated energy needs. Exceptions were inadequate intakes of vitamin E at all energy levels and potassium at lower energy levels, and excessive sodium intakes at higher energy levels. The food intake patterns identified to meet nutritional recommendations form the scientific basis for the *MyPyramid* Food Guidance System.

Step 2 Identification of food selections in each food group that reflects typical intake of Americans, and the nutrient intake expected from consumption of a specified amount of these foods from each group (Marcoe et al. 2006).

Analyses were undertaken to identify food selections in each *MyPyramid* food group or subgroup that were reflective of typical consumption patterns by Americans, and to calculate the nutrient intake that can be expected from consuming a specified amount of these foods from each group, in a low-fat and no-added-sugars form. Data from national food consumption surveys, and food composition databases were used. Foods were disaggregated into component ingredients, similar ingredients combined into "item clusters," and the relative consumption of each was determined. A consumption-weighted nutrient profile was constructed for each food group and subgroup depicted in the *MyPyramid* scheme. The adequacy of the *MyPyramid* food intake patterns were thereby assessed as they were being iteratively developed.

Step 3 Consumer Research for Development of Educational Messages (Britten et al. 2006b).

To assess consumer understanding and use of messages from the original Food Guide Pyramid and potential concepts for a revised Food Guidance System (i.e. *MyPyramid*), focus groups were conducted in Baltimore, Chicago, and Houston in groups comprising (i) general adult consumers (grouped according to younger and older ages); (ii) adults over 60 years of age, (iii) food stamp recipients, and (iv) overweight adults. It was found that key concepts of the original Pyramid were widely understood, but specific knowledge was limited and misunderstandings common, especially related to servings and the food group placement in the Pyramid. Detailed information about whole grains, types of fats, vegetable subgroups, and physical activity was lacking. It was concluded that consumers were aware of general concepts about healthy eating, but lacked specific knowledge to help them implement recommendations depicted by the Pyramid. This information was valuable in constructing the educational messages provided by the new *MyPyramid* food guide that included the provision of concrete examples and specific dietary information.

Step 4 Developing the Consumer Interface for MyPyramid (Haven et al. 2006).

Qualitative research conducted in two phases by professional market research facilities, including focus groups and Web-TV testing, was conducted to assess consumer response to potential graphics, slogans, and messages for the consumer interface of the *MyPyramid* Food Guidance System. Seventy-seven adults in 10 groups took part in the focus group sessions while 407 adults participated in the Web-TV research. Content analysis identified that respondents preferred the familiarity of the pyramid shape and found graphics and slogans that were perceived as new, personal, active, and positive to be most appealing. Consumer feedback from this research identified both appealing and useful elements, as well as elements that were potentially confusing or less meaningful - this was incorporated into development of the final consumer interface for the *MyPyramid* Food Guidance System.

Step 5 Use of updated Food Consumption and Composition Data on MyPyramid nutrient profiles (Yamini et al. 2006).

Methodological aspects related to the use of different nutrient databases for dietary assessment of population groups was investigated. Population-weighted estimates of food group intakes (composites) were developed using 24-hour recall data from two large population surveys that were conducted five years apart, CSFII 1994-96 (N = 14,262) and NHANES 1999-2000 (N = 8070). Nutrient profiles of these composites ere developed using Standard Reference data. The changes observed in five nutrients of selected USDA food subgroups were investigated by partitioning the overall changes into those caused by consumption changes over time, and those caused by nutrient database revisions. Consumption differences resulted in some variations in the food group nutrient content, but a majority of the changes were associated with use of the updated nutrient database. For example, vitamin A level in the orange vegetable subgroup was increased by 2.4% owing to consumption (from CSFII to NHANES), whereas the level was decreased by 38% due to nutrient updates in the database. Consideration of the changes in nutrient databases, as well as in food consumption patterns over time, is essential in monitoring both the trends in the food choices populations make and the adequacy of their diets. This is of relevance when before-after assessments are conducted as a means to establish the effectiveness of the introduction of new food guides.

Step 6 Dietary modelling (Britten et al. 2006c).

This paper describes the most important methodological step in the development of MyPyramid. Modelling analyses using the MyPyramid intake patterns were conducted to determine likely effects of possible recommendations on overall dietary adequacy for various types of eating patterns. Scenarios modelled included the feasibility of using the food patterns for (i) lacto-ovo-vegetarian diets, (ii) of varying fat levels within the patterns, and (iii) of increasing dietary flexibility through food group substitutions. Methods used in the three scenarios are described below.

i. *Lacto-ovo-vegetarian diets*

The *MyPyramid* food intake patterns group animal and plant protein sources into a single food group: the Meat, Poultry, Fish, Dry Beans (i.e. all legumes, including dry beans, dry peas, and soybean products), Eggs, and Nuts (MPFEN) group. The analysis was conducted by modifying the composition of the MPFEN nutrient profile to include only eggs, nuts, and dry beans and determined the changes in nutrient and calorie levels with varying proportions of these foods in this new profile.

The nutrients that can be expected from eating foods in this group (the nutrient profile) were calculated assuming an intake of foods within the group that is proportionate to the distribution of foods in the group consumed by the population. Results from this modelling analysis allowed for adequacy of food intake patterns to be assessed if no meat, poultry, or fish were consumed, in terms of recommended quantities of these foods.

ii. *Modifying fat profiles*

The approach taken to explore the impact on diet quality of modifying fat profiles within the ranges suggested by the Institute of Medicine Dietary Reference Intakes Report on macronutrients (i.e. 20% to 35% of total energy intake). The final food intake patterns of the *MyPyramid* contain about 29% to 31% energy from fat (Britten et al. 2006 a). Within each food group and subgroup, food items in low-fat or fat-free forms are used in determining the nutrient profile of the group (Marcoe et al. 2006). However, some fat is contained in these foods and is considered the minimum 'intrinsic' amount of fat in each pattern. For example, in the 2000-calorie pattern, 23.8 g of total fat comes from recommended amounts of low-fat or fat-free forms of meats and beans (14.5 g of fat), grain (6.5 g), milk (0.6 g), vegetables (1.6 g), and fruits (0.6 g). To bring the amounts of essential fatty acids to recommended levels, to help account for additional calories needed to meet energy needs, and to provide for flexibility in food choices by allowing some higher-fat selections, the working group had originally added a specific amount of additional solid fats and oils (i.e. animal fats such as beef, pork, chicken, and dairy fats, as well as hydrogenated vegetable fats such as shortening and stick margarine), termed 'discretionary' fats, to each food intake pattern. In determining amounts to add, the ratio of solid fats to oils was changed from the 58% solid to 42% oils ratio that is typically consumed to 40% solid and 60% oils in the patterns.

To change the overall percentage of calories from fat in the patterns, the amounts of 'discretionary' fat in the food patterns were calculated at all calorie levels. For each level of fat modelled (20%, 25%, 30%, and 35% energy), the total grams of fat that would be needed to reach the appropriate percentage of calories was estimated. Then, the intrinsic fat already present within each food group was taken away from the total fat allowance to determine the amount of discretionary fat allowed in each food intake pattern at each percentage of calories from fat. The discretionary fat was divided into solid fat and oil in a ratio of 40% solid to 60% oil. These amounts of fats and oils were inserted into the food patterns. At the lowest level of fat intake (20% E), patterns were created containing only oil and no solid fat to determine if this modification would help lower-fat patterns meet the

nutritional goals. For all patterns, after the appropriate levels of fat were included, the caloric deficit was calculated, and sufficient amounts of added sugars were inserted to bring the total calories up to the target levels. The amount of all nutrients in each pattern and the percentage of goal for each nutrient at each level of fat, from 20% to 35% of calories, were calculated.

iii. Flexibility of food choices

In order to investigate flexibility of food choices within a specific food group in the *MyPyramid* food guide, various modelling scenarios were conducted. For example, in the case of fish choice over other items in the meats, poultry, eggs, nuts, and seeds group (MPFEN), modelling was able to determine the impact on the nutrient adequacy if recommendations for all fish and/or high omega-3 fish consumption were increased to eight ounces per week (ie. about two servings of fish per week). Because of different fatty acid profiles of fish, two separate subgroups for fish were created, namely those high and low in omega-3 fat content. Nutrient profiles for the fish subgroups were calculated based on intake of 8 ounces per week of all fish or of only fish high in omega-3 fat. For this analysis, meat and poultry intakes were decreased, whereas egg and nut intakes were held constant. For the eight ounces of all fish per week scenario, the ratio between fish low and high in omega-3 fatty acids was maintained at current intake proportions of about 80 % and 20 %, respectively, as indicated by National Health and Nutrition Examination Survey (NHANES) 1999-2000 data. Including either 8 ounces of all fish or eight ounces of high omega-3 fish per week in the food intake patterns would result in an average intake of almost triple current fish consumption, or more than 10 times current high omega-3 fish consumption.

Similar modelling was performed for choices within the fruit category, and the results helped to drive a decision to change the equivalency for fruit juices so that 1/2 cup of 100% fruit juice is considered equivalent to 1/2 cup of whole fruit in the final intake patterns. This change makes the nutrition contribution of juices more equivalent to that of fruit, with the exception of dietary fibre.

In order to increase uptake of the MyPyramid by consumers, the following processes were followed:

1. Stakeholder input – A *Federal Register* notice was posted to present the plan and to solicit public comment. The notice included the conceptual plan for the graphic design and proposed consumer messages. Comments received were used to help focus the design and development of both motivational and educational aspects of the food guidance system.
2. Design – A new symbol, slogan and educational materials – including Web-based educational materials – were developed.
3. Consumer testing – As part of the design and development process, potential images and messages were tested with consumers to determine how well they communicated the intended content and how appealing they were to consumers. The results from the consumer research were used to revise and finalize the consumer materials so that consumers could more easily understand these messages and incorporate them into their lifestyle.

The educational tools developed for consumer and health professional use were:

- Web-based interactive tools that allow consumers to receive a 'personalized' set of recommendations and provide more information and tips to help them follow the recommendations;
- a new graphic and slogan, "Steps to a Healthier You";
- a poster and mini-poster with the graphic, slogan and key messages; and a core message framework for professionals, which may be used to develop additional educational materials.

The methodology and results of the consumer testing of the web-based educational materials are described in three articles that were published in the *J Nutr Educ Behav* 2006 supplement (Haven et al. 2006b; Juan et al. 2006; French et al. 2006).

Canada: Eating Well with Canada's Food Guide (2007)

A revision was undertaken of Canada's food guide in 2004 to address some of the challenges identified in using the 1992 Food Guide while building on its strengths, which included flexibility, simplicity, visual appeal, widespread awareness, and its consistency with current science. Challenges included confusion about serving sizes and serving ranges, unclear terms such as 'moderation', the perception that the graphics were outdated and not sufficiently inclusive of multicultural foods, and concern that the "Other Foods' category was too vague. A food intake pattern specifying amounts and types of food was created for Canada's revised food guide, *Eating Well with Canada's Food Guide* (2007), using a two-step modeling process (Katamay et al. 2007). In Step One, food composites were manipulated to develop a food intake pattern (see Figure 26.28). The second step used the step one food intake pattern to create 500 simulated diets for each of 16 age and gender groups. The resulting nutrient content distributions were evaluated relative to Dietary Reference Intake reference values. The modeling cycled between these two steps until a satisfactory pattern was achieved. The final pattern reflects modeling, a review of associations between foods and chronic disease, and input received during consultation.

An important part of the process to update dietary guidance in Canada involved ongoing consultation with stakeholders at every stage (Bush et al. 2007). Health Canada worked closely with three advisory groups - an external Food Guide Advisory Committee (representing public health, health policy, nutrition education, disease prevention, industry and communication), an Interdepartmental Working Group (representatives from across a number of federal departments and the Office of Nutrition Policy and Promotion) and the Expert Advisory Committee on Dietary Reference Intakes. Throughout the revision, Health Canada consulted with Canadians across the country including non-government organizations, academics, health professionals, government, industry and consumers.

26.9 Process to develop Canada's revised (2007) food guide (taken from Katamay et al. 2007)

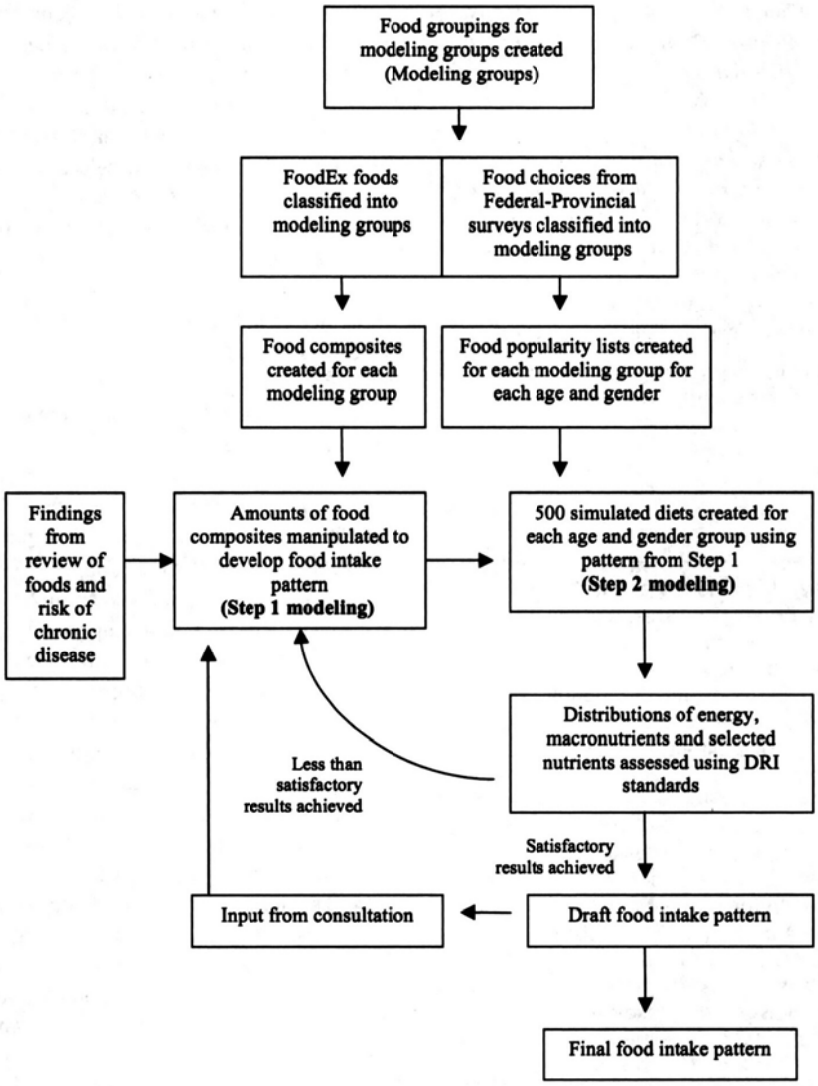


Figure 1. Process to develop the food intake pattern for *Eating Well with Canada's Food Guide (2007).*

A range of evidence helped to shape the revised Food Guide. Nutrient standards and the prevention of chronic disease were key scientific inputs. Research and analysis on issues of both a technical and communications nature were undertaken. Technical matters included addressing issues related to the food groups, number of servings and serving sizes. These technical issues were addressed in part in the context of developing food intake patterns. Communication matters included issues related to terminology, target audiences and graphics. A range of input including results from focus groups, on-line consultations, regional meetings, the review of the 1992 Food Guide and reviews of literature about the environmental context in which Canadians make food choices contributed to the pool of information used to address communication issues.

Development of Guidance on Types of Food in the Food Intake Pattern

Throughout the course of modeling, it was found that some nutrients were prevalent throughout the food supply and adequacy was achieved quite easily. For those nutrients for which adequate amounts could not be achieved within a reasonable amount of energy, specifying the inclusion of particular subgroups of foods improved the nutrient profile of diet patterns without increasing the total amount of food recommended. For example, statements highlighting particular subgroups that were included in the final food intake pattern (and the reason for this in parenthesis) include:

- *"Eat at least one dark green and one orange vegetable each day"*: Dark green and orange vegetables were needed to achieve adequate levels of folate and vitamin A in the food intake pattern.
- *"Have vegetables and fruit more often than juice"*: Vegetables and fruit were recommended more often than juice to maintain the dietary fiber content of the food intake pattern.
- *"Make at least half of your grain products whole grain each day*": Whole grains were needed for the achievement of adequate amounts of magnesium and fiber. In addition, a healthy diet rich in wholegrain products may reduce the risk of heart disease.
- *"Drink skim, 1% or 2% milk each day*": Lower-fat fluid milk was an effective way to obtain adequate calcium and vitamin D while remaining within an appropriate macronutrient profile and total amount of calories.
- *"Include a small amount - 30 to 45 mL (2 to 3 Tbsp) - of unsaturated fat each day. This includes oil used for cooking, salad dressings, margarine, and mayonnaise"*: Foods in the unsaturated fat subgroup were included to achieve appropriate levels of essential fatty acids.
- Likewise, the following statements were included so that the total fat, saturated fat, and calorie content of the pattern remained appropriate, and to encourage food choices lower in salt:
- *"Choose vegetables and fruit prepared with little or no added fat, sugar or salt."*
- *"Choose grain products that are lower in fat, sugar or salt."*
- *"Select lower fat milk alternatives."*
- *"Select lean meat and alternatives prepared with little or no added fat or salt."*
- *"Have meat alternatives such as beans, lentils and tofu often."*

In addition, convincing evidence of the relationship between the consumption of fish, particularly fatty fish, and reduced risk of cardiovascular disease led to the inclusion of the statement: *"Eat at least two Food Guide Servings of fish each week."*

United Kingdom: Balance of Good Health and Getting the Balance Right

The nationally accepted food guide model in the United Kingdom is the *Balance of Good Health* which was released in 1994. In its tilted plate format, the presentation and nutritional content of the *Balance of Good Health* were based on objective dietetic criteria and experimental research, which provided a clear evidence base on the guide's effectiveness as a learning tool (Gatenby et al. 1995;

Hunt et al., 1995b). In its development stages, the guide was tested using consumer research in both professionals and the lay public to identify preferred format and design, as well as tested through performance on various food selection tasks following exposure to versions of the guide (n = 2074). The research showed different preferences for these two groups. Since its release there has been no further published evaluation focused on outcomes associated with usage of the guide. Since portion size guidance was not provided in the original food guide, and it is 15 years since its release, a call for a revision of the national food guide has been made (Hunt 2007).

More recently in 2002 in the UK, the British Meat Nutrition Education Service (BMNES) updated its similar food selection guide *Getting the Balance Right* (also a plate model) to reflect the wider array of foods currently available and bring it in line with the Food Standards Agency's (FSA) *Balance of Good Health.* The nutritional and dietetic principles on which the model is based are described in an article by Strong (2002). *Getting the Balance Right* is targeted at two levels including nutrition educators (dietitians, practice nurses, school nurses, teachers, lecturers, catering trainers) and consumers, and presented in written formats. In 2002, an evaluation of a revised version was undertaken to assess its perceived relevance, suitability, provenance and effectiveness amongst nutrition educators and specialists in design/communication. Qualitative research methods, included 14 in-depth interviews using detailed interview guides to examine detailed knowledge and professional viewpoints. Perceptions related to the content, format, design, presentation, credibility and patterns of use of the guide amongst educators were documented. Responses suggested that key strengths of *Getting the Balance Right* included:

• Its high production quality, which implied that the contents were also of high quality and as a consequence kept and read by consumers.

• The visual impact and pictorial strength of the guide. The central wheel image offered rich potential for discussion with consumers and an inherent ability to show consumers the proportion of types of foods they should be eating.

• Respondents liked the inclusion of a broader range of foods (compared to the FSA's *Balance of Good Health* model) and applauded the inclusion of 'convenience' foods as they felt this gave greater consumer relevance, enabling end users to identify their own food patterns more readily. They liked the use of food photographs instead of illustrations, which introduced realism to the guide.

• The fact that the guide was recommending a healthy style of eating built on everyday recognisable foods, which are easily available in mainstream shops.

• Its motivating nature because it communicated the message that healthy eating is not difficult or about total denial because of the inclusion of 'treat foods' within the guide.

• The practical content of the materials. Many felt that the tone and extent of the materials encouraged end users to use it as a resource, to pick and choose pieces of information relevant and interesting to them.

• The tone within the materials was said to be 'straight forward' and clear – not overly academic or stuffy.

The updated version of the BMNES food guide provides the basis for a useful nutrition education resource. However, effectiveness of the tool has not been evaluated and can only be answered by systematic quantitative research to test the ability of consumers to understand and apply the information within the guide.

Portugal

The *"Knowing how to eat is knowing how to live"* campaign, which included the Food Wheel guide as its symbol was implemented in Portugal in 1977. Several publications referring to and explaining the use of this guide were published but no reference was made to its background methodology. The Food Wheel guide contained five food groups of different sizes, suggesting a recommended proportion between the groups, but without specifying quantity. A revised version of the guide has been published (Rodrigues et al. 2006), composed of seven food groups (fats and oils; milk and dairy products; meat, fish, seafood, and eggs; pulses; potatoes, cereals, and cereal products; vegetables; and fruits), and achieved with the assistance of an expert panel, using existing international recommendations and nutrient composition tables. The development of the revised Portuguese food guide followed nine main steps:

1. Obtaining food and nutrition experts' opinion

2. Establishment of nutritional objectives

Energy requirements were computed by taking the median of 13 age groups of both genders (infants under the age of one were excluded because of their particular needs), as recommended by both the US Recommended Dietary Allowances (RDA, 1989) and the recommended dietary intakes for the Portuguese (1982). A median value of 2200 kcal was considered as a reference value for the general population.

3. Establishment and definition of the food groups and their subgroups

Seven food groups and 21 subgroups were established to be included in the new food guide after taking into account the following: similarities in nutritional composition of food items; common usage in Portuguese food habits; and the five food groups used in the previous food guide (fats and oils; milk and dairy products; meat, fish, seafood, and eggs; potatoes, dried pulses, cereal and cereal products; vegetables, fresh pulses, and fruit).

4. Definition of the standard food portion in each food group

The standard food portion sizes were based on the average weight of current household measures (e.g. a cup of milk, a tablespoon of olive oil) or of usual consumption units. The average weight of the standard portion was calculated when data were not available in the national references used. When necessary, the obtained portion weights were slightly adjusted in order to adopt portions that could easily be divided or multiplied.

5. Establishment of equivalent portions in each food group

In accordance with the established standard portion size, the quantity of the main nutrient supplier for each food group was calculated. The weight of the equivalent portions was determined after taking into account the nutrient quantity of the respective standard portion and the mean nutritional values of the defined subgroups. The obtained values were rounded up in order to adopt portions that could easily be divided or multiplied.

6. Establishment of the recommended number of daily food portions for each food group

Based on the mean nutritional values previously obtained for each food group, dietary plans were calculated for the energy values established in Step 1 (1300 kcal, 2200 kcal, and 3000 kcal). The numbers of portions obtained in each group for the 1300 kcal (children aged one – three years) plan and for the 3000 kcal (active men and male adolescents) plan were taken as extreme values in order to give a range of possible portions, while the median value of 2200 kcal was used for the rest of the population.

The content of foods and on food consumption patterns was used to update food intake patterns of the US population (as published in the *2005 Dietary Guidelines for Americans*). Prior to its release, the *MyPyramid* underwent various phases of development, validation and consumer testing to ensure that various patterns of food intake suggested by the food guide met the nutritional standards.

A multiple component research process was undertaken to revise the original Food Guide Pyramid to result in the *MyPyramid* Food Guidance System. This research has been published as a series of articles in a dedicated supplement to the *Journal of Nutrition Education and Behavior* (November/December 2006); these articles are summarised, according to the steps taken, below.

Despite the limited number of nutrients analyzed in the Portuguese food composition tables and the different analytical methods used in the British food composition tables, an attempt was made to check if the proposed food portion range would supply the recommended daily intakes of some nutrients, other than macronutrients. The average content of vitamins A and C, calcium, phosphorus, iodine, iron, fibre, sodium, and cholesterol were obtained for the three established dietary plans and compared with recommended daily values. Only values for iodine and sodium did not meet the recommendations. Individual-based dietary data from the United Kingdom showed higher sodium intake values than in Portugal, which may indicate higher added salt values in British cooking habits and thus higher sodium values in British cooked foods compared to Portugese varieties. The importance of reducing the use of salt and its possible substitution with herbs and spices is one of the points emphasized in the produced dissemination materials described in Step 9.

8. Transforming results into a captivating and easy to understand food guide

The circle format was adopted, because it can be associated with the image of a plate and because people already recognize it from the previous food guide. The serving dish is an important symbol of Portuguese culture, where eating around the table is still commonplace and very important. Its use also highlights and promotes the relevance of social interaction within food habits. It was decided that the whole circle would represent the maximum possible food weight that could be achieved in

accordance with the dietary plans and number of food portions established in Step 6. This representation was made by multiplying the obtained number of recommended portions by the weight of the heaviest portion of each group; the maximum food weight that would be possible to reach in each food group was obtained. The total maximum food weight was achieved by adding the results of the seven food groups. These procedures were done for the three dietary plans previously established, and the results were 2213 g for the 1300 kcal plan, 3205 g for the 2200 kcal plan, and 4323 g for the 3000 kcal plan. In order to obtain each group contribution in percentage, the maximum weight of each food group was divided by the total food weight of all the groups. The same procedure was used for each dietary plan. The final size of the circle slices resulted from a mean of the obtained proportions: 2% for fats and oils; 18% for milk and dairy products; 5% for meat, fish, seafood and eggs; 4% for pulses; 28% for potato, cereal, and cereal products; 23% for vegetables; and 20% for fruits.

9. Elaboration of dissemination materials

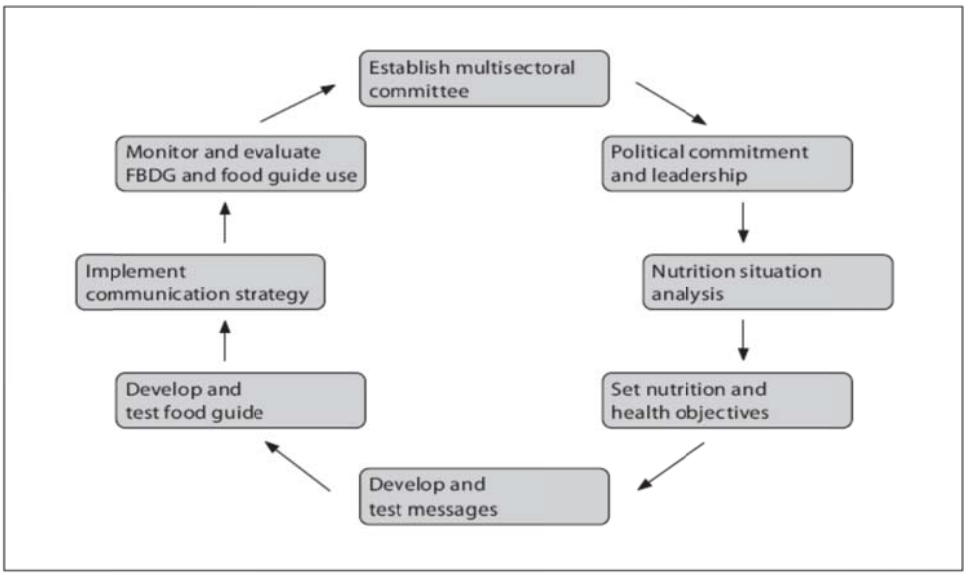
With input from graphic designers, educational materials were produced. A poster based on selected available national foods was conceived for the new food wheel guide. A slogan and some general recommendations were associated with the final, printable version. *"Eat well, live better!"* appeared with the sentences *"eat food from each slice every day," "eat more from the bigger slices and less from the smaller ones,"* and *"eat a variety of foods within each slice, vary them daily, weekly and seasonally."* In order to highlight the importance of hydration, the image of drinking water would be included in the centre of the food circle.

Developing country approach to developing food guides

Over a decade ago, the FAO/WHO (1996) reported on a joint consultation between the two agencies that recommended the development of dietary guidelines that were food, rather than nutrient based (food based dietary guidelines; FBDG) (Figure 26.9). FBDG need to be adapted to a country's specific needs; ensure that the nutrient needs of the population are covered; and contribute in reducing the risk of cardiovascular diseases. In addition, they should be in accord with public policies that promote food safety and physical activity, a healthy environment and a local food economy.

Specific recommendations will vary from country to country based on the availability and cultural acceptance of foods. FAO/WHO (1996) recommended that FBDG should be accompanied by posters or food selection guides. These visual guides should assist users to select a diet that is adequate in nutrients and contains a high level of complex starches and dietary fibre and avoids excessive intakes of fats, salt and added sugars. Guides should reflect a concern for promoting food choices that are consistent with the conservation of national resources, including promoting the concept of "local production for local consumption". A food guide should be culturally inclusive and incorporate foods that are generally available and accessible at a reasonable price. In addition a guide should be based on sound educational principles and be accessible to a wide range of educational levels.

26.10 Recommended steps for developing and implementing FBDG (Albert 2007)



The FBDG approach has been widely adopted. A survey was conducted by the World Health Organization (WHO 2003) to assess the existence of national, government-endorsed food-based dietary guidelines in Member States of the WHO European Region. Of the 48 participating countries, 25 reported having national, government-endorsed food-based dietary guidelines; 8 reported having national food-based dietary guidelines that were either in preparation and/or not yet endorsed by the government; 6 reported not having food-based dietary guidelines and 9 did not reply to the questionnaire.

A workshop on food-based dietary guidelines (FBDG), organised by the European Food Information Council, in conjunction with the Food and Agricultural Organization (FAO) of the United Nations (Regional Office for Europe and Central Asia) and the EURRECA project (European micronutrient recommendations across Europe), was held in Budapest on 18-20 May 2009 (FAO & EURRECA 2009). Information about the FBDG status in Central and Eastern European countries (CEEC) was exchanged, and experiences discussed to compare lessons learned with regards to the development, implementation, communication, monitoring and evaluation of FBDG, which included consideration of food guides, if available in the various participating countries. Fourteen countries (Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Serbia, Slovak Republic, Slovenia) participated in the workshop. The majority of the participating countries had developed FBDG but stages of development varied. Barriers regarding effective communication and dissemination of the FBDGs were similar across all countries and were related to lack of financial resources and local expertise. Consumer research was rarely used in any of the phases of development and implementation of the FBDGs.

Thailand and Chile

The Thai Nutrition Flag, published in 1998, was pre-tested among the public to assess understanding of portion size and quantities (Duenas 2005). The "rice-serving spoon" was developed as the household unit for measuring foods. Use of this flat broad spoon proved to be an effective way for consumers to provide realistic estimates of portion sizes consumed.

Chile is one of the few developing countries that has evaluated its dietary guidelines and food guide. The evaluation included different types of institutional settings and population groups. A study in a clinic found that patients with diet-related chronic diseases received messages to eat more fruits and vegetables but had not heard about reducing animal fats. A study in schools found that children had seen the pyramid but did not understand the portions. A third internet-based study identified that only 30% of the consumers knew about the guidelines and 60% knew about the food pyramid. After the same consumers received information directly, the awareness and willingness to change diets rose to 80% (Olivares 2004). The information obtained from the evaluation was used to revise the FBDG in 2005.

N1.3 Summary

There appears to be a disparity in methods to develop food guides, depending on whether or not the country's national dietary guidelines have been adopted according to the WHO/FAO (1996) approach to developing food based dietary guidelines (FBDG) or whether a more quantitative approach such as the application of population-weighted nutrient composites for food groups as recommended by the USDA, has been undertaken. It is noteworthy that developing countries tend to test their food guides using qualitative consumer research methodology. Interestingly, relative consistency is demonstrated between messages provided by various countries food guides, regardless of the process followed to develop and test the guides. Consumer understanding of nutrition information provided by food guides such as MyPyramid (USA), Balance of Good Health (UK) and Canada (Eating Well with Canada's Food Guide) appears to be good. The challenge for nutrition educators rests in the public's ability to adopt the behaviour changes recommended by the guides. Adherence to dietary recommendations depicted in national food guides has been assessed in various countries using various methods, the most common of which is a Healthy Eating Index instrument developed by the USDA Center of Nutrition Policy and Promotion (Basiotis et al. 2002). Articles related to use of the HEI were excluded for the purpose of this review, but a recently developed version of the HEI in Thailand (Taechangam et al. 2007) demonstrates its applied use that is beginning to emerge in Asian countries. Willet & McCullogh (2008) have demonstrated that adherence to specific dietary guidelines is associated with better health. They reported that adherence to the Dietary Guidelines and the Food Guide Pyramid, assessed using the HEI, were associated with only a small reduction in major chronic disease risk in a population of over 100,000 US adult men and women, suggesting that the Dietary Guidelines were not offering optimal dietary guidance. These authors recommend that dietary guidelines (including food guides) should be evaluated for their ability to predict the occurrence of major illness.

Despite being derived from different types of nutrition research, food guides from around the world essentially share consistent messages: eat more fruits, vegetables, legumes, and whole grains; eat less added sugar and saturated fat; and emphasize plant oils. A comparison of food-based recommendations and nutrient values of three food guides currently in use in the United States (the official national USDA *MyPyramid*; the National Heart, Lung, and Blood Institute's Dietary Approaches to Stop Hypertension (DASH) Eating Plan; and Harvard University's Healthy Eating Pyramid) found that recommendations were similar regarding almost all food groups for both the type and amount of foods (Reedy et al. 2008). Primary differences were seen in the types of vegetables and protein sources recommended and the amount of dairy products and total oil recommended. Overall nutrient values associated with following each of the food guides at the 2,000-calorie level were similar for most nutrients, except vitamin A, vitamin E, and calcium. The analysis compared the three food guides using the USDA evaluation strategy, namely the application of population-weighted nutrient composites for each food group and subgroup, assuming average choices within food groups of the three food guides. The differences identified between the food guides raised questions regarding the optimal way to convey dietary concepts to consumers. The authors identified the following questions to consider in the development of future guides:

- To emphasize intake of whole grains, is it more effective to create a separate food group (the Healthy Eating Pyramid) or to define emphasis within the food group (DASH) and/or through a subgroup (*MyPyramid*)?
- To emphasize increased intake of legumes, is the message clearer with a separate food group (DASH and the Healthy Eating Pyramid), or is it enough to provide emphasis through a subgroup (*MyPyramid*)?
- Conversely, to emphasize decreased intake of fatty red meat, is the message clearer by having a separate food group (the Healthy Eating Pyramid) or to provide guidance for lean choices from red meat and emphasize other protein sources (*MyPyramid* and DASH)?
- To emphasize intake of certain fatty acids, is it better to include a separate group for oils (*MyPyramid* and the Healthy Eating Pyramid), or to create a Nuts and Seeds food group (DASH and the Healthy Eating Pyramid)?
- What is the most effective way to increase calcium and vitamin D intake at the population- and individual-level?
- Should food be emphasized over supplements?

Important lessons can be learned from the extensive process undertaken in the development of the *MyPyramid*. Dietary modelling analyses is required to explore the overall effect of specific dietary recommendations on intake patterns, and determine possible impacts on diet quality of various types of eating patterns, as recommended by the food guide.

In the case of Australia, the national food guide (*Australian Guide to Healthy Eating*) is currently being revised, along with revision of the Core Food Groups and Dietary Guidelines, in order to reflect the most recent scientific information contained in the NHMRC (2006) Nutrient Reference Values. The lack of up-to-date dietary intake data on a population level will undoubtedly hamper the application of established methodology in dietary modelling techniques to inform development of an appropriate new food guide.

Conclusion

There are many different pictorial food guides available from countries around the world. Food guides are not stand-alone tools for nutrition education purposes but are meant to translate a country's dietary guidelines into easy-to-understand messages for consumers. Methodology used to develop food guides is well described in the case of the United States (*MyPyramid*), Canada (*Eating Well with Canada's Food Guide*), United Kingdom (*Balance of Good Health*) and Australia (*Australian Guide to Healthy Eating*). Such nutrition education tools have theoretically been shown to result in adequate nutrient intakes provided that the recommended dietary messages with regard to food choices from various groupings and serving sizes are followed. However few food guides have been formally evaluated as to whether or not they are useful for informing the consumer about healthy eating and how to adhere to the country's dietary guidelines in a real life situation (Yngve & Margetts 2009). Demonstration of the effectiveness of food guides ultimately requires 'hard' outcome data such as changes in health profiles following introduction and implementation of the food guide.

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27. OBESITY INDICES (N1.4)

Evidence Statements

27. OBESITY INDICES (N1.4)

INDICES FOR BODY WEIGHT ETC IN CHILDREN

N1.4. What indices and references are used for the assessment of body weight, growth rates and obesity in children in Australia? What are the current opinions on which indices and references are best?

Purpose

The aim of this narrative review is to answer the question: What indices and references are used for the assessment of body weight, growth rates and obesity in children in Australia? It also aims to summarise international opinion on which indices and references are best.

Methods

A systematic search of scientific literature, available in English from 2002, was conducted in May 2009. The searches used combinations of the following terms: *assessment, reference, index, body weight, measures, body mass index, anthropometry, body composition, growth rate, body height, obesity, overweight, percent body fat, CDC, and skinfold thickness*. Searches were conducted in the following databases: Cinahl, Medline, PreMedline, PsycINFO, Cochrane/DARE, and ERIC. 388 articles were discovered by the searches and after review of titles and abstracts 148 were retrieved for detailed review. Only studies conducted in an Australian population were retrieved. Other reasons for non-retrieval were: not a study (two), not a relevant population (146), not a relevant outcome (85), or duplicated articles (seven). After retrieval of the full articles, 61 others were excluded because the content was not a relevant outcome (14), not a study (three), or not a relevant population (44) for this review, leaving 87 studies used in this narrative review. Additional references were added from the reference lists of included studies and from known organisations with published growth charts. In the reference section, references retrieved from the systematic literature search are identified with an asterisk.

Results

Many different definitions have been used for the assessment of body weight, growth rates, and obesity in children and adolescents in Australian studies. A summary of these is presented in Table 27.1, while details of retrieved Australian studies can be found in the Table 27.2.

Table 27.1 Summary of definitions used to classify children and adolescents according to weight status. BMI: body mass index; WHO: World Health Organization; UK: United Kingdom; CDC: Centers for Disease Control and Prevention; IOTF: International Obesity Task Force; NHMRC: National Health and Medical Research Council.

Category	Measure	Referent	Age group
Severe thinness	BMI z-score for age < 3 standard deviations below normal	WHO	5-19 years
Underweight or thinness	BMI for age < 2nd percentile	UK-WHO growth charts	0-4 years
	Weight for age ≥ 2 standard deviations below normal	WHO	0-5 years
	BMI z-score for age < 2 standard deviations below normal	WHO	5-19 years
At risk for overweight	BMI for age > 85th percentile	CDC growth charts	0-20 years
Overweight	Values equivalent to BMI > 25 kg/m^2 in adults	IOTF age, gender specific charts	2-18 years
	BMI for age > 95th percentile	CDC growth charts	0-20 years
	BMI for age > 85th percentile	NHMRC recommendation with reference to CDC growth charts	0-20 years
	BMI for age > 85th percentile	1990 UK Growth reference curves	4-23 years
	BMI for age > 91st percentile	UK-WHO growth charts	0-4 years
	Weight for height > 2 standard deviations above normal	WHO	0-5 years
	BMI z-score for age > 1 standard deviation above normal	WHO	5-19 years
	Waist circumference > 91st percentile	Child Growth Foundation	11-16 years
	Waist circumference > 90th percentile	Australian Health and Fitness Survey curves	7-15 years
	Waist circumference > 83rd percentile	International Diabetes Federation	6-16 years
	Weight for length > 95th percentile	CDC growth charts	0-2 years
Obese	Values equivalent to BMI > 30 kg/m^2 in adults	IOTF age, sex specific charts	2-18 years
	BMI for age > 95th percentile	NHMRC recommendation with reference to CDC growth charts	0-20 years
	BMI-z score > 2	1990 UK Growth reference curves	0-23 years

	BMI for age > 95th percentile	1990 UK Growth reference curves	4-23 years
	BMI for age > 98th percentile	UK-WHO growth charts	0-4 years
	BMI z-score for age > 2 standard deviations above normal	WHO	5-19 years
	Waist circumference > 98th percentile	Child Growth Foundation	11-16 years
	Waist circumference > 90th percentile	International Diabetes Federation	6-16 years
Very obese	BMI-z score ≥ 3	1990 UK Growth reference curves	0-23 years

Body mass index

Seventy-nine studies measured body mass index (BMI) to indicate body weight, growth, or obesity, and 68 of these compared BMI to reference values to categorise subjects as overweight and obese. Most (58) of these studies used international BMI-for-age charts, developed by Cole et al. (2000), for reference. The International Obesity Task Force (IOTF) has adopted these charts as their standard for defining overweight and obesity in children and adolescents. These curves were developed with data from six different countries, and provide age- and gender-specific BMI cut-off points for children and adolescents from ages 2-18 years that correspond to adult BMI values of 25 kg/m^2 for *overweight* and 30 kg/m^2 for *obesity* (Cole et al. 2000). These reference values are most commonly used to define overweight and obesity in research on Australian children and adolescents.

As an alternative to the IOTF reference charts, 14 of the 68 studies comparing BMI to reference values for overweight/obesity used cut-off values from the Centers for Disease Control and Prevention (CDC) growth charts (CDC 2000). These gender- and age-specific growth charts were last updated in 2000 and show percentile curves of children in the US, using five national surveys undertaken in 1963-1994, the most recent being NHANES III. As body weights of children and adolescents have been increasing in recent years, data from NHANES III from children more than six years of age was not used in these charts, preventing an upward skew appearing on the growth curves. On the CDC scale, BMI-for-age that is greater than or equal to the 85th percentile but less than the 95th percentile is identified as *at risk for overweight*, and BMI-for-age that is greater than or equal to the 95th percentile is identified as *overweight* (CDC 2000). Clinicians in the US have been encouraged to use the CDC growth charts (CDC 2000).

Due to the similarity in prevalence of overweight and obesity in Australia and the US, the Australian government Department of Health and Ageing and the NHMRC has recommended use of the CDC 2000 growth charts for children and adolescents aged 2-18 years (McLennan 2004, NHMRC 2003). However, the definitions are slightly different from those used in the US, as the NHMRC defines *overweight* as above the 85th percentile for BMI-for-age and *obese* as above the 95th percentile for BMI-for-age. According to a review that attempts to develop a standard definition of child and adolescent overweight and obesity for Australia (Denney-Wilson et al. 2003), the IOTF international percentile curves for BMI are the most accurate to use for research, but may not be representative of

non-Western populations and are not considered practical in the clinical setting. For clinical use, the authors of this review suggest use of the CDC gender- and age-specific BMI curves.

Twenty-one studies measured the standard deviation of BMI, or the BMI z-score. BMI can be converted into a BMI z-score using a BMI-for-age growth chart and the formula: z-score = $((BMI/M)^{L}-1)/(LS)$, where M, L, and S are values selected from reference tables corresponding to the age of the child in months (NHMRC 2003). Most (14) (References 10, 18-30) of the studies that reported BMI z-score converted BMI to a BMI z-score using the CDC 2000 growth curves, while seven (Wickramasinghe et al. 2005, Campbell et al. 2006, Haysom et al. 2009, McCallum et al. 2005, Wake et al. 2003, Magarey et al. 2003, Shields 2006) converted to BMI z-score using the 1990 UK Growth Reference curves Cole, Freeman and Preece 1995). Change in BMI z-score can be used to indicate rate of growth: a positive value indicates growth is above the reference, and a negative value indicates growth is below the reference. Five (Hesketh et al. 2009, Timperio et al. 2008, Crawford et al. 2004, Hesketh et al. 2004, Milne et al. 2007) of the 21 studies used z-scores to measure growth in this way, but none defined a fast or slow rate of growth. Alternatively, BMI z-score can be used to indicate overweight or obesity. Using the 1990 UK Growth Reference curves for BMI z-score, two studies (Wickramasinghe et al. 2005, Haysom et al. 2009) defined obesity as a z-score greater than 2, while another (McCallum 2005) defined "very obese" as a z-score ≥ 3.

Although not common in Australia, in the UK, growth of children older than four years and adolescents is commonly monitored against the 1990 UK national BMI percentile charts (Cole et al. 1995). *Overweight* here is defined as a BMI above the 85th percentile while *obesity* is defined as a BMI above the 95th percentile. However, cut-off values of the 91st percentile and 98th percentile for overweight and obesity, respectively, and the IOTF classification system (Cole et al. 2000) are also used in UK clinical practice (Child Growth Foundation 2009).

In conjunction with the World Heath Organization (WHO), the UK has recently developed new growth charts for children from birth to age 4 years (Royal College of Paediatrics and Child Health 2009). These new charts suggest that BMI percentile is a better measure of overweight and obesity than weight percentile. *Overweight* is defined as BMI above the 91st percentile, *obesity* is defined as BMI above the 98th percentile, and *underweight* is defined as BMI below the 2nd percentile. These charts have only recently begun to be used in England, and will be used in Scotland from January 2010. This index is too recent to appear in any Australian studies retrieved by our search.

The WHO uses two sets of growth charts, one for children from birth to age five years (WHO Statistical Information System 2008), and one for children and adolescents from age five to 19 years (WHO 2007). For children younger than five years, tables and charts showing percentiles and z-scores for BMI-for-age, weight-for-age, and weight-for-length were published in 2006. *Overweight* is defined as two standard deviations above normal on the weight-for-height chart and *underweight* is defined as weight-for-age two standard deviations below normal (WHO Statistical Information System 2008). For children and adolescents from age five to 19 years, tables and charts showing percentiles and z-scores for BMI-for-age, height-for-age, and weight-for-age were published in 2007. The BMI z-score-for-age chart defines *overweight* as greater than one standard deviation above normal, *obesity* as greater than two standard deviations above normal, *thinness* as less than two standard deviations below normal, and *severe thinness* as less than three standard deviations below

normal (WHO 2007). However, these WHO growth charts were not used in any of the retrieved Australian studies.

Few Australian studies have used more detailed measures to assess body composition in children. In one study, using either dual energy X-ray absorptiometry (DEXA) three compartment model or a four compartment model to determine body fatness, only weak associations were found between child's BMI and body fatness (Freedman and Sherry 2009). Children with a BMI between the 85th and 95th percentiles on the CDC chart generally do not have excess body fat (Freedman et al. 2009), but the relationship becomes stronger as the degree of body fat and the child's percentile of BMI increases (Freedman and Sherry 2009).

Waist and hip circumference

Waist circumference is becoming a common measure of central obesity in child and adolescents, and has been linked to increased risk of several diseases, including metabolic syndrome, type 2 diabetes, and cardiovascular disease (References 7, 44-47). Multiple waist circumference-for-age charts have been developed, but there is little consensus as to which is best or which cut-offs should be used to define overweight and obesity. Seventeen studies were identified that measured waist circumference. Four studies (Huang et al. 2009, Watts et al. 2008, Valery et al. 2009, Denney-Wilson et al. 2008) used waist circumference measurements to determine overweight and obesity, each employing different reference charts or reference cut-off values. Denney-Wilson et al. (2008) used the 1997 UK Child Growth Foundation Charts. The Child Growth Foundation uses waist circumference-for-age charts for children and adolescents aged 11 to 16 years that derive from data obtained in two large cross-sectional surveys of British children (McCarthy et al. 2003). The Child Growth Foundation defines *overweight* as a waist circumference above the 91st percentile and *obesity* as a weight circumference above the 98th percentile. Watts et al. (2008) used the Australian Health and Fitness Survey curves (Eisenmann 2005), which are derived from a survey of over 8500 Australian school children. *Overweight* was defined by a waist circumference above the 90th percentile. Huang et al. (2009) referred to the International Diabetes Federation (IDF). Using tables published by Fernandez et al. (2004), the IDF defines *obesity* in children and adolescents aged 6-16 years as a waist circumference greater than the 90th percentile (IDF 2009). These tables use US NHANES III data, and separate tables are given for Mexican-American and African-American children. Similarly, Valery et al. (2009) used waist circumference-for-age curves published by Jolliffe and Janssen (2007), which used cut-off values from IDF. However, in contrast to Huang et al., Valery et al. identified *overweight* as a waist circumference above the 83rd percentile.

In addition, two (Sanigorski et al. 2008, Nambiar et al. 2009) of the 17 studies reported waist-to-height ratio (WHtR), and one (O'Connor et al. 2008) reported waist circumference z-score, but neither compared data to a reference value. Due to the limitations mentioned above of using BMI to estimate body fatness, WHtR is being considered as a complementary index, especially in estimating abdominal obesity and predicting cardiovascular risk (Nambiar et al. 2009). The validity of this index was recently examined as part of the Healthy Kids Queensland: Physical Activity and Nutrition Survey (Nambiar et al. 2009). While WHtR was only statistically valid for specific age

groups, the correlation was strong enough to be clinically and biologically acceptable for children and adolescents.

Two studies (Heath and Panaretto 2005, Watts et al. 2006) measured hip circumference, but neither compared data to a standard reference value.

Body weight

Twenty-seven studies measured body weight, although only three (McLennan 2004, Burke et al. 2005, Oddy et al. 2006) measured weight-for-length/height and used cut-off values to identify subjects as overweight or obese. One study used weight-for-age to measure growth. In children one year of age, Oddy et al. (2006) defined weight-for-length above the 85th percentile as *overweight or obese*, as suggested in a relevant systematic review (Baird et al. 2005), but did not identify which growth curves were used for reference. In a review examining the management of childhood overweight in Australia, McLennan et al. (2004) suggests defining *overweight and obesity* as greater than 20% above the normal weight-for-height on standard percentile charts, but again does not refer to specific reference charts. This review also suggests that measuring weight-for-height is less accurate than percentiles on BMI-for-age charts. The third study (Burke et al. 2005) identifies children aged one year who are above the 95th percentile on the CDC weight-for-length chart as *overweight or obese*. This is consistent with the CDC definition of overweight using the weight-for-length chart.

One study has used weight-for-age z-scores to examine growth (Sayers et al. 2004). Using the CDC 2000 growth curves as the reference, a positive value indicated an increase in weight that is greater than the reference population, and a negative value indicated growth that is below the reference population. Fast or slow growth rates were not defined.

Fat mass and lean body mass

Ten studies measured fat mass or percent body fat. Four studies (Telford et al. 2008, Wickramasinghe et al. 2005, Wickramasinghe et al. 2008, Eisenmann et al. 2007) compared percent body fat to reference values to categorise subjects into overfat and obese groups. Eisenmann et al. (2007) determined body fat from a calculation from skinfold measurements, and labelled subjects with percent body fat above the 75th percentile as *high fat*. The authors did not report the source of this reference value. Telford et al. (2008) used DXA to determine body composition, and identified subjects with percent body fat above the 85th percentile as *overfat* and above the 95th percentile as *obese*. These authors used two different percent body fat-for-age scales, one from the US (Mueller 2004) and the other from the UK (McCarthy 2006). While the cut-off percentiles were the same for both scales, the cut-off values for overfatness and obesity were higher on the UK scale than on the US scale. When comparing these two scales to the IOTF cut-offs for BMI, use of the UK's percent body fat scale identified a higher percentage of children as overfat or obese, although with a lower sensitivity (25.4-58.6) than the US scale (78.1-87.5). Wickramasinghe et al. published two studies in 2005 (References 4, 13), one to examine if BMI-based cut-off values were accurate in diagnosing

obesity, and the other to determine if simple measures could accurately predict percent body fat in children. In both, *obesity* was defined as >20% body fat in boys and >30% body fat in girls. In these studies, fat mass was determined by bioelectrical impedance analysis, or using equations based on height, weight, BMI, skinfold thickness, or total body water measured from deuterium labelled water. A relevant review noted that according to the WHO, there is no consistency in the literature on how to define obesity using a percent body fat cut-off value (Freedman and Sherry 2009).

Three studies (Telford et al. 2009, Cleland et al. 2008, McGuigan 2009) measured lean body mass (LBM), two based on DEXA and one calculated from skinfold thicknesses. None of these studies used LBM to define overweight or obesity or to measure growth.

Skinfold thickness

Seven studies (Wickramasinghe et al. 2005, Watts et al. 2006, Eisenmann et al. 2007, Cleland et al. 2008, Dwyer et al. 2009, Huang et al. 2007, Booth et al. 2003) measured at least one skinfold thickness, but none compared to reference values or defined overweight or obesity based on the measurements. As mentioned, four studies used skinfold thickness measurements to calculate fat mass or LBM.

Height-for-age

Three studies measured change in height-for-age z-scores. Two of the studies (O'Connor et al. 2008, Sayers et al. 2004) used the CDC 2000 growth curves to calculate these values; the third referenced a report by Greenacre (1997). Again, a positive value indicated a rate of height growth above the reference, and a negative value indicated a rate of height growth below the reference. Fast or slow change in height was not defined.

Other methods

One study (Kelly et al. 2007) used the Best Guess formulae, a new set of procedures that allows body weight of children and adolescents to be estimated based solely on their age. Overweight or obesity was not defined using these formulae.

Conclusions

Results from this review show that BMI is the most common method used in Australia to define overweight or obesity in children and adolescents, and BMI z-score is the most common method used to define growth. IOTF guidelines for BMI-for-age defining overweight and obesity are the most widely used for research, while reviews suggest that the CDC growth charts are more useful in the clinical setting. Waist circumference is becoming a more common measure of child and

adolescent central adiposity, but standard cut-off values to define overweight and obesity have not yet been determined.

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Table 27.2 Details of retrieved studies

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
Druon 2008	Rural NSW	Children, aged 7-12yrs	BMI	≥ 85th percentile adjusted for age and sex	NG	Explore mothers' knowledge, beliefs and attitudes towards their overweight and obese children
Telford 2008	Commonwealth Institute Lifestyle of our Kids	Children, age 8yrs	% body fat by DEXA % body fat by DEXA BMI BMI Body weight	>85th percentile (overfat); >95th percentile (obese) >85th percentile (overfat); >95th percentile (obese) BMI-for-age 85th-95th percentile (overweight), BMI-for-age ≥ 95th percentile (obese) Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese) Characteristic of population only	UK % BF scale US % BF scale, nonblack CDC BMI growth chart (age- and sex-specific) IOTF BMI chart (age- and sex-specific) None	Investigated variation in incidences of childhood overweight and obesity
Wake 2008	Longitudinal Study of Australian Children - 2004	Children, age 4-5yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese)	IOTF BMI chart (age- and sex-specific)	Determine relationships between BMI status and indicators of health and morbidity

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
Gerner 2006	GPs in Melbourne	Children, age 5-10yrs	BMI Body weight	BMI-for-age 85th-95th percentile (overweight), BMI-for-age ≥ 95th percentile (obese) Percentiles	CDC BMI growth chart (age- and sex-specific) None	Examine if GPs measure weight and height and calculate BMI in children
Kremer 2006	Barwon-South Western region of Victoria	Children, age 4-12yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese)	IOTF BMI chart (age- and sex-specific)	Quantify bias that occurs due to wide age intervals in IOTF BMI-for-age curves
Campbell 2006	Parent Education and Support Program	Children, age 4yrs	BMI BMI z-score	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2); Underweight: <10th percentile for BMI Characteristic of population only	IOTF BMI chart (age- and sex-specific) 1990 UK Growth Reference	Assess maternal concern about their overweight preschool children
Watts 2006	Obese subjects in Perth	Obese children and adolescents, age 10-14yrs	BMI Body weight DEXA - abdominal fat	Cole criteria: BMI equivalent to adult BMI of >30 kg/m^2 (obese) Monitored change - reference baseline Monitored change - reference baseline	IOTF BMI chart (age- and sex-specific) None None	Compared methods for the assessment of body composition

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
			mass DEXA - fat mass Hip circumference Skinfold thickness (triceps, subscapular, iliac crest, abdominal, anterior thigh, medical calf) Waist circumference	 Monitored change - reference baseline Monitored change - reference baseline Monitored change - reference baseline Monitored change - reference baseline	 None None Slaughter equation for triceps and calf only; three-site formula for abdomen, iliac crest, and triceps; four-site formula for abdomen, iliac crest, triceps, and thigh None	
Fisher 2006	10 primary schools from New England Area Health Service	Children, age 5-8yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese)	IOTF BMI chart (age- and sex-specific)	Determine the prevalence of overweight and obese children and assess caregivers' ability to detect adiposity in the children
Wickramasinghe 2005	Sri Lankan children in Brisbane	Sri Lankan migrant and Australian Caucasian	% Fat mass, using deuterium labelled water	>20% for boys; >30% for girls	Dwyer and Blizzard, 1996.	Determine the ability of BMI-based cut-off values to diagnose obesity

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
		children and adolescents, age 5-15yrs	(measure total body water, calculate fat free mass and fat mass by using age- and gender-specific constants for water content of fat free mass)			
			BMI	BMI ≥ 95th percentile (obese)	CDC BMI growth chart (age- and sex-specific)	
			BMI	Cole criteria: BMI equivalent to adult BMI of >30 kg/m^2 (obese)	IOTF BMI chart (age- and sex-specific)	
			BMI z-score	BMI z-score >2	British growth standards BMI z-scores	
			Body weight	Characteristic of population only	None	
McLennan 2004	None (review)	Children and adolescents	BMI	>85th percentile (overweight); ≥ 95th percentile (obese)	CDC BMI growth chart (age- and sex-specific) - NHMRC	Discussion of assessment and management of childhood and adolescent overweight

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
			Weight-for-height	>20% above standard weight-for-height	NG (authors indicate this is less precise)	and obesity (narrative review)
Wang 2002	Australian National Health Survey and National Nutrition Survey	Adolescents, age 15-19yrs	BMI Body weight	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese) Monitored change – reference baseline	IOTF BMI chart (age- and sex-specific) None	Explore relationship between self-reported weight and height to actual weight and height
Renzaho 2009	Longitudinal Study of Australian Children - 2004	Children, age 4-5yrs	BMI BMI z-score	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese) BMI z-score less than -2 (for underweight)	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Examine relationship between childhood nutrition status and ethnicity
Valery 2009	Youth on Mabuiag Island or Sue Island	Children and adolescents, age 5-17yrs	BMI Waist circumference	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2 Combined National Cholesterol Education Program (equiv. to >92nd percentile for adults) and International Diabetes	IOTF BMI chart (age- and sex-specific) Jolliffe and Janssen, 2007	Assess prevalence of obesity and metabolic syndrome in Indigenous youths in Torres Strait region

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
				Foundation (equiv. to >83rd percentile for adults)		
Huang 2009	West Australian Cohort Study	Children followed from birth to age 14yrs	BMI Waist circumference Body weight	BMI ≥ 95th percentile (obese) ≥ 90th percentile Characteristic of population only	CDC BMI growth chart (age- and sex-specific) International Diabetes Federation None	Investigate relationships between inflammatory markers and components of a metabolic syndrome cluster
Dwyer 2009	Childhood Determinants of Adult Health Study	Children, age 7-15yrs	BMI Skinfold thickness - % body fat, then calculated lean body mass from body density and % body fat	Characteristic of population only Characteristic of population only	None None	Examine relationship between fitness in childhood and adulthood and adult obesity and insulin resistance
Telford 2009	Lifestyle of our Kids Project	Children, age 7-8yrs followed to age 11-12yrs	DEXA - fat mass DEXA - lean body mass	None - methods only None - methods only	None None	Investigates how early physical activity contributes to health and development

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
Hesketh 2009	Health of Young Victorians Study	Children, age 5-10yrs	BMI BMI z-score	Cole criteria: BMI equivalent to adult BMI of >25 kg/m^2 (overweight) Positive = growth is above reference; negative - growth is below reference	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Association between potential predictors and change in BMI
Haysom 2009	Schools in NSW with high Aboriginal populations	Children and adolescents, age 9-13yrs	BMI z-score Body weight z-score Height z-score	≥ 2 (obesity) Compared subgroups of cohort - no reference Compared subgroups of cohort - no reference	Goran 1998 Greenacre 1997 Greenacre 1997	Determine if key risk factors for CVD occur more commonly in Aboriginal compared to non-Aboriginal Australian children
Watts 2008	Childhood Growth and Development Study	Children, age 6-13yrs	BMI Waist circumference Body weight	>95th percentile (overweight) ≥ 90th percentile Characteristic of population only	CDC BMI growth chart (age- and sex-specific) Australian Health and Fitness Survey (Eisenmann 2005) None	Investigate clinical markers of CVD risk in children
Booth 2008	NSW Schools	Adolescents,	BMI	Cole criteria: BMI	IOTF BMI	Prevalence of elevated

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	Physical Activity and Nutrition Study	age 15yrs		equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese)	chart (age- and sex-specific)	concentrations of liver enzymes and association with adiposity
			Body weight	Characteristic of population only	None	
			Fat mass index (first calculated % BF from regression equation based on BMI)	Characteristic of population only	None	
			Waist circumference	Characteristic of population only	None	
Cleland 2008	Children Living in Active Neighbourhoods	Children, age 5-6y and age 10-12yrs	BMI	None	CDC BMI growth chart (age- and sex-specific)	Determine if time spent outdoors is associated with physical activity, BMI z-score, and overweight
			BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	
	Australian Schools Health and Fitness Survey 1985	Children and adolescents, age 7-15yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese)	IOTF BMI chart (age- and sex-specific)	

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
			Lean body mass (calculated from % BF, measured from 4 skinfold thicknesses)	None - used in fitness calculation	None	
Hesketh 2007	Health of Young Victorians Study	Children, age 5-10yrs	BMI BMI z-score	Cole criteria: BMI equivalent to adult BMI of >25 (overweight) or >30 kg/m^2 (obese) Compared subgroups of cohort - no reference	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Investigate relationship between TV viewing and electronic game/computer use with BMI
O'Dea 2008	National Youth Cultures of Eating Study	Children and adolescents, age 6-18yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Explore the associations between obesity, weight perceptions and gender, ethnicity, culture and social class
Wake 2007	Longitudinal Study of Australian Children - 2004	Children, age 4-5yrs	BMI BMI	BMI-for-age >85th percentile (at risk for overweight), BMI-for-age >95th percentile (overweight) Cole criteria (BMI equivalent to adult BMI of >25	CDC BMI growth chart (age- and sex-specific) IOTF BMI chart (age- and sex-specific)	Determine prevalence of overweight and obesity, investigate associations between socioeconomic characteristics and overweight/obesity and waist circumference.

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
				(overweight) or >30 (obese) kg/m^2)		
			Waist circumference	Compared subgroups of cohort - no reference	None	
Huang 2007	West Australian Cohort Study	Children, followed from birth to age 8yrs	BMI	None	None	Identify early life influences on development of obesity, hypertension, and dyslipidemia
			Body weight	Compared subgroups of cohort and change - no reference	None	
			Skinfold thickness (triceps)	None	None	
Al Mamum 2007	Mater-University study of pregnancy and its outcomes (MUSP)	Adolescents, age 14yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 kg/m^2 (overweight))	IOTF BMI chart (age- and sex-specific)	Assess if adolescents' BMI and self- or mother's perception of weight status are associated with depression
			Body weight	Characteristic of population only	None	
Hesketh 2007	Children's Leisure Activities Study and Health, Eating and Play Study	Children, grades prep (mean age 6yrs) and 5-6 (mean age 11yrs)	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	Examine associations between weight status and indicators of family circumstance
			BMI z-score	Compared subgroups of cohort - no reference	CDC BMI growth chart (age- and sex-specific)	
Spinks 2007	Childhood	Children,	BMI	Cole criteria: BMI	IOTF BMI	Examine compliance

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	Injury Prevention Study	age 5-12yrs		equivalent to adult BMI of >25 (overweight and obese)	chart (age- and sex-specific)	with the Australian national activity recommendations and examine association with overweight and obesity levels
O'Dea 2006	National study of school children	Children and adolescents, age 6-18yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Examine the socio-cognitive and nutritional factors associated with BMI, and examine associations and interactions between BMI and nutritional knowledge, dietary self-efficacy, dietary locus of control, food variety, breakfast consumption, and SES
Tam 2006	Nepean Study	Children, mean age 7.7yrs followed to mean age 13.0yrs	BMI BMI z-score	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Compared subgroups of cohort and change over time - no reference	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Relationship between soft drink, fruit juice, and milk consumption and BMI
McCallum 2005	Live, Eat and Play study	Children, age 5-9yrs	BMI	Cole criteria (BMI equivalent to adult	IOTF BMI chart (age- and	Determine if GPs and families can be

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
				BMI of >25 (overweight) or >30 (obese) kg/m^2)	sex-specific)	recruited to a RCT and if the GPs can deliver an intervention to families with overweight/obese children
			BMI z-score	Very obese: ≥ 3.0	1990 UK Growth Reference (Cole 1995)	
Hesketh 2004	Health of Young Victorians Study	Children, mean age 7.6yrs followed to mean age 10.8yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Relationship between self-esteem and BMI
			BMI z-score	Monitored change - reference baseline	CDC BMI growth chart (age- and sex-specific)	
Wake 2003	Health of Young Victorians Study	Children, age 5-13.6yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Investigate relationships between children's BMI and parent reports of children's television and video game/computer habits
			BMI z-score	Compared subgroups of cohort - no reference	1990 UK Growth Reference (Cole 1995)	
Magarey 2003	Adelaide Nutrition Study	Children, followed from birth to age 20yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Report tracking of overweight/obesity and relation to parent weight status

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
			BMI z-score	Compared subgroups of cohort - no reference	1990 UK Growth Reference (Cole 1995)	
Wake 2002	Health of Young Victorians Study	Children, age 5-18yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Examine relationship between parent perceptions of child health/wellbeing and overweight/obesity
van den Berg 2002	7 high schools in Melbourne	Girls, mean age 15.5yrs	BMI	Compared subgroups of cohort - no reference	None	Examine predictors of body image, eating dysfunction, and general psychological functioning
Okely 2004	NSW Schools Fitness and Physical Activity Survey	Children and adolescents in grades 4, 6, 8, and 10	BMI Waist circumference	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Characteristic of population only	IOTF BMI chart (age- and sex-specific) None	Examine associations of movement skills with measures of body composition
Rehor 2002	2 primary schools in Launceston area	Children, age 8-11yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Prevalence of overweight and obesity in preschoolers in Tasmania compared to the rest of Australia
Southall 2004	5 schools in Wollongong, NSW	Overweight and non-overweight children,	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and	IOTF BMI chart (age- and sex-specific)	Compared actual vs perceived physical competence of overweight and non-

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
		mean age 10.8yrs	Body weight	obese) Characteristic of population only	None	overweight children
van Zutphen 2007	Be Active Eat Well	Children, age 4-12yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	Describe time children spend watching TV and assess associations between viewing time, family environment, and weight status
Burke 2004	Cohort of Perth children	Children, age 9y, followed to age 25yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	Examine associations between weight status and blood pressure; determine prevalence and degree of tracking in overweight/obesity; examine SES
Valenti 2006	BEACH program	Subjects younger than age 18yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Survey of heights and weights
Murphy 2008	Healthy subjects	Children and adolescents, age 5-18yrs	BMI	Characteristic of population only	None	Examine relationship between height and body cell mass and determine power by which height should be raised to adjust BCM for stature
			BMI z-score	Characteristic of population only	CDC BMI growth chart	

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
					(age- and sex-specific)	
			Body cell mass (estimated from total body potassium, determined from ^{40}K scan)	None	None	
			Body weight	Characteristic of population only	None	
McCabe 2003	10 schools	Children, age 8-11yrs	BMI	Compared subgroups of cohort - no reference	None	Determine nature of body image and body change strategies and determine how age, gender, and BMI are related to these strategies
Denney-Wilson 2008	NSW Schools Physical Activity and Nutrition Survey	Adolescents, grade 10, mean age 15.4yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Determine association between measures of adiposity (BMI and waist circumference) and risk factors for heart disease, type 2 DM, and fatty liver disease
			Waist circumference	>91st percentile (overweight); >98th percentile (obese)	UK Child Growth Foundation Charts 1997 (McCarthy	

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
					2003)	
Shields 2006	Mater-University study of pregnancy and its outcomes (MUSP)	Adolescents, age 14yrs	BMI BMI z-score	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Compared subgroups of cohort - no reference	IOTF BMI chart (age- and sex-specific) 1990 UK Growth Reference	Determine influence of breastfeeding on overweight and obesity in early adolescence
Burke 2005	Western Australian Pregnancy Cohort Study	Children, age 3, 6, and 8yrs	BMI Weight-for-length BMI z-score	>95th percentile (overweight and obese) >95th percentile (overweight and obese) Compared subgroups of cohort - no reference	CDC BMI growth chart (age- and sex-specific)	Examine adiposity in relation to breastfeeding
Oddy 2006	Perth Infant Feeding Study	Children, age 1year	Weight for length	>85th percentile	Baird 2005	Determine association between longer duration of full breastfeeding in early infancy and health outcomes
Finch 2006	18 schools in Hunter region	Children and adolescents, grades 1-6, mean age 9.6yrs	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	Identify sources of food eaten during the school day, the types of foods and frequency of purchases from the canteen and association with SES and weight

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
						status
Booth 2003	Australian Youth Fitness Survey, Australian Health and Fitness Survey, SA Schools Fitness and Physical Activity Survey, NSW Schools Fitness and Physical Activity Survey, Health of Young Victorians Study	Children and adolescents, age 5-17yrs	BMI Body weight Skinfold thickness (sum of biceps, triceps, and subscapular) Waist circumference	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Monitored change - reference baseline Monitored change - reference baseline Monitored change - reference baseline	IOTF BMI chart (age- and sex-specific) None None None	Determine changes in the population prevalence of overweight and obesity among young Australians
Crouch 2007	Mothers attending learn-to-swim school	Children, age 2-6yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Assess relationship between maternal attitudes, beliefs, and child feeding practices
Denney-Wilson 2003	None (review)	Not specified	BMI BMI	85th-95th percentile (at risk of overweight), >95th percentile (overweight) - for clinical use Cole criteria (BMI	CDC BMI growth chart (age- and sex-specific) IOTF BMI	Develop a standard definition of child and adolescent overweight and obesity to be used in the Australian National Health Data

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
				equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) - for research	chart (age- and sex-specific)	Dictionary (narrative review)
Sutherland 2004	Primary school on Central Coast of NSW	Children, grades K-6	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Investigate attitudes of parents, teachers and health professionals on factors contributing to childhood obesity and the role of the school in preventing childhood obesity
McGuigan 2009	Overweight and obese subjects	Overweight and obese children, age 7-12yrs	BMI	≥ 85th percentile (overweight); ≥ 95th percentile (obese)	Freeman 2005	Investigate effect of an 8-week resistance training program on overweight and obese children
			Body weight	Monitored change - reference baseline	None	
			DEXA - % body fat (calculated from fat mass)	Monitored change - reference baseline	None	
			DEXA - fat mass	Monitored change - reference baseline	None	
			DEXA - lean body mass	Monitored change - reference baseline	None	
Zuo 2006	21	Children,	BMI	Cole criteria (BMI	IOTF BMI	Estimate the level of

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	kindergartens in Melbourne and 4 early childhood health centres in Sydney	age 4-5yrs		equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	chart (age- and sex-specific)	overweight and obesity among preschool-aged children
O'Connor 2008	Loozit study	Overweight and obese adolescents, age 13-16yrs	BMI	Range of 1.0-3.5 to indicate overweight and obese	CDC BMI growth chart (age- and sex-specific)	Evaluate a community-based weight management program for overweight and obese adolescents
			BMI	Monitored change - reference baseline	None	
			Body weight	Monitored change - reference baseline		
			Body weight z-score	Monitored change - reference baseline	CDC BMI growth chart (age- and sex-specific)	
			Height z-score	Monitored change - reference baseline	CDC BMI growth chart (age- and sex-specific)	
			Waist circumference	Monitored change - reference baseline	None	
			Waist circumference z-score	Monitored change - reference baseline	Fernandez 2004	
Kelly 2007	Paediatric patients (non-	Children, age 1-11yrs	Best Guess formulae (for	Actual weight	None	Validate the Best Guess formulae, a new method

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	seriously ill) in Sunshine Hospital ED Aug 2005-Feb 2006		body weight) BMI Body weight	 Characteristic of population only Compared to Best Guess Formulae	 None None	for estimation of weight in children
Timperio 2008	Children Living in Active Neighbourhoods	Children, age 10-12yrs, followed for 3years	BMI BMI z-score	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Change: Positive = growth is above reference; negative - growth is below reference	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Examine associations between family physical activity and sedentary environment and changes in BMI z-scores
Eisenmann 2007	Australian Health and Fitness Survey	Children, age 7-15yrs	% body fat (from skinfold thicknesses) Skinfold thickness (triceps, biceps, subscapular, suprailiac, mid-abdominal) Waist circumference	> 75th percentile (high fat) Characteristic of population only Characteristic of population only	None None None	Examine differences in CVD risk factors across 4 groups of cardiorespiratory fitness and body fatness in youth
Williams 2005	Health of	Children,	BMI	Cole criteria (BMI	IOTF BMI	Determine relationships

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	Young Victorians Study - 2000 data only	grades 3-6, age 8-12yrs	BMI z-score	equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Compared subgroups of cohort - no reference	chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	between weight and health-related QOL reported by parent-proxy and child self-report
Sutherland 2008	Primary schools in Hunter region in NSW	Children, grades 1-6	BMI	Cole criteria: BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	Determine the prevalence of overweight and obesity in the Hunter region and examine associations with gender, age, SES and geographical location
Wickramasinghe 2005	Sri Lankan children in Brisbane	Sri Lankan migrant children, age 5-14yrs	% fat mass, bioelectrical impedance analysis equation % fat mass, BMI equation % fat mass, height and weight equation %fat mass, skinfold	> 20% in males and > 30% in females (obese) > 20% in males and > 30% in females (obese) >20% in males and >30% in females (obese) > 20% in males and > 30% in females	Dwyer and Blizzard, 1996. Dwyer and Blizzard, 1996. Dwyer and Blizzard, 1996. Dwyer and Blizzard, 1996.	Evaluate the applicability of bedside techniques in the measurement of percentage body fat

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
			thickness equation	(obese)		
			BMI	BMI-for-age > 95th percentile (obese)	CDC BMI growth chart (age- and sex-specific)	
			BMI	Cole criteria (BMI equivalent to adult BMI of >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	
			Body weight	Characteristic of population only	None	
Sayers 2004	Aboriginal children born at Royal Darwin Hospital Jan 1987-March 1990	Aboriginal children followed from birth to mean age 11.4yrs	BMI	Compared subgroups of cohort - no reference	None	Test hypothesis that birth size interacts with child size to predict glucose and insulin metabolism
			Body weight	Characteristic of population only	None	
			Height z-score	Positive = growth is above reference; negative - growth is below reference	CDC BMI growth chart (age- and sex-specific)	
			Weight-for-age z-score	Positive = growth is above reference; negative - growth is below reference	CDC BMI growth chart (age- and sex-specific)	
Donovan 2006	High schools in Brisbane and Gold Coast	Girls, age 12-14yrs	BMI	BMI-for-age >85th percentile (overweight, including	CDC BMI growth chart (age- and sex-	Examine the validity of a model predicting weight restricting

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
				obese)	specific)	behaviour
Lawlor 2005	Mater-University study of pregnancy and its outcomes (MUSP)	Children, measured at age 5yrs and 14yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Examine the associations between being overweight and behavioural problems
Sawyer 2006	Longitudinal Study of Australian Children - 2004	Children, age 4-5yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Investigate relationship between overweight and obesity and mental health problems
Renzaho 2008	Sub-Saharan African migrant children	Sub-Saharan African migrant children, age 3-12yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Examine the association between acculturation and obesity and its risk factors among African migrant children in Australia
Crawford 2008	Children Living in Active Neighbourhoods	Children, age 8-9yrs and 13-15yrs	BMI BMI z-score	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Change: Positive = growth is above reference; negative - growth is below reference	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Association between density of and proximity to fast food outlets and body weight
Tiggemann 2006	High schools in South Australia	Adolescents, age 13-	BMI	Characteristic of population only	None	Investigate the correlates of missing

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
		16yrs				values on BMI, with a view to distinguishing between potential hypotheses as to their origin
Heath 2005	3 primary schools in Townsville, Queensland with high Indigenous enrolments	Children, preschool to grade 3	BMI Hip circumference Waist circumference	< 5th percentile (underweight), 5th-90th percentile (normal), 90th-95th percentile (overweight), >95th percentile (obese) Characteristic of population only Characteristic of population only	CDC BMI growth chart (age- and sex-specific) None None	Assess the nutritional health status of children in Townsville
Mamun 2008	Mater-University study of pregnancy and its outcomes (MUSP)	Children, measured at age 5yrs and 14yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight and obese); Underweight: <10th percentile for BMI	IOTF BMI chart (age- and sex-specific)	Examine the predictors of maternal misclassifications of their adolescent offspring's weight status
Wake 2007	Longitudinal Study of Australian Children - 2004	Children, age 4-5yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Determine relationships between BMI status at ages 4-5y and mothers' and fathers' parenting dimensions and parenting styles
Sanigorski 2008	Be Active Eat	Children,	BMI	Cole criteria (BMI	IOTF BMI	Evaluate the effects of

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	Well	age 4-12yrs		equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	chart (age- and sex-specific)	Be Active Eat Well on reducing children's unhealthy weight gain
			BMI z-score	Compared subgroups of cohort and change over time - no reference	CDC BMI growth chart (age- and sex-specific)	
			Body weight	Compared subgroups of cohort and change over time - no reference	None	
			Waist circumference	Compared subgroups of cohort and change over time - no reference	None	
			Waist to height ratio	Compared subgroups of cohort and change over time - no reference	None	
Jones 2009	Preschool Activity 'N' Dietary Adiposity study	Children, mean age 4.3yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight and obese)	IOTF BMI chart (age- and sex-specific)	Examine relationships between weight status and child, parent and community characteristics and risk factors
			Body weight	Characteristic of population only	None	
			Waist circumference	Characteristic of population only	None	
O'Dea 2006	Urban high	Females,	BMI	Highest quartile of	None	Examine differences in

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	school in Sydney	grade 7 followed through grade 9	Body weight	BMI, lower 3 quartiles of BMI Compared subgroups of cohort - no reference	None	self-concept among young adolescent females of higher and lower body weight
Hesketh 2004	Health of Young Victorians Study - 1997 and 2000 data	Children, age 5-10y followed for 3yrs	BMI BMI z-score	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Change: Positive = growth is above reference; negative - growth is below reference	IOTF BMI chart (age- and sex-specific) CDC BMI growth chart (age- and sex-specific)	Investigate the prevalence and incidence of overweight and obesity, the frequency of overweight resolution and the influence of parental adiposity during middle childhood
George 2008	NSW Schools Physical Activity and Nutrition Study	Adolescents, age 15yrs	BMI Waist circumference	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2) Characteristic of population only	IOTF BMI chart (age- and sex-specific) None	Describe the distributions of liver tests, to identify the upper normal limits and to describe the correlations among liver tests
Wang 2003	National Nutrition Survey 1995	Children and adolescents, age 7-15yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Explore the association between overweight/obesity and intake of energy and fat
Grant 2008	Seventh-day Adventist high schools in	Adolescents, age 14-15yrs	BMI	Compared subgroups of cohort - no reference	None	Investigate relationships between nutrition and lifestyle behaviours and

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	Sydney-Newcastle area		Body weight	Compared subgroups of cohort - no reference	None	selected biomarkers of health
			Waist circumference	Compared subgroups of cohort - no reference	None	
Milne 2007	Kidskin intervention study	Children, age 5-6y followed for 4yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Investigate if Kidskin sun protection intervention increased children's BMI by reducing time spent outdoors at midday
			BMI z-score	Change: Positive = growth is above reference; negative - growth is below reference	CDC BMI growth chart (age- and sex-specific)	
Salmon 2005	Australian Schools Health and Fitness Survey 1985 and 2001 and Children's Leisure Activities Study Survey	Children, age 9-13yrs	BMI	Cole criteria (BMI equivalent to adult BMI of >25 (overweight) or >30 (obese) kg/m^2)	IOTF BMI chart (age- and sex-specific)	Examine trends in active transport to and from school, in school sport and physical education, and in weight status among children from high and low SES areas
			Body weight	Characteristic of population only	None	
Nambiar 2009	Healthy Kids Queensland: Physical	Children and adolescents,	Waist circumferenc e	Characteristic of population only	None	Assess the statistical validity of the waist-height ratio as an

Citation	Cohort	Age/sex	Index	Reference	Scale	Study objective
	Activity and Nutrition Survey 2005	age 5-17yrs	Waist to height ratio	Converted to percentiles, but no comparison to standard reference	Cole 1990	appropriate method of adjusting waist circumference for height in children and adolescents

28. FOOD SAFETY (N1.5)

Evidence Statements

28. FOOD SAFETY (N1.5)

What are the appropriate food safety processes, for example in food preparation and storage, to maintain a safe food supply for individuals and groups of individuals, including children, adults and pregnant women?

Contents

Introduction

Foodborne disease (or food poisoning) results from consuming contaminated food or drink. The true incidence of foodborne disease is difficult to ascertain because cases are underreported and the majority of cases are sporadic (Redmond & Griffith 2003). Nonetheless it is very common, with an estimated 5.4 million cases per year in Australia, leading to 1.2 million visits to medical practitioners and 2.1 million days of work lost each year (Abelson et al. 2006). From 1995 through to 2000, there were 20 deaths attributed to foodborne illness (Dalton et al. 2004).

Several different diseases with different symptoms can result from eating contaminated food. Common causes are:

- Bacteria, for example *Salmonella, Campylobacter* and *Listeria;*
- Viruses, for example Norovirus and Hepatitis A;
- Toxins, for example toxins made by bacteria such as *Staphylococcus aureus* or *Bacillus cereus,* and *ciguatoxin.*

Anyone can get a foodborne disease, but some people are at increased risk of serious illness, especially:

- Infants;
- Elderly people;
- People with suppressed immune systems; and
- Pregnant women.

Food poisoning can occur with any food and the risk can be reduced if food is properly stored and prepared. While restaurants, cafeterias and other commercial settings are the most frequently cited locations implicated in reported foodborne disease outbreaks, illness from foods consumed in the home accounts for 20-40% of foodborne infections in Australia (Redmond & Griffith 2003). Pathogens can enter the domestic kitchen via a variety or routes: in raw foods (e.g. *Campylobacter* and *Salmonella* spp in poultry); via contamination from food contact surfaces (e.g. knives, cutting boards, dishcloths), or directly from food handlers themselves (Redmond & Griffith 2009).

Foodborne illness has been a growing concern over the past few decades, particularly for elderly people, who represent the largest at-risk segment of the population. Factors that can contribute to increased susceptibility in the elderly are: a weakened immune system (intestinal motility and mucosal immune function decrease with normal aging); decreased level of acid in the lining of the stomach; a loss of sense of smell and taste; and dementia and malnutrition, which can all increase susceptibility to foodborne disease (Almanza et al. 2007, Kendall et al. 2006). Furthermore certain demographic groups, such as men and younger adults aged 19-29 years, have been reported to have more improper food handling behaviours (Almanza et al. 2007).

Pregnancy is also a time when safe food handling becomes more important. Consumption of food contaminated with *Listeria monocytogenes* can cause listeriosis, an uncommon but potentially fatal illness that can also result in miscarriages or premature births (Cates et al. 2004). It has been noted that women seek health advice and often change their diets during pregnancy. It can be a good time to target women with food safety education because the healthy development of the baby may be an incentive and motivator for positive dietary change at this time (Athearn et al. 2004).

The aim of this review was to answer the question: What are the appropriate food safety processes (for example in food preparation and storage) to maintain a safe food supply for individuals and groups of individuals, including children, adults and pregnant women? It aims to summarise the recommended food handling processes for individual consumers in Australia, and also summarise some of the results of studies looking at attitudes towards and compliance with recommended food handling practices.

Methods

A systematic search of scientific literature, available in English from 2002, was conducted in May 2009. The searches used combinations of the following terms: *food, handling, supply, safety, processes, preservation, storage, microbiology, poisoning, standards*. Searches of both original articles and reviews were conducted in the following databases: Cinahl, Medline, PreMedline, Psychinfo, Cochrane/DARE, and ERIC. 1596 articles were discovered by the searches and after review of titles and abstracts 31 were retrieved for detailed review. Reasons for non retrieval were: not a study (81), not a relevant population (16), not a relevant outcome (1461), or duplicated articles (seven). After retrieval of the full articles, six more were excluded because the content was not a relevant outcome for this review.

The remaining 25 articles were used as the basis of this narrative review and are indicated with asterisks in the reference list. Additional references and sources of information were retrieved from references cited in the bibliographies of the included articles. In addition, a Google search of the terms *food safety, standards, recommendations, infant formula* on Australian websites was also used to identify potential sources of authoritative local consumer advice.

Results

Recommendations for safe food handling practices

Table 28.1 lists some authoritative sources of consumer information on safe food handling practices which are available via the internet. The list is not exhaustive. Most of the State and Territory Departments of Health provide educational material, and in general the advice is all quite consistent and similar.

The Food Safety Information Council (FSIC) was founded in 1997, following a well publicised food poisoning outbreak, attributed to mettwurst, which led to the death of a young child in South Australia. It is Australia's leading disseminator of consumer targeted food safety information and is a non-profit entity supported by the Australian Department of Health and Ageing, State and Territory health and food safety agencies, local government, and leading professional, industry and community organisations.

Tables 28.2 and 28.3 summarise consistent recommendations that have been made by a variety of authorities about appropriate food safety processes. Some of these are based on published systematic reviews of the literature (e.g. National Advisory Committee on Microbiological Criteria for Foods 2009), but in many cases the justification for the recommendations is not provided. A number of recommendations from the US are based on structured Delphi consultation processes with national food safety experts (Hillers et al. 2003, Kendall et al. 2003). Nonetheless, there is significant consistency of advice from the various sources.

There are still some areas of uncertainty in recommendations about food safety:

1) The National Advisory Committee on Microbiological Safety of Foods in the US was asked by the US Food and Drug Administration to provide advice on cooking protocols for seafood. After a thorough literature review they reported a lack of data to underpin simple recommendations and concluded there was no single temperature, with or without a specified cooking time, that will ensure the safety of all cooked fishery products and result in a palatable product (National Advisory Committee on Microbiological Criteria for Foods 2008);

2) Recent studies suggest that antimicrobial hand soap is significantly better than plain soap and water at eliminating bacteria on hands and subsequently reducing the transfer of bacteria from hand to food (Fischler et al. 2007). Although this practice has not yet been universally recommended, it may offer additional protection worth consideration;

3) Another newly suggested risk is the increased practice of food waste recycling. Recycling containers are often heavily contaminated around the handle and lid areas and can predispose to cross contamination to foods for consumption without good handwashing practices (Blenkharn 2007). However, to date, no recommendations have yet been made on this topic;

4) Many consumers express concern about the risks of pesticides and other residues on foods and seek organic foods to minimise this risk. Some commentators have suggested that organic production practices, such as use of animal manures and prohibition of some additives and processing techniques, may increase the risk of microbiological contamination, but much of the discussion has arisen from non-scientific articles. A recent review has concluded that there is no peer-reviewed literature suggesting certified organic produce to be at any greater risk of contamination than conventional produce (Bourn & Prescott 2002).

Recommendations for safe preparation and storage of infant formula and breast milk

Table 28.4 summarises recommendations about the preparation of powdered infant formula (PIF) and storage of breast milk. *Enterobacter sakazakii* is recognised as an emerging opportunistic pathogen and the etiological agent of life-threatening bacterial infections in infants. PIF is not a sterile product and PIF has been shown to contain *E. sakazakii*. To reduce the risk of infection, reconstitution of formula should be undertaken by caregivers using good hygienic practice and in accordance with the product manufacturer's food safety guidelines (Drudy et al. 2006, Redmond & Griffith 2009).

Many of the same recommendations apply to the storage of expressed breast milk. However breast milk may be stored frozen for longer term storage, or kept up to 5 days refrigerated up to 4°C, although caution is needed when dealing with preterm infants (Dalidowitz 2005, Eglash 2005).

Table 28.1 Some authoritative sources of safe food handling advice

Organisation	**Website**
Food Safety Information Council	http://www.foodsafety.asn.au/
OzFoodNet	http://www.ozfoodnet.org.au/internet/ozfoodnet/publishing.nsf/Content/Home-1
NSW Food Authority	http://www.foodauthority.nsw.gov.au/consumers/keeping%2Dfood%2Dsafe/
Safe Food Queensland	http://www.safefood.qld.gov.au/index.php?option=com_content&task=view&id=143&Itemid=60
Victorian Department of Health	http://www.health.vic.gov.au/foodsafety/home/athome.htm
Food Standards Australia New Zealand	http://www.foodstandards.gov.au/foodmatters/
WHO	http://www.who.int/foodsafety/publications/micro/pif2007/en/index.html\
Department of Health and Ageing	http://www.healthinsite.gov.au/topics/Food_Storage_and_Handling\

Table 28.2 General recommendations for safe handling and storing food

Practice Category	Recommendations	Organisations
Food purchasing	Only buy food from reputable suppliers with clean and tidy premises	Victorian Department of Health
	Avoid food past its use by date	Victorian Department of Health
	For trips home longer than 30 minutes consider placing chilled and frozen foods in an insulated cooler	Victorian Department of Health
Surface preparation	Use different cutting boards for raw and cooked food	Food Safety Information Council NSW Food Authority
	Wash cutting boards and cutlery with soap and hot water between the use of raw and cooked meats	Food Safety Information Council Food Standards Australia New Zealand NSW Food Authority
Hand washing	Wash hands before preparing food	FSANZ
	Wash hands immediately after preparing uncooked meat or chicken	Food Safety Information Council US Centre of Disease Control and Prevention NSW Food Authority
	Wash for 20-30 seconds with soap and warm running water and dry thoroughly on a clean towel	Food Safety Information Council
Handling raw foods	Rinse fruits, salads and/or vegetables under cold water to remove visible dirt and remove outer leaves of lettuces and cabbages	US Centre for Disease Control and Prevention NSW Food Authority
	Raw meat and poultry should not be washed or rinsed	USFDA
Cooking	Use a thermometer to check food is properly cooked to a minimum safe temperature (roasts and meats 62°C; mince, eggs soups 71°C;	USFDA

	whole poultry 82°C)	
	Most foods should be cooked to at least 75°C	Victorian Department of Health
Handling of cooked foods	Never place cooked meat or chicken where raw meat or chicken has been	Food Safety Information Council US Centre of Disease Control and Prevention Food Standards Australia New Zealand
	Keep cooked foods to be eaten hot at 60°C or hotter	Victorian Department of Health
	Cool cooked foods (to be eaten later) to room temperature or until item stops steaming and refrigerate within 2 hours	Food Standards Australia New Zealand US FDA
	Place food in refrigerator once any part of it drops to 60°C	US Centre for Disease Control and Prevention NSW Food Authority
	Once foods reach room temperature, food should be cooled to less than 5°C in the next 4 hours	Food Standards Australia New Zealand
	Discard cooked food left out for 4 hours or more	Food Safety Information Council Food Standards Australia New Zealand
Food storage in refrigerator	Place raw foods in sealed containers or covered on shelves below cooked or ready-to-eat foods	Food Safety Information Council NSW Food Authority
	Refrigerators should not be higher than 5°C and should have adequate airflow around food to ensure even temperature distribution	NSW Food Authority Victorian Health Department FSANZ
	Food items should be stored carefully away from toxic chemicals such as insect sprays or cleaning agents	NSW Food Authority
Thawing meat	Chicken must be thawed in the refrigerator or by microwaving.	Food Standards Australia New Zealand

	When microwaved, chicken should be cooked immediately	NSW Health
Reheating food	Reheated foods should be quickly reheated until all parts reach 75°C	NSW Food Authority Victorian Department of Health
Cleaning	Consider using paper towels to clean up kitchen surfaces. Or, if using cloth towels, wash them often in the hot cycle of the washing machine	US FDA
	Dish cloths should be sanitised regularly or replaced	NSW Food Authority

Sources: Almanza et al. 2007; Anderson et al. 2004; Anonymous 2004; Cunningham 2005; Fischer et al. 2007; Hillers et al. 2003; Kendall et al. 2003; Mitakakis et al. 2004; National Advisory Committee on Microbiological Criteria For Foods 2008.

Table 28.3 Recommendations for safe food preparation during pregnancy and for at risk older adults

Recommendations	Organisations
Drink only pasteurized milk and fruit juices	FSANZ USDA US expert consultation
Use cheeses and yoghurts made from pasteurized milk	FSANZ USDA
Use a thermometer to make sure meat and poultry are cooked to safe temperatures	US expert consultation
Avoid eating foods containing raw or undercooked eggs	USDA US expert consultation
Avoid eating raw sprouts	US expert consultation
Avoid eating raw or undercooked seafood	FSANZ
Avoid soft cheeses, smoked seafood, paté or cold deli salads	FSANZ USDA
Do not handle pets when preparing foods	USDA
Store eggs in the refrigerator	US expert consultation

Sources: Athearn et al. 2004; Food Standards Australia New Zealand 2009; Hillers et al. 2003; Kendall et al. 2003; Kendall et al. 2006.

Table 28.4 Recommendations for safe preparation and storing of infant formula and breast milk

Recommendations	Organisations
Wash hands with soap and water and use a clean space to work before preparing any formula	WHO DoHA
Boil fresh water and allow to cool before making up formula	WHO DoHA
Prepare formula just before a baby's feed. Extra formula can be stored in the refrigerator at ≤5°C for no more than 24 hours.	WHO DoHA
Always warm bottles in a water bath and not the microwave	WHO DoHA
Discard any food than has not been consumed within 2 hours	WHO
All bottles and teats should be rinsed in cold water, washed in hot soapy water, rinsed and sterilized before being used again	WHO DoHA
Store expressed breast milk in date labelled sterilized containers for up to 2 weeks frozen, or up to 5 days refrigerated at ≤4°C	ABM

Sources: Department of Health and Ageing 2009; Eglash 2005; World Health Organization 2007.

Consumer knowledge, attitudes and practices

Current knowledge of consumer food handling and preparation behaviour is surprisingly limited. Research methods that rely on self reported data are unreliable because there is often a substantial difference between what people say they do and what they actually do, people forget what they do, and people tend to answer questionnaires with what they consider to be appropriate behaviour (Anderson et al. 2004). Observational studies provide a more realistic indication of food hygiene practices actually used in food preparation, but they are relatively rare (Redmond & Griffith 2003).

There are only two recent published studies about Australian practices. The Food Safety Information Council recommends that consumers wash their hands under running water using soap for at least 10 seconds, rubbing hands and rinsing and then drying thoroughly for at least 10 seconds with a clean towel or 20 seconds with a hand dryer. Their initial message of washing hands thoroughly was amended to take into account more recent studies about the need to thoroughly dry hands (Patrick et al. 1997). In 2002, the Council undertook a study to examine handwashing practices, using both a Newspoll survey and an observational study in toilets at a shopping centre food hall (Buchtmann 2002).

Despite nearly all respondents (98%) recognising the correct method of washing hands with soap and water and drying thoroughly, they were not necessarily putting that knowledge into practice. The observational study of 200 people found that only 20% of females and 7% of males used the correct procedure of washing their hands. 8% of females and 29% of males failed to wash their hands at all after going to the toilet. The most common problems observed were washing hands for less than the required ten seconds, failing to use soap and not drying hands for sufficient time.

The study indicated a lower understanding of food safety messages in 18 to 34 year age group. This is an age group that is often higher risk-taking than older age groups. The 35 to 49 year old age group had the best hand washing knowledge which may be linked to the fact that this is an age group more likely to have children at home. Males in all age groups had a lower knowledge of correct hand washing than females. This may be due to the fact the women, especially in older age groups, are more likely to be the household cook and to have had home economics education in their school years. However, food safety knowledge and behaviour in younger male age groups could be a concern as they are more likely to take on less stereotypical roles in the households of the future which could lead to an increase in food safety risks. That research concluded that there is ongoing need for consumer safety messages until behaviour more closely matches understanding about messages such as correct handwashing.

The second Australian study, conducted in 1998 by questionnaires completed in 524 Melbourne households with children, examined the self-reported frequencies of 12 food preparation and storage practices. The percentage of respondents who did not meet Australian recommendations were substantial for each category: food storage in refrigerator (81%)

thawing chicken (76%), surface preparation and handling of cooked foods (70%), handwashing (47%), handling of raw foods (42%). More than half the respondents reported potential cross-contamination from the floor, dishes, and cutting boards via dishcloths, and overall 99% of respondents reported some form of unsafe practice when handling food in the home. Incorrect handwashing and cross contamination from meat products and fresh foods were the most common risky practices, and these results are similar to finding of earlier Australian studies (Jay et al. 1999a; Jay et al. 1999b).

A recent New Zealand questionnaire survey has also examined domestic food handling practices in that country (Gilbert et al. 2007). Only a small proportion of respondents (19%) said they usually used an insulated bag or cooler to carry meat or poultry home, and it was estimated that 41% and 28% would use knives and kitchen surfaces respectively in a manner that could allow cross contamination. Almost half of respondents indicated they would thaw a frozen chicken at room temperature for up to 12 hours.

One major review has summarised the findings from 88 international studies examining consumer food handling and safety practices in the home, including two studies from Australia and four from New Zealand (Redmond & Griffith 2003). Consumers generally have a high level of concern about food safety issues, largely incident-driven. However, analyses of the results indicate that consumers' food safety knowledge fails to correlate with self-reported behaviour, and several intra-study comparisons conclude knowledge does not correlate with actual behaviour (Fischer et al. 2007).

That review reports that the majority (80%) of consumers think themselves adequately informed regarding food safety, but levels of consumer knowledge determined in food safety surveys have differed; most have concluded that consumer knowledge is inadequate and needs improvement. In international studies, up to 95% of consumers do not know the correct refrigeration temperatures and surveys of actual temperatures have reported up to 70% exceed recommended ranges. Observational studies of consumers in Australia in that review reported that: 75% failed to wash their hands or used an inadequate procedure for doing so; 35% failed to wash utensils between preparation of raw and other foods; 30% failed to clean the preparation surface before preparing ready-to-eat foods (Redmond & Griffith 2003).

Elderly consumers receiving meals-on-wheels are a group likely to be at higher risk. A US survey of 869 recipients found more than a third of clients didn't keep hot food safely after meals were delivered, and instead left it on a counter or table, and 18% were regarded as at high risk based on their poor performance on a food safety knowledge questionnaire (Almanza et al. 2007). In another small focus group study with adults aged over 60 years in the US, none of the participants used a thermometer to check whether their home refrigerator was operating at a safe temperature (Cates et al. 2007).

Pregnant women are another at-risk group who are not necessarily well informed about relevant safe food handling issues. In the US, focus groups with pregnant women found most were not very concerned about getting foodborne illness from food prepared at home and

regarded themselves as only somewhat knowledgeable about safe handling practices (Cates et al. 2004).

A few studies have examined actual behaviour in the domestic situation. In one British study with older people living at home, respondents reported that although 'use by' dates were understood and rated as important, they were not necessarily adhered to (Hudson & Hartwell 2002). The print was often too small to read and several participants specifically chose food toward the end of the product's shelf life because it was cheaper. It was also reported than most participants had not measured their refrigerator temperature and did not know what it should be; when measured more than 80% of refrigerators were operating above 5°C. This finding is similar to a French study that reported only 37% of people checked the temperature of their refrigerator (Lagendijk et al. 2008).

In the US, a study videotaping of consumers preparing two recipes in their own homes showed many food handling errors that would increase the risk of foodborne illness (Anderson et al. 2004). The majority of handwashing attempts did not meet recommended standards. An average of seven failures-to-wash were recorded per subject per session (most commonly when switching from handling raw meat to ready-to-eat food) and typically hands were washed for an average of 4-5 seconds only, without soap, and dried on a cloth towel. Surface cleaning was inadequate with only one-third of surfaces thoroughly cleaned. Very few subjects used a thermometer and many of them undercooked meat and poultry dishes.

An interesting Dutch study in 2004 looked at the relationship between consumer knowledge of recommended practices (assessed through interview), observed behaviour (making a chicken salad at home) and the effect of these behaviours on actual bacterial levels in the final product (Fischer et al. 2007). In that study only 14% of participants washed hands appropriately, and cross contamination from raw chicken was the dominant route of exposure to pathogenic bacteria. There was a linear relationship between the determined reductions in bacterial levels and the observed better critical control point scores of the participants, and this was a much better predictor of safe food outcomes than knowledge about food safety per se, implying that motivation was a more important determinant of effective performance than knowledge.

Others have also found food safety knowledge to be a poor predictor of behaviour. In a study of young adults in the US, a risky eating questionnaire asked participants which of 26 foods they consumed. Men were more likely to eat risky food than women, but food safety knowledge (assessed by an 89-item questionnaire) correlated only weakly with risky eating (Byrd-Bredbenner et al. 2008).

Lastly, there has been at least one study specifically examining why high-risk consumers are willing to deviate from best practice guidelines (Brennan et al. 2007). This Irish study found three key reasons:

1. Time and energy investment required to adhere to best practice (e.g. unwilling to defrost food in a refrigerator because of the long time required);

2. Past experience (lack of experience of food poisoning with current practices); and
3. Habit (e.g., always have assessed food temperatures in the refrigerator by touch rather than using a thermometer).

For younger and older single males, an additional reason was a lack of any real interest in food so that they didn't even think about the processes they used, such as the need to wash hands. Similar findings were reported in a study of pregnant women in the US, where resistance to change was expressed to several recommendations that were regarded as too burdensome (e.g., using thermometers, or avoiding soft cheeses) (Athearn et al. 2004).

Conclusion

Conformance with food safety recommendations does reduce the risk of microbial contamination in food. Consumers' failure to associate home food-handling practices with foodborne illness is considered a serious impediment to convincing them to change inappropriate behaviours. Consumers demonstrate judgements of optimistic bias, perceiving themselves to be less at risk from foodborne illness than others and often continue to eat potentially unsafe foods despite knowing the possible consequences of this behaviour. Observational studies suggest that the topics of handwashing, surface cleaning and correct storage of cooked food are often inadequately performed and more research is required to determine why this is so. In developing educational and risk communication materials about food safety, materials that are targeted to a specific population are likely to be more effective than those that are general in nature.

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