Australian Government
Department of Health

MINISTRY OF HEALTH
MANATŪ HAUORA

Australian and New Zealand Nutrient Reference Values for Sodium

Supporting Document 1

Systematic Literature Review

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1. Introduction

The Nutrient Reference Values (NRVs) are a group of recommendations designed to guide the nutritional intake of individuals and/or groups, and are based on current scientific evidence [1]. The current Australian and New Zealand NRVs, published in 2006, were due for revision. Sodium was selected as a key nutrient for revision given the association between high sodium intakes and high blood pressure, a major public health issue.

The methodological framework developed for the revision of the NRVs [1] highlighted the importance of a robust and transparent approach to revising the 2006 NRVs. A systematic approach was applied, which included documentation of decision pathways and justification of the specific nutrient, population group and health outcome to be examined. Relevant recently published expert reviews on the topic were considered, and new studies were identified using a Cochrane style search methodology.

This document outlines the approach and findings of the systematic literature review (SLR) underpinning the revision of the 2006 sodium NRVs for the purposes of proposing an Upper Level (UL) and Suggested Dietary Target (SDT) in adults. The aim of the review was to compare the effect of a high versus a low intake of sodium in the general adult population on blood pressure as the primary health endpoint. The effect of lowering sodium intake on total cholesterol, HDL cholesterol, LDL cholesterol was also investigated as adverse effects on these lipids have been alleged. The effect of lowering sodium intakes on, stroke, myocardial infarction and total mortality was also assessed for beneficial and adverse effects in the general adult population.

2. Methods

2.1 Review of pre-existing reviews

In order to address the scope of this report, the evidence base surrounding the relationship between sodium intake and health effects was examined through a review of SLRs reporting reduced sodium intake and effects on blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, myocardial infarction, total mortality or stroke. A total of six recently published SLRs [2-7] were identified as being relevant to the topic of sodium and the previously outlined health aspects. Several of the included SLRs [2, 3] also included data on the relationship between sodium intake and effects on factors such as renin, aldosterone, renal function and triglycerides that were outside the scope set by the Expert Working Group for this review. All studies included in the SLRs were scrutinised for relevance to the inclusion criteria set for the current review (Section 2.2).

A summary of the key features of the SLRs is shown in Appendix 1. References from the previous Institute of Medicine Dietary Reference Values for sodium were also considered for inclusion in the current review [8].

2.2. Review of literature

The processes followed in this current revision were conducted with reference to the methodological framework provided to the Expert Working Group [1]. The SLR methodology addressed the requirements of the PRISMA statement for Transparent Reporting of Systematic Reviews and Meta-analyses [9].

2.2.1 Research question

The expanded PICO (TS) framework was utilised to inform the search strategy relating to the following research question: 'what is the effect of a high versus a low intake of sodium on blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, stroke, myocardial infarction and total mortality in the general adult population?'

Population:

Adults (defined as individuals aged 18 years and older).

Inclusion criteria: both normotensive individuals and individuals with hypertension (with or without medication), individuals with diabetes (either type 1 or type 2) that has not progressed to nephropathy or chronic kidney disease.

Exclusion criteria: individuals with severe disease such as congestive cardiac failure, end stage renal failure or cancer, pregnant females, children (defined as individuals aged under 18 years).

Intervention:

An intake of sodium achieved either by allocating all subjects to low sodium intakes and randomising all to two or more intakes of sodium via supplements/foods or randomising subjects to two or more different sodium intakes by providing dietary advice and/or foods.

Inclusion criteria:

"Three types of studies were eligible for inclusion in the review:

1. studies involving randomised controlled trials with NaCl supplements or sodium enriched food/drink or placebo or other known sodium dose.

2. co-interventions that use simultaneous interventions whereby the role of sodium can be isolated.

3. unblinded dietary advice to reduce sodium compared to usual intake or a different diet."

Exclusion criteria:

Co-intervention studies where the role of sodium may not be isolated, studies without a minimum of 8 hours of urinary sodium excretion data, studies involving exercise as an intervention due to unknown effects on sodium excretion.

Comparator:

A second arm was required given a different, well-described intake of sodium to subjects.

Outcome:

Studies must report one or more of total mortality, stroke, myocardial infarction, total, LDL or HDL cholesterol or blood pressure (must note method of measurement).

Time:

Study duration of trials measuring blood pressure, total, HDL or LDL cholesterol must be of at least 4 weeks duration. Studies evaluating myocardial infarction, stroke or total mortality must be of at least 6 months duration.

Study design:

Limited to randomised controlled trials.

2.2.2 Identification of literature for inclusion from key reviews

As described in Section 2.1, six SLRs examining reduced sodium intake and effects on blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, myocardial infarction, total mortality or stroke were identified. The studies included within these reviews were added to a database of potential literature to be evaluated against the inclusion and exclusion criteria of the current review.

2.2.3 Identification of literature published 2011 – 2014

2.2.3.1 Databases and search terms

To obtain articles published after the aforementioned systematic reviews, an additional systematic search was conducted. Of the six SLRs used, Graudal et al. [3] was identified as having a wider inclusion criteria than that defined by the Expert Working Group. Therefore, the search terms and combinations were selected to align with its search strategy taking into account the outcomes of interest defined in the present review.

The databases Medline, Web of Science, PubMed and the Cochrane Library were searched with the following key words/combinations and limits:

Sodium OR salt AND Dietary OR restriction AND blood pressure OR hypertension

Sodium OR salt AND Dietary OR restriction AND HDL cholesterol

Sodium OR salt AND Dietary OR restriction AND LDL cholesterol

Sodium OR salt AND Dietary OR restriction AND Total cholesterol

Sodium OR salt AND Dietary OR restriction AND Stroke OR cerebrovascular accident

Sodium OR salt AND Dietary OR restriction AND Myocardial infarction OR heart attack

Sodium OR salt AND Dietary OR restriction AND mortality OR death

The following limits were applied to each search where possible:

Articles published from 22 July 2011 – 10 November 2014 (if the only option was to limit to years, the search was limited to 2011-present/current depending on database), articles published in the English language, humans. The starting date of the search was selected to correspond with the final date of the literature search conducted by Graudal et al. [3]. Initially, the search was conducted to cover the time period of 22 July 2011 – 3 December 2013, with the search updated to cover until 10 November 2014 at a later date. Limits for adults were not set as they were defined as >19 years of age in several databases, and the expert working party defined adults at individuals aged 18 years and above.

All articles identified following both phases of the literature search were scrutinised against the previously defined inclusion and exclusion criteria by experienced researchers to determine their relevance to the current review. Where possible articles were excluded by abstract, with full text sought in the case that an abstract was not available or failed to provide sufficient information to make a decision regarding its inclusion in the current review.

2.3 Extraction of data

All included articles were summarised in tabular form in both Microsoft Word and Excel (Microsoft Corporation, 2010, Version 14.0.7) formats to identify key study components, design and outcomes and allow for further statistical analysis where appropriate. Where available results for the change in study outcome (eg. blood pressure) between the group with the higher sodium excretion (‘control group’) and the group with the lower sodium excretion (‘intervention group’) were obtained from the previously conducted meta-analysis by Graudal et al. [3]. When unavailable this data was calculated using the approach outlined in Section 2.4, or sought from another relevant systematic literature review [2] where appropriate. Data on mean age of participants, hypertension status and blood pressure measurement was also extracted to facilitate the analysis. Additional information on the data management is provided in Section 2.4.

2.3.1 Risk of bias

A risk of bias assessment table was developed for each study in consultation with the Expert Working Group. The table was based on the categories outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [10]. Additional information was added to the table to ensure that all information required for the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method of appraising the quality of evidence in systematic reviews [11] were captured.

2.3.2 Appraisal of evidence quality

The GRADE approach to appraising the quality of evidence for each outcome was adopted for the current review. GRADEProfiler software (Version 3.6) was utilised to facilitate this process, with decisions on the quality of evidence guided by the strategy outlined by Barbui et al. [12] and Guyatt et al. [13]. Due to time constraints meta-analyses were not conducted for diastolic blood pressure and mortality outcomes (see Supporting Document 2), therefore GRADE assessments of the quality of evidence could not be conducted for these outcomes. In addition article summary tables included an assessment of the National Health and Medical Research Council (NHMRC) level of evidence [14].

2.4 Statistical Analyses

A separate report on statistical analyses was developed (Supporting Document 2). Briefly, data from all included articles were summarised in Microsoft Excel to allow for statistical analysis. A summary of the study components extracted is listed in Appendix 2. Where available, data was extracted separately for gender, ethnicity and hypertension status subgroups. Studies were further characterised based on their participants' hypertension status. When investigating the reporting of relevant outcomes, blood pressure measured as supine or sitting was considered to be resting, although these different measurement conditions were noted when extracting the data.

In both parallel and cross-over studies with two groups with different sodium intakes, the group with the lower sodium intake was classified as the intervention group, whereas the group with higher sodium intake was classified as the control group. In the case of Alli [15], this involved reversing the classifications of the original paper, which reported higher urinary sodium excretion in the intervention group. In the case of studies which had more than two groups [16-18], the low and intermediate groups (corresponding to sodium intakes of approximately 50 mmol/day and 100 mmol/day respectively) were selected for analysis based on consensus with the Expert Working Group.

Urinary sodium and potassium data was recorded in the units reported in the paper, with all data converted to mg/24hr, using the conversion of 1 mmol sodium = 23 mg sodium [19]. The difference in urinary sodium and potassium excretion between high and low sodium groups was calculated using the following equation:

Difference in 24 hour urinary excretion = 24 hour urinary excretion at the end of the low sodium period - 24 hour urinary excretion at the end of the high sodium period.

In the case that urinary excretion values were measured over an eight hour period, values were converted to 24 hour values by multiplying by 3.8 and 4.9 for sodium and potassium respectively [20].

As was previously outlined in Section 2.3, data on the change in continuous health outcomes were obtained preferably from Graudal et al. [3] where available. Where data on the change in outcomes was not available from a published SLR, it was calculated from published data using the formulae outlined in Supporting Document 2, or extracted from WHO [2] where the same formula was used.

3. Results

A total of 408 articles were obtained from the six SLRs [2-7] and the additional key document [8]. Of these initial results, a total of 268 studies remained after the removal of duplicates. From this figure, 147 studies were excluded based on irrelevance to the present study from the title or abstract. Of the full text articles assessed for eligibility to the inclusion criteria of the study, 23 were excluded as they involved interventions of less than 4 weeks duration, 10 were excluded as they involved studies where the effect of sodium on the relevant health effect could not be isolated, 9 were excluded due to a lack of urinary sodium data and 9 were excluded as they were not randomised controlled trials. An additional 10 studies were excluded due to uncontrolled changes in anti-hypertensive medication, study participants not meeting the inclusion criteria, not measuring an outcome of interest or not reporting complete outcome data. A list of the full-text articles excluded and the reasons for their exclusion is provided in Appendix 3. In total, 60 articles describing 56 studies were included. A PRISMA [9] flow diagram detailing the selection of the study to be included in the present review is listed as Figure 1.

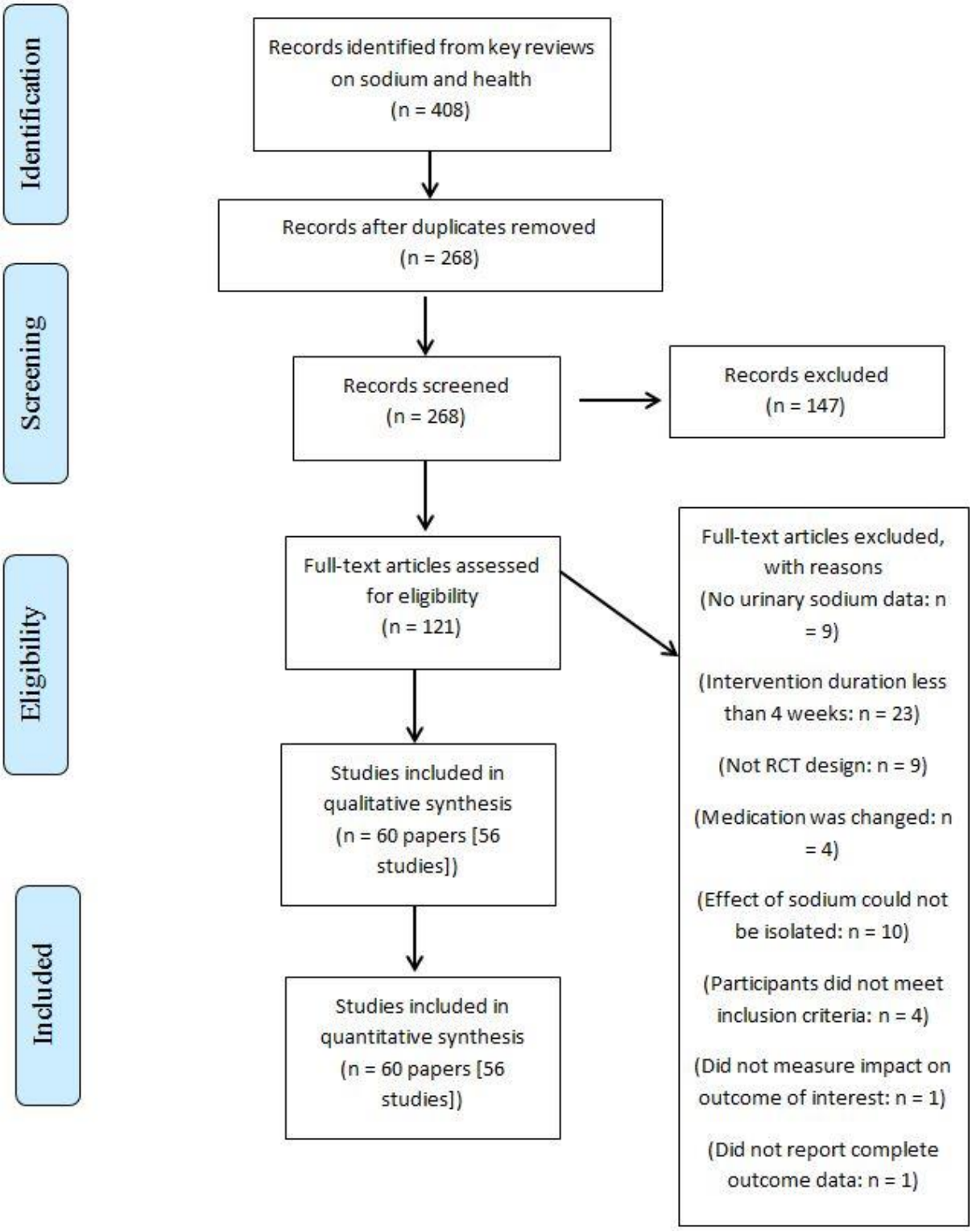

Figure 1. PRISMA flow diagram for studies scrutinized in systematic literature reviews relating to sodium and blood pressure, mortality, lipids, stroke and myocardial infarction

A total of 6067 articles published between 2011 and 2014 were identified from the 4 scientific databases searched. A breakdown of the search results for each topic area (inclusive of duplicates) from each database is shown in the Appendix 4. Of these initial results, a total of 2827 studies remained after the removal of duplicates. From this figure, 2638 studies were excluded based on irrelevance to present study from title or abstract. Of the full text articles assessed for eligibility to the inclusion criteria of the study, 11 were excluded due to a lack of urinary sodium data, 16 were excluded as they involved interventions of less than 4 weeks duration, 112 were excluded as they were not randomised controlled trials, 34 were excluded as they involved studies where the effect of sodium on the relevant health effect could not be isolated (e.g. sodium restriction was coupled with increased dietary fibre or potassium intake), eight did not measure an outcome of interest, and six were excluded due to being in vitro studies, only describing the protocol of studies or being published in a language other than English. One study [21] was identified as meeting the inclusion criteria during the initial 2011 - 2013 search. An additional study [22] was identified in the second search (3 December 2013 – 10 November 2014), however as its results were consistent with the larger body of evidence, inclusion of this study in the quantitative analysis would not influence the results of the review or result in downgrading of the evidence. Therefore it was not included in the meta-analysis. A list of the full-text articles excluded and the reasons for their exclusion is provided in Appendix 3. A PRISMA flow diagram detailing the selection of the study to be included in the present review is listed as Figure 2.

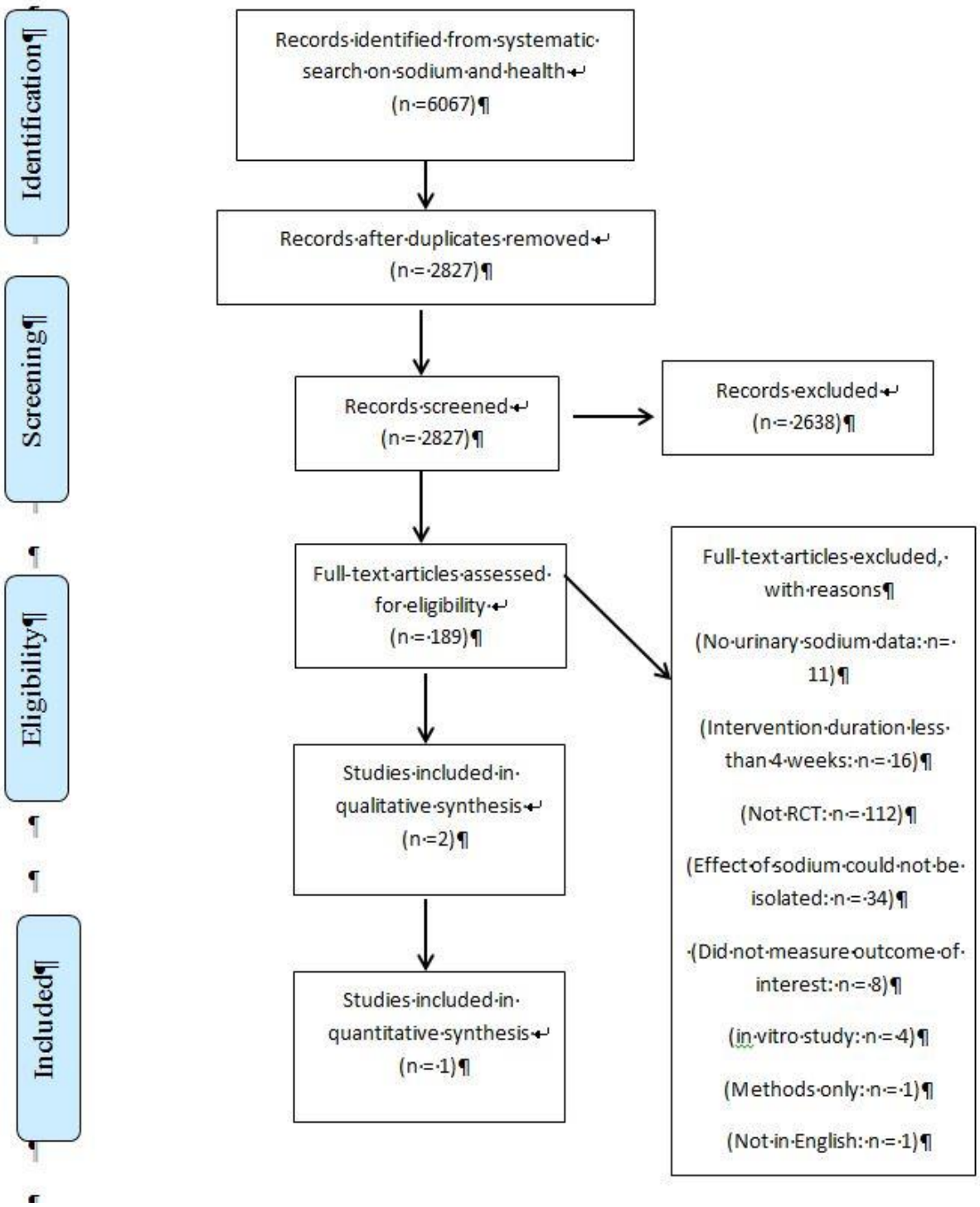

Figure 2. PRISMA flow diagram for systematic literature review inclusive of studies published from 2011-2014

3.1 Risk of bias and appraisal of evidence quality

Summaries of all included studies and corresponding risk of bias assessments are shown in Appendix 5, with risk of bias charts for each health outcome shown in Appendix 6. All evidence was Level II according to the NHMRC Levels of Evidence criteria [23]. The GRADE assessments for each outcome of interest rated the quality of evidence as high for systolic blood pressure in normotensive and hypertensive individuals when analysed separately and moderate for studies involving both normotensive and hypertensive individuals. As previously outlined, a study [22] identified in the second arm of the search (from 3 December 2013 to 10 November 2014) was not included in the meta-analysis. Therefore this study could not be included in the GRADE assessment due to lack of information on inconsistency and imprecision, however a summary of the risk of bias assessment is displayed in Appendix 5. It should also be noted that the consistency of the results of Dickinson et al. [22] with the wider body of evidence means that it would be very unlikely to result in a downgrading of the quality of the evidence base.

The assessment of the quality of evidence involving individuals of mixed hypertensive status was downgraded due to the heterogeneity of the blood pressure responses to reduced sodium intakes in these studies (Appendix 7). The GRADE assessment of the quality of evidence relating to lipids was high for total cholesterol, HDL cholesterol and LDL cholesterol (Appendix 7).

3.2 Locations of research

Pertinent to the objective of this review to update the nutrient reference values relating to sodium in Australia and New Zealand, the number of included studies conducted in Australia was 14 [22, 24-36], with 2 studies included that were conducted in New Zealand [37, 38]. Of the remaining studies, 28 were conducted in European countries [15, 17, 39-63] and 14 studies were conducted in the USA [16, 18, 20, 21, 64-73]. No included studies were conducted in countries in the continents of Asia or Africa.

3.3 Profile of study participants and study design

Data was available for a total of 2315 intervention participants and 2310 control participants in the parallel studies, with data available for 1574 participants (1549 for the meta-analyses) in the cross-over studies. There were 26 parallel studies relating to sodium and a relevant health effect [15, 20, 25-29, 31-33, 35, 36, 38, 42-44, 50, 54, 55, 58, 61, 64, 65, 68-71] and 31 crossover studies (30 included in the meta-analyses) [16, 17, 21, 22, 24, 30, 34, 37, 40-42, 45-49, 51-53, 56, 57, 59-63, 66, 67, 69, 72, 73].

3.4 Outcome measures

3.4.1 Resting systolic blood pressure

Reported changes in resting systolic blood pressure were considered for analyses supporting the derivation of the NRVs. Full details of the statistical analysis and results are reported in Supporting Document 2. Fifty five studies [15-17, 20, 21, 24-27, 29-73] contributing 66 sub-analyses were considered (see Supporting Document 2). Within these studies, 40 studies (46 sub-analyses) [15, 17, 24-27, 31-34, 36-51, 53, 55, 57-59, 63-66, 68, 69, 72, 73] were conducted in participants with a degree of hypertension, 11 studies (14 sub-analyses) [20, 29, 30, 35, 41, 56, 60, 62, 67, 70, 71] were conducted in normotensive participants and 5 studies (6 sub-analyses) [16, 21, 52, 54, 61] were conducted in a both normotensive and hypertensive populations (where the participants could not be separated into either hypertensive or normotensive). It must be noted that due to one study [41] presenting data separately for normotensive and hypertensive participants, this study is included in the total count for both sub-groups. As previously described, an additional study conducted in normotensive participants [22] was not included in the meta-analysis.

Twenty seven sub-analyses [16, 17, 21, 29, 33, 36, 40-42, 45, 47-49, 52, 57, 63, 64, 67, 69, 70, 72, 73] found a significantly greater reduction in systolic blood pressure following consumption of a low sodium diet, compared to a higher sodium diet, whilst 31 sub-analyses [22, 24-27, 29, 31, 32, 34-37, 39, 42-44, 46, 50, 51, 53, 59-62, 65, 66, 68, 71] found a non-significant reduction in systolic blood pressure. Further, one analysis [38] also found a decrease in systolic blood pressure, however data provided was insufficient to calculate significance. Non-significant increases in systolic blood pressure after consuming a low sodium diet were found in seven sub-analyses [20, 30, 31, 54-56, 58], with a significant increase in systolic blood pressure found in one study [15]. Overall, changes in systolic blood pressure in the low sodium intake group compared to the high sodium group ranged from -17 mmHg to 6.3 mmHg.

3.4.2 Resting diastolic blood pressure

Reported changes in resting diastolic blood pressure were also considered for analyses supporting the derivation of the NRVs. Fifty seven studies [15-17, 20-22, 24-38, 40-73] contributing 69 sub-analyses contributed to the analysis of resting diastolic blood pressure. Within these studies, 41 studies (48 sub-analyses) [15, 17, 24-28, 31-34, 36-51, 53, 55, 57-59, 63-66, 68, 69, 72, 73] were conducted in participants with a degree of hypertension, 12 studies (15 sub-analyses) [20, 22, 29, 30, 35, 41, 56, 60, 62, 67, 70, 71] were conducted in normotensive participants and 5 studies (6 sub-analyses) [16, 21, 52, 54, 61] were conducted in a both normotensive and hypertensive populations (where the participants could not be separated into either hypertensive or normotensive).

Twenty four sub-analyses [16, 17, 21, 27, 29, 33, 40, 41, 47-52, 57, 64, 67, 69, 72, 73] found a significantly greater reduction in diastolic blood pressure following consumption of a low

sodium diet, compared to a higher sodium diet, whilst 24 sub-analyses [22, 24-26, 29, 32, 35-37, 39, 42-44, 54, 59, 61, 63-66, 70, 71] found a non-significant reduction in diastolic blood pressure. Two sub-analyses of a single study also found a decrease in diastolic blood pressure, however provided data was insufficient to calculate significance [28]. Two studies found no change in diastolic blood pressure [30, 62]. Non-significant increases in diastolic blood pressure after consuming a low sodium diet were found in 14 sub-analyses [20, 31, 34-36, 45, 46, 53, 56, 58, 60, 68], with a significant increase in diastolic blood pressure found in two studies [15, 55], whilst insufficient data was provided to calculate the significance of the increase in an additional study [38]. Overall, changes in diastolic blood pressure following consumption of a low sodium diet ranged from -9 mmHg to 3.8 mmHg.

3.4.3 Mean arterial pressure (MAP)

A total of 7 studies (8 sub-analyses) evaluated the effect of sodium on mean arterial pressure [22, 39, 40, 56, 59, 60, 73], with changes following a low sodium diet ranging from -10 mmHg to 1 mmHg.

3.4.4 Serum cholesterol levels

The effect of sodium on total cholesterol levels was reported in 14 studies (16 sub-analyses) [18, 21, 36, 41, 46, 50, 51, 56, 62, 66, 69, 73-75]. With outcomes for HDL-cholesterol reported in 11 studies (12 sub-analyses) [21, 36, 50, 51, 56, 62, 66, 69, 74, 75] and results for LDL-cholesterol reported in 8 studies (10 sub-analyses) [21, 36, 56, 62, 66, 69, 74, 75].

Following consumption of a low sodium diet, all studies reported non-significant changes in total, HDL and LDL cholesterol. These changes ranged from -0.20mmol/L to 0.21mmol/L for total cholesterol, -0.20mmol/L to 0.08mmol/L for HDL cholesterol, and -0.23 mmol/L to 0.21mmol/L for LDL cholesterol.

3.4.5 Stroke, myocardial infarction and total mortality outcomes

Three studies reported incidence of total mortality in participants randomised to either a sodium reduced diet or a corresponding control group [20, 27, 71]. There was no significant difference in the relative risk of total mortality between the high and low sodium intake groups in all studies. Only one study reported statistical analyses on the effect of sodium intake on stroke and myocardial infarction [64], finding no significant difference in the incidence of these outcomes between individuals consuming a low and high sodium diet.

3.5 Other data reported

3.5.1 Urinary sodium and potassium excretion

In keeping with the SLR inclusion criteria, all studies reported urinary sodium excretion, although three studies only adequately reported the difference in sodium excretion between the low and high sodium period [65, 67]. Urinary sodium excretion during the low

sodium period ranged from 552 mg/24hr to 3910 mg/24hr, whilst levels of 2438 mg/24hr to 7170 mg/24hr were found during the higher sodium period. The difference between the low and high sodium groups ranged from -6555 mg/24hr to -177.1 mg/24hr.

In contrast, urinary potassium excretion was reported by 31 studies (39 sub-analyses) [15-17, 20-22, 24, 29, 30, 32-34, 36, 37, 40-42, 44-49, 52, 54, 58-60, 63, 73]. Urinary potassium excretion during the low sodium period ranged from 175.5 mg/24hr to 3747.9 mg/24hr, whilst levels of 163.8 mg/24hr to 3357.9 mg/24hr were found during the higher sodium period. The difference between the low and higher sodium groups ranged from -635.7 mg/24hr to 507 mg/24hr.

4. Discussion

Overall the consumption of a lower sodium diet in comparison to a higher sodium diet, was associated with a reduction in systolic blood pressure. The GRADE assessment of the quality of evidence suggests that the evidence for the effect of reduced sodium on systolic blood pressure was of high quality for interventions involving hypertensive and normotensive individuals (when analysed separately). This supports the findings of other SLRs conducted in recent years, which found reductions in systolic blood pressure to be associated with decreased sodium intake [2, 3, 5, 6].

In contrast consumption of a lower sodium diet had no effect on total cholesterol, HDL-cholesterol and LDL-cholesterol in the general adult population (with evidence assessed for lipids to be of high quality according to the GRADE method). These findings are likely to reflect the duration of the studies included, with previous SLRs finding significant increases in cholesterol following sodium restriction in studies of less than 4 weeks duration [3]. It may be that observed increases in cholesterol following sodium reduction are of a transient nature.

Whilst there was some inconsistency between results, reductions were greater and more consistently reported for systolic blood pressure than diastolic blood pressure. In particular, consistently larger reductions were found for both systolic and diastolic blood pressure with lower sodium intakes in hypertensive individuals, whilst studies in normotensive individuals tended to yield smaller effect sizes. When studies included both normotensive and hypertensive participants, heterogeneity between observed effects was evident, resulting in the quality of evidence being moderate according to the GRADE method. These findings were similar to those reported by other SLRs in the area and may reflect different physiological responses to sodium intake under conditions of elevated blood pressure [2, 3, 5, 6].

It has been reported that the favourable changes in blood pressure with a lower sodium diet may be accompanied by increases in cholesterol levels, meaning that the overall effect on

disease outcomes might not be beneficial [3]. This SLR found no evidence for an effect of a decreased sodium diet on total, HDL or LDL cholesterol levels. Whilst this contradicts the results of a previous SLR [3] examining the same question, the previous SLR included short duration studies and did not restrict duration to a minimum of 4 weeks. Consequently, the previous finding may have reflected a transient physiological response on cholesterol levels.

There was no significant effect of a low sodium diet on the incidence of myocardial infarction, stroke or all-cause mortality. However the exclusion of prospective cohort studies in the current review limited the body of available evidence on these outcomes. In future, SLRs using well controlled prospective cohort studies with reliable measurements of sodium intake may provide additional evidence to support conclusions relating to longer term disease outcomes.

The document review strategy applied in the SLR reported here followed one of the options for conducting a SLR outlined in the Methodological Framework for the Revision of the NRVs [1] – the option of updating a review. A potential limitation of this approach was the reliance on published high quality SLRs from the peer-reviewed literature or expert groups to have done a thorough search and retrieved all relevant literature. However, the reviews came from several different groups who were working independently and so the risk of oversight was minimal.

A further limitation of the data compiled for the present report relates to the potential confounding influence of genetic variation between individuals participating in the included studies. Published literature suggests that genetic polymorphisms may result in substantial differences in individuals' blood pressure responses to changes in dietary sodium intake [76, 77]. No studies included in the present review attempted to control for genetic variation, which may have accounted for some residual confounding of the pooled analysis, although some did sub-analyses by ethnicity as a surrogate because the prevalence of the salt-sensitive polymorphism varies by ethnicity [47, 64]. As many of the included studies were conducted prior to the identification of relevant polymorphisms there is a need for future randomised controlled trials to consider these factors to enable more accurate quantification of effect sizes. It should also be noted that not all types of elevated blood pressure respond to sodium reduction [78]. The genetic variation in response might be one reason for the high heterogeneity seen in the current meta-analysis in hypertensive and normotensive individuals.

Conducting the SLR using the approach outlined by the Department of Health and Ageing [1], produced a robust and transparent resource to support the revisions of the 2006 sodium NRVs. Previous reviews report that a reduction in sodium intake reduces both systolic and diastolic blood pressure. The effect of sodium reduction appears most pronounced in individuals with elevated blood pressure and for all systolic blood pressure measures. There was no change in total, HDL, or LDL cholesterol. Little data were available to examine for longer-term outcomes such as stroke, myocardial infarction or mortality

Future research in this area should consider measuring long term health outcomes associated with reduced sodium intake and should take into account genetic variation in blood pressure responses.

Appendices

Appendix 1: Summary table of key aspects of the review papers - sodium intake & health outcomes

The summary table relates to sodium intake and health outcomes including an overview and inconsistencies.

	He et al. (2013) [5]	**Hooper et al (2009) [6]**	**Graudal et al. (2011) [3]**	**WHO (2012a) [2]**	**WHO (2012b) [4]**	**IOM (2013) [7]**
Outcomes measured	Blood pressure (in both normotensive and hypertensive individuals), plasma renin activity, aldosterone, noradrenaline, adrenaline, cholesterol, LDL, HDL and triglycerides	Primary outcomes: - total mortality and combined cardiovascular events (including myocardial infarction, stroke, angina, heart failure, peripheral vascular events, sudden death and non-scheduled cardiovascular interventions Secondary outcomes: - Changes in SBP and DBP, quality of life, weight, nutrient intakes, urinary sodium excretion and anti-hypertensive	-SBP, DBP, mean blood pressure - Mean blood concentrations of renin, aldosterone, catecholamines, cholesterol, HDL, LDL, and triglycerides	- Blood pressure - Renal function - Adverse effects including increased total cholesterol, LDL, or triglycerides; decreased HDL; increased adrenaline or noradrenaline; and any other adverse effects reported by study authors.	- Primary outcome measures: all stroke, CVD and CHD events (incident events, fatal events and non-fatal events) - Secondary outcome measures: all-cause mortality and other outcomes reported by study authors	Cardiovascular disease, congestive heart failure, myocardial infarction, diabetes, mortality, stroke, bone disease, fractures, falls, headaches, kidney stones, skin reactions, immune function, thyroid disease, cancer (listed in research question) - Hypertension not listed in research question but included in list of outcomes in search strategy

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
		medication				
Research question (if defined)	The objective of the study was to assess: (1) the effect of a longer-term modest reduction in salt intake (i.e. of public health relevance) on BP and whether there was a dose-response relationship; (2) the effect on BP by sex and ethnic group; (3) the effect on plasma renin activity, aldosterone, noradrenaline, adrenaline, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides.	The objective of the study was to assess in adults the long term effects (mortality, cardiovascular events, blood pressure, quality of life, weight, urinary sodium excretion, other nutrients and use of anti-hypertensive medications) of advice to restrict dietary sodium using all relevant randomised controlled trials.	The objective of the study were to estimate the effects of low sodium versus high sodium intake on systolic and diastolic blood pressure (SBP and DBP), plasma or serum levels of renin, aldosterone, catecholamines, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides.	The objectives were to assess whether there is any effect on blood pressure, renal function, blood lipids and other adverse outcomes in adults of: - consuming less sodium compared with consuming more sodium; - reducing sodium intake by 1/3 or more compared with reducing sodium intake by < 1/3; - consuming sodium at a level of < 2 g/day compared with consuming ≥ 2 g/day; - consuming sodium at a level of	The objectives of this study were to assess the effect of CVD, stroke and CHD of consuming: - less sodium compared with more sodium; - sodium at a level of < 2 g/day compared with ≥ 2 g/day; - sodium at a level of < 1.2 g/day compared with ≥ 1.2 g/day or 1.2–2 g/day.	1. What is the effect of reducing dietary sodium intake in all individuals compared to habitual intake on health outcomes (see above)? 2. What is the effect of reducing dietary sodium intake in individuals with hypertension, pre-hypertension, aged 51 years and older, African Americans, and individuals with diabetes, CKD or CHF, compared to habitual intake on health outcomes (see above)?

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
				< 1.2 g/day compared with consuming > 1.2 g/day, and compared with consuming 1.2–2 g/day.		
Key findings	The quality of the evidence of the effect of salt reduction on blood pressure was ranked as high for all participants, normotensives and hypertensives in both SBP and DBP (using GRADE). - Modest salt reduction (and a reduction in 24hr urinary sodium excretion) resulted in significant reductions in SBP and DBP in analyses of all participants,	- Effects of reduced sodium diet on mortality and cardiovascular events inconsistent (no significant effect) - SBP was reduced on a low-salt diet in both intermediate and late follow-up, whilst DBP was mainly reduced in intermediate follow-up -Greater effects of salt reduction seen in hypertensive individuals (insufficient data to examine the effect	-In individuals of Caucasian or African descent, sodium reduction resulted in larger reductions in SBP and DBP in hypertensive individuals, whilst reductions in normotensive individuals were only significant for SBP (larger decreases seen in individuals of African descent). Effects were greater in studies of more than 4 weeks duration	- Decreased sodium intake resulted in a significant decrease in resting SBP and DBP (GRADE quality of evidence: high) – greater in individuals with hypertension - Specifically, reducing sodium intake to <2g/day resulted in a decrease in SBP of 3.47mmHg and 1.81mmHg in DBP (GRADE quality of evidence: high), compared to reducing sodium intake but still	- CVD: In cohort studies, the association between higher sodium intake and all CVD was not significant. In RCTs, there was no significant reduction in cardiovascular morbidity with a low-sodium diet compared with usual diet, and there was no power to assess the effects of sodium reduction on cardiovascular mortality (GRADE	- Positive relationship between higher levels of sodium and risk of CVD - However, due to insufficient evidence on direct health outcomes, it could not be concluded that lowering sodium intakes below 2,300 mg/day either increases or decreases risk of CVD outcomes or all-cause mortality in the general population - Low sodium intakes may lead to higher risk of adverse effects in mid- to late-stage CHF patients

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	normotensives and hypertensives. - Results suggest that salt reduction was associated with greater reductions in blood pressure in individuals with hypertension (SBP only) and individuals of African ethnicity (SBP and DBP). Sex was not associated with change in SBP or DBP. - Significant increases in renin activity, aldosterone and noradrenaline with salt reduction. Adrenaline increase near-significant (p=0.06) - Non-significant changes in	of ethnicity or sex)	(analysis only conducted in Caucasian individuals). - In individuals of Asian descent, sodium reduction resulted in larger reductions in SBP and DBP in hypertensive individuals, whilst reductions in normotensive individuals were only significant for DBP. - Sodium reduction resulted in increases in the following measures when studies of all durations were considered, but changes were not significant in studies of 4 weeks or more:	consuming >2g/day (direct comparison) - Non-significant increase in total cholesterol, LDL, noradrenaline, adrenaline found with sodium reduction - Non-significant decrease in HDL, triglycerides found with sodium reduction - Not all of the data on renal function could be combined in a meta-analysis, however the results from the studies suggested that reduced sodium did not have an adverse effect on renal function and may have potentially had a beneficial	quality of evidence: very low) - Stroke: In cohort studies, a significant association was detected between higher sodium intake and increased risk of all stroke. Data from RCTs was insufficient to suggest an effect or lack of effect. (GRADE quality of evidence: low - very low) - CHD: In cohort studies, there was a non-significant association between higher sodium intake and increased risk of all CHD. Data from RCTs was insufficient to	- The current body of evidence addressing the association between low sodium intakes and health outcomes in population subgroups (see above) is limited

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	cholesterol, LDL, HDL and triglycerides		noradrenaline (total: p<0.00001, 4 weeks or more: p=0.06), adrenaline (total: p<0.00001, 4 weeks or more: p=0.10), cholesterol (total: p<0.001, 4 weeks or more: 0.27) and triglycerides (total: p=0.0008, 4 weeks or more: p=0.09) - Changes in LDL (p=0.15), HDL (p=0.91) were not significant regardless of duration	effect.	suggest an effect or lack of effect. (GRADE quality of evidence: very low) - All-cause mortality: In cohort studies, there was a non-significant association between higher sodium intake and increased risk of all-cause mortality. Data from RCTs was insufficient to suggest an effect or lack of effect. (GRADE quality of evidence: very low)	
Search strategy	The following databases were searched: - Cochrane Hypertension Group Specialised Register (1948 – November 2012) - Cochrane Central	The databases searched included: Cochrane Library, Medline, Embase, CAB abstracts, CVRCT registry and SIGLE (to May 1998). - Updated search	The databases searched included: PubMed, Embase, and Cochrane Central (1950 – July 2011) - No language restrictions	In the first phase, relevant systematic reviews were located and their references used. In the second phase, the search strategy involved searching the	In the first phase, relevant systematic reviews were located and their references used. In the second phase, the search strategy involved searching the	Date range: Jan 2003 – Dec 2012. Databases searched: Cochrane reviews, Embase, Medline, PubMed, Web of Science - Peer-reviewed original research

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	Register of Controlled Trials (2012) - Medline (1946 – 2012) - Embase (1974 – 2012) Reference lists of articles also reviewed for additional studies. - No language restrictions	included the Cochrane library and Medline (does not give date) Reference lists of articles also reviewed for additional studies. - No language restrictions		following databases (from the date of the search completed in the reviewed SLRs – August 2011): Cochrane Central Register of Controlled Trials, Medline, Embase, WHO International Clinical Trials Registry Platform, Latin American and Caribbean Health Science Literature Database. - Reference lists of articles also reviewed for additional studies	following databases for additional systematic reviews (from the date of the search completed in the reviewed SLRs – August 2011): Cochrane Central Register of Controlled Trials, PubMed database (to be undertaken if the reviews found in the first phase were more than 2 years old). Reference lists of articles also reviewed for additional studies	studies, systematic reviews and meta-analyses (for background and cross-check of references) published in English
Inclusion criteria	- Adults (18 years or older) with normal or raised blood pressure - Random allocation to either	- Adults (16 years or older) - Randomised controlled clinical trials - Studies which	-Individuals of all ages with normal or elevated blood pressure - Randomised controlled trials	- Adults (16 years and older) with normal or elevated blood pressure - Randomised controlled trials	- Adults (16 years and older) with normal or elevated blood pressure - Included randomised	- Studies used FFQ, 24-hr recall, food record or urinary sodium excretion (included overnight and spot urine with appropriate

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	modestly reduced salt intake or usual salt intake (i.e. control) - Reduction in 24hr urinary sodium excretion must be within the range of 40 – 120mmol/24hr - Duration of salt reduction must have been for 4 or more weeks	were designed to reduce sodium intake, with a control group receiving either a placebo or no active intervention - Study duration of over 6 months	allocating participants to either a low or high sodium diet - Estimation of sodium intake by 24hr urinary sodium excretion (either by 24hr measurement or estimated from a sample of at least 8 hours) - No restriction on study duration	which compared reduced sodium intakes with usual or higher intakes - Healthy individuals as well as those with obesity, diabetes or chronic nephrolithiasis (kidney stones) - Co-interventions allowed if they were identical in the control and intervention groups - Duration of 4 weeks or more - Reduction of sodium intake of >40mmol/day in intervention	controlled trials and prospective cohort studies - Studies included a quantitative measure of exposure (sodium intake) and compared this with an outcome of interest, or compared groups consuming different levels of sodium - Healthy individuals as well as those with obesity, diabetes or chronic nephrolithiasis (kidney stones) - Duration of 1 year or more - Reported on outcome of interest	validation) - RCTs, cohort, case-control studies - studies in all ages, health statuses, races and ethnicities included
Exclusion criteria	- Studies in children, pregnant	- Studies of institutionalised,	- Studies in patients with conditions	- Studies involving individuals who	- Studies involving individuals who	-Case studies and case-series

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	women, or patients with diseases other than hypertension (e.g. diabetes, heart failure) - Studies with concomitant interventions (i.e. non pharmacological interventions, anti-hypertensive or other medications) - Blood pressure not reported - urinary sodium not measured	acutely ill or pregnant individuals - Studies which used a multiple risk factor intervention intending to alter lifestyle or dietary factors other than sodium where the effect of reduced sodium could not be isolated	other than hypertension (e.g. diabetes or heart failure) - Studies treating participants with a concomitant intervention (e.g. hypertensive medication, potassium supplementation) when the intervention was not the same during the low and high sodium diet	were acutely ill or suffering from HIV	were acutely ill or suffering from HIV	-animal and in vitro studies - No data available on dietary sodium intake or health outcome of interest - Did not analyse independent effect of sodium - Method used to estimate sodium intake not described in sufficient detail or numerical sodium levels not calculated
Statistical analyses	Treatment effect was calculated for systolic and diastolic blood pressure and other outcomes measured, variance of treatment effect also calculated. Data was pooled by the inverse	For mortality and cardiovascular events, relative risks were used to examine differences between low sodium and control groups (using random effects model). For	Treatment effect was defined as the mean difference between changes from baseline to end of treatment during a low and a high sodium diet. Meta-analyses were performed, with sub-group	Continuous variables were expressed as mean differences with 95% confidence intervals. Results were calculated based on the random-effects model. Meta-analyses	Dichotomous data were expressed as risk ratio or hazard ratio with 95% confidence intervals (for RCTs, the higher sodium group was treated as the reference group). Results were	No meta-analysis due to heterogeneity of studies (including methods of measuring sodium intake and adjusting for confounders, as well as variation in study populations and sodium intakes examined)

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	variance method in random-effects meta-analysis. Source of heterogeneity was investigated via meta-regression analyses, whilst funnel plot asymmetry was used to investigate publication bias. Separate meta-analyses were also conducted in specific sub-groupings, including blood pressure status (hypertensive or normotensive), ethnicity and sex.	continuous outcomes, weighted mean differences were used (also using random effects model). Meta-analyses were performed on the data, with analyses checked for heterogeneity by visual inspection and Cochran's test. Random effects meta-regression was used to assess the effects of different factors such as initial SBP, ethnicity and sex etc. Sensitivity analyses were also conducted to assess the robustness of the data	analyses performed for studies with a duration of 2 weeks or more (hormones and lipids) and 4 weeks or more (all). Separate meta-analyses were conducted in different ethnicities. Assessment of heterogeneity was conducted using a chi-squared test included in the forest plot. Funnel plots were assessed for asymmetry. Sensitivity analysis was performed excluding studies giving rise to asymmetry in the funnel plots	were performed, with sub-group analyses performed based on gender, hypertensive status, achieved sodium intake level in intervention group (<2g/day vs $\underline{\geq}$2g/day, <1.2g/day vs $\underline{\geq}$ 1.2g/day and reduction relative to control), status of anti-hypertensive medication, duration, study design, type of blood pressure device used and method for measuring blood pressure. Sensitivity analysis conducted.	calculated based on the random-effects model. Meta-analyses were conducted, with sub-group analyses performed based on outcome, sodium intake level in the reference group and the difference in sodium intake level between the reference and comparison group. Sensitivity analyses were also conducted.	

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
Critical appraisal system	Summary tables were created, including relevant statistics which could be used in the pooled analysis. The risk of bias in included studies was evaluated (see below). The quality of the evidence for the effect of salt reduction on blood pressure was assessed using GRADE (ranked separately for all participants, normotensives and hypertensives).	Quality assessment of studies took into account randomisation procedure, allocation concealment, blinding of participants, providers of care and outcome assessors and losses to follow up (using Cochrane Reviewer's Handbook methodology) - GRADE system not used	- Summaries of key points and data for each study were made by reviewers - Risk of bias evaluation conducted (see below) - GRADE system not used	- Summaries of key points and relevant data for each study were made by reviewers - Risk of bias evaluation included (see below) - GRADE methodology used to assess the quality of the body of evidence	- Summaries of key points and relevant data for each study were made by reviewers - Risk of bias evaluation included (see below) - GRADE methodology used to assess the quality of the body of evidence	Rating system not used for individual studies (due to broad range of study designs and sodium intake assessments) Summary tables were developed to present details of study designs, which were critically evaluated based on methodological appropriateness, relevance of study population, interventions and outcome measures and fidelity of implementation of interventions. Broad criteria used to critically appraise each study: generalizability to the population of interest and methodological appropriateness (i.e.

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
						risk of bias)
Bias evaluation included	The risk of bias assessment considered: -allocation concealment: classified as being 'adequate' (participants and investigators could not foresee allocation), 'unclear' (randomisation used but not sufficiently described) or 'inadequate' (participants or investigators could foresee allocation) - Blinding: blinding of investigator, participant and outcome assessor noted - was incomplete outcome data	Risk of bias assessment conducted on each study and included an assessment of the quality of the allocation concealment, which was ranked as being adequate, unclear or inadequate	Risk of bias was assessed for each study using the Cochrane Risk of Bias tool (included recording of allocation, blinding, incomplete outcome data and selective reporting)	Risk of bias was assessed for each study using the Cochrane Handbook for Systematic Reviews of Interventions. The assessment considered: - randomisation - allocation concealment - blinding - management of incomplete outcome data - selective reporting bias - other sources of bias (e.g. similarity of groups at baseline)	Risk of bias was assessed for each study using the Cochrane Handbook for Systematic Reviews of Interventions. The assessment considered: - randomisation (for RCTs only) - For cohort studies, information was collected on potential sources of bias in non-randomised studies, including: characteristics of the sample, the intervention and its implementation, the completeness of follow-up, and the methods used in the analysis to	Risk of bias considered as part of criteria used to critically appraise studies. For RCTs, bias evaluation considered: blinding, method of randomisation, size and characteristics of study population, drop-out rate and relevance of sodium intake level. For observational studies, bias evaluation considered: study design, length, method of measuring sodium intake and adjustment for confounders

	He et al. (2013) [5]	Hooper et al (2009) [6]	Graudal et al. (2011) [3]	WHO (2012a) [2]	WHO (2012b) [4]	IOM (2013) [7]
	addressed: classified as 'yes' (intention-to-treat analysis used, all participants finished study or detailed information given on drop-outs), 'unclear' (no information given) or 'no' (not adequately addressed)				adjust for possible confounding factors.	
Date of publication of last paper cited in review	2009	1998	2011	2010	2011	2012
Additional relevant information						Review noted large degree of inconsistency in methodological approaches used in studies

Appendix 2 – Summary of key study components extracted for further analysis

- Author name and subgroup (for example: males) if appropriate
- Year of publication
- Study design (parallel or cross-over)
- Mean age of participants
- Weight/body mass index pre- and post-study diet
- Hypertension status at the time the study was completed
- Hypertension status by current Australian standards [82]
- Method of obtaining a change in sodium intake (for example: dietary advice)
- Co-intervention if used
- Method of measuring blood pressure
- Sodium excretion in low sodium group (extracted in original units reported in paper and converted to mg/24hr)
- Sodium excretion in high sodium group (extracted in original units reported in paper and converted to mg/24hr)
- Difference in sodium excretion between groups (low sodium excretion minus high sodium excretion)
- Potassium excretion in low sodium group (extracted in original units reported in paper and converted to mg/24hr)
- Potassium excretion in high sodium group (extracted in original units reported in paper and converted to mg/24hr)
- Difference in potassium excretion between groups (low sodium excretion minus high sodium excretion)
- Duration of study phases
- Number of study phases (cross-over studies only)
- Washout period duration (cross-over studies only)
- Number of participants in the intervention and control group
- Mean result for study outcome (for example systolic blood pressure) at baseline for the control and intervention groups, with appropriate variance statistics
- Mean result for study outcome (for example systolic blood pressure) at the end of the study for the control and intervention groups, with appropriate variance statistics
- Mean change in study outcomes over the duration of the study for the control and intervention groups, with appropriate variance statistics
- Difference between the final means of the study phases (cross-over studies) or difference in the changes in the means of each study phase (parallel studies), with appropriate variance statistics

Appendix 3 - Full-text studies excluded from the reviews, with reasons for exclusion

Authors	Reason for exclusion
References obtained from published systematic literature reviews	
Bullpitt et al. 1984	Change in medication
He et al. 2000	Change in medication
Nakamura et al. 2003	Change in medication
Beard et al. 1982	Change in medication in some participants
Chiolero et al. 2000	Duration less than 4 weeks
Delrio et al. 1990	Duration less than 4 weeks
Dimsdale et al. 1990	Duration less than 4 weeks
Draaijer et al. 1995	Duration less than 4 weeks
Ferri et al. 1998	Duration less than 4 weeks
Friberg et al. 1990	Duration less than 4 weeks
Gow et al. 1992	Duration less than 4 weeks
Kawasaki et al. 1978	Duration less than 4 weeks
Kerstens et al. 2003	Duration less than 4 weeks
Luft et al. 1979	Duration less than 4 weeks
Morgan et al. 1988	Duration less than 4 weeks
Myers et al. 1982	Duration less than 4 weeks
Rankin et al. 1981	Duration less than 4 weeks
Resnick et al. 1985	Duration less than 4 weeks
Roos et al. 1985	Duration less than 4 weeks
Ruilope et al. 1993	Duration less than 4 weeks
Skrabal et al. 1984	Duration less than 4 weeks
Starmans-Kool et al. 2011	Duration less than 4 weeks
Stein et al. 1995	Duration less than 4 weeks
Sudhir et al. 1989	Duration less than 4 weeks
Van der Kleij et al. 2002	Duration less than 4 weeks
Weinberger et al. 1988	Duration less than 4 weeks
Zemel et al. 1986	Duration less than 4 weeks
Heerspink et al. 2012	Includes participants with nephropathy
Ambrosioni et al. 1982	Involves children
Costa et al. 1981	Involves children
Trevisan et al. 1981	Involves children
Ana Paula et al. 2012	No urinary sodium data
Cohen et al. 2006	No urinary sodium data
Cohen et al. 2008	No urinary sodium data
Daimon et al. 2008	No urinary sodium data
Gardener et al. 2012	No urinary sodium data
He et al. 1999	No urinary sodium data

Jafar 2006	No urinary sodium data
Kagan et al. 1985	No urinary sodium data
Larsson et al. 2008	No urinary sodium data
Thaler et al. 1982	Not measuring outcome of interest
Chang et al. 2006	Not possible to isolate effects of sodium
Fagerberg et al. 1985	Not possible to isolate effects of sodium
Jula et al. 1992	Not possible to isolate effects of sodium
Jula et al. 1992(b)	Not possible to isolate effects of sodium
Jula et al. 1994	Not possible to isolate effects of sodium
Kempner 1948	Not possible to isolate effects of sodium
Nowson et al. 2009	Not possible to isolate effects of sodium
Skrabal et al. 1984	Not possible to isolate effects of sodium
Takahashi et al. 2006	Not possible to isolate effects of sodium
Whelton et al. 1998	Not possible to isolate effects of sodium
Cook et al 1998	Not RCT
Cook et al. 2007	Not RCT
Cook et al. 2009	Not RCT
Dahl 2005	Not RCT
Hunt et al. 1998	Not RCT
Logan et al. 1986	Not RCT
Miller et al. 1987	Not RCT
Obarzanek et al. 2003	Not RCT
Seals et al. 2001	Not RCT
Silman et al. 1982	Preliminary results of 12 month study
References obtained from systematic literature review of studies published from 2011-2014	
Azadbakht et al. 2011	Cannot isolate effects of sodium
Bautista et al. 2013	Cannot isolate effects of sodium
Bosworth et al. 2011	Cannot isolate effects of sodium
Brader et al. 2014	Cannot isolate effects of sodium
Chen et al. 2012	Cannot isolate effects of sodium
Cottell et al. 2011	Cannot isolate effects of sodium
Epstein et al. 2012	Cannot isolate effects of sodium
Frassetto et al. 2012	Cannot isolate effects of sodium
Huggins et al. 2011	Cannot isolate effects of sodium
Kim et al. 2012	Cannot isolate effects of sodium
Kitaoka et al. 2013	Cannot isolate effects of sodium
Kono et al. 2013	Cannot isolate effects of sodium
Kwok et al. 2012	Cannot isolate effects of sodium
Lima et al. 2013	Cannot isolate effects of sodium
Lin et al. 2012	Cannot isolate effects of sodium
Lin et al. 2013	Cannot isolate effects of sodium
Mok et al. 2013	Cannot isolate effects of sodium

Niiranen et al. 2014	Cannot isolate effects of sodium
Nolan et al. 2011	Cannot isolate effects of sodium
Noori et al. 2014	Cannot isolate effects of sodium
Racine et al. 2012	Cannot isolate effects of sodium
Rayner et al. 2012	Cannot isolate effects of sodium
Reidlinger et al. 2014	Cannot isolate effects of sodium
Robare et al. 2011	Cannot isolate effects of sodium
Sarkkinen et al. 2011	Cannot isolate effects of sodium
Shahnazari et al. 2013	Cannot isolate effects of sodium
Souza et al. 2013	Cannot isolate effects of sodium
White et al. 2013	Cannot isolate effects of sodium
Whitt-Glover et al. 2013	Cannot isolate effects of sodium
Yamada et al. 2014	Cannot isolate effects of sodium
Zair et al. 2013	Cannot isolate effects of sodium
Zhang et al. 2011	Cannot isolate effects of sodium
Zhou et al. 2013	Cannot isolate effects of sodium
Ziv et al. 2013	Cannot isolate effects of sodium
Batch et al. 2013	Did not measure impact on research question outcomes
Bolhuis et al. 2011	Did not measure impact on research question outcomes
Champagne et al. 2011	Did not measure impact on research question outcomes
Cohen et al. 2012	Did not measure impact on research question outcomes
Jablonski et al. 2013	Did not measure impact on research question outcomes
Kostis et al. 2013	Did not measure impact on research question outcomes
Torres et al. 2012	Did not measure impact on research question outcomes
Turban et al. 2013	Did not measure impact on research question outcomes
Azizi et al. 2013	Duration less than 4 weeks
Brown et al. 2014	Duration less than 4 weeks
Chamarthi et al. 2011	Duration less than 4 weeks
Constantinides et al. 2012	Duration less than 4 weeks
Dickinson et al. 2011	Duration less than 4 weeks
Ferrante et al. 2011	Duration less than 4 weeks
Gildea et al. 2013	Duration less than 4 weeks

Kahle et al. 2013	Duration less than 4 weeks
Muller et al. 2011	Duration less than 4 weeks
Preston et al. 2012	Duration less than 4 weeks
Rao et al. 2013	Duration less than 4 weeks
Shafiq et al. 2013	Duration less than 4 weeks
Suckling et al. 2012	Duration less than 4 weeks
Sun et al. 2012	Duration less than 4 weeks
Twist et al. 2013	Duration less than 4 weeks
Zanchi et al. 2011	Duration less than 4 weeks
Cox et al. 2012	in vitro study
Danielsen et al. 2012	in vitro study
Flores et al. 2012	in vitro study
Rajagopal et al. 2011	in vitro study
Zou et al. 2013	Methods only
Diaz et al. 2012	No urinary sodium data
Ferrara et al. 2012	No urinary sodium data
Nozomi et al. 2011	No urinary sodium data
Shea et al. 2011	No urinary sodium data
Todd et al. 2012	No urinary sodium data
Dahlmann and Kopp 2014	Not in English
Abramowicz et al. 2014	Not RCT
Agarwal 2012	Not RCT
Alderman and Cohen 2014	Not RCT
Ando et al. 2012	Not RCT
Anonymous 2011a	Not RCT
Anonymous 2011b	Not RCT
Anonymous 2011c	Not RCT
Anonymous 2011d	Not RCT
Anonymous 2012a	Not RCT
Anonymous 2012b	Not RCT
Anonymous 2012c	Not RCT
Anonymous 2012d	Not RCT
Anonymous 2012e	Not RCT
Anonymous 2013a	Not RCT
Anonymous 2013b	Not RCT
Appel 2014	Not RCT
Appel et al. 2011	Not RCT
Arnett et al. 2012	Not RCT
Aung et al. 2012	Not RCT

Azak et al. 2014	Not RCT
Beaglehole et al. 2011	Not RCT
Ben-Dov et al. 2011	Not RCT
Bochud 2011	Not RCT
Bochud et al. 2011	Not RCT
Brand 2012	Not RCT
Brennen and Williams 2013	Not RCT
Bruce 2011	Not RCT
Campbell et al. 2011	Not RCT
Campbell et al. 2011(b)	Not RCT
Cappuccio 2013	Not RCT
Cappuccio et al. 2011	Not RCT
Cappuccio et al. 2012	Not RCT
Carey 2011	Not RCT
Celermajer et al. 2013	Not RCT
Cohen et al. 2012	Not RCT
Cook et al. 2011	Not RCT
Cook et al. 2014	Not RCT
Cooper et al. 2013	Not RCT
Coxson et al. 2013	Not RCT
de Leeuw et al. 2013	Not RCT
de Simone et al. 2011	Not RCT
Dimke et al. 2011	Not RCT
Dobe 2013	Not RCT
Dobe 2013	Not RCT
Drake-Holland et al. 2011	Not RCT
Elijovich and Laffer 2014	Not RCT
Fang et al, 2012	Not RCT
Frohlich 2011	Not RCT
Frohlich et al. 2011	Not RCT
Graudal et al. 2011	Not RCT
Graudal et al. 2013	Not RCT
Gulland 2012	Not RCT
Ha 2014	Not RCT
Harrap 2012	Not RCT
He and MacGregor 2014	Not RCT
He et al 2011	Not RCT
Heaney 2013	Not RCT

Horikawa et al. 2014	Not RCT
Howard et al. 2011	Not RCT
Ishikawa et al. 2011	Not RCT
Jiang et al. 2013	Not RCT
Judd et al. 2013	Not RCT
Kawada et al. 2011	Not RCT
Kim and Han 2013	Not RCT
Kotchen et al. 2013	Not RCT
Kotchen et al. 2013	Not RCT
Kupferschmidt et al. 2013	Not RCT
Kupferschmidt 2013	Not RCT
Labarthe et al. 2011	Not RCT
Lee 2011	Not RCT
Lee et al. 2011	Not RCT
Li et al. 2013	Not RCT
Lopez-Jaramillo et al. 2013	Not RCT
Mann 2012	Not RCT
Martin et al. 2012	Not RCT
MesserlI and Bangalore 2014	Not RCT
Mugavero et al. 2012	Not RCT
Nakano et al. 2012	Not RCT
Oh 2011	Not RCT
Oliveira de Abreu-Silva et al 2011	Not RCT
Oparil 2014	Not RCT
Pfeifer 2013	Not RCT
Pfeifer 2013	Not RCT
Possner 2011	Not RCT
Price and Nicholls 2014	Not RCT
Quan et al. 2012	Not RCT
Rakova et al. 2013	Not RCT
Rebholz 2011	Not RCT
Satin 2011	Not RCT
Satoh et al. 2012	Not RCT
Sigurdsson 2014	Not RCT
Silver et al. 2011	Not RCT
Silver et al. 2011	Not RCT
Spry 2011	Not RCT

Stigler et al. 2013	Not RCT
Strazzullo 2013	Not RCT
Strazzullo et al. 2011	Not RCT
Streppel et al. 2014	Not RCT
Strom et al. 2013	Not RCT
Svetkey et al. 2011	Not RCT
Temple 2011	Not RCT
Thornton 2013	Not RCT
Titze et al. 2014	Not RCT
Turlova et al. 2013	Not RCT
Vallon et al. 2011	Not RCT
Whelton 2011	Not RCT
Williams et al. 2012	Not RCT
Zanchetti 2014	Not RCT
Asemi et al. 2014	Not urinary sodium data
Cicolini et al. 2014	Not urinary sodium data
Hinderliter et al. 2014	Not urinary sodium data
Koley et al. 2013	Not urinary sodium data
Lima et al. 2014	Not urinary sodium data
Silva-Smith et al. 2013	Not urinary sodium data

Appendix 4 - Initial results of systematic literature search

The results (inclusive of duplicates) relate to sodium intake and health outcomes (published between 2011 and 2014).

	Database			
	Medline	**Web of Science**	**PubMed**	**Cochrane**
Total articles	1764	2360	292	1651
Outcome/area				
Blood pressure	1235	1299	193	472
LDL cholesterol	13	59	0	47
HDL cholesterol	12	55	1	51
Total cholesterol	23	223	0	102
Myocardial infarction	32	74	5	203
Mortality	303	509	40	581
Stroke	146	141	53	195

Appendix 5: Summary tables and risk of bias assessments

The tables relate to studies included in the systematic literature review

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Alli et al. (1992), Italy [15]	Cluster randomised parallel design study	II	Adults (patients of GPs), with mild hypertension (DBP: 90 – 104 mmHg)	GPs were randomised to provide their patients with one of two dietary strategies 1. Dietary advice to reduce dietary sodium to 80mmol/day 2. no dietary advice relating to sodium	Blood pressure (supine after 5min rest)	56	12 months	Low sodium diet: 177.0 ± 32.9 mmol/24hr Normal sodium diet: 169.3 ± 49.4 mmol/24hr (Changes within and between groups all non-significant) Note appears to be very poor	SBP: Control group pre-study: 148.3 ± 10.6mmHg Control group post-study: 148 ± 13.7mmHg (NS change from baseline) Low sodium group pre-study: 150.8 ± 8.7mmHg Low sodium group post-study: 144.2 ± 11.1mmHg ($p<0.05$ compared to baseline, NS compared to control group post-study) DBP: Control group pre-study:

								compliance in low sodium group	97.2 ± 3.8mmHg Control group post-study: 95.6 ± 4.7mmHg (p<0.05 compared to baseline) Low sodium group pre-study: 97 ± 3.1mmHg Low sodium group post-study: 91.6 ± 6.4mmHg (p<0.05 compared to baseline and compared to control group post-study)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Alli et al. (1992)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: unclear risk Providers: high risk Outcome assessors: unclear risk	27.3% (high risk)	Yes (low risk)	No (low risk)	Yes (low risk)	National Council of Research, Italian Federation of Physicians, Fondazione Angelo and Angela Valenti (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Andersson et al. (1984), Sweden [39]	Randomised parallel design study	II	Adult males (41 – 59 years), with hypertension (DBP: 95 - 105mmHg)	Both groups were instructed to consume an energy restricted diet low in sodium. 1. provided with additional sodium via table salt and sodium tablets 2. no sodium provided	Blood pressure (supine after 10 min rest)	23	9-11 weeks	Low sodium diet: 97 $\pm$32 mmol/24hr Normal sodium diet: 200 $\pm$ 56 mmol/24hr	Mean difference between low sodium diet and normal sodium diet SBP: -8.40mmHg (CI: -21.07, 4.27) DBP: -4.60mmHg (CI: -11.31, 2.11)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Andersson et al. (1984)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: unclear risk Providers: high risk Outcome assessors: unclear risk	0% (low risk)	Not required (low risk)	No (low risk)	Yes (low risk)	Swedish National Association Against Heart and Chest Diseases, Goteborg Medical Society (low risk).

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
ANHMRC DSSMC* (1986), Australia [32]	Randomised parallel design study	II	Adults, mild hypertensive (DBP: 90 – 100mmHg)	Participants were then randomised to one of four groups: 1. Normal diet group 2. High potassium group (greater than 100mmol/day) 3. reduced sodium group (50 – 75mmol/day) 4. high potassium, low sodium group (greater than 100mmol/day potassium, 50 - 75mmol/day sodium)	Blood pressure (seated), cholesterol (did not report values for calculating change)	200 (n=100 in sodium and control groups)	12 weeks	Low sodium group: 85.8 $\pm$ 7.1 mmol/24hr Normal sodium group: 155.6 $\pm$ 8.4mmol/24hr	Mean changes between low sodium diet to normal sodium diet (from Graudal): SBP: -4.8mmHg (SEM: 3.92, CI: -12.48, 2.88) DBP: -4.2mmHg (SEM: 1.88, CI: -7.88, -0.52)

				Note only groups 1 and 3 used in this analysis due to confounding effect of potassium (as in Graudal)					

***Australian National Health and Medical Research Council Dietary Salt Study Management Committee**

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
ANHMRCD SSMC* (1986)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: unclear risk Providers: high risk Outcome assessors: unclear risk	<10% (low risk)	Yes (low risk)	No (low risk)	Unclear risk (stated that cholesterol did not change between groups, but did not give exact results)	NHMRC (low risk)

***Australian National Health and Medical Research Council Dietary Salt Study Management Committee**

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
ANHMRCDSSMC* (1989), Australia [33]	Randomised parallel design study	II	Adults, with mild hypertension (DBP: 90 - 100mmHg)	Participants were randomised to one of two groups: 1. low sodium intake group – diet containing less than 80mmol sodium/day plus placebo tablets 2. normal sodium intake group – diet containing less than 80mmol sodium/day plus NaCl tablets	Blood pressure (seated after 5 min rest), plasma cholesterol	103	8 weeks	Low sodium intake: 90 (SEM: 6) mmol/24hr – change: -52 (SEM: 7), p<0.005 Normal sodium intake: 153 (SEM: 6) mmol/24hr – change: +19 (SEM: 7), p<0.05 p-value for change between groups: p<0.005	Mean difference between low sodium diet to normal sodium diet: SBP: -5.5mmHg (SEM: 1.46, CI: -8.36, -2.64) DBP: -2.8mmHg (SEM: 0.84, CI: -4.45, -1.15) States there was no significant change in cholesterol, but does not give specific results

				providing 80mmol daily					

***Australian National Health and Medical Research Council Dietary Salt Study Management Committee**

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
ANHMRCDSSMC * (1989)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: unclear risk Providers: low risk Outcome assessors: unclear risk	<10% (low risk)	Yes (low risk)	No (low risk)	Unclear risk (Reported that there was no significant change in cholesterol but did not report specific results)	NHMRC (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
TONE Appel et al. (2001), USA [64]	Randomised parallel design study	II	Older adults (60 – 80 years) taking 1 anti-hypertensive medication (SBP: <145mmHg, DBP: <85mmHg) (23% African American)	Participants were randomised to one of two groups: 1.reduced sodium intake intervention (goal to achieve urinary sodium excretion of less than 80 mmol/L) 2. control (usual lifestyle) Anti-hypertensive	Blood pressure (seated), cardiovascular events (as trial endpoint)	681 (BP data available for n=142 African American participants and n=471 non- African American participants)	Median duration: 29 months	Differences in change in urinary sodium excretion between study groups: <u>African-American participants:</u> Women: -25 (95% CI: -47, -3) mmol/24hr (p=0.03) Men: -41 (95% CI: -69, -13)mmol/24hr (p=0.007) <u>Non-African-American</u>	Mean difference between reduced sodium and control groups: <u>African-American participants:</u> SBP: -4.9mmHg (SEM: 1.71, CI: -8.25, -1.55) DBP: -3mmHg (SEM: 1.2, CI: -5.35, -0.65) <u>Non-African-American participants:</u> SBP: -4.0mmHg (SEM: 1.01, CI: -5.98, -2.02) DBP: -1.6mmHg (SEM: 0.69, CI: -2.95, -0.25) <u>Cardiovascular events:</u>

				medication was withdrawn for all participants 90 days (± 14 days) after the start of the intervention. Resumption of anti-hypertensive medication, high BP (190/110mm Hg) or a cardiovascular clinical event were treated as trial endpoints.				participants: Women: -28 (95% CI: -41, -15)mmol/24hr (p<0.001) Men: -54 (95% CI: -67, -42)mmol/24hr (p<0.001) Note data not available for genders combined in each group	Stroke: Reduced sodium: 1 (individual and event), control: 2 (individual and event), p>0.99 MI: Reduced sodium: 2 (individual and event), control: 4 (individual and event), p=0.69 Transient ischemic attack: reduced sodium: 7 individuals reporting 8 events, control: 7 individuals reporting 8 events, p>0.99 (not divided into ethnicity)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
TONE Appel et al. (2001)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: unclear risk Providers: high risk Outcome assessors: unclear risk	Unclear risk	Yes (low risk)	No (low risk)	Unclear risk (Reported that there was no significant change in cholesterol but did not report specific results)	National Heart, Lung and Blood Institute, National Institute on Aging, National Centre for Research Resources of the National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Arroll et al. (1995), New Zealand [38]	Randomised parallel design study	II	Adults (aged 20 – 69 years), with hypertension (SBP> 115mmHg or DBP > 70mmHg	Participants randomised to one of four groups: 1. Exercise (walking briskly for 40 mins 3 times/week) 2. Salt reduced diet 3. Exercise (walking briskly for 40 mins 3 times/week) plus salt reduced diet 4. Control As decision was made by EWG to exclude studies	Blood pressure (method not stated)	87 (n=181 in total study)	6 months	<u>Without exercise:</u> Low sodium diet: 107mmol/24hr Normal sodium diet: 120 mmol/24hr	<u>Without exercise:</u> SBP: Control pre-diet: 145.3mmHg Control post-diet: 139.1mmHg (p>0.2) Sodium restriction pre-diet: 145.4mmHg Sodium restriction post-diet: 136.3mmHg (p>0.2) DBP: Control pre-diet: 94.0mmHg Control post-diet: 89.2mmHg (p>0.2) Sodium restriction pre-diet:

				with exercise interventions, only groups 2 and 4 were included in analysis					86.4mmHg Sodium restriction post-diet: 84.7mmHg (p>0.2) Please note SEM for each value not reported, only range of SEM for all SBP and DBP measures

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Arroll et al. (1995)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	13% (did not state from which group)- unclear risk	No (high risk)	No (low risk)	Yes (low risk)	National Heart Foundation of New Zealand (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Benetos et al. (1992), France [40]	Randomised cross-over study	II	Adults (22 – 55 years) with mild-to-moderate hypertension (>90 - <115mmHg DBP)	Participants were randomised to one of two groups: 1. Moderately restricted sodium diet plus 3.5g NaCl/day (59.5mmol/day sodium) in capsules (normal-sodium diet) 2. Moderately restricted sodium diet plus lactose capsules (low-sodium diet)	Resting blood pressure (supine)	20	4 weeks	Normal sodium period: 163 $\pm$ 13.3 mmol/24hr Low sodium period: 85 $\pm$ 9.6 mmol/24hr ($p<0.001$)	Mean changes between low sodium diet to normal sodium diet: SBP: -6.5mmHg (SEM: 1.88, CI: -10.18, -2.82) DBP: -3.7mmHg (SEM: 1.28, CI: -6.21, -1.19)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Benetos et al. (1992)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	<10% (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	Dassault Electronics (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Cappuccio et al. (1997), UK [41]	Randomised cross-over study	II	Older adults (60 – 78 years), both normotensive and hypertensive (SBP range: 123 – 205mmHg, DBP range: 64 – 112mmHg)	All participants were prescribed a reduced sodium diet (80mmol/day) for 2 weeks. Following this period, they were then allocated to a cross-over arm: 1. 12 sodium tablets/day (total of 120mmol/day) 2. 12 placebo tablets/day	Blood pressure (supine), total cholesterol	47 (18 NT, 29 HT)	4 weeks	Normotensive pts.: Normal sodium period: 167 ± 54 mmol/24hr Low sodium period: 91 ± 54 mmol/24hr (p<0.001) Hypertensive pts.: Normal sodium period: 182 ± 46 mmol/24hr Low sodium period: 95 ± 48 mmol/24hr (p<0.001)	Mean changes between low sodium diet to normal sodium diet: Normotensive pts. SBP: -8.1mmHg (SEM: 2.77, CI: -13.53, -2.67) DBP: -3.9mmHg (SEM: 1.54, CI: -6.92, -0.88) Hypertensive pts. SBP: -6.6 mmHg (SEM:2.51, CI: -11.52, -1.68) DBP: -2.8mmHg (SEM: 1.33, CI: -5.41, -0.19) Mean total

									cholesterol was 5.9± 1.1 mg/dL during normal sodium period and 6.0 ± 1.0 mg/dL during low salt period (NS, p-value not given, not given separately for HT and NT pts.)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Cappuccio et al. (1997)	Low risk (Random-generated numbers handled by author not involved in the clinical assessment)	Low risk (handled by author not involved in clinical assessment)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	2% (one participant) – low risk	No (unclear risk)	No (low risk)	Yes (low risk)	International Foundation for the Promotion of Nutrition Research and Nutrition Education (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Carney et al. (1991), Australia [34]	Randomised cross-over study	II	Adults (30 – 65 years), with mild-moderate hypertension, treated with medication	All participants were randomly allocated to a cross-over arm: 1. 100mmol slow-sodium tablets/day 2. Placebo tablets The study did not prescribe a diet, and assumed that participants continued their usual diet	Blood pressure (supine for 10 min, erect for 5 min) Note change in standing BP not able to be calculated as insufficient data in paper	11	6 weeks	Sodium tablets: 272 $\pm$ 24 mmol/24hr Placebo tablets: 170 $\pm$ 24 mmol/24hr ($p<0.001$)	Mean changes between low sodium diet to normal sodium diet: Supine: SBP: -1mmHg (SEM: 3.49, CI: -7.84, 5.84) DBP: 1mmHg (SEM: 2.96, CI: -4.80, 6.80)

				throughout					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Carney et al. (1991)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	0% (low risk)	Not required (low risk)	No (low risk)	Unclear risk (Insufficient data on standing BP to calculate)	Not stated (unclear risk) (company supplied capsules but no indication of funding)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Cobiac et al. (1992), Australia [35]	Randomised parallel design study	II	Older adults aged 60 – 80 years, normotensive and mildly hypertensive (DBP: ≤ 105mmHg) (mean 132/77mmHg)	During the 2 week run-in phase, all participants were encouraged to reduce sodium intake to less than 70mmol/day. Participants were also provided with NaCl tablets providing 80mmol sodium/day and 8g sunflower oil capsules during this time. Participants were then randomised to one of four groups: 1. sunflower oil (5g) with normal	Blood pressure (seated after at least 5 min rest)	106 (54 in sunflower oil groups, 52 in fish oil groups)	4 weeks	Sunflower oil groups: Normal sodium period: 152 ± 10 mmol/24hr Low sodium period: 79 ± 7 mmol/24hr (p<0.001 compared to run-in phase) Fish oil groups: Normal sodium period: 145 ±	Mean changes between low sodium diet to normal sodium diet: Sunflower oil groups: SBP: -2.7mmHg (SEM: 4.99, CI: -12.48, 7.08) DBP: 0.6mmHg (SEM: 3.92, CI: -7.08, 8.28) Fish oil groups: SBP: -3.1mmHg (SEM: 5.86, CI: -14.59, 8.39)

				sodium (with tablets providing 80mmol sodium/day) 2. sunflower oil (5g) with low sodium (with placebo tablets) 3. Fish oil (4.2g n-3 PUFA) with normal sodium (with tablets providing 80mmol sodium/day) 4. Fish oil (4.2g n-3 PUFA) with low sodium (with placebo tablets) 1. sunflower oil (5g) with normal sodium (with tablets providing 80mmol sodium/day)				8 mmol/24hr Low sodium period: 70 ± 8mmol/24hr	DBP: -2.8mmHg (SEM: 3.91, CI: -10.46, 4.86)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Cobiac et al. (1992)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: low risk Providers: low risk Outcome assessors: low risk	7% (low risk)	Yes (low risk)	No (low risk)	Yes (low risk)	National Health and Medical Research Council (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Dickinson et al., (2014), Australia	Randomised cross-over study	II	Adults, overweight or obese (BMI: 27 – 40kg/m^2), with blood pressure lower than 139/89mmHg	Participants were randomised to start on one of two arms: 1. Diet containing 6g of salt/day (100mmol sodium/day) plus 3g of salt capsules/day in capsules (total 150mmol sodium/day) (usual sodium diet) 2. Diet containing 6g of salt/day (100mmol	Blood pressure (seated after 5 min rest), 24 hour ambulatory BP, MAP	25	6 weeks	Urinary sodium excretion: Reduced sodium diet: 113 $\pm$ 45 mmol/24hr Usual sodium diet: 155 $\pm$ 58 mmol/24hr Significantly different between groups (p=0.002)	SBP: Baseline: 120 $\pm$ 13mmHg Usual sodium diet: 118 $\pm$ 16mmHg Reduced sodium diet: 115 $\pm$ 10mmHg Difference between arms not significant (p-value not given) DBP: Baseline: 77 $\pm$ 7mmHg Usual sodium diet: 74 $\pm$ 8mmHg Reduced sodium diet: 73 $\pm$ 6mmHg Difference between arms not significant (p-value

				sodium/day), with no capsules given (total 100mmol sodium/day) (reduced sodium diet)					not given) 24 hr ambulatory BP and MAP data entered into excel sheet

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Dickinson et al., (2014)	Low risk (using computer software)	Low risk (conducted by person independent of study, trialists not aware of allocation)	Participants: high risk Providers: low risk Outcome assessors: low risk	50% (high risk)	No (high risk)	No (low risk)	Yes (low risk)	CSIRO and NHMRC (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Dodson et al. (1989), UK [42]	Randomised parallel design study (1989a) followed by randomised cross-over study (1989b)	II	Adults with type II diabetes and mild hypertension (SBP: >160mmHg, DBP: 95mmHg)	Parallel design study: 1. received dietary advice to reduce sodium intake 2. control (also received dietary education) Cross-over study: 9 participants from the low sodium arm were allocated to one of two cross-over arms: 1. 80mmol sodium tablets/day with	Blood pressure (supine after 5 min rest, erect after 2 min rest)	Parallel design study: 34 Crossover study: 9 participants from the low sodium arm	Parallel design study: 3 months Crossover study: 1 month	Parallel design study: Normal sodium group: 180.7 ±60.4 mmol/24hr Low sodium group: 136.8 ± 37.9 mmol/24hr P<0.05 (between groups) Crossover study design: Normal sodium period: 198.8 ± 37.4 mmol/24hr Low sodium period: 122.6 ±	Mean difference between low sodium diet to normal sodium diet: Supine: Parallel design study: SBP: -13.0mmHg (CI: -25.92, -0.08) DBP: -1.80mmHg (CI: -8.62, 5.02) Crossover design study: SBP: -9.70mmHg (CI: -25.78, 6.38) (from WHO)

				restricted sodium diet continued 2. placebo with restricted sodium diet continued				50.3mmol/24hr	DBP: Change data not provided in WHO, see spreadsheet for means

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Dodson et al. (1989)	Both study designs: Low risk (computerised random number program)	Both study designs: Unclear risk (no description of method of concealment of allocation)	Parallel design study Participants: unclear risk Providers: high risk Outcome assessors: low risk Crossover study Participants: low risk Providers: low risk Outcome assessors: low risk	Parallel design study: <5% (low risk) Crossover design study: >20% (high risk)	Parallel design study: No (unclear risk) Crossover design study: No (high risk)	No (low risk)	Yes (low risk)	Not stated (unclear risk) (company supplied capsules but no indication of funding)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Dubbert et al. (1995), USA [65]	Randomised parallel design study	II	Older adults (aged 60 – 80 years), with essential hypertension (mean SBP: 142.3mmHg, mean DBP: 85.6mmHg)	Participants were randomised to one of three groups: 1. Dietary sodium goal of 87mmol/day supported by dietary education, with feedback on urinary sodium levels given (DI/FB) 2. Dietary sodium goal of 87mmol/day supported by dietary education, with no feedback given	Blood pressure (seated)	122	3 months	Mean change in urinary sodium levels by group: <u>DI/FB:</u> Caucasian participants: -87.7mmol/24hr (sig greater than changes in DI or C, also sig greater than in African-American participants) African-American participants: -40.6mmol/24hr (not sig different from DI, but both DI/FB and DI sig different from C) <u>DI:</u>	Mean difference between low sodium diet to normal sodium diet: SBP: -1.4mmHg (SEM: 3.76, CI: -8.77, 5.97) DBP: -0.5mmHg (SEM: 1.67, CI: -3.77, 2.77) (Note these results are for all participants, however Graudal included these results in the African American participant

				(DI) (merged with group 1 for analysis) 3. Instructed to continue usual diet (C)				Caucasian participants: -25.5mmol/24hr African American participants: -56.6mmol/24hr <u>C:</u> Caucasian participants: 4.4mmol/24hr African-American participants: -15.3mmol/24hr	subgroup analysis, as they were the largest subgroup and separate data was not given)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Dubbert et al. (1995)	Low risk (random number table)	Unclear risk (randomisation procedure stratified by race)	Participants: unclear risk Providers: high risk Outcome assessors: unclear risk	>20% (high risk)	No (high risk)	No (low risk)	Unclear risk (Limited detail available on significance level of changes in urinary sodium levels)	Department of Veteran's Affairs (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Erwteman et al. (1984), Netherlands [43]	Randomised parallel design study	II	Adults with mild hypertension (DBP: 95 – 110mmHg)	Participants allocated to either: 1. Normal diet 2. Sodium restricted diet – limited to 70mmol/day All participants received in random order chlorthalidone, metoprolol, a fixed combination of these drugs for 4 weeks each, alternated with 4 weeks of placebo	Blood pressure (after 10 mins supine rest and after 2 mins standing), cholesterol and HDL	94	24 weeks (placebo duration 12 weeks)	During placebo period: Normal sodium period: 130 $\pm$ 50 mmol/24hr Low sodium period: 72 $\pm$ 31 mmol/24hr ($p<0.05$)	Mean difference between low sodium diet to normal sodium diet (from Graudal, not clear if this is placebo period only): SBP: -2.7mmHg (SEM: 4.01, CI: -10.56, 5.16) DBP: -2.5mmHg (SEM: 2.46, CI: -7.32, 2.32) From the article: mean difference in BP during placebo period: SBP: -2.7 $\pm$2.2 (p=0.12) (supine), -4.4 $\pm$ 2.3 (p=0.025) (standing) DBP: -3.4 $\pm$1.7 (p=0.025) (supine), -1.0 $\pm$ 1.6 (p=0.25) (standing)

									States there was no significant change in cholesterol and HDL, but does not give specific results for normal and low sodium diets

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Erwteman et al. (1984)	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: high risk Providers: high risk Outcome assessors: low risk	12% (however unclear from which study group) (unclear risk)	No (high risk)	No (low risk)	Unclear risk (Reported that there was no significant change in cholesterol, HDL and glucose but did not report specific results)	Funding source not stated (unclear risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Fagerberg et al. (1984), Sweden [44]	Randomised parallel design study	II	Obese adult males with hypertension (DBP: 94 – 115mmHg)	Following a 3 – 4 week basal period, participants were randomly allocated to one of two groups: 1. Energy restricted diet (aimed at weight reduction of 1kg /week) with unchanged sodium intake for 12 weeks 2. Following the basal period, participants in this group underwent a 4	Auscultatory blood pressure (after 60 mins supine rest), resting intra-arterial blood pressure	30	12 weeks (sodium restriction period: 9 weeks)	Energy restricted, normal sodium diet: 194.6 (SEM: 13.4) mmol/24hr Energy restricted, low sodium diet: 95.5 (SEM: 7.7) mmol/24hr (significantly lower than measurement at start of study: $p<0.001$)	Mean difference between low sodium diet to normal sodium diet (not stated whether this is auscultatory or intra-arterial BP in Graudal): SBP: -3.7mmHg (SEM: 7.14, CI: -17.69, 10.29) DBP: -3.1mmHg (SEM:4.06, CI: -11.06, 4.86)

				week control period with their normal energy and sodium intake. For the final 9 weeks, participants were instructed to follow an energy restricted diet (aimed at weight reduction of 1kg /week) and restrict sodium to 100mmol/24 hrs					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Fagerberg et al. (1984)	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: high risk Providers: high risk Outcome assessors: unclear risk	12% (however unclear from which study group) – unclear risk	No (high risk)	No (low risk)	Yes (low risk)	Swedish National Association Against Heart and Chest Diseases, Swedish Medical Research Council, Goteborg Medical Society (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Fotherby et al. (1993) and Fotherby et al. (1997), UK [45, 74]	Randomised cross-over study	II	Older adults (aged 66 – 79 years) with essential hypertension (SBP: ≥ 160mmHg, DBP: ≥ 95 mmHg)	All participants were prescribed a reduced sodium diet (80-100mmol/day) for 4 weeks. Following this period, they were then randomly allocated to a cross-over arm: 1. 8 slow sodium tablets/day (total of 80mmol/day) 2. 8 placebo tablets/day	Blood pressure (supine after 5 min rest and after 1 min standing) (reported in Fotherby et al., 1993). Total cholesterol, HDL and LDL (reported in Fotherby et al., 1997)	17	5 weeks	Normal sodium period: 174 ± 40 mmol/24hr Low sodium period: 95 ± 36 mmol/24hr ($p<0.01$)	Mean difference between low sodium diet to normal sodium diet: Supine: SBP: -8mmHg (SEM: 3.5, CI: -14.86, -1.14) DBP: 1.0 mmHg (SEM:2, CI: -2.92, 4.92) Cholesterol: -7.70mg/dL (CI: -31.03, 15.63) HDL: -7.70mg/dL (CI: -20.03, 4.63) LDL: 0.0mg/dL (CI:

									-20.77, 20.77) Lipid data from Graudal, does not appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Fotherby et al. (1993) and Fotherby et al. (1997)	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	One participant (5.6%) lost to follow-up (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	British Heart Foundation (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Gates et al. (2004), USA [66]	Randomised cross-over study	II	Adults (aged over 50 years) with stage 1 systolic hypertension	Participants randomly allocated to start on one of two cross-over arms: 1. Reduced sodium diet plus salt tablets (intended to return participants to their usual sodium intakes) 2. Reduced sodium diet plus placebo	Blood pressure (seated and supine), 24hr ambulatory BP, total cholesterol, HDL, LDL	12	4 weeks	Normal sodium period: ~ 160 – 170mmol/24hr (estimated from figure, exact values not given) Low sodium period: ~60 – 70mmol/24hr (estimated from figure, exact values not given) ($p<0.05$)	Mean difference between low sodium diet to normal sodium diet: Supine: SBP: -3mmHg (SEM: 1.84, CI: -6.61, -0.61) DBP: -1.2mmHg (SEM: 1.46, CI: -4.06, 1.66) Cholesterol: 5.00mg/dL (CI: -38.21, 48.21) HDL: -1.90mg/dL (CI: -29.44, 25.64) LDL: 8.10mg/dL (CI: -29.92, 46.12) Lipid data from Graudal, does not

									appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Gates et al. (2004)	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	No loss to follow up (low risk)	Not required (low risk)	No (low risk)	Yes (low risk)	National Institute of Aging, NCRR General Clinical Research Centre, American Heart Association (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Gillies et al. (1984), Australia [24]	Randomised cross-over study	II	Adults with moderate hypertension, some receiving anti-hypertensive medication (information on number of participants on medication not given)	Participants randomly allocated to start on one of two cross-over arms: 1. Dietary advice for moderate dietary salt restriction 2. normal diet	Blood pressure (supine and standing), MAP Note: specific values for MAP not given in study, stated as having no significant changes.	24	6 weeks	Salt restriction resulted in decrease from 169mmol/24hr (SEM: 13) to 92mmol/24hr (SEM: 7) – unclear if this change was from baseline or compared to normal sodium diet ($p>0.001$)	Mean difference between low sodium diet to normal sodium diet: Supine: SBP: -2.4mmHg (SEM: 2.51, CI: -7.32, 2.52) DBP: -2.6mmHg (SEM: 2.21, CI: -6.93, 1.73) Note data also given for patients on and not on diuretics, however insufficient information given to calculate

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Gillies et al. (1984), Australia	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: unclear risk Providers: high risk Outcome assessors: unclear risk	14.2% loss to follow up (unclear from which group) (unclear risk)	No (high risk)	No (low risk)	Unclear risk (Insufficient data on MAP to calculate change in BP)	Not stated (unclear risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Grobbee et al. (1987), Netherlands [46]	Randomised cross-over study	II	Young adults (18 – 28 years) with mild hypertension (SBP $\geq$ 140mmHg, DBP$\geq$ 90mmHg)	Participants randomly allocated to start on one of three cross-over arms: 1. Low sodium diet plus sodium supplementation (90mmol/day) 2. Low sodium diet plus potassium supplementation (72mmol/day) 3. Low sodium diet plus placebo	Blood pressure (supine), serum cholesterol	40	6 weeks	Normal sodium period: 129 $\pm$5 mmHg Low sodium period: 57 $\pm$ 5 mmHg Low sodium/high potassium: 69 $\pm$ 6 mmHg ($p<0.005$)	Mean difference between low sodium diet to normal sodium diet (assuming that the potassium group was excluded by Graudal, although this is not clearly stated): SBP: -0.8mmHg (SEM: 1.51, CI: -3.76, 2.61) DBP: -0.8mmHg (SEM: 1.44, CI: -3.62, 2.02) Cholesterol: 0.0 mg/dL (CI: -15.31, 15.31) Lipid data from Graudal, does not appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Grobbee et al. (1987)	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	<5% loss to follow-up (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	Netherlands Heart Foundation (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
He et al. (2009), UK [47]	Randomised cross-over study	II	Caucasian, African and Caribbean and Asian adults (30 – 75 years), with mild hypertension (SBP: 140 – 170mmHg, DBP: 90 – 105mmHg)	Following consuming a reduced salt diet (with a goal of 85mmol/day) for 2 weeks, participants were randomly allocated to start one of the two cross-over arms: 1. Reduced salt diet with sodium supplementation (90mmol/day) 2. Reduced salt diet with placebo	Blood pressure (sitting after 5 – 10 min rest), 24hr ambulatory BP	169 (n=71 Caucasian, n=29 Asian, n=69 African and Caribbean)	6 weeks	All participants: Normal sodium period: 165 ±58 mmHg Low sodium period: 110 ± 49 mmHg (p<0.001) Caucasian pts. Normal sodium period: 163 ±54 mmHg Low sodium period: 104 ± 54 mmHg (p<0.001) Asian pts. Normal sodium period: 176 ± 64	Mean difference between low sodium diet to normal sodium diet: Seated: Caucasian pts. SBP: -4.8mmHg (SEM: 1.24, CI: -7.23, -2.37) DBP: -2.2mmHg (SEM: 0.66, CI: -3.49, -0.91) Asian pts. SBP: -5.40mmHg (SEM: 1.93, CI: -9.18, -1.62) DBP: -2.2mmHg (SEM: 1.04, CI: -4.24, -0.16) African and Caribbean pts.

								mmHg Low sodium period: 108 ± 49 mmHg (p<0.001) <u>African and Caribbean pts.</u> Normal sodium period: 162 ±59 mmHg Low sodium period: 116 ± 44 mmHg (p<0.001)	SBP: -4.80mmHg (SEM: 1.24, CI: -7.23, -2.37) DBP: -2.2mmHg (SEM: 0.67, CI: -3.51, -0.89)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
He et al. (2009)	Low risk (computer generated random number)	Low risk (computer generated random number, conducted by individuals not involved in the conduct of the study)	Participants: low risk Providers: low risk Outcome assessors: low risk	<10% loss to follow-up (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	UK Food Standards Agency (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Howe et al. (1994), Australia [25]	Randomised parallel design study	II	Adults (aged 34 – 82 years) with hypertension (DBP<105mm Hg) treated with ACE inhibitors	Participants were instructed to reduce dietary sodium to 70mmol/day during a 4 week run-in phase (also included 80mmol/day NaCl tablets, providing a total sodium intake of 150mmol/day). Participants were then randomly assigned to one of four intervention groups: 1. low sodium diet (70mmol/day) with placebo and fish oil (5g/day) 2. low sodium diet (70mmol/day) plus NaCl tablets (total	Blood pressure (seated after at least 5 min rest), total cholesterol (however did not report changes in cholesterol)	56 (n=28 in olive oil groups, n=28 in fish oil groups)	6 weeks	Olive oil groups: Normal sodium period: 155 mmol/24hr Low sodium period: 75mmol/24hr Fish oil groups: Normal sodium period: 160mmol/24hr Low sodium period: 85mmol/24hr (note values are estimated from figure) For oil groups	Mean changes between low sodium diet to normal sodium diet: Olive oil groups: SBP: -5mmHg (CI: -17.55, 7.55) DBP: -2mmHg (CI: -7.54, 3.54) Fish oil groups: SBP: -4.0mmHg (CI: -18.13, 10.13) DBP: -1.0mmHg (CI: -7.50, 5.50)

				sodium intake:150mmol/day) with fish oil 3. low sodium diet (70mmol/day) plus placebo and olive oil 4. low sodium diet (70mmol/day) plus NaCl tablets (total sodium intake:150mmol/day) with olive oil				combined: Normal sodium period: 158mmol/24hr Low sodium period: 78mmol/24hr	

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Howe et al. (1994)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: low risk Providers: low risk Outcome assessors: low risk	8.2% (but unclear from which group) – unclear risk	No (unclear risk)	No (low risk)	Unclear risk (Cholesterol reported as not changing but exact results not provided)	Bristol Myers Squibb (pharmaceutical company) – unclear risk

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Hypertension Prevention Trial Research Group (1990), USA [20]	Randomised parallel design study	II	Adults (aged 25 – 49 years) with diastolic blood pressure of 76 – 90mmHg	Participants randomly assigned to one of five groups: 1. control (no dietary counselling) - 2. reduced calories (participants with high BMI only) 3. reduced sodium (goal of urinary sodium excretion ≤ 70mmol/day) 4. reduced sodium and calories (participants with high BMI only) (goal of urinary sodium excretion ≤ 70mmol/day) 5. reduced sodium and increased potassium (goal of urinary sodium excretion ≤	Blood pressure (sitting after 5 min rest), mortality also noted.	351 (in groups 1 and 3, n= 841 in whole study)	3 years	Difference in change in urinary sodium between reduced sodium and control groups (sodium – control): -4.2 (SEM: 2.1) mmol/8 hr	Mean difference between reduced sodium and control groups: SBP: 0.1mmHg (SEM: 0.99, CI: -1.84, 2.04) DBP: 0.2mmHg (SEM: 0.71, CI: -1.19, 1.59) Mortality reported as one death each in control and reduced sodium groups (no statistical analysis reported)

				70mmol/day, urinary potassium excretion ≥ 100mmol/day) Note: only groups 1 and 3 used in analysis to avoid confounding effect of calories and potassium					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Hypertension Prevention Trial Research Group (1990)	Unclear risk (method of randomisation not described)	Unclear risk (method of allocation concealment not described)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	10% loss to follow-up (for groups 1 and 3) (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	National Heart, Lung and Blood Institute (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Jablonski et al. (2013), UK [21]	Randomised cross-over study	II	Adults (50 – 79 years), with high-normal or Stage 1 systolic hypertension (SBP: 130 – 159mmHg, DBP: <99mmHg)	All participants were instructed to reduce their dietary sodium intake to ~50mmol/day. Participants were randomised to start one of two study arms: 1. Reduced salt diet with 100mmol sodium/day from NaCl tablets 2. Reduced salt diet with placebo	Blood pressure (supine), total cholesterol, LDL, HDL. Note: vascular endothelial function appears to be the primary outcome	17	5 weeks	Normal sodium diet: 153 ± 27 mmol/day Low sodium diet: 70 ± 30 mmol/day (p<0.001)	SBP: Baseline: 138 ± 7 mmHg Low sodium: 128 ± 10mmHg (p<0.01) Normal sodium: 140 ± 15mmHg DBP: Baseline: 83 ± 7 mmHg Low sodium: 79 ± 6mmHg Normal sodium: 82 ± 6mmHg Total cholesterol: Baseline: 196 ± 27 mg/dL Low sodium: 187 ± 27mg/dL

									Normal sodium: 194 ± 22 mg/dL LDL: Baseline: 123 ± 23 mg/dL Low sodium: 118 ± 21mg/dL Normal sodium: 127 ± 23 mg/dL HDL: Baseline: 52 ± 16 mg/dL Low sodium: 49 ± 16mg/dL Normal sodium: 50 ± 15 mg/dL Lipid data from Graudal, however does not appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Jablonski et al. (2013)	Unclear risk (no description of method of sequence generation)	Unclear risk (method of allocation concealment not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	15% loss to follow-up (prior to completing vascular measurements) – unclear risk	Unclear risk	No (low risk)	Yes (low risk)	National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Kirkendall et al. (1975), USA [18]	Randomised cross-over study	II	Adult males (24 - 47 years), with normotensive BP (below 150/90mmHg)	Participants were randomised to start one of three study arms: 1. Liquid dietary supplement containing 10mEq sodium/day 2. Liquid dietary supplement containing 210mEq sodium/day 3. Liquid dietary supplement containing 410mEq sodium/day	Blood pressure (supine, standing), total cholesterol. Only mean BP (calculated as diastolic plus 40% pulse pressure) reported	8	4 weeks	High sodium diet: 307 ± 56 mEq/24hr Intermediate sodium diet: 159 ± 31 mmol/day Low sodium diet: 10 ± 10 mmHg ($p<0.05$)	Mean BP supine Low sodium: 90 ± 3mmHg Intermediate sodium: 88 ± 7 mmHg High sodium: 90 ± 5 mmHg Total cholesterol: Low sodium: 200 ± 26 mg%/100mL Intermediate sodium: 200 ± 25 mg%/100mL High sodium: 211 ± 29 mg%/100mL

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Kirkendall et al. (1975)	Low risk (modified Latin square design)	Unclear risk (method of allocation concealment not described)	Participants: low risk Providers: unclear risk Outcome assessors: low risk	No loss to follow up (low risk)	Not required (low risk)	No (low risk)	Reported no significant change in BP, but only reported mean BP values	National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
MacGregor et al. (1982), UK [48]	Randomised cross-over study	II	Adults (aged 30-66), with mild to moderate hypertension (SBP: 135 – 185mmHg, DBP: 90 – 110mmHg)	Following dietary instructions to consume a reduced salt diet (with a goal of 60 - 80mmol/day) for 2 weeks, participants were randomly allocated to start one of the two cross-over arms: 1. Reduced salt diet with "slow" sodium supplementation (designed to restore sodium intake to match pt.'s baseline urinary sodium excretion) 2. Reduced salt diet with placebo	Blood pressure (supine and standing), mean arterial pressure Insufficient data in paper to calculate MAP	19	4 weeks	Normal sodium diet: 160 mmHg (estimated from figure, exact values not given) Low sodium diet: 83 $\pm$ 11 mmHg ($p<0.001$)	Mean difference between low sodium diet to normal sodium diet: Seated: SBP: -10mmHg (SEM: 2.76, CI: -15.41, -4.59) DBP: -5mmHg (SEM: 1.76, CI: -8.45, -1.55)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
MacGregor et al. (1982)	Unclear risk (no description of method of sequence generation)	Unclear risk (not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	0% loss to follow-up (low risk)	Not required (low risk)	No (low risk)	Unclear risk (Insufficient data in paper to calculate changes in MAP for group)	Welcome Trust (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
MacGregor et al. (1987), UK [49]	Randomised cross-over study	II	Adults (aged 33 - 71), with hypertension (DBP> 95 mmHg) (mean BP: 162/107mmHg)	All participants were provided with captopril 50mg twice daily for one month. Following this period, participants were instructed to reduce dietary sodium to 70 – 80 mmol/day for two weeks. Participants were then randomised to start one of two cross-over arms: 1. Restricted sodium diet + captopril and 100mmol sodium (NaCl) tablets/day 2. Restricted sodium diet + captopril and placebo	Blood pressure (supine and standing), mean arterial pressure Insufficient data in paper to calculate MAP	15	4 weeks	Normal sodium diet: 183 (SEM: 11) mmHg Low sodium diet: 83 (SEM: 10) mmHg (p<0.001)	Mean difference between low sodium diet to normal sodium diet: Seated: SBP: -13mmHg (SEM: 3.29, CI: -19.45, -6.55) DBP: -9mmHg (SEM: 3.05, CI: -14.98, -3.02)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
MacGregor et al. (1987)	Unclear risk(no description of method of sequence generation)	Unclear risk (not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	0% loss to follow-up (low risk)	Not required (low risk)	No (low risk)	Unclear risk (Insufficient data in paper to calculate changes in MAP for group)	Not stated (unclear risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
MacGregor et al. (1989), UK [17]	Randomised cross-over study	II	Adults (aged 42 - 72), with hypertension (DBP> 90 – 110 mmHg)	Participants were instructed to reduce dietary sodium to 30 – 50 mmol/day for two weeks. Participants were then randomised to start one of three cross-over arms: 1. Restricted sodium diet plus placebo (total 50mmol sodium/day) 2. Restricted sodium diet plus 70mmol NaCl tablets/day and placebos (total 100mmol sodium/day) 3. Restricted sodium diet plus 160mmol NaCl tablets/day (total	Blood pressure (supine and standing), mean arterial pressure (results not reported in paper) Changes in standing BP also not able to be calculated due to insufficient data on baseline levels in paper	20	1 month (n = 15 pts. also followed up for 1 year after study)	200mmol sodium/day arm: 190 (SEM: 11, CI: 168, 212) mmHg 100mmol sodium/day arm: 108 (SEM: 10, CI: 88, 129) mmHg 50mmol sodium/day arm: 49 (SEM: 8, CI: 34, 65) mmHg ($p<0.001$) Note: Groups 2 and 3 used for analysis	Mean results at end of low sodium diet and intermediate sodium diet: <u>SBP:</u> Low: 147mmHg (SEM: 4) Intermediate: 155mmHg (SEM: 3) <u>DBP:</u> Low: 91mmHg (SEM: 2) Intermediate: 95mmHg (SEM: 2)

				200mmol sodium/day) Note: Groups 1 and 3 used for analysis by Graudal (insufficient data in paper to allow manual extraction for excel sheet)					In follow-up 1 year after study completed, SBP was: 142mmHg (SEM: 3), DBP was: 87mmHg (SEM: 2). 24hr urinary sodium excretion was 54mmol/24hr (SEM: 7)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
MacGregor et al. (1989)	Unclear risk (no description of method of sequence generation)	Unclear risk (method of concealment of allocation not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	0% loss to follow-up (low risk)	Not required (low risk)	No (low risk)	High risk (Mean arterial pressure measured but results not reported)	Not stated (company supplied capsules but no indication of funding) – unclear risk

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Mascioli et al. (1991), USA [67]	Randomised cross-over study	II	Adults (aged 30-59), normotensive (SBP: <150mmHg, DBP: 80 – 89mmHg)	Following dietary instructions to consume a reduced salt diet for 8 weeks, participants were randomly allocated to start one of the two cross-over arms: 1. Reduced salt diet with salt supplementation (providing 96 mEq sodium/day) 2. Reduced salt diet with placebo	Blood pressure (seated)	48	4 weeks	Pooled values not given for urinary sodium levels in both diets. Difference between the normal sodium and low sodium periods was reported as 20.2 $\pm$ 3.6 mEq/8hr	Mean difference between low sodium diet to normal sodium diet: SBP: -3.60mmHg (SEM: 0.9, CI: -5.36, -1.84) DBP: -2.30mmHg (SEM: 0.8, CI: -3.87, -0.73)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Mascioli et al. (1991)	Low risk (block randomisation)	Unclear risk (block randomisation but not clear who was responsible etc.)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	4% loss to follow-up (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Maxwell et al. (1984), USA [68]	Randomised parallel design study	II	Obese adults, with hypertension (DBP: ≥ 90mmHg)	Participants were randomised to consume one of two dietary supplements as meal replacements: 1.320 calories/day as 30g of CHO and 45g of protein, plus 600mg calcium, 350mg phosphorus, 150mg magnesium, 100% daily allowance of iron, copper, zinc, and all vitamins. Total potassium intake was 60mEq/day, sodium was 40mEq/day 2. Same dietary supplement with same potassium intake,	Blood pressure (seated)	30	12 weeks	Low sodium supplement: 39 ± 4mEq/24hr Normal sodium supplement: 200 ± 30mEq/24hr Note results are from week 8 of 12 week study, results from week 12 not given	Mean difference between low sodium supplement and normal sodium supplement: SBP: -2mmHg (SEM: 6.72, CI: -15.17, 11.17) DBP: 2mmHg (SEM: 3.84, CI: -5.53, 9.53)

				however sodium was 210mEq/day (via NaCl tablets)					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Maxwell et al. (1984)	Unclear risk (method of randomisation not stated)	Unclear risk (method of randomisation not stated)	Participants: unclear risk Providers: unclear risk Outcome assessors: unclear risk	0% loss to follow-up (low risk)	Not required (low risk)	No (low risk)	Unclear risk (Urinary sodium data only reported for week 8 in paper)	University Medical Research Foundation (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
McCarron et al. (1997), USA [69]	Randomised cross-over study	II	Adults (mean age 51.6 years) with mild to moderate essential hypertension (DBP: 95 – 115mmHg)	For 4 weeks prior to the study starting, participants consumed an ad libitum NaCl diet (100-200mmol/24hr). Following this, over a 4 week period, all participants then received the required amount of isradipine (2.5mg or 5mg/day) to maintain their DBP at <90mmHg. Participants were instructed to consume a low sodium diet (60 – 80mmol/24hr), and were randomised to start one of two study arms: 1. Restricted sodium diet plus supplementary NaCl	Blood pressure (seated after 15 min rest), total cholesterol, LDL, HDL	99	4 weeks	Low sodium period: 120.5 ± 68.9mmol/24hr Normal sodium period: 175.9 ± 68.7 mmol/24hr ($p<0.0001$)	Mean difference between low sodium period and normal sodium period: SBP: -4.90mmHg (SEM: 1.23, CI: -7.31, -2.49) DBP: -2.9mmHg (SEM: 0.81, CI: -4.49, -1.31) Total cholesterol: 8.20 mg/dL (CI: -2.89, 19.29) HDL: 0.10 mg/dL (CI:-3.79, 3.99) LDL: 5.90 mg/dL (CI: -4.36, 16.16) Lipid data from Graudal, does not

				(100mmol/24hr) 2. 1. Restricted sodium diet plus placebo					appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
McCarron et al. (1997)	Low risk (computer generated sequence)	Unclear risk (method of concealment of randomisation not described)	Participants: low risk Providers: low risk Outcome assessors: low risk	2% loss to follow-up (low risk)	Yes (low risk)	No (low risk)	Unclear risk (Reported that creatinine, albumin, haemocrit and haemoglobin were unchanged but did not report specific results)	Sandoz Research Institute, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Meland et al. (1997), Norway [51]	Randomised cross-over study	II	Adults (aged 20-69, mean age:50) with mild to moderate hypertension (mean SBP: 146mmHg, mean DBP: 95mmHg)	Participants were randomly allocated to start one of the two cross-over arms: 1. Moderately reduced salt diet with salt supplementation (providing 50mmol sodium/day) 2. Moderately reduced salt diet with placebo	Blood pressure (seated after 3 min rest), total cholesterol, HDL	16	8 weeks	Low sodium period: 125 (95% CI: 104 – 146) mmol/24hr Normal sodium period: 191 (95% CI: 159 – 223) mmol/24hr (not stated if significantly different)	Mean difference between low sodium period and normal sodium period: SBP: -4mmHg (SEM: 2.47, CI: -8.84, 0.84) DBP: -3mmHg (SEM: 1.36, CI: -5.67, -0.33) Total cholesterol: 0.0 mg/dL (CI: -27.32, 27.32) HDL: -3.80 mg/dL (CI:-14.47, 6.87) Lipid data from Graudal, however does not appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Meland et al. (1997)	Unclear risk (method of randomisation not stated)	Unclear risk (method of concealment of randomisation not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	0% loss to follow-up (low risk)	Not required (low risk)	No (low risk)	Yes (low risk)	Research Council of Norway (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Meland et al. (2009), Norway [50]	Randomised parallel design study	II	Adults (aged 20-70) with hypertension (SBP: >160mmHg, DBP: >90mmHg) (on antihypertensive drug treatment)	All participants received dietary advice to consume a moderate salt-restricted diet, then randomised into one of two groups: 1. Moderately reduced salt diet with salt supplementation (providing 50mmol sodium/day) 2. Moderately reduced salt diet with placebo	Blood pressure (seated after 2 min rest), total cholesterol, HDL	46	8 weeks	Low sodium period: 83 mmol/24hr Normal sodium period: 126 mmol/24hr (p=0.11) Note values calculated from table of mean differences	Mean difference between low sodium period and normal sodium period: SBP: -5mmHg (SEM: 3.79, CI: -12.43, 2.43) DBP: -5mmHg (SEM: 1.38, CI: -7.70, -2.30) Total cholesterol: -0.2 mmol/L (CI: -0.65, 0.25) (from WHO) HDL: -0.05 mmol/L (CI:-0.25, 0.15) (from WHO)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Meland et al. (2009)	Unclear risk (method of randomisation not stated)	Low risk (randomisation list concealed from investigators)	Participants: Low risk Providers: Low risk Outcome assessors: unclear risk	0% loss to follow-up (low risk)	Not required (low risk)	No (low risk)	Yes (low risk)	University of Bergen, Solstrandsfondet (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Melander et al. (2007), Sweden [52]	Randomised cross-over study	II	Adults (mean age 53±11 years), without known hypertension (mean SBP: 139mmHg, mean DBP: 86.3mmHg)	All participants received all meals and drinks throughout the study duration to provide a total daily intake of 50mmol of sodium/salt (NaCl). Participants were randomly allocated to start one of the two cross-over arms: 1. Provided food and drinks plus 100mmol NaCl/day 2. Provided food and drinks plus placebo	Blood pressure (supine after 30 min rest), 24hr ambulatory BP	39	4 weeks	Low sodium period: 50.7 $\pm$ 17.3 mmol/24hr Normal sodium period: 140 $\pm$ 39.5 mmol/24hr ($p<0.0001$)	Mean difference between low sodium period and normal sodium period: Supine: SBP: -6mmHg (SEM: 1.18, CI: -8.31, -3.69) DBP: -2.3mmHg (SEM: 0.86, CI: -3.99, -0.61)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Melander et al. (2007)	Unclear risk (method of randomisation not stated)	Unclear risk (method of allocation concealment not stated)	Participants: low risk Providers: low risk Outcome assessors: unclear	15% loss to follow-up (and unclear from which study period) – unclear risk	No (high risk)	No (low risk)	Yes (low risk)	Swedish Medical Research Council and other research bodies (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Morgan et al. (1978), Australia [27]	Randomised parallel design study	II	Adult males (more than 50 years), with borderline hypertension (DBP: 95 – 109mmHg)	Participants randomly divided into four groups: 1. Control group (no treatment) 2. Dietary advice to reduce sodium intake to 70 – 100mmol/day 3. chlorothiazide (500 mg twice daily) 4. propranolol (up to 480 mg/day) and a diuretic Note: only groups 1 and 2 used in this analysis	Blood pressure (supine), mortality BP also measured standing, however insufficient data reported in paper to analyse	62	2 years	Restricted sodium group: 157 (SEM: 7) mmol/24hr Control group : 180 (SEM: 9) mmol/24hr ($p<0.05$)	Mean difference between restricted and control sodium diet: Supine: SBP: -1.5mmHg (SEM: 5.55, CI: -12.38, -9.38) DBP: -7mmHg (SEM: 2.77, CI: -12.43, -1.57) Mortality: 1 participant in the restricted sodium group died due to MI (compared to 0 participants in control, statistical analysis not conducted)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Morgan et al. (1978)	Unclear risk (method of randomisation not stated)	Unclear risk (method of allocation concealment not stated)	Participants: low risk Providers: high risk Outcome assessors: low risk	7.5% (low risk)	No (unclear risk)	No (low risk)	Unclear risk (Reported that biochemical values were similar at the end of the study but did not report values.)	Department of Veterans Affairs and National Heart Foundation of Australia (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Morgan et al. (1981), Australia [28]	Randomised parallel design study	II	Adult (aged 28 – 50 years), with hypertension (DBP: ≥90 - <105mmHg)	Participants randomly divided into four groups: 1. Control group (no treatment) 2. Advised to reduce dietary sodium to 70mmol/day Note study also included a group of pts. with DBP >105mmHg, control group was treated with chlorothiazide. As it is not possible to isolate the effect of sodium in these participants, they were not included	Blood pressure (supine after 10 mins, standing after 5 mins) Note: data on standing BP not given in sufficient detail to calculate	12 (in sodium and control arms only) (6 males, 6 females) Due to the way data was presented, it had to be divided by gender	8 weeks	Males Restricted sodium group: 78 ± 8 mmol/24hr (p<0.001 compared to start) Control group: 170 ± 15 mmol/24hr Females Restricted sodium group: 58 ± 7 mmol/24hr (p<0.001 compared to start) Control group:	Males DBP: Control pre-diet: 96mmHg (SD not given, stated to be 'less than ± 7') Control post-diet: 94mmHg Sodium restriction pre-diet: 97mmHg Sodium restriction post-diet: 87mmHg (p<0.01 compared to start value, p<0.05 compared to control) Females

				in this analysis (results given separately in the paper).				125 ± 10 mmol/24hr	DBP: Control pre-diet: 94mmHg (SD not given, all SD's stated to be 'less than ± 7') Control post-diet: 92mmHg Sodium restriction pre-diet: 95mmHg Sodium restriction post-diet: 89mmHg ($p<0.01$ compared to start value)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Morgan et al. (1981)	Unclear risk (method of randomisation not stated)	Unclear risk (method of allocation concealment not stated)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	None reported (low risk)	Not required (low risk)	No (low risk)	Unclear risk (Did not report changes in SBP in sufficient detail to be able to calculate for each group (same for standing SBP and DBP))	Department of Veterans Affairs and National Health and Medical Research Council (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Morgan et al. (1987), Australia [26]	Randomised parallel design study	II	Adult males (aged 50 – 65 years), with hypertension treated with anti-hypertensive medication	Participants randomly divided into two groups: 1. normal diet 2. Reduced sodium diet (between 50 – 75mmol/day)	Blood pressure (supine, standing) Note: results not provided for standing BP	20	6 months	Restricted sodium group: 75 ± 7 mmol/24hr ($p<0.005$ compared to start) Control group: 155 ± 12 mmol/24hr ($p<0.005$ compared to control group)	SBP: Control initial (prior to medication cessation: 143 ± 5mmHg Control post drug cessation (week 1): 158 ± 6 mmHg Control post-diet: 178 ± 7 mmHg Sodium restriction pre-diet: 143 ± 5 mmHg Sodium restriction post drug cessation (week 1): 152 ± 7 mmHg Sodium restriction post-diet: 155 ± 5mmHg ($p<0.05$ compared to change in control)

									DBP: Control initial (prior to medication cessation: 81 ± 2mmHg Control post drug cessation (week 1): 91 ± 5 mmHg Control post-diet: 98 ± 3 mmHg Sodium restriction pre-diet: 83 ± 2 mmHg Sodium restriction post drug cessation (week 1): 86 ± 3 mmHg Sodium restriction post-diet: 90 ± 2mmHg ($p<0.05$ compared to change in control)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Morgan et al. (1987)	Unclear risk (method of randomisation not stated)	Unclear risk (method of allocation concealment not stated)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	None reported (low risk)	Not required (low risk)	No (low risk)	Unclear risk (Change in standing BP not reported)	Department of Veterans Affairs and National Health and Medical Research Council (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Nestel et al. (1993), Australia [29]	Randomised parallel design study	II	Older adults aged 60 – 79 years, normotensive (mean SBP: 124.5mmHg, mean DBP: 72.5mmHg)	Participants were all advised to reduce dietary sodium intake and consume a diet low in fat, and linoleic acid. Dietary sodium targets were 80mmol/day men, 70mmol/day women. Low sodium foods were provided Participants were then randomised into one of 4 groups: Group 1: low sodium, with 1g dihommo-gammalinolenic acid Group 2: added sodium (participants consumed 80mmol/day sodium	Blood pressure (seated after at least 5 min rest)	66 (n=30 females, n= 36 males) Breakdown not shown for different oils	6 weeks	Females: Normal sodium period: 150 ± 45 mmol/24hr Low sodium period: 77 ± 33 mmol/24hr Males: Normal sodium period: 162 ± 49 mmol/24hr Low sodium period: 106 ± 49	Females: SBP: Normal sodium period (pre): 118 ± 14mmHg Normal sodium period (post): 125 ± 17mmHg Low sodium period (pre): 121 ± 12mmHg Low sodium period (post): 118 ± 9mmHg DBP: Normal sodium period (pre): 68 ± 9mmHg Normal sodium period (post): 72 ± 9mmHg Low sodium period (pre):

				(NaCl) supplements) + 1g DGLA Group 3: Low sodium, with 1g safflower oil Group 4: added sodium + safflower oil Note: due to insufficient data on sodium excretion and numbers in each oil group, groups 1 and 3 combined (low sodium) and groups 2 and 4 combined (high sodium)				mmol/24hr (Note paper does not separate male and female data into oils used)	68 ± 9mmHg Low sodium period (post): 67 ± 9mmHg <u>Males:</u> SBP: Normal sodium period (pre): 128 ± 12mmHg Normal sodium period (post): 130 ± 10mmHg Low sodium period (pre): 129 ± 10mmHg Low sodium period (post): 127 ± 10mmHg DBP: Normal sodium period (pre): 75 ± 8mmHg Normal sodium period (post): 77 ± 9mmHg Low sodium period (pre): 80 ± 7mmHg Low sodium period (post):

									77 ± 6mmHg Study reports oil did not affect blood pressure

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Nestel et al. (1993), Australia	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation)	Participants: low risk Providers: low risk Outcome assessors: low risk	5.2% (low risk)	Yes (low risk)	No (low risk)	High risk (Cholesterol, HDL cholesterol, and triglycerides not reported)	Hoffmann La Roche (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Nowson et al. (2003), Australia [30]	Randomised cross-over study	II	Adults (aged 33 – 74 years), both normotensive (n=92) (mean SBP: 121.9mmHg, mean DBP: 78.1mmHg) and hypertensive (n=16)(mean SBP: 151.7mmHg, mean DBP: 151.7mmHg, 85.7mmHg)	Participants received dietary advice to reduce dietary sodium (to 50mmol/day) and to increase potassium intake (to a target of 80mmol/day). Participants were then randomly allocated to start one of the two cross-over arms: 1. reduced sodium diet plus 120mmol sodium supplements /day 2. reduced sodium diet plus placebo	Blood pressure (clinic - seated after a 5 min rest, home – after 10 min rest, and 24hr ambulatory BP)	92 normotensive pts. (data on change in outcomes not given for hypertensive pts.)	64 weeks	Low sodium period: 50.9 $\pm$4.1 mmol/24hr Normal sodium period: 138.7 $\pm$ 4.0 mmol/24hr (p=0.001)	Mean difference between low sodium period and normal sodium period (NT pts. only): Seated (office): SBP: 0.4mmHg (SEM: 0.8, CI: -1.17, 1.97) DBP: 0.0mmHg (SEM: 0.6, CI: -1.18, 1.18)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Nowson et al. (2003)	Low risk (random number generator used)	Low risk (Examiners blinded to allocation, randomisation procedure stratified by household)	Participants: low risk Providers: low risk Outcome assessors: low risk	15.6% loss to follow-up (and unclear from which study period) – unclear risk	No (high risk)	No (low risk)	High risk (data on changes in outcomes not reported for hypertensive pts.)	National Health and Medical Research Committee and the Rebecca Cooper Foundation (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Parker et al. (1990), Australia [31]	Randomised parallel design study	II	Adult males(aged 20 – 70 years), with stable, treated hypertension (SBP: 125-180mmHg, DBP<115mmHg)	Participants consumed a low sodium diet (60mmol/day) plus 100mmol NaCl tablets/day for a 2 week run-in period. They were then randomly assigned to one of four groups: 1. low sodium diet plus 100mmol NaCl tablets/day and usual alcohol intake 2. low sodium diet plus placebo and usual alcohol	Blood pressure (supine and standing)	59 (normal alcohol: n= 28, low alcohol: n= 31)	4 weeks	All participants: Low sodium diet: 68.6 ± 8.0 mmol/24hr Normal sodium diet: 141.7 ± 7.6 mmol/24hr Regular alcohol participants: Low sodium diet: 70 mmol/24hr Normal sodium diet: 130 mmol/24hr (estimated from figure) Low alcohol participants:	Mean difference between low sodium period and normal sodium period: Supine: Regular alcohol participants: SBP: -0.1mmHg (SEM: 2.72, CI: -5.43, 5.23) DBP: 0.8mmHg (SEM: 1.57, CI: -2.28, 3.88) Low alcohol participants: SBP: 2.2mmHg (SEM: 2.15, CI: -

				intake 3. low sodium diet plus 100mmol NaCl tablets/day and low alcohol beer 4. low sodium diet plus placebo and low alcohol beer				Low sodium diet: 60 mmol/24hr Normal sodium diet: 140 mmol/24hr (estimated from figure)	2.01, 6.41) DBP: 0.5mmHg (SEM: 1.17, CI: -1.79, 2.79)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Parker et al. (1990)	Unclear risk (no description of method of sequence generation)	Unclear risk (no description of method of concealment of allocation, stratified for age, BMI, BP, alcohol consumption)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	6.3% (low risk)	No (unclear risk)	No (low risk)	Unclear risk (Reported that creatinine, potassium, calcium and magnesium were unchanged but did not report specific results. HDL not separately reported for different sodium levels)	National Heart Foundation of Australia, Royal Perth Hospital Medical Research Foundation (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Parijs et al (1973), Belgium [53]	Randomised cross-over study	II	Adult (mean age: 41.2 ± 8.21 years), with hypertension (SBP:>140mmHg, DBP>90mmHg)	Participants consumed a regular diet and took 4 placebo tablets/day for a 2 -4 week run-in period. They were then randomly assigned to one of four groups: 1. Regular diet + placebo 2. moderate sodium restriction + placebo (participants instructed to avoid all foods with added sodium and select low sodium bread) (only groups 1 and 2 used by Graudal in analysis) 3. regular diet + diuretics (100mg spironolactone + 100mg	Blood pressure (supine and standing, measured office and home) Home BP not able to be calculated due to insufficient information on baseline data in paper	17 (outpatient values only available for n=15 participants in low sodium, placebo group)	4 weeks	Low sodium period: 92.8 ± 41.8 mmol/24hr Normal sodium period: 191.1 ± 61.2 mmol/24hr (p<0.0005) (note data is for placebo periods only)	Mean difference between low sodium period and normal sodium period : Supine: SBP: -6.7mmHg (SEM: 9.75, CI: -25.81, 12.41) DBP: 3.2mmHg (SEM: 5.91, CI: -8.38, 14.78)

				hydrochlorothiazide) 4. moderate sodium restriction + diuretics					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Parijs et al (1973)	Unclear risk (Intervention group decided by odd or even number; manner in which numbers were generated and given to participants not clear)	High risk (Allocation was based on odd/even number already known by trialist)	Participants: High risk Providers: High risk Outcome assessors: unclear risk	22.7% (high risk)	No (high risk)	No (low risk)	Unclear risk (Home BP not able to be calculated due to insufficient information on baseline data in paper)	Not stated (unclear risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Puska et al. (1983), Finland [54]	Randomised parallel design study	II	Adults (aged 30-50 years), mixed normotensive and hypertensive	Participants were randomised to either: 1. low fat diet (25% energy from fat) 2. low salt diet (reduced from 192mmol-77mmol/day, following advice from dietitians & provision of low salt items) 3. control (maintain usual diet) (note only groups 2 and 3 used in analysis by Graudal)	Blood pressure (seated after 5 min rest)	107 (n=72 in groups 2 and 3)	6 weeks	<u>All participants:</u> Low sodium period: 77 <u>+</u> 5mmol/24hr ($p<0.001$) Normal sodium period: 167 <u>+</u> 8mmol/24hr	Mean difference between low sodium period and normal sodium period: SBP: 0.1mmHg (CI:-6.28, 6.48) DBP: -0.7mmHg (CI: -5.22, 3.82)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Puska et al. (1983)	Unclear risk (randomisation method not stated)	Unclear risk (method of concealment of allocation not described, stratified by locality and age)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	6.1% (low risk)	No (unclear risk)	No (low risk)	Yes (low risk)	US Department of Agriculture (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Redon-Mas et al. (1993), Spain [55]	Randomised parallel design study	II	Adults (aged 18-80 years), mild-moderate hypertension (DBP:90 – 114mmHg)	All participants consumed a reduced salt diet for 2 weeks. Participants were then randomised to one of two groups: 1. Low salt diet plus slow release verapamil once a day 2. Unrestricted salt diet plus slow release verapamil once a day	Blood pressure (seated after 2 min rest), 24 hr. ambulatory BP (only in 61 pts.)	418	4 weeks	Low sodium diet: 81.9 ± 26.6mmol/24hr (NS) Normal sodium diet: 186.0 ± 36.3mmol/24hr ($p<0.001$ compared to low salt run-in period)	Mean difference between low sodium diet and normal sodium diet: SBP: 1mmHg (SEM: 1.94, CI: -2.80, 4.80) DBP: 1.9mmHg (SEM: 0.94, CI: -0.06, 3.74)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Redon-Mas et al. (1993), Spain	Unclear risk (randomisation method not stated)	Unclear risk (method of concealment of allocation not described, stratified by locality and age)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	>45% (many excluded due to compliance cut-offs) – high risk	No (high risk)	No (low risk)	Yes (low risk)	Not stated (unclear risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Richards et al. (1984), New Zealand [37]	Randomised cross-over study	II	Adults (aged 19-52 years) with mild essential hypertension (140/90 – 180/105mm Hg)	Participants were randomised to start one of three cross-over arms: 1. control diet (180mmol sodium/day and 60mmol potassium/day) 2. Sodium restricted diet (80mmol sodium/day and 60mmol potassium/day) 3. Potassium supplemented diet (200mmol potassium/day) (not used in this analysis)	Blood pressure (supine after 20 min rest, standing after 5 min), 24 hr. ambulatory pressure (during wash-out period) Note change in standing BP and 24hr ambulatory BP not able to be calculated as insufficient data in paper	12	4 - 6 weeks	Low sodium diet: 100mmol/24hr Normal sodium diet: 200mmol/24hr ($p<0.001$) Note: estimated from figure	Mean difference between low sodium period and normal sodium period: SBP: -4mmHg (SEM: 2.79, CI: -9.47, 1.47) DBP: -3mmHg (SEM: 2.26, CI: -7.43, 1.43)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Richards et al. (1984)	Unclear risk (randomisation method not stated)	Unclear risk (method of concealment of allocation not described)	Participants: high risk Providers: high risk Outcome assessors: unclear risk	25% (high risk)	No (high risk)	No (low risk)	Unclear risk (insufficient information provided for calculation of changes in standing and 24hr ambulatory BP)	National Heart Foundation, Medical Research Council of New Zealand (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Ruppert et al. (1993), Germany [56]	Randomised cross-over study	II	Adults (aged 27 – 75 years) normotensive (<140/90mmHg) who had previously participated in one week study of NaCl and placebo (cannot be included in current analysis due to duration)	All participants were instructed to consume a diet containing 85mmol sodium/day. Participants were then randomised to start one of two cross-over arms: 1. Restricted sodium diet plus NaCl capsules (total daily sodium intake: 200mmol/day) 2. Restricted sodium diet plus placebo (total daily sodium intake: 85mmol/day)	Blood pressure (supine after 30 min rest), mean arterial pressure, total cholesterol, LDL, HDL	25	4 weeks	Low sodium diet: 82 $\pm$ 3.4mmol/24hr Normal sodium diet: 199.6 $\pm$ 5.3 mmol/24hr ($p<0.001$)	Mean difference between low sodium period and normal sodium period: SBP: 1.70mmHg (CI: -4.98, 8.38) DBP: 1mmHg (CI: -3.47, 5.47) Cholesterol: 0.00mmol/L (CI: -0.46, 0.46) HDL:-0.04mmol/L (CI: -0.23, 0.15) LDL: 0.13mmol/L (CI: -0.28, 0.54) (All values from WHO)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Ruppert et al. (1993)	Unclear risk (randomisation method not stated)	Unclear risk (method of concealment of allocation not described)	Participants: low risk Providers: low risk Outcome assessors: unclear risk	0% (low risk)	Not required (low risk)	No (low risk)	Yes (low risk)	Not stated (unclear risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
DASH 2001 - Sacks et al. (2001) - Vollmer et al. (2001) - Harsha et al. (2004) USA [16, 75, 79]	Randomised cross-over study	II	Adults (22 years and older), normotensive and hypertensive (SBP: 120 – 159mmHg, DBP: 80 – 95mmHg)	Participants consumed a high sodium (150mmol/day) control diet for a 2 week run-in period. They were then randomised to either a control diet (usual USA style diet) or DASH. Participants in both diet groups were then randomised to start one of three cross-over arms: 1. Low sodium (50mmol/day) plus DASH or	SBP (primary outcome), DBP (BP measured seated), serum total cholesterol, HDL and LDL	390	30 days	Control diet: Low sodium diet: 64 ± 37mmol/24hr Normal sodium diet (Intermediate dietary period): 106 ± 44 mmol/24hr DASH diet: Low sodium diet: 67 ± 46mmol/24hr Normal sodium diet (Intermediate dietary period): 107 ± 52	Mean difference between low sodium period and normal sodium period (intermediate period) Control diet: SBP: -4.6mmHg (CI: -5.9, -3.2) DBP: -2.4mmHg (CI: -3.3, -1.5) DASH diet: SBP: -1.7mmHg (CI: -3.0, -0.4) DBP: -1.0mmHg (CI: -1.9, -0.1) Control diet: Cholesterol: 0.07mmol/L (CI: -0.02, 0.15)

				control diet 2. Intermediate sodium (100mmol/day) plus DASH or control diet 3. High sodium (150mmol/day) plus DASH or control diet				mmol/24hr	HDL: -0.01mmol/L (CI: -0.03, 0.01) LDL: 0.07mmol/L (CI: 0.00, 0.15) <u>DASH diet:</u> Cholesterol: 0.04mmol/L (CI: -0.04, 0.13) HDL: 0.01mmol/L (CI: -0.02, 0.03) LDL: 0.01mmol/L (CI: -0.06, 0.09)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
DASH 2001 - Sacks et al. (2001) - Vollmer et al. (2001) - Harsha et al. (2004)	Low risk (computer generated sequence used)	Low risk (Allocation occurred at central location)	Participants: High risk Providers: high risk Outcome assessors: low risk	5.4% loss to follow-up (low risk)	Yes (low risk)	No (low risk)	Yes (low risk)	National Heart, Lung and Blood Institute, General Clinical Research Center Program of the National Center for Research Resources (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
TOHP, Phase I -Whelton et al. (1992) Kumanyika et al. (1993) -Whelton et al. (1997a) USA [70, 80, 81]	Randomised parallel design study	II	Adults (30 – 54 years), with high normal diastolic blood pressure (mean: 124.8/83.7mmHg in sodium reduction group and 125.1/83.9mmHg in control)	Participants were randomly assigned to either lifestyle (18 months) or supplement interventions (6 months each, compared with placebo): Lifestyle 1: weight reduction (group and individual education) Lifestyle 2: sodium reduction (group and individual education) Lifestyle 3: stress management (group and individual education) Lifestyle 4: usual care Supplement 1: calcium Supplement 2: magnesium	BP (seated after 5 min rest) (note DBP was primary outcome, SBP secondary outcome)	744 (in sodium reduction and control groups, n=2182 for total study)	18 months	Mean difference in the change in urinary sodium excretion between groups (active – control): -43.86 (CI: -56.88, -30.84) mmol/24hr (p<0.01)	Mean difference between sodium reduction and control period: SBP: -1.7mmHg (SEM: 0.59, CI: -2.86, -0.54) DBP: -0.8mmHg (SEM: 0.42, CI: -1.62, 0.02)

				Supplement 3: fish oil Supplement 4: potassium Note: Lifestyle 2 and 4 only are used in this analysis					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
TOHP, Phase I -Whelton et al. (1992) Kumanyika et al. (1993) -Whelton et al. (1997a)	Unclear risk (method of randomisation not described)	Low risk (Concealment of allocation at a central location)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	<5% loss to follow-up (low risk)	Yes (low risk)	No (low risk)	Yes (low risk)	National Heart, Lung, and Blood Institute, National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
TOHP, Phase II -Whelton et al. (1997b) USA [71]	Randomised parallel design study	II	Moderately overweight adults (30 – 54 years), with high normal diastolic blood pressure (mean DBP:86.1mmHg in sodium reduction group and 85.1mmHg in control)	Participants were randomly assigned to one of four treatment groups: 1. weight loss (goal achievement of desirable body weight or mean weight loss of at least 4.5kg) (group and individual education) 2. sodium reduction (goal sodium intake of 70 - 80mmol/day or less) (group and individual education) 3. weight loss plus sodium reduction (same goals as individual sodium and weight loss groups) (group and individual education)	BP (seated) (note DBP was primary outcome, SBP secondary outcome)	1190	36 – 48 months	Mean difference in the change in urinary sodium excretion between groups (active – control): -40.4 $\pm$ 5.7 ($p<0.001$)	Mean difference between sodium reduction and control period: SBP: -1mmHg (SEM: 0.52, CI: -2.02, 0.02) DBP: -0.5mmHg (SEM: 0.4, CI: -1.28, 0.28)

				4. usual care (control) Note: Groups 2 and 4 only are used in this analysis					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
TOHP, Phase II	Unclear risk (method of randomisation not described)	Low risk (Concealment of allocation at a central location)	Participants: unclear risk Providers: high risk Outcome assessors: low risk	<5% loss to follow-up (low risk)	Yes (low risk)	No (low risk)	Yes (low risk)	National Heart, Lung, and Blood Institute, National Institutes of Health (low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Schorr et al. (1996), Germany [62]	Randomised, placebo controlled double-blind cross over trial	II	Normotensive adults (aged 60-72 years)	Participants were all counselled to reduce dietary salt intake to <100mmol/day prior to interventions (participants remained on low salt diet for study duration) Participants randomised in cross-over order to consume 1.5L of a mineral water with the following composition: 1. NaCl rich (sodium 84.5mmol/l,	Resting BP, lipids, 24 hour ambulatory BP	16	4 weeks per treatment	<u>24 hour urinary excretion data:</u> 1.High NaCl mineral water treatment: 175.2±29.6mmol/day 2. High sodium bicarbonate mineral water treatment: 124.7±17.0mmol/day 3. Low	<u>Comparison between high sodium chloride and placebo treatment (from Graudal which compared high sodium chloride treatment and placebo):</u> SBP: -1mmHg (SEM:2.7, 95%CI: -6.29, 4.29) DBP: 0mmHg (SEM: 1.73, 95%CI: -3.39, 3.39) Insufficient BP data to work out change between bicarbonate rich treatment and either SBP, DBP or 24 hour ambulatory BP (data given as day and night time 24 hour ambulatory BP or a figure without further detail) Change in Total Cholesterol between high NaCL mineral

				chloride 63.7mmol/l, bicarbonate 21.9mmol/l) 2. Sodium bicarbonate rich: (sodium 39.3mmol/l, chloride 6.5mmol/l, bicarbonate <0.02mmol/l 3. Placebo (sodium, chloride & bicarbonate <0.02mmol/l) *note: study excluded from WHO SLR due to sodium level not the only thing to change between interventions (e.g. Differing bicarbonate levels), but included in				sodium & bicarbonate (placebo), mineral water treatment: 104.6±21.7mmol/day	water and placebo treatments: 5 mg/dl (95%CI:-20.93, 30.93) Change in HDL-cholesterol 3mg/dl (95%CI: -2.97, 8.97) Change in LDL cholesterol: 7mg/dl (95%CI: -15.59, 29.59) Baseline total cholesterol: 237±30mg/dl Total cholesterol following low sodium (placebo) treatment: 233±33mg/dl Total cholesterol following high sodium bicarbonate treatment: 234±35mg/dl Total cholesterol following high sodium chloride treatment: 228±41mg/dl Baseline LDL cholesterol: 173±30mg/dl LDL cholesterol following low sodium (placebo) treatment:

				Graudal review					172±32mg/dl LDL-C following high sodium bicarbonate treatment: 154±45mg/dl LDL-C following high sodium chloride treatment: 165±33mg/dl HDL-C at baseline: 40±105mg/dl HDL-C following low sodium (placebo) treatment: 36±9mg/dl HDL-C following high sodium bicarbonate treatment: 36±9mg/dl HDL-C following high sodium chloride treatment: 33±8mg/dl *Lipid data from Graudal does not appear to be based on change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Schorr et al. (1996)	Unclear (no description of method of sequence generation)	Unclear (not described)	Participants: blinded, low risk Providers: blinded, low risk Outcome assessors: unclear	19.2% (loss of 5), data only analysed for completers/those considered compliant, high risk	No, high risk	No (Low risk)	Unclear, some data missing (e.g. Baseline ambulatory BP)	Unclear, not specified

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Sciarrone et al (1992), Australia [36]	Randomised parallel, double blind placebo controlled trial (with a 2x2 factorial design)	II	95 hypertensive adults, some on medication (mean BP 137/83mmHg) – now considered high normal BP), mean age: 53.5 years N=79 participants were undergoing anti-hypertensive treatment and were asked not to change medication for	Participants prescribed a low sodium diet (target <60mmol/day) and randomised to one of two groups: 1. Low sodium, low fat, high fibre diet (<60mmol sodium/day; 30% energy from fat, P:S ratio=1, 50-50g fibre/day) 2. Low sodium, normal fat, normal fibre (<60mmol sodium/day; 40% energy from fat; P:S	SBP (supine & resting), DBP (supine & resting), Total cholesterol, HDL cholesterol, LDL cholesterol	95 (4 drop outs but included data for all participants)	8 weeks	<u>24 hour urinary sodium excretion:</u> <u>Low sodium diet:</u> 52.0mmol/24 hours (CI: 42.9, 61.2) (data provided grouped both low sodium arms together) <u>Normal sodium diet:</u> 133.9mmol/24 hours (CI: 125.4, 142) (data provided grouped both normal sodium	<u>Data grouped according to sodium intake:</u> <u>Change in relevant outcomes:</u> <u>Normal sodium (n=21) & low sodium (n=27) groups (both low fat/high fibre dietary prescription):</u> SBP: -7.5mmHg (95%CI: -13.19, -1.81) DBP: -1.4mmHg (95%CI: -5.54, 2.74) <u>Total cholesterol:</u> 0.00mmol/l(95%CI: -0.54, 0.54) HDL-C: -0.10mmol/l

			study duration	ration=0.3, 15g fibre/day) Half of each treatment group were then randomised to receive either 100mmol NaCl tablets per day or a placebo				arms together)	(95%CI: -0.21, 0.01) <u>LDL-C:</u> 0.10mmol/l (95%CI: -0.37, 0.57) <u>Normal sodium (n=24) & low sodium (n=19) groups (both normal fat/normal fibre dietary prescription):</u> SBP: -4.3mmHg (95%CI: -9.85, 1.25) DBP: 0.80mmHg (95%CI: -2.70, 4.30) <u>Total cholesterol:</u> -0.10mmol/l (95%CI: -0.43, 0.23) <u>HDL-C:</u> -0.10mmol/l 95%CI: -0.25, 0.05) <u>LDL-C:</u> -0.10mmol/; (95%CI: -0.52, 0.32) Insufficient data to calculate standing BP

									*data from WHO SLR

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Sciarrone et al (1992)	Unclear (no description of method of sequence generation)	Unclear (not described)	Participants: blinded, Low risk Providers: blinded, Low risk Outcome assessors: unclear	<5%, Low risk	No, unclear	No (Low risk)	Yes (Low risk)	NHMRC, Royal Perth Hospital research funding

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Silman et al (1983), UK [58]	Randomised controlled parallel design trial	II	Adults aged 50-64 years, with DBP 95-104mmHg for past 13 months, not taking antihypertensive	Participants were randomised to either: <u>Low sodium diet:</u> (aim 100mmol sodium/day) based on dietary advice <u>Control:</u> Standard monitoring of BP, regular health check-ups, no advice related to sodium restriction	SBP, DBP (method described as 'the standard way')	28 participants randomised	1 year	Low sodium diet group: At 12 months: 117mmol/24 hours (based on available urinary data for 7 out of 12 participants), mean change from baseline: -26.4mmol/24 hours Control group: At 12 months: 159.5mmol/24 hours (based on available urinary data for 11 out of 16 participants), mean change from baseline:	Mean changes between low sodium and control groups: SBP: 3.5mmHg (SEM: 11.39, 95%CI: -18.82, 25.82) DBP: 0.5mmHg (SEM: 4.91, 95%CI: -9.12, 10.12)

								+26.35mmol/day	

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Silman et al (1983)	Unclear (no description of method of sequence generation)	Unclear (no description of method of concealment of allocation)	Participants: not blinded as given advice but blinded to purpose of urinary sodium excretion data (unclear) Providers: not blinded Outcome assessors: unclear	<10%, low risk	Unclear, used weighted mean average of available data	No (Low risk)	Yes (Low risk)	Unclear, assume hospital funding

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Singer et al (1991), UK [63]	Double-blind cross over placebo controlled randomised cross over study	II	Adults with essential hypertension (mean age 53±2.5 years), taking captopril (50mg twice daily) and hydrochlorothiazide (diuretic) 25mg/day for at least a month prior to commencement of study	Whilst remaining on medications (and following 1 month run in phase of usual diet), participants were instructed by a dietitian to reduce dietary sodium (aim 80-100mmol/day) for two weeks prior to being randomised to one of two treatments: 1. Low sodium/placebo: participants remain on low sodium diet and take 10x placebo tablets/day 2. High sodium: participants remain	SBP, DBP, MAP	21	4 weeks per treatment	24 hour urinary sodium excretion: 1. Low sodium/placebo treatment: 104±11mmol/day 2. High sodium treatment: 195±14mmol/day	Comparison between change in placebo and high sodium treatments (supine BP): SBP: -9mmHg (SEM: 3, 95%CI: -14.88, -3.12) DBP: -3(SEM: 3, 95%CI: -14.88, -3.12) Insufficient baseline data to calculate change in MAP between treatments

				on low sodium diet and take 10x slow sodium tablets per day (total 100mmol/day)					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Singer et al (1991)	Unclear (no description of method of sequence generation)	Unclear (not described)	Participants: blinded, low risk Providers: Blinded, low risk Outcome assessors: unclear	0% drop outs, Low risk	Low risk (no drop outs)	No (Low risk)	Unclear, baseline MAP data not provided	Unclear (not specified)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Suckling et al. (2010), UK (*conference abstract) [61]	Randomised controlled cross over study	II	Adults with type 2 diabetes or impaired glucose tolerance, with untreated normal or high BP	Participants were randomised to the following interventions: 1. Reduced sodium diet + (unspecified amount of slow sodium tablets/day) 2. Reduced sodium diet + placebo (control group)	SBP, DBP (measured in a clinic), 24 hour ambulatory BP, urinary albumin excretion	46	6 weeks	24 hour urinary sodium excretion for: High sodium group: 165±9mmol/day Control (placebo) group: 117±10mmol/day	Mean difference between groups: SBP: -4.3mmHg (95% CI:-9.71, 1.11) (from WHO SLR) DBP: -1.6mmHg (95%CI: -4.79, 1.59) (From WHO SLR) • No baseline data to calculate change in ambulatory BP

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Suckling et al (2010) *conference abstract	Unclear (not enough information in abstract)	Unclear (not enough information in abstract)	Participants: unclear Providers: Unclear Outcome assessors: Unclear	Unclear	unclear	Unclear	Unclear	Unclear

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Swift (2005), UK [57]	Randomised, double blind, placebo controlled cross over trial	II	African or African – Caribbean descent (mean age 50±10 years), hypertensives not taking medication (SBP≥140mmHg, DBP ≥90mmHg) Mean SBP 156±12, mean DBP 100±7mmHg	Following a run in period on usual diet, then advice to reduce salt intake to 5g/day, Participants were randomised to one of two groups: 1.Reduced sodium (low salt diet + placebo tablets) 2. Higher sodium (low salt diet + 120mmol/day slow sodium tablets) in a cross over design	Blood pressure (measured semi-supine by a nurse), 24 hour ambulatory BP	46 randomised, 40 completed trial	4 weeks	urinary sodium excretion in study groups: <u>Higher sodium group:</u> 169±73mmol/24 hours <u>Placebo (lower sodium) group:</u> 89±52mmol/24 hours Mean fall in urinary sodium excretion was 78±62mmol.24 hours (P<0.001)	Mean changes between low sodium and higher sodium groups (based on supine BP): SBP: -8.0mmHg (SEM: 2.06, 95%CI: -12.04, -3.96) DBP: -3mmHg (SEM: 1.11, 95%CI: -5.18, -0.82) *no baseline 24 hour ambulatory BP available to calculate change

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Swift et al (2005)	Unclear (method of randomisation not described)	Low risk (pharmacy conducted)	Participants: blinded, Low risk Providers: blinded to allocation, Low risk Outcome assessors: unclear	7 lost (1 during run-in phase, 6 following randomisation), 14% (low risk)	Only reported data from participants that completed the study, but unlikely to affect results, Low risk	No (Low risk)	unclear, reported baseline total cholesterol, triglycerides but no data post intervention, also 24hr ABP baseline data not provided	Placebo & slow sodium tablets provided by CIBA, unlikely conflict, Low risk(low risk)

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Van Berge-Landry (2004), USA [73]	Randomised cross over study	II	Middle aged adults with mild, borderline hypertension (not on medication for duration of trials) (BP range >140/190mmHg-<160/105mmHg –Grade 1– grade 2)	Participants were randomised to either: 1. Low sodium diet: target <40mmol/day 2. High sodium diet: target >225mmol/day Participants also maintained sodium intakes of: 120-160mmol/day during the first and third 4 week periods All sodium targets were achieved	BP, SBP, MAP, total cholesterol	48	4 weeks (4x 4 week intervention periods)	Mean 24 hour urinary sodium excretion: Low sodium diet: 24±13mmol/day High sodium diet: 309±88mmol/day	Change in SBP between low sodium & higher sodium diets: -16mmHg (SEM: 1.51, 95%CI: -18.96-13.04) Change in DBP between diets: -8mmHg (SEM: -10.04, 95%CI: -5.96) Insufficient baseline data to calculate change in MAP Change in total cholesterol between low sodium & high sodium diets: 3mg/dl(95%CI: -11.82, 17.82) (from Graudal)

				through intensive counselling with a dietitian					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Van Berge-Landry et al. (2004)	Unclear (no description of method of sequence generation)	Unclear (not described)	Participants: received dietary counselling, high risk Providers: not blinded, high risk Outcome assessors: Unclear	Low risk	Low risk	No (Low risk)	Yes (low risk)	NIH

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Watt et al, (1983), Wales [59]	Double blind, randomised cross over trial	II	Adults aged between 31-64, with stable hypertension (mean BP 144/93 mmHg) not taking anti-hypertensive medication	Participants were provided with dietary advice and access to foods to reduce total sodium intake for the duration of the intervention periods (8 weeks in total), participants were randomised to either: Higher sodium diet: Provided with 8x slow sodium tablets/day (total 80mmol/sodium) Or Placebo group:	SBP, DBP (measured seated), MAP	18 (2 drop outs, data presented for those that completed only)	4 weeks (per intervention)	Mean 24 hour urinary excretion for the higher sodium diet: 143mmol/day Mean 24 hour urinary excretion for the placebo group: 87mmol/day	Mean changes between placebo and higher sodium groups: SBP: -0.5mmHg (SEM: 1.5, 95%CI: -3.44, 2.44) DBP: -0.3mmHg (SEM: 0.8, 95% CI: -1.87, 1.27) MAP data entered into excel spreadsheet (SD data available)

				Provided with 8x placebo tablets					

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Watt et al. (1983)	Unclear (methods of randomisation not described)	Unclear	Participants: Low risk Providers: Low risk Outcome assessors: unclear	Low risk (two participants lost one from each group)	Unclear	No (Low risk)	Yes (Low risk)	British Heart Foundation

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Watt et al. (1985), Wales [60]	Double blind, randomised cross over trial	II	Adults aged 22-23 years, normotensive, and determined from a previous trial involving their parents to be either at a low genetic risk of hypertension (based on their parent's BP) or a high risk of hypertension	All participants were randomly allocated to a cross-over arm for 4 weeks each intervention: 1. 80mmol slow-sodium tablets/day 2. Placebo tablets All participants were provided with dietary advice to reduce sodium intake for the duration of the study	SBP, DBP (measured seated), MAP	66 (statistical analyses were conducted for the two groups: 1. Individuals identified as being at low risk of hyper-tension (n=31) 2. Those identified as being at high risk of hyper-tension (n=35)	4 weeks each intervention arm	Data presented based on the two groups: Group 1 (low risk for HT): 128.4mmol sodium/24 hours during high sodium phase & 68.4mmol sodium/24 hours during low sodium phase Group 2 (high risk for HT): 130.6mmol sodium/24 hours during high sodium phase & 56.3mmol sodium/24 hours during low sodium phase	Mean changes between placebo and higher sodium group (for low risk HT group 1): SBP: -0.5mmHg (SEM: 0.82, 95% CI: -2.11, 1.11) DBP: 1.4mmHg (SEM: 0.9, 95%CI: -0.36, 3.16) (for high risk HT group 2): SBP: -1.4mmHg (SEM:0.74, 95%CI: -

									2.85,0.05) DBP: 1.2mmHg (SEM: 0.93, 95%CI: -0.62,3.02)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Watt et al. (1985), Wales	Unclear (no description of method of sequence generation)	Low risk (statistician completed separate from researchers)	Participants: Low risk Providers: Low risk Outcome assessors: unclear	Low risk (9 drop outs from original recruited, but authors state Low risk statistical power with remaining participants	Unclear, no intention to treat but did additional analysis according to level of compliance	No (Low risk)	Yes (Low risk)	British Heart Foundation & the Medical Research Council

Summary table

Citation & location	Study design	NHMRC level of evidence	Population	Intervention	Outcomes measured relevant to research question	Sample size	Intervention duration	Compliance to sodium target (urinary data)	Results
Weir et al. (2010), USA [72]	Randomised open-label, blinded end point multi-centre, cross over study	II	Adults with hypertension (range SBP ≥135-160mmHg), aged 16-60 years, taking 300mg/day aliskiren (direct renin inhibitor for treatment of HT)	Participants were randomised to intervention groups in a cross over design (no washout period) 1. Low sodium diet (≤100mmol sodium/day), dietitian advice provided 2. High sodium diet (≥200mmol sodium/day), dietitian advice provided	Resting BP, 24 hour ambulatory BP, including mean arterial diastolic and systolic (maDBP, MASBP)	132	4 weeks per intervention	<u>Mean 24 hour urinary sodium excretion:</u> <u>Low sodium diet:</u> 84.8mEq sodium/ 24 hours <u>High sodium diet:</u> 207.6mEq sodium/24 hours (P<0.0001)	Difference in resting SBP between groups: -9.4mmHg (0.97SEM, 95%CI: -11.3, -7.50) Difference in resting DBP between groups: -5.7mmHg (0.66SEM, 95%CI: -6.99, -4.41) maDBP was lower with the lower sodium diet compared to the higher sodium diet (LSM difference: 5.7mmHg, 95%CI, 4.4-6.9, p<.0001) (raw data entered into excel sheet) maSBP was lower with the low sodium diet compared with the high sodium diet (LSM difference: 9.4mmHg, 95%ci: 7.5-11.4) (raw data

									entered into excel sheet)

Key features for bias assessment of randomised trials

Citation	Method of randomisation	Allocation concealment	Blinding	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Weir et al. (2010)	Unclear (no methods given)	High risk (no method of concealment used)	Participants: Not blinded, high risk Providers: not blinded, high risk Outcome assessors: not blinded, high risk	<15% Low risk (loss to follow up equal between groups), low risk	Unclear	No (Low risk)	All outcomes reported, low risk	Novartis Pharmaceuticals Corporation, unclear

Appendix 6: Risk of bias summary charts and tables

The risk of bias summary charts and tables are for included literature according to health outcomes

Table 1: Brief summary of bias assessment (GRADE) – SBP (total group)

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Alli et al. (1991)	?	?	?	-	?	-	+	+	+	+
Andersson et al. (1984)	?	?	?	-	?	+	+	+	+	+
ANHMRC DSSMC* (1986)	?	?	?	-	?	+	+	+	?	+
ANHMRC DSSMC* (1989)	?	?	?	+	?	+	+	+	?	+
TONE Appel et al. (2001)	?	?	?	-	?	?	+	+	?	+
Arroll et al. (1995)	?	?	?	-	+	?	-	+	+	+
Benetos et al (1992)	?	?	+	+	?	+	?	+	+	+
Cappuccio et al. (1997)	+	+	+	+	?	+	?	+	+	+
Carney et al. (1991)	?	?	+	+	?	+	+	+	?	?
Cobiac et al. (1992)	?	?	+	+	+	+	+	+	+	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Dodson et al. (1989a) (parallel design study)	+	?	?	-	+	+	?	+	+	?
Dodson et al. (1989a) (crossover design study	+	?	+	+	+	-	-	+	+	?
Dubbert et al. (1995)	+	?	?	-	?	-	-	+	?	+
Erwteman et al. (1984)	?	?	-	-	+	?	-	+	?	?
Fagerberg et al (1984)	?	?	-	-	?	?	-	+	+	+
Fotherby et al (1993) and Fotherby et al (1997)	?	?	+	+	?	+	?	+	+	+
Gates et al. (2004)	?	?	+	+	?	+	+	+	+	+
Gillies et al. (1984)	?	?	?	-	?	?	-	+	?	?
Grobbee et al. (1987)	?	?	+	+	?	+	?	+	+	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
He et al. (2009)	+	+	+	+	+	+	?	+	+	+
Howe et al. (1994)	?	?	+	+	+	?	?	+	?	?
Hypertension Prevention Trial Research Group (1990)	?	?	?	-	+	+	?	+	+	+
Jablonski et al. (2013)	?	?	+	+	?	?	?	+	+	+
MacGregor et al. (1982)	?	?	+	+	?	+	+	+	?	+
MacGregor et al. (1987)	?	?	+	+	?	+	+	+	?	?
MacGregor et al. (1989)	?	?	+	+	?	+	+	+	-	?
Mascioli et al. (1991	+	?	+	+	?	+	?	+	+	+
Maxwell et al. (1984)	?	?	?	?	?	+	+	+	?	+
McCarron et al. (1997	+	?	+	+	+	+	+	+	?	+
Meland et al. (1997)	?	?	+	+	?	+	+	+	+	+
Meland et al. (2009)	?	+	+	+	?	+	+	+	+	+
Melander et al.	?	?	+	+	?	?	-	+	+	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
(2007)										
Morgan et al. (1978)	?	?	+	-	+	+	?	+	?	+
Morgan et al. (1987)	?	?	?	-	+	+	+	+	?	+
Nestel et al. (1993)	?	?	+	+	+	+	+	+	-	+
Nowson et al. (2003)	+	+	+	+	+	?	-	+	?	+
Parker et al. (1990)	?	?	+	+	?	+	?	+	?	+
Parijs et al (1973)	?	-	-	-	?	-	-	+	?	?
Puska et al. (1983)	?	?	?	-	+	+	?	+	+	+
Redon-Mas et al. (1993)	?	?	?	-	+	-	-	+	+	?
Richards et al. (1984)	?	?	-	-	?	-	-	+	?	+
Ruppert et al. (1993)	?	?	+	+	?	+	+	+	+	?
DASH 2001	+	+	-	-	+	+	+	+	+	+
TOHP, Phase I	?	+	?	-	+	+	+	+	+	+
TOHP, Phase II	?	+	?	-	+	+	+	+	+	+
Swift et al (2005)	?	+	+	+	?	+	+	+	?	+
Silman et al (1983)	?	?	?	-	?	+	?	+	+	?

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Watt et al. 1983	?	?	+	+	?	+	?	+	+	+
Watt et al 1985	?	+	+	+	?	+	+	+	+	+
Suckling et al (2010)	?	?	?	?	?	?	?	?	?	?
Weir (2010)	?	-	-	-	-	+	?	+	+	?
Van Berge-Landry (2004)	?	?	-	-	?	+	+	+	+	+
Schorr et al. (1996)	?	?	+	+	?	-	-	+	?	?
Singer et al (1991)	?	?	+	+	?	+	+	+	?	?
Sciarrone et al (1992)	?	?	+	+	?	+	?	+	+	+
Dickinson et al (2014)	+	+	-	+	+	-	-	+	+	+

Legend: '+' = low risk of bias, '?' = unclear risk of bias, '-' = high risk of bias

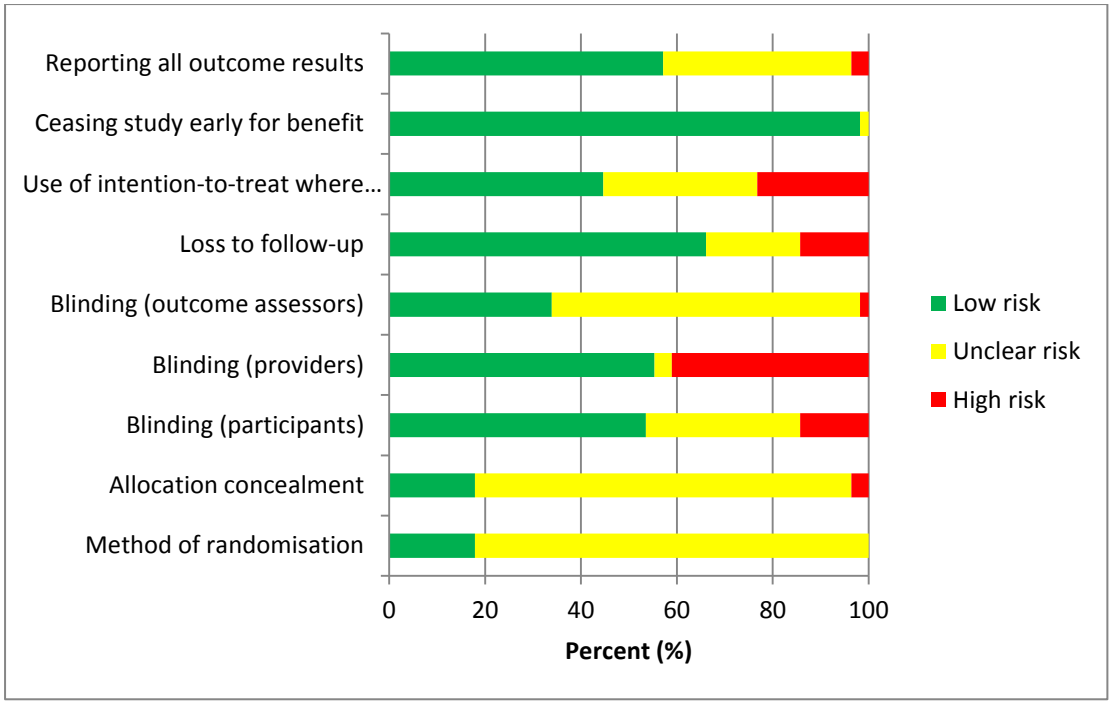

Figure 1: Risk of bias assessment summary, resting systolic blood pressure

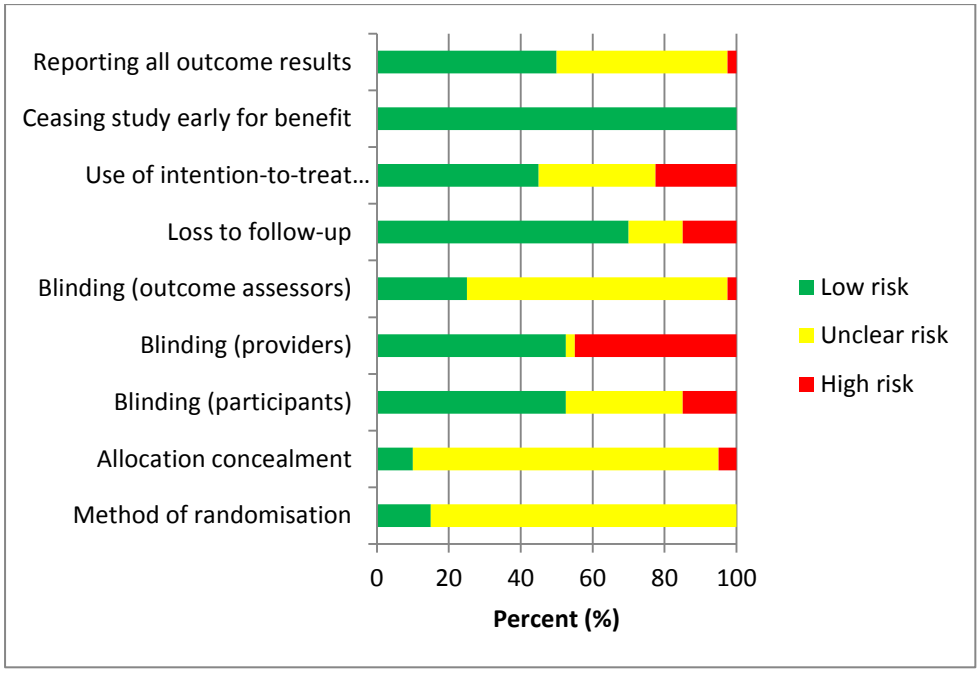

Figure 2: Risk of bias assessment summary, resting systolic blood pressure (hypertensive participants)

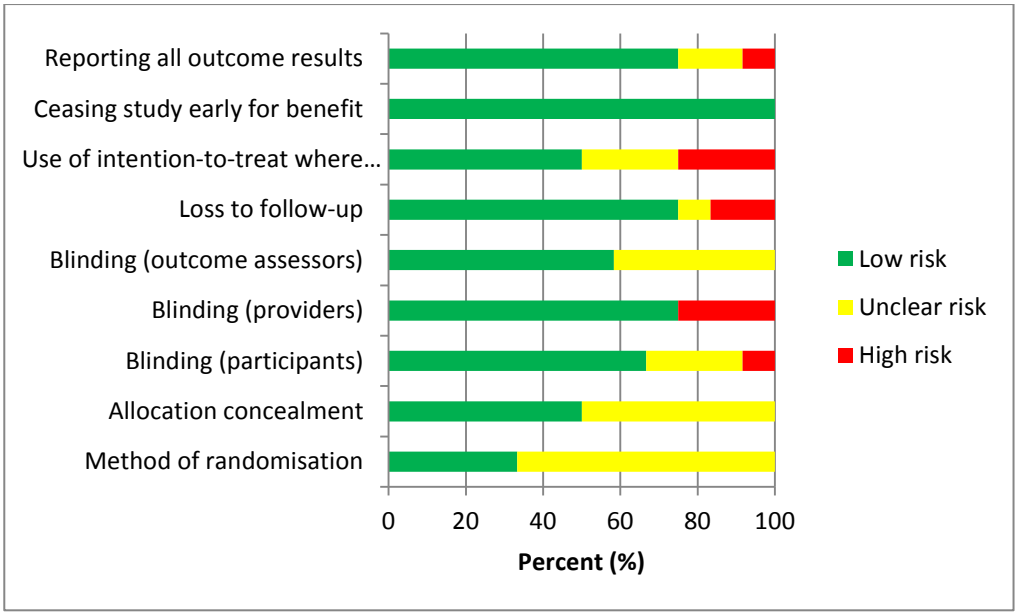

Figure 3: Risk of bias assessment summary, resting systolic blood pressure (normotensive participants)

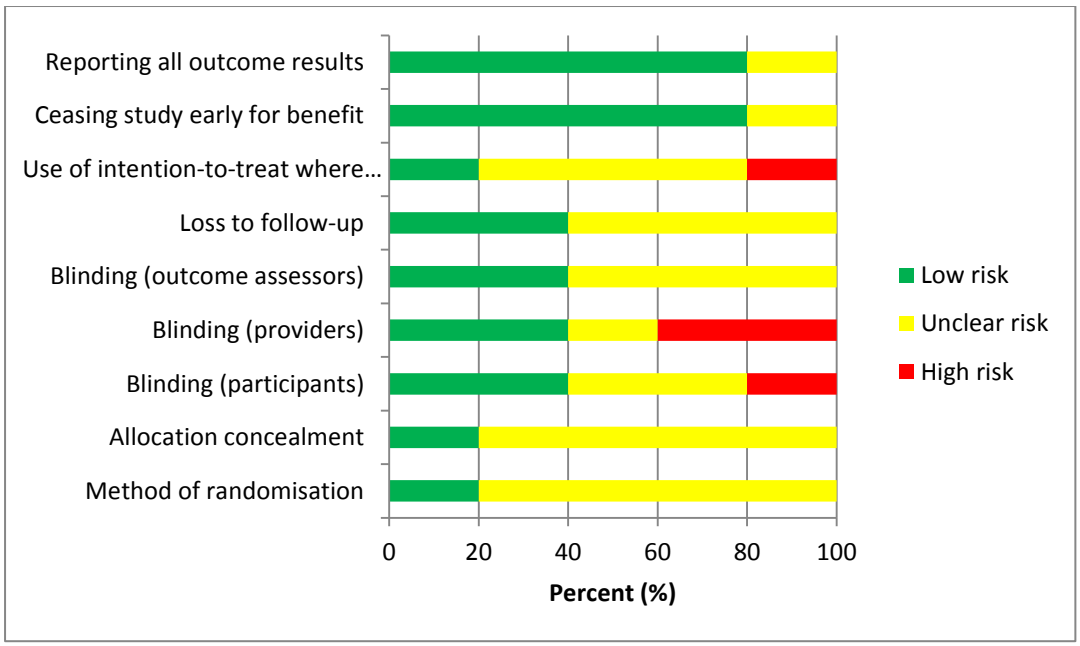

Figure 4: Risk of bias assessment summary, resting systolic blood pressure (studies involving both hypertensive and normotensive participants)

Table 2: Brief summary of bias assessment (GRADE) – DBP (total group)

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Alli et al. (1991)	?	?	?	-	?	-	+	+	+	+
Andersson et al. (1984)	?	?	?	-	?	+	+	+	+	+
ANHMRC DSSMC (1986)	?	?	?	-	?	+	+	+	?	+
ANHMRC DSSMC (1989)	?	?	?	+	?	+	+	+	?	+
TONE Appel et al. (2001)	?	?	?	-	?	?	+	+	?	+
Arroll et al. (1995)	?	?	?	-	+	?	-	+	+	+
Benetos et al (1992)	?	?	+	+	?	+	?	+	+	+
Cappuccio et al. (1997)	+	+	+	+	?	+	?	+	+	+
Carney et al. (1991)	?	?	+	+	?	+	+	+	?	?
Cobiac et al. (1992)	?	?	+	+	+	+	+	+	+	+
Dodson et al. (1989a) (parallel design study)	+	?	?	-	+	+	?	+	+	?
Dodson et al. (1989a) (crossover design study	+	?	+	+	+	-	-	+	+	?

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Dubbert et al. (1995)	+	?	?	-	?	-	-	+	?	+
Erwteman et al. (1984)	?	?	-	-	+	?	-	+	?	?
Fagerberg et al (1984)	?	?	-	-	?	?	-	+	+	+
Fotherby et al (1993) and Fotherby et al (1997)	?	?	+	+	?	+	?	+	+	+
Gates et al. (2004)	?	?	+	+	?	+	+	+	+	+
Gillies et al. (1984)	?	?	?	-	?	?	-	+	?	?
Grobbee et al. (1987)	?	?	+	+	?	+	?	+	+	+
He et al. (2009)	+	+	+	+	+	+	?	+	+	+
Howe et al. (1994)	?	?	+	+	+	?	?	+	?	?
Hypertension Prevention Trial Research Group (1990)	?	?	?	-	+	+	?	+	+	+
Jablonski et al. (2013)	?	?	+	+	?	?	?	+	+	+
MacGregor et al.	?	?	+	+	?	+	+	+	?	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
(1982)										
MacGregor et al. (1987)	?	?	+	+	?	+	+	+	?	?
MacGregor et al. (1989)	?	?	+	+	?	+	+	+	-	?
Mascioli et al. (1991	+	?	+	+	?	+	?	+	+	+
Maxwell et al. (1984)	?	?	?	?	?	+	+	+	?	+
McCarron et al. (1997)	+	?	+	+	+	+	+	+	?	+
Meland et al. (1997)	?	?	+	+	?	+	+	+	+	+
Meland et al. (2009)	?	+	+	+	?	+	+	+	+	+
Melander et al. (2007)	?	?	+	+	?	?	-	+	+	+
Morgan et al. (1978)	?	?	+	-	+	+	?	+	?	+
Morgan et al. (1981)	?	?	?	-	+	+	+	+	?	+
Morgan et al. (1987)	?	?	?	-	+	+	+	+	?	+
Nestel et al. (1993)	?	?	+	+	+	+	+	+	-	+
Nowson et al. (2003)	+	+	+	+	+	?	-	+	?	+
Parker et al. (1990)	?	?	+	+	?	+	?	+	?	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Parijs et al (1973)	?	-	-	-	?	-	-	+	?	?
Puska et al. (1983)	?	?	?	-	+	+	?	+	+	+
Redon-Mas et al. (1993)	?	?	?	-	+	-	-	+	+	?
Richards et al. (1984)	?	?	-	-	?	-	-	+	?	+
Ruppert et al. (1993)	?	?	+	+	?	+	+	+	+	?
DASH 2001	+	+	-	-	+	+	+	+	+	+
TOHP, Phase I	?	+	?	-	+	+	+	+	+	+
TOHP, Phase II	?	+	?	-	+	+	+	+	+	+
Swift et al (2005)	?	+	+	+	?	+	+	+	?	+
Silman et al (1983)	?	?	?	-	?	+	?	+	+	?
Watt et al. 1983	?	?	+	+	?	+	?	+	+	+
Watt et al 1985	?	+	+	+	?	+	+	+	+	+
Suckling et al (2010)	?	?	?	?	?	?	?	?	?	?
Weir (2010)	?	-	-	-	-	+	?	+	+	?
Van Berge-Landry (2004)	?	?	-	-	?	+	+	+	+	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Schorr et al. (1996)	?	?	+	+	?	-	-	+	?	?
Singer et al (1991)	?	?	+	+	?	+	+	+	?	?
Sciarrone et al (1992)	?	?	+	+	?	+	?	+	+	+
Dickinson et al (2014)	+	+	-	+	+	-	-	+	+	+

Legend: '+' = low risk of bias, '?' = unclear risk of bias, '-' = high risk of bias

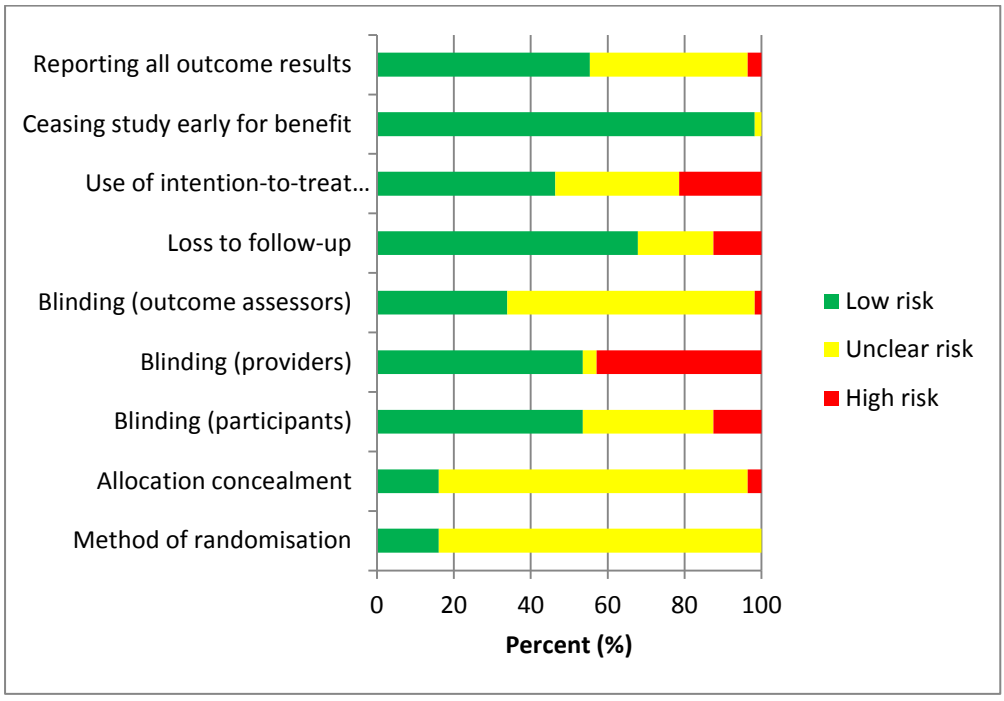

Figure 5: Risk of bias assessment summary, resting diastolic blood pressure

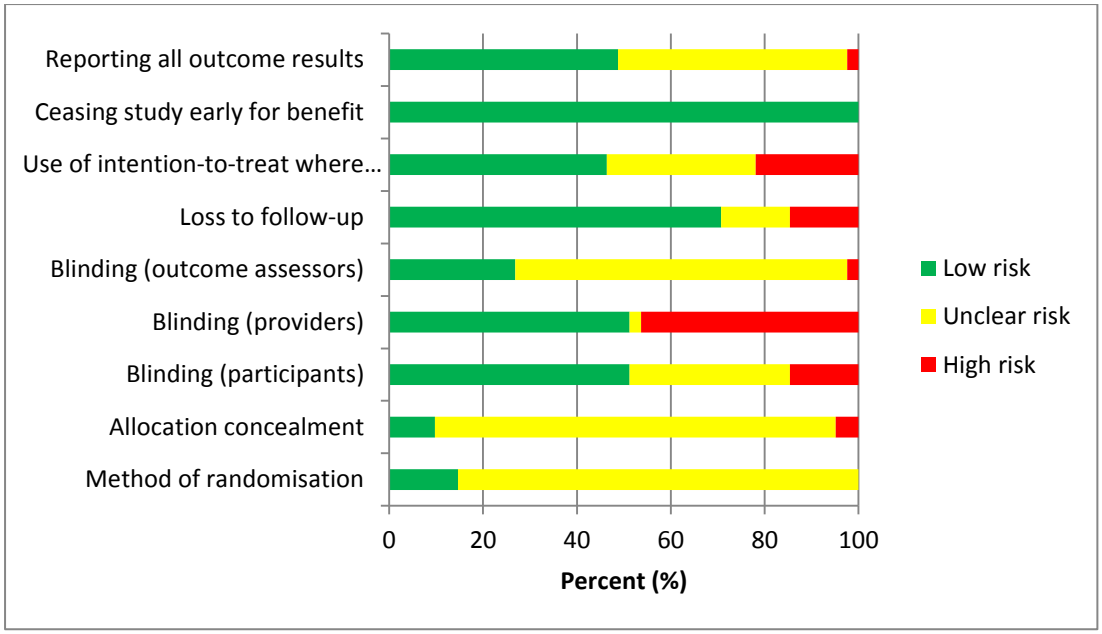

Figure 6: Risk of bias assessment summary, resting diastolic blood pressure (hypertensive participants)

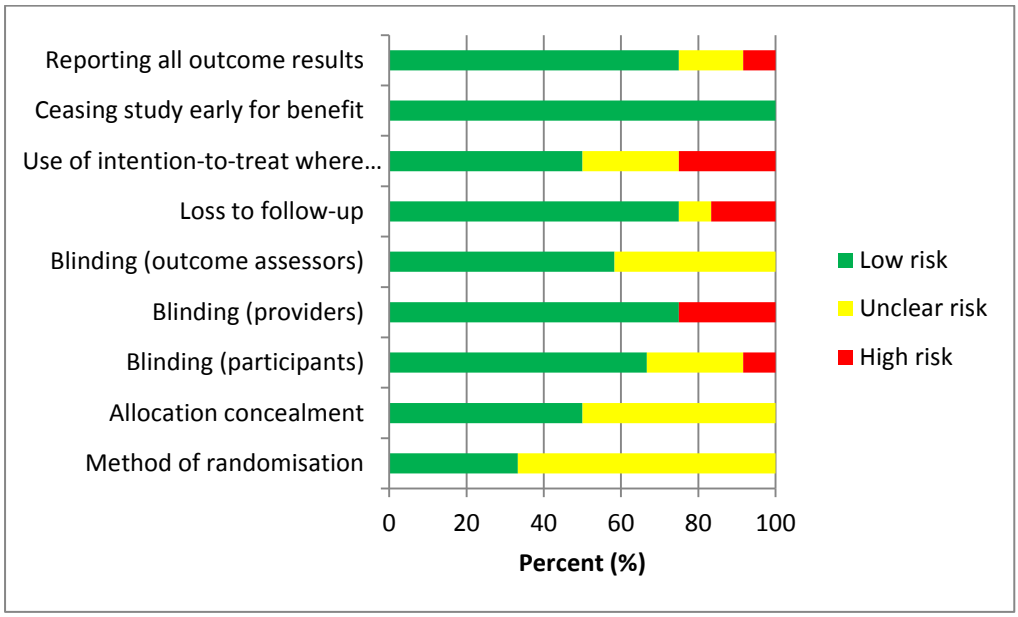

Figure 7: Risk of bias assessment summary, resting diastolic blood pressure (normotensive participants)

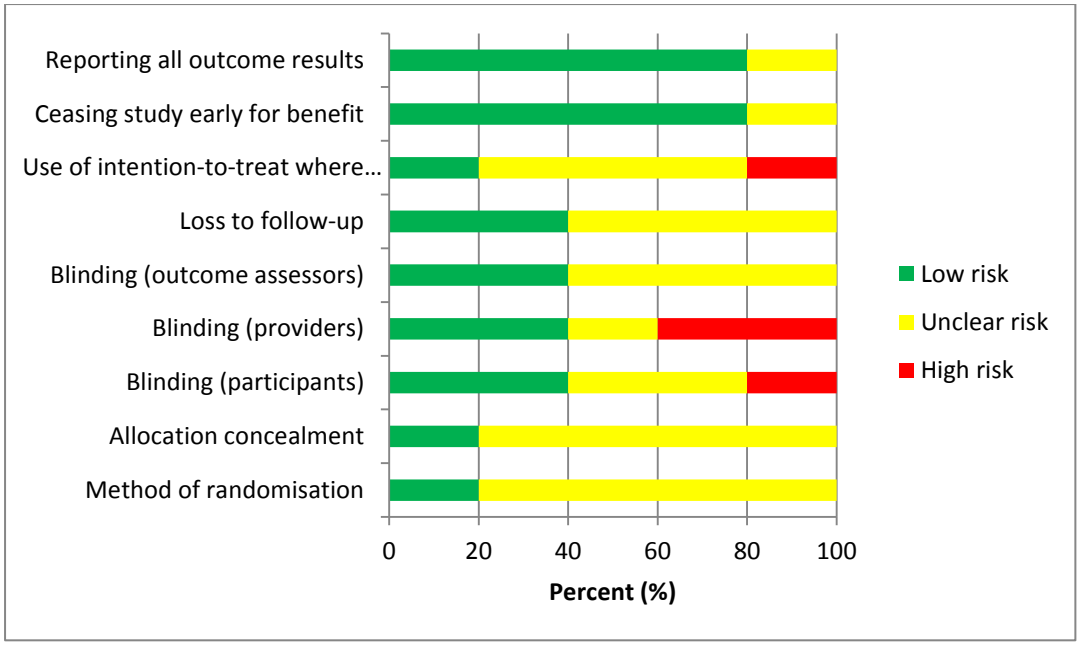

Figure 8: Risk of bias assessment summary, resting diastolic blood pressure (studies involving both hypertensive and normotensive participants)

Table 3: Brief summary of bias assessment (GRADE) – total cholesterol

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Cappuccio et al. (1997)	+	+	+	+	?	+	?	+	+	+
Erwteman et al. (1984)	?	?	-	-	+	?	-	+	?	?
Fotherby et al (1993) and Fotherby et al (1997)	?	?	+	+	?	+	?	+	+	+
Gates et al. (2004)	?	?	+	+	?	+	+	+	+	+
Grobbee et al. (1987)	?	?	+	+	?	+	?	+	+	+
Jablonski et al. (2013)	?	?	+	+	?	?	?	+	+	+
McCarron et al. (1997	+	?	+	+	+	+	+	+	?	+
Meland et al. (1997)	?	?	+	+	?	+	+	+	+	+
Meland et al. (2009)	?	+	+	+	?	+	+	+	+	+
Ruppert et al. (1993)	?	?	+	+	?	+	+	+	+	?
DASH 2001	+	+	-	-	+	+	+	+	+	+
Van Berge-Landry (2004)	?	?	-	-	?	+	+	+	+	+

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Schorr et al. (1996)	?	?	+	+	?	-	-	+	?	?
Sciarrone et al (1992)	?	?	+	+	?	+	?	+	+	+
Kirkendall et al. (1975)	+	?	+	?	+	+	+	+	?	+

Legend: '+' = low risk of bias, '?' = unclear risk of bias, '-' = high risk of bias

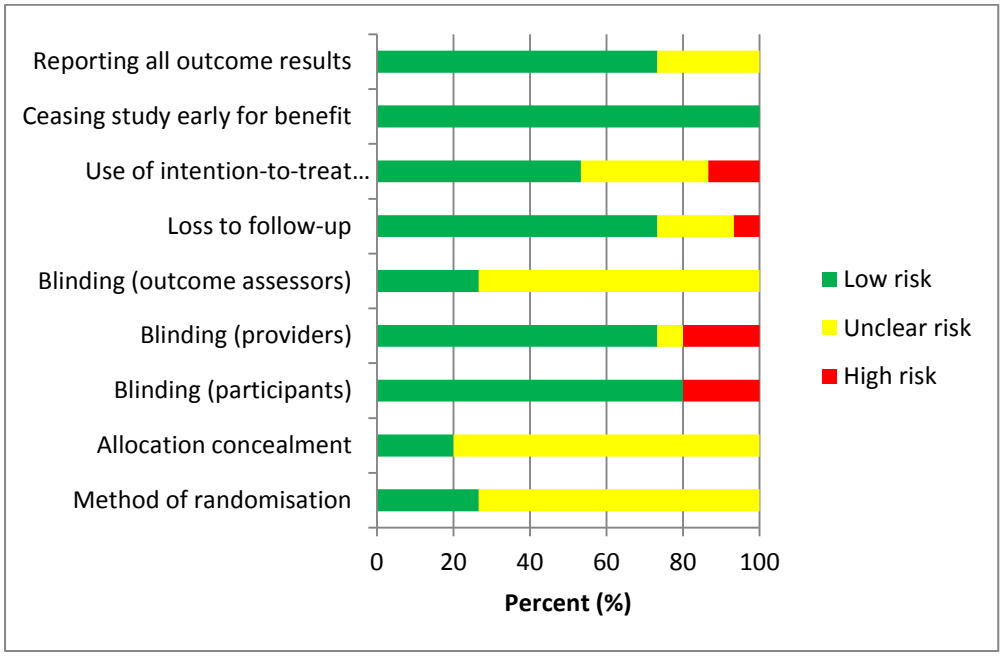

Figure 9: Risk of bias assessment summary, total cholesterol

Table 4: Brief summary of bias assessment (GRADE) – HDL cholesterol

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Fund-ing source
Erwteman et al. (1984)	?	?	-	-	+	?	-	+	?	?
Fotherby et al (1993) and Fotherby et al (1997)	?	?	+	+	?	+	?	+	+	+
Gates et al. (2004)	?	?	+	+	?	+	+	+	+	+
Jablonski et al. (2013)	?	?	+	+	?	?	?	+	+	+
McCarron et al. (1997	+	?	+	+	+	+	+	+	?	+
Meland et al. (1997)	?	?	+	+	?	+	+	+	+	+
Meland et al. (2009)	?	+	+	+	?	+	+	+	+	+
Ruppert et al. (1993)	?	?	+	+	?	+	+	+	+	?
DASH 2001	+	+	-	-	+	+	+	+	+	+
Schorr et al. (1996)	?	?	+	+	?	-	-	+	?	?
Sciarrone et al (1992)	?	?	+	+	?	+	?	+	+	+

Legend: '+' = low risk of bias, '?' = unclear risk of bias, '-' = high risk of bias

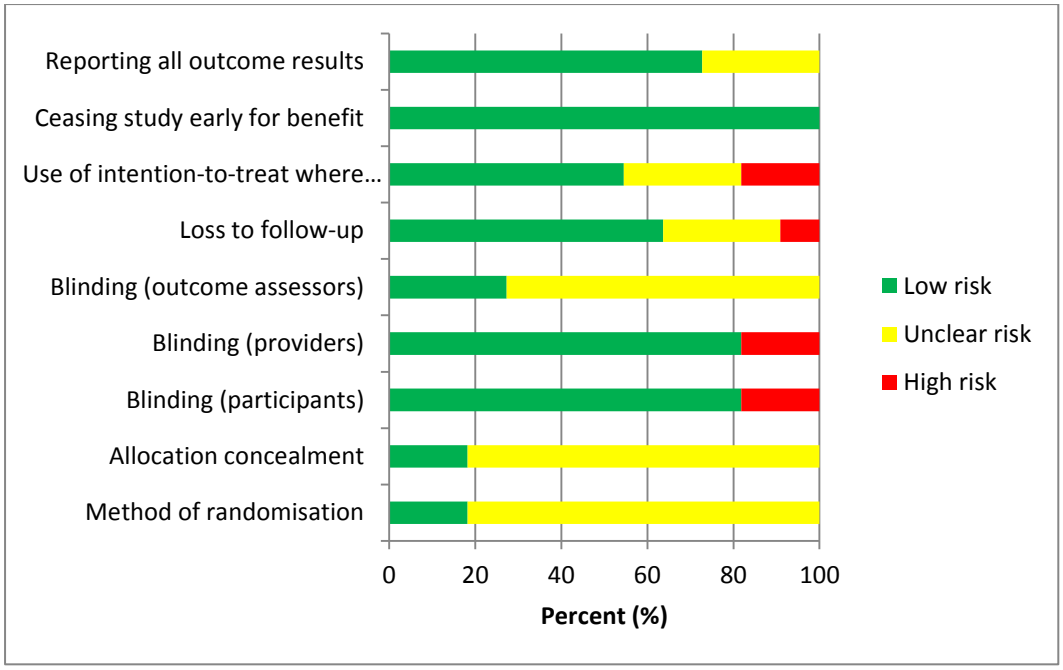

Figure 10: Risk of bias assessment summary, HDL cholesterol

Table 5: Brief summary of bias assessment (GRADE) – LDL cholesterol

Citation	Method of randomisation	Allocation concealment	Blinding (pts)	Blinding (provider)	Blinding (outcome assessor)	Loss to follow-up	Use of intention-to-treat where required	Ceasing study early for benefit	Reporting all outcome results	Funding source
Fotherby et al (1993) and Fotherby et al (1997)	?	?	+	+	?	+	?	+	+	+
Gates et al. (2004)	?	?	+	+	?	+	+	+	+	+
Jablonski et al. (2013)	?	?	+	+	?	?	?	+	+	+
McCarron et al. (1997	+	?	+	+	+	+	+	+	?	+
Ruppert et al. (1993)	?	?	+	+	?	+	+	+	+	?
DASH 2001	+	+	-	-	+	+	+	+	+	+
Schorr et al. (1996)	?	?	+	+	?	-	-	+	?	?
Sciarrone et al (1992)	?	?	+	+	?	+	?	+	+	+

Legend: '+' = low risk of bias, '?' = unclear risk of bias, '-' = high risk of bias

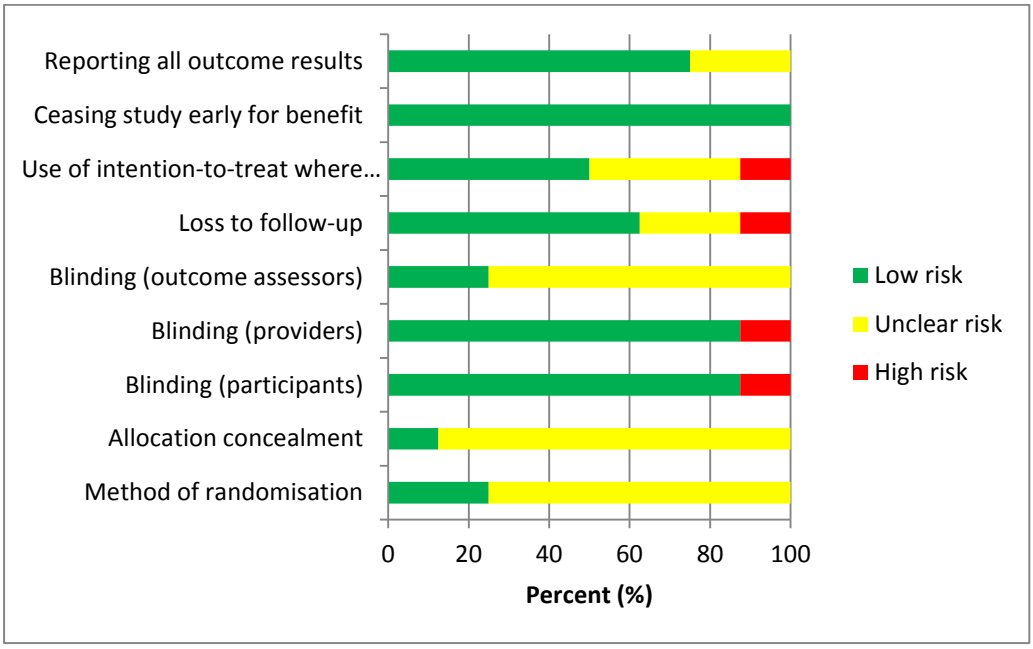

Figure 11: Risk of bias assessment summary, LDL cholesterol

Appendix 7: GRADE evidence profile

Quality assessment							No of patients		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A low intake of sodium	A high intake of sodium	Absolute		
systolic blood pressure (all participants) (follow-up 4 - 156 weeks; measured with: resting; Better indicated by lower values)											
61	randomised trials	no serious risk of bias[1]	serious[2]	no serious indirectness[3]	no serious imprecision[4]	none[5]	3592	3634	MD 3.9 lower (4.7 to 3 lower)	⊕⊕⊕O MODERATE	CRITICAL[6]
systolic blood pressure (HT participants only) (follow-up 4 - 104 weeks; measured with: resting; Better indicated by lower values)											
42	randomised trials	no serious risk of bias	no serious inconsistency[7]	no serious indirectness	no serious imprecision[8]	none[9]	1672	1609	MD 4.7 lower (5.8 to 3.6 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
systolic blood pressure (NT participants only) (follow-up 6 - 156 weeks; measured with: resting; Better indicated by lower values)											
13	randomised trials	no serious risk of bias	no serious inconsistency[10]	no serious indirectness	no serious imprecision[11]	none[12]	1394	1495	MD 1.0 lower (1.8 to 0.2 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
systolic blood pressure (mixed hypertension status) (follow-up 4 - 6 weeks; measured with: resting; Better indicated by lower values)											
6	randomised trials	no serious risk of bias	serious[13]	no serious indirectness	no serious imprecision[14]	none[15]	526	530	MD 4.4 lower (6.7 to 2.1 lower)	⊕⊕⊕O MODERATE	CRITICAL
Total cholesterol (follow-up 4 - 8 weeks; Better indicated by lower values)											
16	randomised trials	no serious risk of bias	no serious inconsistency[16]	no serious indirectness	no serious imprecision[17]	none[18]	804	803	MD 0.03 higher (0.02 lower to 0.08 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
HDL cholesterol (follow-up 4 - 8 weeks; Better indicated by higher values)											
12	randomised trials	no serious risk of bias	no serious inconsistency[19]	no serious indirectness	no serious imprecision[20]	none[21]	661	660	MD 0.01 lower (0.02 lower to 0.01 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

LDL cholesterol (follow-up 4 - 8 weeks; Better indicated by lower values)											
10	randomised trials	no serious risk of bias	no serious inconsistency[22]	no serious indirectness	no serious imprecision[23]	none[24]	622	621	MD 0.01 higher (0.06 lower to 0.09 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

[1] The studies were viewed as bring in the category of 'no limitation'. This category was selected as the risk of bias assessments for each study resulted in mainly 'low risk' and 'unclear risk' (see risk of bias assessment charts). In accordance with the GRADE guidelines, 'unclear risk' needed to be categorised as either 'no limitations' or 'serious limitations'. In view of the potential implications of the 'unknown risk' aspects on the quality of the body of evidence, 'no limitations' was selected

[2] Based on the results of a meta-analysis, heterogeneity was detected between studies (I squared = 72%, p=0.000), resulting in the decision to downgrade the quality of evidence

[3] Choice of comparisons and PICO in the reviewed studies closely matches the present review's study question

[4] Population size sufficient (>400 participants) and 95% CI includes an effect, therefore the decision was made not to downgrade the quality of evidence

[5] Based on funding bodies (largely government or not-for-profit etc.)

[6] Systolic BP is critical outcome when investigating impact of reduced sodium diet on health

[7] Based on the results of a meta-analysis, medium heterogeneity was detected between studies (I squared = 53%, p=0.000). However, 95% CI's overlapped with similar direction of effect in most studies, suggesting it should not be downgraded for heterogeneity

[8] Population size sufficient (>400 participants) and 95% CI includes an effect, therefore the decision was made not to downgrade the quality of evidence

[9] Based on funding bodies (largely government or not-for-profit etc.)

[10] Based on the results of a meta-analysis, low heterogeneity was detected between studies (I squared = 33%, p=0.120), resulting in the decision not to downgrade the quality of evidence

[11] Population size sufficient (>400 participants) and 95% CI includes an effect, therefore the decision was made not to downgrade the quality of evidence

[12] Based on funding bodies (largely government or not-for-profit etc.)

[13] Based on the results of a meta-analysis, high heterogeneity was detected between studies (I squared = 78%, p=0.000), resulting in the decision to downgrade the quality of evidence

[14] Population size sufficient (>400 participants) and 95% CI includes an effect, therefore the decision was made not to downgrade the quality of evidence

[15] Based on funding bodies (largely government or not-for-profit etc.)

[16] Based on the results of a meta-analysis, heterogeneity was not detected between studies (I squared = 0%, p=0.86), resulting in the decision not to downgrade the quality of evidence

[17] Population size sufficient (>400 participants). 95% CI does not include an effect, 95% CI does not include appreciable benefit or harm (crossing effect size of 0.5 in either direction), therefore the decision was made not to downgrade the quality of evidence

[18] Based on funding bodies (largely government or not-for-profit etc.), funnel plot appears symmetrical

[19] Based on the results of a meta-analysis, heterogeneity was not detected between studies (I squared = 0%, p=0.58), resulting in the decision not to downgrade the quality of evidence

[20] Population size sufficient (>400 participants). 95% CI does not include an effect, 95% CI does not include appreciable benefit or harm (crossing effect size of 0.5 in either direction), therefore the decision was made not to downgrade the quality of evidence

[21] Based on funding bodies (largely government or not-for-profit etc.), funnel plot appears somewhat symmetrical

[22] Based on the results of a meta-analysis, low heterogeneity was detected between studies (I squared = 25.6%, p=0.29), resulting in the decision not to downgrade the quality of evidence

[23] Population size sufficient (>400 participants). 95% CI does not include an effect, 95% CI does not include appreciable benefit or harm (crossing effect size of 0.5 in either direction), therefore the decision was made not to downgrade the quality of evidence

[24] Based on funding bodies (largely government or not-for-profit etc.), funnel plot is symmetrical indicating low risk of publication bias

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