



**Australian Government**  
**Department of Health**



# **Australian and New Zealand Nutrient Reference Values for Fluoride**

Supporting Document 4  
Literature review

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## **Acknowledgments**

This report was prepared for the Australian Government Department of Health and the New Zealand Ministry of Health, by the Expert Working Group for Fluoride; Ms Janis Baines, Dr Michael Foley, Emeritus Professor Andrew John Spencer, Professor Marco Peres, Dr Utz Mueller and Associate Professor Loc Do, with research assistance from Dr Judy Cunningham, Mr Emmanuel Gnanamanickam, and Dr Najith Amarasena.

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## Introduction

A comprehensive literature search rather than a full systematic review was undertaken in December 2013–February 2014 to assist with the nominated task of estimating an AI and UL for fluoride for young children. Although the task of the EWG was to review any new evidence on fluoride and its related nutritional reference data since the 2006 NHMRC report was published, the EWG reviewed the bibliographies of the major international reports on fluoride noting that some of the critical papers were published prior to 2005 (see Section 5.3.1. and Supporting Document 3 for a summary of the major international reports reviewed). The literature review was conducted specifically to confirm that there was no new post-2005 data that could be used to estimate the AI and UL as it appeared from the more recent international major review reports that this was the case.

The approach to the comprehensive literature search for studies published since 2005 is outlined in the main report in Section 5.3.2 Review of new literature. The research questions addressed in the search are given in Section 5.3.2.1; the approach taken for the comprehensive literature review is outlined in Section 5.3.2.2; and, the results of the literature search is summarised in Section 5.3.3. This latter section includes two PRISMA diagrams, one for fluoride and fluorosis and one for fluoride and dental caries. This document (Supporting Document 4) provides details of the studies identified in the literature search, as summarised in the PRISMA diagrams in the main report, and the specific database search strategies used. It should be read in conjunction with Sections 5.3.2 and 5.3.3 of the main report.

The research questions are replicated here for convenience:

1. What is the recommended UL for fluoride intake among children up to 8 years of age?
2. What is the recommended AI for fluoride among children up to 8 years of age?

The PICO models extended beyond these two main questions to include the health outcomes of interest; dental caries and dental fluorosis (see Section 3.5.3.2).

**Table 1: Literature search results – Question 1: Fluoride intake and fluorosis**

**Title Sifting**

Inclusion and Exclusion Criteria	Established economies	Epidemiological study*/Review	Fluoride intake from all sources of potential intake	Fluorosis	Children under 8 years	Relationship between fluoride intake and fluorosis	Total papers identified
<b>Number of papers eliminated based on title #</b>	27	104	195	348	213	356	401

# Exclusion of studies was not done on a hierarchical basis, failure to meet one or more of any of the criteria was considered adequate to be excluded.

\*Epidemiological studies referred to all observational studies

**Abstract Sifting**

Year	Authors	Established economies	Epidemiological study/Review	Fluoride intake from all sources of potential intake	Fluorosis	Children under 8 years	Relationship between fluoride intake and Fluorosis	Full paper Review
2005	Beltran-Aguilar et al.	Yes	Yes	No	Yes	Yes	No	
2005	Erdal & Buchanan	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2005	Hamasha et al.	Yes	Yes	Yes	Not Clear	Yes	Not clear	Yes
2005	Jones et al.	Yes	No	Yes	No	Not clear	No	
2006	Ahiropoulous	Yes	Yes	Yes	No	No	No	
2006	Bassin et al.	Yes	Yes	Yes	No	Yes	No	
2006	Hong et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2007	Banoczy & Rugg-Gunn	Yes	Yes	No	No	Yes	No	
2007	Sagheri, McLoughlin & Clarkson	Yes	Yes	Yes	Yes	No	Yes	
2009	Bergman et al.	Yes	Yes	Not clear	Not clear	Yes	Not Clear	Yes
2009	Clifford et al.	Yes	Yes	Not clear	Not clear	Yes	Not Clear	Yes

Year	Authors	Established economies	Epidemiological study/Review	Fluoride intake from all sources of potential intake	Fluorosis	Children under 8 years	Relationship between fluoride intake and Fluorosis	Full paper Review
2009	Do, Spencer and Ha	Yes	Yes	No	Yes	Yes	No	
2009	Graves et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2009	Kanagaratnam et al.	Yes	Yes	No	Yes	No	No	
2009	Lida & Kumar	Yes	Yes	No	Yes	Yes	No	
2009	Siew et al.	Yes	Yes	Yes	Not Clear	Yes	Not Clear	Yes
2009	Sohn, Noh & Burt	Yes	Yes	Yes	Not clear	Yes	Not Clear	Yes
2009	Vandevijere et al.	Yes	Yes	Yes	No	No	No	
2010	Armfield	Yes	Yes	Yes	No	Yes	No	
2010	Beltran-Aguilar, Barker & Dye	Yes	Yes	No	Yes	No	No	
2010	Cressey	Yes	Yes	Yes	Not Clear	Yes	Not Clear	Yes
2010	Cressey, Gaw & Love	Yes	Yes	Yes	Not Clear	Not Clear	Not Clear	Yes
2010	Martinez-Mier & Soto-Rojas	Yes	Yes	Yes	No	Yes	No	
2010	Mills, Falconer & Cook	Yes	Yes	Yes	No	No	No	
2010	Moseley-Stevens et al.	Yes	Yes	No	Yes	Yes	Yes	
2010	Pendrys et al.	Yes	Yes	Yes	Yes	No	Yes	
2010	Ritter, Catalanotto & Lossius	Yes	No	Yes	No	No	No	
2010	Rozier et al.	Yes	Yes	No	No	Not Clear	No	
2010	Verkerk	Yes	Not clear	Not Clear	Not Clear	Not Clear	Not Clear	Yes
2011	Jedra et al.	Yes	Yes	Yes	No	Yes	No	

Year	Authors	Established economies	Epidemiological study/Review	Fluoride intake from all sources of potential intake	Fluorosis	Children under 8 years	Relationship between fluoride intake and Fluorosis	Full paper Review
2011	Kobayashi et al.	No	yes	No	No	Yes	No	
2011	Lee & Brearley Messer	Yes	Yes	Yes	No	Yes	No	
2011	Nohno, Zohoori & Maguire	Yes	Yes	Yes	Not Clear	Yes	Not Clear	Yes
2011	Tubert-Jeannin et al.	Yes	Yes	No	No	Yes	No	
2011	Vargas	Yes	Yes	No	Yes	Yes	No	
2011	Vernacchio et al.	Yes	Yes	No	No	Yes	No	
2012	Do, Levy & Spencer	Yes	Yes	No	Yes	Yes	No	
2012	Levy and Leclerc	Yes	Yes	No	No	Yes	No	
2012	Maguire et al.	Yes	Yes	Yes	Not Clear	Yes	Not Clear	Yes
2012	Mis, Kobe & Stimec	Yes	Yes	Yes	No	No	No	
2012	Zohoori et al.	Yes	Yes	No	No	Yes	No	
2013	Chou et al.	Yes	Yes	No	No	Yes	No	
2013	de Carvalho et al.	Not clear	Yes	No	Yes	Yes	No	
2013	Fojo, Figueria & Almeida	Yes	Yes	Not Clear	Not Clear	Yes	Not Clear	Yes
2013	Zohoori et al.	Yes	Yes	Yes	Not Clear	Yes	Not Clear	Yes
2014	Zohoori et al.	Yes	Yes	Yes	Not Clear	Yes	Not Clear	Yes
2014	Levy et al.	Yes	Yes	Yes	No	No	No	No



## Full paper review - additional information

Year	Authors	Established economies	Epidemiological study*/Review	Fluoride intake from all sources of potential intake	Fluorosis	Children under 8 years	Relationship between fluoride intake and fluorosis	Eligible for Full Quality Assessment
2005	Erdal & Buchanan	Yes	Yes – Study is mathematical modelling of hypothetical data	Yes – Theoretical intake	Yes – Theoretical intake	Yes	Yes	No
2005	Hamasha et al.	Yes	Yes	Yes – But only fluoride intake from supplements was used for this analysis	No	Yes	No	No
2006	Hong et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2009	Bergman et al.	Yes	Yes – Review	No	No	Yes	No	No
2009	Clifford et al.	Yes	Yes	No – Only fluoride in powdered formula was studied	No	Yes	No	No
2009	Graves et al.	Yes	Yes	Yes – Only fluoride content of water from private wells	Yes	Yes	Yes	No
2009	Siew et al.	Yes	Yes	Yes – Fluoride concentrations in infant formula and various concentrations of water used to prepare them	No	Yes	No	No
2009	Sohn, Noh & Burt	Yes	Yes	Yes	No	Yes	No	No
2010	Cressy	Yes	Yes	Yes – Fluoride from infant formula and water used to	No	Yes	No	No

Year	Authors	Established economies	Epidemiological study*/Review	Fluoride intake from all sources of potential intake	Fluorosis	Children under 8 years	Relationship between fluoride intake and fluorosis	Eligible for Full Quality Assessment
				reconstitute it				
2010	Cressy, Gaw & Love	Yes	Yes	Yes – Fluoride intake from diet and toothpaste use	No	Yes	No	No
2010	Verkerk	Yes	Yes – A Review	No	No	No	No	No
2011	Nohno, Zohoori & Maguire	Yes	Yes	Yes – All exposure to fluoride was considered for these study participants (infants), i.e. infant milk formulas and water	No	Yes	No	No
2012	Maguire et al.	Yes	Yes	Yes – for infants	No	Yes	No	No
2013	Fojo, Figueria & Almeida	Yes	Yes	No – Only liquids measured	No	Yes	No	No
2013	Zohoori et al.	Yes	Yes	Yes	No	Yes	No	No
2014	Zohoori et al.	Yes	Yes	Yes	No	Yes	No	No

\*Epidemiological studies referred to all observational studies

**Table 2: Summary of review of full papers following search results from abstract sifting – Question 1: Fluoride intake and fluorosis**

Report	Overview	Methodology	Findings/estimates	Comments
<b>Bergman et al. 2009</b>	Authors have attempted to review the new evidence on Dietary Reference Intakes (DRI) for fluoride along with calcium, phosphorus, magnesium and vitamin D since these were established by IOM in 1997.	A specific search strategy is not available although the relevant publications since 1997 have been reviewed.	<p>The importance of considering various fluoride sources including water, food, beverages and food prepared with fluoridated water in estimating total fluoride intake has been highlighted.</p> <p>Authors stressed that defining optimal intakes and establishing individual and synergistic activities of these nutrients considered would be rather complicated and therefore reviewing DRIs for these nutrients could be an uphill task.</p>	No new information about either AI or UL was available.
<b>Clifford et al. 2009</b>	Fluoride content of powdered infant formula available in Brisbane, Australia, was analysed and compared with that reported a decade ago.	A total of 53 different samples of infant formula powder tins were purchased and their fluoride content was determined using a modification of micro-diffusion method. Average consumption of reconstituted formula was estimated based on Queensland Health formula feeding guidelines.	Fluoride content of formula powder ranged from 0.24–0.92 µg F/g with a mean of 0.49 µg F/g. On average, infant formula contributes 0.04 to 1.04 mg F/day from milk-based formula and 0.11 to 1.12 mg F/day from soy-based formula to daily fluoride intake and it depends on weight and age of the infants. Fluoride content in infant formula has been decreased by about one third (milk-based formula) to half (soy-based formula) the fluoride content that was reported over a decade ago. Fluoride intake was less from formulas when reconstituted with non-fluoridated water than with fluoridated water.	<p>Formula powders include in this study were not representative of all products available in Australia.</p> <p>All sources of fluoride intake were not considered.</p>
<b>Cressey (2010)</b>	Fluoride content in infant and toddler formulas	A total of 32 products including 19 infant, 8 follow-on and 5 toddler formulas purchased and analysed for their fluoride content using a modified micro-	Mean fluoride content was 0.069, 0.065 and 0.081 mg F/L, respectively for infant, follow-on and toddler formulas. These values were	Formulas purchased were considered to be all products available in New

Report	Overview	Methodology	Findings/estimates	Comments
	available on the New Zealand market was analysed and dietary fluoride intake for fully formula-fed infants estimated.	diffusion method. Dietary fluoride intake was estimated using a stochastic model.	significantly lower than those reported in 1997. Formulas reconstituted with non-fluoridated water did not exceed the UL for fully formula-fed infants while those prepared with fluoridated water at 0.7 and 1 mg F/L would have the probability of exceeding UL by 30% and 93% for fully formula-fed infants. Authors suggest that the risk of developing fluorosis is high in fully formula-fed infants when water used to reconstitute formulas is optimally fluoridated.	Zealand. There was a positive linear relationship between fluoride concentration of reconstituted formulas and the fluoride content of water used to reconstitute them.
<b>Cressey et al. 2010</b>	Fluoride intake from diet and toothpaste use for New Zealanders was estimated using existing data.	Results from the New Zealand Total Diet Survey (NZTDS), which was conducted in 1987–88 and 1990–9, were used to estimate the fluoride content of New Zealand foods while overseas data were used when no information was available from the NZTDS. Simulation diets and 24 hour dietary recall records (24HDR) were used for food consumption data whereas dietary fluoride intake was ascertained through use of the total diet study results and dietary modelling approaches for each sub-population with non-fluoridated and fluoridated water supply.	Irrespective of water fluoride status both the mean and 95 <sup>th</sup> percentile estimations of dietary fluoride intake were below the UL. Despite toothpastes contributing to additional fluoride intake many people, except for infants aged 6–12 months, had mean intakes which were lower than the AI regardless of water fluoride status. Thus none of the population sub-groups were at increased risk of surpassing the UL apart from 6–12 month old infants who were using high-fluoride toothpaste and living in areas with fluoridated water, while a majority of adults was not receiving an adequate fluoride level required for caries prevention.	Both the fluoride content and food intake data were rather old and may not be comparable to current data, however no new data are available for NZ children since the 2002 Children’s National Nutrition Survey. Contribution from toothpaste use to fluoride intake was assessed based on international sources and may not be representative of NZ.
<b>Erdal &amp; Buchanan 2005</b>	Amidst reports of increasing prevalence of dental fluorosis in the US the authors used a mathematical model to assess mean daily	A health risk assessment approach consisting of hazard identification, dose-response assessment, exposure assessment and risk characterisation was used. Both the average (central tendency exposure - CTE) and high-end (reasonable maximum exposure - RME) exposures were calculated.	The RME and CTE in fluoridated areas were 0.20 and 0.11 mg F/kg bw/day, respectively, for infants while the RME and CTE estimates for children were 0.23 and 0.06 mg F/kg bw/day, respectively. In non-fluoridated areas, the RME and CTE estimates were 0.11 and 0.08 mg F/kg bw/day for infants and 0.21 and 0.06 mg F/kg bw/day for children. Although the CRE estimates were within the	Uncertainties in the overall intake and risk estimates which ranged from medium to high level may have made the authors overly cautious of their findings.

Report	Overview	Methodology	Findings/estimates	Comments
	fluoride intake from all possible sources including drinking water, beverages, food, soil, infant formula, F supplements and toothpaste in infants (<1 year old) and 3–5 year old children living in hypothetical fluoridated and non-fluoridated areas.		optimal range the RME estimates were greater than the UL. This might have prompted authors to caution that some children could be at increased risk for fluorosis.	
<b>Fojo et al. 2013</b>	Fluoride (F) concentration in beverages including soft drinks, juices and teas marketed in Portugal was estimated.	Fluoride content was analysed using a potentiometric method which was optimised and validated.	The total number of samples selected was 183. Fluoride concentration in descending order was from extract-based soft drinks, juice drinks, juice and teas to carbonated soft drinks. All samples had F concentrations that would lead to F intakes below the acceptable daily intake (0.05 mg/kg bw/day); hence these beverages would be unlikely to cause fluorosis if considered individually.	Only the beverages were considered as the source of fluoride intake in this analysis.
<b>Graves et al. 2009</b>	As about 15% of US households with private wells were ignored in a national water fluoridation program, the authors aimed to	Household drinking water samples were assessed and fluoride exposures were estimated based on parental information, while primary school children were examined to diagnose dental fluorosis.	Drinking water had a fluoride content ranging from 0.08 to 1.3 mg F/L which was lower than that expected to cause health concerns and also 94% were below the level required for caries protection. The prevalence of mild dental fluorosis was about 19% which was in line with national level.	Contrary to the previous reports these findings suggested relatively a lower exposure to fluoride.

Report	Overview	Methodology	Findings/estimates	Comments
	estimate fluoride content in water from private wells and prevalence of dental fluorosis among children who live in these households.			
<b>Hamasha et al. 2005</b>	The aim of this study was to report fluoride supplement use from birth to 96 months of age in 1388 participants.	Use of supplements was ascertained through the questionnaires mailed at 3 to 6-month intervals. Fluoride intake from supplements was derived in such a way to allow reporting of it as a daily fluoride intake in milligrams.	Daily average fluoride intake contribution from supplements increased with age from 0.06 mg (birth-12 months) to 0.07 mg (12–60 months) to 0.18 mg (60–96 months) although the proportion of users decreased with age.  About 7–23% of the participants were living in areas with 0.6 mg F/L fluoride in water and hence inappropriately receiving supplements.	Participants were not representative of any population group and were over-represented by Whites with high education levels. Self-reported data were not validated. Dental fluorosis levels were not reported.
<b>Hong et al. 2006</b>	This study was conducted as part of Iowa Fluoride study in view of reporting the prevalence of fluorosis by fluoride intake levels over the first 3 years of life in 628 participants	Participants were followed every 3–4 months from birth to 3 years and beyond. Questionnaires were used to collect fluoride exposure and ingestion information from various sources including water, beverages, selected food, supplements and toothpastes based on information provided by the parents.  Twelve permanent teeth including 8 incisors and 4 first molars were examined using Fluorosis Risk Index (FRI) to diagnose fluorosis in the participants at the age of 8–10 years.	Only 8 participants (1.3%) had severe fluorosis while a majority had mild to moderate fluorosis. A dose-response effect on fluorosis reported using the Fluorosis Risk Index was seen with increasing levels of fluoride (low: <0.04 mg F/kg bw/day, moderate: 0.04–0.06 mg F/kg bw/day, high: >0.6 mg F/kg bw/day).  Duration of fluoride intake along with its long-term cumulative effect was associated with increased risk for fluorosis.	Findings have limited robustness and generalisability because of convenience nature of sampling that biased towards high social strata, high rate of loss to follow-up (>80%), incomplete and non-verified intake data based on self-reported questionnaires, not controlling for potential risk factors in fluorosis development, and not assessing daily fluctuation of

Report	Overview	Methodology	Findings/estimates	Comments
				fluoride ingestion. Eligible for full quality review.
<b>Maguire et al. 2011</b>	Stressing the importance of knowing total fluoride intake from all sources, particularly in infants and young children, the authors have attempted to measure fluoride concentration of ready-to-feed (RTF) infant foods and drinks in the UK.	Indirect acid diffusion method and direct F-ion-selective electrode method was used to analyse fluoride content of 122 infant foods.	The median fluoride content ranged from 0.02 mg F/L for milks to 0.2 mg F/kg for baked goods.  Authors suggested that RTF infant foods had fluoride levels which were not as high as to cause dental fluorosis if consumed within the recommended limits.	Only RTF infant foods were analysed.
<b>Nohno et al. 2011</b>	All infant milk formulas (IMF) in Japanese market were assessed for their fluoride content and fluoride exposure of infants was estimated in infants whose primary source of nutrition was IMF.	From 6 manufacturers 21 milk-based and 1 soy-based IMF products were purchased. The hexamethyldisiloxane diffusion and a fluoride ion-selective electrode technique were used to estimate F content in each sample. Both distilled water and fluoridated water [0.13 mg F/L] were used to reconstitute each IMF.	While the F content ranged from 0.15–1.24 mg/kg with a mean of 0.41 mg/kg, no significant differences were observed among different products.  The mean F intake from IMF reconstituted with fluoridated water was almost double that of the IMF reconstituted with distilled water.	Fluoride concentration of IMF depends on fluoride content of water that is used to reconstitute IMF.
<b>Siew et al.</b>	Fluoride	A total of 49 infant formulas including 9 RTF, 13	Fluoride content of formula was generally low	Estimates were based on

Report	Overview	Methodology	Findings/estimates	Comments
<b>2009</b>	concentration in infant formulas and fluoride intake in infants fed mainly on formula were estimated and compared with the AI and UL recommended by IOM.	liquid concentrate and 27 powdered formulas were purchased and analysed for their fluoride content using modified diffusion method by Taves. Both deionised water and fluoridated water containing 0–1 mg F/L fluoride were used to reconstitute formula.	though soy-based formulas had a higher content which was statistically not significant. If formula were reconstituted with water containing F less than 0.4 mg F/L, infants aged 6–12 months would be likely to receive F intakes below the AI, while the UL could be exceeded in some infants if formulas were reconstituted with water containing 1 mg F/L.	exclusive formula feeding during the first year of life. Fluoride intake of infants mainly fed on formulas depends on the fluoride content of water used to reconstitute formula.
<b>Sohn et al. 2009</b>	Fluoride intake in US children based on their fluid consumption pattern was determined based on National Health and Nutrition Survey (NHANES III) data.	A 24-hour recall diet survey was used to estimate fluid intakes of children aged 1–10 years. Fluoride intake from fluids was based on several assumptions as NHANES III had no information about individual sources.	The amount of F ingested by children at the 75 <sup>th</sup> and 90 <sup>th</sup> percentile or higher F intake, from fluids, was estimated to be 0.05 and 0.07 mg F/kg bw/day or more which was consistent across all ages. Fluoride ingested by African-American children was significantly higher than that by White children.	Socio-demographic factors might have an effect on fluoride ingestion which needs to be further studied since fluoride intake estimates were based on assumptions and was underestimated.
<b>Verkerk 2010</b>	Given that the existing model for risk analysis for nutrients used in Europe and the USA has an over-simplified two-tailed risk approach that may not consider beneficial effects of exceeding	The new conceptual model points to a zone of overlap between risks and benefits and is more realistic than the conventional model which might prevent the majority of the population from experiencing benefits from higher dosages.	Dean's data have still been widely used to depict the dose–response relationship for fluoride although fluoride in drinking water was the only major source at that time. The authors questioned the logic of IOM 1997 in estimating ULs by setting an uncertainty factor (UF) of 1 given the uncertainties in data collection, exposure amount, timing and duration as well as genetic predisposition. In light of caries (infection) preventive action of F the authors suggest using F as a medicine rather	Verkerk criticised the existing approach in 1977 IOM report of determining the risk based on the most sensitive endpoint for fluoride, moderate dental fluorosis, for estimating a UL and estimating the AI based on the perceived benefit of reducing the caries prevalence in children as being contradictory to that



Report	Overview	Methodology	Findings/estimates	Comments
	certain thresholds, a new model with overlapping risks and benefits has been suggested for risk/benefit analysis.		than a nutritional supplement. Reappraisal of fluoride based on the conventional model would result in lowering the current value for AI and this in turn would be an obstacle to the continuation of water fluoridation programs.	adopted for setting NRVs for other nutrients.
<b>Zohoori et al. 2013</b>	The relationship between total daily F intake (TDFI) and daily urinary F excretion (DUFE) as well as TDFI and fractional urinary F excretion (FUFE) in 6–7 year old children living in low-fluoridated and naturally fluoridated areas in north-east England was explored.	TDFI from diet and tooth brushing was estimated through duplicate dietary plate and tooth brushing expectorate whereas DUFE was through F-ion-selective electrode. The ratio between DUFE and TDFI was computed as FUFE.	A total of 33 children, 21 from low-fluoridated water (0.3 mg F/L) and 12 from naturally higher fluoridated water (1.06 mg F/L) areas was included.  While TDFI and DUFE were not correlated ( $r=+0.22$ , $P=0.22$ ), FUFE and TDFI had a statistically significant negative correlation ( $r= -0.63$ , $P<0.001$ ).	Further studies in different age groups using adequate sample sizes with sufficient power are essential to confirm the findings.
<b>Zohoori et al. 2014</b>	Total daily fluoride intake (TDFI) in infants aged 1–12 months living in fluoridated and non-fluoridated areas in north-east England was ascertained.	A three-day food diary was used to estimate fluoride intake and F content was analysed using an F-ion selective electrode and a diffusion method. Information on tooth brushing habits was obtained through a questionnaire combined with an interview.	A total of 38 infants, 19 each from fluoridated and non-fluoridated areas, completed the study with a mean TDFI of 0.11 and 0.02 mg F/kg bw/day, respectively. Mean fluoride content of drinking water in the fluoridated and non-fluoridated areas was 0.97 mg F/L and 0.19 mg F/L, respectively. For 87% of infants diet was the only source of fluoride; no one used fluoride supplements. TDFI from toothpastes ranged from 24–78% in infants whom tooth brushing/cleaning	Sample size was small. Fluoride intake of infants from all sources was considered.

Report	Overview	Methodology	Findings/estimates	Comments
			<p>started. About 53 % of infants living in fluoridated areas had estimated fluoride intakes that exceeded the UL while almost all infants in non-fluoridated areas did not receive optimal levels of fluoride.</p>	

**Table 3: Literature search results – Question 2: Fluoride intake and dental caries**

**Title Sifting**

Inclusion and Exclusion Criteria	Established economies	Epidemiological study*/Review	Fluoride intake from all sources of potential intake	Caries experience	Children under 8 years	Relationship between fluoride intake and caries experience	Total papers identified
Number of papers eliminated based on title#	66	109	462	318	312	543	576

#Exclusion was not done on a hierarchical basis, failure to meet one or more of any of the criteria was considered adequate to be excluded.

\* Epidemiological studies referred to all observational studies.

**Abstract Sifting**

Year	Authors	Established economies	Epidemiological study*/Review	Fluoride intake from all sources of potential intake	Caries experience	Children under 8 years	Relationship between fluoride intake and caries experience	Full paper Review
2005	Marshall et al.	Yes	Yes	Not Clear	Yes	Yes	Not clear	Yes
2005	Moynihan	yes	Yes	No	Yes	Yes	No	
2005	Tinanoff	Yes	Not clear	No	Yes	Yes	No	
2005	Toumba & Curzon	Yes	Yes	No	Yes	No	No	
2006	Al-Ansari, Al-Jairan and Gillespie	No	Yes	No	No	No	No	
2006	Tagliaferro et al.	No	Yes	Not clear	Yes	Yes	Not clear	
2006	Van Loveren & Duggal	Yes	No	No	No	No	No	
2007	Broffitt et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2007	Do & Spencer	Yes	Yes	Yes	Yes	No	Yes	
2007	Karjalainen	Yes	No	No	No	NO	No	

Year	Authors	Established economies	Epidemiological study*/Review	Fluoride intake from all sources of potential intake	Caries experience	Children under 8 years	Relationship between fluoride intake and caries experience	Full paper Review
2007	Ohlund et al.	Yes	Yes	Not clear	Yes	Yes	Not clear	Yes
2007	Vallejos-Sanchez et al.	No	Yes	Yes	Yes	Yes	Yes	
2008	Llena and Forner	Yes	Yes	No	Yes	Yes	No	
2008	Spencer, Armfield and Slade	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2009	Foster et al.	Yes	Not clear	Yes	Yes	Yes	No	
2009	Kanagaratnam et al.	Yes	Yes	No	Yes	No	No	
2009	Warren et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2010	Kirskeskov et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2010	Marya et al.	No	Yes	Yes	Yes	Yes	Yes	
2010	Tanaka, Miyake and Sasaki	Yes	Yes	No	Yes	Yes	No	
2011	Chankanka et al.	Yes	Yes	No	Yes	Yes	No	
2011	Downer et al.	Yes	Yes	No	Yes	Yes	No	
2011	Dyer	Yes	Yes	No	Yes	Yes	No	
2011	Jimenez-Farfan et al.	No	Yes	Yes	Yes	Not clear	Yes	
2011	Lee and Messer	Yes	Not clear	No	No	Yes	No	
2011	Meiers	Yes	No	Not clear	Not clear	Not clear	Not Clear	
2012	Charone et al.	No	Yes	Yes	Yes	Yes	Yes	
2012	Do, Levy and Spencer	Yes	Yes	No	Yes	No	No	
2012	Rugg-Gunn and Do	Not Clear	Not Clear	No	Yes	Yes	Yes	
2013	Armfield et al.	Yes	Yes	Yes	Yes	Yes	No	
2013	Iheozor-Ejiofor et al.	Not Clear	No	Yes	Yes	Not clear	Yes	
2013	Kamel, Thomson and Drummond	Not Clear	Yes	No	Yes	Yes	No	
2014	Lewis	Yes	No	No	No	Yes	No	

\* Epidemiological studies referred to all observational studies.

### Full paper - additional information

Year	Authors	Established economies	Epidemiological study*/ Review	Fluoride intake from all sources of potential intake	Caries experience	Children under 8 years	Relationship between fluoride intake and caries experience	Eligible for Full Quality Assessment
2005	Marshall et al.	Yes	Yes	Fluoride intake from all sources were recorded in the study	Yes	Yes	Fluoride intake was used only for adjusting the relationship between caries and sugary foods	No
2007	Broffitt et al.	Yes	Yes	Yes – Water was used but the main comparison was with bottled water	Yes	Yes	Yes – But the focus was on a comparison between bottle water and tap water users.	No
2007	Ohlund et al.	Yes	Yes	Fluoride exposure from toothpaste and tablets alone	Yes	Yes	Fluoride exposure variable was only tested in the relationship between other foods and caries.	No
2008	Spencer et al.	Yes	Yes	Yes – exposure was for fluoride in water alone	Yes but as net caries increment across years	Yes	Yes	No
2009	Warren et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2010	Kirskeskov et al.	Yes	Yes	Yes - Drinking water fluoridation	Yes	Yes	Yes	Yes

\* Epidemiological studies referred to all observational studies.

**Table 4: Summary of review of full papers following search results from abstract sifting – Question 2: Fluoride intake and dental caries**

Paper	Overview	Methodology	Findings/estimates	Comments
<b>Marshall et al. 2005</b>	Using data from the Iowa Fluoride study this paper examines the relationship between caries experience and meals, snacks and exposure to food and beverages in children	Subjects were from the Iowa Fluoride study. Caries experience was collected through oral examinations between 4.5–6.8 years of age and was dichotomised to any caries or no caries, based on cavitated or filled surfaces. Food and beverage intake information was collected through 3-day parental food diaries starting at 6 weeks, 3, 6, 9 and 12 months and every four months till 3 years and every 6 months thereafter. Diet abstraction was done on a yearly basis up to 5 years of age. The food diaries/questionnaires were also used to estimate fluoride exposure from water and other beverages and food items prepared with water and also fluoride supplements and dentifrice use. Caries risk in first versus the fourth quartile of food and beverage exposure was examined using logistic regression models and was adjusted for cumulative fluoride intake and age of dental examination.	25.7% of the children had caries experience in the primary dentition; median cumulative fluoride exposure was 0.55 and 0.63 mg F/day in children with and without caries. Children in the highest quartile of number of eating events and snack eating events through the 5 year period had higher caries experience compared to those in the lowest quartile. Caries risk was also increased by exposure to 100% juice with snacks at 2 years, soda-pop use with meals and snacks at different time points and total soda-pop use at different time points. Across the 5 years, higher exposure to sugars and starches at meals decreased caries risk while higher exposure to sugars as snacks increased caries risk.	The main focus of this paper was to examine the relationship between different food and beverage intake as meals and snacks and dental caries. Though fluoride intake information was collected, apart from the mention of median cumulative fluoride intake levels no analysis of the relationship between fluoride intake and caries was done.
<b>Broffitt et al. 2007</b>	Against the backdrop of increased bottled water use and its lower fluoride content, the association between bottled water use and caries was examined using data from the Iowa Fluoride	This study was a secondary analysis of data from the Iowa fluoride study. For this analysis data was from a 6 monthly questionnaire to parents from age 6 years until the time of the mixed dentition exam. Water consumption information along with source of water (whether mostly tap or bottled water) was collected. Respondents were categorised into bottled water users, tap water users or half users for each time point of data collection. Overall bottled water users were classified so if they were estimated to use 25% or more of bottled water. Varying fluoride levels in different brands of bottled water were not considered. Other fluoride intake information was	413 children were included in the analysis with complete information. 10% (42) of the participants were classified as bottled water users. Bottled water users and non-users were similar in most demographic characteristics. Among all fluoride sources, fluoride ingested from water was the only source that was significantly different between the two groups. No significant differences was found between the two groups in relation to permanent tooth caries or primary second molar caries.	The main study was not designed to answer the question on bottled water use and caries. Number of participants classified as bottled water users were very small in proportion and number.

Paper	Overview	Methodology	Findings/estimates	Comments
	study.	also collected as part of the main study. Mixed dentition oral examinations were done at about age 9 years. Caries was defined as children with cavitated or filled surfaces.		
<b>Ohlund et al. 2007</b>	Study on the association between dental caries and the presence of mutans in saliva and carbohydrate and dairy diet in 4 year olds in a low-prevalence area. Information on fluoride habits were also collected	The study was a cohort of children who were followed up at 4 years of age after joining the initial study at 6 months. Monthly food and medical information was collected from 6 to 18 months of age. Parents consented to provide dietary and physical information up to 4 years of age and an oral examination. Caries experience was recorded at an oral examination where information on tooth brushing and fluoride use was also collected through a parental questionnaire and whole saliva was also collected. Step wise regression was used to model food intake, bacterial counts and oral hygiene measures against caries	Of the 86 who had their oral examination 70% had no sign of dental caries. Mean dfs was 2.8 among those with caries lesions/restorations. Only 68 samples of saliva were collected and 44% of them had the mutans streptococci and 25% had the lactobacilli mutan. Both correlated with caries prevalence. 46% of children with caries had visible plaque, more than twice as high (19%) as those without caries. All children used fluoridated toothpaste. Cheese and black pudding were the only two items that co-related with caries experience, cheese negatively and black pudding positively. There was no co-relation with intake or frequency of any other food group, energy intake or intake of particular nutrients.	Only 86 of the entire cohort had their oral examination done and caries experience recorded. No fluoride intake was measured or recorded in dietary intake and all the children in the study used fluoridated toothpaste and only 3 had any fluoride supplements in their lifetime.
<b>Spencer, Armfield and Slade 2008</b>	Cohort study comparing two states with contrasting fluoridation patterns with the respective increment in caries experience in 5–15 year olds over three years.	Data was from the Child Fluoride Study which started in 1991. Data for this paper was from 1991 to 1995 from a stratified random sample of the school dental services (SDS) of 5–12 year olds in South Australia (SA) and 5–15 year olds in Queensland(QLD). Caries experience was collected by SDS staff and exposure to fluoride in water through a parental questionnaire. Caries increment was annualised based on data at baseline and last oral-examination.	Children lost to follow up were more likely to be from non-fluoridated areas and were from extremes of SES in SA and low SES in QLD. In SA less than 10% of children has 0% exposure to fluoridation and over one third had 100% lifetime exposure while in Qld over two thirds had 0% exposure and only 5% had 100% exposure. Annualised caries increment for deciduous teeth was 0.34 for SA (30% less than Qld) and 0.50 in Qld. For permanent teeth it was 0.12 (50% less) and 0.24 respectively. In relation to fluoridation exposure of 0% and 100%, caries increment was 78.6% higher in the 0% exposure group in SA and 86.2% higher in	The main explanatory variable in this study was water fluoridation. Only the relationship between caries increment and water fluoridation was reported. Caries experience was not directly compared with fluoride exposure.



Paper	Overview	Methodology	Findings/estimates	Comments
			Qld. In multivariate analysis after controlling for sex, age, fluoride exposure from other sources and SES, fluoridated water showed a significant association with decreased caries in both states for deciduous teeth. For permanent teeth a statistically significant effect was seen in Qld and not in SA, while controlling for sex and age alone and while controlling for all control variables. An inverse relationship between lifetime exposure and caries increment was evident.	
<b>Warren et al. 2009</b>	Data from the Iowa Fluoride study was used to estimate the optimal level of fluoride intake that would be necessary to prevent any fluorosis or caries among children (n=602)	Fluoride intake was estimated through regular parental questionnaires collected from the age of 6 weeks. The main sources of fluoride that were considered were water (by itself and in reconstituted form), other beverages, fluoride toothpaste and supplements. Dental examinations were done at about 5 years and 9 years of age to establish fluorosis and caries experience. All levels of fluorosis were considered. The analysis was based on four groups of fluorosis/caries experience: Neither caries at the two time points or fluorosis at the 9 year stage; both caries at least one of the time points and fluorosis at 9 years; Caries at least at one of the time points and no fluorosis; and No caries and fluorosis at 9 years.	Two main results were shown mainly through figures: <ul style="list-style-type: none"> <li>Those in the neither fluorosis nor caries group had fluoride exposure of less than 0.05 mg F/kg bw/day throughout the period of study. Those with fluorosis alone or along with caries had higher exposure and those with caries alone was consistently below the 'Neither' group.</li> </ul> Among those who neither had fluorosis nor caries, there was considerable individual variation of fluoride exposure. No summary or variation measures were provided.	Caries and fluorosis were analysed in the same analysis of the four groups. No measures of dispersion were provided. The authors conclude that recommendation of an optimum level of fluoride intake is not possible because of the individual variability of fluoride exposure in those without either fluorosis or caries. Eligible for full quality review.
<b>Kirkeskov et al. 2010</b>	Health registry data was used to study the association between public water fluoridation and dental caries in children in Denmark over a 10 year period	For this NRV review we are interested in the data of the 5 year olds only. Data was derived from 5 different administrative databases to provide information on dental caries, housing, water, and income (used as a proxy for SES). Two cohorts of 5 year old children were used – those born in 1989 and 1999 (41,000-48,000 children in cohorts). Data on water supplied only by public or private water works was used. Fluoride exposure was calculated as a weighted	Analysis showed that children from higher family income and lower level of caries were more represented in the study. For 5 year olds mean dmfs was 2.01 (in 1989) and 1.44 (in 1999) for the two cohorts with 90 <sup>th</sup> percentile being 6 and 4 respectively. Proportion of dmfs= $\geq$ 2 was 20.77% (1989) and 15.23% (1999). Negative association between fluoride exposure through drinking water and caries after adjusting for gender and family income was confirmed.	Only public water fluoridation was considered as a source of fluoride exposure in this study. The sample size is large. Dental caries was dichotomised at dmfs= $\geq$ 2 which is a conservative cut off. The study did not provide

Paper	Overview	Methodology	Findings/estimates	Comments
	among 5 and 15 year olds.	mean – a product of the fluoride concentration at each dwelling and the time spent at that address divided by the total number of years of exposure. Caries was measured as dmfs and was dichotomised at dmfs $\geq$ 2 for 5 year olds.	Children with $>1$ mg F/L exposure were half as likely (OR=0.51) to have caries as those with 0–0.1249 mg F/L exposure and the dose response relationship was seen at different levels of fluoride exposure. The authors noted that their findings were significant in light of the widespread use of fluoridated toothpaste.	prevalence rates of caries at different levels of drinking water fluoridation. Eligible for full quality review.

# Database search strategies – fluorosis

## Fluoride intakes and fluorosis

### Cochrane

ID Search

- #1 exposure or intake or Excret\* or diet\* or concentration\* or ingesti\* or content or bio\* next marker\* or Bio\* next availabilit\*
- #2 Fluorid\* or Fluoros\*
- #3 child\* or Infan\* (Word variations have been searched)
- #4 Australia or New next Zealand or EU\* or USA or United next States\* or America or Canad\* or UK or OECD or United next Kingdom (Word variations have been searched)
- #5 Adequate next Intake or AI or Upper next Limit or UL or Upper next Intake next Level or UI or NRV\* or Nutritional next reference next value\* or Dietary next Reference next Intake or DRI or Dietary next Reference next value\* or DRV\* or Average next Requirement\* or AR or \*Maximum next Contaminant next Level\* or \*MCL\* or \*observed next adverse next effect next level\* or \*OAEL\* or Estimated next Average next requirement\*
- #6 #2 and #3 and #4 and #5
- #7 #1 or #5
- #8 #7 and #2 and #3 and #4
- #9 Fluoride
- #10 #8 and #9

The Cochrane database does not have a filter option so the citations prior to 2005 were filtered out after importing into endnote. In the final search line #6 was redundant.

### PUBMED (National Centre for Biotechnology Information interface)

((((((((((((((((((((Average intake) OR "AI") OR "Upper limit") OR UL) OR Upper Intake Level) OR "Nutritional Reference values") OR "Nutritional Reference value\*") OR "NRV\*") OR "Dietary Reference Intake") OR "DRI") OR "Dietary reference value\*") OR "DRV\*") OR "Average Requirement\*") OR "AR\*") OR "\*Maximum Contaminant level\*") OR "\*MCL\*") OR "\*observed adverse effect level\*") OR "\*OAEL\*") OR "Estimated Average Requirement")) AND ((Fluorid\*) OR Fluoros\*)) AND ((Infan\*) OR Child\*)) AND (((((((((((Australia) OR "New Zealand") OR NZ) OR Europe\*) OR EU) OR USA) OR United States\*) OR America) OR Canada) OR OECD) OR uk) Filters: Publication date from 2005/01/01 to 2014/02/28; Humans; English

## Web of science (database is included in Web of knowledge platform)

#17	#11 AND #10 AND #4 AND #3 Refined by: <b>LANGUAGES:</b> (ENGLISH) AND <b>PUBLICATION YEARS:</b> (2009 OR 2012 OR 2005 OR 2006 OR 2010 OR 2007 OR 2008 OR 2014 OR 2011 OR 2013) <i>DocType=All document types; Language=All languages;</i>
#16	#11 AND #10 AND #4 AND #3 Refined by: <b>LANGUAGES:</b> (ENGLISH) <i>DocType=All document types; Language=All languages;</i>
#15	#11 AND #10 AND #4 AND #3 <i>DocType=All document types; Language=All languages;</i>
#14	#12 AND #11 AND #4 AND #3 Refined by: <b>LANGUAGES:</b> (ENGLISH) <i>DocType=All document types; Language=All languages;</i>
#13	#12 AND #11 AND #4 AND #3 Refined by: <b>LANGUAGES:</b> (ENGLISH) AND <b>PUBLICATION YEARS:</b> (2009 OR 2012 OR 2005 OR 2006 OR 2010 OR 2007 OR 2008 OR 2014 OR 2011 OR 2013) <i>DocType=All document types; Language=All languages;</i>
#12	#10 OR #7 <i>DocType=All document types; Language=All languages;</i>
#11	<b>TOPIC:</b> (Fluorid*) OR <b>TOPIC:</b> (Fluoros*) <i>DocType=All document types; Language=All languages;</i>
#10	<b>TOPIC:</b> (exposure) OR <b>TOPIC:</b> (intake) OR <b>TOPIC:</b> (excret*) OR <b>TOPIC:</b> (diet*) OR <b>TOPIC:</b> (concentration*) OR <b>TOPIC:</b> (ingesti*) OR <b>TOPIC:</b> (content) OR <b>TOPIC:</b> ("bio* marker*") OR <b>TOPIC:</b> ("bio* availabilit*") <i>DocType=All document types; Language=All languages;</i>
#9	#8 AND #7 AND #4 AND #3 <i>DocType=All document types; Language=All languages;</i>
#8	<b>TOPIC:</b> ("dental Caries") OR <b>TOPIC:</b> ("dental decay") <i>DocType=All document types; Language=All languages;</i>
#7	<b>TOPIC:</b> ((Adequate Intake) OR <b>TOPIC:</b> (AI) OR <b>TOPIC:</b> (Upper Limit) OR <b>TOPIC:</b> (UL) OR <b>TOPIC:</b> (Upper Intake Level) OR <b>TOPIC:</b> (UI) OR <b>TOPIC:</b> (NRV*) OR <b>TOPIC:</b> (Nutritional reference value*) OR <b>TOPIC:</b> (Dietary Reference Intake) OR <b>TOPIC:</b> (DRI) OR <b>TOPIC:</b> (Dietary Reference value*) OR <b>TOPIC:</b> (DRV) OR <b>TOPIC:</b> (Average Requirement*) OR <b>TOPIC:</b> (AR) OR <b>TOPIC:</b> (*Maximum Contaminant Level*) OR <b>TOPIC:</b> (*MCL*) OR <b>TOPIC:</b> (*observed adverse effect level*) OR <b>TOPIC:</b> (*OAEL*) OR <b>TOPIC:</b> (EAR) OR <b>TOPIC:</b> (Estimated Average requirement*))

	<i>DocType=All document types; Language=All languages;</i>
#6	<b>TOPIC:</b> <i>(TOPIC: (Adequate Intake) OR TOPIC: (AI) OR TOPIC: (Upper Limit) OR TOPIC: (UL) OR TOPIC: (Upper Intake Level) OR TOPIC: (UI) OR TOPIC: (NRV*) OR TOPIC: (Nutritional reference value*) OR TOPIC: (Dietary Reference Intake) OR TOPIC: (DRI) OR TOPIC: (Dietary Reference value*) OR TOPIC: (DRV) OR TOPIC: (Average Requirement*) OR TOPIC: (AR) OR TOPIC: (*Maximum Contaminant Level*) OR TOPIC: (*MCL*) OR TOPIC: (*observed adverse effect level*) OR TOPIC: (*OAEL*) OR TOPIC: (EAR) OR TOPIC: (Estimated Average requirement*))</i> <i>DocType=All document types; Language=All languages;</i>
#5	#4 AND #3 AND #2 AND #1 <i>DocType=All document types; Language=All languages;</i>
#4	<b>TOPIC:</b> <i>(Australia) OR TOPIC: (New Zealand) OR TOPIC: (EU) OR TOPIC: (US) OR TOPIC: (America) OR TOPIC: (Canad*) OR TOPIC: (U K) OR TOPIC: (OECD) OR TOPIC: (Europ*) OR TOPIC:(USA)</i> <i>DocType=All document types; Language=All languages;</i>
#3	<b>TOPIC:</b> <i>(Child*) OR TOPIC: (Infan*)</i> <i>DocType=All document types; Language=All languages;</i>
#2	<b>TOPIC:</b> <i>(Fluorid*)</i> <i>DocType=All document types; Language=All languages;</i>
#1	<b>TOPIC:</b> <i>(Average Intake) OR TOPIC: (AI) OR TOPIC: (Upper Limit) OR TOPIC: (UL) OR TOPIC: (Upper Intake Level) OR TOPIC: (UI) OR TOPIC: (NRV*) OR TOPIC: (Nutritional reference value*) OR TOPIC: (Dietary Reference Intake) OR TOPIC: (DRI) OR TOPIC: (Dietary Reference value*) OR TOPIC: (DRV) OR TOPIC: (Average Requirement*) OR TOPIC: (AR) OR TOPIC: (*Maximum Contaminant Level*) OR TOPIC: (*MCL*) OR TOPIC: (*observed adverse effect level*) OR TOPIC: (*OAEL*) OR TOPIC: (EAR) OR TOPIC: (Estimated Average requirement*)</i> <i>DocType=All document types; Language=All languages;</i>

In the final Web of Science search line #13 was used therefore lines #1, #2, #5, #6, #7, #8, #9, #12, #14 and #17 were redundant.

## **MEDLINE (Ovid)**

- 1 "Estimated Average Requirement\*".mp. (372)
- 2 Fluoros\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (27710)
- 3 United States/ or "United States\*".mp. (820480)
- 4 United States/ or USA.mp. (789541)

- 5 "Average Intake".mp. (531)
- 6 "AI".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (16765)
- 7 "Upper Limit".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (9104)
- 8 UI.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3155)
- 9 "upper Intake Level".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (153)
- 10 UI\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (12252)
- 11 "NRV".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (55)
- 12 "Nutritional reference value\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2)
- 13 "Dietary reference Intake".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (163)
- 14 "DRI".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (624)
- 15 "Dietary reference value\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (102)
- 16 "DRV".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (275)
- 17 "Average Requirement\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (437)
- 18 AR\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (20577433)

- 19     "\*Maximum Contaminant Level\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (261)
- 20     "\*MCL\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8474)
- 21     "\*observed adverse effect level\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2738)
- 22     "\*OAEL\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)
- 23     5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (20577981)
- 24     Fluorid\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (45109)
- 25     child\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1854002)
- 26     infan\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1032174)
- 27     Australia/ (72754)
- 28     New Zealand/ (29946)
- 29     NZ.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1306)
- 30     European Union/ or EU\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (516838)
- 31     Canad\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (112764)
- 32     Great Britain/ or UK.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (224197)
- 33     Developed countries/ or OECD.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (20693)

- 34 1 or 23 (20577981)
- 35 2 or 24 (70337)
- 36 25 or 26 (2289573)
- 37 3 or 4 or 27 or 28 or 29 or 30 or 31 or 32 or 33 (1715017)
- 38 34 and 35 and 36 and 37 (1071)
- 39 limit 38 to (english language and humans and yr="2005 -Current") (292)
- 40 "Adequate Intake".mp. (712)
- 41 1 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 40 (20577982)
- 42 35 and 36 and 37 and 41 (1071)
- 43 limit 42 to (english language and humans and yr="2005 -Current") (292)
- 44 exposure.mp. (595143)
- 45 intake.mp. (188657)
- 46 excret\*.mp. (145839)
- 47 Diet/ or diet\*.mp. (496732)
- 48 concentration\*.mp. (1574254)
- 49 ingesti\*.mp. (56542)
- 50 content.mp. (423968)
- 51 Biological Markers/ or "bio\* marker\*".mp. (175812)
- 52 Biological Availability/ or "bio\* availability\*".mp. (31822)
- 53 41 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 (20618053)
- 54 35 and 36 and 37 and 53 (1082)
- 55 limit 54 to (english language and humans and yr="2005 -Current") (296)
- 56 (fluorid\* or fluorosis).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (45841)
- 57 Fluorides/ or fluorid\*.mp. (45109)
- 58 Fluorosis, Dental/ or fluorosis.mp. (3040)
- 59 57 or 58 (45841)
- 60 36 and 37 and 53 and 59 (973)
- 61 limit 60 to (english language and humans and yr="2005 -Current") (235)

In the final Medline search terms lines 2, 5, 23, 24, 34, 35, 38, 39, 42, 43, 54, 55 and 56 were redundant.



## Embase

child\* OR infan\* AND ('australia'/exp OR australia OR 'new zealand'/exp OR 'new zealand'  
OR europe\* OR eu OR usa OR 'united next states' OR america\* OR canad\* OR 'uk'/exp OR uk  
OR 'united kingdom'/exp OR 'united kingdom' OR oecd)

AND (fluorid\* OR fluoros\*)

AND ('exposure' OR intake OR excret\* OR diet\* OR concentration\* OR ingesti\* OR content  
OR 'adequate intake' OR ai OR 'upper limit' OR ul OR 'upper intake level' OR ui OR nrv\* OR  
'nutritional reference value' OR 'nutritional reference values' OR 'dietary reference  
intake'/exp OR 'dietary reference intake' OR dri OR 'dietary reference value' OR 'dietary  
reference values' OR drv OR 'average requirement' OR 'average requirements' OR ar OR  
'maximum contaminant level' OR mcl\* OR 'observed adverse effect level' OR oael\* OR  
'ear'/exp OR 'estimated average requirement' OR 'estimated average requirements' OR bio\*  
NEXT/1 marker\* OR bio\* NEXT/1 availabilit\*)

AND (2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR  
2012:py OR 2013:py OR 2014:py)

AND 'human'/de

## Dental & Oral Sciences (DOSS); ANZ Reference Centre

S1 "Average Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\*  
OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary  
Reference Value\*" OR DRV

S2 "Average Requirement\*" OR AR OR "\*\*maximum contaminant level\*" OR \*MCL\* OR  
\*\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*\*"

S3 S1 or S2

S4 Fluorid\* OR Fluoros\*

S5 child\* OR infan\*

S6 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\*  
OR Canad\* OR UK OR "United Kingdom" OR OECD

S7 S3 AND S4 AND S5 AND S6

S8 "Average Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\*  
OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary  
Reference Value\*" OR DRV

S9 "Average Requirement\*" OR AR OR "\*\*maximum contaminant level\*" OR \*MCL\* OR  
\*\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*\*"

S10 S8 OR S9

S11 Fluorid\* OR Fluoros\*

S12 child\* OR infan\*

S13 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\*  
OR Canad\* OR UK OR "United Kingdom" OR OECD

S14 S10 AND S11 AND S12 AND S13

S15 "Average Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary Reference Value\*" OR DRV

S16 "Average Requirement\*" OR AR OR "\*maximum contaminant level\*" OR \*MCL\* OR "\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*"

S17 S15 OR S16

S18 Fluorid\* OR Fluoros\*

S19 child\* OR infan\*

S20 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S21 S17 AND S18 AND S19 AND S20

S22 child\* OR infan\*

S23 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S24 "Adequate Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary Reference Value\*" OR DRV

S25 exposure OR intake OR excret\* OR diet\* OR concentration\* OR content OR "bio\* Marker\*" OR "bio\* availabilit\*"

S26 "dental caries" OR "tooth decay"

S27 Fluorid\*

S28 (exposure OR intake OR excret\* OR diet\* OR concentration\* OR content OR "bio\* Marker\*" OR "bio\* availabilit\*") AND (S24 OR S25)

S29 S22 AND S23 AND S26 AND S27 AND S28

S30 S22 AND S23 AND S26 AND S27 AND S28 (Limiters - Publication Date: 20040101-20141231)

S31 "Average Requirement\*" OR AR OR "\*maximum contaminant level\*" OR \*MCL\* OR "\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*"

S32 Fluorid\* OR Fluoros\*

S33 child\* OR infan\*

S34 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S35 "Adequate Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary Reference Value\*" OR DRV

S36 S31 OR S35

S37 S32 AND S33 AND S34 AND S36

S38 exposure OR intake OR excret\* OR diet\* OR concentration\* OR content OR "bio\* Marker\*" OR "bio\* availabilit\*"

S39 S35 OR S38

S40 S32 AND S33 AND S34 AND S39

S41 (S2 AND S3 AND S4 AND S39) AND (S2 AND S3 AND S4 AND S38)

S42 S32 AND S33 AND S34 AND S39 (Limiters - Publication Date: 20040101-20141231)

In the DOSS/ANS Reference Centre final searches, lines S32, S33, S34, S35, S38, S39 and S49 were used; all the other search terms were redundant.

## **Toxline**

Toxline is a US National Library of Medicine database. At the time of running the searches the platform did not have a function to save the search terms. So when the search terms were required to be included in the report at a later date they were not available, however they were consistent with the above searches.

## **Summary for fluoride intakes and fluorosis**

A total of 419 abstracts were retrieved, 401 after duplicate removal (Cochrane 26, PubMed 35, Web of Science 2, Medline 259, Embase 74, DOSS 9, ANZ Ref Centre 3, Toxline 11 retrieved).

## Fluoride intakes and dental caries

### Cochrane

ID Search

- #1 exposure or intake or Excret\* or diet\* or concentration\* or ingesti\* or content or bio\* next marker\* or Bio\* next availabilit\*
- #2 Fluorid\*
- #3 child\* or Infan\* (Word variations have been searched)
- #4 Australia or New next Zealand or EU\* or USA or United next States\* or America or Canad\* or UK or OECD or United next Kingdom (Word variations have been searched)
- #5 Adequate next Intake or AI or Upper next Limit or UL or Upper next Intake next Level or UI or NRV\* or Nutritional next reference next value\* or Dietary next Reference next Intake or DRI or Dietary next Reference next value\* or DRV\* or Average next Requirement\* or AR or \*Maximum next Contaminant next Level\* or \*MCL\* or \*observed next adverse next effect next level\* or \*OAEL\* or Estimated next Average next requirement\*
- #6 #2 and #3 and #4 and #5
- #7 #1 or #5
- #8 "dental caries" or "tooth decay"
- #9 #2 and #3 and #4 and #7 and #8

The Cochrane database does not have a filter option so the citations prior to 2005 were filtered out after importing into endnote. In the final search line #6 was redundant.

### PUBMED (National Centre for Biotechnology Information interface)

```
(((Fluorid*) AND (((((((Infan*) OR Child*)) AND (((((((Australia) OR "New Zealand") OR NZ) OR Europe*) OR EU) OR USA) OR United States*) OR America) OR Canada) OR OECD) OR uk)))) AND (("dental caries") OR "dental decay")))) AND (((((((Exposure) OR intake) OR excret*) OR diet*) OR concentration*) OR ingesti*) OR content) OR "bio* marker*") OR "Bio* Availabilit*") OR (((((((((((((((Adequate intake) OR "AI") OR "Upper limit") OR UL) OR Upper Intake Level) OR "Nutritional Reference values") OR "Nutritional Reference value*") OR "NRV*") OR "Dietary Reference Intake") OR "DRI") OR "Dietary reference value*") OR "DRV*") OR "Average Requirement*") OR "AR*") OR "*Maximum Contaminant level*") OR "*MCL*") OR "*observed adverse effect level*") OR "*OAEL*") OR "Estimated Average Requirement")))) AND ( ( "2005/01/01"[PDat] : "2014/12/31"[PDat] ) AND Humans[Mesh] AND English[lang])
```

## Web of Science (database is included in Web of knowledge platform)

#14	#11 AND #8 AND #4 AND #3 AND #2 Refined by: <b>PUBLICATION YEARS:</b> (2011 OR 2010 OR 2008 OR 2013 OR 2009 OR 2012 OR 2007 OR 2006 OR 2005) AND <b>LANGUAGES:</b> (ENGLISH) <i>DocType=All document types; Language=All languages;</i>
#13	#11 AND #8 AND #4 AND #3 AND #2 Refined by: <b>PUBLICATION YEARS:</b> (2011 OR 2010 OR 2008 OR 2013 OR 2009 OR 2012 OR 2007 OR 2006 OR 2005) <i>DocType=All document types; Language=All languages;</i>
#12	#11 AND #8 AND #4 AND #3 AND #2 <i>DocType=All document types; Language=All languages;</i>
#11	#10 OR #1 <i>DocType=All document types; Language=All languages;</i>
#10	<b>TOPIC:</b> (exposure) OR <b>TOPIC:</b> (intake) OR <b>TOPIC:</b> (excret*) OR <b>TOPIC:</b> (diet*) OR <b>TOPIC:</b> (concentrati on*) OR <b>TOPIC:</b> (ingesti*) OR <b>TOPIC:</b> (content) OR <b>TOPIC:</b> ("bio* marker*") OR <b>TOPIC:</b> ("bio* availabilit*") <i>DocType=All document types; Language=All languages;</i>
#9	#8 AND #7 AND #4 AND #3 <i>DocType=All document types; Language=All languages;</i>
#8	<b>TOPIC:</b> ("dental Caries") OR <b>TOPIC:</b> ("dental decay") <i>DocType=All document types; Language=All languages;</i>
#7	<b>TOPIC:</b> ((Adequate Intake) OR <b>TOPIC:</b> (AI) OR <b>TOPIC:</b> (Upper Limit) OR <b>TOPIC:</b> (UL) OR <b>TOPIC:</b> (Upper Intake Level) OR <b>TOPIC:</b> (UI) OR <b>TOPIC:</b> (NRV*) OR <b>TOPIC:</b> (Nutritional reference value*) OR <b>TOPIC:</b> (Dietary Reference Intake) OR <b>TOPIC:</b> (DRI) OR <b>TOPIC:</b> (Dietary Reference value*) OR <b>TOPIC:</b> (DRV) OR <b>TOPIC:</b> (Average Requirement*) OR <b>TOPIC:</b> (AR) OR <b>TOPIC:</b> (*Maximum Contaminant Level*) OR <b>TOPIC:</b> (*MCL*) OR <b>TOPIC:</b> (*observed adverse effect level*) OR <b>TOPIC:</b> (*OAE*) OR <b>TOPIC:</b> (EAR) OR <b>TOPIC:</b> (Estimated Average requirement*)) <i>DocType=All document types; Language=All languages;</i>
#6	<b>TOPIC:</b> (TOPIC: (Adequate Intake) OR <b>TOPIC:</b> (AI) OR <b>TOPIC:</b> (Upper Limit) OR <b>TOPIC:</b> (UL) OR <b>TOPIC:</b> (Upper Intake Level) OR <b>TOPIC:</b> (UI) OR <b>TOPIC:</b> (NRV*) OR <b>TOPIC:</b> (Nutritional reference value*) OR <b>TOPIC:</b> (Dietary Reference Intake) OR <b>TOPIC:</b> (DRI) OR <b>TOPIC:</b> (Dietary Reference value*) OR <b>TOPIC:</b> (DRV) OR <b>TOPIC:</b> (Average Requirement*) OR <b>TOPIC:</b> (AR) OR <b>TOPIC:</b> (*Maximum Contaminant Level*) OR <b>TOPIC:</b> (*MCL*) OR <b>TOPIC:</b> (*observed adverse effect level*) OR <b>TOPIC:</b> (*OAE*) OR <b>TOPIC:</b> (EAR) OR <b>TOPIC:</b> (Estimated Average requirement*)) <i>DocType=All document types; Language=All languages;</i>
#5	#4 AND #3 AND #2 AND #1

	<i>DocType=All document types; Language=All languages;</i>
#4	<b>TOPIC: (Australia) OR TOPIC: (New Zealand) OR TOPIC: (EU) OR TOPIC: (US) OR TOPIC: (America) OR TOPIC: (Canad*) OR TOPIC: (UK) OR TOPIC: (OECD) OR TOPIC: (Europ*) OR TOPIC:(USA)</b> <i>DocType=All document types; Language=All languages;</i>
#3	<b>TOPIC: (Child*) OR TOPIC: (Infan*)</b> <i>DocType=All document types; Language=All languages;</i>
#2	<b>TOPIC: (Fluorid*)</b> <i>DocType=All document types; Language=All languages;</i>
#1	<b>TOPIC: (Average Intake) OR TOPIC: (AI) OR TOPIC: (Upper Limit) OR TOPIC: (UL) OR TOPIC: (Upper Intake Level) OR TOPIC: (UI) OR TOPIC: (NRV*) OR TOPIC: (Nutritional reference value*)OR TOPIC: (Dietary Reference Intake) OR TOPIC: (DRI) OR TOPIC: (Dietary Reference value*) OR TOPIC: (DRV) OR TOPIC: (Average Requirement*) OR TOPIC: (AR) OR TOPIC: (*Maximum Contaminant Level*) OR TOPIC: (*MCL*) OR TOPIC: (*observed adverse effect level*) OR TOPIC: (*OAEL*) OR TOPIC: (EAR) OR TOPIC: (Estimated Average requirement*)</b> <i>DocType=All document types; Language=All languages;</i>

In the final Web of Science search lines #5, #6, #7, #9, #12 and #13 were redundant.

## **MEDLINE (Ovid)**

1. "Estimated Average Requirement\*".mp.
2. Fluoros\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
3. United States/ or "United States\*".mp.
4. United States/ or USA.mp.
5. "AI".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
6. "Upper Limit".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
7. UI.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
8. "upper Intake Level".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

9. UI\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
10. "NRV".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
11. "Nutritional reference value\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
12. "Dietary reference Intake".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
13. "DRI".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
14. "Dietary reference value\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15. "DRV".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
16. "Average Requirement\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
17. AR\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
18. "\*Maximum Contaminant Level\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
19. "\*MCL\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
20. "\*observed adverse effect level\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
21. "\*OAEL\*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

22. Fluorid\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23. child\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
24. infan\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
25. Australia/
26. New Zealand/
27. NZ.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
28. European Union/ or EU\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
29. Canad\*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
30. Great Britain/ or UK.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
31. Developed countries/ or OECD.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
32. 2 or 22
33. 23 or 24
34. 3 or 4 or 25 or 26 or 27 or 28 or 29 or 30 or 31
35. "Adequate Intake".mp.
36. 1 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 35
37. 32 and 33 and 34 and 36
38. limit 37 to (english language and humans and yr="2005 -Current")
39. exposure.mp.
40. intake.mp.
41. excret\*.mp.
42. Diet/ or diet\*.mp.



43. concentration\*.mp.
  44. ingesti\*.mp.
  45. content.mp.
  46. Biological Markers/ or "bio\* marker\*".mp.
  47. "dental Caries".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
  48. Biological Availability/ or "bio\* availability\*".mp.
  49. 36 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 48
  50. 32 and 33 and 34 and 49
  51. limit 50 to (english language and humans and yr="2005 -Current")
  52. "tooth decay".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
  53. 47 or 52
  54. 22 and 33 and 34 and 49 and 53
  55. limit 54 to (english language and humans and yr="2005 -Current")
- In the final Medline search lines 37, 38, 50 and 51 were redundant.

## Embase

child\* OR infan\* AND ('australia'/exp OR australia OR 'new zealand'/exp OR 'new zealand' OR europe\* OR eu OR usa OR 'united next states' OR america\* OR canad\* OR 'uk'/exp OR uk OR 'united kingdom'/exp OR 'united kingdom' OR oecd)

AND ('dental caries' OR 'tooth decay')

AND fluorid\*

AND 'exposure' OR intake OR excret\* OR diet\* OR concentration\* OR ingesti\* OR content OR bio\* NEXT/1 marker\* OR bio\* NEXT/1 availabilit\* OR 'adequate intake' OR ai OR 'upper limit' OR ul OR 'upper intake level' OR ui OR nrv\* OR 'nutritional reference value' OR 'nutritional reference values' OR 'dietary reference intake'/exp OR 'dietary reference intake' OR dri OR 'dietary reference value' OR 'dietary reference values' OR drv OR 'average requirement' OR 'average requirements' OR ar OR 'maximum contaminant level' OR mcl\* OR 'observed adverse effect level' OR oael\* OR 'ear'/exp OR 'estimated average requirement' OR 'estimated average requirements')

AND (2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py)

AND 'human'/de

## **Dental & Oral Sciences (DOSS); ANZ Reference Centre**

S1 "Average Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary Reference Value\*" OR DRV

S2 "Average Requirement\*" OR AR OR "\*maximum contaminant level\*" OR \*MCL\* OR "\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*"

S3 S1 or S2

S4 Fluorid\* OR Fluoros\*

S5 child\* OR infan\*

S6 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S7 S3 AND S4 AND S5 AND S6

S8 "Average Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI OR "Dietary Reference Value\*" OR DRV

S9 "Average Requirement\*" OR AR OR "\*maximum contaminant level\*" OR \*MCL\* OR "\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*"

S10 S8 OR S9

S11 Fluorid\* OR Fluoros\*

S12 child\* OR infan\*

S13 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S14 S10 AND S11 AND S12 AND S13

S15 "Average Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI

OR "Dietary Reference Value\*" OR DRV

S16 "Average Requirement\*" OR AR OR "\*maximum contaminant level\*" OR \*MCL\* OR "\*Observed adverse effect level\*" OR \*OAEL\* OR "Estimated Average Requirement\*"

S17 S15 OR S16

S18 Fluorid\* OR Fluoros\*

S19 child\* OR infan\*

S20 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S21 S17 AND S18 AND S19 AND S20

S22 child\* OR infan\*

S23 Australia\* OR "new Zealand" OR Europe\* OR EU OR United States\* OR USA OR America\* OR Canad\* OR UK OR "United Kingdom" OR OECD

S24 "Adequate Intake" OR AI OR "Upper Limit" OR UL OR "Upper Intake Level" OR UI OR NRV\* OR "Nutritional Reference Value\*" OR "Dietary Reference Intake" OR DRI  
OR "Dietary Reference Value\*" OR DRV

S25 exposure OR intake OR excret\* OR diet\* OR concentration\* OR content OR "bio\* Marker\*" OR "bio\* availabilit\*"

S26 "dental caries" OR "tooth decay"

S27 Fluorid\*

S28 (exposure OR intake OR excret\* OR diet\* OR concentration\* OR content OR "bio\* Marker\*" OR "bio\* availabilit\*") AND (S24 OR S25)

S29 S22 AND S23 AND S26 AND S27 AND S28

S30 S22 AND S23 AND S26 AND S27 AND S28 (date limited 20040101-20141231)

In the DOSS/ANS Reference Centre final searches lines S22, S23, S24, S25, S26, S27, S28 and S30 were used; all the other search terms were redundant.

## **Toxline**

Toxline is a US National Library of Medicine database. At the time of running the searches the platform did not have a function to save the search terms. So when the search terms were required to be included in the report at a later date they were not available, however they were consistent with the above searches.

## **Summary for fluoride intakes and dental caries**

A total of 655 abstracts were retrieved, 576 after duplicate removal (Cochrane 54, PubMed 30, Web of Science 70, Medline 99, Embase 305, DOSS 94, ANZ Ref Centre 1, Toxline 2 retrieved).

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