

Supporting Document 4: Literature review

Table 1 Review of search results (for Question 1) – Fluoride intake and Dental Caries

Paper	Overview	Methodology	Findings/estimates	Comments
Marshall et al 2005	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 exposure 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 Vs fourth quartile of food and beverage exposure was examined using logistic regression models and was adjusted for cumulative fluoride intake and age of dental exam.	25.7% of the children had caries experience in the primary dentition with median cumulative fluoride exposure in was .55 and .63 mg/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 at 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.
Broffitt et al 2007	Against the backdrop of increased bottled water use and its lower fluoride content the association between bottled water use and	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 till 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	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 were found between the two	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.

	<p>caries was examined using data from the Iowa Fluoride study.</p>	<p>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 also collected as part of the main study. Mixed dentition oral examinations were done at about age 9. Caries was defined as children with cavitated or filled surfaces.</p>	<p>groups in relation to permanent tooth caries or primary second molar caries.</p>	
<p>Ohlund et al 2007</p>	<p>Study on the association between dental caries and the presence of mutants in saliva and carbohydrate and dairy diet in low-prevalence area of 4 year olds. Information on fluoride habits were also collected</p>	<p>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</p>	<p>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 was collected and 44% of them had the mutan 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 with cheese co-relating negatively and black pudding positively. There was no co-relation with intake or frequency of any other food group or energy intake or intake of particular nutrients.</p>	<p>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.</p>
<p>Spencer, Armfield and Slade 2008</p>	<p>Cohort study comparing two states with contrasting fluoridation patterns with the respective increment in caries experience in 5-15 year olds over three years.</p>	<p>Data was from the Child Fluoride Study 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 Fluoride exposure through a parental questionnaire. Caries increment was annualised based on data at baseline and last oral-examination.</p>	<p>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.</p> <p>In SA less than 10% of children has 0% exposure to Fluoride 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.</p>	<p>The main explanatory variable in this study was water fluoridation. Only relationship between caries increment and water fluoridation was reported. Caries experience was not directly compared with fluoride exposure.</p>

			<p>In relationship 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 Qld. In Multivariate analysis after controlling for sex, age, fluoride exposure from other sources and SES fluoridated water showed a significant association with increased caries in both states for deciduous teeth while 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 though an inverse relationship between lifetime exposure and caries increment was evident.</p>	
Warren et al 2009	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	<p>Fluoride intake was collected through regular parental questionnaire 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 was considered.</p> <p>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.</p>	<p>Two main results were shown mainly through figures;</p> <ol style="list-style-type: none"> 1. Those in the neither fluorosis nor caries group had fluoride exposure of less than 0.05 mg F/kg/bw 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. 2. Among those who neither had fluorosis or caries, there was considerable individual variation of fluoride exposure – No summary or variation measures were provided. 	Caries and Fluorosis was 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.
Kirkeskov et al 2010	Health registry data was used to study the association between public water fluoridation and	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 children were used – those born in 1989 and 99 for 5 year olds. Data on water supplied only by public or private waster work was used.	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(89) and 1.44(99) for the two cohorts. Proportion of dmfs= \geq 2 was 20.77 and 15.23 respectively with 90 th percentile being 6 and 4.	Only public water fluoridation was considered as a source of fluoride exposure in this study. The sample size is huge.

dental caries in children in Denmark over a 10 year period among 5 and 15 year olds. For this review we are interested in the data of the 5 years olds only.

Fluoride exposure was calculated as a weighted 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.

Negative association between fluoride exposure through drinking water and caries after adjusting for gender and family income was confirmed. Children with $>1\text{mg/l}$ exposure were half as likely ($OR=0.51$) to have caries as those with $0-0.1249\text{mg/l}$ 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.

Dental caries was dichotomised at $dmfs \geq 2$ which is a conservative cut off. The study did not provide prevalence rates of caries at different levels of drinking water fluoridation.

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Table 2 Review of search results (Question 2) – Fluoride intake and Fluorosis

Report	Overview	Methodology	Findings/estimates	Comments
Bergman et al. 2009	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 would be rather complicated and therefore reviewing DRI for these nutrients could be an uphill task.</p>	No new information about either AI or UL was available.
Clifford et al. 2009	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 formulae 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>
Cressey (2010)	Fluoride content in infant and toddler formulae available on the New Zealand	A total of 32 products including 19 infant, 8 follow-on and 5 toddler formulae purchased and analysed for their fluoride content using a modified microdiffusion method. Dietary fluoride intake was estimated using a stochastic model.	Mean fluoride content was 0.069, 0.065 and 0.081 mg/L, respectively for infant, follow-on and toddler formulae. These values were significantly lower than those reported in 1997. Formulae reconstituted with non-	Formulae purchased were considered to be all products available in New Zealand. There was a positive

	market was analysed and dietary fluoride intake for fully formula-fed infants was estimated.		fluoridated water did not exceed the UL while those prepared with fluoridated water at 0.7 and 1mg/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 formulae is optimally fluoridated.	linear relationship between fluoride concentration of reconstituted formulae and the fluoride content of water used to reconstitute them.
Cressey et al. 2010	Fluoride intake from diet and toothpaste use for New Zealanders was estimated using existing data.	Results from New Zealand Total Diet Survey (NZTDS) which was conducted in 1987-88 and 1990-91 were used to estimate the fluoride content of New Zealand foods while overseas data were used when no information was available from NZTDS. Simulation diets and 24 hour dietary recall records (24HDR) were used for food consumption data whereas dietary fluoride intake was ascertained through total diet 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 th percentile estimations of dietary fluoride intake were quite below the UL. Despite toothpastes had contributed to additional fluoride intake many people, except for infants aged 6-12 months, had mean intakes which were lower than 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. Contribution from toothpaste use to fluoride intake was assessed based on international sources and may not be representative of real picture in NZ.
Erdal & Buchanan 2005	Amidst the reports of increasing prevalence of dental fluorosis in the US the authors used a mathematical model to assess mean daily fluoride intake from all possible sources including drinking water,	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/kg/day, respectively, for infants while the RME and CTE estimates for children were 0.23 and 0.06 mg/kg/day, respectively. In non-fluoridated areas, the RME and CTE estimates were 0.11 and 0.08 mg/kg/day for infants and 0.21 and 0.06 mg/kg/day for children. Although the CRE estimates were within the 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	Uncertainties in this analysis which ranged from medium to high level have affected the findings to a greater extent.

	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.		fluorosis.	
Fojo et al. 2013	Fluoride 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 the descending order was from extract-based soft drinks, juice drinks, juice and teas to carbonated soft drinks. All analysed samples had fluoride concentrations that were lower than the AI and hence these beverages would unlikely to cause fluorosis if considered individually.	Only the beverages were considered as the source of fluoride exposure in this analysis.
Graves et al. 2009	Given that about 15% of US households with private wells were ignored in national water fluoridation program the authors were aiming to estimate the fluoride content in private wells and the prevalence of dental fluorosis	Household drinking water samples were assessed and fluoride exposures were obtained from parents while primary school children were examined to diagnose dental fluorosis.	Drinking water had fluoride ranging from 0.08 to 1.3mg/L which was not only lower than that expected to cause health concerns and also 94% 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.

	among the children who live in these households.			
Hamasha et al. 2005	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 indicate it as a daily fluoride intake in mg.	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 was living in areas with 0.6ppm fluoride in water and hence was inappropriately receiving supplements.	Participants were not representative of any population group and over-represented by Whites with high education levels. Self-reported data were not validated. Dental fluorosis levels were not reported.
Maguire et al. 2011	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 0.02µg/ml for milks to 0.2µg/g 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.
Moseley-Stevens et al. 2010	This study was carried out to estimate fluoride content in RTF infant food and to detect if there are significant	Taves microdiffusion method was used to compare 150 samples of five infant food flavours from two different manufacturers.	The range of fluoride content was 0.01 to 0.60ppm for all samples. For all flavours there existed significant differences between samples of two manufacturers. More importantly, all foods tested had fluoride levels below IOM recommended	Only RTF infant foods were considered.

	differences among flavours and brands.		upper daily intake level. Authors suggested that RTF infant foods should be taken into account when estimating total fluoride intake.	
Nohno et al. 2011	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(mu) g F/ml] were used to reconstitute each IMF.	While the F content ranged from 0.15-1.24 (mu) g/g with a mean of 0.41 no significant differences were observed among manufacturers or different products. The mean F intake from IMF reconstituted with fluoridated water was almost doubled that reconstituted with distilled water.	Fluoride concentration of IMF depends on fluoride content of water that is used to reconstitute IMF.
Siew et al. 2009	Fluoride concentration in infant formulas and fluoride intake in infants fed mainly on formula were estimated and compared with AI and UL recommended by IOM.	A total of 49 infant formulas including 9 RTF, 13 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 0-1ppm fluoride were used to reconstitute formula.	Fluoride content of formula was generally low though soy-based formulas had a higher content which was statistically not significant. If reconstituted with water containing F less than 0.4ppm infants aged 6-12 months would likely to receive F levels below AI while UL could be exceeded in some infants if formulas were reconstituted with water containing 1ppm F.	Estimates were based on 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.
Sohn et al. 2009	Fluoride intake in the US children based on their fluid consumption pattern was determined	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 th and 90 th percentile or higher F intake from fluids was 0.05 and 0.07mg F/kg/day or more which was consistent across all ages. Fluoride ingested by African-American children was significantly higher than that by	Socio-demographic factors might have an effect on fluoride ingestion which needs to be further studied since fluoride intake was based on assumptions and was

	based on National Health and Nutrition Survey (NHANES III).		White children.	under-estimated.
Verkerk 2010	Given that the existing model has an over-simplified two-tailed risk approach that may not consider beneficial effects of exceeding certain threshold a new model with overlapping risks and benefits has been suggested for risk/benefit analysis.	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.	<p>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.</p> <p>The authors questioned the logic of IOM 1997 in estimating UL by setting UF as 1 given the uncertainties in data collection, exposure amount, timing and duration as well as genetic predisposition.</p> <p>In light of caries (infection) preventive action of F the authors suggest using F as a medicine rather than a nutritional supplement.</p> <p>Reappraisal of fluoride based on the conventional model would result in lowering the current value for AI and this in turn would be a blockade to the continuation of water fluoridation programs.</p>	Authors have criticised the existing approach of detecting the risk based on moderate dental fluorosis and estimating the UL based on reducing the caries prevalence in children being contradictory to that adopted for other nutrients.
Zohoori et al. 2013	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	TDFI from diet and toothbrushing was estimated through duplicate dietary plate and toothbrushing expectorate whereas DUFE was through F-ion-selective electrode. The ratio between DUFE and TDFI was computed as FUFE.	<p>A total of 33 children, 21 from low-F (0.3mg F/l) and 12 from naturally F (1.06mg F/l) areas was included.</p> <p>While TDFI and DUFE were not correlated ($r=+0.22$, $P=0.22$) FUFE and TDFI had a statistically significant negative correlation ($r=-0.63$, $P<0.001$).</p>	Further studies in different age groups using adequate sample sizes with sufficient power are essential to confirm the findings.

	living in low-fluoridated and naturally fluoridated areas in north-east England was explored.			
Zohoori et al. 2014	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 toothbrushing 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 0.12mg/kg/bw/day, respectively. For 87% of infants diet was the only source of fluoride while no one used fluoride supplements. TDFI from toothpastes ranged from 24-78% in infants whom toothbrushing/cleaning started. About 53 % of infants living in fluoridated areas exceeded the UL while almost all infants in non-fluoridated areas did not receive below optimal levels of fluoride.	Sample size was rather small. Fluoride intake of infants from all sources was considered.

The main findings from these 16 papers in regards to specific topics that may be referred to elsewhere in the report are summarised below.

Infant formula and other infant foods

Some studies only estimated the fluoride content of infant formula (Clifford et al. 2009; Siew et al. 2009; Cressey 2010; Nohno et al. 2011) while others also considered infant foods, such as ready to feed (RTF) food (Moseley-Stevens et al. 2010; Maguire et al. 2011). Almost all studies based on infant formula were in agreement that the fluoride content in formulas has been on the decline over time and that it is a function of the fluoride concentration of water which has been used to reconstitute formulas rather than the fluoride content of the formula per se. While the overall risk of developing fluorosis is low in formula-fed infants it may be enhanced with increasing fluoride concentration in water that is used to reconstitute the formula. Likewise, the fluoride content in RTF foods were not high enough to cause fluorosis in children although the authors suggested that the contribution from RTF products should be considered in calculating total fluoride intake in infants.

Fluoride intake from diet and toothpaste use

While one study dealt with national fluoride intake information based on historical data in New Zealand (Cressey et al. 2010) another couple of studies investigated the total fluoride intake in infants and its relationship with urinary excretion of fluoride in 6-7 year old children living in north-east England (Zohoori et al. 2013; 2014). The findings of the study on fluoride intake in New Zealand suggested that none of the population sub-groups were at increased risk of exceeding 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 (Cressey et al. 2010). Taking into account all sources of fluoride intake in infants of north-east England Zohoori and colleagues (2014) observed that diet was the main source of fluoride intake (87%) and a little over half of infants living in fluoridated areas exceeded the UL while almost all infants in non-fluoridated areas did not receive optimal levels of fluoride. On the other hand their investigation on total dietary fluoride intake (TDFI)-daily urinary excretion of fluoride (DUFE) relationship revealed that TDFI and DUFE were not correlated though fractional urinary fluoride excretion (FUFE) and TDFI had a statistically significant negative correlation (Zohoori et al. 2013). Caution should be exercised, however, in interpreting these findings because of the small number of participants included in these two studies.

Theoretical/hypothetical concepts of fluoride intake/fluorosis

Erdal & Buchanan (2005) used a mathematical model to assess mean daily 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. Computing both the average (central tendency exposure - CTE) and high-end (reasonable maximum exposure - RME) exposures they suggested that some children might be at increased risk of fluorosis. However, the uncertainties associated with this analysis limit the interpretation of the findings.

Reviewing 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 (IOM 1997), Bergman et al highlighted the importance of including multiple fluoride sources including water, food, beverages and food prepared with fluoridated water in estimating total fluoride intake. They also pointed out that defining optimal intakes and establishing individual and synergistic activities of these nutrients would be rather complicated and therefore reviewing DRI for these nutrients could be an arduous task (Bergman et al 2009).

While criticising the conventional model for its over-simplified two-tailed risk approach that may not consider beneficial effects of exceeding a certain threshold a new model with overlapping risks and benefits has been suggested for risk/benefit analysis by Verkerk (Verkerk 2010). The author questioned the logic of IOM 1997 Report in estimating the UL by setting the Uncertainty Factor (UF) as 1 given the uncertainties in data collection, exposure amount, timing and duration as well as genetic predisposition and cautioned that reappraisal of fluoride based on the conventional model could lower the AI further and this in turn could negatively affect the continuation of ongoing water fluoridation programs.

Miscellaneous studies

There were few other studies focusing on fluoride supplement use (Hamasha et al. 2005), fluoride content in beverages (Fojo et al. 2013) as well as private wells (Graves et al. 2009) and the relationship between fluoride intake and fluid consumption pattern (Sohn et al. 2009). In general, excessive fluoride content/intake from these sources was not reported in these studies despite Sohn and colleagues raising some concerns about socioeconomically disadvantaged children being at a higher risk of ingesting more fluoride than their counterparts from high social background.

References

Refer to Section 8 References in main report.