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Systematic review of evidence pertaining to factors that modify risk of early childhood caries

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Abstract:	INTRODUCTION: A systematic review of evidence on the impact of modifiable risk factors on early childhood caries (ECC) was conducted to inform recommendations in a WHO Manual on ECC prevention. OBJECTIVES: To systematically review published evidence pertaining to the effect on ECC of modifiable risk factors. METHODS: Twelve questions, prioritized by a WHO Expert Panel, relating to infant feeding, diet, oral hygiene and fluoride were addressed. Due to proven efficacy, questions pertaining to use of fluoride toothpaste were excluded. The target population was children aged <72 months. Data sources included MEDLINE, EMBASE, CINAHL, and PubMed. Included were all human epidemiological studies. The highest-level of evidence was used for evidence synthesis and where possible, meta-analysis. The review was conducted in accordance with the PRISMA statement. Evidence was assessed using the GRADE method. RESULTS: 627 of the 13,831 papers identified were screened in duplicate; of these 139 were included. The highest-level evidence indicated breastfeeding ≤ 24 months does not increase ECC risk, but suggested longer duration breastfeeding increases risk (low quality evidence). Low quality evidence indicated increased risk associated with consumption of sugars in bottles. Only one study had data on the impact of sugars in complementary foods; which increased risk. Moderate quality evidence showed a benefit of oral health education for care-givers (OR (95% CI) 0.39 (0.19, 0.80) P=0.009). Meta-analysis of data on the impact on ECC of living in a fluoridated area showed a significant effect (mean difference (95% CI) -1.25 (-1.24,-0.36) P=0.006). Limited, moderate and low quality data indicated a benefit of fluoride exposure from salt and milk respectively. CONCLUSION: The best available evidence indicates breastfeeding up to

	2 years of age does not increase ECC risk. Providing access to fluoridated water and educating care-givers are justified approaches to ECC prevention. Limiting sugars in bottles and complementary foods should

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Systematic review of evidence pertaining to factors that modify risk of early childhood caries

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Knowledge Transfer Statement:

This research is being used by the WHO in developing a toolkit on the prevention and management of ECC. The information will guide governments in developing national oral health plans, and clinicians when providing preventive advice, including advice regarding infant feeding practices. It will help ensure advice is in line with current WHO guidelines and the best available evidence.

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Abstract

INTRODUCTION: A systematic review of evidence on the impact of modifiable risk factors on early childhood caries (ECC) was conducted to inform recommendations in a WHO Manual on ECC prevention.

OBJECTIVES: To systematically review published evidence pertaining to the effect on ECC of modifiable risk factors.

METHODS: Twelve questions, prioritized by a WHO Expert Panel, relating to infant feeding, diet, oral hygiene and fluoride were addressed. Due to proven efficacy, questions pertaining to use of fluoride toothpaste were excluded. The target population was children aged <72 months. Data sources included MEDLINE, EMBASE, CINAHL, and PubMed. Included were all human epidemiological studies. The highest-level of evidence was used for evidence synthesis and where possible, meta-analysis. The review was conducted in accordance with the PRISMA statement. Evidence was assessed using the GRADE method.

RESULTS: 627 of the 13,831 papers identified were screened in duplicate; of these 139 were included. The highest-level evidence indicated breastfeeding ≤ 24 months does not increase ECC risk, but suggested longer duration breastfeeding increases risk (low quality evidence). Low quality evidence indicated increased risk associated with consumption of sugars in bottles. Only one study had data on the impact of sugars in complementary foods; which increased risk. Moderate quality evidence showed a benefit of oral health education for care-givers (OR (95% CI) 0.39 (0.19, 0.80) P=0.009). Meta-analysis of data on the impact on ECC of living in a fluoridated area showed a significant effect (mean difference (95% CI) -1.25 (-1.24,-0.36) P=0.006). Limited, moderate and low quality data indicated a benefit of fluoride exposure from salt and milk respectively.

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CONCLUSION: The best available evidence indicates breastfeeding up to 2 years of age does not increase ECC risk. Providing access to fluoridated water and educating care-givers are justified approaches to ECC prevention. Limiting sugars in bottles and complementary foods should be part of this education.

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Introduction

Early childhood caries (ECC) is a worldwide pandemic and is increasing rapidly in low and middle income countries where exposure to sugars has increased following nutrition transition. ECC may be defined as the presence of one or more non-cavitated or cavitated lesions, missing (due to caries), or filled tooth surfaces in any primary tooth in a child 71 months of age or younger (American Academy of Pediatric Dentistry 2015).

The highest prevalence of ECC is in Asia and Africa where the disease affects 36-85% and 38-45% of children aged under 6 years respectively. Prevalence is also higher in lower socioeconomic groups (Phantumvanit et al. 2018). The highest reported levels are in Cambodia and Indonesia where 90% of 3-5 year olds have a dmft >6.0. In many countries, especially in lower socioeconomic populations, ECC is untreated and, if severe, impacts on health and wellbeing, causing pain and potentially leading to life threatening infections requiring hospitalization. It is beyond the capacity of healthcare resources of most low and middle income countries to treat ECC as prevalence is high and treatment is expensive, especially if general anesthesia is required. An effective means of prevention is therefore of paramount importance.

ECC is caused by exposure to sugars through the diet (Moynihan and Kelly 2014); but a child is exposed to many factors that modify ultimate risk. There are factors that will modify exposure to sugars such as dietary patterns and drinking habits. There are also factors that potentially mitigate ECC and the effect of sugars, including oral hygiene practices and exposure to fluoride through a variety of means. WHO recommends exclusive breastfeeding for the first 6 months of life, followed by

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continued breastfeeding with appropriate complementary feeding (foods and drinks other than breastmilk and infant formula) for up to 2 years or beyond (WHO 2018), although concerns over the impact on risk of ECC of breast feeding after 12 months of age have been raised (Tham et al. 2015). However, to date, no systematic review has specifically compared the impact of breastfeeding up to 12 months with breastfeeding up to two years, or the impact of breastfeeding up to 2 years with breastfeeding beyond 2 years. Moreover, most research has focused on comparing bottle versus breastfeeding and not on comparisons of breast versus cow's milk. Knowledge of which modifiable risk factors have most impact on risk of ECC is essential to inform programs of prevention.

In view of the global problem of ECC, a WHO Expert Consultation on Public Health Intervention against Early Childhood Caries was held in January 2016. The aim was to agree on a set of recommendations for a future action plan. The Consultation included narrative review of evidence for factors that impact on risk of ECC (WHO 2016). However, recommendations need to be based on systematic review of the best available evidence (WHO 2014) and be in line with WHOs common risk factor approach to prevention. Based on the evidence presented at the Expert Consultation, research questions pertaining to the prevention of ECC that required systematic review were prioritised by the panel. Questions pertaining to the use of fluoride toothpaste were excluded as the panel concluded its efficacy as a mitigating factor against ECC was already proven through systematic review (dos Santos et al 2013a; 2013b; Wright et al 2014). Nonetheless it was recognised that accessibility of affordable fluoride toothpaste was not universal, especially in less affluent countries and that other means of prevention and mitigation were essential. This systematic

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review was commissioned by WHO and the aim of this paper is to report the outputs. The objective was to systematically identify and review all available published evidence pertaining to the effect on ECC of modifiable risk and protective factors. The overall question underpinning the review was 'which is the best way to maintain health of the primary dentition? The specific questions addressed are presented in Table 1.

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Methods

Guided by the WHO Guideline Development Process (WHO 2014) a systematic review was conducted and reported according to the PRISMA statement. The review methods were established prior to the conduct of the review. The protocol is published on PROSPERO (Hillier-Brown et al. 2017) and is described, in brief, below.

Eligibility criteria

All relevant randomized controlled trials (RCTs), other intervention studies and observational studies (including cohort, case-control, ecological and cross-sectional studies), were included. Participants were apparently healthy (without acute illness, but may be overweight or have chronic illness such as diabetes) infants and children aged <72 months, and caregivers, in countries that are low, middle or high income. For RCTs an intervention period of at least one year for dental caries was required. The American Academy of Pediatric Dentistry (American Academy of Pediatric Dentistry 2016) definition of ECC was adopted for this review. The intervention/exposures and the comparator/controls according to each research question are presented in Table 1. Excluded were studies with participants of different age groups, studies specifically targeting children with medical conditions, and articles not peer-reviewed and published. Non-English articles were included if they contained an English language abstract. No date restrictions were used. The questions were limited to risk and protective factors that can be described as 'modifiable' (i.e. could lead to a recommendation or policy for a change in practice). Therefore, genetics and acquisitions of mutans streptococci, salivary protein profile and

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antioxidant capacity were all excluded.

Dental caries outcomes included the primary dentition only, including caries increment, incidence and/or severity, measured as decayed, missing/exfoliated and filled teeth (dmft, dmfs, deft, dft ECC and S-ECC (Severe Early Childhood Caries)); and/or comparisons of higher or lower levels of dental caries.

Search Strategy

Four electronic databases were searched in August 2017. The databases included MEDLINE, EMBASE, CINAHL, PubMed. Moreover, registers of the ongoing systematic reviews (SRs) were searched using the Cochrane Library (Dentistry and Oral Health) and PROSPERO (Centre for Reviews and Dissemination). Clinical trials were also identified by accessing and searching the U.S. National Library of Medicine and the WHO International Clinical Trials Registry Platform. Abstracts and unpublished studies were not included. The search strategy is presented in the Appendix.

Study selection

An initial screen of titles and abstracts of all records identified in the electronic search was conducted by a single reviewer (LT, RH, BA, AM, PK). A random 5% sample of titles and abstracts were screened by all reviewers and inter-rater reliability was assessed qualitatively. Studies that apparently met the inclusion criteria or where there was not enough information in the abstract to inform a decision, underwent independent duplicate screening of the full article. Differences between reviewers

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were resolved by discussion and by a third reviewer where consensus could not be reached. Data extraction was undertaken by one reviewer and checked by a second reviewer. Evidence was grouped according to the 12 review questions and each organised by study type, according to the hierarchy: systematic review; RCT; cohort, case-control, other interventions (e.g. quasi-experimental studies); cross-sectional, ecological, to enable a pragmatic data synthesis of the 'best available evidence' (Petticrew and Roberts 2006). For each research question the highest level of evidence retrieved was used for evidence synthesis and where appropriate meta-analysis. Meta-analysis and forest plots of data that could be pooled, were created using RevMan software. Evidence was also reported narratively. When data from the highest level of evidence were scant, the next level of evidence was referred to narratively.

Quality assessment

Risk of bias for individual studies was assessed using the Cochrane 'Risk of Bias' tool for RCTs (Cochrane Collaboration) and the ROBINS-I for non-randomised trials and all other studies (Cochrane Collaboration). The Grading of Recommendations Assessment Development and Evaluation (GRADE) (Atkins et al. GRADE Working Group, 2004) was used to assess the quality of the overall body of evidence in relation to each review question, based on the WHO Handbook for Guideline Development (WHO 2014). The quality of the evidence was categorised as high, moderate, low or very low. The GRADE assessment was conducted by using GRADEpro software. The GRADE method classifies observational studies as 'low quality' and upgrading to a higher level requires evidence of a large effect size or a dose response. RCTs are classified as 'high quality' but in some instances, the GRADE method requires

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downgrading of evidence if there is serious risk of bias, imprecision, inconsistency of results, indirectness, or if publication bias is likely.

Results

Figure 1 presents the PRISMA flow chart. In total 13,831 papers were retrieved, reducing to 9,449 following de-duplication. Of those, 627 papers full papers were retrieved and screen. Following this screening, 137 papers (133 studies) were eligible for inclusion and 493 papers were excluded. The reasons for exclusions are provided in Figure 1 and the Appendix (Appendix Table 1). A breakdown of the number of studies for each main research question is presented in Appendix Table 2. Information from the data extraction, for each paper identified as the highest level of evidence retrieved for each question, is presented in the Appendix (Appendix Table 3). The results, by research question, are considered below and a summary of the highest-level evidence pertaining to each question is provided in Table 2. The GRADE evidence profiles are presented in the Appendix (Appendix Tables 4-13).

Question 1. Does breastfeeding beyond one year increase the risk of early childhood caries compared with breastfeeding until less than one year of age?

Twenty one studies had data that enabled comparison of dental caries in children breast fed beyond one year with up to one year of age. Of these, one was a case control study and 19 were cross sectional studies. The highest level of evidence came from one prospective cohort study (Peres et al. 2017). This study showed no significant difference in severity of caries at 5 years between children breastfed up to 23 months with those breastfed up to one year. Overall risk of bias rating for this study was moderate. In relation to confounding, all participants entered the study at

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the same time. Additionally, fluoridated area and sugars intake was controlled for. A GRADE evidence profile analysis of these data, that showed no increased risk of ECC with breastfeeding up to 23 months, classified the evidence as 'low quality'. This finding was supported by the next level of evidence: a case control study in which multivariate analysis indicated that breastfeeding >13 months compared with <12 months, was not predictive of high dmft. Moreover, of the 19 cross sectional studies, 9 included multivariate analysis to explore an independent effect of breastfeeding up to 2 years compared with up to one year. Six of 9 studies showed breastfeeding up to 24 months of age was not a primary risk factor for ECC (Appendix Table 14).

QUESTION 2. Does breastfeeding beyond one year increase the risk of early childhood caries compared with cow's (or similar) milk consumption as main milk source from one year of age?

No studies were identified that had data to enable risk of ECC to be compared between children breast fed beyond one year compared with children who consumed cow's milk as the main source of milk.

QUESTION 3. Does breastfeeding beyond two years increase the risk of early childhood caries compared with breastfeeding until less than two years of age?

Eight studies provided data that enabled levels of ECC to be compared when breast feeding extended beyond 2 years of age compared with when it ceased by age 2. Included were: 2 cohort studies; 1 case control study and 5 cross sectional studies. The highest-level evidence was the cohort studies (Chaffee et al. 2014; Peres et al. 2017). The aforementioned study by Peres et al, which showed breastfeeding beyond 2 years of age increased caries risk, demonstrated a large effect size. However, the

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study by Chaffee found a non-significant trend towards increased prevalence of ECC with breastfeeding at 24 months and beyond compared with breastfeeding between 6 and 23 months (adjusted Prevalence Ratio (95% CI) 1.17 (0.85, 1.78). This evidence was classified as 'low quality' using the GRADE process.

QUESTION 4. Does breastfeeding beyond two years increase the risk of early childhood caries compared with cow's (or similar) milk consumption as main milk source from two years of age?

No studies were identified that had data to enable risk of ECC to be compared between children breast fed beyond two years of age compared with children who consumed cow's milk as the main source of milk from two years of age.

QUESTION 5. Does consumption of liquids that contain free sugars from an infant feeding bottle, increase the risk of early childhood caries?

Thirty one studies provided data relating to the risk of ECC from consumption of liquids containing free sugars from an infant feeding bottle. These included: 3 cohort studies, 2 case control studies and 25 cross sectional studies. The highest level evidence came from the cohort studies, all of which showed a positive relationship between consumption of sugars as liquids in feeder bottles, however, two of these were rated as being at critical risk of bias (in relation to confounding) (Tanaka et al. 2013; Wendt and Birkhed 1995; Wendt et al. 1996) and were therefore excluded from the GRADE evidence profile as recommended (Guyatt et al. 2013). The remaining cohort study was rated as having a low risk of bias (Feldens et al. 2010). This study showed a significant increased risk of severe ECC with use of bottles containing fruit juices or soft drinks at 12 months of age (Relative Risk 1.41 (95% CI 1.08, 1.86). A

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GRADE evidence profile classified this evidence as 'low quality'. This finding is supported by the data from the next level of evidence; two case control studies, both of which showed sugars in bottles to be independently associated with ECC (Appendix Table 14).

QUESTION 6. Does consumption of complementary drinks that contain free sugars increase the risk of early childhood caries?

Data pertaining to the risk of ECC from consumption of drinks containing free sugars were found in 8 studies: 6 cohort studies and 2 cross sectional studies. The highest level evidence came from the 6 cohort studies for which analysis of risk of bias classified risk as very serious primarily due to risk of confounding and weaknesses in experimental design. Five of the 6 studies showed significantly higher ECC in children that consumed a higher compared with lower/no drinks containing free sugars

(Warren et al. 2009; Watanabe et al. 2014; Wendt and Birkhed 1995; Wendt et al. 1996; Wigen and Wang 2014) and one study found no significant difference (Yonezu et al. 2006). However, this study compared ECC between those consuming 3 vs. 2 drinks/week and not with non-consumers. The GRADE profile analysis of these data, suggesting increased risk of ECC from consumption of sugars containing drinks, classified the evidence as 'very low quality'.

QUESTION 7. Does consumption of complementary foods to which free sugars have been added increase the risk of early childhood caries?

One cohort study (Feldens et al. 2010) provided data that enabled the comparison of levels of ECC according to consumption of complementary foods (foods consumed in addition to breast or bottle feeding up to the age of 2 years) containing free sugars.

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This study showed a relative risk of severe ECC of 1.43 (95% CI 1.08, 1.89) P=0.003) with consumption of items with a high density of added sugars compared with no consumption of items of high added sugars density. A GRADE profile analysis of these data, showing increased risk of ECC with consumption of foods high in free sugars, classified the evidence as 'low quality'

QUESTION 8. Does oral hygiene provided by a parent/carer reduce the risk of early childhood caries?

Twenty one studies had data on the impact on ECC of oral hygiene provided by a care giver. These included: 2 cohort studies, 1 quasi experimental study and 17 cross sectional studies. The highest level of evidence came from the cohort studies (Leroy et al. 2012; Okuno et al. 1994) both studies had serious risk of bias due to lack of control for confounding. Neither study showed a significant independent effect. In the study by Leroy, multivariate analysis showed that oral hygiene provided by parent or care-giver was not an independent factor for risk of ECC. Okuno et al. (1994) found that oral hygiene conditions and eating habits between meals were stronger determinants of ECC than oral hygiene provided by parent. The evidence therefore suggests little effect of oral hygiene provided by parent or care-giver on ECC risk. The quality of the data were also classified as 'very low' quality by the GRADE profile analysis.

QUESTION 9. Is oral health education for care-givers' effective for preventing early childhood caries?

Fourteen studies had data pertaining to the impact of oral health education for care-givers on children's risk of ECC. These included: 6 RCTs, 2 cohort and 6 quasi-

experimental studies. The highest level of evidence was provided by the RCTs, 4 showed lower levels of ECC in children, resulting from oral health education programmes for care givers (Feldens et al. 2007; Harrison et al. 2007; Mohebbi et al. 2009; Plutzer and Spencer 2008), and two showed no significant effect (Jiang et al. 2014; Vachirarojpisan et al. 2005). It was not possible to conduct a meta-analysis on all 6 RCTs due to differences in outcomes reported. A random effect meta-analysis of 3 RCTs reporting data as odds ratio showed children of caregivers who received oral health education had a reduced risk of ECC compared with those of caregivers who had never received oral health education (OR (95% CI) 0.39(0.19,0.79 P=0.009; with moderate heterogeneity between studies (I^2=52%; p=0.12). A random effect meta-analysis of three studies reporting outcomes as mean (SD) dmft, showed a non-significant trend (Standardized mean difference (95% CI) -0.15 (-0.34, 0.05) P=0.140 (Harrison et al. 2007; Jiang et al. 2014; Vachirarojpisan et al. 2005); with low to moderate heterogeneity between studies (I^2 = 43%; p=0.17). Forest plots are presented in Figure 2. A GRADE evidence profile classified the evidence as 'moderate quality' as data were downgraded for inconsistency of findings.

QUESTION 10. Does an optimum concentration of fluoride in water reduce the risk of early childhood caries?

Thirty two studies had data relating to the above question; 13 cohort studies; 15 cross sectional studies and 4 ecological studies. The highest level of evidence came from the cohort studies that reported ECC in children that had resided in fluoridated areas from birth compared with those residing in non-fluoridated areas (Blinkhorn et al. 1981; Booth et al. 1992; Evans et al. 1996; French et al. 1984; Jackson et al. 1980; Jackson et al. 1975a; Jackson et al. 1985; Jackson et al. 1975b; O'Mullane 1997;

Rugg-Gunn et al. 1988; Rugg-Gunn et al. 1981; Tank 1964; Thomas 1995). All studies showed lower development of ECC in children exposed to fluoridated water and there was evidence of a large effect size in individual studies. Only 2 studies (Booth et al. 1992; Jackson et al. 1975a) reported data comparing levels of fluorosis between groups; none showed a difference between fluoridated and non-fluoridated populations. Four studies had a serious risk of bias due to failure to measure and account for any socioeconomic difference between groups and these were excluded from the analyses (Jackson et al. 1980; Jackson et al. 1975a; Jackson et al. 1985; Jackson et al. 1975b). It was possible to pool data for dmft from 4 studies for meta-analysis (Figure 3) which showed evidence of significant protective moderate size effect of exposure to fluoridated water (mean difference between fluoridated and non-fluoridated -1.25, 95% CI -2.14, -0.36), P=0.006). There were high levels of heterogeneity between studies I^2 = 92%; p<0.00001). Most studies were rated as having a moderate risk of bias. A GRADE evidence profile of these data classified the evidence as 'moderate quality'

Question 11. Does consumption of fluoridated milk reduce the risk of early childhood caries?

Three studies with data pertaining to the impact of drinking fluoridated milk on risk of ECC were identified. These included: 1 quasi-experimental and 2 cross sectional studies. The highest level of evidence was the quasi-experimental study (Bian et al. 2003), which showed a strong protective effect on ECC of consumption of fluoridated milk. However, risk of bias was assessed as serious, as socioeconomic status of control and intervention groups was not controlled for. There was also a lack of control for dietary factors (e.g. sugars intake). The findings of the cross sectional

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studies supported the findings of a protective effect of fluoridated milk (Appendix Table 14). The GRADE evidence profile classified the evidence as 'low quality'.

Question 12. Does salt fluoridation reduce the risk of early childhood caries?

Four studies had data pertaining to the impact on risk of ECC of consumption of fluoridated salt. These included: 1 RCT, 1 cohort and 2 quasi-experimental studies. The highest level of evidence was provided by the RCT (Jordan et al. 2017). This study received a high risk of bias rating due to lack of blinding of the outcome assessors and was therefore downgraded for risk of bias. This study showed a lower level of cavitation in the test population. Data for pre-cavitated lesions showed higher mean lesions in the test compared with control group (i.e. opposite effect as observed for caries into dentine measured by dmft), however 95% CI suggest this difference was not significant. A GRADE evidence profile of this study rated the quality as 'moderate'. The next level of evidence was provided by one cohort study that indicated a significant protective effect of the use of fluoride salt on caries experience (dmft) (Appendix Table 14).

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Discussion

The best available evidence indicates that breastfeeding up to 2 years of age does not increase risk of ECC, compared with breastfeeding up to one year of age. The findings show consistent albeit low quality evidence that consumption of liquids containing free sugars, including from a feeding bottle, increases the risk of ECC. Limited data indicate that adding free sugars to complementary foods also increases risk. This systematic review has identified moderate quality evidence that provision of oral health education to carers, exposure to optimally fluoridated water and salt fluoridation (limited data), decrease risk of ECC. Evidence, albeit low quality, also shows a protective effect of fluoridated milk. There was limited opportunity for meta-analysis. However where these analysis were undertaken the findings support the conclusion of a protective effect. All three meta-analysis showed heterogeneity between studies; although only one was considered high.

This systematic review has largely identified low/very low quality evidence pertaining modifiable factors for risk of ECC, which reflects the observational nature of most of the data and the serious risk of bias in many studies. There is a need for better quality research including where appropriate, trials and well-designed cohort studies that collect data on, and control for, relevant confounders and that also adopt robust and objective measures of risk exposure.

This review focused on factors known to be modifiable, but excluded factors if pre-existing evidence from systematic review was sufficient (e.g. amount of sugars consumed, use of fluoride toothpaste). It is acknowledged that socioeconomic factors (i.e. low level of general education, low income, family dynamics) may increase the likelihood of being exposed to risk factors for ECC (Phantumvanit et al. 2018),

however, it is unlikely such factors are independent risk factors and questions specific to these factors were therefore not included.

The current review indicated that breastfeeding up to 2 years did not increase risk of ECC compared with breastfeeding up to one year. A previous systematic review (Tham et al. 2015) suggested that breastfeeding beyond one year of age increased the risk of ECC, but cautioned that until the confounding effects of dietary habits and oral hygiene are adequately controlled for it cannot be certain if prolonged breastfeeding can be principally associated with ECC. Moreover, the meta-analysis included studies of breastfeeding beyond 12 months, with no upper limit on duration, whereas the current review focused on breastfeeding up to 2 years of age. The current review also included more recent longitudinal data (Peres et al. 2017). The review by Tham et al. (2015) included only one cohort study (Tanaka et al. 2013) and one cross sectional study (Nobile et al. 2014) that enabled comparison of breastfeeding up to 2 years with up to one year. Tanaka et al. (2013) found a non-significant trend towards a lesser protective effect against S-ECC of breastfeeding 12-17 months (OR 0.81 (95% CI 0.16, 4.01)) compared with breastfeeding for 6-11 months (OR 0.4 (0.07-2.01) p=0.09. Nobile et al.(2014) showed that prevalence of ECC increased with increased breastfeeding duration and those breastfed 11-19 months had a higher dmft (0.44 (SD 1.07) compared with infants breastfed for 5-10 months duration (dmft = 0.22 (SD 0.62). Neither study adequately controlled for important confounders.

An aim of the review was to determine if weaning from breast milk to cow's milk from one year of age effected ECC risk; however, no data were identified to address this. Human breast milk contains approximately 7% sugars compared with cow's

milk which contains <5% sugars (primarily lactose). Cow's milk is also high in calcium and phosphorus which protect against demineralisation and therefore it is reasonable to suggest that weaning to cow's milk would lower caries risk. However, studies have reported only on duration of breastfeeding and not on the alternative source of milk on its cessation – which could be formula or cow's milk. Moreover, cessation of breastfeeding might lead to the introduction of sugars-sweetened beverages. There are therefore many factors to consider when investigating the impact of breastfeeding duration on risk of ECC (Peres et al. 2017) and future research should pay more careful attention to controlling for confounding form complementary foods and drinks. The impact on ECC risk of weaning onto cow's milk also warrants further exploration in well conducted studies that consider and control for the intake of all drinks. It is unknown if there are benefits to oral health of weaning a child onto cow's milk at one year and from a general health perspective, for both child and mother, breastfeeding to age 2 years and beyond has considerable benefits (WHO 2018).

A previous systematic review has shown moderate quality evidence for an increased risk of dental caries, including ECC, from increasing the amount of free sugars consumed (Moynihan and Kelly 2014). The current review has indicated that data pertaining to specific dietary practices and risk of ECC are more limited. Notwithstanding the importance of limiting intake of free sugars per se, the current systematic review found only one study that had examined specifically the effect of consuming complementary foods containing free sugars. This study did however, clearly show an independent effect indicating that complementary foods should not contain added free sugars. The data also support the avoidance of sugars-containing

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drinks including from a feeding bottle. Studies on the impact on ECC risk of interventions promoting the avoidance of adding sugars in complementary foods and drinks are needed.

A larger volume of data pertaining to the impact of providing oral health education to care givers on ECC risk, including that from RCTs were available. Information on the difference approaches used is given in Table 2. Meta-analysis of studies reporting risk as odds ration indicated a reduced risk of 39% but there was inconsistency between studies. Nonetheless, overall the evidence supports oral health education for care-givers as a means of ECC prevention.

Unsurprisingly there was a larger body of moderate quality evidence to support water fluoridation as a means of ECC prevention, thus indicating the importance of promoting exposure to optimally fluoridated water wherever possible. The findings suggest that for areas without access to public water supplies to fluoridate, that exposure to fluoride via alternative means such as kindergarten/school milk fluoridation programmes or salt fluoridation programmes is effective. However, the results of the one RCT on salt fluoridation showed lower cavitation lesions and a trend towards higher pre-cavitation lesions in the test group, suggesting an arresting effect of salt fluoridation on existing dental caries. Moreover, salt *per se* is detrimental to health and therefore fluoridation must be achieved within the WHO recommended limits for sodium intake (WHO 2018b).

Conclusion

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Based on the best available, albeit limited, evidence, breastfeeding up to 24 months is not associated with an increased risk of ECC. The evidence indicates that breastfeeding beyond 24 months carries an increased risk of ECC; this risk should be balanced against the nutritional and health benefits of breastfeeding children beyond 2 years of age.

Based on the best available evidence, providing access to fluoridated water and delivering oral health education to care givers are justified approaches to ECC prevention. The evidence suggests that limiting sugars in feeder bottles and avoiding addition of sugars to complementary foods and drinks should be part of this education. Evidence that pre-existed this review indisputably proves the efficacy of fluoride toothpastes which should be made accessible and affordable to all. Evidence from this review shows efforts to increase access to fluoridated water should also be given priority. In populations without access to a fluoridated public water supply, the evidence shows that exposure to fluoride through milk schemes, and to a lesser extent salt, are justifiable as a means of prevention.

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Table 1. Review questions with related definitions of intervention and control (intervention studies) and exposure and comparator (observational studies)

Question	Intervention/control*. Exposure/comparator **	
Q1.Does breastfeeding beyond one year increase the risk of early childhood caries compared with breastfeeding until less than one year of age?	Exposure	Breastfeeding beyond one year.
	Comparator	Breastfeeding less than one year.
Q2. Does breastfeeding beyond one year increase the risk of early childhood caries compared with cow's (or similar) milk consumption as main milk source from one year of age?	Exposure	Breastfeeding beyond one year.
	Comparator	Cow's (or similar) milk consumption as main milk source from one year of age.
Q3. Does breastfeeding beyond two years increase the risk of early childhood caries compared with breastfeeding until less than two years of age?	Exposure	Breastfeeding beyond two years.
	Comparator	Breastfeeding less than two years.
Q4. Does breastfeeding beyond two years increase the risk of early childhood caries compared with cow's (or similar) milk consumption as main milk source from two years of age?	Exposure	Breastfeeding beyond two year.
	Comparator	Cow's (or similar) milk consumption as main milk source from two years of age.
Q5. Does consumption of liquids that contain free sugars from an infant feeding bottle, increase risk of early childhood caries?	Intervention	Any intervention intended to reduce the consumption of liquids that contain free sugars from an infant feeding bottle in one arm of the study, compared to consumption of such liquids in another arm of the study. To be included a trial must report this feeding practice status in both arms.
	Control	Consumption of liquids that contain free sugars from an infant feeding bottle.

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	Exposure	Consumption of liquids that contain free sugars from a bottle. When assessing the quality of the evidence, the separation or controlling for the effects of other lifestyle or medical interventions (for example, use of bottle per se, prolonged breast feeding, exposure to fluoride, sugars intake from other dietary sources, feeding practices, oral hygiene behaviour) will be considered.
	Comparator	No or lower free sugars containing drinks consumed from an infant feeding bottle.
Q6. Does consumption of complementary drinks[$] that contain free sugars increase the risk of early childhood caries?	Intervention	Any intervention intended to reduce the consumption of complementary drinks that contain free sugars in one arm of the study, compared to consumption of such complementary in another arm of the study. To be included a trial must report this feeding practice status in both arms.
	Control	Consumption of complementary drinks that contain free sugars.
	Exposure	Consumption of complementary drinks that contain free sugars.
	Comparator	No or lower free sugars containing complementary drinks consumed.
Q7. Does consumption of complementary foods[$] to which free sugars have been added increase risk of early childhood caries?	Intervention	Any intervention intended to reduce the consumption of free sugars in complementary foods in one arm of the study, compared with no intervention in the other arm. To be included a trial must report this feeding practice status in both arms.
	Control	Consumption free sugars in the complementary diet.
	Exposure	Consumption free sugars in the complementary diet.
	Comparator	No or lower consumption of free sugars in complementary diet.
Q8. Does oral hygiene	Exposure	Good oral hygiene as indicated by

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provided by a parent/carer reduce the risk of early childhood caries?		the absence of a high plaque volume and or daily tooth brushing by carer.
	Comparator	Poor oral hygiene (as defined above).
Q9. Is oral health education for care givers' effective for preventing early childhood caries?	Intervention	Any intervention where care givers receive oral health education in one arm of the study, compared with no intervention in the other arm.
	Control	No or lower oral health education to caregivers.
	Exposure	Caregiver exposure to oral health education.
	Comparator	No or less caregiver exposure to oral health education.
Q10. Does an optimum concentration of fluoride in water reduce the risk of early childhood caries?	Intervention	Any intervention where participants are exposed to fluoridated water or water naturally containing fluoride (at a concentration of >0.6 PPM (mg/L)) in one arm of the study, compared with non-fluoridated water or water that is naturally low in fluoride (<0.3PPM) in the other arm.
	Control	No exposure to fluoridated water or water naturally containing fluoride at a level of >0.6 PPM.
	Exposure	Participants living in areas where water is fluoridated or naturally contains fluoride (at a concentration of >0.6 PPM).
	Comparator	Participants living in areas where water is not fluoridated nor naturally high in fluoride (i.e. the concentration of fluoride in water is <0.3 PPM).
Q11. Does consumption of fluoridated milk reduce the risk of early childhood caries?	Intervention	Any intervention intending to increase the consumption of fluoridated milk in one arm of the study, compared with no intervention, or no consumption of fluoridated milk, in the other arm.
	Control	No consumption of fluoridated milk.

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	Exposure	Consumption of fluoridated milk.
	Comparator	No consumption of fluoridated milk.
Q12. Does salt fluoridation reduce the risk of early childhood caries?	Intervention	Any intervention intending to encourage the exposure to/consumption of fluoridated salt in one arm of the study, compared with no intervention, or no consumption of fluoridated salt, in the other arm.
	Control	No exposure/consumption of fluoridated salt.
	Exposure	Consumption of/exposure to fluoridated salt.
	Comparator	No consumption of fluoridated salt/exposure to salt fluoridation.

* for intervention studies
** for observational studies
$ all foods and drinks consumed in addition to breastmilk and infant formula are referred to as 'complementary foods and drinks' and sometimes commonly referred to as 'weaning foods and drinks'

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Table 2. Summary of studies contributing to the top level of evidence for review questions.

Q1. Does breastfeeding beyond one year increase the risk of early childhood caries compared with breastfeeding until less than one year of age?	
Reference	**Evidence**
Peres et al 2017	Cohort study to investigate if there is a controlled direct effect of breastfeeding on dental caries in Brazilian children aged 5 years. Risk of dental caries amongst children who were breastfed for 13-23 was not significantly different to those breastfed to up to 12 months. Multi-source method for caries amongst children who were breastfed for 13-23 months compared to up to 12 months showed the mean ratio (95% CI) = 0.9 (0.6, 1.3). For severe dental caries -relative risk (95% CI) = 1.0 (0.6, 1.6).
Q2. Does breastfeeding beyond one year increase the risk of early childhood caries compared with cows (or similar) milk consumption as main milk source from one year of age?	
N/A	No evidence
Q3. Does breastfeeding beyond two years increase the risk of early childhood caries compared with breastfeeding until less than two years of age?	
Peres et al 2017	Cohort study investigating risk of dental caries amongst children who were breastfed for ≥24 months was significantly increased. Multi-source method for caries amongst children who were breastfed ≥ 24 months compared to up to 24 months showed the mean ratio (95% CI) = 1.9 (1.5, 2.4). For severe dental caries -relative risk (95% CI) = 2.4 (1.7, 3.3).
Chaffee et al 2014	Cohort study investigating the risk of severe ECC in children from a low income population in Brazil who were breastfed for 24 months compared with lesser durations. Severe early childhood caries (S-ECC) was assessed at aged 38 months. Breastfeeding ≥24 months was associated with a higher adjusted population-average severe-ECC prevalence (0.45, 95% CI: 0.36, 0.54) compared with 12–23 months (0.39, 95% CI: 0.20, 0.56). The Prevalence Ratio for ECC (95% CI) with breastfeeding for 24 or months was 1.17 (0.85, 1.78) which failed to reach statistical significance.
Q4. Does breastfeeding beyond two years increase the risk of early childhood caries compared with cows (or similar) milk consumption as main milk source from two years of age?	
N/A	No evidence
Q5. Does consumption of liquids that contain free sugars from an infant feeding bottle, increase the risk of early childhood caries?	
Feldens et al 2010	Cohort study that compared S-ECC at 4 years of age in Brazilian children exposed to bottle use for fruit juices / soft drinks at 12 months compared with no use of bottle for juices/soft drinks. Relative risk for S-ECC (95% CI) = 1.41 (1.08, 1.86), (P=0.025).
Wendt and	Cohort study of caries free Swedish children at age one

Birkhed 1995; Wendt et al 1996	year, examining the factors associated with the development of ECC at age 2 years. Compared with children remaining caries free at age 3 years , a higher proportion of children with caries at age 3 consumed soft drinks more than once a day (12% vs 23% respectively) p<0.04).
Tanaka et al 2013	Cohort study of children followed from age 2 to 50 months in Japan. Of 1002 recruited 315 completed all aspects of the study. Logistic regression indicated that consuming sweetened liquids from a bottle compared with never consuming these drinks from a bottle, significantly increased risk of ECC. Adjusted OR 2.17 (95% CI 1.23, 5.05).
Q6. Does consumption of complementary drinks that contain free sugars increase the risk of early childhood caries?	
Warren et al 2009	A cohort study to assess the effect of sugar-sweetened beverage consumption on 18-month caries prevalence (as part of a longitudinal study) of high-risk children in the USA. The odds ratio (95% CI) for development of dental caries in those consuming sugars drinks was 3.04 (1.07, 8.64).
Watanbe et al 2014	Cohort study that examined how lifestyle, household environment, and caries activity test score of Japanese children at age 1.5 years, affected their dental caries incidence at age 3. The odds ratio (95%CI) for ECC with daily sugar-sweetened beverage consumption was 1.56 (1.46, 1.65) p= <0.001.
Wendt et al 1995;1996	Cohort study of caries-free Swedish children at age on years examining the factors associated with the development of ECC at age 2 and 3 years. Not drinking sugars sweetened drinks to quench thirst at age one was an independent significant factor determining being free of dental caries at age 3 (OR 2.26 (95% CI 1.07, 4.77) p=0.033. No comparative data were provided on the proportion of children with caries and caries-free at 3 years of age who got milk or water when thirsty.
Wigen & Wang 2014	Cohort study in which exposure to sugars in drinks in Norwegian children aged 1.5 years of age was related to caries experience at 5 years. Risk (OR, 95% CI) of ECC with consumption of sugars-containing drinks at night was 1.5 (0.8–2.8) for consumption sometimes, and 2.2 (1.1–4.5) for nightly consumption, compared with never.
Yonezu et al 2006	Cohort study that compared ECC between Japanese children that consumed sweetened beverages 2/week versus 3/week at age 18 months. Logistic regression analysis of effect on ECC experience at 24 months of age showed sweet beverages intake was no significant OR(95%CI): 0.99 (0.25, 4.01).
Q7. Does consumption of complementary foods to which free sugars have been added increase the risk of early childhood caries?	
Feldens et al	Cohort study investigating feeding practices in the first year

2010	of life associated with S-ECC at the age of 4 years. 47.3% of children who consumed foods with a high density of added sugars had ECC compared with 32% in non-consumers. Multivariate analysis showed consumption of foods with a high density of added sugars increased risk of ECC. Relative risk 1.43 (1.08, 1.89) P =0.003.
Q8. Does oral hygiene provided by a parent/carer reduce the risk of early childhood caries?	
Leroy et al 2012	Cohort study that examined risk factors for the incidence of visible caries experience in pre-school children in Belgium. Help with brushing >1/day compared with <daily was associated with reduced risk of ECC between 3 and 5 years of age in univariate analysis. However, help with brushing was not an independent factor in multivariate analysis.
Okuno 1994	Cohort study of children aged 18 months in Japan. Exposure to risk factors at 18 months was related to ECC at age 3 years. Logistic regression analysis showed that oral hygiene conditions and eating habits between meals were more important than mother-aided daily tooth brushing.
Q9. Is oral health education for care givers' effective for preventing early childhood caries?	
Feldens et al 2007	RCT to investigate the impact of home visits for advising mothers about breast feeding and weaning on ECC in Brazil. The intervention was initially delivered from 10 days – 14 months; dental examination took place between 12 and 14 months. 10.2% of the intervention group had ECC and the mean dmft was 0.37 compared with 18.3% in the control group with a mean dmft of 0.63 (p=0.03). Odds Ratio for the intervention group 0.52 (95% CI 0.27, 0.97) (p = 0.03).
Harrison et al 2007	RCT to investigate the effect of an oral health intervention employing motivational interviewing (MI) to prevent ECC in S. Asian immigrants in Canada. The dmft in the intervention group was 3.35 (SD 7.8) versus 7.59 (SD 14.2) in the control (p=0.001). Poisson regression showed protective effect of MI relative to the control condition on the rate of dmfs after 2 years (hazard ratio = 0.54 (95% CI 0.35, 0.84).
Plutzer et al 2008	RCT to investigate the efficacy of an oral health promotion programme during pregnancy and when the child was 6 and 12 months of age, on S-ECC at 18 months of age in offspring (in Australia). For the intervention group the adjusted OR for S-ECC (95.0% CI) was 6.8 (2.1, 21.9), P<0.001. The cumulative incidence of S-ECC in the test group was 1.7% and in the control group 9.6% (P < 0.01).
Mohebbi et al 2009	RCT to evaluated the impact of a 6-month educational intervention (educational pamphlet with or without 5 minutes of oral health instructions, plus two recall phone

	calls of the oral health instructions at 2-month intervals) on ECC in children in Iran. The mean age of the children was 12.3 months (SD= 0.4) at baseline and 18.3 months (SD 0.6) at outcome. No new decayed/exfoliated (de) teeth appeared in intensive intervention group. With pamphlet only, the mean de increment was 0.2 (SD 0.6), and in the controls 0.4 (SD = 0.7) (p =0.05).
Vachirarojpisan et al. 2005	RCT of the effectiveness of a one year participatory dental health education programme aimed at care givers to increase tooth brushing and use of fluoride toothpaste in children initially aged 6-19 months in Thailand. Caries increment (cavitated) was 3.46 (SD 3.36) in the test compared with 3.24 (3.53) in the control group. There were no statistically significant differences in oral health outcomes at 1 year follow up.
Jiang et al 2014	RCT of the effectiveness oral health education talk and parental tooth brushing training, reinforced every 6 months, in preventing ECC in children in Hong Kong, China aged 15 months at baseline, followed up for 24 months. Mean dmft (including non cavitated lesions) was 0.2 (SD 0.6) in the test compared with 0.3 (sd 1.2) in the control group. Caries incidence was 11.8 vs 11.9%.
Q10. Does an optimum concentration of fluoride in water reduce the risk of early childhood caries?	
Tank et al 1965	Cohort study of the effect of exposure to fluoridated water on ECC in children in Canada aged 1-6 years. For children aged 5, mean dmft was 3.29 in fluoridated group compared with 6.0 in non-fluoridated. Only 4% of those in non-fluoridated community were caries free compared with 39% in those exposed to fluoride in drinking water since birth (significant differences at $p<0.05$).
Jackson et al 1975a	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of Cumbria England since birth. Mean dmft was 2.38 (SE 0.3) vs 4.40 (SE 0.35) for fluoridated and non- fluoridated groups respectively.
Jackson et al 1975b	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of Wales since birth. Mean dmft was 2.83 (SE 0.26) vs 4.58 (SE 0.34) for fluoridated and non- fluoridated groups respectively.
Jackson et al 1980	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of Leeds England since birth. Mean dmft was 1.23 (SE 0.15) vs 3.38 (SE 0.25) for fluoridated and non- fluoridated groups respectively.
Rugg-Gunn et al 1981	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of North East England since birth. Mean deft was 2.5 (SD 2.79) for fluoridated and 6.1 (4.03) for non-fluoridated groups respectively. There was a higher proportion of lower SES in the non-fluoridated group.
Blinkhorn et al	Compared ECC at age 4-5 years in children residing in

1981	fluoridated compared with non-fluoridated areas of Scotland since birth. Mean dmft was 2.48 (SD 3.16) vs 4.34 (SD 4.04) in the fluoridated and non-fluoridated groups respectively. Those residing in a fluoridated area had a 65% reduction in ECC.
French et al 1984	Compared ECC at age 5 in children living in fluoridated and non-fluoridated areas in North East England. In children from social class III mean dmft was 1.51 (SD 2.28) vs 3.55 (3.69) for children from fluoridated vs non-fluoridated area respectively ($p<0.001$).
Jackson et al 1985	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of Wales since birth Mean dmft was 1.58 (SE0.17) vs 3.55 SE 0.33) for fluoridated and non- fluoridated groups respectively.
Rugg-Gunn et al 1988	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of North East England since birth. In children from social class III, mean deft was 1.70 (SD 2.53) for fluoridated and 3.71 (SD 4.05) for non-fluoridated groups respectively. Overall there was a 54% reduction in caries in children residing in the fluoridated area.
Booth et al 1992	Compared ECC at age 3 in children residing in fluoridated compared with non-fluoridated areas of England since birth. Mean dmft was 0.3 (SD 1.0) for fluoridated and 0.74 (SD 2.0) for non-fluoridated groups respectively ($p<0.03$).
Thomas et al 1995	Retrospective cohort study investigating ECC in 5 year old children who had resided in a fluoridated area for at least 35% of their life compared with those who had resided in a fluoridated area for <10% of life: dmft were 1.81 (SD 2.86) vs 2.28 (SD 3.48) respectively.
Evans et al 1996	Retrospective cohort study investigating ECC in 5 year old children who had resided in fluoridated or non fluoridated areas of Northumberland England since birth. Mean dmft was significantly lower for children from fluoridated areas for all social classes. For high social class dmft was 0.59 (SD 1.37) vs 1.46 (SD2.62), and for low social classes mean dmft was 1.19 (2.73) vs 2.74 (SD 3.05) for children residing in fluoridated and non-fluoridated areas respectively.
O'Mullane & Whelton 1997	Compared ECC at age 5 in children residing in fluoridated compared with non-fluoridated areas of the Republic of Ireland, since birth. Mean dmft was 1.8 for fluoridated and 3.0 for non-fluoridated groups respectively.
Q11. Does consumption of fluoridated milk reduce the risk of early childhood caries?	
Bian 2003	Quasi-experimental study to investigate the effect of fluoridated milk on ECC in children from Beijing China, aged 54 (SD 4.0) month at baseline followed up for 21 months. Test group received approximately 200ml of milk fluoridated at 2.5mg F\L each day. Caries increment was 0.4 (SD 1.9) dmft for test group compared with 1.3 (SD 1.2) dmft for control group, $P<0.001$.

Q12. Does salt fluoridation reduce the risk of early childhood caries?	
Jordon et al 2017	RCT of children aged 3-5 years in Gambia that investigated the effect of fluoridated salt in a communal feeding program for pre-school children. At 12 month follow up the mean (95% CI) for dmft for test and control groups were 4.64 (4.04, 5.23) vs 6.57 (5.52, 7.61) respectively. The percentage of children free of caries into dentine was 25.0 vs 16.8 for test and control groups respectively but this was not significant with relative risk RR 0.88 (0.79, 1.01). For pre-cavitated lesions, the test group had higher values compared with control group: 8.14 (7.45, 8.83) vs 7.70 (6.56, 8.83) respectively). There was high bias in measurement of the outcome.

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Figure 1: PRISMA Flow Diagram

Figure 2. Meta-analysis of randomised controlled trials pertaining to question 9: Is oral health education for care-givers' effective for preventing early childhood caries?

Figure 3. Meta-analysis of data from cohort studies pertaining to question 10: Does an optimum concentration of fluoride in water reduce the risk of early childhood caries? Mean difference (Random effect)

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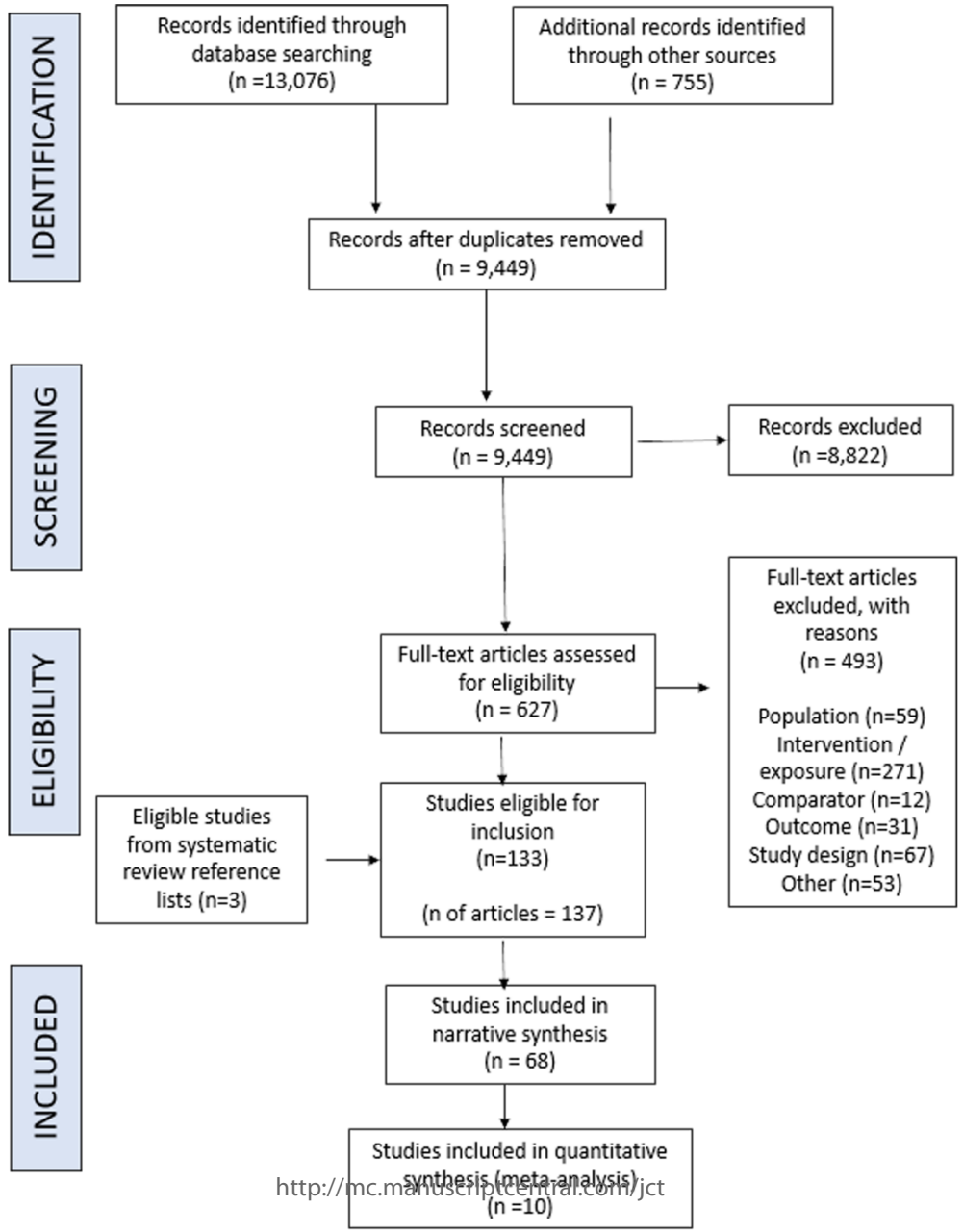

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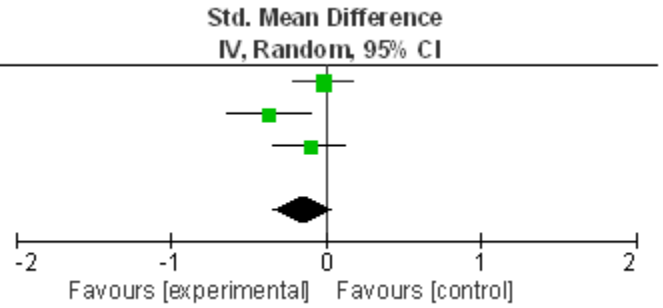
a

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Vachirarojpisan 2005	3.98	3.08	213	4.04	2.99	191	38.9%	-0.02 [-0.22, 0.18]	2005
Harrison 2007	3.35	7.8	105	7.59	14.2	100	28.0%	-0.37 [-0.65, -0.09]	2007
Jiang 2014	0.2	0.6	144	0.3	1.2	134	33.1%	-0.11 [-0.34, 0.13]	2014
Total (95% CI)			**462**			**425**	**100.0%**	**-0.15 [-0.34, 0.05]**	

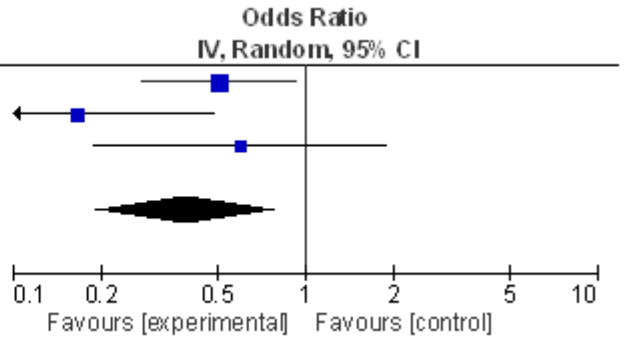
Heterogeneity: Tau² = 0.02; Chi² = 4.19, df = 2 (P = 0.12); I² = 52%
Test for overall effect: Z = 1.47 (P = 0.14)



b

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Year
Feldens 2007	16	157	40	219	47.8%	0.51 [0.27, 0.94]	2007
Plutzer 2008	4	232	20	209	27.1%	0.17 [0.06, 0.49]	2008
Mohebbi 2009	5	55	9	63	25.0%	0.60 [0.19, 1.91]	2009
Total (95% CI)		**444**		**491**	**100.0%**	**0.39 [0.19, 0.79]**	
Total events	25		69				

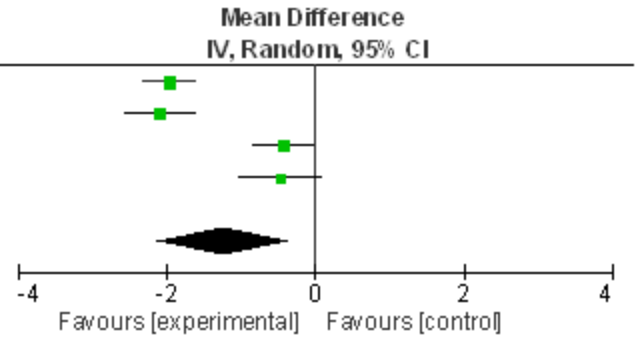
Heterogeneity: Tau² = 0.17; Chi² = 3.51, df = 2 (P = 0.17); I² = 43%
Test for overall effect: Z = 2.59 (P = 0.009)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
French 1981	1.41	2.21	533	3.37	3.65	536	25.7%	-1.96 [-2.32, -1.60]	1981
Rugg-Gunn 1988	1.81	2.56	457	3.9	4.22	370	24.8%	-2.09 [-2.58, -1.60]	1988
Booth 1992	0.3	1	121	0.74	2	107	25.3%	-0.44 [-0.86, -0.02]	1992
Thomas 1995	1.81	2.86	230	2.28	3.48	268	24.3%	-0.47 [-1.03, 0.09]	1995
Total (95% CI)			**1341**			**1281**	**100.0%**	**-1.25 [-2.14, -0.36]**	

Heterogeneity: Tau² = 0.77; Chi² = 47.42, df = 3 (P < 0.00001); I² = 94%

Test for overall effect: Z = 2.74 (P = 0.006)



Appendix

Medline search strategy

1 Infant Formula/
2 Beverages/
3 Bottle Feeding/
4 exp Breast Feeding/
5 Milk, Human/
6 Cariogenic Agents/
7 Diet, Cariogenic/
8 exp Cariostatic Agents/
9 complementary food*.mp.
10 Infant Food/
11 exp Feeding Behavior/
12 Fluoridation/
13 Milk/
14 follow on formula.mp.
15 follow-on formula.mp.
16 free sugar*.mp.
17 Oral Health/
18 Health Education, Dental/
19 Oral hygiene/
20 Dietary Sucrose/
21 Toothbrushing/
22 1 or 2 or 3 or 4 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
23 exp Dental Caries/
24 carious dentine.mp.
25 carious lesion*.mp.
26 carious lesion*.mp.
27 cavit*.mp.
28 tooth decay.mp.
29 dental decay.mp.
30 deft.mp.
31 dft.mp.
32 dmf index/
33 exp dental materials/ or dental amalgam/
34 Dental Restoration, Permanent/
35 Tooth Demineralization/
36 Tooth Remineralization/
37 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38 Infant/
39 Child, Preschool/
40 Infant, Newborn/
41 38 or 39 or 40
42 22 and 37 and 41
43 limit 42 to ‘humans’

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Appendix Table 1. Excluded studies

Reason for exclusion
Article not peer-reviewed
1. Aeck MA. 1995. The prevalence of nursing caries among head start early childhood education and assistance program for children by ethnicity, age, gender, and nursing practices. Gonzaga University.
Full text not available
1. Bordoni N, Bellagamba H, Dono R, Marcantoni M, Sabelli C, Macchi R, Squassi A. 1985. Dental condition in a preventive program for school children. Acta odontologica latinoamericana: AOL. 2(2-3):91-96. 2. Government funding body Oral Health Program LBA, Metro South Health Service District. 2009. A controlled longitudinal study of caries prevention in children aged 2 to 4 years. 3. University Menzies School of Health Research. 2009. Improved dental health for remote aboriginal children: A cluster randomised trial. 4. University of Michigan, National Institute of Dental and Craniofacial Research (NIDCR). 2012. Predicting caries risk in underserved toddlers in primary healthcare settings. https://ClinicalTrials.gov/show/NCT01707797.
Comparator did not meet the inclusion criteria
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12. Wendt LK, Hallonsten AL, Koch G, Birkhed D. 1996. Analysis of caries-related factors in infants and toddlers living in Sweden. Acta Odontol Scand. 54(2):131-137.

Population did not meet the inclusion criteria

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Study design did not meet inclusion criteria

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Appendix Table 2. Total number and type of studies by review question

Review question	Study type	Number of studies identified
Q1. Does breastfeeding beyond one year increase the risk of early childhood caries compared with breastfeeding until less than one year of age?	All	28
	Cohort	1
	Cross sectional	27
Q2. Does breastfeeding beyond one year increase the risk of early childhood caries compared with cows (or similar) milk consumption as main milk source from one year of age?	All	0
Q3. Does breastfeeding beyond two years increase the risk of early childhood caries compared with breastfeeding until less than two years of age?	All	8
	Cohort	2
	Case control	1
	Cross sectional	5
Q4. Does breastfeeding beyond two years increase the risk of early childhood caries compared with cows (or similar) milk consumption as main milk source from two years of age?	All	0
Q5. Does consumption of liquids that contain free sugars from an infant feeding bottle, increase the risk of early childhood caries?	All	31
	Cohort	4
	Case control	2
	Cross sectional	25
Q6. Does consumption of complementary drinks that contain free sugars increase the risk of early childhood caries?	All	8
	Cohort	5
	Cross sectional	3
Q7. Does consumption of complementary foods to which free sugars have been added increase the risk of early childhood caries?	All	1
	Cohort	1
Q8. Does oral hygiene provided by a parent/carer reduce the risk of early childhood caries?	All	21
	Cohort	2
	Case control	1
	Cross sectional	17
	Quasi experimental	1
Q9. Is oral health education for care givers' effective for preventing early childhood caries?	All	14
	RCTs	6
	Cohort	2
	Quasi-experimental	6
Q10. Does an optimum concentration of fluoride in water reduce the risk of early childhood caries?	All	32
	Cohort	13
	Cross sectional	15
	Ecological	4
Q11. Does consumption of fluoridated milk reduce the risk of early childhood caries?	All	3
	Quasi-experimental	1
	Cross sectional	2
Q 12. Does salt fluoridation reduce the risk of early childhood caries?	All	4
	RCTs	1
	Cohort	1
	Quasi-experimental	2

Appendix Table 3. Details of data extraction for the top level of evidence pertaining to each review question

Research question 1: Does breastfeeding beyond one year increase the risk of early childhood caries compared with breastfeeding until less than one year of age?

Citation	Peres, K. G., et al. (2017). Impact of prolonged breastfeeding on dental caries: A population-based birth cohort study. Pediatrics, **140**,(1):e20162943		
Study design (including statistical analysis):	Prospective Cohort (marginal structural modelling)		
Aims/objectives:	RQ – is there a controlled direct effect of prolonged breastfeeding on dental caries at age 5 years?		
Participants	Total sample size at baseline:	1303	
	Country:	Brazil	
	Region (urban (city)/rural):	Not stated	
	Ethnicity:	Not stated (native)	
	Socioeconomic status:	Not stated	
	Gender:	Mixed	
	Age (including adults/children):	5 years (final data collection)	
	Health background/status:	Not stated	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Models (table 2) adjusted for family income, maternal schooling, maternal age, sugar consumption, and bottle feeding at 5 years	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Exposure: Breast feeding 13-23 months N= 129	Comparator: Breast feeding up to 12 months N= 741
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Participants were followed from birth; breastfeeding data were collected at birth and when participants were 3, 12 and 24 months. Outcome data were collected when the children were aged 5 years.	
	Oral outcomes measured:	WHO criteria – dmfs S-ECC = dmfs ≥6	
	Scale/measure:		
	Means and SD or events for	Mean dmfs (95% CI)	Mean dmfs (95% CI)

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	each group at post-treatment or follow-up	amongst children breastfed 13-23 months: 3.1 (2.2 – 4.0) 1.0	amongst children breastfed 0-12 months: 3.4 (2.9-3.9)
	Other relevant statistical results	Table 1 data (crude, not adjusted): Crude rate ratio for dmfs (95% CI) amongst children breastfed 13-23 months: 0.9 (0.6-1.3) S-ECC for dmfs amongst children breastfed 13-23 months: 20.1 (13.1-27.2) Crude risk ratio for dmfs (95% CI) amongst children breastfed 13-23 months: 1.0 (0.6-1.6) Table 2 data (adjusted): Dental caries amongst children who were breastfed for 13-23 months compared to up to 12 months MSM: Mean ratio (95% CI) = 0.9 (0.6 to 1.3) Severe Dental Caries MSM: Relative risk (95% CI) = 1.0 (0.6 to 1.6)	Table 1 data (crude, not adjusted): Crude rate ratio for dmfs amongst children breastfed 0-12 months (ref): 1.0 S-ECC for dmfs amongst children breastfed 0-12 months: 19.8 (16.9-22.7) Crude risk ratio for dmfs amongst children breastfed 0-12 months: 1.0 (ref) Ref for both = 1.0

Research question 3: Does breastfeeding beyond two years increase the risk of early childhood caries compared with breastfeeding until less than two years of age?

Citation	Chaffee, Benjamin W., Carlos Alberto Feldens, and Márcia Regina Vítolo. "Association of long-duration breastfeeding and dental caries estimated with marginal structural models." Annals of Epidemiology 24.6 (2014): 448-454.
Study design (including statistical analysis):	Prospective cohort
Aims/objectives:	Estimate the association between breastfeeding ≥24 months and severe early childhood caries.

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Participants	Total sample size at baseline:	715	
	Country:	Brazil	
	Region (urban (city)/rural):	Porto Alegre	
	Ethnicity:	395 (55.2%) of participants self-identified as maternal white race	
	Socioeconomic status:	Data were from low income families	
	Gender:	Male and female	
	Age (including adults/children):	38 months	
	Health background/status:	Not specified	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Data were from low income families (household income ≤1500 Brazilian Reais monthly; approximately 900 US dollars in 2008) Participants were from the same city (Porto Alegre), presumably with similar exposure to water fluoride Analysis adjusted for: Clinic allocation (intervention); Maternal age (years); Maternal education (≤8 years);Maternal smoking (current); Parity (has previous child); Social class (C or lower);Pre-pregnancy BMI; Child age at dental assessment (years); Child sex (male); Length-for-age Zscore at 11–15 months (per SD) ; First-year feeding index (per unit);Daily bottles at 5–9 months (1–3;Daily bottles at 5–9 months (≥ 4);Added sugar in bottle at 5–9 months; Ever formula fed; Frequency of fruits at 11–15 months; Frequency of vegetables at 11–15 months; Frequency of beans at 11–15 months; Frequency of meat at 11–15 months; Frequency of organ meat at 11-15 months.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Exposure: Breastfeeding ≥24 months	Comparator: Breastfeeding <6 months (reference) Breastfeeding 6-11 months Breastfeeding 12-23 months
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	Outcome data were collected when participants were aged 38 months	
	Oral outcomes measured:	Population-average severe-ECC prevalence	
	Scale/measure:	severe-ECC was defined as ≥4 affected tooth surfaces or ≥1 affected maxillary anterior teeth	
	Means and SD or events for each group at post-treatment		

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	or follow-up		
	Other relevant statistical results	Breastfeeding ≥24 months was associated with the highest adjusted population-average severe-ECC prevalence (0.45, 95% CI: 0.36, 0.54) compared with breastfeeding <6 months (0.22, 95% CI: 0.15, 0.28), 6–11 months (0.38, 95% CI: 0.25, 0.53), or 12–23 months (0.39, 95% CI: 0.20, 0.56).	

Citation	Peres, K. G., et al. (2017). Impact of prolonged breastfeeding on dental caries: A population-based birth cohort study. Pediatrics, **140** (1):e20162943.		
Study design (including statistical analysis):	Prospective Cohort (marginal structural modelling).		
Aims/objectives:	Research question – is there a controlled direct effect of prolonged breastfeeding on dental caries at age 5 years?		
Participants	Total sample size at baseline:	1303	
	Country:	Brazil	
	Region (urban (city)/rural):	Not stated	
	Ethnicity:	Not stated (native)	
	Socioeconomic status:	Not stated	
	Gender:	Mixed	
	Age (including adults/children):	5 years (final data collection)	
	Health background/status:	Not stated	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Models (table 2) adjusted for family income, maternal schooling, maternal age, sugar consumption, and bottle feeding at 5 years	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Exposure: Breast feeding ≥24 months N= 258	Comparator: Breast feeding <24 months N= 870
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Participants were followed from birth; breastfeeding data were collected at birth and when participants were 3, 12 and 24 months. Outcome data were collected when the children were aged 5 years.	
	Oral outcomes measured:	WHO criteria – dmfs S-ECC = dmfs ≥6	
	Scale/measure:		

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	Means and SD or events for each group at post-treatment or follow-up		

Research question 5: Does consumption of liquids that contain free sugars from an infant feeding bottle, increase the risk of early childhood caries?

Citation	Feldens et al. (2010). Early Feeding Practices and Severe Early Childhood Caries in Four-Year-Old Children from Southern Brazil: A Birth Cohort Study. Caries Res. 44(5),445-52		
Study design (including statistical analysis):	Prospective cohort study (univariable poisson regression, multivariable modelling)		
Aims/objectives:	To investigate the relationship between feeding practices in the first year of life and the occurrence of severe early childhood caries (S-ECC) at 4 years of age.		
Participants	Total sample size at baseline:	500	
	Country:	Brazil	
	Region (urban (city)/rural):	São Leopoldo	
	Ethnicity:	-	
	Socioeconomic status:	71.2% of the mothers having ≤8 years of schooling, and the family income was low for most families, of which 82% had an income per capita below 1 national monthly minimum wage (R$ 180.00; approximately USD 80.00)	
	Gender:	Both male and female	
	Age (including adults/children):	48–50 months: N=171 51–53 months: N=169 48 to 53 months (mean = 50.5; SD = 1.7)	
	Health background/status:	Mothers were included in the study if they gave birth to apparently normal, single, full-term (≥ 37 weeks) baby with normal birth weight (≤ 2,500 g) were invited to take part in the study. The exclusion criteria were: impediment to breastfeeding (HIV/AIDS) or congenital malformation	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Relative risk estimate of the exposure of interest was adjusted for other variables in the multivariable model (maternal schooling, daily breastfeeding frequency at 12 months, daily meals and snacks at 12 months, high density of sugar at 12 months, teeth at 12 months). Fluoride level of the water supply in the area was 0.7 ppm.	
	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es	Exposure: bottle use for fruit juices / soft drinks at 12 months (n children assessed for caries at 4	Comparison: bottle not used for fruit juices / soft drinks at 12 months (n children assessed for caries

	used):	years= 129)	at 4 years= 205)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Exposure data were collected from mothers when the children were aged 12 months; clinical examinations took place at 4 years of age.	
	Oral outcomes measured:	severe early childhood caries (S-ECC) incidence	
	Scale/measure:	Defined as ≥1 cavitated, missing or filled smooth surfaces in primary maxillary anterior teeth or d 1+ mfs ≥ 5	
	Means and SD or events for each group at post-treatment or follow-up	**Univariable regression:** **S-ECC (N; %) among children aged 4 years** Bottle use for fruit juices/soft drinks at 12 months: Yes: 57; 44.2% No: 67; 32.7% **RR (95% CI)** Bottle use for fruit juices/soft drinks at 12 months (P=0.032): Yes: 1.35 (1.03–1.78) No: 1 **Multivariable regression:** **RR (95% CI)** Bottle use for fruit juices/soft drinks at 12 months (P=0.025): Yes: 1.41 (1.08–1.86) No: 1	
	Other relevant statistical results		

Citation	Tanaka et al. (2013). Infant feeding practices and risk of dental caries in Japan: The Osaka Maternal and Health Study. Pediatric Dentistry, 35(3), 267-71.	
Study design (including statistical analysis):	Prospective cohort (multiple logistic regression)	
Aims/objectives:	To investigate the relationship between feeding practice and the risk of ECC	
Participants	Total sample size at baseline:	1,002 children
	Country:	Japan
	Region (urban (city)/rural):	Osaka
	Ethnicity:	-
	Socioeconomic status:	-
	Gender:	Both male and female
	Age (including adults/children):	41-50 months old
	Health background/status:	-
	Any information on confounders (e.g. water, milk	The association between the exposure and outcome of interest was presented as crude ORs and ORs adjusted for

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	or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	the following variables: Breastfeeding duration, bottle-feeding while falling asleep, age of introduction of foods, maternal age at baseline survey, maternal smoking during pregnancy, family income, paternal and maternal education levels, child's sex, birth weight, age at first tooth eruption, tooth-brushing frequency at fourth and fifth surveys, use of fluoride.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Bottle use for sweetened liquids other than milk Sometimes or usually (n = 148)	Bottle use for sweetened liquids other than milk Never (n = 167)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Study duration: November 2001 to March 2003 Information about the variables under study and potentially confounding factors were collected at: pregnancy, 2-9, 16-24, 29-39 and 41-49 months old; Outcome data were collected at 41-50 months	
	Oral outcomes measured:	ECC	
	Scale/measure:	Presence of one or more caries teeth (decayed or filled)	
	Means and SD or events for each group at post-treatment or follow-up	Odds ratio for early childhood caries according to bottle use for sweetened liquids other than milk: **Never:** N: 167 Prevalence (%): 19 Crude OR ratio (95% CI): 1.00 Adjusted OR (95% CI): 1.00 **Sometimes or usually:** N: 148 Prevalence (%): 28 Crude OR ratio (95% CI): 1.67 (0.99-2.84) Adjusted OR (95% CI): 2.47 (1.23-5.05) Odds ratio for moderate and severe early childhood caries according to bottle use for sweetened liquids other than milk: **Never:** Adjusted OR for moderate ECC vs caries free (95% CI): 1.00 Adjusted OR for severe ECC vs caries free (95% CI): 1.00 **Sometimes or usually:** Adjusted OR for moderate ECC vs caries free (95% CI): 2.63 (1.17-6.08)	

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		Adjusted OR for severe ECC vs caries free (95% CI): 2.58 (0.74-9.57) The time point during the study when exposure data were collected was not specified
	Other relevant statistical results	Bottle use for sweetened liquids other than milk (n; %): Never: 167; 53% Sometimes or usually : 148; 47%

Citation	Wendt et al. (2009). Analysis of caries-related factors in infants and toddlers living in Sweden. Acta Odontol Scand. 54(2)131-7.		
Study design (including statistical analysis):	Prospective cohort (logistic regression analysis, chi-square test and Fisher's exact test w).		
Aims/objectives:	Oral hygiene and dietary factors (in percentage) at 2 years of age in children who got sugar-containing liquid in a feeding bottle at 1 year of age (n = 48)		
Participants	Total sample size at baseline:	671	
	Country:	Sweden	
	Region (urban (city)/rural):	community of Jonkoping	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	Both male and female	
	Age (including adults/children):	One year old at baseline, re-examinations were undertaken when the children were 2 and 3 years of age	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Children with carious lesions at baseline were excluded	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Exposures: Consumption of sugar sweetened liquid from an infant feeding bottle at 1 and 2 years of age.	Comparator Consumption of milk or water from an infant feeding bottle at 1 and 2 years of age.
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Between 1988 and 1990 clinical examinations took place at 1, 2 and 3 years of age; data on independent variables were collected at 1 and 2 years of age.	

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	Oral outcomes measured:	Caries incidence
	Scale/measure:	Percentage
	Means and SD or events for each group at post-treatment or follow-up	Oral hygiene and dietary factors (in percentage) at 2 years of age in children who got sugar-containing liquid in a feeding bottle at 1 year of age (n = 51):
	Other relevant statistical results	children caries-free at 3 years of age (n = 28): 32% children with caries at 3 years of age (n = 23): 44% NS, p> 0.05 Lack of data on the comparator (i.e. the N / proportion of children with caries and caries free at 3 years of age who got milk or water. Oral hygiene and dietary factors (in percentage) at 2 years of age in children who got sugar-containing liquid when thirsty at 1 year of age (n = 48):

Citation	Wendt et al. (2009). Dietary habits related to caries development and Immigrant status in infants and toddlers living in Sweden. Acta Odont Scand, 53(6), 339-344.	
Study design (including statistical analysis):	Prospective cohort (chi-square test and Fisher's exact test w)	
Aims/objectives:	To describe the dietary habits of infants and toddlers living% Sweden with special reference to caries prevalence at 2 and 3 years of age and to immigrant status.	
Participants	Total sample size at baseline:	Children invited into the study, n= 671
	Country:	Sweden
	Region (urban (city)/rural):	community of Jonkoping; the areas included town, suburb, and countryside
	Ethnicity:	Caries-free at one year children with at least one parent born in Sweden (n = 532) Caries free at one year children with both parents born outside Sweden (n=61) Nineteen percent of the children were immigrants
	Socioeconomic status:	The areas were chosen to reflect the socioeconomic levels of the population living in the community of Jonkoping.
	Gender:	Both male and female
	Age (including adults/children):	One year old
	Health background/status:	-
	Any information on confounders (e.g. water, milk	The results were stratified according to whether children were immigrants or not

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	or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):		
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Exposure: daily intake of a feeding bottle with sugar-containing liquid	Comparator no daily intake of a feeding bottle with sugar-containing liquid
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Between 1988 and 1990 Children were recruited into the study at 1 year; follow up took place at the ages of 2 and 3 years	
	Oral outcomes measured:	Caries incidence	
	Scale/measure:	No scale was defined.	
	Means and SD or events for each group at post-treatment or follow-up	**Sugar-containing liquid in feeding bottle in 8 groups (%):**	
	Other relevant statistical results	**Non-Caries I-** Children caries-free at one and three years (n=434): 13% **Caries I-** Children caries-free at one year but with caries at three years (n=159): 22% P-value <0.01 **Non-Caries II-** Children caries-free at one and two years (n=276): 16% **Caries II-** Children caries-free at one year but with caries at two years (n=22): 50% P-value <0.001 **Non-Caries III-** Children caries-free at one, two and three years (n=210): 6% **Caries III-** Children caries-free at one and two year but with caries at three years (n=60): 12% P>0.05 **Non-immigrant children-** Children with at least one parent born in Sweden (n=532): 14% **Immigrant children-** Children with both parents born outside Sweden (n=61): 31% P-value <0.001	

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Research question 6: Does consumption of complementary drinks that contain free sugars increase the risk of early childhood caries?

Citation	Wendt et al. (2009). Analysis of caries-related factors in infants and toddlers living in Sweden. Acta Odontol Scand.54 (2)131-7.		
Study design (including statistical analysis):	Prospective cohort (logistic regression analysis, chi-square test and Fisher's exact test w)		
Aims/objectives:	Oral hygiene and dietary factors (in percentage) at 2 years of age in children who got sugar-containing liquid in a feeding bottle at 1 year of age (n = 48)		
Participants	Total sample size at baseline:	671	
	Country:	Sweden	
	Region (urban (city)/rural):	community of Jonkoping	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	Both male and female	
	Age (including adults/children):	One year old at baseline, re-examinations were undertaken when the children were 2 and 3 years of age; exposure data were collected at 1 and 2 years of age	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Children with carious lesions at baseline were excluded	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Exposures: Consumption of sugar sweetened liquid when thirsty at 1 and 2 years of age	Comparator Consumption of milk or water when thirsty at 1 and 2 years of age
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	between 1988 and 1990 clinical examinations took place at 1, 2 and 3 years of age; data on independent variables were collected at 1 and 2 years of age	
	Oral outcomes measured:	Caries incidence	
	Scale/measure:	Percentage	
	Means and SD or events for each group at post-treatment or follow-up	Dietary factors (in percentage) at 2 years of age in children who got sugar-containing liquid when thirsty at 1 year of age (n = 48): **Sugar-containing liquid when thirsty at 2 years of age:**	

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	Other relevant statistical results	children caries-free at 3 years of age (n = 23): 52% children with caries at 3 years of age (n = 25): 60% NS, p> 0.05 Lack of data on the comparator (i.e. the N / proportion) of children with caries and caries free at 3 years of age who got milk or water when thirsty at 2 years of age.

Citation	Warren et al. (2009). A Longitudinal Study of Dental Caries Risk among Very Young low SES children. Community Dent Oral Epidemiol. 37(2), 116–122.		
Study design (including statistical analysis):	Cohort study (Logistic regression models for baseline predictors of d2-3f caries at the 18-month follow-up).		
Aims/objectives:	To assess the effect of Sugar-Sweetened Beverage Consumption for 18-month caries prevalence as part of a longitudinal study of high-risk children.		
Participants	Total sample size at baseline:	212	
	Country:	USA	
	Region (urban (city)/rural):	southeast Iowa community	
	Ethnicity:	Among those who remained in the study at follow-up, there were higher proportions who were Caucasian children	
	Socioeconomic status:	low-income and minority families	
	Gender:	Both male and female	
	Age (including adults/children):	6 to 24 months	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Logistic regression models were adjusted for age	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	**Exposure of interest: sugar-Sweetened Beverage Consumption** N=44 (Sugar Sweetened Beverages included regular soda pop, sugared beverages made from powder, sports drinks, juice drinks and other sugared beverages)	**Comparator: no Sugar-Sweetened Beverage Consumption** N=81
	Other relevant baseline	**Sugar-Sweetened Beverage Consumption**	

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	statistics for each group (for the analysis/es used):	**Yes:** ID/ month=0.019 **No:** ID/ month=0.006 IDR=3.44 (P-value=0.001) OR (95%CI)=5.2 (2.0-13.3) *ID: Incidence dentistry *IDR: Incidence dentistry ratio - Incidence density of caries was estimated as the number of new caries developed during 18 months divided by the total person time at risk during the follow-up period
	Duration:	Risk factor data were collected at 6, 12 and 18 months, dental examinations were undertaken at baseline and at 18 months
	Oral outcomes measured:	Caries prevalence
	Scale/measure:	No. w/frank decay (d2-3 or filled surfaces)
	Means and SD or events for each group at post-treatment or follow-up	**Sugar-Sweetened Beverage Consumption** **Yes:** n=25 **No:** n=103 OR (95%CI)=3.04 (1.07-8.64) p-value=0.04
	Other relevant statistical results	

Citation	Watanbe et al. (2014). The Influence of Lifestyle on the Incidence of Dental Caries Among 3-Year-Old Japanese Children. Int J Environ Res Public Health, 11(12), 12611-22.	
Study design (including statistical analysis):	Cohort (multivariate logistic regression analysis)	
Aims/objectives:	To examine how lifestyle, household environment, and caries activity test score of Japanese children at age 1.5 years affected their dental caries incidence at age 3.	
Participants	Total sample size at baseline:	33, 655
	Country:	Japan
	Region (urban (city)/rural):	Kobe City Public Health Centre
	Ethnicity:	-
	Socioeconomic status:	-
	Gender:	Both male and female
	Age (including adults/children):	1.5 years of age
	Health background/status:	-
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	The OR was adjusted for nationality, gender, birth order, and Cariostat score.

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Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	**Exposure:** **Daily sugar-sweetened beverage consumption answer "Yes"**	**Comparator** **Daily sugar-sweetened beverage consumption answer "No"**
	Other relevant baseline statistics for each group (for the analysis/es used):	Children were caries free at 1.5 years	
	Duration:	June 2006 and August 2009 Follow-up duration: 21 months	
	Oral outcomes measured:	Incidence of dental caries in 3-years old subjects	
	Scale/measure:	No scale was defined	
	Means and SD or events for each group at post-treatment or follow-up	**Daily Sugar-Sweetened Beverage Consumption All (n = 31,202) (n; %)** **Yes:** 2782 (20.4) **No:** 2324 (13.2) P-value= <0.001 **Daily Sugar-Sweetened Beverage Consumption Boy (n = 16,052) (n; %)** **Yes:** 1532 (21.5) **No:** 1254 (14.0) P-value= <0.001 **Daily Sugar-Sweetened Beverage Consumption Girl (n = 15,150) (n; %)** **Yes:** 1259 (19.2) **No:** 1070 (12.5) P-value= <0.001 **Daily Sugar-Sweetened Beverage Consumption All OR (95%CI)** **Yes:** 1.56 (1.46, 1.65) **No:** 1 P-value= <0.001 **Daily Sugar-Sweetened Beverage Consumption Boy OR (95%CI)** **Yes:** 1.55 (1.42, 1.69) **No:** 1 P-value= <0.001 **Daily Sugar-Sweetened Beverage Consumption Girl OR (95%CI)** **Yes:** 1.55 (1.41, 1.70) **No:** 1 P-value= <0.001
	Other relevant statistical results		

Citation	Wigen and Wang (2014). Health behaviours and family characteristics in early childhood influence caries development. A longitudinal study based on data from MoBa. Norsk Epidemiologi, **24** (1-2), 91-95.
Study design	Cohort study (multivariable logistic regression).

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(including statistical analysis):			
Aims/objectives:	To study how family characteristics and health behaviour in pregnancy and early childhood influence caries development in preschool children.		
Participants	Total sample size at baseline:	1607	
	Country:	Norway	
	Region (urban (city)/rural):	Akershus	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	Both male and female	
	Age (including adults/children):	1.5 years of age	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Multivariable models included the exposure of interest (see below) in addition to the following variables: • Tooth brushing frequency • Sugary drink consumption level • Maternal health and lifestyle variables (dietary sugar, dietary fat, BMI) • Family characteristics (maternal education, parental origin (western or non-western), family status from pregnancy to age 5 (change from two to one parent family)	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Consumption of sugary drinks at night a) sometimes or b) each night Consumption of sugary drinks at least once per week Age = 1.5 years	Consumption of sugary drinks at night: never Consumption of sugary drinks less than once per week Age = 1.5 years
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Exposure data at 1.5 years of age in relation to caries experience at 5 years	
	Oral outcomes measured:	Caries prevalence	
	Scale/measure:	No scale was defined	
	Means and SD or events for each group at post-treatment or follow-up	Sugary drinks at night (OR, (95%CI)) Never (ref) Sometimes: 1.5 (0.8–2.8) Each night: 2.2 (1.1–4.5)	
	Other relevant statistical results	Sugary drinks less than once a week (reference) Sugary drinks at least once a week 1.7 (1.1-2.08)	

Citation	Yonezu et al. (2006). Characteristics of Breast-fed Children with Nursing Caries. Bull Tokyo Dent Coll. 47(4)161-5.		
Study design (including statistical analysis):	Cohort (logistic regression)		
Aims/objectives:	To investigate the characteristics and risk factors of prolonged breast feeding in children.		
Participants	Total sample size at baseline:	105	
	Country:	Japan	
	Region (urban (city)/rural):	-	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	Both male and female	
	Age (including adults/children):	18 months	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Logistic regression analysis included the following variables: • Bedtime breast-feeding • Sweets intake • Tooth brushing frequency • Oral hygiene at 18 months exam • Sweet beverage intake (exposure of interest)	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Sweet beverages intake 3 times-/ week at 18 months	Sweet beverages intake - 2 times/ week at 18 months
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Study duration: 2003-2005 Exposure data were collected at 18 months Follow up (caries experience examined) 6 months later, at 24 months	
	Oral outcomes measured:	Initial and manifest caries	
	Scale/measure:		
	Means and SD or events for each group at post-treatment or follow-up	**Results of logistic regression analysis of effect of variables for caries (Experience at 24 months of age):** Sweet beverages intake (OR (95%CI)): 0.99 (0.25– 4.01) (not significant).	
	Other relevant statistical results		

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Research question 7: Does consumption of complementary foods to which free sugars have been added increase the risk of early childhood caries?

Citation	Feldens et al. (2010). Early Feeding Practices and Severe Early Childhood Caries in Four-Year-Old Children from Southern Brazil: A Birth Cohort Study. Caries Res. 44(5),445-52		
Study design (including statistical analysis):	Prospective cohort study (Poisson regression models)		
Aims/objectives:	Investigate feeding practices in the first year of life associated with S-ECC at the age of 4 years.		
Participants	Total sample size at baseline:	500 (Final = 340)	
	Country:	Brazil	
	Region (urban (city)/rural):	Unclear	
	Ethnicity:	-	
	Socioeconomic status:	Low-income	
	Gender:	Mixed	
	Age (including adults/children):	4 years	
	Health background/status:	Apparently healthy at birth	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Adjusted models incorporated (and therefore controlled for the effects of). Maternal schooling, daily breastfeeding frequency at 12 months, daily meals and snacks at 12 months, bottle use for fruit juices / soft drinks at 12 months, number of teeth at 12 months.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	No high density of sugar at 12 months (n=240) Proportion of >50% simple carbohydrates in 100g food (but proportion not reported)	High density of sugar at 12 months (n=91)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Feeding practices were assessed using standardized methods at 6 and 12 months of age, severe early childhood caries (S-ECC) was assessed at 4 years	
	Oral outcomes measured:	S-ECC	
	Scale/measure:	≥1 cavitated, missing or filled smooth surfaces in primary maxillary anterior teeth or dmfs ≥5	
	Means and SD or events for each group at post-treatment or follow-up	S-ECC prevalence N=78 (32.5%) Univariate Poisson regression analysis RR (95% CI) 1.0 (ref)	S-ECC prevalence N=43 (47.3%) Univariate Poisson regression analysis RR (95% CI) 1.45 (1.10-1.93) p=0.010

		Adjusted multivariable model RR (95% CI) 1.00 (ref)	Adjusted multivariate model RR (95% CI) 1.43 (1.08-1.89) p=0.003

Research question 8: Does oral hygiene provided by a parent/carer reduce the risk of early childhood caries?

Citation	Leroy et al. (2012). Risk factors for caries incidence in a cohort of Flemish preschool children. Clin Oral Invest. 16: 805-812.		
Study design (including statistical analysis):	Prospective cohort (multivariable logistic regression models).		
Aims/objectives:	To identify the risk factors for the incidence of visible caries experience in a cohort of preschool children living in Flanders.		
Participants	Total sample size at baseline:	1, 057 children	
	Country:	Belgium	
	Region (urban (city)/rural):	Flanders	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	Male and female	
	Age (including adults/children):	3 & 5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	The following variables were included in multivariable regression models: age, gender, ranking of the child, watching television at age 3 and 5, family smoking status at birth, family smoking status at age 3 and 5 years**,** educational level of mother, parental brushing frequency at birth and at ages 3 and 5, interdental cleaning aids at birth, interdental cleaning aids at 3 and 5 years, help with brushing at 3, help with brushing at 5, brushing frequency at age, plaque accumulation at ages 3 and 5, baby feeding at birth, in between meals sugar containing drinks, in between meals sugar containing snacks, drinks at night at ages 3 and 5, snacks at night at ages 3 and 5, fruit juice consumption at age 5, soda consumption at age 5.* These variables were include in multivariable regression models, for which data concerning the association between plaque and caries was presented.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	**<u>Intervention:</u>** Indicators of oral hygiene provided by parent or caregiver, measured in relation to plaque* and supervised daily tooth	**<u>Comparator</u>** Indicators of poor oral hygiene provided by parent or caregiver:

		brushing: No plaque accumulation at age 3 years No plaque accumulation at age 5 years Help with brushing at age 3 (daily) Help with brushing at age 5 (daily day)	 Plaque accumulation at age 3 years Plaque accumulation at age 5 years Help with brushing at age 3 (<1/day) Help with brushing at age 5 (<1/day)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Children were recruited at birth; parents completed questionnaires which yielded data on sociodemographic variables and on children's and parental oral health behaviour at birth (2003-4) and when the children were 3 (2007) and 5 (2009). Clinical examinations took place at 3 and 5 years	
	Oral outcomes measured:	Caries increment between ages 3 and 5	
	Scale/measure:	Dental caries lesions at the d1 level (cavitated and non-cavitated)	
	Means and SD or events for each group at post-treatment or follow-up	--	-
	Other relevant statistical results	**<u>*Multivariable models:</u>** OR (95% CI) for the association between increment in caries experience between age 3 and 5 and caries experience at age 3: 2.79 (1.82-4.29) OR (95% CI) for the association between increment in caries experience between age 3 and 5 and plaque accumulation at age 5: 2.20 (1.50-3.23) Data were available concerning the association between daily help with	

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		tooth brushing >1/day versus <1 / day at age 3 and 5 and caries at 3 and 5 OR (95% CI), however, these data were from univariable models.	

Citation	Okuno, M. (1994). A Cohort Study on Dental Caries in Infants. Nihon Koshu Eisei Zasshi. 41(7), 625-8.		
Study design (including statistical analysis):	Cohort Study (Chi-square, Logistic regression analysis)		
Aims/objectives:	To determine what techniques are effective in dental caries prevention in infants.		
Participants	Total sample size at baseline:	878 (18 months children without dental caries)	
	Country:	Japan	
	Region (urban (city)/rural):	Gifu city, Gifu Prefecture	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	N/A (The author described that there were almost no difference by gender with regards to prevalence of dental caries and other indicators. Therefore, all statistical analysis was conducted by combing both gender information.)	
	Age (including adults/children):	Baseline 18 months children Follow up 3 yrs children	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	The baseline information on; oral hygiene situation including plaque score, tooth brushing habit, and snack intakes	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Baseline information at 18 months – 1) Plaque score b) low 2) Toothbrushing behaviour by a) brushing teeth more than one time by parents or b) not brushing teeth by parents	Baseline information at 18 months – 1) Plaque score high 2) Toothbrushing behaviour not brushing teeth by parents
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-

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	Duration:	Dental caries prevalence was assessed at 3 yrs in relation to oral health behaviour measured at the baseline (18 months)	
	Oral outcomes measured:	Prevalence of dental caries at 3 yrs	
	Scale/measure:	Percent	
	Means and SD or events for each group at post-treatment or follow-up	Results from Chi-square test 1) Plaque score at 18 months (baseline) a) low or b) high 2) Toothbrushing behaviour at 18 months a) brushing teeth more than one time per day by parents or b) not brushing teeth by parents.	1) Dental Caries Prevalence at 3 yrs among a) 31.5% (n=192) b) 43.3% (n=116) (p=0.001) 2) Dental Caries Prevalence at 3 yrs among a) 30.9% (n=121) b) 38.5% (n=187) (p=0.019)
	Other relevant statistical results	Results from Logistic regression analysis (a is reference) 1) Plaque score at 18 months (baseline) a) low or b) high 2) Toothbrushing behaviour at 18 months a) brushing teeth more than one time by parents or b) not brushing teeth by parents.	X^2 score (P-value) 1) 7.9763 (0.0047) 2) 1.8712 (0.1713)

Research question 9. Is oral health education for care givers' effective for preventing early childhood caries?

Citation	Feldens, C., Vítolo, M., & Drachler, M. (2007). A randomized trial of the effectiveness of home visits in preventing early childhood caries. Community Dent Oral Epidemiol, 35(3), 215-223.
Study design (including statistical	RCT. Mann-Whitney U test and Logistic regression.

analysis):			
Aims/objectives:	Assess the effectiveness of home visits for advising mothers about breast feeding and weaning on early childhood caries (ECC) at the age of 12 months.		
Participants	Total sample size at baseline:	500 (intervention group: 200 and control group: 300)	
	Country:	Brazil	
	Region (urban (city)/rural):	The city of San Leopoldo	
	Ethnicity:	-	
	Socioeconomic status:	Mother-child pairs were recruited from a publicly funded hospital that mainly serves the low-income population The income was low for most of the families, with 10.7% (17/159) of the families of the intervention group and 11.1% (25/225) of the controls living with an income below one minimum wage of the national salary; the income was between 1 and 3 minimum wages for 63.5% (101/ 159) of the intervention group and 58.7% (132/225) of the controls, and it was more than three minimum wages only for 25.8% (41/159) of the intervention group and 30.2% (68/225) of the controls. (v2 for differences in proportions between the two groups ¼ 0.600).	
	Gender:	Both male and female	
	Age (including adults/children):	Intervention delivered when babies were 10 days, 1-6 months, 8, 10 and 12 months; caries assessment for both groups at 12-14 months	
	Health background/status:	Apparently normal, single, full term babies with birth weight equal to or greater than 2500g and who did not have an impediment to breastfeeding (HIV/AIDS)	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	There were no evidence of imbalance between the intervention and control groups in the distribution of family income, maternal education and age at the child's birth. No significant differences were reported between groups in relation to other socioeconomic variables. Adjustment for: the confounding effect of number of teeth.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention: received home visits for advising mothers about breastfeeding and weaning at 10 days, monthly up to 6 months, and at 8, 10 and 12 months following their child's birth Almost all households in the city have access to public water supply with fluoride level of 0.7ppm	Control: routine assistance by their paediatricians in the health service, research assessment usually within 1 month following the child's 6-12 month anniversary and dietary advice by a fieldworker after the 12 month research assessment
	Other relevant baseline statistics for each group (for		

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	the analysis/es used):	
	Duration:	Intervention was initially delivered from 10 days – 4 months; dental examination took place between 12 and 14 months
	Oral outcomes measured:	ECC incidence
	Scale/measure:	Caries status number of decayed surfaces
	Means and SD or events for each group at post-treatment or follow-up	Mean number of decayed surfaces (SD): Control group: 0.63 (1.62) Intervention group: 0.37 (1.37) (Mann Whitney U, P = 0.03)
	Other relevant statistical results	The proportion of children with ECC (defined as at least one decayed surface) was 10.2% (16/157) among the intervention group and 18.3% (40/219) among the controls and significantly higher in the control group relative to the intervention group: OR (adjusted for number of teeth) for the control group 1.0, OR for the intervention group 0.52 (95% CI 0.27-0.97) (p = 0.03)

Citation	Mohebbi, S. Z., et al. "A cluster randomised trial of effectiveness of educational intervention in primary health care on early childhood caries." Caries Res 43.2 (2009): 110-118.	
Study design (including statistical analysis):	Cluster RCT (Logistic regression, Kruskal-Wallis, Mann-Whitney U test and x2)	
Aims/objectives:	To evaluate the impact of a 6-month educational intervention on ECC	
Participants	Total sample size at baseline:	Total= 242 (group A = 77, group B = 85, group C = 80) 18 public health centres
	Country:	Iran
	Region (urban (city)/rural):	Tehran
	Ethnicity:	-
	Socioeconomic status:	The parents' level of education was low for 14%, moderate for 49% and high for 37%. The parents' level of education was low for 12% in group A, 12% in group B and 16% in group C. Family income was low for 10% of families; moderate for 50% and high for 40% of families. The family income was low for 7% in group A, for 12% in group B, and for 11% in group C. The parents' level of education and family income showed no differences between the groups.
	Gender:	Of the children who received outcome examinations, 50% were boys: 40% in group A, 59% in group B and 54% in group C (p = 0.11).
	Age (including	The mean age of the children was 12.3 months (SD = 0.4)

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	adults/children):	(12 to 15 months old) at baseline and 18.3 months (SD = 0.6) at outcome. The groups showed no differences regarding children's age or dental findings at baseline	
	Health background/status:	Children suffering from any severe disease that could pose a barrier to the practice of oral health were excluded	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Child's age, Child's gender, Parent's level of education, Family income.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Group A = educational pamphlet, 5 min of oral health instructions, 2 recall phone calls of the oral health instructions at 2-month intervals. (n = 55) Group B = pamphlet only (n = 59)	C = control (n = 63)
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	6 month interval between intervention and follow-up	
	Oral outcomes measured:	Increments in the number of teeth with new dt or de, as percentages of children developing new dt or de, and as the number needed to treat (NNT).	
	Scale/measure:	Number and percentages of new de or dt dt = Number of teeth with dentinal caries; de = number of upper central incisors with enamel caries	
	Means and SD or events for each group at post-treatment or follow-up	Factors related to development of any new caries, either enamel caries (de) on upper central incisors or new decayed teeth (dt) during the 6-month intervention (n = 177). Intervention groups (control = 0) Pamphlet only (group B) = 1 Estimate of strength= –0.893 Standard error= 0.441 OR= 0.4 95%CI= 0.2–1.0 P= 0.043 Pamphlet + reminder (group A) = 2	

		Estimate of strength= –2.249 Standard error= 0.662 OR= 0.1 95%CI= 0.0–0.4 P= 0.001
	Other relevant statistical results	<u>Number of children at risk of developing new decayed enamel (de) on upper central incisors:</u> A: 48 B: 56 C: 61 <u>Increment in the new 'de' during the 6-month intervention:</u> A: 0 (SD=0) B: 0.2 (SD= 0.6) C: 0.4 (SD = 0.7) P (A vs C) < 0.001 P (B vs C) 0.066 <u>All children with de at the outcome examination:</u> A: 4 (7%), C: 18 (29%) (p<0.01) B: 10 (17%), C: 18 (29%) (p = 0.14) <u>Increment in percentages of children developing new de:</u> A: 0 B: 14 C: 26 P (A vs C) < 0.001 P (B vs C) 0.208 <u>No significant differences regarding the number or percentage of children developing new dt during the 6 month intervention were found between groups</u> <u>NNT, children with new de:</u> A: 4 B: 9 <u>Increment in the new dt during the 6-month intervention:</u> A: 0 .1 (SD=0.6) B: 0.1 (SD= 0.1) C: 0.2 (SD = 0.7)

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		P (A vs C) 0.188 P (B vs C) 0.265 <u>Increment in percentages of children developing new dt:</u> A: 5 B: 7 C: 13 P (A vs C) 0.177 P (B vs C) 0.276 <u>NNT, children with new dt:</u> A: 13 B: 17

Citation	Plutzer, Kamila, and A. John Spencer. "Efficacy of an oral health promotion intervention in the prevention of early childhood caries." Community Dent Oral Epidemiol 36.4 (2008): 335-346.		
Study design (including statistical analysis):	RCT; Fisher's Exact test		
Aims/objectives:	The purpose of this study was to test the efficacy of an oral health promotion programme targeting nulliparous women starting during the pregnancy to reduce S-ECC at 18 months of age.		
Participants	Total sample size at baseline:	649 (Nulliparous pregnant women in the test group=327 and control group=322)	
	Country:	Australia	
	Region (urban (city)/rural):	South Australia	
	Ethnicity:	No information	
	Socioeconomic status:	No information	
	Gender:	Female (no data on this variable with respect to the children)	
	Age (including adults/children):	Intervention delivered during pregnancy and when the child and 12 months of age. In a test sub-group, a structured telephone consultation was given when the child was 6-12 months of age. Children's teeth were assessed at the age of 20 ± 2.5 months	
	Health background/status:	Mothers with high risk pregnancies were excluded	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Mother's age, examination-age, number of parent family, mother's employment, country of born, education	
Intervention	Comparison/exposure	Intervention group (n	Comparison (n

	(including n, age and gender (if different from above) for each group for the analysis/es used):	randomized =327): Oral health promotion information during pregnancy, and later when the child reached 6 and 12 months of age. After the second round of information the test group mothers were randomized again. The information was reinforced in one of the test subgroups (n randomized= 165; n analysed = 123) through a telephone consultation. In the second test subgroup (n randomized= 156; n analysed = 109) no telephone conversation was received.	randomized = 322; n analysed = 209): There was no contact with mothers in the control group after enrolment
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	Intervention delivered during pregnancy and when the child was 6 and 12 months of age	
	Oral outcomes measured:	S-ECC incidence %	
	Scale/measure:	A case of S-ECC was defined when one or more upper incisor teeth labial surfaces were carious, either non-cavitated or cavitated. Diagnosis was based on visual criteria only	
	Means and SD or events for each group at post-treatment or follow-up	Bivariate and multivariate logistic regression analyses of severe early childhood caries (S-ECC) with unadjusted and adjusted odds ratios:	
	Other relevant statistical results	Control group***(ref. test group): Un-adjusted odds ratio (95.0% CI): 6.1 (2.0-18.1) adjusted odds ratio (95.0% CI): 6.8 (2.1-21.9) *** $P < 0.001$ Cumulative incidence of S-ECC in the test and control groups, including test A and test B groups (Fisher's exact test): Test group (A+B) = 1.7%; Control group 9.6% ($P < 0.01$)	

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		Tests group A = 1.6%; test group B = 1.8% (P = 0.903) Test group A = 1.6%; control group = 9.6% (P < 0.01) Test group B = 1.8%; control group = 9.6% (P < 0.01) (test B and control group). Number of children with S-ECC: A+B=4 (from total n=232) A=2 (from total n=123) B=2 (from total n=109) Control=20 (from total n=209)

Citation	Vachirarojpisan, Thongchai, Kayoko Shinada, and Yoko Kawaguchi. "The process and outcome of a programme for preventing early childhood caries in Thailand." Community Dent Health 22.4 (2005): 253-259.	
Study design (including statistical analysis):	Cluster- RCT (two-sample t-test to compare the differences in cavitated carious increment between the two groups).	
Aims/objectives:	To investigate the effectiveness of a participatory DHE approach to increase tooth brushing and fluoride toothpaste behaviour for preventing ECC.	
Participants	Total sample size at baseline:	520 mothers/caregivers of 6-19 month old children
	Country:	Thailand
	Region (urban (city)/rural):	One rural district of Suphanburi Province
	Ethnicity:	-
	Socioeconomic status:	Family income per month above Thai average: • Intervention group: 46% • Control group: 44% Family income per month below Thai average: • Intervention group: 54% • Control group: 56%
	Gender:	Both male and female
	Age (including adults/children):	6-19 month old children Children's average age at baseline Inter group: 12.9 (3.66%) Cont group: 12.24 (3.78%) Mother's/caregiver's average age at baseline: Inter group: 30.28 (9.65%) Cont group: 29.70 (9.35%)
	Health background/status:	-
	Any information on confounders (e.g. water, milk	No significant differences were reported concerning consumption of sweet food between meals between

	or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	intervention and control groups at baseline or in relation to measures of oral hygiene (tooth brushing habits).	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention: Small group discussion with 6-8 mothers/caregivers on their children's oral health, the cause and prevention of ECC three times (40-60 minutes/time), at 3-months interval +providing free toothbrushes and fluoride toothpaste (500 ppm F) N randomized (initial clinical examination and questionnaire interview Nov 2001): 11 health centres; 270 mothers / caregivers At the clinical examination and questionnaire interview (follow-up stage – Nov 2002), n= 213 mothers / caregivers participated	Control: Didactic teaching about the ECC prevention method + providing free toothbrushes conducted at the same time as vaccination program. N randomized (initial clinical examination and questionnaire interview Nov 2001): 10 health centres; 250 mothers / caregivers At the clinical examination and questionnaire interview (follow-up stage – Nov 2002), n= 191 mothers / caregivers participated
	Other relevant baseline statistics for each group (for the analysis/es used):	Intervention group: n=270	Control group: n=250
	Duration:	One-year intervention program	
	Oral outcomes measured:	Non-cavitated carious lesions, cavitated carious lesions, ECC (non-cavitated and cavitated carious lesions), Mean cavitated carious increment	
	Scale/measure:	Mean and SD	
	Means and SD or events for each group at post-treatment or follow-up	**Intervention group (Mean (SD))** Non-cavitated carious lesions: Baseline=1.38 (2.12) 1 year=3.98 (3.08) cavitated carious lesions: Baseline=0.36 (1.06) 1 year=3.82 (3.65) ECC (non-cavitated and	**Control group (Mean (SD))** Non-cavitated carious lesions: Baseline=1.47 (2.14) 1 year=4.04 (2.99) cavitated carious lesions: Baseline=0.51 (1.38) 1 year=3.74 (3.93) ECC (non-cavitated and

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		cavitated carious lesions): Baseline=1.73 (2.60) 1 year=7.80 (4.99) There is no statistical differences in all above variables between 2 groups at the base line and 1-year follow-up. Mean cavitated carious increment=3.46 (3.36)	cavitated carious lesions): Baseline=1.97 (2.76) 1 year=7.78 (5.22) Mean cavitated carious increment= 3.24 (3.53)
	Other relevant statistical results	Intervention group: n=213 Male: 120 (56.3) Female: 93 (43.7)	Control group: n=191 Male: 96 (50.3) Female: 95 (49.7)

Citation	*Harrison, R. et al. Effect of motivational interviewing on rates of early childhood caries: a randomized trial.'Pediatric Dentistry 29.1 (2007): 16-22.*		
Study design (including statistical analysis):	RCT (Poisson regression)		
Aims/objectives:	To investigate the effect of motivational interviewing to prevent early childhood caries.		
Participants	Total sample size at baseline:	240	
	Country:	Canada	
	Region (urban (city)/rural):	Surrey, British Columbia	
	Ethnicity:	South Asian immigrant	
	Socioeconomic status:	Proportion of children with a household income of $31,000 / y: (control group: 51%, intervention group: 50%)	
	Gender:	Both male and female	
	Age (including adults/children):	6 to 18 months	
	Health background/status:	Proportion of children in 'fair or poor health': 24% in the intervention and control groups. Proportion of children with a major illness: 13% (control group), 8% (intervention group)	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	No significant differences between groups in relation to baseline characteristics presented in relation to: caries prevalence at baseline, age, recruitment age, socioeconomic factors, health status, whether mother pre-chews food, antibiotic and vitamin use and the child's mood disposition	
Intervention	Comparison/exposure	Intervention group (N=122)	Control group (N=118)

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	(including n, age and gender (if different from above) for each group for the analysis/es used):	Boys (n, %): 69 (57%) Recruitment age (mean (SD)): 10.8 (5.3) The intervention (MI) group received the following: 1. The pamphlet and video 2. One 45-minute counselling session, in which a 'menu of options' for infant oral care were discussed 3. Two brief follow-up telephone calls up to 6 months after the initial contact 4. 2 postcard reminders	Boys (n, %): 61 (52%) Recruitment age (mean (SD)): 12.1 (5.3) The control group received 'traditional information' consisting of: a pamphlet on infant oral health; mother's also watched an 11-minute video 'preventing tooth decay for infants and toddlers'.
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Follow up period: 2 years	
	Oral outcomes measured:	Number of decayed surfaces, white spot surfaces, Missing surfaces, Filled surfaces, Dmfs, Dmfs plus white spots at 2 years post-intervention	
	Scale/measure:	Number of decayed surfaces, white spot surfaces, Missing surfaces, Filled surfaces, Dmfs, Dmfs plus white spots	
	Means and SD or events for each group at post-treatment or follow-up	Intervention group (n=105): mean (SD) Decayed surfaces: 2.03 (4.9) White spot surfaces: 0.17 (0.6) Missing surfaces:0.33 (2.5) Filled surfaces:0.99 (5.1) Dmfs: 3.35 (7.8) Dmfs plus white spots: 3.52 (8.0)	Control group (n=105): mean (SD) Decayed surfaces: 2.91 (5.6) White spot surfaces: 0.32 (1.1) Missing surfaces: 1.25 (5.8) Filled surfaces: 3.43 (9.7) Dmfs:7.59 (14.2) Dmfs plus white spots:7.91 (14.2)
	Other relevant statistical results	Significant ($p \leq 0.05$) differences were found between intervention and control groups in relation to the following:	

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		Filled surfaces (p = 0.03) Dmfs: 3.35 (p = 0.001) Dmfs plus white spots: (p = 0.1) Poisson regression results support a protective effect of MI relative to the control condition on the rate of dmfs after 2 years (hazard ratio = 0.54 (95% CI 0.35-0.84).

Citation	Jiang, Emily Ming, et al. "Prevention of early childhood caries (ECC) through parental tooth brushing training and fluoride varnish application: a 24-month randomized controlled trial." J Dent 42.12 (2014): 1543-1550.		
Study design (including statistical analysis):	RCT (independent samples Kruskal-Wallis test)		
Aims/objectives:	To investigate the effectiveness of hands-on training in parental tooth brushing in preventing ECC.		
Participants	Total sample size at baseline:	Intervention group=152 Control group=149	
	Country:	China	
	Region (urban (city)/rural):	Hong Kong	
	Ethnicity:	-	
	Socioeconomic status:	Monthly household income: Intervention group (n=144): <15,000: 24 (17%) 15,000-25,000: 35 (24%) >25,000: 85 (59%) Control group (n=134): <15,000: 20 (15%) 15,000-25,000: 23 (17%) >25,000: 91 (68%)	
	Gender:	Both male and female	
	Age (including adults/children):	8-23 Months	
	Health background/status:	Good general health and not on long term medication	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	There are no statistically significant difference (at $p \leq 0.05$ level) between the two groups in terms of the children's age, gender, monthly household income, parents' education level, parental tooth brushing and child self-tooth brushing at baseline.	
Intervention	Comparison/exposure (including n, age and gender	Intervention group (G2): Mean age at base line: 15.6	Control group (G1): Mean age at base line:

	(if different from above) for each group for the analysis/es used):	(3.8) Boys: 62 (43%) Girls: 82 (57%) The intervention group received oral health education talk and parental tooth brushing training, reinforced every 6 months.	15.5 (3.9) Boys: 58 (43%) Girls: 76 (57%) The control group received one-off oral health education talk to parents and printed materials information on children's tooth eruption, suggested method for cleaning baby's mouth, parental tooth brushing methods, healthy oral health-related dietary practice, need for regular dental visits, and a brief introduction to early childhood caries. There was no reinforcement of the oral health education messages by the investigators during the study period.
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	Follow up: 24 months (every 6 months)	
	Oral outcomes measured:	ECC incidence	
	Scale/measure:	Dmft	
	Means and SD or events for each group at post-treatment or follow-up	Mean dmtf increment at 24 month follow up: Intervention group: (n=144) Mean (included non-cavitated and cavitated lesions)=0.2 (SD=0.6) Mean (included cavitated lesions)=0.1 (SD=0.5)	Mean dmft increment at 24 month follow up: Control group: (n=134) Mean((non-cavitated and cavitated)=0.3 (SD=1.2) Mean (cavitated)=0.2 (SD=1.0)
	Other relevant statistical results	Incidence of ECC in the intervention group (non-cavitated+cavitated) (n-144) = 17 (11.8%) (cavitated)=10 (6.9%)	Incidence of ECC in the control group (non-cavitated+cavitated) (n=134) =16 (11.9%) (cavitated)=11 (8.2%)

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Research question 10: Does an optimum concentration of fluoride in water reduce the risk of early childhood caries?

Citation	Blinkhorn, A., Brown, M., Attwood, D., & Downer, M. (1981). The effect of fluoridation on the dental health of urban Scottish Schoolchildren. Journal of Epidemiology and Community Health, 35(2), 98-101.		
Study design (including statistical analysis):	Retrospective cohort (two way ANOVA)		
Aims/objectives:	To demonstrate the likely benefits of introducing fluoridation to urban areas of Scotland by comparing the dental health of children from Stranraer, a fluoridated area, with similar children from Anan, a non-fluoridated area.		
Participants	Total sample size at baseline:	262 eligible children; 230 examined and lifetime residents	
	Country:	Scotland	
	Region (urban (city)/rural):	Annan and Stranraer; seaport towns with a mixture of rural activities and light industry	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	-	
	Age (including adults/children):	4-5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	The number of dentists serving the two towns was also comparable, five in Stranraer and four in Annan. Only children who were lifetime residents were included in the analysis	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Stranraer received water with an optimally adjusted 1mg /l fluoride N=129	Annan did not have fluoridated drinking water (the concentrate of naturally occurring fluoride was not specified) N=101
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Exposure (or not) to fluoridated water from birth. Data collected at 4-5 years	
	Oral outcomes measured:	Number of decayed deciduous teeth Number of decayed, missing and filled deciduous teeth	
	Scale/measure:	Mean (SD)	
	Means and SD or events for each group at post-treatment or follow-up	Stranraer (fluoridated) : Adjusted* mean dt score:	Annan (non-fluoridated) : Adjusted* mean dt score:

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		1.34 Adjusted mean dmft score: 2.47 *adjusted for differences between two examiners	3.34 Adjusted mean dmft score: 4.41 *adjusted for differences between two examiners
	Other relevant statistical results	Mean difference in adjusted mean dt scores in 4-5 year olds between Stranraer (Fluoridated) and Annan (Non-fluoridated): 2.0, F(31.5), p<0.01 Mean difference in adjusted mean dmft scores in 4-5 year olds between Stranraer (Fluoridated) and Annan (Non-fluoridated): 1.94, F(17.0), p<0.01 (Results specific to anterior teeth also reported (as fluoridation shows particular benefit to these) – but I wouldn't have extracted these data either as overall results is our main interest)	

Citation	Booth et al. (1992). A comparison between the dental health of 3-year-old children living in fluoridated Huddersfield and non-fluoridated Dewsbury in 1989. Community Dent Health, 9(2):151-7.	
Study design (including statistical analysis):	Retrospective cohort	
Aims/objectives:	To compare the prevalence if dental caries and developmental defects of enamel between 3 year old children who were lifelong residents of fluoridated areas of Huddersfield and non-fluoridated Dewsbury.	
Participants	Total sample size at baseline:	480 (240 from Huddersfield and 240 from Dewsbury)
	Country:	England, UK
	Region (urban (city)/rural):	Huddersfield and Dewsbury
	Ethnicity:	White children
	Socioeconomic status:	A representative cross-section of all social classes was obtained from each location
	Gender:	Male and female
	Age (including adults/children):	3 years
	Health background/status:	-
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration,	Included children had never taken fluoride tablets Areas were matched according to socio-economic data Participants were randomly selected All participants had to be lifelong residents of the area to which they were grouped in this study There was no significant difference regarding response

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	frequency) and oral hygiene behaviour):	rate between areas No significant difference between social class or mean ages of the two samples No significant differences were found with respect to demarcated developmental defects of enamel between intervention and control areas Significant differences were found between groups with respect to diffuse defects of the upper and lower first molars	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention: (n = 240 randomly sampled, 225 contacted, 126 attended the first appointment, 22 attended the second appointment, 121 children were included in the analysis) Fluoridated water supply (1 ppm F)	Control: (n = 240 randomly samples, 206 contacted, 206 were contacted, 101 attended the first appointment, 21 the second, of theses 122 children, 107 were included in the analysis) Non-fluoridated water supply (<0.3ppm)
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	The intervention area received fluoridated water (1 ppm F) from 1970 – 31st Oct 1989. In the fluoridated area, dental examinations took place in September and October 1989; in the non-fluoridates area, dental examinations took place in October and November 1989	
	Oral outcomes measured:	Number of DMFT	
	Scale/measure:	Mean	
	Means and SD or events for each group at post-treatment or follow-up	Mean (SD) values in Fluoridated Huddersfield: dt: 0.24 (0.84) mt: 0.03(0.29) ft: 0.03(0.20) dmft: 0.30 (1.00)* *denotes a significant effect p =0.03	Mean (SD) values in non-Fluoridated Dewsbury: dt: 0.60 (1.87) mt: 0.10(0.53) ft: 0.04 (0.23) dmft: 0.74 (2.00)*
	Other relevant statistical results	1) Caries free (dmft = 0) 87% 2) Carious teeth (dt>0)	1) Caries free (dmft = 0) 75%, p = 0.03 2) Carious teeth

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		11% 3) Teeth extracted (mt>0) 2%	(dt>0) 11%, p = 0.04 3) Teeth extracted (mt>0) 5%, p = 0.35

Citation	Evans, D.J., Rugg-Gunn, A.J., Tabari, E.D. and Butler, T. (1996) The effect of fluoridation and social class on caries experience in 5-year-old. Community Dent Health, 13(1), 5-10.		
Study design (including statistical analysis):	Historical cohort; Chi-square and Mann-Whitney U tests		
Aims/objectives:	To compare the dental health of children who had lived in continuously fluoridated compared to non-fluoridated areas of Northumberland.		
Participants	Total sample size at baseline:	662	
	Country:	England, UK	
	Region (urban (city)/rural):	North-East	
	Ethnicity:	-	
	Socioeconomic status:	Children in social groups from I-V from intervention and control areas were included in the analyses	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	There was a statistically significant difference in the distribution of subjects in three social class groups between the two areas – in Northumberland (NF) a higher proportion of social class III (manual) were included whereas in Newcastle (F) a higher proportion of social group 1 were included. This was not controlled for in overall analysis but results were presented by social group.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Newcastle was continuously fluoridated (at 0.1 mg/lF) n = 327 children	South-East Northumberland was non-Fluoridated (0.1 mg/lF) n = 335
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Children lived in areas since birth and examinations tool place when they were 5 years old	
	Oral outcomes measured:	Caries prevalence	
	Scale/measure:	Number / Percentage	
	Means and SD or events for each group at post-treatment	-	-

	or follow-up	
	Other relevant statistical results	

	Fluoridated area	Non-Fluoridated area	Difference	%
No of sound teeth	18.37	17.19**	1.18	6
dt	0.79	1.63**	0.84	52
mt	0.19	0.42**	0.23	55
ft	0.22	0.24 NS	0.02	8
dmft	1.20	2.29**	1.09	48
dmfs	2.52	5.49**	2.97	54
dfs	1.59	3.41**	1.82	53
%dmft>0	36%	52%	16%	
%dmft>4	12%	26%	14%	

NS = Non significant
*P = <0.05
** P<0.001

Social class	F	NF	Difference
dmft			
I + II	0.59 (1.37)	1.46 (2.61)	0.87 (60%)*
III	1.21 (2.36)	2.04 (3.42)	0.83 (41%) NS
IV + V	1.17 (2.73)	2.74 (3.05)	1.57 (57%)**
dfs			
I + II	0.85 (2.28)	2.18 (4.46)	1.33 (61%)*
III	1.25 (2.84)	3.13 (6.94)	1.88 (60%)*
IV + V	1.17 (2.65)	3.65 (4.51)	2.48 (68%)

Mean (SD)
*P= <0.05, **P= <0.001

Citation	French, A. D., et al. Fluoridation and dental caries experience in 5-year-old children in Newcastle and Northumberland in 1981." Brit Dent J 156.2 (1984): 54.	
Study design (including statistical analysis):	Retrospective cohort (Chi-squared test and Mann-Whitney U test)	
Aims/objectives:		
Participants	Total sample size at baseline:	1069
	Country:	UK
	Region (urban (city)/rural):	North East
	Ethnicity:	-

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	Socioeconomic status:	All social classes	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Social class: In the fluoridated Newcastle locality slightly more social class I, II and III children were obtained in the sample, while in low fluoride Northumberland more social class IV and V were found to be present.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Children were continuous residents of a fluoridated area (Newcastle), n = 533 children	Children were continuous residents of a low-fluoride area (Northumberland), n = children 536
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	5 years	
	Oral outcomes measured:	Caries experience	
	Scale/measure:	dmft, dmfs, dfs	
	Means and SD or events for each group at post-treatment or follow-up	See tables 1 and 2 (below)	See tables 1 and 2 (below)
	Other relevant statistical results	See tables 1 and 2 (below)	

Table I: Caries experience (dmft and dmfs) of 5-year old children in each area for all subjects and for social class III children only

				dmft		*dmfs*	
	N	*Percent caries free (dmft=0)*	*Difference*	*Mean (SD)*	*Difference (%)*	*Mean (SD)*	*Difference (%)*
All subjects							
Newcastle (Fluoridated)	533	55	24~	1.41 (2.21)	1.96*(58)	2.14 (4.13)	3.56 (62)
Northumberland (Fluoride low)	536	31		3.37 (3.65)		5.70 (7.19)	
Class III only							
Newcastle (Fluoridated)	295	52	21~	1.54 (2.28)	2.01* (57)	2.32 (4.13)	3.61* (61)
Northumberland (Fluoride low)	253	31		3.55 (3.69)		5.93 (7.08)	
P<0.001 (Mann-Whitney U test)							
~P<0.001 (Chi-squared)							

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Table 2 dfs experience for each surface type separately for all subjects and for social class III children only						
	Fissure		Free smooth surface		Approximal	
	Mean (SD)	Difference (per cent)	Mean (SD)	Difference (per cent)	Mean (SD)	Difference (per cent)
All subjects						
Newcastle (Fluoridated)	0.98 (1.65)	0.74* (43%)	0.14 (0.64)	0.37* (73%)	0.30 (1.0)	1.22*(76%)
Northumberland (Fluoride low)	1.72 (1.99)		0.51(1.29)		1.60 (2.51)	
Class III only						
Newcastle (Fluoridated)	1.04 (1.62)	0.75* (42%)	0.18 (0.79)	0.42* (70%)	0.43 (1.03)	1.32* (75%)
Northumberland (Fluoride low)	1.79 (2.06)		0.60(1.49)		1.75(2.56)	
*P<0.001 (Mann-Whitney U test)						

Citation	Jackson et al (1975). Fluoridation in Anglesey A Clinical Study. Brit Dent J, 138 (5), 165-71.		
Linked studies	Jackson et al. (1980). Fluoridation in Leeds. Brit Dent J, 149, 231-4. Jackson D, James PM, Thomas FD. 1985. Fluoridation in Anglesey 1983: a clinical study of dental caries. Brit Dent J. 158(2):45. Jackson et al. (1975). Fluoridation in Cumbria A Clinical Study. Brit Dent J , 139, 319-322.		
Study design (including statistical analysis):	Historical cohort		
Aims/objectives:	To find out the possible benefits of water fluoridation		
Participants	Total sample size at baseline:	600	
	Country:	Wales, UK	
	Region (urban (city)/rural):	-	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Children were excluded from the study for the reasons including the following: - The child had left the area - The child did not have continuity of residence - The home of the child did not have a piped water supply for his/her whole life No information on similarity of the two areas although close geographically	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention area: Anglesey Intervention: drinking water had contained 0.9ppm fluoride for the whole lives of participants	Control area: Bangor / Caernarvon Intervention: drinking water contained <0.01 ppm fluoride

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		N of children examined: 153 (50% of baseline)	N of children examined: 145 (49% of baseline)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Drinking water contained 0.9ppm fluoride in Anglesey from 1955; clinical examinations for this study took place in 1974	
	Oral outcomes measured:	D,m,f, dmf	
	Scale/measure:	Number, mean	
	Means and SD or events for each group at post-treatment or follow-up	See accompanying data (below)	See accompanying data (below)
	Other relevant statistical results	See accompanying data (below)	See accompanying data (below)

Accompanying data

Table IV: Caries experience (dmf or DMF) of children aged 5 years in Anglesey and in non-fluoridated Bangor / Caernarvon (NF<0.1PPM)

Area	N	d	m	f	dmf	SE
Anglesey	Total	306	48	79	433	-
	Mean per person	2.00	0.31	0.52	2.83	0.261
Bangor / Caernarvon	Total	412	91	161	664	-
	Mean per person	2.84	0.63	1.11	4.58	0.338

Citation	Jackson et al. (1980). Fluoridation in Leeds. Brit Dent J. 149, 231-4.	
Linked studies	Jackson et al (1975). Fluoridation in Anglesey A Clinical Study. Brit Dent J. 138 (5), 165-71. Jackson D, James PM, Thomas FD. 1985. Fluoridation in Anglesey 1983: a clinical study of dental caries. Brit Dent J. 158(2):45. Jackson, D. et al. (1975). Fluoridation in Cumbria A Clinical Study. Brit Dent J. 139, 319-322.	
Study design (including statistical analysis):	Historical cohort	
Aims/objectives:	To find out the possible benefits of water fluoridation	
Participants	Total sample size at baseline:	910
	Country:	England, UK
	Region (urban (city)/rural):	Leeds (urban)
	Ethnicity:	-
	Socioeconomic status:	-

	Gender:	-	
	Age (including adults/children):	5-year-old	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Children were excluded if their parents reported that they in receipt of fluoride - topical or supplements, or if they were in receipt of mixed water supplies Children who were continuous residents were included in the analysis	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention: 4 districts of Leeds that had been fluoridated continuously at an average level of 0.9 ppm fluoride since 1968 n =470 children examined and n = 349 questionnaires returned in 1979; n = 190 acceptable for the study after disqualifications	Control: Low fluoride districts of Leeds where the water supply is about 0.1ppm F n =440 children examined and n = 317 questionnaires returned in 1979; n = 198 acceptable for the study after disqualifications
	Other relevant baseline statistics for each group (for the analysis/es used):	All included participants were continuous residents of the districts they were assigned to in the study	
	Duration:	Intervention implemented in 1968, clinical examination took place in 1979	
	Oral outcomes measured:	Dmf, d,m,f,df	
	Scale/measure:	Mean, percentage	
	Means and SD or events for each group at post-treatment or follow-up	See accompanying data (below)	See accompanying data (below)
	Other relevant statistical results	See accompanying data (below)	See accompanying data (below)

Table 1: Caries experience (mean dmf ±SE) in 5-year old children

	Total caries experience. Mean values			
	d	**m**	**f**	**dmf±SE**
Fluoridated districts (n= 190)	0.71	0.11	0.41	1.23 ±0.1462
Low fluoride districts (n= 198)	2.30	0.43	0.54	3.38 ±0.2543

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Table 2: Caries experience of approximal sites in 5-year old children

	Total no approximal sites	Total no df approximal sites	Percentage df
Fluoridated districts (n=190)	7,432	73	0.98
Low fluoride districts (n= 198)	7,590	302	3.98

Table 3: Caries experience of occlusional and approximal sites on deciduous molars in 5-year old children

	Occlusional sites					Approximal sites				
	no	df	Df percent	f	f/f+d percent	no	df	Df percent	f	f/f+d percent
Fluoridated districts (n=190)	1,503	115	7.65	52	45	3,006	46	1.53	16	35
Low-fluoride districts (n=198)	1,488	209	14.05	62	30	2,976	194	6.52	34	18

Citation	Jackson, D., P. M. James, and F. D. Thomas. "Fluoridation in Anglesey 1983: a clinical study of dental caries." Brit Dent J 158.2 (1985): 45. (A follow-up study from Jackson 1975. Fluoridation in Anglesey A Clinical Study)	
Linked studies	Jackson et al (1975). Fluoridation in Anglesey A Clinical Study. *British Dental Journal*, 138 (5), 165-71. Jackson et al. (1980). Fluoridation in Leeds. *British Dental Journal*, 149, 231-4. Jackson, D. et al. (1975). Fluoridation in Cumbria A Clinical Study. *British Dental Journal*, 139, 319-322.	
Study design (including statistical analysis):	Historical cohort	
Aims/objectives:	It has recently been noticed that caries experience has fallen in English children from both fluoridated and non-fluoridated communities. It was important to know whether a similar phenomenon had occurred in fluoridated Anglesey and in the non-fluoridated adjacent mainland part of Gwynedd.	
Participants	Total sample size at baseline:	600

	Country:	Wales, UK	
	Region (urban (city)/rural):	Anglesey and Gwynedd	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Children who were discontinuous residents, had fluoride supplements or who received water from a well or from a well and the mains water supply were excluded*	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention group (5 year old children from Anglesey) had received a mains water supply containing F=0.9 PPM fluoride for all of their lives (since 1964, the study including clinical examinations were undertaken in 1983). N children examined = 314 Number of children in the final sample following exclusions due to the presence of confounders* = 219	Control group (5 year old children from Gwynedd) received un-fluoridated water containing F=0.1 PPM fluoride. N children examined = 172 Number of children in the final sample following exclusions due to the presence of confounders* = 128
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Water fluoridation to 0.9 ppm fluoride was implemented in Anglesey in 1964; clinical examinations were conducted of children in the intervention and control areas in 1983.	
	Oral outcomes measured:	D, m, f, dmf	
	Scale/measure:	Mean, difference	
	Means and SD or events for each group at post-treatment or follow-up	See accompanying data (below)	See accompanying data (below)
	Other relevant statistical results	See accompanying data (below)	See accompanying data (below)

Table IV: Caries experience (dmf or DMF) of children aged 5 years in Anglesey and in non-fluoridated

Gwynedd (NF<0.1PPM)

Age 5 years	N	d	m	f	*dmf±SE
Anglesey	219	1.03	0.10	0.46	1.58±0.174
Gwynedd	128	2.24	0.45	0.86	3.55±0.328

Table V. Caries experience in children aged 5 years in fluoridated (F) Anglesey and non-fluoridated Gwynedd 1974-83 data compared

	Anglesey (F=0.9 PPM) Mean dmf	Gwynedd (F=0.1 PPM) Mean dmf
1974	2.83	4.58
1983	1.38	3.55
Diff. 1974-83	44%	22%

Citation	Jackson, D. et al. (1975). Fluoridation in Cumbria A Clinical Study. Brit Dent J. 139, 319-322.	
Linked studies	Jackson et al (1975). Fluoridation in Anglesey A Clinical Study. *British Dental Journal*, 138 (5), 165-71. Jackson et al. (1980). Fluoridation in Leeds. Brit Dent J. 149, 231-4. Jackson et al. 1985. Fluoridation in Anglesey 1983: a clinical study of dental caries.	
Study design (including statistical analysis):	Historical cohort	
Aims/objectives:	-	
Participants	Total sample size at baseline:	830
	Country:	England, UK
	Region (urban (city)/rural):	Cumbria (rural)
	Ethnicity:	-
	Socioeconomic status:	-
	Gender:	-
	Age (including adults/children):	5 years
	Health background/status:	-
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration,	Children were excluded from the study for reasons including the following: - Non continued residence in their community - Non continuous receipt of mains water supply - Receipt of one of the following preventative

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	frequency) and oral hygiene behaviour):	measures against caries: fluoride tablets, topical fluoride, fissure sealant or other No information given on how the areas were comparable	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention area: Cockermouth / Workington Intervention: water supply fluoridated to 1ppm N of children examined: 106 (26% of baseline)	Control area 1: Carlisle / Penrith Intervention: drinking water contained <0.01 ppm fluoride N of children examined: 130 (31% of baseline)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Drinking water contained 0.9ppm fluoride in Anglesey from 1955; clinical examinations for this study took place in 1974	
	Oral outcomes measured:	D, m, f, d+m+f teeth	
	Scale/measure:	Number, mean	
	Means and SD or events for each group at post-treatment or follow-up	See accompanying data (below)	See accompanying data (below)
	Other relevant statistical results	See accompanying data (below)	See accompanying data (below)

Table II: Caries experience of 5-year-old children in fluoridated and in non-fluoridated communities of Cumbria

	Cockermouth and Workington F = 1ppm N = 106		Carlisle and Penrith F = <0.1ppm N = 130		Decoys N= 143	
	Total	Mean	Total	Mean	Total	Mean
d teeth	194	1.83	426	3.28	431	3.01
m teeth	40	0.38	105	0.81	95	0.66
f teeth	18	0.17	41	0.32	81	0.57
d+m+f teeth	252	2.38±0.304 (SE)	572	4.40 ±0.349 (SE)	607	4.24 ±0.365 (SE)

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Citation	O'Mullane D, Whelton H. Efficacy of fluoride against dental caries; fluoride in water. Fogorvosi szemle. 1997 Apr; 90:7.		
Study design (including statistical analysis):	Retrospective cohort		
Aims/objectives:	To consider the effectiveness of fluoridated water		
Participants	Total sample size at baseline:	1995	
	Country:	Republic of Ireland	
	Region (urban (city)/rural):	All	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	Males and females	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Subjects in the intervention (Full FI) group may have had exposure to school fluoridation, fluoride tablets or fluoride mouth rinses Subjects in the control ("Non FI") group never had fluoride tablets or mouth rinses.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention ("Full FI") group: Home water supply fluoridated continuously (0.8-1.0mg'l fluoride) since birth.	Control ("Non FI") group Home water supply never fluoridated. Present school water supply is not fluoridated. Subject never had fluoride tablets or mouth rinses.
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	Home water supply of the "Full FL" fluoridated continuously since birth.	
	Oral outcomes measured:	Number of decayed, missing and filled teeth	
	Scale/measure:	Mean	
	Means and SD or events for each group at post-treatment or follow-up	See table 1, below	See table 1, below
	Other relevant statistical results	-	

Table 1: Mean number of decayed missing and filled teeth in 5-year-old children (dmft) in 1984

	Group	
Health board	Full FL	Non-FL
Eastern	1.3	2.9
Midland	1.9	3.0
M-western	2.3	4.0
N-Eastern	1.0	2.1
N-Western	1.7	3.0
S-Eastern	1.9	2.8
Southern	2.5	4.0
Western	1.5	2.2
All health boards	1.8	3.0

Citation	Rugg-Gunn et al. (1981). Caries Experience of 5-year-old children living in four communities in N.E. England Receiving Differing Water Fluoride Levels. Brit. Dent. J. 150, 9-12.		
Linked studies	Rugg-Gunn, A.J., Carmichael, C.L. and Ferrell, R.S. (1988) Effect of fluoridation and secular trend in caries in 5-year-old children living in Newcastle and Northumberland. Brit Dent J. 19;165(10):359-64.)		
Study design (including statistical analysis):	Historical cohort (T test)		
Aims/objectives:	To assess the relationship between water fluoride levels and caries experience.		
Participants	Total sample size at baseline:	N= 2,023 consent forms issued N=1,038 subjects studied (following exclusion of participants who failed to return their consent form and of children who failed to meet the inclusion criteria*)	
	Country:	England, UK	
	Region (urban (city)/rural):	North-East (urban)	
	Ethnicity:	Caucasian	
	Socioeconomic status:	Children from social classes I –V	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	* • Non-caucasian children were excluded • All consenting children had lived in the area throughout their lives were examined • Proportion of individuals from each social class I-V were well balanced between groups, except for a significantly higher proportion of social class IV&V children from Ashington (ppm<0.1)	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es	Intervention: Residence in Newcastle , which had ppm 1.0 F for	Comparators: Residence in Ashington, and Houghton, which had

	used):	the last seven years N = 438 subjects studied	ppm <0.1 and 0.2 F, respectively N = 132 subjects studied (Ashington) N= 112 subjects studied (Houghton)
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Fluoride levels had remained constant for the past seven years; participants' teeth were examined at 5 years of age	
	Oral outcomes measured:	Caries experience (deft and DMFS)	
	Scale/measure:	Mean (SD), %	
	Means and SD or events for each group at post-treatment or follow-up	See accompanying data (below)	See accompanying data (below)
	Other relevant statistical results	See accompanying data (below)	See accompanying data (below)

Table III – caries experience (deft and defs) of 5-year-old children in each of the 4 areas. Data also given for social class III children only

			Ashington (<0.1ppm)	Sig. [1]	Houghton (0.2 ppm)	Newcastle (1.0 ppm)
deft (all subjects)		Mean (sd)	6.1 (4.03)		4.9 (4.42)	2.5 (2.79)
deft (social class III)		Mean (sd)	5.9 (3.92)	n.s.	4.9 (4.10)	2.4 (2.73)
defs (all subjects)		Mean (sd)	11.6 (9.54)	[1]	8.9 (9.86)	4.1 (5.76)
defs (social class III only)		Mean (sd)	11.5 (9.64)	[1]	8.2 (8.34)	4.0 (5.67)

Sig. = significance between adjacent pairs (Welsh or t test); [1] P<0.05

Table IV – Percentage of children caries-free or with gross caries

	Ashington (<0.1ppm)	Houghton (0.2 ppm)	Newcastle (1.0 ppm)
Caries free	11	24	33
Deft 5+	65	47	20
Defs 15 +	36	29	8

Citation	Rugg-Gunn, A.J., Carmichael, C.L. and Ferrell, R.S. (1988**)** Effect of fluoridation and secular trend in caries in 5-year-old children living in Newcastle and Northumberland. Brit Dent J. 19;165(10):359-64.		
Linked studies	Rugg-Gunn et al. (1981). Caries Experience of 5-year-old children living in four communities in N.E. England Receiving Differing Water Fluoride Levels. Brit Dent J. 150, 9-12.		
Study design (including statistical analysis):	Historical cohort (Chi-square and Mann-Whitney U)		
Aims/objectives:	This study compared the dental health of 457 5-year-old children who had lived in continuously fluoridated (at 1.0 mg F/litre) Newcastle with the dental health of 370 5-year old children of the same age in non-fluoridated (less than 0,1 mg F/litre) south Northumberland.		
Participants	Total sample size at baseline:	827	
	Country:	England, UK	
	Region (urban (city)/rural):	Newcastle (urban) and Northumberland (rural)	
	Ethnicity:	Caucasian	
	Socioeconomic status:	-	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Only Caucasian participants were included in the study, as the study authors reported that ethnicity influences caries experience in young children and the control area contained very few non-Caucasians Children had to have lived in their locality since birth to be included in the study Data from the analyses were presented for all subjects and for children from social class III only	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention: Residence since birth in Newcastle-upon-Tyne, the water supply of this city had been fluoridated since 1967; the level of fluoridated was between 0.9 and 1 mg F/ litre since 1981 N = 457 participants included in the analysis	Control: Residence since birth in south Northumberland, a non-fluoridated area (<0.1 mg F / litre) N = 370 participants included in the analysis
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-

	Duration:	The water in Newcastle-upon-Tyne had been fluoridated to 0.9 and 1 mg F/ litre since 1981; caries was examined in 5-year-old children in 1987	
	Oral outcomes measured:	Caries experience (dmft, dmfs)	
	Scale/measure:	Mean, mean difference, %	
	Means and SD or events for each group at post-treatment or follow-up	See accompanying data (below)	See accompanying data (below)
	Other relevant statistical results	See accompanying data (below)	See accompanying data (below)

Table III Caries experience (dmft and dmfs) of 5-year-old children in each area, for all subjects and for social class III children only

	dmft		dmfs	
All subjects	**Mean (SD)**	**Difference (%)**	**Mean (SD)**	**Difference (%)**
F (n = 457)	1.81 (2.56)	2.09[a] (54%)	2.81 (4.77)	4.19[a] (60%)
NF (n = 370)	3.90 (4.22)		7.00 (9.28)	
Social class III only				
F (n = 170)	1.70 (2.53)	2.01[a] (54%)	2.49 (4.24)	3.72[a] (60%)
NF (n = 146)	3.71 (4.05)		6.21 (8.15)	

P<0.001 (Mann-Whitney test)

Table IV Percentage of children caries-free or with gross caries in each area, for all subjects and for social class III

	% caries free	% dmft 5+	% dmfs 15+
All subjects			
F	50[a]	16[a]	4[a]
NF	32	37	17
Social class III only			
F	54[a]	15[a]	4[b]
NF	33	33	14

[a] P<0.001

[b] P <0.01 (chi-squared test)

Citation	Tank, Gertrude, and Clara A. Storvick. "Caries experience of children one to six years old in two Oregon communities (Corvallis and Albany)." JADA 70.2 (1965): 394-403.	
Study design (including statistical analysis):	Prospective cohort	
Aims/objectives:	To investigate the effect of pre- and post-natal exposure to a fluoridated water supply on the teeth of children from one to six years old	
Participants	Total sample size at baseline:	246 (aged 1- 5 years)
	Country:	Canada
	Region (urban (city)/rural):	Ontorio

	Ethnicity:	All included children were white	
	Socioeconomic status:	-	
	Gender:	Male and female	
	Age (including adults/children):	1- 6 years (data were presented for individual years, therefore data on 1-5 year old children were extracted for this review)	
	Health background/status:	Healthy children	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	The authors indicated that Corvallis and Albany were comparable in climate, topography and population. Mother had used the municipal water during pregnancy. All children in the study had consumed the municipal water since birth and had not been absent from their respective areas for more than two months in any year. Children who had received topical applications of fluoride or who were taking fluoride by prescription were excluded, as were those children whose parents refused to allow roentgenograms to be taken.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention group (Corvallis residents) Pre- and post-natal exposure to water adjusted to 1.0 ppm of fluoride	Control group (Albany residents) Lack of pre- or post-natal exposure to artificially fluoridated water
	Other relevant baseline statistics for each group (for the analysis/es used):		
	Duration:	Annual assessments of caries took place annually for 5 years	
	Oral outcomes measured:	Mean dmft; N decayed teeth; N missing teeth; N filled teeth; N decayed surfaces (all per child) Percent difference (between Corvallis and Albany) in the above measures; percent of children caries-free (without dmft) Percent of teeth caries free (no dmft).	
	Scale/measure:	Mean values Percentages	
	Means and SD or events for each group at post-treatment or follow-up	See table 3 (below)	
	Other relevant statistical results	See table 3 (below)	

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Table 3: Decayed, missing and filled deciduous teeth of children with a fluoride-free water supply (Albany) and a fluoridated water supply (Corvallis)

		Age on last birthday				
	Community	**1**	**2**	**3**	**4**	**5**
Mean no. of dmft per child	Albany	0.14	1.26	4.25	5.51	6.0
	Corvallis	0.08	0.59	1.44	2.31	3.29
Percent difference	Corvallis	-43	-53*	-66*	-58*	-45*
Mean no. of decayed teeth per child	Albany	0.14	1.26	3.89	4.95	4.96
	Corvallis	0.08	0.59	1.30	2.0	2.0
Percent difference	Corvallis	-43	-53*	-67*	-60*	-60*
Mean no. of missing teeth per child	Albany	0	0	0.09	0.06	0.17
	Corvallis	0	0	0	0	0
Percent difference	Corvallis	-	-	-100	-100	-100
Mean no. of filled teeth per child	Albany	0	0	0.32	0.68	1.0
	Corvallis	0	0	0.11	0.41	1.32
Percent difference	Corvallis	-	-	-66	-40	+32
Mean no. of decayed surfaces per child	Albany	0.14	1.34	5.08	7.28	8.83
	Corvallis	0.09	0.56	1.45	2.66	2.89
Percent difference	Corvallis	-36	-58*	-71*	-63*	-67*
Percent of children caries-free (without dmft)	Albany	89	54	11	8	4
	Corvallis	97	79*	55*	38*	39*
Percent of teeth caries-free	Albany	99	93	79	72	69
	Corvallis	99	97	93*	88	83

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(no dmft)						

- = reduction. + = increase. Calculated as follows: Corvallis-Albany/ Albany (100)
*Difference significant at the 5 percent level

Citation	Thomas, F.D., Kassab, J.Y. and Jo, B.M. Fluoridation in Anglesey: a clinical study of dental caries in in 5-year-old children who had experienced sub-optimal fluoridation. Br Dent J. 1995 Jan 21; 178(2):55-9.		
Study design (including statistical analysis):	Retrospective cohort		
Aims/objectives:	1. To ascertain and compare dental caries experience amongst Anglesey 5-year-old children residing in zones which had experienced different periods of fluoridation, and 2. To compare dental caries experience amongst Anglesey 5-year-old children who experienced sub-optimal fluoridation in the earlier part of their lives only, with previous caries experience related to whole life fluoridation and to that of contemporaries with low or negligible experience of fluoridation.		
Participants	Total sample size at baseline:	725 (all children examined in the survey) 498 children examined had continually resided in specific water district zones (the cohort of interest)	
	Country:	Wales	
	Region (urban (city)/rural):	Anglesey	
	Ethnicity:	-	
	Socioeconomic status:	-	
	Gender:	-	
	Age (including adults/children):	5 years	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	Children whose parents indicated in the questionnaire that they had received fluoride supplements were eliminated from the inter-zone comparisons. Children whose parents indicated in the questionnaire that the child had consumed non-mains water from well, spring or bottle were also eliminated from the inter-zone comparison.	
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	<u>Intervention group:</u> Child had resided in an area (Alaw zone) of optimal fluoridation during approximately 35% of their lives (n=230)	<u>Comparison group:</u> Child had resided in an area (Cefni and Penmynydd zones) of optimal fluoridation for less than 10% of their lives (n=268)
	Other relevant baseline statistics for each group (for the analysis/es used):		

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	Duration:	Outcome data were collected when the children were aged 5 years.	
	Oral outcomes measured:	dmft and components (d,m,f)	
	Scale/measure:	mean	
	Means and SD or events for each group at post-treatment or follow-up	<u>Intervention group:</u> Mean dmft (SD): 1.81 (2.86) Mean d: 1.13 Mean m: 0.38 Mean f: 0.31	<u>Control group:</u> Mean dmft (SD): 2.28 (3.48) Mean d: 1.36 Mean m: 0.45 Mean f: 0.47
	Other relevant statistical results		

Research question 11: Does consumption of fluoridated milk reduce the risk of early childhood caries?

Citation	Bian et al. 2003. Effect of fluoridated milk on caries in primary teeth: 21-month results. Community Dent Oral Epidemiol. 31(4), 241-5.	
Study design (including statistical analysis):	Quasi experimental (t-tests)	
Aims/objectives:	To investigate the effect of fluoridated milk on caries in primary teeth	
Participants	Total sample size at baseline:	534 (intervention group)-305 (control group)
	Country:	China
	Region (urban (city)/rural):	Beijing
	Ethnicity:	-
	Socioeconomic status:	-
	Gender:	Both male and female
	Age (including adults/children):	3-5 years old
	Health background/status:	-
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):	The fluoride concentration in the drinking water in all kindergartens was determined before starting the program and every 3 months after the program was implemented. Results showed that it was less than 0.3mg/l. The fluoride content in the local fresh cow milk was found to be below 0.02mg/l No oral health education program was implemented in any of the kindergartens There was no statistically significant difference in the baseline mean dmft scores between the two groups (3.2 vs. 3.5, p = 0.312)

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Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention group: Each participant consumed 200 ml of fluoridated milk (concentration 2.5mgF per litre) per day from Monday to Friday in the kindergarten, and was given two packs of fluoridated milk (250ml) for consumption at home on Saturday and Sunday every week. Parents of the children were asked to ensure that the children drank the fluoridated milk. There were 534 children (mean age 54±4 months) in the test group at baseline and 417 at the 21 month follow up	control group: Fresh milk without addition of sugar or fluoride There were 305 children (mean age 53±4 months) in the control group at baseline and 247 at the 21 month follow up
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Follow up duration: 21 months	
	Oral outcomes measured:	caries experience, new caries, reversals, and net caries increment	
	Scale/measure:	dmft	
	Means and SD or events for each group at post-treatment or follow-up	Baseline caries experience, new caries, reversals, and net caries increment of test and control children **Test group (n=417)- Control group (n=247)- P-value** Mean baseline dmft (SD): 3.2 (3.7)-3.5 (1.4)- 0.312 % dmft>0 at baseline: 66- 68- 0.723 % dmft>0 at 21 months: 72- 82- 0.003 Mean new caries (SD)(dmft): 1.2 (1.5)- 1.8 (1.6)- <0.001 % with new caries: 51- 73- <0.001 Mean reversal (SD)(dmft) Mean arrested caries: 0.3 (0.9)- 0.1 (0.5)- <0.001 Mean examiner reversal: 0.5 (0.9)- 0.4 (0.9)- 0.578 Mean net increment (SD)(dmft): 0.4 (1.9)- 1.3 (1.2)- <0.001	
	Other relevant statistical results		

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Research question 12: Does salt fluoridation reduce the risk of early childhood caries?

Citation	Jordan et al. (2017). Caries preventive effect of salt fluoridation in preschool children in the Gambia: A prospective, controlled, interventional study. Caries Res. 15;51 (6):596-604.		
Study design (including statistical analysis):	RCT (Wilcoxon rank-sum test)		
Aims/objectives:	To investigate the effect of fluoridated salt in a communal feeding program for pre-school children.		
Participants	Total sample size at baseline:	700 assessed for eligibility; 441 randomized 304 (intervention group)-137 (control group)	
	Country:	Gambia	
	Region (urban (city)/rural):	Brikama	
	Ethnicity:	-	
	Socioeconomic status:		
	Gender:	Both male and female	
	Age (including adults/children):	3-5 years old	
	Health background/status:	-	
	Any information on confounders (e.g. water, milk or salt fluoridation, sugars intake from diet, feeding practices (e.g. breastfeeding, bottle feeding – duration, frequency) and oral hygiene behaviour):		
Intervention	Comparison/exposure (including n, age and gender (if different from above) for each group for the analysis/es used):	Intervention group: Meals were prepared with fluoridated (250mg F^-/kg) salt Mean age=4.7 years Female=184 (60.5%) Male=120 (39.5%) N analyzed = 304	control group: Meals were not prepared with fluoridated table salt Mean age=4.9 years Female=90 (65.7%) Male=47 (34.3%) N analyzed = 137
	Other relevant baseline statistics for each group (for the analysis/es used):	-	-
	Duration:	Follow up duration: 12 months	
	Oral outcomes measured:	Caries incidence	
	Scale/measure:	$D_{3/4}$mft; $G_{2\text{-}4}$; TCT $D_{3/4}$: decayed with cavitation into dentine. M: missing	

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		F: filled T: teeth $G_{2\text{-}4}$: teeth with white lesions from slight white spot formation to white spot formation with cavitation into enamel TCT: weighted sum score according to the following weights
	Means and SD or events for each group at post-treatment or follow-up	**Caries experience at t_0: (Baseline)** **Test group:** $D_{3/4}$mft: 3.35 (2.83-3.86) $G_{2\text{-}4}$: 4.65 (4.17-5.14) TCT: 23.95 (21.51-26.39) **Control group:** $D_{3/4}$mft: 2.74 (1.76-3.72) $G_{2\text{-}4}$: 5.41 (4.33-6.49) TCT: 23.26 (18.14-28.39) **Caries experience at t_1: (After 12-month)** **Test group:** $D_{3/4}$mft: 4.63 (4.04-5.23) $G_{2\text{-}4}$: 8.14 (7.45-8.83) TCT: 36.80 (34.10-39.50) **Control group:** $D_{3/4}$mft: 6.57 (5.52-7.61) $G_{2\text{-}4}$: 7.70 (6.56-8.83) TCT: 47.74 (42.78-52.70) **Proportion (%) of dentine caries-free individuals in the test and control groups at t_0 and t_1** **Test group:** $D_{3/4}(t_0)$: 33.0% $D_{3/4}(t_1)$: 26.7% **Control group:** $D_{3/4}(t_0)$: 25.9% $D_{3/4}(t_1)$: 16.8% **RR (95%CI):** $D_{3/4}(t_0)$: 0.90 (0.80-1.04) $D_{3/4}(t_1)$: 0.88 (0.79-1.01)

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Appendix: GRADE Evidence Profiles

Appendix Table 4. Question 1: Does breastfeeding beyond one year increase the risk of early childhood caries compared with breastfeeding until less than one year of age?

Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Breastfeeding until less than one year	Breastfeeding beyond one year	Relative (95% CI)	Absolute (95% CI)		
ECC												
1	observational studies	not serious [a]	not serious	not serious	not serious	none	741	129	-	**0** (0 to 0)	⨁⨁◯◯ LOW	CRITICAL

Explanations

a. Overall risk of bias rating for this study was moderate, as determined by the ROBINS-I tool. In relation to confounding, all participants entered the study at the same time. Additionally, fluoridated area and sugars intake was controlled for. All participants fell within our specified time frame (<1 year versus >=24 months).

Reference:
Peres KG, Nascimento GG, Peres MA, Mittinty MN, Demarco FF, Santos IS, Matijasevich A, Barros AJD. 2017. Impact of prolonged breastfeeding on dental caries: A population-based birth cohort study. Pediatrics. 140 (1): e20162943.

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Appendix Table 5. Question 3: Does breastfeeding beyond two years increase the risk of early childhood caries compared with breastfeeding until less than two years of age?

Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Breastfeeding for 24 months or longer	Breastfeeding for less than 24 months	Relative (95% CI)	Absolute (95% CI)		
ECC												
2	observational studies	not serious	not serious	not serious	not serious	none	414	1251	-	**0** (0 to 0)	⨁⨁◯◯ LOW	CRITICAL

References:

1. Chaffee BW, Feldens CA, Vítolo MR. 2014. Association of long-duration breastfeeding and dental caries estimated with marginal structural models. Annals of Epidemiology. 24(6):448-454.
2. Peres KG, Nascimento GG, Peres MA, Mittinty MN, Demarco FF, Santos IS, Matijasevich A, Barros AJD. 2017. Impact of prolonged breastfeeding on dental caries: A population-based birth cohort study. Pediatrics. 140 (1): e20162943.

For Peer Review

Appendix Table 6. Question 5: Does consumption of liquids that contain free sugars from an infant feeding bottle, increase the risk of early childhood caries?
Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No free sugars from an infant feeding bottle	Free sugars from an infant feeding bottle	Relative (95% CI)	Absolute (95% CI)		
ECC												
1	observational studies	not serious [a]	not serious	not serious	not serious	none	205	129	-	**0** (0 to 0)	⨁⨁◯◯ LOW	

Explanations

a. One of the articles (Feldens et al. 2010) was rated as having a low risk of bias; two* were rated as being at critical risk of bias (in relation to confounding)

Reference

Feldens CA, Giugliani ERJ, Vigo A, Vitolo MR. 2010. Early feeding practices and severe early childhood caries in four-year-old children from Southern Brazil: A birth cohort study. Caries Res. 44(5):445-452.

Two additional cohort studies were identified but were excluded from the GRADE analysis due to serious risk of bias (based on information from Gordon et al. J Clinical Epidemiol. 2011, 64:407). The excluded references were:

*Tanaka K, Miyake Y, Sasaki S, Hirota Y. 2013. Infant feeding practices and risk of dental caries in Japan: The Osaka maternal and child health study. Pediatric Dentistry. 35(3):267-271.

* Wendt LK, Hallonsten AL, Koch G, Birkhed D. 1996. Analysis of caries-related factors in infants and toddlers living in Sweden. Acta Odont Scanda. 54(2):131-137.

For Peer Review

Appendix Table 7. Question 6: Does consumption of complementary drinks that contain free sugars increase the risk of early childhood caries?
Setting: population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No/ lower intake of free sugars from complementary drinks	Intake /higher intake of free sugars from complementary drinks	Relative (95% CI)	Absolute (95% CI)		
ECC												
6	observational studies	very serious [a]	not serious	not serious	not serious	strong association	36250		-	**0** (0 to 0)	⨁◯◯◯ VERY LOW	

Explanations

a. Assigned based on ROBINS-I overall risk of bias scores.

Total sample size for all studies at baseline is specified in the table

References:

1. Warren JJ, Blanchette D, Dawson DV, Marshall TA, Phipps KR, Starr D, Drake DR. 2016. Factors associated with dental caries in a group of American Indian children at age 36 months. Community Dent Oral Epidemiol. 44(2):154-161.
2. Warren JJ, Weber-Gasparoni K, Marshall TA, Drake DR, Dehkordi-Vakil F, Dawson DV, Tharp KM. 2009. A longitudinal study of dental caries risk among very young low ses children. Community Dent Oral Epidemiol. 37(2):116-122.
3. Watanabe M, Wang DH, Ijichi A, Shirai C, Zou Y, Kubo M, Takemoto K, Masatomi C, Ogino K. 2014. The influence of lifestyle on the incidence of dental caries among 3-year-old Japanese children. Int J Environ Res Public Health. 11(12):12611-12622.
4. Wendt LK, Hallonsten AL, Koch G, Birkhed D. 1996. Analysis of caries-related factors in infants and toddlers living in Sweden. Acta Odont Scand. 54(2):131-137.
5. Wigen TI, Wang NJ. 2014. Health behaviors and family characteristics in early childhood influence caries development. A longitudinal study based on data from Moba. Norsk Epidemiologi. 24(1):91-95.
6. Yonezu T, Yotsuya K, Yakushiji M. 2006. Characteristics of breast-fed children with nursing caries. Bull Tokyo Dent Coll. 47(4):161-165.

Appendix Table 8. Question 7: Does consumption of complementary foods to which free sugars have been added increase the risk of early childhood caries?
Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Free sugars not added to complementary food	Free sugars added to complementary food	Relative (95% CI)	Absolute (95% CI)		
ECC												
1	observational studies	not serious	not serious	not serious	not serious	none	240	91	-	**0** (0 to 0)	⨁⨁◯◯ LOW	

Reference:
Feldens CA, Giugliani ERJ, Vigo A, Vitolo MR. 2010. Early feeding practices and severe early childhood caries in four-year-old children from Southern Brazil: A birth cohort study. Caries Res. 44(5):445-452.

For Peer Review

Appendix Table 8. Question 9: Does oral hygiene provided by a parent/carer reduce the risk of early childhood caries?
Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral hygiene provided by parent / carer	No oral hygiene provided by parent / carer	Relative (95% CI)	Absolute (95% CI)		
ECC												
2	observational studies	serious [a]	not serious	not serious	not serious	none	-/1935 [b]		not estimable		⨁◯◯◯ VERY LOW	IMPORTANT

Explanations

a. Serious risk of bias due to lack of information on water fluoride

b. Overall number of participants from both studies is specified in the GRADE table. In Okuno et al. (1994), the number of participants analysed in the intervention and control groups were 121 and 187, respectively. The number of participants in intervention and control groups were not provide for Leroy et al. (2012)

References:

1. Leroy R, Bogaerts K, Martens L, Declerck D. 2012. Risk factors for caries incidence in a cohort of Flemish preschool children. Clinical Oral Investigations. 16(3):805-812.
2. Okuno M, Kani T, Shimizu H. 1994. A cohort study on dental caries in infants. Japanese Journal of Public Health. 41(7):625-628.

For Peer Review

Appendix Table 9. Question 10: Is oral health education for care givers' effective for preventing early childhood caries?
Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral health education for care givers	No or lower exposure to oral health education for caregivers	Relative (95% CI)	Absolute (95% CI)		
ECC												
6	randomised trials	not serious	serious [a]	not serious	not serious	none	1185	1202	-	**0** (0 to 0)	⨁⨁⨁◯ MODERATE	CRITICAL

a. Four out of six studies indicated a significant protective effect of oral health education for caregivers, whereas two studies, with sufficient power, indicated a non-significant effect. Meta-analysis of studies reporting odds ratio reported significant effect.

References:

1. Feldens CA, Vitolo MR, Drachler Mde L. 2007. A randomized trial of the effectiveness of home visits in preventing early childhood caries. Community Dent Oral Epidemiol. 35(3):215-223.
2. Harrison R, Benton T, Everson-Stewart S, Weinstein P. 2007. Effect of motivational interviewing on rates of early childhood caries: A randomized trial. Pediatric Dentistry. 29(1):16-22.
3. Jiang EM, Lo EC, Chu CH, Wong MC. 2014. Prevention of early childhood caries (ecc) through parental toothbrushing training and fluoride varnish application: A 24-month randomized controlled trial. J. Dent. 42(12):1543-1550.
4. Mohebbi SZ, Virtanen JI, Vahid-Golpayegani M, Vehkalahti MM. 2009. A cluster randomised trial of effectiveness of educational intervention in primary health care on early childhood caries. Caries Res. 43(2):110-118.
5. Plutzer K, Spencer AJ. 2008. Efficacy of an oral health promotion intervention in the prevention of early childhood caries. Community Dent Oral Epidemiol. 36(4):335-346.
6. Vachirarojpisan T, Shinada K, Kawaguchi Y. 2005. The process and outcome of a programme for preventing early childhood caries in Thailand. Community Dent Health. 22(4):253-259.

Appendix Table 11. Question 10: Does an optimum concentration of fluoride in water reduce the risk of early childhood caries? (Fluoridated water compared with non-fluoridated water / water with a low fluoride concentration for children)

Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fluoridated water	Non-fluoridated water/ water with lower concentration of fluoride	Relative (95% CI)	Absolute (95% CI)		
ECC												
9	observational studies	not serious	not serious	not serious	not serious		2367	2075 [a]	-	0 (0 to 0)	MODERATE-	CRITICAL

a. No of patients in intervention and control groups were unavailable from the study: O'Mullane, D., and H. Whelton. "Efficacy of fluoride against dental caries; fluoride in water." Fogorvosi szemle 90 (1997): 7.

References:

Blinkhorn AS, Brown MD, Attwood D, Downer MC. 1981. The effect of fluoridation on the dental health of urban Scottish schoolchildren. Journal of Epidemiology & Community Health. 35(2):98-101.

Booth JM, Mitropoulos CM, Worthington HV. 1992. A comparison between the dental health of 3-year-old children living in fluoridated Huddersfield and non-fluoridated Dewsbury in 1989. Community Dent Health. 9(2):151-157.

Evans DJ, Rugg-Gunn AJ, Tabari ED, Butler T. 1996. The effect of fluoridation and social class on caries experience in 5-year-old Newcastle children in 1994 compared with results over the previous 18 years. Community Dent Health. 13(1):5-10.

French AD, Carmichael CL, Rugg-Gunn AJ, Furness JA. 1984. Fluoridation and dental caries experience in 5-year-old children in Newcastle and northumberland in 1981. Brit Dent J. 156(2):54-57.

O'Mullane D, Whelton H. 1997. Efficacy of fluoride against dental caries; fluoride in water. Fogorvosi szemle. 90 Spec No: 7-12.

Rugg-Gunn AJ, Carmichael CL, Ferrell RS. 1988. Effect of fluoridation and secular trend in caries in 5-year-old children living in Newcastle and Northumberland. Brit Dent J. 165(10):359-364.

Tank G, Storvick CA. 1964. Caries experience of children one to six years old in two Oregon communities (Corvallis and Albany). I. Effect of fluoride on caries experience and eruption of teeth. JADA (1939). 69:749-757.

Studies with serious risk of bias, excluded from GRADE Profile analysis:

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Jackson D, Goward PE, Morrell GV. 1980. Fluoridation in Leeds. A clinical survey of 5-year-old children. Brit Dent J. 149(8):231-234.
Jackson D, Gravely JF, Pinkham IO. 1975a. Fluoridation in Cumbria. A clinical study. Brit Dent J.l. 139(8):319-322.
Jackson D, James PM, Thomas FD. 1985. Fluoridation in Anglesey 1983: A clinical study of dental caries. Brit Dent J. 158(2):45-49.
Jackson D, James PM, Wolfe WB. 1975b. Fluoridation in Anglesey. A clinical study. Brit Dent J.l. 138(5):165-171.

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Appendix Table 12. Question 11: Does consumption of fluoridated milk reduce the risk of early childhood caries?
Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fluoridated milk	Unfluoridated milk	Relative (95% CI)	Absolute (95% CI)		
ECC												
1	observational studies	serious [a]	not serious	not serious	not serious	strong association	417	247	-	**0** (0 to 0)	⨁⨁◯◯ LOW	CRITICAL
New outcome												
									not estimable		-	

Explanations

a. Socioeconomic status of control and intervention groups was not controlled for. There was also a lack of lack of control for dietary factors (e.g. sugar intake).

Reference:

Bian JY, Wang WH, Wang WJ, Rong WS, Lo EC. 2003. Effect of fluoridated milk on caries in primary teeth: 21-month results. Community Dent Oral Epidemiol. 31(4):241-245.

For Peer Review

Appendix Table 13. Question 12: Does salt fluoridation reduce the risk of early childhood caries?
Setting: Population

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Salt fluoridation	unfluoridated salt	Relative (95% CI)	Absolute (95% CI)		
ECC												
1	randomised trials	serious [a]	not serious	not serious	not serious	none	304/-	137/-	not estimable		⨁⨁⨁◯ MODERATE	
New outcome												
									not estimable		-	

Explanations

a. This study received a high risk of bias rating due to lack of blinding of the outcome assessors.

- Regarding other considerations: follow-up period was relatively short. Data for pre-cavitated lesions shows higher mean lesions in test compared with control group (i.e. opposite effect as observed for caries into dentine measured by dmft).
- A cohort study* was identified that fulfilled the inclusion criteria for research question 12 but was not included in the narrative synthesis or GRADE process as it provided lower quality evidence compared to the RCT for addressing this intervention evaluation research question due to its study design. The cohort study indicated a significant protective effect of the use of fluoride salt on caries experience (dmft).

Study reference:

Jordan RA, Schulte A, Bockelbrink AC, Puetz S, Naumova E, Warn LG, Zimmer S. 2017. Caries-preventive effect of salt fluoridation in preschool children in the Gambia: A prospective, controlled, interventional study. Caries Res. 51(6):596-604.

Appendix Table 14. Summary of lower level evidence

Q1: Does breastfeeding beyond one year increase the risk of ECC compared with breastfeeding until less than one year of age?

Case control			
Reference	**Country**	**+, 0, - ***	**Summary of study and findings**
Al-Ghanim et al 1998	Saudi Arabia	0	445 children aged 4.13 years, comparing practices in cases with dmft ≥ 8 those with dmft 0. A higher % of children in the ECC group were breastfed for longer duration, but breastfeeding duration was not predictive of ECC in the multivariate logistic regression model.
Cross sectional			
Lida et al 2017	USA	0	1576 children aged 2-5 years. Using data from NHANES, the association of breastfeeding and its duration was examined in bivariate analyses and by multivariable logistic and Poisson regression analyses. After adjusting for potential confounders significant in bivariate analyses, breastfeeding and its duration were not associated with the risk for ECC.
Folayan et al 2015	Nigeria	0	497 children aged 6 – 71 months. Duration of breastfeeding (up to 12 months compared with over 12 months duration) was not associated with ECC in multivariate analysis.
Correa-Faria et al 2015	Brazil	0	381 children aged 1-5 years. In bivariate chi square analysis, a greater proportion of children breastfed beyond 12 months had ECC. However, duration of breastfeeding was not identified as an independent risk factor in multivariate analysis.
Nobile et al 2014	Italy	+	515 children aged 36-71 months. Prevalence of ECC was 12.2% in those breastfed 5-10 months compared with 20.1% in those breastfed 11-19 months. Multivariate analysis showed prevalence of ECC increased with breastfeeding duration OR 1.26, 96% CI 1.01-1.57) P=0.039.
Bissar et al 2014	Germany	+	1007 children aged 3-5 years. Breastfeeding >12 months was a significant risk factor for S-ECC in multivariate analysis OR 3.27 (1.63, 6.59) p=0.0009.
Olatoshi 2014	Nigeria	+	302 children aged 6-70 months. Odds ratio for ECC with breastfeeding 7-12 months compared with >12 months was 0.12 (0.05, 0.27) in multivariate analysis – however, it is unclear which confounders were controlled for (e.g. age, sugars intake).

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Nunes et al 2012; 2014	Brazil	0	Measured ECC in 260 children aged 18-42 months and compared those still being breastfed with those who ceased breastfeeding by 12 months in a low-income population. Analysis adjusted for some known confounders, using a hierarchical approach. Prolonged breast-feeding was not associated with ECC (IDR 1.15; 95%CI 0.84–1.59; P = 0.363).
Al Malik et al 2003	Saudi Arabia	0	Children aged 2-5 years, n= 987. ECC was more prevalent with longer breastfeeding (but confounded by education level). However this association was not found in multivariate analysis
Mattee et al 1994	Tanzania	0	2912 children aged 1 to 4 years. Duration of breastfeeding was non-significant in multivariate analysis but a wide variability in effect was observed OR 2.4 95% CI 0.7, 9.1
Q3: Does breastfeeding beyond two years increase the risk of ECC compared with breastfeeding until less than two years of age?			
Case control			
Ayhan H 1996		+	161 children aged 2-5 years with ECC compared with 181 children aged 2-5 years without caries. Breastfeeding beyond 2 years was more common in cases (43%) compared with controls (1%). However this observation does not control for confounding.
Q5: Does consumption of liquids that containing free sugars from an infant feeding bottle increase the risk of ECC?			
Case control			
Ye et al 1999	China	+	Study of 2094 children aged 2-5 years, 404 cases or 'rampant' caries compared with 1690 controls stratified by age. Odds ratio for ECC when sweet liquids were consumed from a bottle 1.71, P=0.002.
Wang et al 2008	China	+	Study of 204 children aged 4 and 5 years, with dmft >6 compared with 237 children that were caries free. Odds ratio for ECC when sweet liquids were consumed in a bottle was 2.25 (logistic Regression), P<0.05.
Q6: Does consumption of complementary drinks that contain free sugars increase the risk of ECC			
Cross sectional			
Detsomboonrat and Pisarnturakit 2015	Thailand	+	Children aged 9-18 months, N=151. Hierarchial multiple regression was used to determine factors predictive of dental caries. Frequency of drinking sweeting milk was a significant predictor, β= -.17-0.18, P<0.005.

Warran et al 2016	USA	+	American Indian Children (n=232) aged 36 months followed from birth. The relationship between dental caries (dmft) at 36 months and intake of sugars-containing drinks at 36 months was explored in logistic regression. Analysis identified higher added sugar beverage consumption as a significant risk factor for dmft ($p<0.05$).
Hoffmeister et al 2016	Chile	+	Children aged 2-4 years in southern Chile. Zero inflated negative binomial regression model was used to determine the factors associated with dental caries. In the 4 year old age group, a high frequency of consuming sugar containing drinks at bedtime was associated with increased ECC (OR 1.30) 1.06, 1.59).
Q8: **Does oral hygiene provided by a parent/carer reduce the risk of early childhood caries**			
Quasi-experimental			
Manowiec 2003	Poland	-	A study of 4-6 year old children. Two models of supervised tooth brushing: brushing supervised by teachers and parents and brushing supervised by teacher only with a control group not supervised. The dft values differed between groups at baseline and were 6.53, 4.5 and 5.4 for control, teachers and parent supervision and teacher only. The increases in dft were 1.27 for the control group and 0.95, 0.13 for the parent/teacher and teacher only intervention groups respectively. Difference between groups at baseline, or other confounders, did not appear to be accounted for in analysis.
Q9: **Is oral health education for care-givers' effective for preventing early childhood caries?**			
Cohort			
Wagner et al 2012	Austria	-	A case-cohort study of 5 year old children whose mothers had (intervention) or had not (control) participated in a one off oral health education programme following the child's birth. At 5 years 33.2% of the intervention group had caries ($d_{3\ 4}$mfs 7.4) compared with 42.6% of the control group ($d_{3\ 4}$mfs 6.4).
Da Silva et al 2013	Brazil	-	Mothers with babies aged 0-8 months at baseline, n=112. Followed up for one year following educational lectures (oral hygiene dietary practices). The educational intervention resulted in a decrease in the percent of caries in dental surfaces. Initally 5.6% of surfaces had white spot or

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				cavities. This decreased to 0.4% after one year (NB the number of surfaces increased as teeth erupted).
Q10: **Does an optimum concentration of fluoride in water reduce the risk of early childhood caries?**				
Cross sectional				
	Beal and James 1971	England	-	Caries levels of 5 year olds residing in fluoridated areas compared with non-fluoridated area, 5.5 years after the introduction of water fluoridation,.n=2280. Before water fluoridation the % of children who were caries free (and % with def >10) were 8.9 (30.4) and 28.6 (18.1) for two areas to receive fluoridation and 16.1 (12.0) for a control area. Following 5.5 years of water fluoridation these values changed to: 47.0 (def >10, 1.5%) and 41.2 (def >10 4.9%) and for the control area, 24.1 (def >10 20.1).
	McInnes et al 1982	S. Africa	-	331 children aged 1-5 years living in areas with water fluoride at 2.2-4.0 mg/l had on average dmft 0.8 +/- 2.1 and 82% were caries free (51% had enamel opacities). 177 children aged 1-5 years living in non-fluoridated areas had an average dmft of 5.4 9+/_ 5.8) and 28% were caries free, none had opacities.
	Gu et al 1989	China	-	Measured dental caries in children aged 3-6 years, 31 and 52 months after stopping water fluoridation. Caries significantly increased in the 3 year old group but not in the 4-6 year old children who were born during the water fluoridation period.
	Seaman et al 1989	UK (Wales)	-	5 year old children attending schools in fluoridated and non-fluoridated areas of Wales, UK. For fluoridated areas mean dmft was 0.8 (+/- 1.43) for non-fluoridated it was 2.26 (+/- 1.46).
	Treasure and Dever 1991	New Zealand	-	345 5 year old children. Significantly lower dmft in those residing in fluoridated compared with non-fluoridated communities. The average dmft for fluoridated areas were 1.08 (=/- 1.64) and 1.03 (+/- 1.86) and for non-fluoridated communities the average dmft were 2.0 (+/- 2.93) and 2.91 (=/- 2.82). In non-fluoridated communities there was a clear social gradient in caries levels that was not observed for fluoridated communities.
	Vignarajan and Williams 1992	Antigua	-	3-4 year old children attending nursery schools, 146 from a low water fluoride concentration area (0.1-0.3 ppm) and 66 from an optimum fluoride area (0.6-1.0 ppm). Caries

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			experience in the low fluoride area was 29% higher than in optimum area. Average dmft values were 0.9 (=/- 2.29) and 0.64 (+/- 1.65) for children from low and optimally fluoridated areas respectively.
Serwint et al 1993	USA	-	Convenience sample of 110 sequential children aged 18-36 months attending a general paediatric clinic. 27% of those with caries drank fluoridated tap water compared with 54% of those without caries. P<0.05.
Cisternas et al 1994	Chile	-	780 pre-school children from cities in Chile. Children from non-fluoridated areas had dmft of 4.7 +/- 3.9 and 4.7 +/- 3.7 and those from fluoridated areas had dmft 3.7 =/- 3.5 and 1.2 +/- 2.0.
Gray and Slowick 2001	UK (England)	-	Used data from national dental surveys to observe change in the percentage of 5 year olds without dental caries before and following the introduction of water fluoridation. In the areas where water fluoride was introduced the prevalence of caries free children increased whereas in non-fluoridated areas it decreased or remained the same.
Tickle et al 2003	UK (England)	-	All 5 year old children residing in fluoridated and non-fluoridated areas of Cheshire, England. Prevalence of ECC was 12.4% higher and dmft 29.4% higher in children from non-fluoridated areas. For non-fluoridated areas prevalence of ECC was 37% and mean dmft 1.34. For fluoridated areas prevalence was 32.4 and mean dmft 1.01. Analysis demonstrated that water fluoridation was effective in reducing ECC after controlling for confounding including SES.
Postma et al 2008	S. Africa	-	Data from national oral health survey of children aged 36-71 months, n=5822. Factors associated with ECC were explored in multivariate analysis. Area based fluoride level was included. Decreased water fluoride concentration was significantly associated with ECC.
Chi et al 2013	USA	-	Pilot study of 115 children aged 3-5 years to explore if developmental delays increased risk of dmfs. Multiple variable Poisson regressions models were used to test the factors associated with risk of dmfs. Living in a non-fluoridated community was associated with increased caries risk.

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	Q11: **Does consumption of fluoridated milk reduce the risk of ECC?**			
	Cross sectional			
	Marino et al 2001 and 2004	Chile	-	Cross sectional sample of children aged 3-6 years from communities receiving fluoridated milk (n=152) compared with control (n=150). After 4 years of the milk fluoridation programme the proportion of caries free children in the study community increased from 22% to 48.4%. Following termination of the fluoride milk scheme, dental caries levels in children aged 3, 4, and 5 years increased to levels similar to the control group.
	Q12: **Does salt fluoridation reduce the risk ECC?**			
	Cohort study			
	Wagner et al 2012	Austria	-	A case-cohort study of 5 year old children whose mothers had (intervention) or had not (control) participated in a one off oral health education programme following the child's birth. Analysis of data for total sample of the 471 children showed lower dmft in those that used fluoridated salt; average dmft was 1.81 compared with 2.22 in those using non fluoridated salt (p=0.015).

* '+' denotes a positive association, '0' denotes a null association and '-'denotes a negative association between risk factor and risk of ECC.

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

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