Water fluoridation for the prevention of dental caries

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[Intervention Review]

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ABSTRACT

Background

Dental caries is a major public health problem in most industrialised countries, affecting 60% to 90% of school children. Community water fluoridation was initiated in the USA in 1945 and is currently practised in about 25 countries around the world; health authorities consider it to be a key strategy for preventing dental caries. Given the continued interest in this topic from health professionals, policy makers and the public, it is important to update and maintain a systematic review that reflects contemporary evidence.

Objectives

To evaluate the effects of water fluoridation (artificial or natural) on the prevention of dental caries.

To evaluate the effects of water fluoridation (artificial or natural) on dental fluorosis.

Search methods

We searched the following electronic databases: The Cochrane Oral Health Group's Trials Register (to 19 February 2015); The Cochrane Central Register of Controlled Trials (CENTRAL; Issue 1, 2015); MEDLINE via OVID (1946 to 19 February 2015); EMBASE via OVID (1980 to 19 February 2015); Proquest (to 19 February 2015); Web of Science Conference Proceedings (1990 to 19 February 2015); ZETOC Conference Proceedings (1993 to 19 February 2015). We searched the US National Institutes of Health Trials Registry (ClinicalTrials.gov) and the World Health Organization's WHO International Clinical Trials Registry Platform for ongoing trials. There were no restrictions on language of publication or publication status in the searches of the electronic databases.

Selection criteria

For caries data, we included only prospective studies with a concurrent control that compared at least two populations - one receiving fluoridated water and the other non-fluoridated water - with outcome(s) evaluated at at least two points in time. For the assessment of fluorosis, we included any type of study design, with concurrent control, that compared populations exposed to different water fluoride concentrations. We included populations of all ages that received fluoridated water (naturally or artificially fluoridated) or non-fluoridated water.

Data collection and analysis

We used an adaptation of the Cochrane 'Risk of bias' tool to assess risk of bias in the included studies.

We included the following caries indices in the analyses: decayed, missing and filled teeth (dmft (deciduous dentition) and DMFT (permanent dentition)), and proportion caries free in both dentitions. For dmft and DMFT analyses we calculated the difference in mean change scores between the fluoridated and control groups. For the proportion caries free we calculated the difference in the proportion caries free between the fluoridated and control groups.

For fluorosis data we calculated the log odds and presented them as probabilities for interpretation.

Main results

A total of 155 studies met the inclusion criteria; 107 studies provided sufficient data for quantitative synthesis.

The results from the caries severity data indicate that the initiation of water fluoridation results in reductions in dmft of 1.81 (95% CI 1.31 to 2.31; 9 studies at high risk of bias, 44,268 participants) and in DMFT of 1.16 (95% CI 0.72 to 1.61; 10 studies at high risk of bias, 78,764 participants). This translates to a 35% reduction in dmft and a 26% reduction in DMFT compared to the median control group mean values. There were also increases in the percentage of caries free children of 15% (95% CI 11% to 19%; 10 studies, 39,966 participants) in deciduous dentition and 14% (95% CI 5% to 23%; 8 studies, 53,538 participants) in permanent dentition. The majority of studies (71%) were conducted prior to 1975 and the widespread introduction of the use of fluoride toothpaste.

There is insufficient information to determine whether initiation of a water fluoridation programme results in a change in disparities in caries across socioeconomic status (SES) levels.

There is insufficient information to determine the effect of stopping water fluoridation programmes on caries levels.

No studies that aimed to determine the effectiveness of water fluoridation for preventing caries in adults met the review's inclusion criteria.

With regard to dental fluorosis, we estimated that for a fluoride level of 0.7 ppm the percentage of participants with fluorosis of aesthetic concern was approximately 12% (95% CI 8% to 17%; 40 studies, 59,630 participants). This increases to 40% (95% CI 35% to 44%) when considering fluorosis of any level (detected under highly controlled, clinical conditions; 90 studies, 180,530 participants). Over 97% of the studies were at high risk of bias and there was substantial between-study variation.

Authors' conclusions

There is very little contemporary evidence, meeting the review's inclusion criteria, that has evaluated the effectiveness of water fluoridation for the prevention of caries.

The available data come predominantly from studies conducted prior to 1975, and indicate that water fluoridation is effective at reducing caries levels in both deciduous and permanent dentition in children. Our confidence in the size of the effect estimates is limited by the observational nature of the study designs, the high risk of bias within the studies and, importantly, the applicability of the evidence to current lifestyles. The decision to implement a water fluoridation programme relies upon an understanding of the population's oral health behaviour (e.g. use of fluoride toothpaste), the availability and uptake of other caries prevention strategies, their diet and consumption of tap water and the movement/migration of the population. There is insufficient evidence to determine whether water fluoridation results in a change in disparities in caries levels across SES. We did not identify any evidence, meeting the review's inclusion criteria, to determine the effectiveness of water fluoridation for preventing caries in adults.

There is insufficient information to determine the effect on caries levels of stopping water fluoridation programmes.

There is a significant association between dental fluorosis (of aesthetic concern or all levels of dental fluorosis) and fluoride level. The evidence is limited due to high risk of bias within the studies and substantial between-study variation.

PLAIN LANGUAGE SUMMARY

Water fluoridation to prevent tooth decay

Background

Tooth decay is a worldwide problem affecting most adults and children. Untreated decay may cause pain and lead to teeth having to be removed. In many parts of the world, tooth decay is decreasing. Children from poorer backgrounds still tend to have greater levels of decay. Fluoride is a mineral that prevents tooth decay. It occurs naturally in water at varying levels. Fluoride can also be added to the water with the aim of preventing tooth decay. Fluoride is present in most toothpastes and available in mouthrinses, varnishes and gels. If young children swallow too much fluoride while their permanent teeth are forming, there is a risk of marks developing on those teeth. This is called ‘dental fluorosis’. Most fluorosis is very mild, with faint white lines or streaks visible only to dentists under good lighting in the clinic. More noticeable fluorosis, which is less common, may cause people concern about how their teeth look.

Review question

We carried out this review to evaluate the effects of fluoride in water (added fluoride or naturally occurring) on the prevention of tooth decay and markings on teeth (dental fluorosis).

Study characteristics

We reviewed 20 studies on the effects of fluoridated water on tooth decay and 135 studies on dental fluorosis. The evidence is up to date at 19 February 2015.

Nineteen studies assessed the effects of starting a water fluoridation scheme. They compared tooth decay in two communities around the time fluoridation started in one of them. After several years, a second survey was done to see what difference it made. Around 70% of these studies were conducted before 1975. Other, more recent studies comparing fluoridated and non-fluoridated communities have been conducted. We excluded them from our review because they did not carry out initial surveys of tooth decay levels around the time fluoridation started so were unable to evaluate changes in those levels since then. We reviewed one study that compared tooth decay in two fluoridated areas before fluoridation was stopped in one area. Again, after several years, a second survey was done to see what difference it made.

Around 73% of dental fluorosis studies were conducted in places with naturally occurring – not added – fluoride in their water. Some had levels of up to 5 parts per million (ppm).

Key results

Our review found that water fluoridation is effective at reducing levels of tooth decay among children. The introduction of water fluoridation resulted in children having 35% fewer decayed, missing and filled baby teeth and 26% fewer decayed, missing and filled permanent teeth. We also found that fluoridation led to a 15% increase in children with no decay in their baby teeth and a 14% increase in children with no decay in their permanent teeth. These results are based predominantly on old studies and may not be applicable today.

Within the 'before and after' studies we were looking for, we did not find any on the benefits of fluoridated water for adults.

We found insufficient information about the effects of stopping water fluoridation.

We found insufficient information to determine whether fluoridation reduces differences in tooth decay levels between children from poorer and more affluent backgrounds.

Overall, the results of the studies reviewed suggest that, where the fluoride level in water is 0.7 ppm, there is a chance of around 12% of people having dental fluorosis that may cause concern about how their teeth look.

Quality of the evidence

We assessed each study for the quality of the methods used and how thoroughly the results were reported. We had concerns about the methods used, or the reporting of the results, in the vast majority (97%) of the studies. For example, many did not take full account of all the factors that could affect children's risk of tooth decay or dental fluorosis. There was also substantial variation between the results of the studies, many of which took place before the introduction of fluoride toothpaste. This makes it difficult to be confident of the size of the effects of water fluoridation on tooth decay or the numbers of people likely to have dental fluorosis at different levels of fluoride in the water.

Summary of findings for the main comparison.

Initiation of water fluoridation compared with low/non-fluoridated water for the prevention of dental caries

Patient or population: people of all ages

Settings: community setting

Intervention: initiation of water fluoridation

Comparison: low/non-fluoridated water

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk in area with low/non-fluoridated water	Risk in area with initiation of water fluoridation				
Caries in deciduous teeth (dmft)[1] Scale from: 0 to 20 (lower = better) Follow-up: range from 3-12 years	The mean dmft at follow-up in the low/non-fluoridated areas ranged from 1.21 to 7.8 (median 5.1)	The mean dmft in the areas with water fluoridation was 1.81 lower (1.31 lower to 2.31 lower)		44,268[2] (9 observational studies)	⊕⊕⊖⊖[3,4,5,6]	This indicates a reduction in dmft of 35% in the water fluoridation groups over and above that for the control groups We have limited confidence in the size of this effect due to the high risk of bias within the studies and the lack of contemporary evidence
Caries score in permanent teeth (DMFT)[7] Scale from: 0 to 32 (lower better) Follow-up: range from 8-11 years	The mean DMFT at follow-up in the low/non-fluoridated areas ranged from 0.7 to 5.5 (median 4.4)	The mean DMFT in the areas with water fluoridation was 1.16 lower (0.72 lower to 1.61 lower)		78,764[2] (10 observational studies)	⊕⊕⊖⊖[3,4,5,6]	This indicates a reduction in DMFT of 26% in the water fluoridation groups over and above that for the control groups We have limited confidence in the size of this effect due to the high risk of bias within the studies and the lack of contemporary evidence

Change in proportion of caries-free children (deciduous teeth) Scale: 0 to 1 Follow-up: range 3-12 years	The proportion of caries-free children at follow-up in the low/non-fluoridated areas ranged from 0.06 to 0.67 (median 0.22)	The proportion of caries-free children increased in the areas with water fluoridation 0.15 (0.11 to 0.19)		39,966[2] (10 observational studies)	⊕⊕⊖⊖[3,4,5,6]	We have limited confidence in the size of this effect due to the high risk of bias within the studies and the lack of contemporary evidence
Change in proportion of caries-free children (permanent teeth) Scale: 0 to 1 Follow-up: range 8-12 years	The proportion of caries-free children at follow-up in the low/non-fluoridated areas ranged from 0.01 to 0.67 (median 0.14)	The proportion of caries-free children increased in the areas with water fluoridation 0.14 (0.05 to 0.23)		53,538[2] (8 observational studies)	⊕⊕⊖⊖[3,4,5,6]	We have limited confidence in the size of this effect due to the high risk of bias within the studies and the lack of contemporary evidence.
Disparities in caries by socioeconomic status (SES)[8]				> 35,399[9] (3 observational studies)	⊕⊕⊖⊖[3]	There is insufficient information to determine whether initiation of a water fluoridation programme results in a change in disparities in caries levels across SES
Adverse effects Dental fluorosis of aesthetic concern[10] (measured by Dean's Index, TFI, TSIF)[11]	For a fluoride level of 0.7 ppm the percentage of participants with dental fluorosis of aesthetic concern was estimated to be 12% (95% CI 8% to 17%). Controlling for study effects, we would expect the odds of dental fluorosis to increase by a factor of 2.90 (95% CI 2.05 to 4.10) for each one unit increase in fluoride level (1 ppm F).			59,630 (40 observational studies)	⊕⊕⊖⊖[3,12]	The estimate for any level of dental fluorosis at 0.7ppm was 40% (95% CI 35% to 44%; 90 studies). This includes dental fluorosis that can only be detected under clinical conditions and other enamel defects We have limited confidence in the size of this effect due to the high risk of bias and substantial between-study variation.

⊕⊕⊕⊕: We are very confident that the true effect lies close to that of the estimate of the effect. Further research is very unlikely to change the estimate of effect.
⊕⊕⊕⊖: We are moderately confident in the effect estimate. Further research may change the estimate.
⊕⊕⊖⊖: Our confidence in the effect estimate is limited. Further research is likely to change the estimate.
⊕⊖⊖⊖: We are very uncertain about the estimate.

1. dmft - decayed, missing and filled deciduous teeth

2. Total number of participants measured. Analysis undertaken on average number of participants measured at baseline and follow-up for each study
3. Studies at high risk of bias; quality of the evidence downgraded
4. Substantial heterogeneity present, however, given that the direction of effect was the same in all but on of the studies/outcomes we did not downgrade due to heterogeneity
5. Indirectness of evidence due to lack of contemporary evidence; quality of the evidence downgraded. 71% of the studies conducted prior 1975; the use of fluoridated toothpaste, the availability of other caries prevention strategies, diet and tap water consumption are all likely to have changed in the populations in which the studies were conducted. No studies on the effect of water fluoridation in adults met the inclusion criteria
6. Very large effect size; quality of the evidence upgraded twice
7. DMFT - decayed, missing and filled permanent teeth
8. SES - socioeconomic status
9. Number of participants not stated in one study
10. Data come from studies of both naturally occurring and artificially fluoridated areas (i.e. not just areas where water fluoridation has been initiated). Dental fluorosis of aesthetic concern only with levels of reported fluoride exposure of 5 ppm or less
11. TFI - Thylstrup-Fejerskov Index: TSIF - Tooth Surface Index of Fluorosis
12. Substantial heterogeneity; quality of the evidence downgraded

Summary of findings 2.

Cessation of water fluoridation compared with fluoridated water for the prevention of dental caries

Patient or population: people of all ages

Settings: community setting

Intervention: cessation of water fluoridation

Comparison: fluoridated water

Outcomes	No of participants (studies)	Quality of the evidence (GRADE)	Comments
Caries in permanent teeth (DMFS)[1] Follow-up: 3 years	9249[2] (1 observational study)	⊕⊖⊖⊖ [3]	Insufficient evidence to determine the effect of the cessation of water fluoridation on caries
Caries in deciduous teeth (dmft/dmfs)[4]			No evidence to determine the effect of the cessation of water fluoridation on caries
Change in proportion of caries-free children (deciduous or permanent teeth)			No evidence to determine the effect of the cessation of water fluoridation on caries

Disparities in caries by socioeconomic status (SES)[5]		No evidence to determine the effect of the cessation of water fluoridation on disparities
Adverse effects		No evidence to determine whether cessation of a water fluoridation programme is associated with any harms

⊕⊕⊕⊕: We are very confident that the true effect lies close to that of the estimate of the effect. Further research is very unlikely to change the estimate of effect.
⊕⊕⊕⊖: We are moderately confident in the effect estimate. Further research may change the estimate.
⊕⊕⊖⊖: Our confidence in the effect estimate is limited. Further research is likely to change the estimate.
⊕⊖⊖⊖: We are very uncertain about the estimate.

1. DMFS - decayed missing and filled surfaces in permanent teeth
2. Total number of participants measured
3. Study at high risk of bias; quality of evidence downgraded
4. dmft/dmfs - decayed, missing and filled deciduous teeth/surfaces
5. SES - socioeconomic status

BACKGROUND

Description of the condition

Dental caries is a chronic and progressive disease of the mineralised and soft tissues of the teeth. Its aetiology is multifactorial and is related to the interactions over time between tooth substance and certain micro-organisms and dietary carbohydrates, producing plaque acids. Demineralisation of the tooth enamel (non-cavitated dental caries) follows and in the absence of successful treatment, can extend into the dentine and the dental pulp, impairing its function (Ten Cate 1991). Despite reductions in the prevalence and severity of dental caries over time (CDC 2005), social inequalities in dental health persist (OECD 2011), with significant numbers of individuals and communities having a clinically significant burden of preventable dental disease. Dental caries is associated with pain, infection, tooth loss and reduced quality of life (Sheiham 2005). In children, the burden of dental disease also includes lost school time and restricted activity days, as well as problems in eating, speaking and learning. This especially affects those from lower income families owing to their higher prevalence of caries (Feitosa 2005). Given the progressive nature of the condition and widespread prevalence in adulthood, most children are at risk of dental caries.

Dental caries is a major public health problem in most industrialised countries, affecting 60% to 90% of school children (Petersen 2003). It has been estimated that in the USA 42% of children aged between two to 11 years have caries experience in their primary teeth and 59% of those aged 12 to 19 years have caries experience in their permanent teeth (Dye 2007). Prevalence studies in South America, Asia and Europe have indicated that caries may affect between 20% and 100% of the population (Bagramian 2009). Increasing levels of dental caries are observed in some developing countries, especially those where community-based preventive oral care programmes are not established (Petersen 2004). Studies also suggest that the growing retention of teeth has also been accompanied by a rise in dental caries among ageing adults in different parts of the world (Selwitz 2007). This has major implications especially in high-income countries experiencing an increase in life expectancy.

The link between fluoride and the prevention of dental caries dates back to the 1930s. There are many ways in which fluoride can be provided, including toothpastes, gels, varnishes, milk and water. An adverse effect associated with the use of fluoride is the development of dental fluorosis due to the ingestion of excessive fluoride by young children with developing teeth. Dental fluorosis occurs due to the hypomineralisation of the dental enamel caused by the chronic ingestion of sufficiently high concentrations of fluoride while the dentition is still forming (Pendrys 2001). Clinically, the appearance of teeth with fluorosis depends on the severity of the condition. In its mildest form, there are faint white lines or streaks visible only to trained examiners under controlled examination conditions. In more involved cases, fluorosis manifests as mottling of the teeth in which noticeable white lines or streaks often have coalesced into larger opaque areas. In the more severe forms, brown staining or pitting of the tooth enamel may be present and actual breakdown of the enamel may occur (Rozier 1994).

Description of the intervention

Water can be artificially fluoridated (also known as community water fluoridation) through the controlled addition of a fluoride compound to a public water supply (Department of Health and Human Services 2000). Water that is artificially fluoridated is set at the 'optimum level', considered to be around 1 ppm (Dean 1941; WHO 2011). The European Union water quality directive specifies 1.5 ppm as the maximum level for human consumption (European Union 1998). Community water fluoridation was initiated in the USA in 1945 and is currently practiced in about 25 countries around the world (The British Fluoridation Society 2012). Health authorities consider it to be a key strategy for preventing dental caries. In Western Europe around 3% of the population receive water with added fluoride (Cheng 2007), mainly in England, Ireland, and Spain. In the USA, over 70% of the population on public water systems receive fluoridated water (CDC 2008), as do a similar proportion of Australians (NHMRC 2007). The rationale behind the role of community water fluoridation is that it benefits both children and adults by effectively preventing caries, regardless of socioeconomic status or access to care. It is believed to have played an important role in the reductions in tooth decay (40% to 70% in children) and of tooth loss in adults (40% to 60%) in the USA (Burt 1999). Fluoridation is an intervention that occurs at the environmental level, meaning that individual compliance is not relied upon. Interventions at this level can have greater impact upon populations than those at the individual and clinical levels (Frieden 2010), although concerns have been raised around the ethics of 'mass intervention' (Cheng 2007).

Fluoride is also naturally present in the soil, in water and the atmosphere at varying levels depending on geographic location. In areas of Africa, Asia, the Middle East, Southern Europe and the Southern USA, ground waters have been found to contain particularly high concentrations of fluoride, well above the 'optimum level' of 1 ppm. However, while ground waters in some areas can contain high concentrations of fluoride, fluoride content in drinking water in many locations is too low to prevent and control tooth decay.

How the intervention might work

Fluoride impedes the demineralisation of the enamel and also enhances its remineralisation, if it is present in high enough concentrations in the saliva (Ten Cate 1991). This function is very important in caries prevention as the progression of cavities depends on the balance of the demineralisation and remineralisation processes (Selwitz 2007). The presence of fluoride in drinking water therefore confers the advantage of providing a constant exposure to fluoride ions in the oral cavity. The effectiveness of fluoridated water (McDonagh 2000; Truman 2002), and other fluoride sources, such as toothpastes and varnishes, have previously been documented (Marinho 2013; Walsh 2010). Some adverse effects of fluoridated water that have been explored are widely perceived to be dependent on dose, duration and/or time of exposure (Browne 2005). Within community water fluoridation programmes, maximum fluoride concentrations are set to prevent other harms related to very high fluoride concentrations. Supra-optimal levels of fluoride (occurring naturally) have been linked to severe dental fluorosis and skeletal fluorosis. There is a lack of evidence for other postulated harms such as cancer and bone fractures; no evidence of a strong association with water fluoridation has been shown for these conditions (McDonagh 2000).

Why it is important to do this review

Water fluoridation was identified as a priority topic in the Cochrane Oral Health Group's international priority setting exercise, incorporating views from clinicians, guideline developers and members of the public.

The use of water fluoridation as a means of improving dental health has been endorsed by many national and international health institutions, including the World Health Organization (MRC 2002). It has been hailed by the US Surgeon General as "one of the most effective choices communities can make to prevent health problems while actually improving the oral health of their citizens" (ADA 2013). Opponents have raised concerns about ethical issues and its potential harms (Cheng 2007), as a result of which the practice has remained controversial. A comprehensive systematic review of water fluoridation has previously been published (McDonagh 2000). The review showed a benefit in terms of a reduction in caries as well as an increased risk of dental fluorosis. However, there was insufficient evidence to draw conclusions regarding other potential harms or health disparities. The review findings have often been misinterpreted and have been used to support arguments on both sides of the water fluoridation debate (Cheng 2007). In addition, little comment has been made on the applicability of the evidence to today's society. Many of the caries studies presented in the McDonagh 2000 review were conducted prior to the widespread use of fluoride toothpastes in the late 1970s, and the introduction and uptake of other preventative strategies, such as fluoride varnish. The McDonagh 2000 review was conducted 15 years ago. Given the continued interest in this topic, from both health professionals, policy makers and the public, it is important to update and maintain a systematic review that reflects any emerging, contemporary evidence.

This review updates the McDonagh 2000 review. It aims to contextualise the evidence to inform current national and international guidelines.

It should be noted, the original systematic review had a broader remit and aimed to evaluate the differential effects of natural and artificial fluoridation as well as adverse effects other than dental fluorosis (McDonagh 2000). The inclusion criteria for the objectives covered in this review follow those stated in McDonagh 2000.

OBJECTIVES

To evaluate the effects of water fluoridation (artificial or natural) on the prevention of dental caries.

To evaluate the effects of water fluoridation (artificial or natural) on dental fluorosis.

METHODS

Criteria for considering studies for this review

Types of studies

Water fluoridation for the prevention of dental caries

For caries data, we included only prospective studies with a concurrent control, comparing at least two populations, one receiving fluoridated water and the other non-fluoridated water, with at least two points in time evaluated. Groups had to be comparable in terms of fluoridated water at baseline. For studies assessing the initiation of water fluoridation the groups had to be from non-fluoridated areas at baseline, with one group subsequently having fluoride added to the water. For studies assessing the cessation of water fluoridation, groups had to be from fluoridated areas at baseline, with one group subsequently having fluoride removed from the water.

For the purposes of this review, water with a fluoride concentration of 0.4 parts per million (ppm) or less (arbitrary cut-off defined a priori) was classified as non-fluoridated.

Water fluoridation and dental fluorosis

For the assessment of dental fluorosis, we included any study design, with concurrent control, comparing populations exposed to different water fluoride concentrations.

It should be noted that, due to the nature of the research question, randomised controlled trials are unfeasible.

Types of participants

Populations of all ages receiving fluoridated water (naturally or artificially) and populations receiving non-fluoridated water.

Types of interventions

Water fluoridation for the prevention of dental caries

Caries data: a change in the level of fluoride in the water supply of at least one of the study areas within three years of the baseline survey. Exposure to fluoridated water or non-fluoridated water (less than 0.4 ppm) could be in conjunction with other sources of fluoride (e.g. fluoridated toothpaste), provided the other sources were similar across groups. Where specific information on the use of other sources of fluoride was not supplied, we assumed that populations in studies conducted after 1975 in industrialised countries had been exposed to fluoridated toothpaste.

Water fluoridation and dental fluorosis

Fluoride at any concentration present in drinking water.

Types of outcome measures

Primary outcomes

Any measure of dental caries including the following.

- Change in the number of decayed, missing and filled deciduous, and permanent teeth, (dmft and DMFT, respectively).
- Change in the number of decayed, missing and filled deciduous, and permanent, tooth surfaces (dmfs and DMFS, respectively).
- Incidence of dental caries.
- Percentage of caries-free children.

We also recorded data on disparities in dental caries across different groups of people, as reported in the included studies.

An a priori set of rules regarding the prioritisation of caries measures has been developed previously (Marinho 2013). We would have adopted these, if the data had required.

Secondary outcomes

Dental fluorosis, as measured by the following.

- Percentage of children with fluorosis (any level of fluorosis, or fluorosis of aesthetic concern).
- Dean's Fluorosis Index.
- Tooth Surface Index of Fluorosis (TSIF).
- Thylstrup and Fejerskov index (TFI).
- Modified Developmental Defects of Enamel (DDE).

We aimed to record the prevalence of dental fluorosis for each dentition if reported in the studies. In measuring the percentage prevalence of dental fluorosis, we classified children with dental fluorosis according to the index used in the individual studies. As measured by the common epidemiologic indices for dental fluorosis (Rozier 1994), we classified children with a DDE, TSIF, TFI score greater than zero or Dean's classification of 'questionable' or higher as having dental fluorosis. If other indices had been used, we would have considered and adopted the percentage prevalence of dental fluorosis as reported by the original investigators using other methods (e.g. photographic method or other index). Any dental fluorosis scoring ≥ 3 (TFI), ≥ 2 (TSIF) and 'mild' or worse (Dean's) were considered to be of aesthetic concern. We restricted analysis on dental fluorosis of aesthetic concern to TFI, TSIF and Dean's indices as it is not easily determined from the modified DDE index.

Within the context of this review dental fluorosis is referred to as an 'adverse effect'. However, it should be acknowledged that moderate fluorosis may be considered an 'unwanted effect' rather than an adverse effect. In addition, mild fluorosis may not even be considered an unwanted effect.

We also recorded data on any other adverse effects (e.g. skeletal fluorosis, hip fractures, cancer, congenital malformations, mortality) reported in the included studies. However, this review did not aim to provide a comprehensive systematic review of adverse effects other than dental fluorosis.

Search methods for identification of studies

The original review involved searching a wide range of databases from their starting date to June/October 1999 (Appendix 1). Full details of all the strategies initially used have been published previously (McDonagh 2000).

For the identification of studies included or considered for this updated review, we developed detailed search strategies combining controlled vocabulary and free text terms for each database searched. These were based on the search strategy developed for MEDLINE (Appendix 4) but revised appropriately for each database to take account of differences in controlled vocabulary and syntax rules.

Electronic searches

We searched the following electronic databases (from inception):

- The Cochrane Oral Health Group's Trials Register (to 19 February 2015; see Appendix 2);
- The Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2015, Issue 1; see Appendix 3);
- MEDLINE via OVID (1946 to 19 February 2015; see Appendix 4);
- EMBASE via OVID (1980 to 19 February 2015; see Appendix 5);
- Proquest (all databases; to 19 February 2015; Appendix 6);
- Web of Science Conference Proceedings (1990 to 19 February 2015; see Appendix 7);
- ZETOC Conference Proceedings (1993 to 19 February 2015; see Appendix 8).

There were no restrictions on language of publication and non-English studies were translated, unless a translator could not be found through Cochrane.

Searching other resources

We searched the following databases for ongoing trials (see Appendix 9):

- US National Institutes of Health Trials Register (clinicaltrials.gov to 19 February 2015);
- The WHO Clinical Trials Registry Platform (apps.who.int/trialsearch/default.aspx to 19 February 2015).

Only handsearching conducted as part of the Cochrane Worldwide Handsearching Programme and uploaded to CENTRAL was included (see the Cochrane Masterlist for the details of journals searched to date). We reviewed the reference lists of identified trials and review articles for additional appropriate studies.

Data collection and analysis

Selection of studies

Two review authors independently and in duplicate screened the titles and abstracts (when available) of all reports identified through the electronic search update. We obtained the full report for all studies that appeared to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision. Two review authors independently assessed the full reports obtained from the electronic and other methods of searching to establish whether or not the studies met the inclusion criteria. Disagreements were resolved by discussion. Where resolution was not possible, a third review author was consulted. Studies rejected at this or subsequent stages were recorded in the 'Characteristics of excluded studies' table, and reasons for their exclusion recorded.

Data extraction and management

Two review authors extracted data independently using specially designed data extraction forms (produced in Excel). We piloted the data extraction forms on several papers and modified them as required before use. Any disagreements were discussed and a third review author consulted where necessary.

For each study we aimed to record the following data.

- Year of publication, country of origin and source of study funding.
- Details of the participants including demographic characteristics (socioeconomic status (SES), ethnicity), age, deciduous/permanent dentition and criteria for inclusion and exclusion.
- Details of the type of intervention, comparator and co-interventions.
- Details of the outcomes reported, including method of assessment, and time intervals.

- Details of confounding factors considered (potential confounders of relevance to this review include sugar consumption/dietary habits, SES, ethnicity and the use of other fluoride sources).
- Details on comparability of groups with regard to confounding factors.
- Details on methods used to control for confounding.
- Details regarding both unadjusted and adjusted effect estimates.

Assessment of risk of bias in included studies

McDonagh 2000 used specially designed validity assessment checklists that provided a 'validity score' and assigned a 'level of evidence' for each study. In this update, we aimed to assess all included studies (including those from the previous review by McDonagh 2000) for risk of bias using the Cochrane 'Risk of bias' assessment tool adapted for non-randomised controlled studies (Higgins 2011). The domains assessed for each included study included: sampling, confounding, blinding of outcome assessment, completeness of outcome data, risk of selective outcome reporting and risk of other potential sources of bias. We did not include random sequence generation or allocation concealment, as these were not relevant for the study designs included and are covered by the domain for confounding. We had identified the following factors as important confounders for the primary and secondary outcomes: sugar consumption/dietary habits, SES, ethnicity and the use of other fluoride sources.

We tabulated a description of the 'Risk of bias' domains for each included trial, along with a judgement of low, high or unclear risk of bias.

We undertook a summary assessment of the risk of bias for the primary outcome (across domains) across studies (Higgins 2011). Within a study, we gave a summary assessment of low risk of bias when there was a low risk of bias for all key domains, unclear risk of bias when there was an unclear risk of bias for one or more key domains, and high risk of bias when there was a high risk of bias for one or more key domains.

Measures of treatment effect

We included the following caries indices in the analyses: dmft, DMFT, and proportion caries free in both dentitions. For dmft and DMFT analyses we calculated the difference in mean change scores between fluoridated and control groups. For the proportion caries free, we calculated the difference in the proportion caries free between the fluoridated and control groups.

For dental fluorosis data we calculated the log odds and presented them as probabilities for interpretation.

We have presented data on other adverse effects, reported in the included studies, as a narrative.

We intended to present data on both adjusted and unadjusted results, but the data allowed only for unadjusted values.

Dealing with missing data

Where outcome data were missing from the published report, or could not be calculated from the information presented in the report of a trial, we attempted to contact the authors to obtain the data and clarify any uncertainty. The analyses generally included only the available data (ignoring missing data). When the number of participants evaluated was not reported, we did not include outcome data in the analyses. Where standard deviations were missing for DMFT and dmft data we used the equation: log(SD) = 0.17 + 0.56 x log(mean) to estimate the standard deviations for both the before and after mean caries values. This equation was estimated from available data where the standard deviations were given ($R^2 = 0.91$; Appendix 10). We undertook no other imputations.

We undertook sensitivity analyses to determine the effect of the imputed standard deviations.

Assessment of heterogeneity

We planned to explore differences in fluoridation technique, fluoride concentration, outcome measurement index and technique as possible sources of heterogeneity. Initial consideration of heterogeneity would be via the DerSimonian-Laird model (commonly referred to as a random-effects meta-analysis). When between study variance was deemed to be both robustly estimated and substantial (judged as the estimate being larger than twice its standard error), we favoured the random-effects model over a fixed-effect approach. We would have investigated any heterogeneity further via Baujat and normal quantile-quantile (Q-Q) plots, alongside influence diagnostics (for example **diff**erence in **fit**ted values (DFFITS), Cook's distance, hat values and leave-one-out methods) as appropriate. However, due to the limited data and lack of clarity in reporting we were unable to undertake any of these analyses for the caries data. Fluoride concentration was explored as part of the fluorosis analysis.

Assessment of reporting biases

If more than 10 trials had been identified for any meta-analysis of the primary outcome caries, we would have assessed publication bias according to the recommendations described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Had asymmetry been identified in the contour-enhanced funnel plots, we would have investigated possible causes. The number of studies presented in each caries meta-analyses precluded this.

Data synthesis

The primary analyses was based on all included studies, irrespective of risk of bias.

Caries

For the analyses of mean dmft and DMFT severity data, we used Review Manager (RevMan 2014; not shown) to calculate weighted (for age) mean change score for water fluoridation and control group separately, and the summary effect estimates across all age groups for each study (we only analysed data for dmft for children eight years and younger). The resulting effect estimates for the water fluoridation and control groups were then entered into RevMan for each study to calculate the mean difference in change scores for the review (see Analysis 1.1; Analysis 1.2). We decided to display this data using the average n for the before and after data for each study to give an indication of the size of the studies. The raw data and summary statistics are shown in Table 1; Table 2.

Where standard deviations (SDs) are missing for the dmft, DMFT data we used the equation: log(SD) = 0.17 + 0.56 x log(mean) to estimate the SDs for both before and after mean caries values. We

undertook a sensitivity analysis omitting all the data for studies/age groups where the standard deviation was imputed.

For the caries free data for both dentitions, we calculated the risk differences in RevMan (not shown) for water fluoridation and control groups separately, for each study, undertaking a meta-analyses across age groups. These summary effect estimates and standard deviations were then combined in a meta-analysis in RevMan (not shown) as continuous data to provide summary estimates of the change in the proportion caries free for both groups. For each dentition (rather than age group), we then combined the resulting data as a meta-analysis in the review. Once again we decided to display this data using the average n for the before and after data for each study to give an indication of the size of the studies. Table 3 and Table 4 provide the raw data and summary estimates of the risk differences for each water fluoridation and control group separately, for each study, across age groups.

Fluorosis

In line with the previous systematic review (McDonagh 2000), the primary analysis was carried out on data where fluoride exposure was 5 ppm or less, for reasons of applicability and robustness of evidence (the concentration of most naturally occurring fluoride will be below than this threshold, and the paucity of information from higher exposures leads to less precise estimates). We analysed two aspects of fluorosis: aesthetic concerns of fluorosis (as defined in Types of outcome measures), and any level of fluorosis. We used random-effects models with random intercept and random slope to model the log odds of fluorosis as a function of fluoride exposure. In this model we allowed the intercept and slope to vary from study to study. The slope of the linear relationship between fluoride level (the predictor) and the log odds of fluorosis is the value of the coefficient for fluoride level plus the study specific random effect for that specific study. Fluoride exposure was centred upon the grand mean, and results presented as probabilities to aid interpretation.

Subgroup analysis and investigation of heterogeneity

We undertook subgroup analyses according to whether data were collected prior to the widespread use of fluoride toothpaste, or after: we used a cut-off of 1975 for this purpose. We made the decision to undertake subgroup analyses by date of study conduct post hoc, following peer review comments.

We had planned to use meta-regression to investigate and explain sources of heterogeneity among studies where possible (potential confounders of relevance to this review include sugar consumption/dietary habits, SES, ethnicity and the use of other fluoride sources). Dental caries results were to be analysed using meta-regression in order to assess the impact of potential sources of heterogeneity and estimate the underlying effect of water fluoridation. We also planned to conduct subgroup analyses by study design. However, due to the small number of studies and lack of clarity in the reporting within the caries studies, we did not undertake these sub-group analyses

Sensitivity analysis

We would have undertaken sensitivity analyses based on risk of bias if sufficient trials had been included. We had planned to undertake further sensitivity analyses to determine if the results of the meta-analysis were influenced by the timing of baseline measurement, as appropriate. We did undertake sensitivity analyses to determine the effect of the imputed standard deviations.

Presentation of main results

We assessed the quality of the evidence for the primary and secondary outcomes for this review using GRADE methods (gdt.guidelinedevelopment.org). Due to the observational nature of the studies included in the review, GRADE stipulates that the quality of the body of evidence starts at 'low'. We considered susbequent downgrading of the quality of the body of evidence with reference to the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results and the precision of the estimates. We considered upgrading the quality of the evidence on the basis of an assessment of the risk of publication bias, the magnitude of the effect and whether or not there was evidence of a dose response.

We presented the results and quality of evidence for each outcome in a 'Summary of findings' table. We made a post hoc decision not to use the GRADE terminology of high, moderate, low and very low to describe the quality of the evidence (see Quality of the evidence).

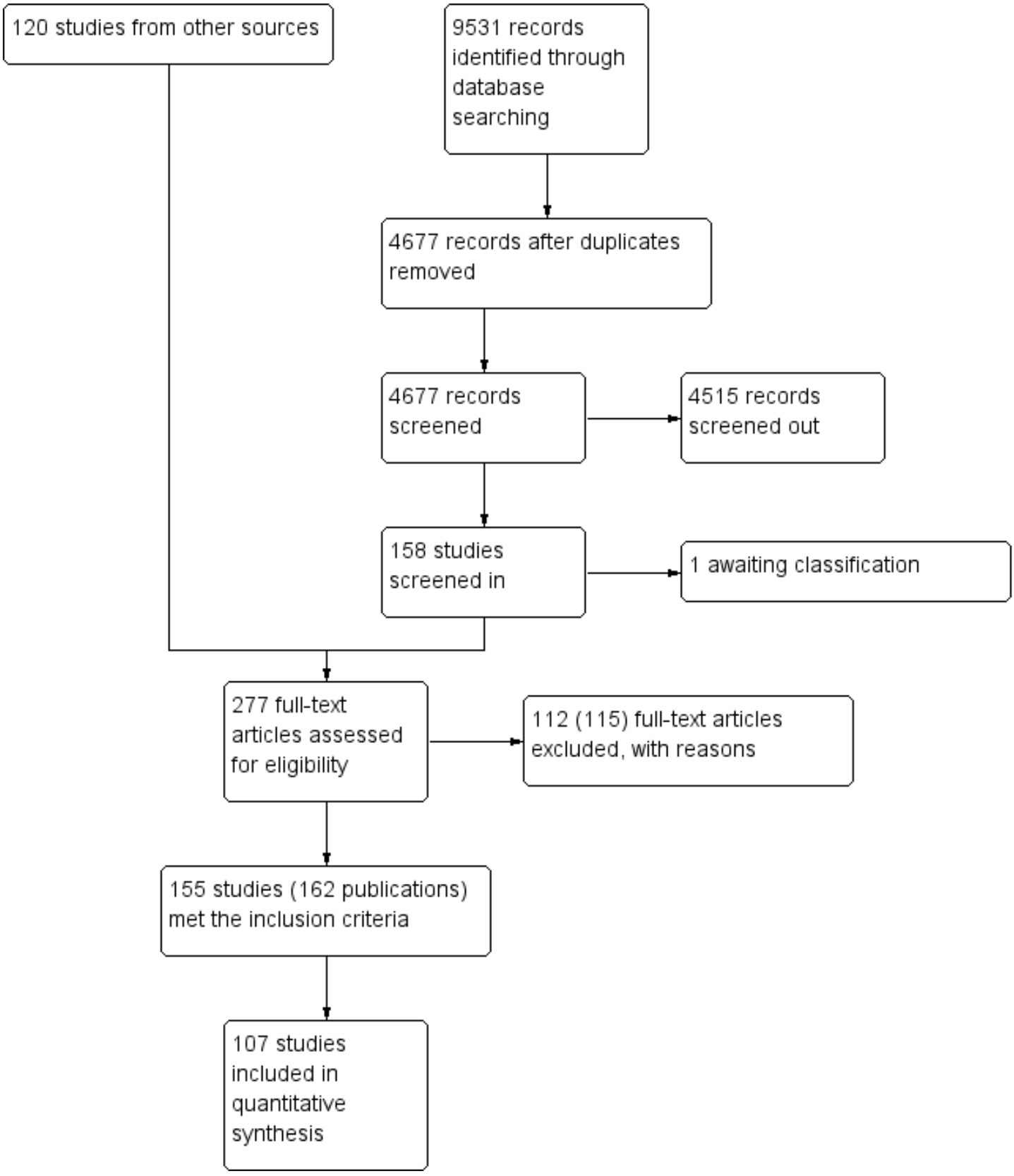
RESULTS

Description of studies

Results of the search

The search for literature produced a total of 4677 records after de-duplication. Two reviewers in duplicate screened these records independently. Any disagreements were resolved by a third reviewer. After this initial screening, we obtained 158 articles, combined with 120 articles from additional sources (including McDonagh 2000; NHMRC 2007 and an unpublished paper, Blinkhorn (unpublished)) and read them in detail. We assessed 277 of these 278 articles for eligibility; 155 studies (162 publications) met the inclusion criteria for the review. However, only 107 studies (15 caries studies; 92 studies reporting data on either all fluorosis severities or fluorosis of aesthetic concern) presented sufficient data for inclusion in the quantitative syntheses. One study awaits classification. The search, screening results and selection of included studies are illustrated in the PRISMA flow diagram (Figure 1).

Figure 1. Figure 1. Study flow diagram.



Included studies

A total of 20 prospective observational studies provided data on caries or disparities in caries, or both (Adriasola 1959; Arnold 1956; Ast 1951; Backer-Dirks 1961; Beal 1971; Beal 1981; Blinkhorn (unpublished); Brown 1965; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Gray 2001; Guo 1984; Hardwick 1982; Holdcroft 1999; Kunzel 1997; Loh 1996; Maupome 2001; Pot 1974; Tessier 1987).

Caries

Nineteen prospective observational studies (22 publications) published between 1951 and 2015 met the inclusion criteria for the caries outcome. Eighteen of these studies looked at the effect of the initiation of water fluoridation programme on dental caries (Adriasola 1959; Arnold 1956; Ast 1951; Backer-Dirks 1961; Beal 1971; Beal 1981; Blinkhorn (unpublished); Brown 1965; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Gray 2001; Guo 1984; Hardwick 1982; Kunzel 1997; Loh 1996; Pot 1974; Tessier 1987), and one study focused on the effect of cessation of fluoridation on caries (Maupome 2001). Only one study followed the same participants over time (Hardwick 1982), evaluating 12-year old children in a fluoridated and a non-fluoridated area and following them for four years. All other studies evaluated specific age groups within three years of a change in fluoridation status and undertook a follow-up evaluation of the same age groups (different children) at at least one other time point. A low/non-fluoridated area was used as a control. These have been analysed as controlled before-and-after studies.

The studies were conducted in multiple centres in Europe (Backer-Dirks 1961; Beal 1971; Beal 1981; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Gray 2001; Hardwick 1982; Kunzel 1997; Pot 1974), North America (Arnold 1956; Ast 1951; Brown 1965; Maupome 2001; Tessier 1987), South America (Adriasola 1959), Australia (Blinkhorn (unpublished)) and Asia (Guo 1984; Loh 1996). Five studies were funded by research grants from research organisations, health authorities and government organisations (Beal 1971; Blinkhorn (unpublished); Booth 1991; Kunzel 1997; Maupome 2001), one study was funded in collaboration with members of the committee pro-fluoridation (Adriasola 1959), while the other studies did not state their funding sources.

Participants, aged from three to 16 years, were mostly recruited from schools; the period of time between baseline and final measurement ranged from two to 12 years.

The intervention groups in all 'fluoride initiation' studies were exposed to naturally low fluoride at baseline and artificially fluoridated water at follow-up, while the control groups were exposed to naturally low fluoride at both time points. In studies where it was not stated clearly, fluoride concentration was reported as 'high' or 'fluoridated' for the intervention group and 'low' or 'non-fluoridated' for the control group. For the 'fluoride cessation' study that met our inclusion criteria, the intervention group was exposed to artificially fluoridated water at baseline and naturally low fluoride at follow-up, while the control group remained artificially fluoridated at both time points.

Measures of dental caries reported were dmft (decayed missing and filled deciduous teeth), DMFT (decayed missing and filled permanent teeth), DMFS (decayed missing and filled surfaces in permanent teeth), and proportion of caries-free children (deciduous and permanent dentition).

Disparities in caries

Three prospective observational studies (four publications) met the inclusion criteria for disparities in caries but did not provide data suitable for analysis (Beal 1971; Gray 2001; Holdcroft 1999). They all assessed the effect of the initiation of water fluoridation on caries in different SES groups receiving fluoridated and non-fluoridated water. All three studies evaluated specific age groups within three years of a change in fluoridation status and undertook a follow-up evaluation of the same age groups (different children) at a least one other time point. A low/non-fluoridated area was used as a control. All these studies were conducted in the UK. Caries measures reported were decayed, extracted and filled deciduous teeth (deft; Beal 1971), dmft (Gray 2001; Holdcroft 1999), and percentage of caries-free children (Beal 1971; Gray 2001).

Dental fluorosis

For dental fluorosis, 135 studies were included. These were published between 1941 and 2014. Of these studies, 28% were conducted in Europe, 23% in Asia, 19% in North America, 13% in South America, 10% in Africa, 5% in Australia and 2% in multiple centres in Europe and Asia. Forty-four studies were supported by research grants from government organisations and health authorities, non-governmental organisations, research organisations, universities or a combination of these sources (Adair 1999; Alarcon-Herrera 2001; AlDosari 2010; Angelillo 1999; Awadia 2000; Azcurra 1995; Bao 2007; Butler 1985; Chen 1989; Clark 1993; Correia Sampaio 1999; de Crousaz 1982; Garcia-Perez 2013; Hernandez-Montoya 2003; Ibrahim 1995; Indermitte 2007; Indermitte 2009; Kanagaratnam 2009; Kumar 1999; Kumar 2007; Mackay 2005; Mandinic 2010; Milsom 1990; Nanda 1974; Narwaria 2013; Nunn 1992; Pontigo-Loyola 2008; Ray 1982; Riordan 2002; Ruan 2005; Rwenyonyi 1999; Skinner 2013; Stephen 2002; Szpunar 1988; Tsutsui 2000; Vilasrao 2014; Villa 1998; Vuhahula 2009; Wang 1999; Wang 2012; Warren 2001; Whelton 2004; Whelton 2006; Wondwossen 2004); six studies were funded by: a sugar association (McInnes 1982), a water company (Firempong 2013; Warnakulasuriya 1992), the dental industry (Machiulskiene 2009; Wenzel 1982), or associated with a dental industry through authorship (McGrady 2012). Sources of support were not explicitly stated in 86 studies. One study explicitly stated that no funding had been obtained (Shanthi 2014).

Out of the 135 studies that met the inclusion criteria for fluorosis we aimed to extract cross-sectional data. Ninety studies reported sufficient data for inclusion in the analysis for all severities of dental fluorosis (Appendix 11). Forty studies were included in the analysis for fluorosis of aesthetic concern (Appendix 11). The remaining studies did not report sufficient data for inclusion in the analysis, typically due to failure to indicate water fluoride concentration of the study areas or reporting inappropriate measure of fluorosis (e.g. mean value or Community Fluorosis Index (CFI)). Where studies reported fluorosis outcomes as CFI only, we could not use the data. The CFI is a composite score calculated by summing the scores of Dean's Index and dividing the total by the sample size. This gives an indication of the experience and severity of fluorosis at a population level, but individual level data cannot be derived from it alone.

Dean's index, TFI, TSIF, DDE were reported in 41%, 19%, 10%, 6% of the included studies, respectively, while 23% of the studies either reported on other indices, specific enamel defects, or did not state the index used at all.

Other adverse effects

Five studies that reported on the dental fluorosis outcome also presented data on other adverse effects associated with water fluoridation (Table 5). The outcomes reported were skeletal fluorosis (Chen 1993; Jolly 1971; Wang 2012), bone fracture (Alarcon-Herrera 2001), and skeletal maturity (Wenzel 1982). Outcomes were assessed in participants using radiographs (Chen 1993; Jolly 1971; Wenzel 1982), the diagnostic criteria of endemic skeletal fluorosis (WS 192-2008; Wang 2012), or methods that were not clearly stated (Alarcon-Herrera 2001).

Excluded studies

Of the 277 studies that were assessed for eligibility, we excluded 112 studies (115 publications; see Characteristics of excluded studies). The reasons for exclusion were most frequently due to inappropriate study design, including:

- absence of data from two time points for one or both study groups (Agarwal 2014; Ajayi 2008; Aldosari 2004; Antunes 2004; Archila 2003; ARCPOH 2008; Armfield 2004; Armfield 2005; Arora 2010; Bailie 2009; Baldani 2002; Baldani 2004; Binbin 2005; Blagojevic 2004; Bradnock 1984; Carmichael 1980; Carmichael 1984; Carmichael 1989; Evans 1995; Gillcrist 2001; Gushi 2005; Han 2011; Jones 1997; Jones 2000a; Jones 2000b; Kirkeskov 2010; Kumar 2001; Lee 2004; Peres 2006; Provart 1995; Rihs 2008; Riley 1999; Rugg-Gun 1977; Sagheri 2007; Sales-Peres 2002; Saliba 2008; Sampaio 2000; Slade 2013; Tagliaferro 2004; Tiano 2009; Tickle 2003; Zimmermann 2002);
- unsuitable control group (Attwood 1988; Hobbs 1994; Kalsbeek 1993; Seppa 1998; Wragg 1999; Murray 1984; Murray 1991);
- absence of concurrent control group (Buscariolo 2006; Kunzel 2000a; Wong 2006).

Risk of bias in included studies

The review authors' judgements about each risk of bias item for each included study is summarised in Figure 2.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

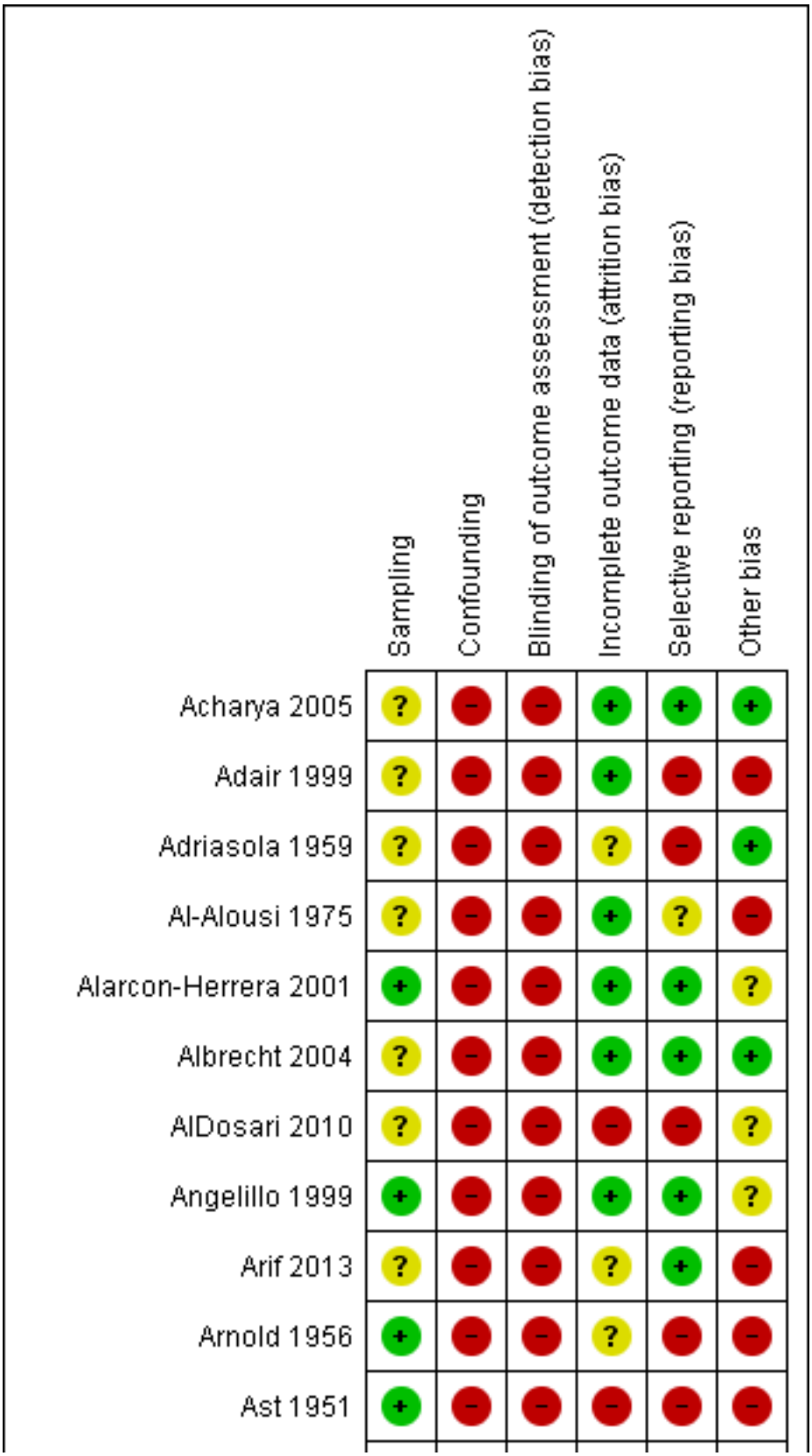
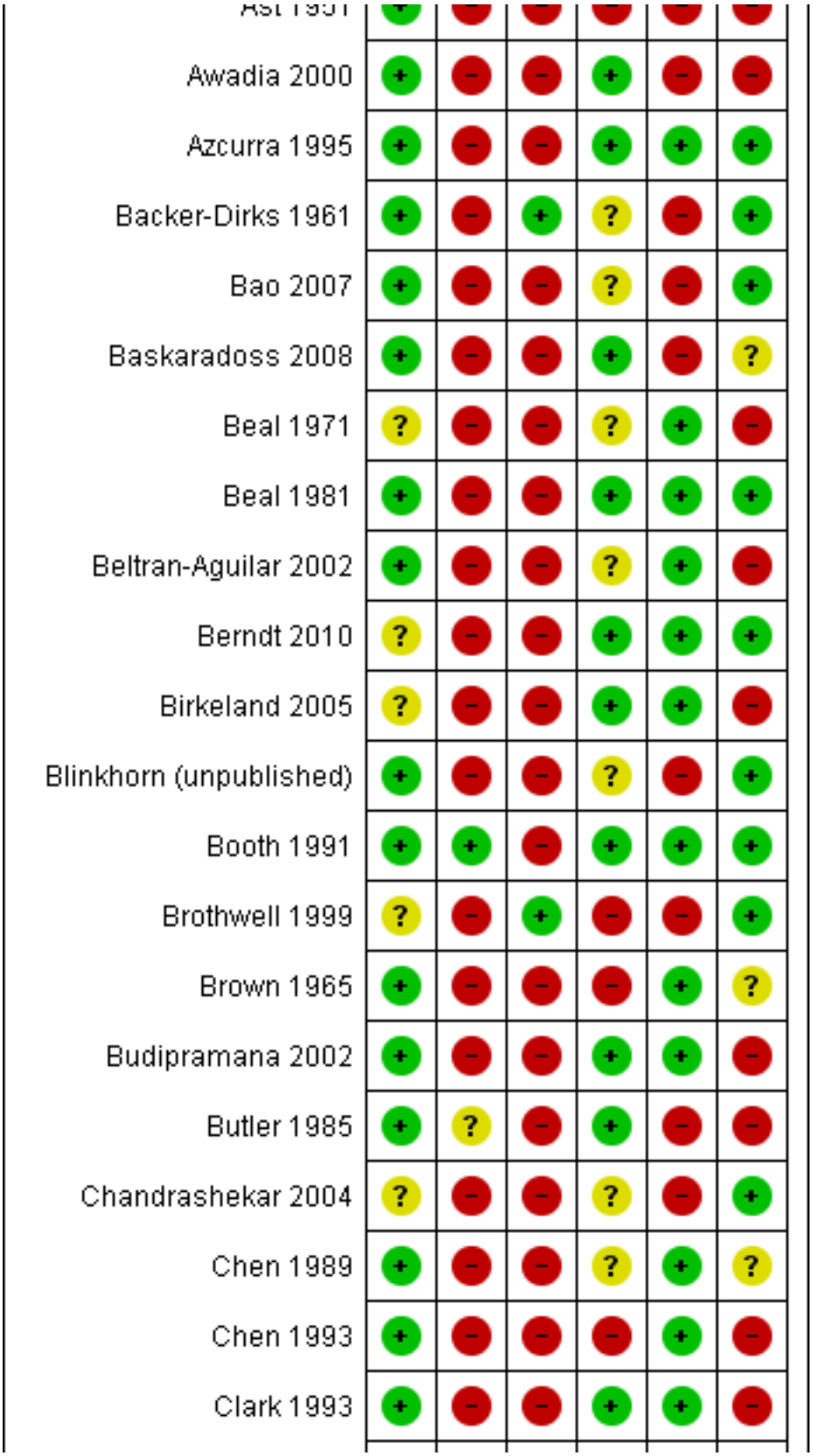


Figure 2. (Continued)



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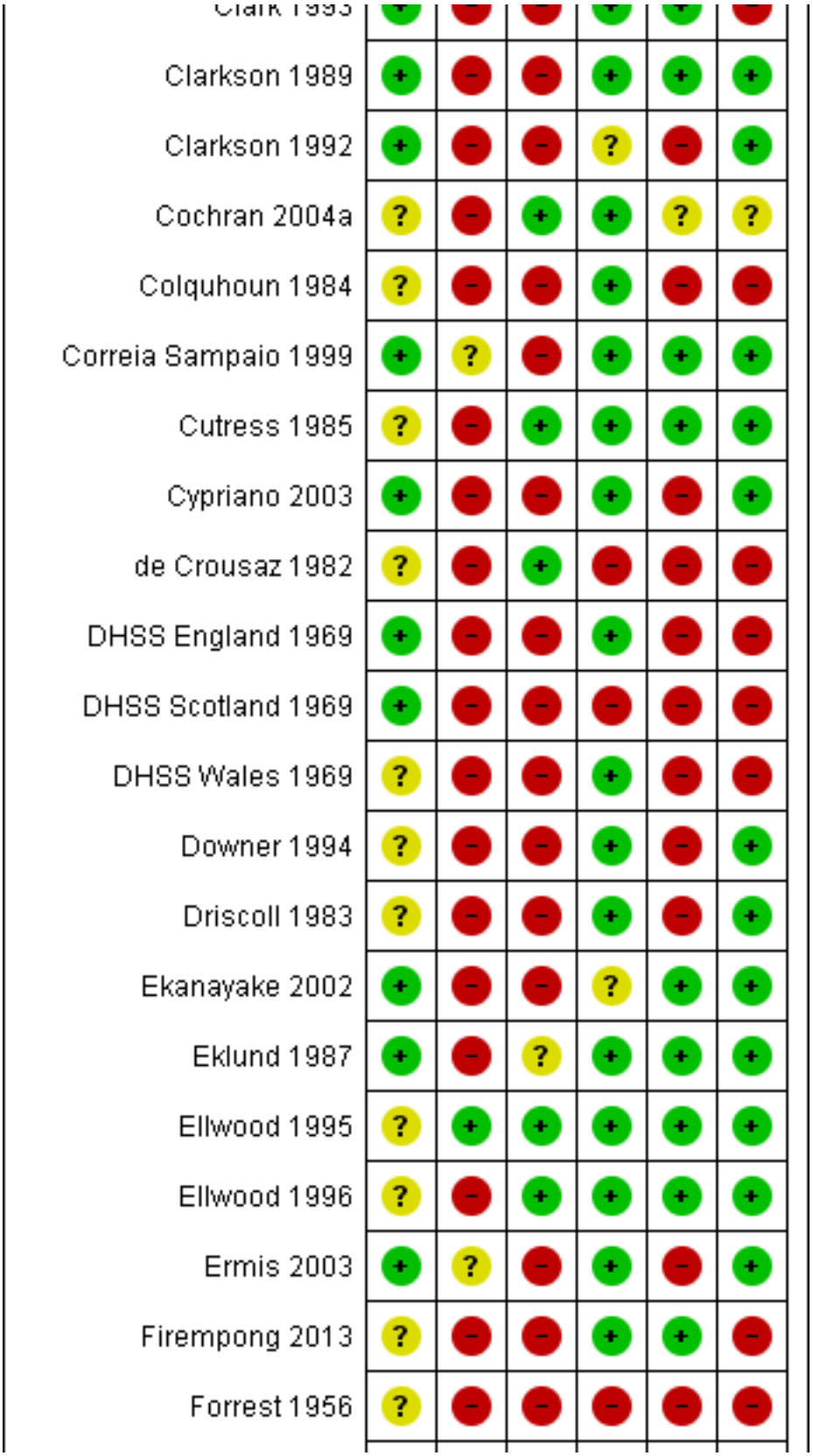

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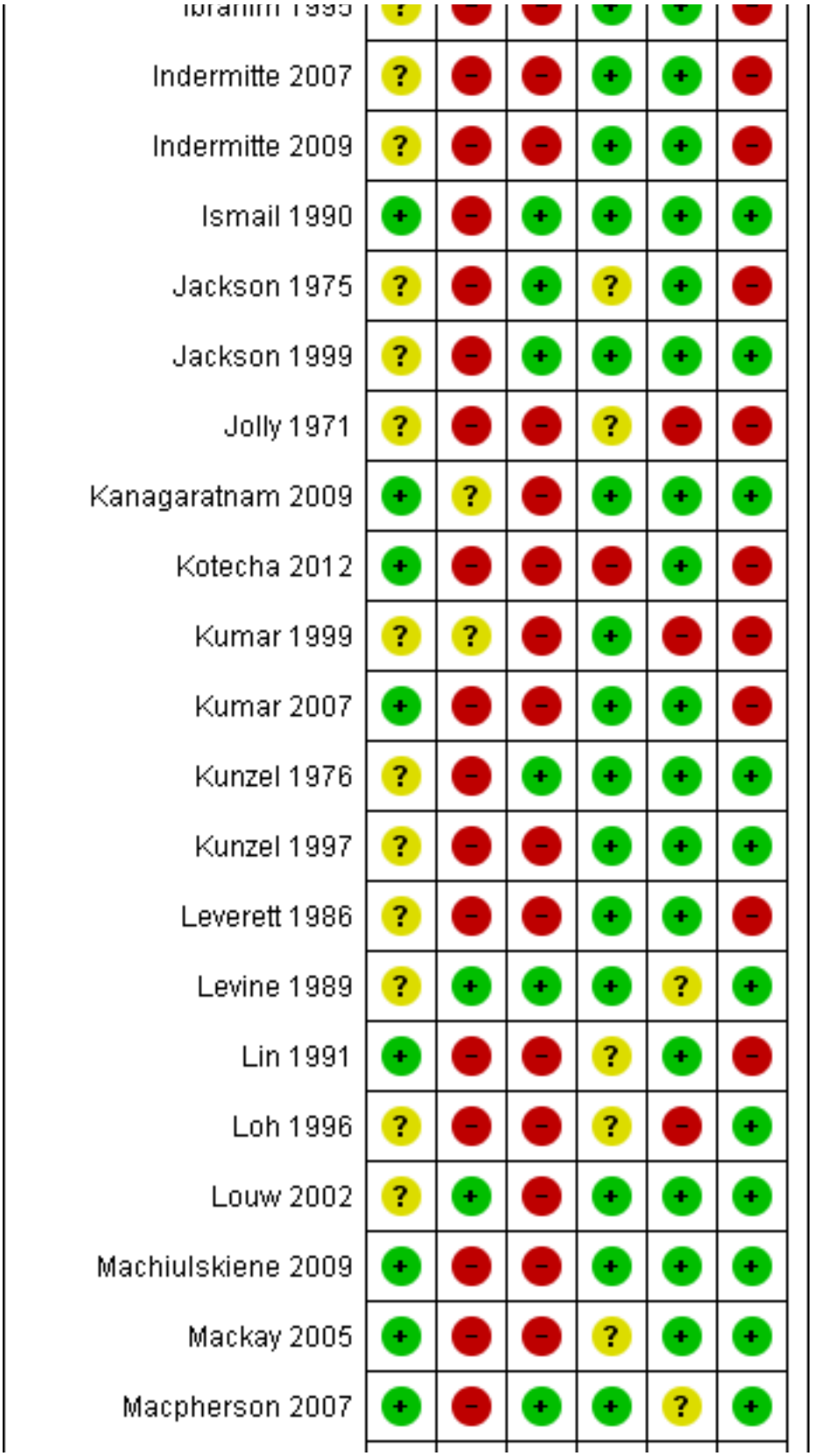

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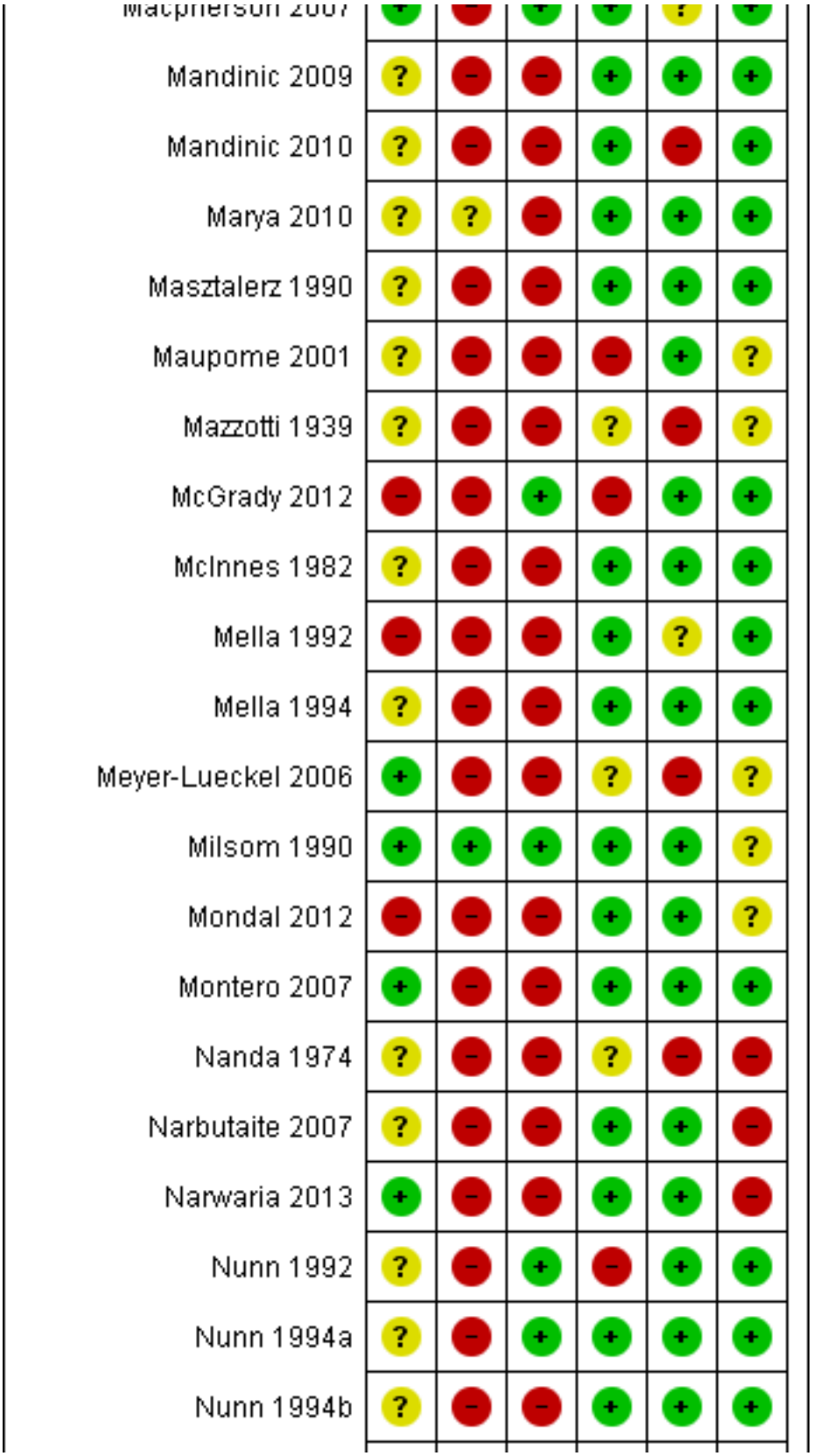

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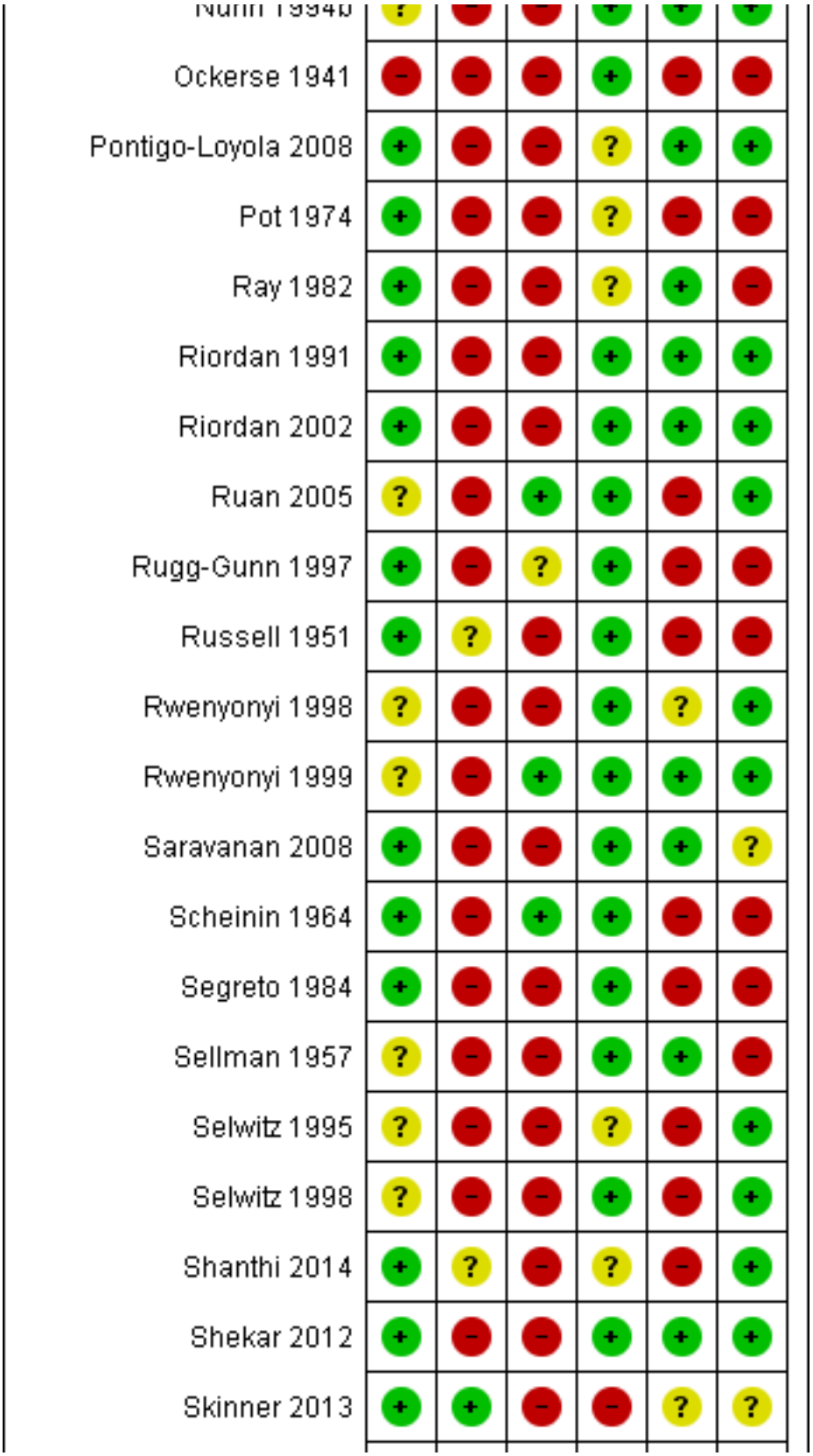

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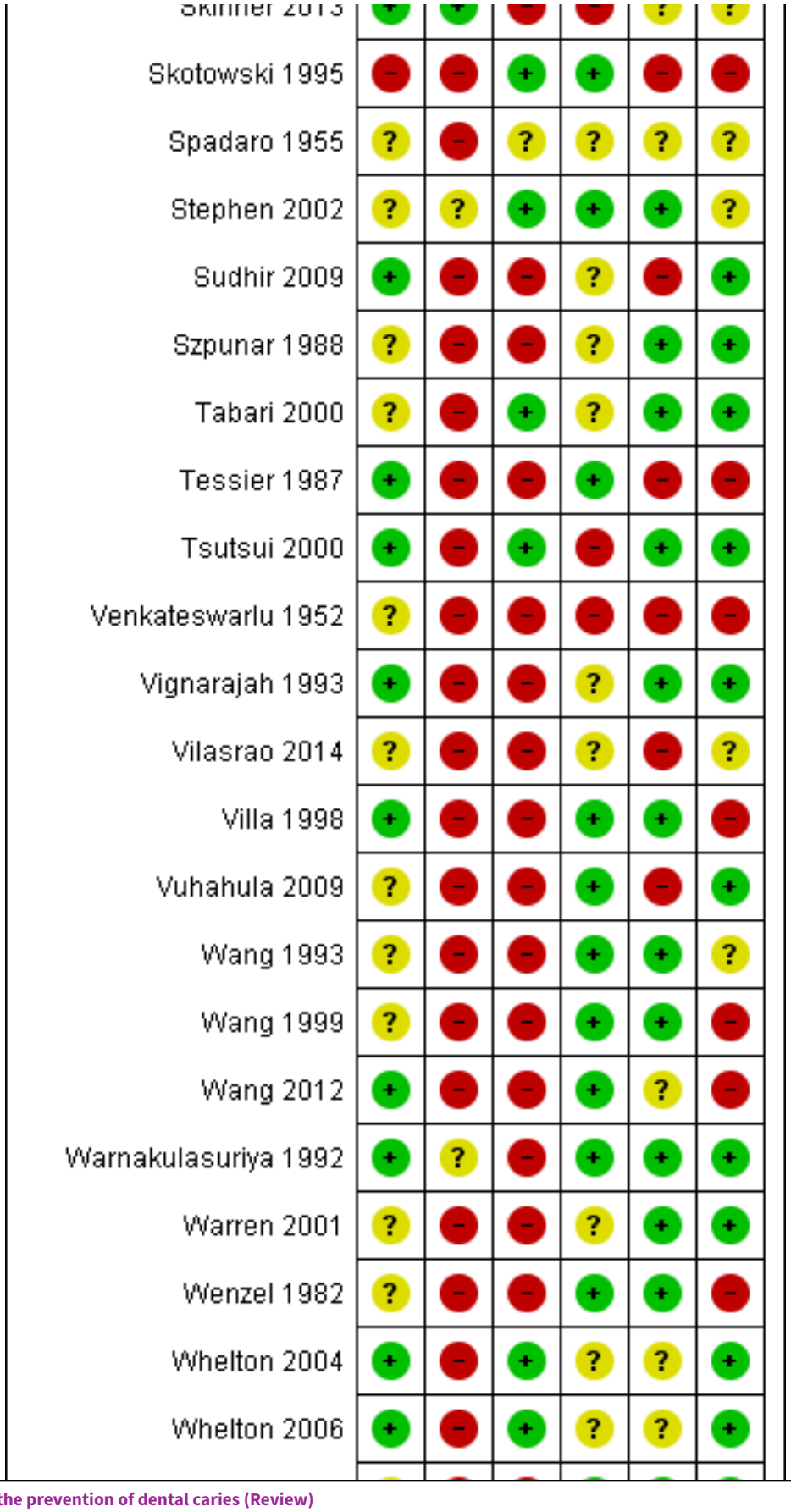


Caries outcome

We judged that all the 20 studies included for the caries outcome (including disparities in caries) were at high risk of bias overall. The bias may occur in either direction.

Sampling

We judged 13 of the studies as being at low risk of bias in terms of sampling (Arnold 1956; Ast 1951; Backer-Dirks 1961; Beal 1981; Blinkhorn (unpublished); Brown 1965; DHSS England 1969; DHSS Scotland 1969; Gray 2001; Guo 1984; Hardwick 1982; Pot 1974; Tessier 1987). For these studies, sampling was achieved either randomly or by including the entire eligible population of the study area. We judged seven studies to be at unclear risk of bias for sampling (Adriasola 1959; Beal 1971; DHSS Wales 1969; Holdcroft 1999; Kunzel 1997; Loh 1996; Maupome 2001). This judgement was based on insufficient or unavailable information in most cases, however in the study by Kunzel 1997, there was an unexplained exclusion of disabled children. In the DHSS Scotland 1969 study, different age criteria were used for each group resulting in an imbalance between the groups; the reason for this was not explained. No studies were found to be at high risk for selection bias for this outcome.

Confounding

We found all studies to be at high risk of bias for confounding. We considered confoundng factors for this outcome to be sugar consumption/dietary habits, SES, ethnicity and the use of other fluoride sources. We would have judged studies to be at low risk of confounding bias only if they had successfully controlled for all factors. Six of the studies attempted to control for none of these factors (Adriasola 1959; Ast 1951; Brown 1965; Guo 1984; Loh 1996; Pot 1974). Eight controlled for SES, but not for other sources of fluoride or for dietary habits (Arnold 1956; Backer-Dirks 1961; Beal 1971; Beal 1981; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Gray 2001). Hardwick 1982 matched for SES and reported the use of fluoride from other sources to be broadly similar across groups, but did not report on dietary habits. Maupome 2001 reported on dietary habits and the use of fluoride from other sources; this study showed that dietary habits did not confound the relationship between water fluoridation and caries.

Detection bias

The majority of the studies did not blind outcome assessors. This is perhaps unsurprising when considering the efforts that may be required to blind assessors for this type of study. We judged only two studies to be at low risk of bias for this domain (Backer-Dirks 1961; Hardwick 1982). Backer-Dirks 1961 utilised radiographs in order to blind assessors, and in the Hardwick 1982 study children were brought to a central examination centre for assessment.

Incomplete outcome data

Eight studies were judged as being at low risk of bias (Beal 1971; Beal 1981; Brown 1965; Gray 2001; Guo 1984; Hardwick 1982; Kunzel 1997; Maupome 2001), or unclear risk of bias for the domain of incomplete outcome data (Adriasola 1959; Arnold 1956; Backer-Dirks 1961; Beal 1971; Blinkhorn (unpublished); Holdcroft 1999; Loh 1996; Pot 1974). We found four studies to be at high risk. In two studies (Ast 1951; Maupome 2001), the outcome data for participants was substantially lower than at baseline. The Brown 1965 study, which ran from 1948 to 1959, sampled and examined children aged six to eight years up until 1957, but ceased this activity after 1957 as no significant differences were found to exist in that age group. The DHSS Scotland 1969 study did not present data for all children examined.

Selective reporting

We found 11 of the studies to be at high risk of bias for selective reporting. Four studies recorded data on dental fluorosis, but this was not reported (Arnold 1956; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969). Six studies did not report standard deviations (Arnold 1956; Blinkhorn (unpublished); DHSS England 1969; DHSS Wales 1969; Kunzel 1997; Tessier 1987), and Adriasola 1959 did not report complete baseline data for the proportion of caries-free children aged six, seven, 11 and 15 years. Eight studies were found to be at low risk of bias for this domain with all expected data having been reported (Beal 1971; Beal 1981; Brown 1965; Gray 2001; Guo 1984; Hardwick 1982; Kunzel 1997; Maupome 2001). For one study the risk of bias remains unclear (Holdcroft 1999).

Other bias

We found 12 studies to be at high risk of other bias; for ten of these studies this was due to an apparent lack of reliability or consistency of the outcome assessments in terms of either calibration of examiners or tests for inter- and intra-rater reliability (Arnold 1956; Ast 1951; Beal 1971; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Gray 2001; Guo 1984; Pot 1974; Tessier 1987). In the Gray 2001 study the baseline fluoridation status of the children was determined by the location of the school they attended, which may not have taken into account any children attending schools in fluoridated areas who residede outside those areas. We assessed four studies as being at unclear risk of bias (Beal 1981; Brown 1965; Holdcroft 1999; Maupome 2001). The remaining six studies were not assessed as having any other apparent risk of bias.

Dental fluorosis outcome

Of the 135 studies included for this outcome, we found 131 to be at high risk of bias and four to be at unclear risk overall (Ellwood 1995; Levine 1989; Milsom 1990; Stephen 2002). We judged no studies as being at low risk.

We assessed five studies as being at high risk for sampling bias, 60 as being at low risk of bias and the remainder as 'unclear'. We found the majority of studies (114) to be at high risk for confounding; we assessed 11 as being at low risk of bias for this domain. For detection bias, we assessed 103 as being at high risk of detection bias, and 15 at low risk of bias. Overall, we found studies to be at low risk of bias for incomplete outcome data (92), with only 12 assessed as being at high risk of bias. For selective reporting, we assessed 42 as being at high risk of bias, with 82 at low risk of bias. With regard to other bias, we assessed 48 studies as being at high risk, 66 at low risk and all others at unclear risk. In most cases the reason for studies having high risk of other bias was that they did not report on the reliability or consistency of the outcome assessments.

Effects of interventions

See: **Summary of findings for the main comparison**; **Summary of findings 2**

Caries

Nineteen studies met the inclusion criteria (18 fluoride initiation studies and one fluoride cessation studies), with 15 providing sufficient data for analysis of caries levels following a change in fluoridation status. Only one of these studies examined the effect of water fluoridation on adults (Pot 1974); the reported outcome for this study was the percentage of participants with dentures. There are no data to determine the effect of water fluoridation on caries levels in adults.

Four studies provided insufficient data for analysis (Backer-Dirks 1961; DHSS Scotland 1969; Loh 1996; Pot 1974).

Initiation of water fluoridation

The caries studies are presented in forest plots, sub-grouped according to when they were conducted (those conducted in 1975 or before, and those conducted after 1975; Figure 3; Figure 4; Figure 5; Figure 6). Given the limited data post-1975 and this being a post-hoc analysis, the results presented below are for the overall body of evidence for each outcome.

Figure 3. Initiation of water fluoridation compared with low/non-fluoridated water: change in dmft

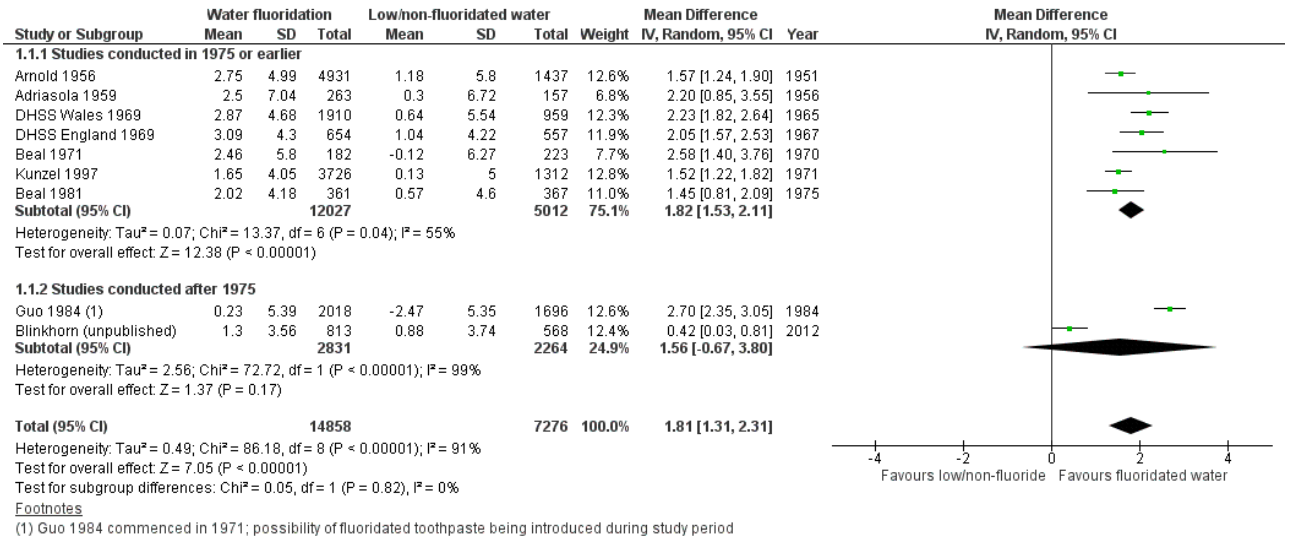


Figure 4. Initiation of water fluoridation compared with low/non-fluoridated water: change in DMFT

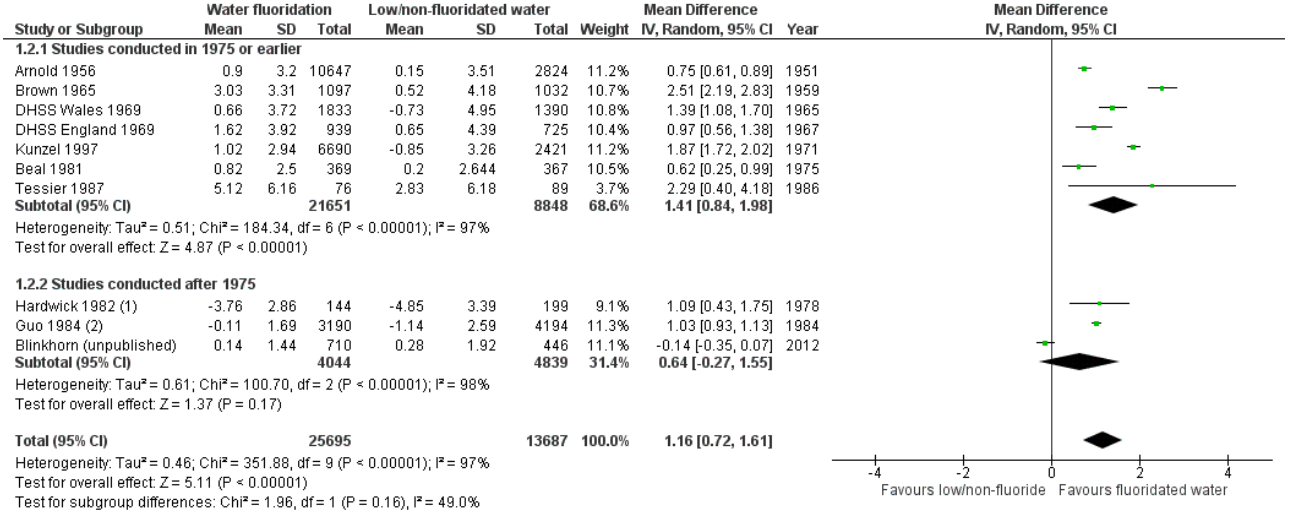
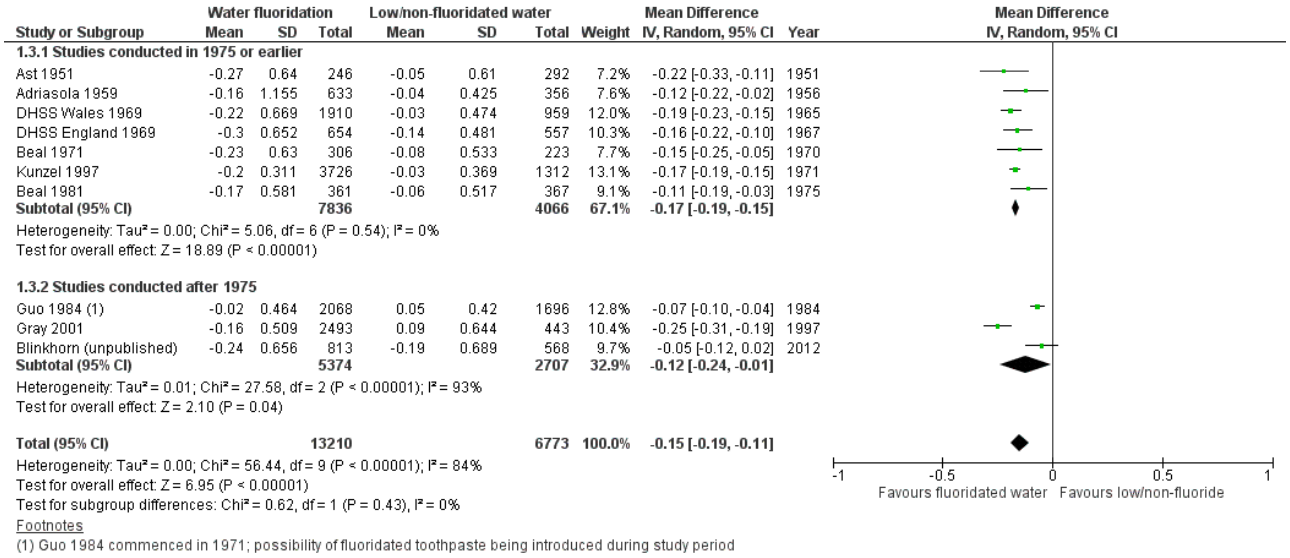
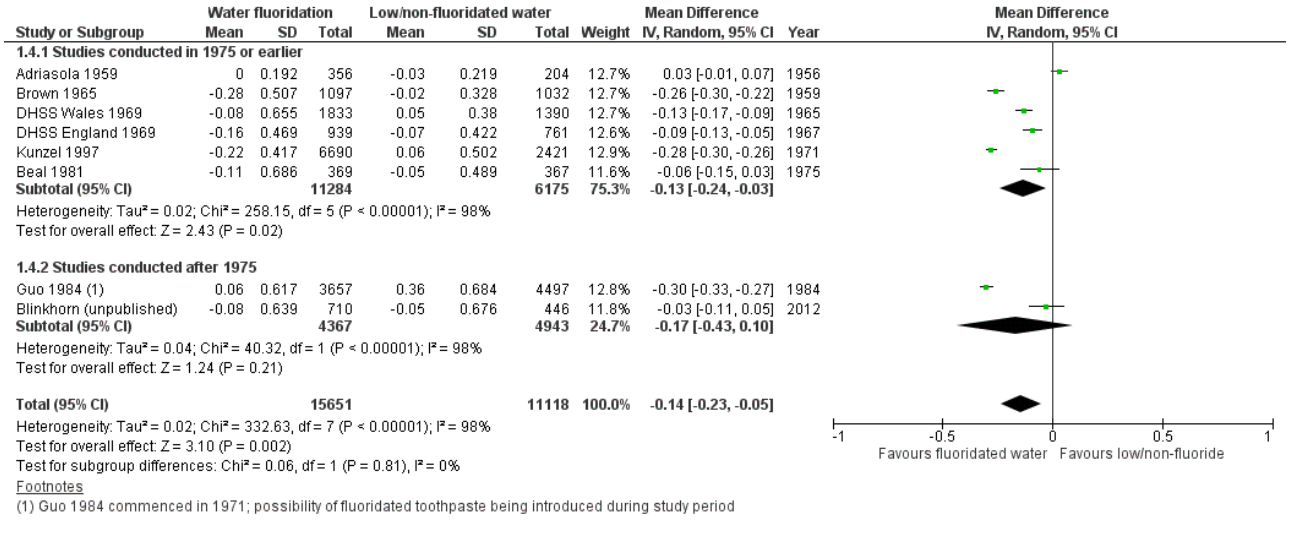


Figure 5. Initiation of water fluoridation compared with low/non-fluoridated water: change in proportion of caries-free children (deciduous teeth)



Footnotes
(1) Guo 1984 commenced in 1971; possibility of fluoridated toothpaste being introduced during study period

Figure 6. Initiation of water fluoridation compared with low/non-fluoridated water: change in proportion of caries-free children (permanent teeth)



Footnotes
(1) Guo 1984 commenced in 1971; possibility of fluoridated toothpaste being introduced during study period

Change in dmft/dmfs

Nine studies, with data from 44,268 participants, provided data for dmft (Adriasola 1959; Arnold 1956; Beal 1971; Beal 1981; Blinkhorn (unpublished); DHSS England 1969; DHSS Wales 1969; Guo 1984; Kunzel 1997). We judged all studies to be at high risk of bias and only two (22%) studies were conducted post-1975. Data collection following initiation of water fluoridation ranged from two to 12 years. Data did not allow for an evaluation of effect by duration of exposure to fluoridated water.

The mean difference in change in dmft was 1.81 (95% CI 1.31 to 2.31; P value < 0.00001; Figure 3). At final assessment, the dmft means for the control groups ranged from 1.21 to 7.8, with a median of 5.1. A mean reduction of 1.81 indicates a 35% reduction in dmft in the water fluoridation groups over and above that for the control groups. Although there was considerable heterogeneity (P value < 0.00001; I^2 = 91%), we decided to pool the data as all the mean difference estimates were in the same direction. Some of the heterogeneity is expected due to the large size of the studies ensuring narrow confidence intervals.

Sensitivity analysis, excluding studies with imputed standard deviations gave rise to a similar effect estimate, mean difference in change score 1.83 (95% CI 0.68 to 2.98; 5 studies).

There were no data for dmfs.

Change in DMFT/DMFS

Ten studies, with data from 78,764 participants, provided data for DMFT (Arnold 1956; Beal 1981; Blinkhorn (unpublished); Brown 1965; DHSS England 1969; DHSS Wales 1969; Guo 1984; Hardwick 1982; Kunzel 1997; Tessier 1987). We judged all the studies to be at high risk of bias and only three studies (30%) were conducted post-1975. Data collection following initiation of water fluoridation ranged from two to 11 years. Data did not allow for an evaluation of effect by duration of exposure to fluoridated water.

The mean difference in change in DMFT was 1.16 (95% CI 0.72 to 1.61; P value < 0.00001;Figure 4). At final assessment, the DMFT means for the control groups ranged from 0.71 to 5.5, with a median of 4.4. A mean reduction of 1.16 indicates a 26% reduction in DMFT in the water fluoridation groups over and above that for the control groups. It should be noted that in Guo 1984 the before mean DMFT values for both the control and water fluoridation groups were low at 0.8, and this increased in both groups, however the increase was greater for the control group. This explains why the changes are both negative. The data for Hardwick 1982 are mean DMFT increment data for both groups from the paper, following the same children over time. A lower increment was observed for the water fluoridation group and, as they are caries increments, they have been entered as negative values.

Although there was considerable heterogeneity (P value < 0.00001; I^2 = 97%), once again we decided to pool the data as all but one of the mean difference estimates were in the same direction (ranging from -0.14 to 2.51). Some of the heterogeneity is expected due to the large numbers in the studies ensuring narrow confidence intervals.

Sensitivity analysis in which we excluded studies with imputed standard deviations gave rise to a slightly larger effect estimate; mean difference in change score 1.32 (95% CI 0.53 to 2.11; 4 studies).

Only one study, with data from 343 participants, presented data on DMFS (Hardwick 1982). The study presented increment data for both groups, with a lower increment being observed for the water fluoridation group; mean difference 2.46 (95% CI 1.11 to 3.81).

Change in proportion of children caries free: deciduous dentition

Ten studies, with data from 39,966 children, provided data for the proportion of caries-free children for deciduous dentition (Adriasola 1959; Ast 1951; Beal 1971; Beal 1981; Blinkhorn (unpublished); DHSS England 1969; DHSS Wales 1969; Gray 2001; Guo 1984; Kunzel 1997). We judged all studies to be at high risk of bias. Three studies (30%) were published post-1975. For all studies combined, there was a 0.15 absolute increase in the proportion of caries-free children in fluoridated areas with mean difference 0.15 (95% CI 0.11 to 0.19; Figure 5). At final assessment, the proportion of caries-free children in the low/non-fluoridated areas ranged from 0.06 to 0.67, with a median of 0.22; an increase of 0.15 in the proportion of caries-free children could be considered substantial. There was considerable heterogeneity (P value < 0.00001; I^2 = 84%), but the value of Tau^2 from the random-effects analysis was low (< 0.001; mean differences ranged from 0.05 to 0.25). Therefore we decided to pool the data.

Change in proportion of children caries free: permanent dentition

Eight studies, with data from 53,538 participants, provided data for the proportion of caries-free children for permanent dentition (Adriasola 1959; Beal 1981; Blinkhorn (unpublished); Brown 1965; DHSS England 1969; DHSS Wales 1969; Guo 1984; Kunzel 1997). We judged all studies to be at high risk of bias and only two (25%) were conducted post-1975. There was a 0.14 absolute increase in the proportion of caries-free children in fluoridated areas with mean difference 0.14 (95% CI 0.05 to 0.23; Figure 6). At final assessment, the proportion of caries-free children in the low/non-fluoridated areas ranged from 0.01 to 0.67, with a median of 0.14; the increase of 0.14 doubles this. There was considerable heterogeneity (P value < 0.00001; I^2 = 98%), but the value of Tau from the random-effects analysis was low at 0.02 (mean differences ranged from -0.03 to 0.30). Therefore we decided to pool the data.

Other caries measures

We did not include four studies that met the inclusion criteria in the quantitative analysis (Backer-Dirks 1961; DHSS Scotland 1969; Loh 1996; Pot 1974). We judged all studies to be at high risk of bias and excluded them from the analysis due to insufficient data (e.g. no data on number of participants evaluated) or different measures of caries, or both. The Backer-Dirks 1961 study reported dentinal approximal lesions as the caries measure, while Pot 1974 reported the percentage with false teeth. The other two studies did not report on the number of participants (DHSS Scotland 1969; Loh 1996). Three of the studies assessing children between the ages of four and 15 years showed a reduction in caries following the initiation of water fluoridation (Backer-Dirks 1961; DHSS Scotland 1969; Loh 1996). Pot 1974 assessed participants between five and 55 years of age and showed an increase in percentage with dentures following fluoridation.

Cessation of water fluoridation

Change in DMFT/DMFS

Only one study, at high risk of bias, presented data on DMFS: the Maupome 2001 fluoride cessation study was conducted over three years. The study was conducted in a population with "generally low caries experience, living in an affluent setting with widely accessible dental services". The results did not demonstrate an increase in caries in the children in the fluoride-ended group compared with the still-fluoridated group, in fact there was a statistically significant decrease in caries severity (including incipient and cavitated lesions) for the fluoride-ended group, which was not found in the still-fluoridated group, for both of the age groups examined. A complex pattern of disease was found when different caries indices were examined.

No studies that met the inclusion criteria reported on change in dmft or proportion of caries-free children (deciduous/permanent dentition) following the cessation of water fluoridation.

Disparities across social class

Three included studies' reported on the effect of water fluoridation on disparities in caries across social class (Beal 1971; Gray 2001; Holdcroft 1999; Table 6). The number of participants was reported in only two of the studies (Beal 1971; Gray 2001). The total number of participants measured for caries in these studies was 35,399. The studies focused on the initiation of water fluoridation in study areas that were reasonably comparable. Measures of caries reported in the studies were dmft, deft and percentage caries-free subjects. All three studies were judged to be at high risk of bias.

Beal 1971 studied three areas, in two of which water fluoridation was initiated (one classed as 'poor' and the other 'industrial').

The control group was classed as 'industrial'. Given the lack of a validated measure of deprivation, and without knowing the composition of the groups under comparison, it is not possible to draw conclusions from this study.

Holdcroft 1999 and Gray 2001 both used the Jarman score (an index to measure socioeconomic variation across small geographical areas, originally developed as a measure of General Practice workload; a positive score equates to deprivation). The Holdcroft 1999 study contained insufficient information about fluoride levels at baseline or follow-up and the number of participants measured at each time point was unclear. In both studies the Jarman scores at baseline for the control (non-fluoridated areas) were all less than zero. The Jarman scores at baseline in the fluoridated areas ranged from -7.85 to 15.03 in the Holdcroft 1999 study, and from -23.09 to 21.57 in the Gray 2001 study.

Given the reasons above we are unable to draw robust conclusions about the initiation of water fluoridation and its effect on disparities in caries across social class.

Dental fluorosis

Aesthetic concern

Fluoride levels of 5 ppm or less

We included 40 studies, at high risk of bias, that reported data from 59,630 participants in the analysis of dental fluorosis of aesthetic concern. The reported fluoride exposure ranged from 0 to 4.9 ppm with a mean of 0.80 ppm (SD 0.90).

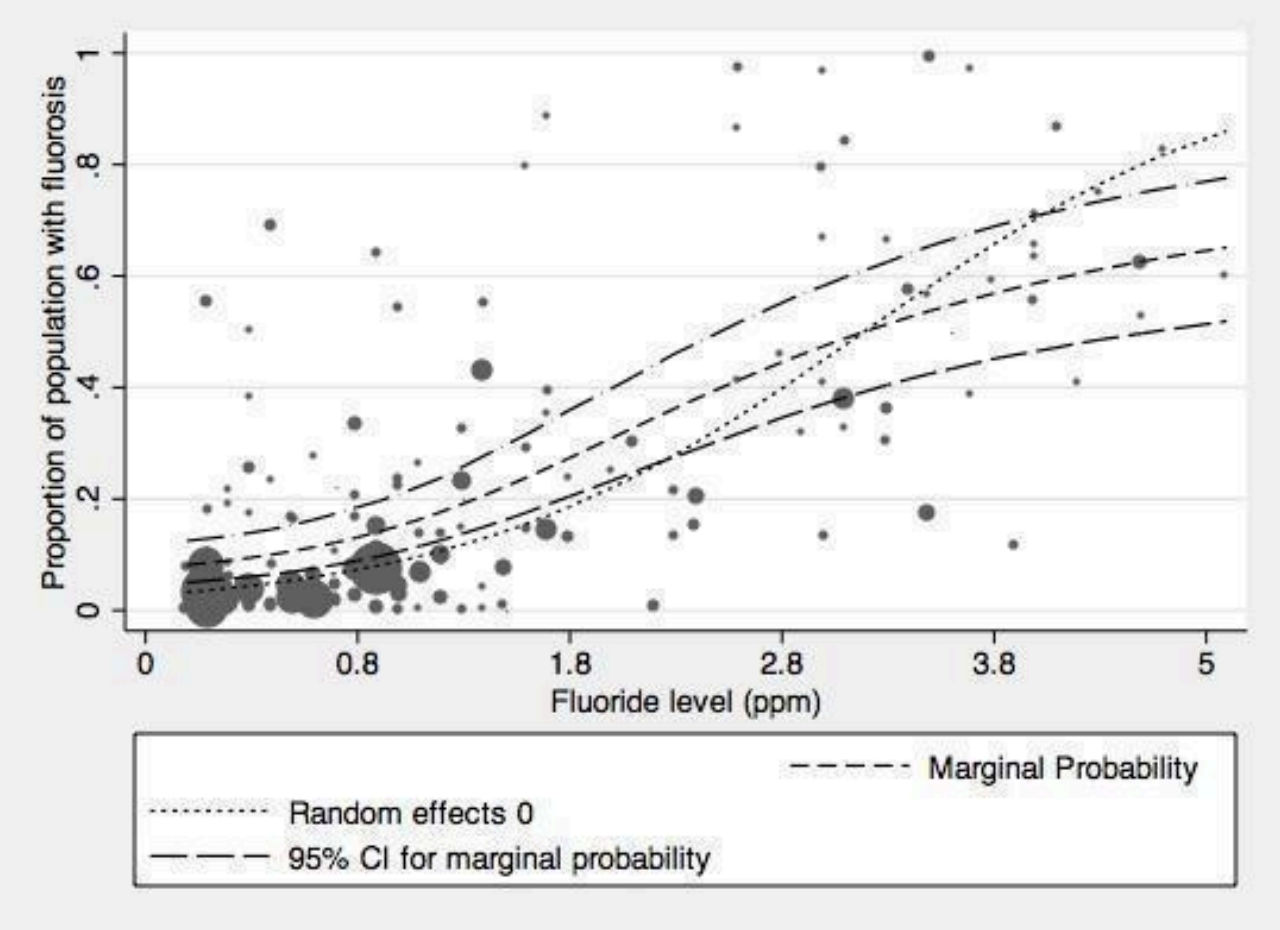
In order to assess the assumption of linearity we plotted the log odds of the prevalence of dental fluorosis with fluoride level and with log of fluoride level (not shown). A positive linear relationship could be assumed in both cases, indicating that as fluoride levels increase so does the prevalence of dental fluorosis. The reported fluoride level was used as a predictor rather than the log of reported fluoride exposure. This was then centred by taking away the grand mean (0.80) from the reported fluoride level.

Caterpillar plots (not shown) of the residuals for slope and intercept indicated that many of the studies differed significantly from the average (random effects at zero) at the 0.05 level of significance. The effect of fluoride exposure was positive and statistically significant; a higher prevalence of dental fluorosis is associated with increased fluoride exposure (OR 2.90, 95% CI 2.05 to 4.10). When controlling for study effects, we would expect the odds of dental fluorosis to increase by a factor of 2.90 for each one unit increase in fluoride exposure.

The random intercept and random slope model indicated that the effect of fluoride exposure differed across studies. The statistically significant negative covariance of -0.82 implies that studies with a higher than average probability of dental fluorosis tend to have a more shallow slope.

The results presented so far have been based on study-specific values. This is indicated in the following graphic, where the random effects of intercept and slope are set to zero, in effect the plotted prevalence of dental fluorosis in an 'average' study. An alternative approach is to calculate the prevalence of dental fluorosis in all studies combined, to obtain the marginal probability of dental fluorosis. The study-specific values indicate the probability of dental fluorosis in terms of 'any given participant' whereas the marginal probabilities indicate the probability of dental fluorosis 'among the participants' (Figure 7).

Figure 7. Proportion of the population with dental fluorosis of aesthetic concern by water fluoride level together with 95% confidence limits for the proportion (studies reporting up to and including 5ppm).



The marginal probabilities of dental fluorosis of aesthetic concern at different fluoride levels are given below.

Fluoride exposure (ppm)	Probability of dental fluorosis of aesthetic concern (95% CI)
0.1	0.08 (0.05 to 0.12)
0.2	0.09 (0.06 to 0.13)
0.4	0.10 (0.06 to 0.15)
0.7	0.12 (0.08 to 0.17)
1	0.15 (0.11 to 0.21)
1.2	0.18 (0.13 to 0.24)
2	0.31 (0.23 to 0.40)
4	0.59 (0.46 to 0.71)

All fluoride levels

The analysis of dental fluorosis of aesthetic concern at all reported fluoride exposure was based on 60,030 observations from 40 studies. The reported fluoride levels ranged from 0 to 7.6 ppm with a mean of 0.85 ppm (SD 1.03).There was very little difference in the results from the analysis restricted to 5 ppm or less. The effect of fluoride exposure is positive and statistically significant; a higher prevalence of dental fluorosis is associated with increased fluoride exposure (OR 2.84, 95% CI 2.00 to 4.03). When controlling for study effects, we would expect the odds of dental fluorosis to increase by a factor of 2.84 for each one unit increase in fluoride level (1 ppm F).

Any dental fluorosis

Fluoride levels of 5 ppm or less

We included 90 studies, at high risk of bias, that reported data from 180,530 participants in this analysis. The reported fluoride levels in the studies ranged from 0 to 5 ppm, with a mean of 1.22 ppm (SD 0.92). When restricted to studies reporting fluoride exposure of 5 ppm or less, there is a clearer positive relationship between the proportion of children with dental fluorosis and fluoride level.

The relationship between the log odds of dental fluorosis and fluoride level and log fluoride level were both approximately linear. Consequently the reported fluoride exposure was used as a predictor rather than the log of reported fluoride exposure. This was then centred by taking away the grand mean (1.22) from the reported fluoride exposure level.

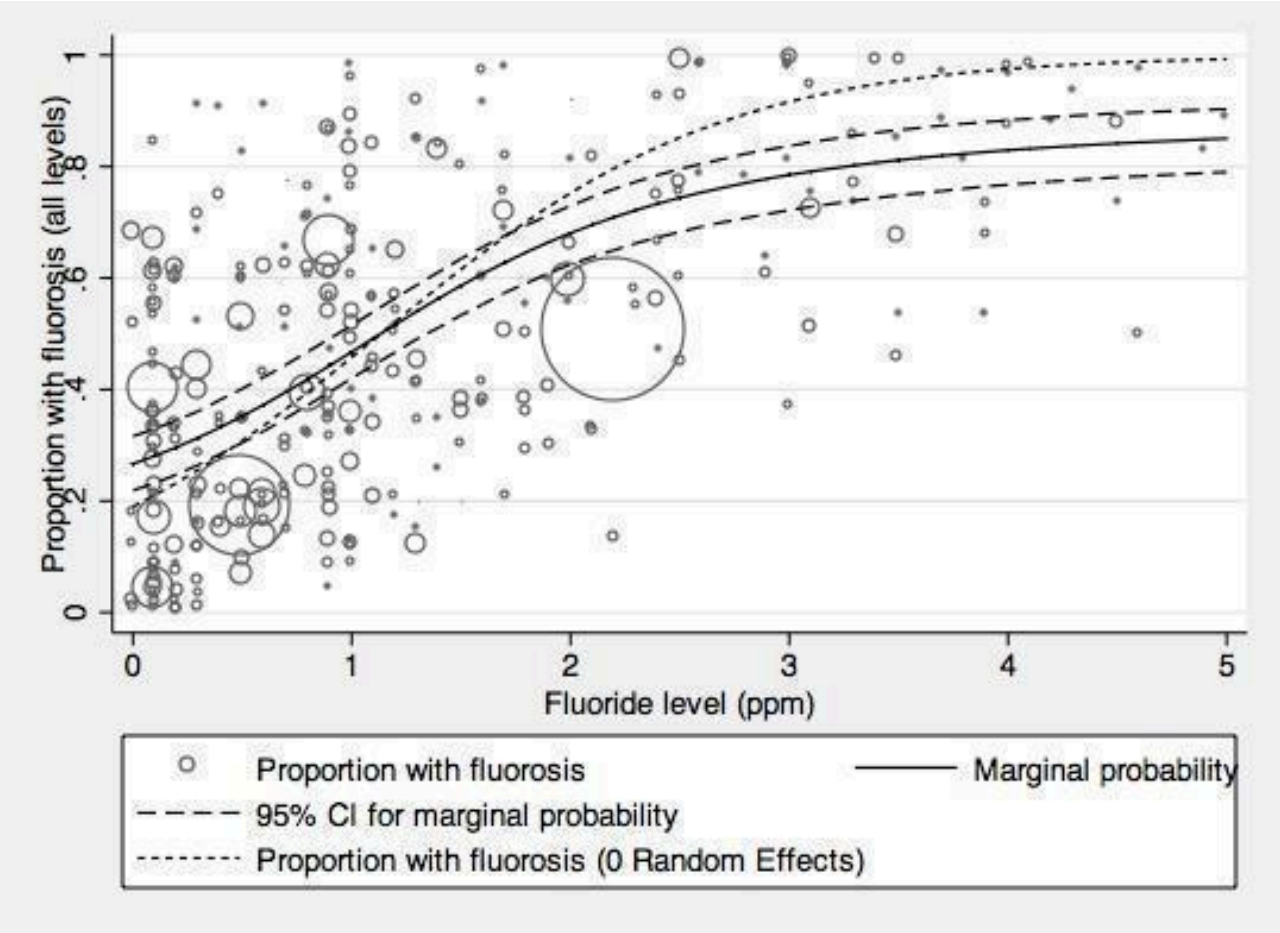
The effect of fluoride exposure is positive and statistically significant; a higher prevalence of dental fluorosis is associated with increased fluoride exposure (OR 3.60, 95% CI 2.86 to 4.53). Controlling for study effects, we would expect the odds of dental fluorosis to increase by a factor of 3.60 for each one unit increase in fluoride exposure (1 ppm F).

The random intercept and random slope model indicated that the effect of fluoride exposure differed across studies. The statistically significant negative covariance of -1.05 implies that studies with a higher than average probability of dental fluorosis tend to have a more shallow slope.

The results presented so far have been based on study-specific values. This is indicated in the following graph, where the random effects of intercept and slope are set to zero, in effect the plotted prevalence of dental fluorosis in an 'average' study

(Figure 8).

Figure 8. Proportion of the population with dental fluorosis of any level by water fluoride level together with 95% confidence limits for the proportion (studies reporting up to and including 5ppm F)



The marginal probabilities of any dental fluorosis are presented in the table below.

Fluoride exposure (ppm)	Probability of any dental fluorosis (95% CI)
0.1	0.28 (0.23 to 0.33)
0.2	0.30 (0.25 to 0.34)
0.4	0.33 (0.28 to 0.38)
0.7	0.40 (0.35 to 0.44)
1	0.47 (0.42 to 0.52)
1.2	0.52 (0.47 to 0.56)
2	0.68 (0.62 to 0.73)
4	0.83 (0.77 to 0.88)

All fluoride levels

We included 90 studies that reported data from 182,233 participants in this analysis. The reported fluoride levels ranged from 0 to 14 ppm with a mean fluoride level of 1.28 ppm (SD 1.11). There was little change in the pooled estimates when all fluoride levels were included in the analysis. The effect of fluoride exposure is positive and statistically significant; a higher prevalence of dental fluorosis is associated with increased fluoride exposure (OR 3.13, 95% CI 2.55 to 3.85). When controlling for study effects, we would expect the odds of dental fluorosis to increase by a factor of 3.13 for each one unit increase in fluoride exposure (1 ppm F).

The statistically significant negative covariance of -0.87 implies that studies with a higher than average probability of dental fluorosis tend to have a shallower slope. The between study variance increases as fluoride level increases.

Post hoc analysis

We used a multivariate analysis to investigate possible sources of heterogeneity in the model. We explored the effects of source of fluoride and its interaction with fluoride concentration by including them as fixed covariates in the models above. Source of fluoride was classed as natural or artificial. We excluded studies that reported mixed sources of fluoridation, or where the source of fluoridation was not reported, from the analysis. This analysis was carried out separately for the outcomes of fluorosis and fluorosis of aesthetic concern, and for studies reporting fluoride concentrations at any level and restricted to 5 ppm or less.

The results from the models with the additional covariates and the ones containing fluoride concentration only as a covariate are not directly comparable, as the additional covariate analyses included fewer studies due to missing data (source of fluoride). For fluorosis of aesthetic concern at all concentrations, fluoride concentration and source of fluoride explain a proportion of the variation between estimates, whereas the interaction between these estimates does not (the OR for fluorosis due to fluoridation becomes 3.16 (95% CI 2.12 to 4.71) when controlling for source of fluoride (OR 0.25, 95% CI 0.09 to 0.70) and interaction (OR 1.89, 95% CI 0.74 to 4.82). The conclusions are the same for fluorosis of aesthetic concern at fluoride concentrations of 5 ppm or less (the OR for fluorosis due to fluoridation becomes 3.22 (95% CI 2.16 to 4.79) when controlling for source of fluoride (OR 0.25, 95% CI 0.10 to 0.70) and interaction (OR 1.82, 95% CI 0.71 to 4.62)).

For the outcome of fluorosis at all levels, the additional covariates do not contribute significantly to the model.

Other dental fluorosis studies

Approximately one third of the dental fluorosis studies that met the review's inclusion criteria did not report data in a way that allowed for further analysis (Appendix 11).

Other adverse effects reported in the included studies

Five studies that reported on dental fluorosis also presented data on the association of water fluoridation with skeletal fluorosis (Chen 1993; Jolly 1971; Wang 2012), bone fracture (Alarcon-Herrera 2001), and skeletal maturity (Wenzel 1982), in participants between the ages of six and over 66 years. Four of the studies included a total of 596,410 participants (Alarcon-Herrera 2001; Chen 1993; Wang 2012; Wenzel 1982), and fluoride concentration in all four studies ranged from less than 0.2 ppm to 14 ppm. The studies were all at high risk of bias and we did not analyse their results further (Table 5).

DISCUSSION

Summary of main results

Of the 155 studies that met the inclusion criteria, 107 studies provided sufficient data for quantitative synthesis. Fourteen studies provided adequate data for the assessment of the effect of the initiation of a water fluoridation programme on dental caries, one study focused on the effect of the cessation of water

fluoridation. Although three studies evaluated disparities in dental caries across social class, no data were suitable for further analysis. Ninety studies provided sufficient data for inclusion in the analysis of dental fluorosis of any level (40 in the analysis of dental fluorosis of aesthetic concern).

Our confidence in the size of the effect estimates obtained for the prevention of caries is limited (see Quality of the evidence and Summary of findings for the main comparison; Summary of findings 2).

The results from the caries severity data indicate that the initiation of water fluoridation results in reductions in the order of 1.8 dmft and 1.2 DMFT for deciduous and permanent dentitions. This translates to reductions of 35% and 26% compared to the median control group mean values. In addition, there was an increase in the percentage of children who were caries free (15% increase when evaluating deciduous dentition and 14% in the permanent dentition).

There is insufficient information to determine whether initiation of a water fluoridation programme results in a change in disparities in caries levels across SES.

There is insufficient information to determine the effect of stopping water fluoridation programmes on caries levels.

There were no studies that met the review's inclusion criteria that investigated the effectiveness of water fluoridation for preventing caries in adults.

With regard to dental fluorosis, the percentage of participants with dental fluorosis of aesthetic concern was estimated to be approximately 12% for a fluoride level of 0.7 ppm. This increases to 40% when considering dental fluorosis of any level, however, this includes fluorosis that can only be detected under very controlled, clinical conditions and other enamel defects.

Adverse effects, other than dental fluorosis, were rarely reported in the included studies.

Overall completeness and applicability of evidence

The applicability of the evidence on water fluoridation to today's societies is unclear and highly likely to vary according to setting.

The evidence included in the review pertains to caries in children only. Only one study, that met the review's inclusion criteria, examined the effect of water fluoridation on adults (Pot 1974); the reported outcome for this study was the percentage of participants with dentures. There are no data to determine the effect of water fluoridation on caries levels in adults. Research, utilising data from 26 countries, indicates that dental caries levels in permanent dentition in adults are significantly higher than in children (Bernabe 2014). It has been suggested that greater attention needs to be directed at preventing caries at all stages of life, not just childhood.

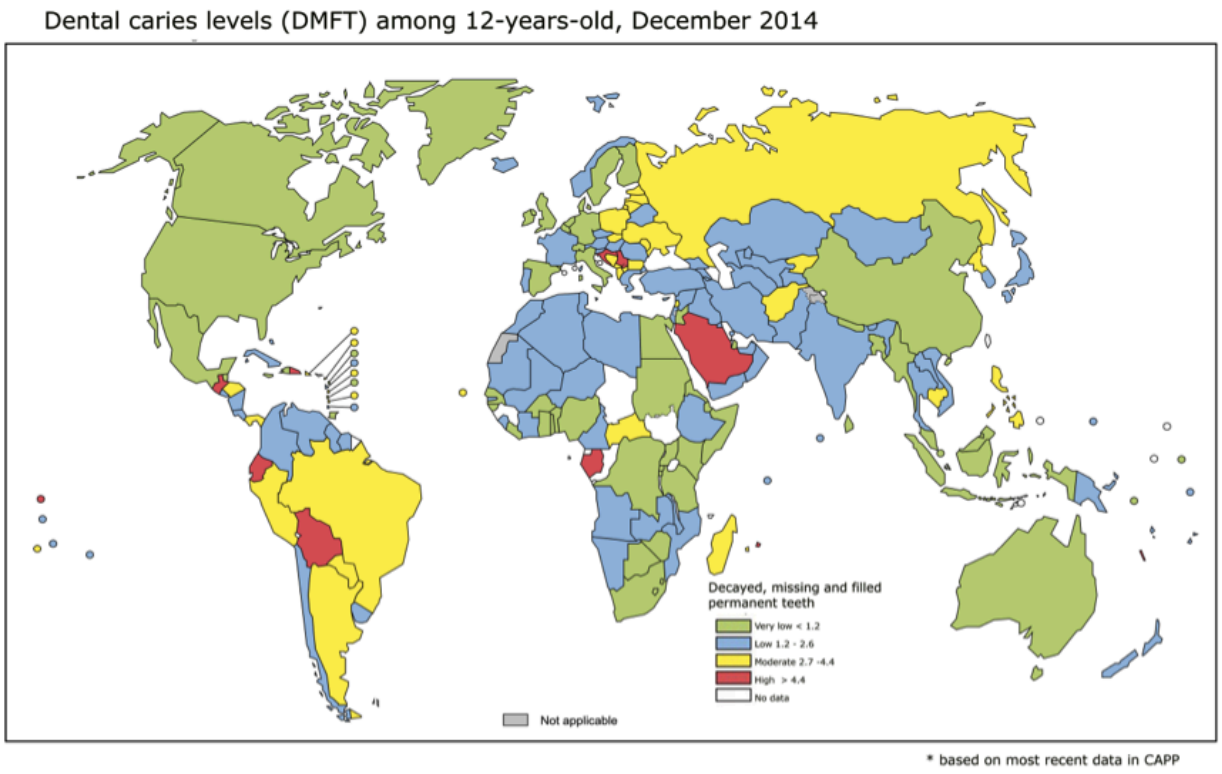
Approximately 71% of the included caries studies that evaluated the initiation of water fluoridation were conducted prior to 1975.

In developed countries, the widespread use of fluoride toothpastes from the mid to late 1970s, along with increased access to other caries-preventive strategies of proven effectiveness, such as fluoride varnishes (Marinho 2013), and dental sealants (Ahovuo-Saloranta 2013), may mean that the benefit of water fluoridation is reduced in such populations. However, the Marinho 2003a review evaluated the effect of topical fluorides for preventing dental caries in children and adolescents, and found no evidence that the effect of topical fluoride was dependent on background exposure to other fluoride sources. The reviewers did find evidence that the relative effect of topical fluoride may be greater in those who have higher baseline levels of caries.

Globally, caries levels have been reducing. In 1980 the global DMFT for 12 year olds was estimated to be 2.43 (Leclercq 1987). In 2011, this global estimate had reduced to 1.67 DMFT (although there is variation by World Health Organisation region; Table 7). Within the studies included in the review, the mean values for DMFT at follow-up in the non-fluoridated areas were higher, ranging from 0.7 to 5.5.

Figure 9 shows global dental caries levels (DMFT) among 12 year olds. Out of the 189 countries that provided data, 148 (78%) have a DMFT of 3 or less. Areas where a large percentage of the population (more than 60%) receive fluoridated water (either natural or artificial fluoridation) include: North America, Australasia, parts of South America (namely Brazil, Columbia and Chile), the Republic of Ireland, and Malaysia. Whilst these areas tend to have low to very low DMFT (Figure 9), there are many other parts of the world where fluoridated water is not widespread that also have low caries levels. Equally, there are areas with relatively high distribution of water fluoridation and moderate caries levels (e.g. Brazil).

Figure 9. Source:CAPP database, 2015



The applicability of the evidence around water fluoridation has to be considered in the context of reductions in caries levels over time, the uptake of other strategies proven to prevent caries, and global changes in patterns of food consumption (Kearney 2010). Annual sugar consumption, specifically, has risen dramatically since the start of the 20th century when it was approximately 5.1 kg per capita. The consumption of sugar continues to rise with the average sugar consumption now estimated at 23 kg per capita; the greatest rates of growth are currently seen in Asia, the Middle East and Africa (SucDen 2015). In addition, in many parts of the world more industrially processed foods are consumed, with less food being prepared and cooked in the home using locally sourced water (Slimani 2009). Variation in fluoride concentrations in water across regions and countries, and the increase in processed foods and beverages and their transportation, make it difficult to assess dietary fluoride intake. Such changes may mean that, although the tap water is fluoridated in a particular area, some members of the population do not consume a sufficient volume, either through beverages or foods prepared with tap water, to provide a benefit to their oral health.

Ten of the 14 studies used in the analysis of water fluoridation initiation schemes included lifetime residents only. Whilst this is a valid approach it evaluates the absolute effect rather than the benefit to the whole population. The effect size shown in the review may, therefore, be larger than that found in the population, depending on population movement/migration.

There was limited reporting of adverse effects, other than dental fluorosis, in the included studies. The broader literature speculates about harms associated with higher levels of fluoride in water (e.g. cancer, lowered intelligence, endocrine dysfunction), however, there has been insufficient evidence to draw conclusions (MRC 2002).

Quality of the evidence

The GRADE approach was used to assess the quality of the evidence within the review. GRADE has developed over recent years as an internationally recognised framework for systematically evaluating the quality of evidence within both systematic reviews and guidelines. It aims to overcome the confusion that arises from having multiple systems for grading evidence and recommendations, and, because of this key aim, the GRADE working group discourages the use of modified GRADE approaches. However, there has been much debate around the appropriateness of GRADE when applied to public health interventions, particularly for research questions where evidence from randomised controlled trials is never going to be available due to the unfeasibility of conducting such trials. Community water fluoridation is one such area.

When applying GRADE to non-randomised studies, the quality of the evidence automatically starts at 'low', as opposed to 'high' for RCTs. There has been some criticism of GRADE with regard to its inability to discriminate between stronger and weaker

observational designs (Rehfuess 2013). It has been proposed that certain designs, such as quasi-experimental designs and interrupted-time-series studies should begin at 'moderate' quality. Indeed, WHO have previously employed such a modified approach (Bruce 2014). Others suggest that starting non-randomised studies at 'low' simply acknowledges our reduced certainty that observed effects are actually due to the intervention itself. With regard to the current review, using a modified approach to differentiate between stronger and weaker study designs would have no impact on the overall quality assessment as the study designs would still not merit commencing at 'moderate'.

Another concern about applying GRADE is the limited possibilities for 'upgrading' the quality of evidence from observational studies. Modified approaches to GRADE have incorporated the option to upgrade for consistency in findings (Bruce 2014). Within the current review, it was not felt appropriate to upgrade for consistency as there was statistically significant heterogeneity present in all four caries analyses. However, given that the direction of effect was the same for all but one of the outcomes in one of the studies, we have not downgraded with regard to inconsistency.

In our review protocol we stated that we would produce a 'Summary of findings' table, applying the GRADE criteria. We have attempted to be transparent in our decisions regarding the downgrading/upgrading of the quality of the evidence, and feel our decisions are justified. The quality of the evidence, when GRADE criteria are applied, is judged to be low. However, we accept that the terminology of 'low quality' for evidence may appear too judgmental. We acknowledge that studies on water fluoridation, as for many public health interventions, are complex to undertake and that researchers are often constrained in their study design by practical considerations. For many public health interventions, the GRADE framework will always result in a rating of low or very low quality. Decision makers need to recognise that for some areas of research, the quality of the evidence will never be 'high' and that, as for any intervention, the recommendation for its use depends not just upon the quality of the evidence but also on factors such as acceptability and cost-effectiveness (Burford 2012). In order to overcome some of the concerns around the use of GRADE within this review, a decision was made to omit the GRADE terminology of 'low quality' and discuss the findings in terms of our confidence in the results.

With regard to the caries outcomes, all included studies were observational and our confidence in the effect estimate is limited. We downgraded the quality of the evidence due to an overall high risk of bias in the included studies (excluding domains associated with randomisation, allocation concealment, blinding of participants). The main areas of concern were confounding and lack of blind outcome assessment. The evidence was additionally downgraded for indirectness due to the fact that about 71% of the caries studies that evaluated the initiation of water fluoridation were conducted prior to 1975 (Overall completeness and applicability of evidence). Present day reductions in caries may be of a smaller magnitude in developed countries. Also, there were no included studies evaluating caries levels in adults. There was statistically significant heterogeneity present in all four caries analyses (Analysis 1.1; Analysis 1.2; Analysis 1.3; Analysis 1.4), with I^2 statistics of 84% or more. However, given that the direction of effect was the same for all but one of the outcomes in one of the studies, we have not downgraded with regard to inconsistency. The study showing an effect in the opposite direction was the most recently conducted study, with low baseline caries levels, and, as yet, the shortest duration of follow-up (Blinkhorn (unpublished)); both these factors could influence the effect estimate. It is also possible, given the widespread coverage of fluoridated water in Australia, that the low baseline caries reflects diffusion of fluoride from other areas through commercial foods and beverages.

With regard to dental fluorosis, again, all studies were observational and we downgraded the quality of the evidence due to an overall high risk of bias and inconsistency due to substantial between-study variation. Our confidence in the effect estimate is limited.

Potential biases in the review process

Within the review, water with a fluoride concentration of 0.4 ppm or less was classified as non-fluoridated. This cut-off was arbitrary, based on a priori clinical judgement. It is acknowledged that that this cut-off might be high for equivalence of non-fluoridation in hot climates. In practice, only one of the 15 studies that provided sufficient data for analysis of caries levels following a change in fluoridation status had a fluoride concentration greater than 0.2 ppm in the non-fluoridated area.

We imputed the standard deviation for four studies included in the analysis of water fluoridation for preventing caries (dmft and DMFT). This was not prespecified in the protocol. The equation for imputing the standard deviations was estimated from available data where the standard deviations were given (Appendix 10). Sensitivity analysis, excluding those studies for which the standard deviation had been imputed gave similar results.

An arbitrary cut-off date of 1975 was used as an indication of when fluoridated toothpaste use became widespread in industrialised countries. There is no indication in the included studies of the extent to which this is true.

We only reported on dmft in children eight years old and younger. This decision was based on clinical judgement, but was not prespecified in the protocol. The cut-off is unlikely to alter the review's findings as very little data was excluded due to this cut-off.

When analysing the dental fluorosis data, our primary analysis focused on fluoride concentrations of 5 ppm or less. Again, this was an arbitrary cut-off; there was little difference in the results obtained when all fluoride concentrations were examined.

Agreements and disagreements with other studies or reviews

The most widely recognised systematic review of water fluoridation was published in 2000 (McDonagh 2000). Our review aimed to update this review, but has adopted different methods in certain areas. Importantly, these included changes to the evaluation of the cessation of water fluoridation programmes and the evaluation of disparities in caries levels.

The McDonagh 2000 review included 26 studies that looked at the effect of water fluoridation on oral health. No pooling of data was undertaken. The mean difference in change in dmft/DMFT and increase in proportion of caries-free children were presented for selected ages/age groups. The range of mean reduction in dmft/DMFT score was from 0.5 to 4.4, with a median of 2.25 dmft/DMFT. In

our review, we did undertake statistical pooling, imputing standard deviations where necessary. Rather than selecting specific ages from the data provided in the included studies, we undertook the analyses by dentition, utilising all data for deciduous teeth for children aged eight years and younger, and all available data for permanent teeth. The analyses showed mean reductions of 1.81 in dmft and 1.16 in DMFT, due to water fluoridation.

In terms of the proportion of caries-free children following water fluoridation, the McDonagh 2000 review reported a range of mean differences from -0.05 to an increase of 0.64, with a median of 0.15. The pooled estimate obtained in our review demonstrates an increase in proportion of caries-free children in the areas with water fluoridation of 0.15 for deciduous teeth and 0.14 for permanent teeth.

With regard to the cessation of water fluoridation programmes, the McDonagh 2000 review included eight studies, whereas our review included only one (Maupome 2001). This difference is due to the inappropriate choice of control group in the cessation studies. In a controlled before-and-after study, the groups should be comparable at baseline. Therefore, in the water fluoridation cessation studies, the two groups should both be fluoridated areas, one of which (the 'intervention' group) subsequently has the fluoride removed from the water. The area that remains fluoridated acts as the control. In the majority of the cessation studies, a non-fluoridated area was used as the control at baseline. The intervention and control groups, therefore, were not comparable at the start of the study. Whilst the McDonagh 2000 review suggested that caries prevalence increases following the withdrawal of water fluoridation, this result was not confirmed in the study included in our review.

Neither the McDonagh 2000 review nor our review included studies that evaluated the effectiveness of water fluoridation for preventing caries in adults. However, Griffin 2007 undertook a comprehensive systematic review evaluating the effectiveness of fluoride in preventing caries in adults, including nine studies that examined the effectiveness of water fluoridation. The studies included fell outside the scope of both the McDonagh 2000 review and our review. One of the nine studies they included was a prospective cohort trial, and the remaining eight were cross-sectional studies, with single time-point data. In our review, we only included studies that reported caries data if they had a concurrent control, with at least two points in time evaluated. In the analyses, Griffin 2007 demonstrated a prevented fraction of 34.6% (95% CI 12.6% to 51.0%), when pooling data from seven studies of lifelong residents of control or fluoridated-water communities (5409 participants). When the analysis was limited to studies published after 1979 the prevented fraction was 27.2% (95% CI 19.4% to 34.3%; 5 studies; 2530 participants). The most recent of these post-1979 papers was published in 1992. The fluoride concentration evaluated in these more recent studies was not reported in two studies and was above what is considered the 'optimal level' in a further two studies. Griffin and colleagues acknowledge that the paucity of studies and the quality of the included studies limits their review.

A more recent evaluation of the effects of fluoridated drinking water on dental caries in adults has been conducted in Australia (Slade 2013). A comparison in caries levels was made between a cohort of adults born before the widespread implementation of fluoridation (before 1960; n = 2270) and a cohort born after widespread implementation (n = 1509). Greater lifetime exposure to water fluoridation was associated with lower levels of caries experience in both cohorts. In the study, 31% of participants were excluded from the complete-case analysis due to missing data. The authors report that imputation to account for missing data "did not markedly alter estimated associations between fluoride exposure and caries experience" (Slade 2013).

When addressing the issue of whether water fluoridation results in a reduction in disparities in caries levels across different groups of people, the McDonagh 2000 review included 15 studies, all except two of which were cross-sectional surveys. The authors concluded that, based on a small number of low quality, heterogeneous studies, there was "some evidence that water fluoridation reduces the inequalities in dental health across social classes in five and 12 year-olds, using the dmft/DMFT measure. This effect was not seen in the proportion of caries-free children among five year-olds. The data for the effects in children of other ages did not show an effect." They suggested caution in interpreting these results due to the small number of studies and their low quality rating (McDonagh 2000). There were no data for disparities in caries levels amongst adults.

The cross-sectional studies, whilst able to provide information on whether water fluoridation is associated with a reduction in disparities, are not able to address the question of whether water fluoridation results in a reduction in disparities in caries levels. There were insufficient data to determine whether initiation of a water fluoridation programme results in a change in disparities in caries levels across different groups of people.

In the past 20 years, the majority of research evaluating the effectiveness of water fluoridation for the prevention of dental caries has been undertaken using cross-sectional studies with concurrent control, with improved statistical handling of confounding factors (Rugg-Gunn 2012). We acknowledge that there may be concerns regarding the exclusion of these studies from the current review. A previous review of these cross-sectional studies has shown a smaller measured effect in studies post-1990 than was seen in earlier studies, although the effect remains significant. It is suggested that this reduction in size of effect may be due to the diffusion effect (Rugg-Gunn 2012); this is likely to only occur in areas where a high proportion of the population already receive fluoridated water. The authors of the review conclude that "There is need for further thought to strengthen study design" (Rugg-Gunn 2012).

The results from our review of the dental fluorosis data are fairly comparable with those of the McDonagh 2000 review. The McDonagh 2000 review fluorosis analysis excluded areas with natural fluoride levels above 5 ppm. It was acknowledged that this is significantly above the level recommended for artificial fluoridation, however the range of concentration of 0 ppm to 5 ppm allowed exploration of a dose-response relationship. In the current review, we also conducted analyses of studies of fluoride concentrations of 5 ppm or lower, in addition to an analyses of all studies irrespective of fluoride concentrations. In the McDonagh 2000 review, the estimated percentage of the population with dental fluorosis of aesthetic concern at a fluoride concentration of 0.7 ppm was 9% (95% CI 4% to 17%; based on studies with fluoride concentration of 5 ppm or lower); in our review this was slightly higher at 12% (95% CI 8% to 17%). There was little change in

the pooled estimates when all fluoride levels were included in the analysis.

The broader literature speculates about harms associated with higher levels of fluoride in water (e.g. cancer, lowered intelligence, endocrine dysfunction). These harms have not been systematically evaluated in this review, however, previous reviews suggest there is insufficient evidence to draw conclusions about them (MRC 2002; NHMRC 2007).

AUTHORS' CONCLUSIONS

Implications for practice

There is very little contemporary evidence, meeting the review's inclusion criteria, evaluating the effectiveness of water fluoridation for the prevention of caries.

The data come predominantly from studies conducted prior to 1975, and indicate that water fluoridation is effective at reducing caries levels in both the deciduous and permanent dentition in children. Our confidence in the size of the effect estimates is limited by the observational nature of the study designs, the high risk of bias within the studies, and, importantly, the applicability of the evidence to current lifestyles. The decision to implement a water fluoridation programme relies upon an understanding of the population's oral health behaviours (e.g. use of fluoride toothpaste), the availability and uptake of other caries-prevention strategies, diet and consumption of tap water, and the movement/migration of the population. There is insufficient evidence to determine whether water fluoridation results in a change in disparities in caries levels across socioeconomic status. There are no studies that met the review's inclusion criteria, from which to determine the effectiveness of water fluoridation for preventing caries in adults.

There is insufficient information to determine the effect of stopping water fluoridation programmes on caries levels.

There is a significant association between dental fluorosis (of aesthetic concern or all levels of dental fluorosis) and fluoride level. The evidence is limited due to high risk of bias within the studies and substantial between-study variation.

The studies that have examined dental fluorosis as an outcome are generally more recent than those that have examined caries and, consequently, may be influenced by other sources of fluoride. These additional sources are seldom reported.

Implications for research

More contemporary studies, evaluating the effectiveness of water fluoridation for the prevention of caries, are needed. These studies should include a concurrent control with comparable caries levels at baseline. Caries data should therefore be measured at at least two time points (i.e baseline and follow-up).

Since all the included studies examined the effectiveness of water fluoridation in children, research on effectiveness among adults is needed.

Standardised diagnostic criteria and reporting techniques for caries and dental fluorosis would improve comparability of results across studies.

More research is also needed to understand the contribution of fluoride from sources other than water; the consumption of tap water within a population; the effect of water fluoridation over and above other caries preventive measures, namely dental sealants and fluoride varnishes; the impact of water fluoridation on disparities in oral health; and adverse effects associated with fluoridated water (particularly in areas with naturally high levels of fluoride).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Acharya 2005

Methods	**FLUOROSIS STUDY**

Acharya 2005 *(Continued)*

	Country of study: India Geographic location: Davangere-Nallur, Naganur, Doddabathi, Kundawada and Holesirigere Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children aged 12-15 years; lifetime residency Exclusion criteria: absence on the day of the survey Other sources of fluoride: not stated Social class: socioeconomic position was similar in all villages Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.43 ppm Group 2: 0.72 ppm Group 3: 1.1 ppm Group 4: 1.22 ppm Group 5: 3.41 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 12-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	5 villages were selected out of a possible 90. There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for use of other fluoride sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Adair 1999

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Warren County, Georgia Year of study: not stated Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: children attending sole elementary and middle schools in study area Exclusion criteria: children whose homes were served with well-water. Other sources of fluoride: parents completed questionnaire regarding dentifrice use, home water source and current use of systemic fluoride supplements; all subjects received school water fluoridated at 0.5 ppm Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not considered Other confounding factors: not stated
Interventions	Group 1: 0.5-1.2 ppm (both natural and artifical fluoridation) Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index); caries data collected but not presented in this review due to study design Age at assessment: 8-10 and 11-13 years
Funding	NIDR Grant DE-06113
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Participants were children attending the sole elementary and middle/high schools in Warren county. There was insufficient detail reported to determine how selection took place
Confounding	High risk	SES was not accounted for
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for over 80% of participants were reported
Selective reporting (reporting bias)	High risk	Outcome of interest reported. However, data were not presented clearly enough to be considered reliable

Adair 1999 *(Continued)*

Other bias	High risk	Exposure to fluoride water could not be controlled for. Some children had fluoride water at school across groups. Some had non-fluoridated well-water at home

Adriasola 1959

Methods	**CARIES STUDY** Country of study: Chile Geographic location: Curico (F); San Fernando (non-F) Year study started: 1953 Year study ended: 1956 Year of change in fluoridation status: 1953 Study design: CBA
Participants	Inclusion criteria: children aged 3-15; children from 2 primary schools in the study areas Exclusion criteria: none stated Other sources of fluoride: not stated Social class: based on knowledge of their demographics, culture and social economy, it was assumed that the study areas were comparable Ethnicity: not stated Residential history: not stated Other confounding factors: none stated
Interventions	**Initiation of water fluoridation** Group 1: low fluoride content (ppm not reported; natural fluoridation) Group 2: low fluoride content (ppm not reported; natural fluoridation)
Outcomes	% caries-free participants Age at baseline measure: 3-8 years and 11, 12 and 15 years (unclear if deciduous or permanent dentition) Age at final measure: 3-8 years and 11, 12 and 15 years (unclear if deciduous or permanent dentition)
Funding	In collaboration with members of the committee Pro-Fluoridation
Notes	Data extracted from Adriasola 1959 differs from that presented in CRD review (additional data extracted) Paper translated from Spanish

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Following on from the 1953 survey, the authors re-established contact with local authorities, teachers and health educators in 1956 and in a period of 2 months examined children in Curicco and San Fernando attending private and public technical schools, kindergartens, primary and secondary schools. There was insufficient detail reported to determine how selection took place
Confounding	High risk	Study groups assumed comparable for SES. No details were reported on the use of fluoride from other sources or on the dietary habits of the children

Adriasola 1959 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Different children examined at before and after time points. Unclear if all eligible children examined at each time point
Selective reporting (reporting bias)	High risk	Baseline data for proportion of children caries free incomplete for ages 6, 7, 11 and 15 years
Other bias	Low risk	No other apparent bias

Al-Alousi 1975

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: Anglesey (F); Leeds (non-F) Year of study: 1973 Year of change in fluoridation status: 1955 Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; children aged 12-16 years Exclusion criteria: missing, fractured or crowned teeth; refusal to participate (1 school in Leeds) Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 0.9 ppm (artificial fluoridation) Group 2: < 0.01 ppm (natural fluoridation)
Outcomes	Dental fluorosis Age at assessment: 12-16 years
Funding	Not stated
Notes	Data extracted from Al-Alousi 1975 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Children were selected from schools in Leeds in a quasi-random way whereby every nth child (n = total children in school/20) from the register was selected. Eligible children in Anglesea were selected from schools randomly
Confounding	High risk	Did not account for use of other fluoride sources or SES

Al-Alousi 1975 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	A clinical investigation and double-blinded photographic examination were conducted. However, the results reported are those of the unblinded clinical investigation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Unclear risk	Outcome of interest reported
Other bias	High risk	Diagnoses had to be "agreed" on by the two examiners and there was no mention of any sort of calibration of the examiners. This may have resulted in measurement bias

Alarcon-Herrera 2001

Methods	**FLUOROSIS STUDY** Country of study: Mexico Geographic location: Durango Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 6-12 years who had established permanent residence in the area Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: permanent residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: non-detectable-1.5 ppm Group 2: 1.51-4.99 ppm Group 3: 5.0-8.49 ppm Group 4: 8.5-11.9 ppm Group 5: > 12 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 6-12 years
Funding	Project grant from the Mexican National Council of Science and Technology Conacyt-Sivilla, Project 9502160
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Alarcon-Herrera 2001 *(Continued)*

Sampling	Low risk	Through a polystage conglomerate random sampling, 380 families were selected and prorated into 77-80 families per concentration area zone. The division yielded a total of 1437 individuals from the five different areas
Confounding	High risk	Did not account for use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Unclear risk	No information examiner calibration with regard to detection of the outcome variable

Albrecht 2004

Methods	**FLUOROSIS STUDY** Country of study: Hungary Geographic location: Bár and Dunaszekcső Year of study: 2004 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: healthy schoolchildren, aged 6-18 years; lifelong residents in the communities Bár or Dunaszekcső; only permanent teeth were investigated Exclusion criteria: any systemic disease Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.7 ppm Group 2: 2 ppm
Outcomes	Dental fluorosis (Dean's Index and TSIF) Age at assessment: 6-18 years
Funding	Not stated
Notes	Paper translated from Hungarian

Albrecht 2004 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

AlDosari 2010

Methods	**FLUOROSIS STUDY** Country of study: Saudi Arabia Geographic location: Riyadh Year of study: 2010 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria:Saudi nationality; lifetime residence in the area Exclusion criteria: non-Saudi nationality; absence from school on the day of dental examination Other sources of fluoride: not stated Social class: both schools from urban and rural areas were included in the sample frame Ethnicity: Saudi nationals, no further details Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0-0.3 ppm Group 2: 0.31-0.6 ppm Group 3: 0.61-1 ppm Group 4: 1.01-1.5 ppm Group 5: 1.51-2 ppm Group 6: 2.01-2.5 ppm Group 7: ≥ 2.51 ppm
Outcomes	Dental fluorosis (TF Index)

AlDosari 2010 *(Continued)*

	Age at assessment: 6-18 years
Funding	Supported by a grant from King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	A list of zones was considered as the sampling frame for the schools, and municipalities were randomly chosen from each zone to represent the urban area. Additionally, rural areas in the municipality with at least one school were surveyed. However there was insufficient detail reported to determine how selection of schools and children within those schools took place
Confounding	High risk	Did not account for use of other fluoride sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Over 95% of the subjects sampled were examined. However, it is not clear why fluorosis was not scored in permanent teeth of the 6- to 7-year olds
Selective reporting (reporting bias)	High risk	The authors did not report or justify not presenting fluorosis data for the age group 15-18 years
Other bias	Unclear risk	Clinical examination was carried out by 2 dentists, but no information on whether the examiners were calibrated with regard to detection of the outcome variable was given

Angelillo 1999

Methods	**FLUOROSIS STUDY** Country of study: Italy Geographic location: areas around Naples (F); Catanzaro (non-F) Year of study: 1997 Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: lifetime residents of study areas (children only); children aged 12 years; used community water supply as main sources of drinking water Exclusion criteria: partially erupted teeth; orthodontic banding Other sources of fluoride: tooth brushing habits (frequency of tooth brushing); fluoride tablets; fluoride dentifrices Social class: parents' employment status Ethnicity: not stated Residential history: lifetime residents Other confounding factors: sweet consumption; climate

Angelillo 1999 *(Continued)*

Interventions	All natural fluoridation Group 1: ≥ 2.5 ppm Group 2: ≤ 0.3 ppm
Outcomes	Dental fluorosis; caries data evaluated in study but not included in review due to study design Age at assessment: 12 years
Funding	Partially supported by a grant of Acquedotto Vesu- viano S.p.A.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Schools were selected at random, as were classes with the schools. All eligible children within the selected class were recruited to the study
Confounding	High risk	There was a reported imbalance between groups in the use of fluoride supplements, toothbrushing behaviour and in SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for the majority of participants presented
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Unclear risk	The 2 examiners involved had previously been trained and calibrated, but details not presented

Arif 2013

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Nagaur district Year of study: 2013 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: only villages where the mean fluoride concentration was > 1.0 mg/L were selected for the dental fluorosis survey. No other information provided for participants Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated

Arif 2013 *(Continued)*

	Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	54 villages receiving water with different natural fluoride concentrations ranging from 0.9 5.8 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: not stated
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Only villages where the mean fluoride concentration was > 1.0 ppm were selected. There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to determine whether data presented for all participants as study details were poorly reported
Selective reporting (reporting bias)	Low risk	Outcome of interest not reported in paper, but made available by authors via email
Other bias	High risk	Fluoride concentration for the different villages overlapped making the data impossible to interpret

Arnold 1956

Methods	**CARIES STUDY** Country of study: USA Geographic location: Grand Rapids (F); Muskegon (non-F) Year study started: 1944 Year study ended: 1951 (after which time the control group became fluoridated; evaluated until 1954) Year of change in fluoridation status: 1945 Study design: CBA
Participants	Inclusion criteria: children aged 4-16 years; used city water supplies since birth Exclusion criteria: children who lived outside study areas for more than 3 months of any 1 year

Arnold 1956 *(Continued)*

	Other sources of fluoride: author stated that there were no concerted efforts to commence special caries control programmes e.g. topical fluoride programmes, in either of the cities since the study began Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1: 1 ppm (artificial fluoridation) Group 2: < 0.2 ppm (natural fluoridation)
Outcomes	DMFT; deft Age at baseline measure: 5-13 years (deciduous dentition); 6-16 years (permanent dentition) Age at final measure: 5-13 years (deciduous dentition); 6-16 years (permanent dentition)
Funding	Not stated
Notes	Data extracted from Arnold 1956 differed from that presented in CRD review (additional data extracted)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Children were selected through schools. Almost all eligible children in the areas of study were examined
Confounding	High risk	No efforts were made to stop topical fluoride application in either control or test group. However it is not known if the areas differed in terms of the programmes/services on offer. No details on the dietary habits of the children were reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "samples consist of all available children in certain grades (or in sections of the grades)" Number of children examined each year presented, however, numbers varied across each age group and each year (not a continuous study sample)
Selective reporting (reporting bias)	High risk	It is noted in the results that fluorosis observations had been made, but no details were given for the methods and data (just % increase). Also, standard deviation not reported
Other bias	High risk	Calibration of examiners not mentioned

Ast 1951

Methods	**CARIES STUDY**

Ast 1951 *(Continued)*

	Country of study: USA Geographic location: Newburgh (F); Kingston (non-F) Year study started: 1945 Year study ended: 1952 Year of change in fluoridation status: 1945 Study design: CBA
Participants	Inclusion criteria: all 5- to 12-year-old children present at school on days of examination; lifetime residents of study areas Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1 baseline: < 0.1 ppm (natural fluoridation) Group 1 post intervention: 1-1.2 ppm (artificial fluoridation) Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	DMFT rate per 100 erupted permanent teeth; % caries-free children (deciduous dentition) Age at baseline measure: 5 years (deciduous dentition); 6-12 years (permanent dentition) Age at final measure: 5 years (deciduous dentition); 6-12 years (permanent dentition)
Funding	Not stated
Notes	Data extracted from Ast 1951 differs from that presented in CRD review (additional data extracted)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All 5- to 12-year-old school children present in the schools within the study areas on the days of examination were included in the study
Confounding	High risk	Did not account for SES, the use of other fluoride sources, or the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	The number of participants for whom outcome data was reported (F = 3054; non-F = 2812) varied from the number of participants reported to have been included in the study (F = 3200; non-F = 3100)

Ast 1951 *(Continued)*

Selective reporting (reporting bias)	High risk	Baseline dates of children in the intervention (1944-45) and control (1945-46) groups varied, which would result in incomparability of data from both study groups
Other bias	High risk	There was no mention of examiner calibration

Awadia 2000

Methods	**FLUOROSIS STUDY** Country of study: Tanzania Geographic location: Arusha and Moshi Year of study: 1996 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: age 9-14 years; lifelong residence in respective towns or villages Exclusion criteria: not stated Other fluoride sources: toothpaste use: Arusha = 94%; Arusha Meru = 100%; Moshi = 97.1% and Kibosho = 40%Magadi use: Arusha = 31(47%); Arusha Meru = 1(2.9%); Moshi = 41 (58.6%); Kibosho = 83(97.6%) Social class: peasant mothers: Arusha = 1 (1.5%); Arusah Meru = NR; Moshi = 7 (10%); Kibosho = 33 (38.8%); other: Arusha = 65 (98.5%); Arusha Meru = 35 (100%); Moshi = 63 (90%); Kibosho = 52 (61.2%) Ethnicity: Arusha area (Arusha and Arusha Meru) – mainly ethnic Asians; Kilimanjaro region (Moshi and Kibosho) - Africans Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.2 ppm Group 2: 0.3 ppm Group 3: 3.6 ppm
Outcomes	Dental fluorosis (TF Index) Age at assessment: 9-14 years
Funding	Supported by the Norwegian State Educational Loan fund, NUFU project 61/96, and the committee for Research and Postgraduate Training, Faculty of Dentistry, University of Bergen, Norway
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Schools in all villages (except in Arusha Meru) as well as participants were randomly selected. For schools where participants were not randomly selected,

Awadia 2000 *(Continued)*

		including the school in Arusha Meru, all the registered school children were chosen to participate
Confounding	High risk	There was a reported imbalance between groups in terms of SES and use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Outcome of interest not fully reported, rather presented as a median score
Other bias	High risk	Only one examiner was involved; no testing for intra-rater reliability with regard to detection of the outcome variable.

Azcurra 1995

Methods	**FLUOROSIS STUDY** Country of study: Argentina Geographic location: Sampacho (F); Porteña (non-F) in the Cordoba province Year of study: 1993 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 6-7 years (1st grade) and 12-13 years (7th grade) at primary school Exclusion criteria: none stated Other sources of fluoride: frequency of tooth brushing. Group 1 (aged 6-7): 56% brushed at least once a day (28/50) Group 1 (aged 12-13): 74% brushed at least once a day (37/50) Group 2 (aged 6-7): 46% brushed at least once a day (23/50) Group 2 (aged 12-13): 50% brushed at least once a day (25/50) Social class: determined by occupation and highest attained level of schooling attained by main breadwinner in familyClassified as high, medium, and low social class Group 1 (aged 6-7): 80% low SES (40/50) Group 1 (aged 12-13): 82% low SES (41/50) Control (aged 6-7): 74% low SES (37/50) Control (aged 12-13) 80% low SES (40/50) Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 9.05 ppm

Azcurra 1995 *(Continued)*

	Group 2: 0.19 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data evaluated in study but not included in review due to study design Age at assessment: 6-7 years and 12-13 years
Funding	Part of this work was subsidised by the Ministry of Science and Technology (SeCyT) of the National University of Córdoba , Córdoba, Argentina
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Stratified random selection was used. Following stratification by age, gender and SES,100 school children were randomly selected from each village
Confounding	High risk	Although SES was considered during sampling, it was not controlled for within the analysis. No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding not stated, however the two calibrated operators, as authors of the study, were likely to have knowledge of the study areas
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across both groups
Other bias	Low risk	No other apparent biases

Backer-Dirks 1961

Methods	**CARIES STUDY** Country of study: Holland Geographic location: Tiel (F); Culemborg (non-F) Year study started: 1952 Year study ended: 1959 Year of change in fluoridation status: 1953 Study design: CBA
Participants	Inclusion criteria: children aged 11-15; lifelong residents of the study areas; used the piped water supply; 100 children of each age examined Exclusion criteria: not stated Other fluoride sources: not stated Social class: areas similar in social class structure and proportional numbers of subjects selected from each school type Ethnicity: not stated

Backer-Dirks 1961 *(Continued)*

	Residential history: lifetime residents Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1: 1.1 ppm (artificial fluoridation) Group 2: 0.1 ppm (natural fluoridation)
Outcomes	Average number of all approximal lesions; average number of approximal dental lesions Age at baseline measure: 11-15 years (permanent dentition) Age at final measure: 11-15 years (permanent dentition)
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A proportion of children were chosen at random from different types of schools (public school, Roman Catholic, Protestant)
Confounding	High risk	No details were reported on the use of fluoride from other sources or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The radiographs made in Tiel and Culemborg were put into unlabelled envelopes, and examined at random". Each examiner evaluated the same number of radiographs without knowledge of the origin of the films
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is not clear whether the outcome data were reported for all participants
Selective reporting (reporting bias)	High risk	Outcome of interest reported, however, data not in useable format
Other bias	Low risk	No other bias apparent

Bao 2007

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: 3 cities (Harbin, Mudanjiang, Zhaodong) and 3 rural areas (Zhaoyuan, Shuangcheng, Linkou) in the Heilongjiang province Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: 12-year-old children in Heilongjiang

Bao 2007 *(Continued)*

	Exclusion criteria: not reported. Other sources of fluoride: not reported Social class: 396 (198 male; 198 female) from cities; 396 (198 male; 198 female) from rural areas Ethnicity: Chinese Residential history: not reported Other confounding factors: not reported
Interventions	All natural fluoridation Group 1 (Linkou): 0.29 ppm Group 2 (Mudanjiang): 0.40 ppm Group 3 (Shuangcheng): 0.68 ppm Group 4 (Harbin): 0.77 ppm Group 5 (Zhaoyuan): 0.80 ppm Group 6 (Zhaodong): 1.14 ppm
Outcomes	Dental fluorosis (CFI); caries data evaluated in study, but excluded from review due to study design Age at assessment: 12 years
Funding	Research Fund of Bureau of Health of Heilongjiang Province (grant no.2005[122])
Notes	Translation from Chinese

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Quote: "Representative samples were selected by multi-stage, stratified and random sampling" "For each site, 66 12-year-old boys and 66 12-year-old girls were randomly chosen".
Confounding	High risk	3 groups were from cities and 3 groups were from rural areas. The authors did not record/report or adjust for other confounding factors (e.g. other fluoride sources, diet, residential history)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The authors did not report any information on loss of follow-up or exclusion of participants. Judging by the number of people they chose randomly (792), and the number of people (792) with results of caries examination, there was no loss of follow-up or exclusion of participants
Selective reporting (reporting bias)	High risk	Data not presented in a format that allowed for further evaluation Quote: "Dean's Index was used to classify fluorosis." The authors did not report the number of affected people for each Dean's Index category. They did not report the prevalence fluorosis (number of affected people/number of people examined)

Bao 2007 *(Continued)*

Other bias	Low risk	No other apparent bias

Baskaradoss 2008

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: 9 villages (Munchirai, Thovalai, Melpuram, Rajakkamangalam, Kurunthencode, Thiruvattar, Agasteeswaram, Thuckalay, Killiyoor) in Kanyakumari district Year of study: 2006 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: brushing patter (toothbrush) = 84.6%; toothpaste (Colgate) = 92.2%; frequency (once daily) = 80.7%; age of starting to brush (< 2 years) = 69.2% Social class: low SES (46.1%); urban residence (44.2%) Ethnicity: not stated Residential history: not stated Other confounding factors: Information was collected on diet, seafood intake and tea
Interventions	All natural fluoridation Groups 1–9: specific ppm not presented. Groups listed according to number of Panchayats in the various Blocks of Kanyakumari district with water fluoride level more than 1.5 and 1.7 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 10-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A stratified cluster sampling method was used to select the samples. 2 schools from each block were selected at random from a list of higher secondary schools. After examining an entire class, only the first 20 were taken until sample size was achieved
Confounding	High risk	Participants had different oral hygiene habits and there was no mention of duration of residency
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias)	Low risk	Outcome data for all participants reported

Baskaradoss 2008 *(Continued)*
All outcomes

Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Unclear risk	No mention of calibration

Beal 1971

Methods	**CARIES STUDY** Country of study: England Geographic location: Balsall Heath and Northfield, Birmingham (F); Dudley (non-F) Year study started: 1967 Year study ended: 1970 Year of change in fluoridation status: 1964 Study design: CBA
Participants	Inclusion criteria: children aged 5 attending schools that participated in each year of the study Exclusion criteria: none stated Other sources of fluoride: not stated Social class: Quote: "The socio-economic composition of the districts has been described previously ...". Balsall Heath is a poor area of the city with high proportion of immigrants; Northfield and Dudley are both industrial areas with comparable populations, but there were more immigrants in Dudley Ethnicity: all areas have some proportion of immigrants Residential history: no attempt was made to select continuously resident children from the samples Other confounding factors: not stated
Interventions	Initiation of water fluoridation Group 1 and Group 2: 1 ppm (artificial fluoridation) Group 3: < 0.1 ppm (natural fluoridation)
Outcomes	dmft; % caries-free children Age at baseline measure: 5 years (deciduous dentition) Age at final measure: 5 years (deciduous dentition)
Funding	MRC grant funded trial
Notes	Quote: "The children, who were 5 years old in 1967, were aged about 3 years when the fluoride in their drinking water reached the recommended level; they had erupted all their deciduous, and these would be expected to have derived only slight benefit at this time. These children do not represent a true baseline; any dental advantage that this group had received, compared with the true but unexamined baseline before fluoride was added would have the effect of decreasing the observed reduction, if any, over subsequent years."

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place

Beal 1971 *(Continued)*

Confounding	High risk	No details were reported on the use of fluoride from other sources or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Different children examined at before and after time points. Unclear if all eligible children examined at each time point
Selective reporting (reporting bias)	Low risk	Reporting of outcome of interest balanced across groups
Other bias	High risk	No detail of who performed examinations, their training/consistency

Beal 1981

Methods	**CARIES STUDY** Country of study: England Geographic location: Scunthorpe (F); Corby (non-F) Year study started: 1969 Year study ended: 1975 Year of change in fluoridation status: 1968 Study design: CBA
Participants	Inclusion criteria: lifetime residents in study areas; children aged 5, 8 and 12 Exclusion criteria: teeth extracted for orthodontic purposes Other sources of fluoride: not stated Social class: both areas had iron/steel as main industry-socioeconomic; composition of the 2 areas was similar Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	**Fluoride initiation** Group 1: 0.9 ppm (artificial fluoridation) Group 2: 0.35 ppm (natural fluoridation)
Outcomes	dmft; DMFT; % caries-free subjects (deciduous teeth); % caries-free subjects (permanent teeth) Age at baseline measure: 5, 8 and 12 years Age at final measure: 5, 8 and 12 years
Funding	Not stated

Beal 1981 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Schools were chosen by random selection and every child of eligible age in these schools was examined
Confounding	High risk	No details were reported on the use of fluoride from other sources or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants appears to be presented
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	The authors reported that was no difference in level of reproducibility of the examiners

Beltran-Aguilar 2002

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: not stated Year of study: 1986 Year study ended: 1987 Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: aged 12-14 years; availability of data on type of water system and fluorosis; having residences served by the same type of public water system with respect to fluoride status; determinable date of public water system fluoridation initiation and residence at area before initiation of water fluoridation; availability of continuous residence history if more than 1 residence; fewer than 5 residences; ascertainable exposure to fluoride drops or tables; served by public water systems with ascertainable fluoride status in residences Other fluoride sources: tablets = 623 (14.9%); drops = 627 (14.5%); tablets and drops = 317 (8.4%). Suboptimal fluoride: drops only = 507 (23.0); tablets only = 512 (22.5); tablets and drops = 279 (13.2). Optimal fluoride:drops only = 103 (6.8); tablets only = 98 (6.0); tablets and drops = 32 (2.2) Natural fluoride: drops only = 13 (5.5); tablets only = 17 (7.5);tablets and drops = 6 (2.5) Exclusion criteria: any criterion in discord with the inclusion criteria

Beltran-Aguilar 2002 *(Continued)*

	Social class: not stated Ethnicity: not stated Residential history: all the children were continuous residents of areas with the reported water systems Other confounding factors: not stated
Interventions	Group 1: < 0.7 ppm (natural fluoridation) Group 2: 0.7-1.2 ppm (artificial fluoridation) Group 3: 0.7-4 ppm (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 12-14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	The sampling frame was specified and the sample represented 41 percent of all 12- to 14-year olds and more than 4 million schools children, there is no evidence that any eligible children were excluded
Confounding	High risk	The use of other fluoride sources was similar in those that consumed water with optimal and natural fluoride, but very different from those in the suboptimal fluoride group. Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Children with missing outcome data were excluded. It is not clear whether there was an imbalance across groups in excluded children
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	There is an overlap in fluoride concentration between the exposure groups (0.7-1.2 ppm and 0.7-4.0 ppm) which is likely to dilute the observable effect of exposure to intervention across groups. It is unclear whether the examiners were calibrated as the paper provides insufficient information and we were unable to access associated reports which may have contained examination protocols

Berndt 2010

Methods	**FLUOROSIS STUDY** Country of study: Namibia Geographic location: Ombili, Ondera, Vryheid, Kakuse

Berndt 2010 *(Continued)*

	Year of study: October 2004 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: aged 8-21 years Other fluoride sources: 47 (39.3%) reported oral hygiene practice with fluoridated toothpaste (1400 ppm); 8 (6.7%) used traditional 'natural' toothbrush. Different ethnic groups differed markedly in their oral hygiene behaviour (P value 0.02) Exclusion criteria: not stated Social class: not stated Ethnicity: !Kung (45%); Heikum (35%); Damara (13%); Bantu (7%) Residential history: residents of Ombili had been resident since 1991 and the residents of the other farms were lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.28 ppm Group 2: 0.38 ppm Group 3: 1.06 ppm Group 4: 1.43 ppm
Outcomes	Dental fluorosis (Dean's Index; CFI) Age at assessment: 8-21 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Children selected from Ombill Primary School and divided into groups according into place of birth and ethnicity
Confounding	High risk	Imbalance in oral health behaviour and duration of residency between ethnic groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for in analysis
Selective reporting (reporting bias)	Low risk	Outcome data fully reported

Berndt 2010 *(Continued)*

Other bias	Low risk	No other apparent bias

Birkeland 2005

Methods	**FLUOROSIS STUDY** Country of study: Sudan Geographic location: Triet el Biga, Abu Delaig and Abu Groon Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: residence in the village from the age of 1 year Exclusion criteria: not stated Other fluoride sources: not stated Social class: similar socioeconomic conditions Ethnicity: similar ethnicity Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.3-1.4 ppm Group 2: 0.8-2.2 ppm Group 3: 2-4.2 ppm
Outcomes	Dental fluorosis (TF Index) Age at assessment: 11-13 years
Funding	Not stated
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	The schools were selected from an unspecified sampling frame and insufficient detail was reported to determine how selection of schools took place. However children were selected at random from the schools
Confounding	High risk	No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias)	Low risk	Data presented for all participants

Birkeland 2005 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	There is inconsistency in the number of water samples tested (Triet el Biga = 6, Abu Delaig = 11, Abu Groon = 8) and an overlap in range of fluoride concentrations between the 3 study areas. Also examinations were done by a dental assistant and it is not clear whether reliability testing was carried out

Blinkhorn (unpublished)

Methods	**CARIES STUDY** Country of study: Australia Geographic location: Gosford city (newly-F); Wyong Shire (F); Ballina and Byron (non-F) Year study started: 2008 Year study ended: 2012 Year of change in fluoridation status: 2008 Study design: ITS
Participants	Inclusion criteria: children aged 5-7 years (data for 10- to 12-year olds also provided) Exclusion criteria: not stated Other fluoride sources: information on toothbrushing habit was collected, but not reported in details Social class: Shires of Ballina and Byron were more rural and less industrialised than Wyong Shire and Gosford CityInformation on parent's educational attainment and cardholder status was recorded, but not reported in details Ethnicity: aboriginal status was recorded, but not reported in details Residential history: not stated Other confounding factors: information on sugary drink was collected, but not reported in details
Interventions	Group 1: fluoridated (data not included in review) Group 2: newly fluoridated Group 3: non-fluoridated
Outcomes	dmft; DMFT; % caries free (deciduous dentition); % caries free (permanent dentition) Age at baseline measure: 5-7 years Age at final measure: 5-7 years
Funding	Centre for Oral Health Strategy, New South Wales Health, the Australian Dental Association (New South Wales Branch) and Northern Sydney and Central Coast Local Health Service
Notes	All data unpublished
Risk of bias	

Blinkhorn (unpublished) *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Children were drawn from Catholic and state schools in the 3 areas and schools were randomly selected from a master list until the individual school rolls for primary school children aged 5-7 years added up to around 900
Confounding	High risk	Multivariate analysis of dmft was done taking educational attainment of parents, toothbrushing behaviour and sugary drink consumption into account, however this was done by year, not by study area, and there was insufficient information to determine whether these confounding factors were balanced across study groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Though response rate was unbalanced across groups, data were presented for all examined participants
Selective reporting (reporting bias)	High risk	Standard deviation not reported
Other bias	Low risk	No other apparent bias

Booth 1991

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: Huddersfield (F); Dewsbury (non-F) Year of study: 1989 Year of change in fluoridation status: 1989 Study design: cross-sectional
Participants	Inclusion criteria: all 3-year-old white children; lifetime residents of study areas; positive informed consent Exclusion criteria: children who had moved out of the area; children who were ill; children taking fluoride tablets Other sources of fluoride: children taking fluoride tablets excluded from study Social class: areas matched using socioeconomic data from the 1981 census and recent unemployment data; parents asked about occupation of head of household during interview Ethnicity: white children only Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: < 0.3 ppm (natural fluoridation)

Booth 1991 *(Continued)*

Outcomes	Dental fluorosis (modified developmental defects of enamel index), caries data evaluated in study but excluded from review due to study design Age at assessment: 3 years
Funding	North Western Regional Health Authority
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Eligible children were identified from a list of all children in the health district and were randomly sampled from each population. The numbers required were based on a pilot study (no reference provided). No further details reported
Confounding	Low risk	Fluoride from other sources was controlled for using inclusion/exclusion criteria and there was no significant difference in SES between the groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data were presented for the majority of those recruited (attending appointments)
Selective reporting (reporting bias)	Low risk	All expected data reported
Other bias	Low risk	No other apparent bias

Brothwell 1999

Methods	**FLUOROSIS STUDY** Country of study: Canada Geographic location: Wellington and Dufferin (neighbouring counties), South-Western Ontario Year of study: 1996-1997 (academic year) Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children resident in Wellington-Dufferin-Guelph Health Unit area; parental consent; children aged 7-8 years Exclusion criteria: children with non-erupted or insufficiently erupted central incisors; children absent on day of examination Other sources of fluoride: amount of toothpaste usually used ("48.9% use > pea sized amount, 365/747"); fluoride supplements ("14.5% take supplements, 107/740"); age started brushing; use of mouthwash ("4% routinely use fluoridated mouthwash, 30/752"); breast/bottle fed; whether toothpaste used when brushing Social class: household income; highest level of education received. "It is likely that respondents under-represented the disadvantaged segment of the population. How the low response rate in this sub-

Brothwell 1999 *(Continued)*

	group affects the estimates of prevalence is unknown; however, it is unlikely to be a major source of bias." Ethnicity: not stated Residential history: "The questionnaire assessed … years at current residence", 39% lifelong residents (293/752); 64.8% (487/752 resided at tested source from before the age of 3 (fluorosis-sensitive period – multivariate analysis restricted to these 487 participants) Other confounding factors: breast-feeding duration
Interventions	Group 1: ≥ 0.7 ppm (natural fluoridation) Group 2: < 0.7 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TSIF score > 1) Age at assessment: 7-8 years
Funding	Not stated
Notes	Data extracted from Brothwell 1999 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Children were selected via schools, however insufficient detail was reported regarding sampling
Confounding	High risk	Bivariate analysis showed that fluoridated mouthwash use and professional fluoride treatments were significantly associated with fluorosis prevalence, however, the data were not reported/presented in a manner which demonstrated adjustment for imbalance at baseline occurred, or was measured well and controlled for
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Testing of water samples for fluoridation level was conducted after screening examination (at the University of Toronto); examinations conducted by a single dental hygienist (in school clinics). It does not appear that, despite the lack of any attempt to blind being reported, that blinding would have had any effect on reducing bias
Incomplete outcome data (attrition bias) All outcomes	High risk	Significant missing data (e.g. 34 participants from the water sample)
Selective reporting (reporting bias)	High risk	Comment: there is much that is either not reported in a sufficient manner to be able to glean the necessary information from (i.e. TSIF scores against fluoridation levels of water samples), or has significant missing data (e.g. 34 participants from the water sample) and so is difficult to draw the conclusions required for this review. No evidence of protocol in advance of obtaining data/undertaking analysis
Other bias	Low risk	Reporting dental fluorosis as TSIF score > 1 rather than ≥ 1 puts the results at risk of misclassification bias

Brown 1965

Methods	**CARIES STUDY**

Brown 1965 *(Continued)*

	Country of study: Canada Geographic location: Brantford (F); Stratford (natural F); Sarnia (non-F), Ontario Year study started: 1948 Year study ended: 1959 Year of change in fluoridation status: 1945 Study design: CBA
Participants	Inclusion criteria: children aged 9-14 years; lifetime residents (absence of < 6 weeks since birth); all primary and secondary schools in study areas Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1: artifical fluoridation - ppm not stated Group 2: natural fluoridation - ppm not stated Group 3: 'negligible' - ppm not stated (natural fluoridation)
Outcomes	DMFT, % caries-free subjects (permanent teeth) Age at baseline measure: 9-11 years and 12-14 years Age at final measure: 9-11 years and 12-14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	The study sample was selected by random sampling (by school and grade) described in "A Suggested Methodology for Fluoridation Surveys in Canada" (Department of National Health and Welfare 1952)
Confounding	High risk	Did not account for use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Children 6-8 years were sampled and initially examined up until 1957, but were no longer included after 1957 as no significant differences were found to exist in that age group
Selective reporting (reporting bias)	Low risk	Outcome of interest reported

Brown 1965 *(Continued)*

Other bias	Unclear risk	Inorder to maintain a uniform scale of observation, all examinations were done by the same examiner and intra-examiner, reproducibility not reported

Budipramana 2002

Methods	**FLUOROSIS STUDY** Country of study: Indonesia Geographic location: 10 villages in Asembagus subdistrict Year of study: 1999 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children aged 6-12 years who were lifetime residents Exclusion criteria: not stated Other sources of fluoride: not stated Social class: the villages all had identical SES Ethnicity: the villages all had identical ethnic profiles Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.51 ppm Group 2: 0.81 ppm Group 3: 2.25 ppm Group 4: 3.16 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data evaluated in study, but excluded from review due to study design Age at assessment: 6-12 years
Funding	Not stated
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Low risk	The authors reported that participants were chosen randomly from 1 selected primary school in each of the 10 villages. However, it is not clear why only 1 school was selected in each village and if the resulting sample was representative
Confounding	High risk	The use of other fluoride sources was not considered
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported

Budipramana 2002 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome data for all participants was reported
Selective reporting (reporting bias)	Low risk	All expected outcome were reported
Other bias	High risk	No mention of examiner calibration

Butler 1985

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: 16 Texas communities (selected to reflect a wide range of fluoride levels in drinking water) Year of study: 1980 Year study ended: 1981 Year of change in fluoridation status: unclear if natural or artifical fluoridation Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; enrolled in grades 2-6 (aged 7-13 years) and 9-12 (aged 14-19 years) in public schools Exclusion criteria: none stated Other sources of fluoride: fluoride toothpaste, fluoride drops, number of fluoride treatments Social class: mother's education Ethnicity: white/Spanish/black (ethnicity judged by surname?) Residential history: lifetime residents Other confounding factors: home air-conditioning; air temperature; number of months breastfed; children in the family; mother's age at child's birth; total dissolved solids in drinking water and zinc in drinking water; age
Interventions	Unclear as to whether the fluoridation was natural in all areas Group 1: 0.2 ppm Group 2: 0.2 ppm Group 3: 0.3 ppm Group 4: 0.7 ppm Group 5: 1.0 ppm Group 6: 1.0 ppm Group 7: 1.1 ppm Group 8: 1.8 ppm Group 9: 1.9 ppm Group 10: 1.9 ppm Group 11: 2.1 ppm Group 12: 2.1 ppm Group 13: 2.3 ppm Group 14: 2.3 ppm Group 15: 2.4 ppm Group 16: 3.3 ppm
Outcomes	Dental fluorosis (CFI score; prevalence of observed mottling (moderate)) Age at assessment: 7-19 years

Butler 1985 *(Continued)*

Funding	Supported by grants from the US Environmental Protection Agency
Notes	Data extracted from Butler 1985 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were invited to participate
Confounding	Unclear risk	While some confounders were measured well and some controlled for in the analysis, it is not clear whether the necessary adjustment was done to the data relevant to this review
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Comment: reporting balanced across all groups; however not all data presented in a form that can be interrogated. Despite collecting data on the CFI's 6 categories of severity of mottling, only data for moderate mottling was presented independently of the overall CFI score for each group. Furthermore, identified confounders were not presented for each group, but for the portion of the study sample as a whole (despite being possible from authors having collected the data)
Other bias	High risk	Each child received a dental examination performed by one of the authors, however, calibration was not mentioned

Chandrashekar 2004

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Davangere district Year of study: 2002 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residency; age 12-15 years Exclusion criteria: not stated Other fluoride sources: not stated Social class: similar socioeconomic conditions Ethnicity: not stated Residential history: lifetime residents

Chandrashekar 2004 *(Continued)*

	Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.22 ppm Group 2: 0.43 ppm Group 3: 0.74 ppm Group 4 0.93 ppm Group 5: 1.1 ppm Group 6: 1.22 ppm Group 7: 1.63 ppm Group 8: 2.08 ppm Group 9: 2.33 ppm Group 10: 2.64 ppm Group 11: 2.91 ppm group 12: 3.41 ppm
Outcomes	Dental fluorosis (TF Index) Age at assessment: 12-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Villages satisfying eligibility criteria were selected randomly and children were accessed via schools. It is not clear, however, how the children within the schools were selected
Confounding	High risk	No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The number of participants analysed was not reported
Selective reporting (reporting bias)	High risk	Dean's fluorosis index was measured but not reported
Other bias	Low risk	No other apparent bias

Chen 1989

Methods	**FLUOROSIS STUDY** Country of study: Taiwan Geographic location: Shenkang Hsiang, Changwa Year of study: 1987-1988 Year of change in fluoridation status: NA

Chen 1989 *(Continued)*

	Study design: cross-sectional
Participants	Inclusion criteria: children aged 6-16 years; lifetime residents of study areas; always used water wells as primary source of drinking water Exclusion criteria: not stated Other fluoride sources: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: author states that project communities had approximately the same location, climate, diet, food habits and customs, mean average daily temp = 25 ºC, range = 13 ºC-37 ºC
Interventions	All natural fluoridation Group 1: 4.2-4.9 ppm Group 2: 2.1-2.8 ppm Group 3: 1.4-2.1 ppm Group 4: 0.7-1.4 ppm Group 5: 0.4-0.7 ppm Group 6: < 0.4 ppm
Outcomes	Dental fluorosis prevalence (Dean's Index); caries data evaluated in study but not included in review due to study design Age at assessment: 6-16 years
Funding	National Science Council, Taiwan, ROC (NSC-77-0412-B-039-05)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible participants in the were included in the study
Confounding	High risk	Did not account for use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	5172 children recruited and examined, however, data presented for 5072 participants. Unclear if missing data balanced across groups
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Unclear risk	Examiners were calibrated before actual assessments of caries and fluorosis were initiated, however, kappa values were not reported

Chen 1993

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: Anquan village (low F); Hubei village (high F), Fenshun county, Guangdong Province Year of study: 1984 Year study ended: 1991 Year of change in fluoridation status: 1984 Hubei, 1986 Anquan Study design: before-and-after
Participants	Inclusion criteria: native born children aged 8-12 years for dental fluorosis Exclusion criteria: not stated Other sources of fluoride: not stated Social class: author stated that economic and living habits were similar in all study areas Ethnicity: not stated. Residential history: only native born children were assessed. Other confounding factors: not stated
Interventions	Water source from wells changed to river water Group 1: Hubei 4.1 mg/l (1984 pre-intervention – natural from wells); 0.8 mg/l (1984 at point of intervention – natural from river); 3.1 mg/l*(1991, 7 years post-intervention – natural from river) * Increase due to damaged walls of well at bottom of river bed allowing hot spring water with high fluoride content to amalgamate. No regular monitoring took place after changing water supply and therefore unclear when water fluoride content increased in Hubei Group 2: Anquan 12.5 mg/l (1984 pre-intervention – natural from wells); 0.3 mg/l (1986 at point of intervention – natural from river); 0.4 mg/l (1991, 5 years post-intervention – natural from river)
Outcomes	Dental fluorosis (Dean's Index); skeletal fluorosis Age at baseline measure: 8-12 years (dental fluorosis) and 16-65 years (skeletal fluorosis) Age at final measure: 8-12 years (dental fluorosis) and 16-65 years (skeletal fluorosis)
Funding	Not stated
Notes	Data extracted from Chen 1993 differs from that presented in CRD review Discrepancies between text and table with regard to fluoride concentration

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were included in the study examined for dental fluorosis and for skeletal fluorosis, adults aged 16-65 years were randomly sampled to have roentgenograms taken in pelvis
Confounding	High risk	Did not account for use of other fluoride sources

Chen 1993 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	For both study areas, n = 800 (Anquan) and n = 1331 (Hubei), however, data not reported for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	No mention of examiner calibration. Also, quote: "by investigation, it was found that the walls of the well for storing water at the bottom of river bed and water pipe were damaged, the hot spring water with high fluoride content gushed into the well and pipe. Because there was no regular monitoring on the water fluoride after changing water sources, it was unclear when the water fluoride content increased in Hubei".

Clark 1993

Methods	**FLUOROSIS STUDY** Country of study: Canada Geographic location: Kelowna (F); Vernon (non-F), British Columbia Year of study: not stated Year of change in fluoridation status: 1954 Study design: cross-sectional
Participants	Inclusion criteria: children in selected schools Exclusion criteria: children with fixed orthodontic appliances; missing anterior teeth Other sources of fluoride: not stated Social class: 2 communities selected because of regional and socioeconomic similarities Ethnicity: not stated Residential history: information recorded in questionnaire and verified by telephone, but doesn't appear to have been prohibitive for inclusion in study Other confounding factors: 274 participants had been exposed to fluoride supplements
Interventions	Group 1: 1.2 ppm (artificial fluoridation) Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TSIF) Age at assessment: school age
Funding	Supported by the British Columbia Health Research Foundation
Notes	
Risk of bias	

Clark 1993 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Primary schools were stratified into low, medium and high SES categories from a specified sampling frame. Schools were then randomly selected and all eligible children within the selected schools were included in the studies
Confounding	High risk	Did not account for use of other fluoride sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	Kappa value of 0.44 suggests a moderate degree of inter-examiner agreement

Clarkson 1989

Methods	**FLUOROSIS STUDY** Country of study: Ireland and England Geographic location: Cork (low and high F; 2 separate areas) and Manchester (low F) Year of study: not stated Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: children aged 8 and 15 years Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	Group 1: 'optimal' level - ppm not stated (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation) Gruop 3: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Enamel defects (DDE) Age at assessment: 8 and 15 years
Funding	Not stated

Clarkson 1989 *(Continued)*

Notes	Data extracted from Clarkson 1989 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Sampling was by stratified random selection of eligible children in the study areas. Stratification based on school size and gender
Confounding	High risk	Did not account for the use of other fluoride sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	To assess reproducibility, 46 children were examined twice without the examiner's knowledge, however, there is no indication of the examiner being blind to fluoridation status of participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported and balanced across groups
Other bias	Low risk	No other apparent bias

Clarkson 1992

Methods	**FLUOROSIS STUDY** Country of study: Ireland Geographic location: Ireland Year of study: 1984 Year of change in fluoridation status: 1964 Study design: cross-sectional
Participants	Inclusion criteria: children aged 8 and 15 years Exclusion criteria: none stated Other sources of fluoride: increase in use of fluoride-containing toothpaste and infant formula made with fluoridated water Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: problems of consistent levels in the fluoridated supply during the 1960s and early 1970s
Interventions	Group 1: 'optimal' level - ppm not stated (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (Deans Index); enamel defects (DDE)

Clarkson 1992 *(Continued)*

	Age at assessment: 8 and 15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A stratified proportional random sampling procedure was used with size of school with fluoridation status and sex as stratifying factors
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The number of participants recruited was not reported and there was a variation in the number of children examined for enamel defects and children interviewed on perception of defects. It is not clear whether data were presented for all recruited participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Cochran 2004a

Methods	**FLUOROSIS STUDY** Country of study: Ireland, England, Greece, Netherlands, Finland, Iceland, and Portugal Geographic location: Cork, Haalem, Athens, Reykjavik, Oulu, Knowsley, Almada/Setubal Year of study: 1997-1998 Year of change in fluoridation status: varies Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: information about use of fluoride supplements, age at which toothpaste was first used and the amount and type of toothpaste used were collected but not reported Social class: the sampling ensured a wide socioeconomic spread of participants Ethnicity: not stated Residential history: parents were given questionnaires to supply information on history of living a fluoridated area. No further details reported Other confounding factors: not stated

Cochran 2004a *(Continued)*

Interventions	Group 1: < 0.01 ppm (natural fluoridation) Group 2: 0.05 ppm (natural fluoridation) Group 3: 0.08 ppm (natural fluoridation) Group 4: < 0.1 ppm (natural fluoridation) Group 5: 0.13 ppm (natural fluoridation) Group 6: 1 ppm (artificial fluoridation)
Outcomes	Dental fluorosis (TF Index); enamel defects (DDE) Age at assessment: 8 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	The sampling frame was specified, but the eligibility criteria were not stated. It is not clear whether the number of children photographed as a percentage of the total population of children in the age group (12-23%) is representative
Confounding	High risk	Data were collected on the use of fluoride from other sources but not reported on
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Fluorosis was assessed using photographs and was done without reference to the area from which they were collected
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 5250 transparencies was taken, of which 114 (2.2%) were not suitable for analysis" Unlikely to influence results
Selective reporting (reporting bias)	Unclear risk	Outcome of interest fully reported, however data relating to confounding variables was collected but not reported
Other bias	Unclear risk	Reliability testing was carried out. The Kappa statistic from all the study sites showed substantial to excellent agreement with the 'gold standard', except for one study site that showed moderate agreement (0.49; Cochran 2004b). It is not clear what effect this moderate agreement would have on the results given that agreement at the other study sites was substantial to excellent

Colquhoun 1984

Methods	**FLUOROSIS STUDY** Country of study: New Zealand Geographic location: Auckland Year of study: 1983 Year of change in fluoridation status: 1953 Study design: cross-sectional

Colquhoun 1984 *(Continued)*

Participants	Inclusion criteria: school children aged 7-12 years Exclusion criteria: children with mottling who were known to have grown up in areas with different fluoridation status from the place in which they were examined Other sources of fluoride: fluoride toothpaste use accounted for 76% of toothpaste sales in New Zealand in 1980. Though there had been a marked increase in fluoride toothpaste use since 1970, there was no trend toward a greater severity of dental fluorosis among younger children Social class: results stratified on social class - incidence of advanced dental fluorosis inversely related to social class but prevalence of dental fluorosis slightly higher in lower social class Ethnicity: ethnic composition of study areas was similar except for higher proportion of Maori and Pacific Island people in the lower socioeconomic areas Residential history: proportion of children at each clinic who were not life-long residents of the suburb was not ascertained, but there was no reason to suppose that proportions differed between areas Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (diffuse opacities) Age at baseline measure: 7-12 years
Funding	Not stated
Notes	Data extracted from Colquhoun 1984 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	A population of 458 school children in the fluoridated area had initially been investigated, so the author made further observations on school children of the same age in 6 additional dental clinics chosen at random. An additional 342 children of same age were examined from the non-fluoridated area, but how they were selected was not reported
Confounding	High risk	Some children had used fluoride tablets, but were not excluded from the analysis. The fluoridated area had participants that were of low, middle and high SES while the non-fluoridated area had only participants of low SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	Intra- and inter-examiner reliability not mentioned

Correia Sampaio 1999

Methods	**FLUOROSIS STUDY** Country of study: Brazil Geographic location: rural areas of Paraiba Year of study: 1997 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; children attending public schools (aged 6-11 years) Exclusion criteria: children who refused to be examined; those without permanent teeth; undetermined place of birth Other sources of fluoride: no topical or systemic fluoride programme implemented in schools; children interviewed about oral health habits and use of toothpaste Social class: all study areas were of low socioeconomic status Ethnicity: not stated Residential history: lifetime residents Other confounding factors: nutritional status
Interventions	Group 1: > 1.0 ppm (natural fluoridation) Group 2: 0.7-1.0 ppm (natural fluoridation) Control: < 0.7 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TF Index) Age at assessment: 6-11 years
Funding	Brazilian Ministry of Education CAPES (1666/95-4)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Low risk	All eligible children attending schools in the study area were included
Confounding	Unclear risk	It was reported that the areas of study were generally low SES. Data were collected on the use of fluoride toothpaste and brushing habits, but showed that those brushing their teeth less frequently had higher levels of fluorosis. It was also reported that the levels of fluorosis in the area had not changed since the introduction of fluoride toothpastes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants

Correia Sampaio 1999 *(Continued)*

Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported and balanced across groups
Other bias	Low risk	No other apparent biases

Cutress 1985

Methods	**FLUOROSIS STUDY** Country of study: New Zealand Geographic location: Auckland, Frankton and Rodney Year of study: not stated Year of change in fluoridation: 1953 Study design: cross-sectional
Participants	Inclusion criteria: children returning parental consent forms and completed questionnaires; lifetime residents of study areas; children aged 9 Exclusion criteria: none stated Other sources of fluoride: ingestion of fluoride tablets Social class: not stated Ethnicity: European (80% F; 84% non F); Polynesian (16%F; 11% non-F); Asian (2% F; 1% Non-F); Mixed (2% F; 4% non-F). Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1.0 ppm (artificial fluoridation) Group 2: < 0.3 ppm (natural fluoridation)
Outcomes	Any enamel defect Age at assessment: 9 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Schools in the fluoridated area were randomly selected. All schools in the control area were selected. No details were reported about how the children were selected for the study
Confounding	High risk	There was an imbalance in lifetime residents using fluoride tables in the fluoridated area compared to the non-fluoridated area. SES was not accounted for
Blinding of outcome assessment (detection bias)	Low risk	Children were taken to the examination centre by bus to prevent the examiner from identifying residence or fluoridation status

Cutress 1985 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Cypriano 2003

Methods	**FLUOROSIS STUDY** Country of study: Brazil Geographic location: Porto Feliz, Ipero, Itaoca and Barra do Chapeu (F); Bom Sucesso do Itarare and Itapirapua Paulista (non-F) Year of study: 2003 Year of change in fluoridation status: 1981 Study design: cross-sectional
Participants	Inclusion criteria: pre-school children aged 5-6 years and students aged 7-12 years Exclusion criteria: individuals outside the 5-12 years age bracket Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	Group 1: 'optimal' level - ppm not stated (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (Community Fluorosis Index) Age at assessment: 5-12 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	7 out of 48 counties were randomly selected by raffle, based on size and the presence or absence of fluoridated water. Children were then randomly selected from schools

Cypriano 2003 *(Continued)*

Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants appears to be presented
Selective reporting (reporting bias)	High risk	Fluorosis data were not reported for children between 5 and 6 years and no explanations were provided.
Other bias	Low risk	No other apparent bias

de Crousaz 1982

Methods	**FLUOROSIS STUDY** Country of study: Switzerland Geographic location: Bale-Ville (F); Friburg and Neuchatel (non-F) Year of study: 1979 Year of change in fluoridation status: 1961 Study design: cross-sectional
Participants	Inclusion criteria: not stated for control areas, for fluoride area only Exclusion criteria: children born outside Switzerland Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (TFI) Age at assessment: 6-13 years
Funding	Subsidy from SSO research funds
Notes	Data extracted from de Crousaz 1982 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement

de Crousaz 1982 *(Continued)*

Sampling	Unclear risk	The children were accessed via schools, however the sampling frame was unspecified
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Examiners worked independently without knowledge of the origin of the children
Incomplete outcome data (attrition bias) All outcomes	High risk	Data were not presented for all participants and missing outcome data varied greatly across study groups
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	Examiners were calibrated and trained but kappa values for reliability not reported. The authors assume that a combination of clinical and photographic examination are sufficient for the verification of intra-and inter-examiner reproducibility, so kappa values may not have been calculated

DHSS England 1969

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: Watford (F); Sutton (non-F) Year of study: 1956 Year study ended: 1967 Year of change in fluoridation status: 1956 Study design: CBA
Participants	Inclusion criteria: lifetime residents of study areas; consumed piped water at home and at school Exclusion criteria: children that were not continuous residents Other sources of fluoride: none stated Social class: none stated, however, study areas and associated control area had be situated near to each other and be of the same character (e.g. industrial, semi-industrial, rural or residential) Ethnicity: none stated Residential history: lifetime residents Other confounding factors: information on oral hygiene was recorded
Interventions	**Initiation of water fluoridation** Group 1 at baseline: 'low' level - ppm not stated (natural fluoridation) Group 1 post intervention: 0.89-0.99 ppm (artificial fluoridation) Group 2: 'low level' - ppm not stated (natural fluoridation)
Outcomes	dmft, DMFT, % caries-free subjects (deciduous teeth), % caries-free subjects (permanent teeth) Age at baseline measure: 3-14 years Age at final measure: 3-14 years

DHSS England 1969 *(Continued)*

Funding	Not stated
Notes	Data extracted from DHSS England 1969 differs from that presented in CRD review (additional data extracted)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Representative groups of children of all ages included in the study were examined in each area and as far as possible the same standards of examination were maintained in the pairs of areas for which the dental findings were to be compared (HMSO 1962)
Confounding	High risk	No details were reported on the use of fluoride from other sources or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants appears to have been presented
Selective reporting (reporting bias)	High risk	Enamel defects, white or stained, which might be confused with fluoride mottling were also noted but not presented in the report; standard deviation not reported
Other bias	High risk	No mention of calibration and reliability testing of the examiners

DHSS Scotland 1969

Methods	**CARIES STUDY** Country of study: Scotland Geographic location: Kilmarnock (F); Ayr (non-F) Year study started: 1961 Year study ended: 1968 Year of change in fluoridation status: 1956 Study design: cBA
Participants	Inclusion criteria: lifetime residents of study areas; consumed piped water at home and at school Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: continuous residents Other confounding factors: not stated
Interventions	**Initiation of fluoridation**

DHSS Scotland 1969 *(Continued)*

	Group 1: 1 ppm (artificial fluoridation) Group 2: 'low' level - ppm not reported (natural fluoridation)
Outcomes	dmft, % caries-free subjects (primary teeth) Age at baseline measure: 5 years Age at final measure: 5 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Representative groups of children of all ages included in the study were examined in each area and as far as possible the same standards of examination were maintained in the pairs of areas for which the dental findings were to be compared (HMSO 1962)
Confounding	High risk	The effect of sugary diet consumption and use of fluoride from other sources were not taken into account
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blind outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	A cross-section of children were examined each year, together with some children in nurseries and nursery schools, but findings for the later were not presented
Selective reporting (reporting bias)	High risk	Enamel defects, white or stained, which might be confused with fluoride mottling were also noted but not presented in the report; standard deviation not reported
Other bias	High risk	No mention of calibration of examiners and reliability testing

DHSS Wales 1969

Methods	**CARIES STUDY** Country of study: Wales Geographic location: Gwalchmai zone (F); Holyhead (mainly F - gets most of water from Gwalchmai, but occasionally also receives water from Bodafon); and Bodafon zone (non-F) Year study started: 1956 Year study ended: 1965 Year of change in fluoridation status: 1955 Study design: CBA
Participants	Inclusion criteria: continuous residents of study areas; consumed piped water both at home and school; up to 15 years (Gwalchmai and Bodafon); up to 11 years (Holyhead) Exclusion criteria: not stated Other sources of fluoride: not stated

DHSS Wales 1969 *(Continued)*

	Social class: none stated, however, study areas and associated control area had be situated near to each other and be of the same character (e.g. industrial, semi-industrial, rural or residential) Ethnicity: not stated Residential history: continuous residents Other confounding factors: information on oral hygiene was recorded
Interventions	**Initiation of water fluoridation** Group 1 baseline: 'low' level - ppm not stated (natural fluoridation) Group 1 post intervention: 0.8-0.9 ppm (artificial fluoridation) Group 2 baseline: 'low' level - ppm not stated (natural fluoridation) Group 2 post intervention: 0.8-0.9 ppm (artificial fluoridation) Group 3: 'low' level - ppm not stated (natural fluoridation)
Outcomes	dmft, DMFT, % caries-free subjects (deciduous teeth), % caries-free subjects (permanent teeth) Age at baseline measure: 3-14 years Age at final measure: 3-14 years
Funding	Not stated
Notes	Data extracted from DHSS Wales 1969 differs from that presented in CRD review (additional data extracted)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Pre-school children examined were a reasonably good cross-section of Anglesey children of that age, however, different age criteria were used for school children in different study areas (up to 15 years in Gwalchmai and Bodafon; up to 11 years in Holyhead). The reason for this was not reported. (HMSO 1962)
Confounding	High risk	No details were reported on the use of fluoride from other sources or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants appears to be presented
Selective reporting (reporting bias)	High risk	Enamel defects, white or stained, which might be confused with fluoride mottling were also noted but not presented in the report
Other bias	High risk	No mention of calibration and reliability testing of examiners

Downer 1994

Methods	**FLUOROSIS STUDY** Country of study: England, Scotland and Ireland Geographic location: Dublin (F); north London, Edinburgh and Glasgow (non-F)

Downer 1994 *(Continued)*

	Year of study: not stated Year of change in fluoridation status: 1965 Study design: cross-sectional
Participants	Inclusion criteria: children aged 12 years; lifetime residents of study areas Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated, however, sampling in the fluoridated areas was done to achieve a mix of participants from different SES Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 0.9 ppm (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation) Group 3: 'low' level - ppm not stated (natural fluoridation) Group 4: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Enamel defects (DDE); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 12 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	25% of the secondary schools in Glasgow and Dublinwere randomly selected to participate, and participants were selected at random. Sampling in London was aimed at examining all 12-year-old children in secondary schools in 3 districts and 14 out of 19 schools. The reason for non-participation of 5 out of the 19 eligible schools in the non-fluoridated area was logistical and the authors state that this was (Quote:) *"unlikely to have caused sampling bias".* In Edinburgh a random selection of 20% of children in 20 out of 50 eligible schools, drawn at random, formed the sample
Confounding	High risk	No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis

Downer 1994 *(Continued)*

Other bias	Low risk	No other apparent bias

Driscoll 1983

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: 7 rural Illinois communities within 75 miles of each other Year of study: 1980 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children in grades 3-10 (age 8-16 years); lifetime residents of study areas; consumed public water Parental consent Exclusion criteria: not stated Other sources of fluoride: not stated Social class: relatively small, rural communities chosen because they shared several similar characteristics Ethnicity: < 5% non white Residential history: lifetime residents Other confounding factors: same climatic zone
Interventions	Group 1: 3.84-4.07 ppm (natural fluoridation) Group 2: 2.84-3.77 ppm (natural fluoridation) Group 3: 2.08 ppm (natural fluoridation) Group 4: 1.06 ppm (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index; CFI; TSIF was also used but reported in a later paper); caries data were measured but excluded from this review due to study design Age at assessment: 8-16 years
Funding	Not stated
Notes	None of the communities had made any change in its water source that was likely to alter the fluoride concentration during the period relevant to the study

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Different examiners carried out measurements in order to avoid bias, however, this may not have been sufficient to avoid detection bias

Driscoll 1983 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All findings were based only on those children assessed for both fluorosis and majority of the children fall under this category. Also, the higher-than-optimal study area had considerably fewer children compared to the other areas due to small size of the communities and other similar communities in same geographic area were not available. This was not considered sufficient to introduce bias
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Ekanayake 2002

Methods	**FLUOROSIS STUDY** Country of study: Sri Lanka Geographic location: Uda Walawe Year of study: 2001 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: completion of the 14th but not the 15th birthday; availability in school on the day of the examination Exclusion criteria: not stated Other sources of fluoride: not stated Social class: almost all belonged to the low socioeconomic group Ethnicity: not stated Residential history: resident at present address since birth Other confounding factors: no details reported; nearly 75% of the subjects had used fluoride toothpaste from the age of about 9-12 months (discussion section)
Interventions	All natural fluoridation Group 1: ≤ 0.3 ppm Group 2: 0.31-0.49 ppm Group 3: 0.5-0.7 ppm Group 4: > 0.7 ppm
Outcomes	Enamel defect (DDE) Age at assessment: 14 years
Funding	Not stated
Notes	
Risk of bias	

Ekanayake 2002 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	6 schools were selected on the basis of being sufficiently large for study. All eligible children present on day of study were examined
Confounding	High risk	While it is stated in the paper that "Less than 75% of the participants started teeth brushing with fluoride toothpaste from 9-12 months of age", the use of other fluoride sources was not controlled for, neither was it reported by fluoridation status
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	6.25% of the children examined were not included in the analysis. The authors did not report their fluoride exposure, and it is not clear whether their exclusion may have introduced bias
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Eklund 1987

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Lordsburg (high-F); Deming (lower-F), New Mexico Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: resident in study areas for the first 6 years of life; subjects aged approximately 30-60 years old; consumed city water supplies Exclusion criteria: not stated Other sources of fluoride: not stated Social class: areas similar for education and income level; number of years of education similar between areas Ethnicity: Lordsburg: 89.6% = Hispanic; Deming: 74.2% = Hispanic Residential history: residence for the first 6 years of life Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 3.5 ppm Group 2: 0.7 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design

Eklund 1987 *(Continued)*

	Age at assessment: 27-65 years
Funding	Not stated
Notes	Data extracted from Eklund 1987 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Efforts were made to recruit all eligible adults in all the communities and 80%-90% of eligible people consented and participated
Confounding	High risk	No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Ellwood 1995

Methods	**FLUOROSIS STUDY** Country of study: Ireland and Wales Geographic location: Chester (non-F); Bala (non-F); Anglesey (F); Cork (F) Year of study: 1991 Year study ended: not reported Year of change in fluoridation status: NA Study design: cross-sectional study
Participants	Inclusion criteria: lifetime residents of study areas (children only); agreement to participate Exclusion criteria: fixed orthodontic appliances Other sources of fluoride: tooth brushing behaviour - age started brushing; weekly tooth brushing frequency Social class: children from all 3 groups were from schools with a similar social profile Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated

Ellwood 1995 *(Continued)*

Interventions	Group 1: 0.7 ppm (artificial fluoridation) Group 2: 0.9 ppm (artificial fluoridation) Group 3: < 0.1 ppm (natural fluoridation)
Outcomes	Enamel defect (DDE) Age at assessment: 14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	Low risk	SES and reported tooth brushing frequency were similar across groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Photographs were taken, identified randomly and examined without reference to subject details
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Ellwood 1996

Methods	**FLUOROSIS STUDY** Country of study: England and Wales Geographic location: Anglesey (F); Chester and Bala (non-F) Year of study: 1991 Year of change in fluoridation status: 1955 Study design: cross sectional
Participants	Inclusion criteria: children in their 3rd year of secondary education; lifelong residents of study areas Exclusion criteria: children with fixed orthodontic appliances; absence at the time of examination Other sources of fluoride: not stated Social class: not stated, however, the schools in the non-fluoridated areas had similar catchment areas to those from the fluoridated area. No further details reported Ethnicity: not stated

Ellwood 1996 *(Continued)*

	Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 0.7 (artificial fluoridation) Control: < 0.1 (natural fluoridation)
Outcomes	Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	3 schools from Anglesey were selected and for the control group, schools with catchment areas as similar as possible to those from Anglesey were chosen from Chester and Bala using national census statistics.There was no random selection of schools in Anglesey, and it is not clear whether the selected schools were a representative sample
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Photographs were taken, randomly mixed and scored without reference to subject details
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Ermis 2003

Methods	**FLUOROSIS STUDY** Country of study: Turkey Geographic location: Izmir and Isparta Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifelong residence; use of the public water supply continuously as source of drinking water; absence of nutrition deficiency

Ermis 2003 *(Continued)*

	Exclusion criteria: not stated Other sources of fluoride: not stated Social class: the selected schools were public secondary schools Ethnicity: not stated Residential history: lifetime residents Other confounding factors: toothbrushing frequency: did not brush = 22 (7.9%); irregularly = 49 (17.6%); once a day = 115 (41.4%); more than once = 92 (33.1%)
Interventions	All natural fluoridation Group 1: 0.3-0.4 ppm Group 2: 1.42-1.54 ppm Group 3: 1.55-1.66 ppm
Outcomes	Dental fluorosis prevalence (TSIF); caries data also evaluated within the study but excluded from review due to study design due to study design Age at assessment: 12-14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	4 schools were selected using a random sampling technique from a list of all public secondary schools. Within these schools eligible children were selected randomly
Confounding	Unclear risk	Toothbrushing habits differed between participants, however it is not clear whether they varied across study groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Fluorosis prevalence was measured, but only reported for the high fluoride areas and not for the low fluoride area
Other bias	Low risk	No other apparent bias

Firempong 2013

Methods	**FLUOROSIS STUDY** Country of study: Ghana

Firempong 2013 *(Continued)*

	Geographic location: Bongo district (Zone A: Atampiisi, Soeboko and Aliba; Zone B: Nayire, Boyrigo, Anabisa, Amagre and Tigre; Zone C: Soe, Kuyeligo, and Kunduo; Zone D: Yakanzanway, Gurigo, Ababorobiisi, Zaasi, and Anafobiisi) Year of study: 2008-2009 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lived in the area for the first 7 years of childhood; using water from a constant source that could still be traced Exclusion criteria: medically confirmed dental problem different from dental fluorosis; history of tobacco or kola use Other sources of fluoride: information on frequency of toothbrushing (P value 0.101) and type of oral health product (P value 0.179) were collected and there was no difference between the 4 zones Social class: the children had similar educational backgrounds Ethnicity: not stated Residential history: lifetime residents for first 7 years of childhood Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.95 ppm Group 2: 1 ppm Group 3: 1.86 ppm Group 4: 2.36 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 7-18 years
Funding	Supported by the Regional Laboratory of the Ghana Water Company/Aqua Viten Rands Limited in Tamale, Ghana
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Stated that eligible children were randomly selected, but insufficient detail provided to make a clear judgement
Confounding	High risk	While there appears to be little difference in the use of oral hygiene habits across groups, did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants

Firempong 2013 *(Continued)*

Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	Quote: "A professional examiner was engaged to carry out all the testing measurements ..." Comment: intra-examiner reliability test not reported and may not have been conducted

Forrest 1956

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: West Mersey (5.8 ppm); Burnham-on-Crouch (3.5 ppm); Harwich (2/1.6 ppm); Slough (0.9 ppm) Saffron Walden and District (non-F); Stoneleigh and Malden West (non-F) Year of study: 1954 Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: lifetime residents of study areas; children aged 12-14 years Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 5.8 ppm Group 2: 3.5 ppm Group 3: 2.0 ppm Group 4: 0.9 ppm Group 5: 0.1-0.2 ppm Group 6: 0.1 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design due to study design Age at assessment: 12-14 years
Funding	Not stated
Notes	Data extracted from Forrest 1956 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement

Forrest 1956 *(Continued)*

Sampling	Unclear risk	Areas were selected opportunistically. Entire populations of children in some areas were selected for study but insufficient detail is given on how they were accessed
Confounding	High risk	SES and the use of other fluoride sources was not sufficiently reported and controlled for
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Results are presented for the majority of participants. However, while the results are presented in full for 4 of the 5 areas the area of highest F ppm appears to have 10% of participants missing from results
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	There is risk of measurement bias as examiner calibration was not mentioned

Forrest 1965

Methods	**FLUOROSIS STUDY** Country of study: Wales Geographic location: Gwalchmai (F); Bodafon (non-F), Anglesey Year of study: 1963 Year of change in fluoridation status: 1955 Study design: cross-sectional
Participants	Inclusion criteria: children aged 8 years from a selection of schools Exclusion criteria: schools in Holyhead; schools in Llangefni and Beaumaris, as changed supply from fluoridated to non-fluoridated in 1961 Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not clearly stated, however, the participants were chosen for being the only ones who had had fluoride for most of their lives Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: ≤ 0.2 ppm (natural fluoridation)
Outcomes	Outcome: enamel defects Age at assessment: 8 years
Funding	Not stated

Forrest 1965 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Schools were selected for study and then children within these schools, however it is not clear how the children were examined
Confounding	High risk	SES and the use of fluoride from other sources were not reported on
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The examiners were unaware of the children's fluoridation status since they all resided in the same county.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Franzolin 2008

Methods	**FLUOROSIS STUDY** Country of study: Brazil Geographic location: Sao Paulo Year of study: not stated Year of change in fluoridation status: 1975 Study design: cross-sectional
Participants	Inclusion criteria: residence in the same geographical area as the school since birth Exclusion criteria: not stated Social class: homogenous population comprising entirely of public school students Ethnicity: white = 243 (67.5%); black = 41 (11.4%); admixture = 73 (20.3%); Asian = 3 (0.8%) Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 'optimal' level - ppm not stated (artificial fluoridation via water treatment station) Group 2: 'optimal' level - ppm not stated (artificial fluoridation via direct fluoridation in well) Group 3: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (TF Index); caries data collected, however, excluded from the review due to study design Age at assessment: 12 years

Franzolin 2008 *(Continued)*

Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Multi-stage random sampling was used whereby schools were selected randomly and the children within them
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The examiner and recorder were reported to have been blinded to the type of water supply of the schools
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Unclear risk	Examinations carried out by a single, previously calibrated examiner, however, kappa score not reported

Garcia-Perez 2013

Methods	**FLUOROSIS STUDY** Country of study: Mexico Geographic location: Morelos Year of study: 2013 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children who had been born in the community, lived in the community from 1 year of age onwards, or had not moved in or out of the community for more than 6 months Exclusion criteria: systemic diseases requiring premedication; absence on the days of the oral examination; children who had brackets Other sources of fluoride: bottled water often containing 0.3-0.6 ppm fluoride levels; dentifrice use; number of times brushing teeth per day Social class: both communities had a low socioeconomic level Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation

Garcia-Perez 2013 *(Continued)*

	Group 1: 0.56-0.76 ppm Group 2: 1.45-1.61 ppm
Outcomes	Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 12 years
Funding	Partially funded by the Metropolitan Autonomous University, Xochimilco (Universidad Autonoma Metropolitana, UAM-X) and the National Council of Science and Technology (Consejo Nacional de Ciencia y Tecnologia, CONACYT)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	Low risk	Both villages were of low SES, participants were lifetime residents and there was no difference in toothbrushing frequency or bottled water consumption
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data presented as percentages making it difficult to determine if all participants are accounted for
Selective reporting (reporting bias)	High risk	Fluorosis prevalence was not reported for all severities of dental fluorosis
Other bias	Low risk	No other apparent bias

Gaspar 1995

Methods	**FLUOROSIS STUDY** Country of study: Brazil Geographic location: Piracicaba (F); Iracemapolis (non-F) Year of study: not stated Year of change in fluoridation status: 1974 Study design: cross-sectional
Participants	Inclusion criteria: children aged 10-14; lifetime residents of study areas Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: not stated Social class: not stated

Gaspar 1995 *(Continued)*

	Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: < 0.2 ppm (natural fluoridation) Group 2: 0.7 ppm (artificial fluoridation)
Outcomes	Dental fluorosis prevalence (TF Index) Age at assessment: 10-14 years
Funding	Not stated
Notes	Data from CRD review (unverified data)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Unable to make a judgement as study was unavailable
Confounding	High risk	Did not appear to account for the use of other fluoride sources or SES in analysis
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unable to make a judgement as study was unavailable
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unable to make a judgement as study was unavailable
Selective reporting (reporting bias)	Unclear risk	Unable to make a judgement as study was unavailable
Other bias	Unclear risk	Unable to make a judgement as study was unavailable

Goward 1982

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: 2 adjacent districts of Leeds with different fluoride levels Year of study: 1979 Year of change in fluoridation status: 1968 Study design: cross sectional
Participants	Inclusion criteria: lifetime residents of study areas (children only); children aged 5 Exclusion criteria: not clear, though children using systemic or topical fluoride supplements were excluded from the study Other sources of fluoride: children using systemic or topical fluoride supplements excluded from the study

Goward 1982 *(Continued)*

	Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: difference in breast fed vs bottle fed children
Interventions	Group 1: 0.9 ppm (artificial fluoridation) Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	Dental fluorosis (defined by Al-Alousi) Age at time of measurement: 5 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	No information on calibration of examiners

Gray 2001

Methods	**CARIES STUDY** Country of study: England Geographic location: Dudley (F), Sedgeley and Cosely (F), Halesowen (F), Brierly Hill and Kingswinford (F); Stourbridge (non-F) Year study started: 1988 Year study ended: 1997 Year of change in fluoridation status: 1987 Study design: CBA
Participants	Inclusion criteria: children living in study area since 1988

Gray 2001 *(Continued)*

	Exclusion criteria: not stated Other sources of fluoride: not stated Social class: participants were all from state-funded primary schools and might have been socioeconomically similar Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1: 1 ppm (artificial fluoridation) Group 2: 1 ppm (artificial fluoridation) Group 3: 1 ppm (artificial fluoridation) Group 4: 1 ppm (artificial fluoridation) Group 5: 0.3 ppm (natural fluoridation)
Outcomes	% caries free (deciduous teeth) Age at baseline measure: 5 years Age at final measure: 5 years
Funding	Not stated
Notes	Data extracted from Gray 2001 differs from that from Gray 2000 (unpublished) which was originally presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	According to Pitts 1997, representative samples were drawn from a whole population of Dudley health authority
Confounding	High risk	No details were reported on the use of fluoride from other sources or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "...blinding was not possible"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome was reported
Other bias	High risk	At baseline the fluoridation status of the children was determined by the location of their school

Grimaldo 1995

Methods	**FLUOROSIS STUDY** Country of study: Mexico Geographic location: San Luis Potasi Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents at same address; children aged 11-13 years in selected schools; parental consent Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: local diet rich in calcium, reduces fluoride absorption
Interventions	All natural fluoridation Group 1: > 2.0 ppm Group 2: 1.2-2.0 ppm Group 3: 0.7-1.2 ppm Group 4: < 0.7 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 11-13 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	The authors reported that schools and participants from the study areas were selected at random. No further details reported
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	There was a variation in the numbers of children reported to have been examined for dental fluorosis compared to the number of children initially reported to be receiving different water fluoride levels
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups

Grimaldo 1995 *(Continued)*

Other bias	High risk	No indication that the examiners were calibrated

Grobler 1986

Methods	**FLUOROSIS STUDY** Country of study: South Africa Geographic location: Nourivier (low F); Tweeriviere (high F) in North Western Cape province Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; children aged 12-13 years Exclusion criteria: not stated Other sources of fluoride: both communities had virtually no dental care or fluoride therapy Social class: similar socioeconomic status in both study areas (reported by authors) Ethnicity: similar ethnicity in both study areas (reported by authors) Residential history: lifetime residents Other confounding factors: areas similar in nutrition and dietary habits (reported by authors); temperature 27 °C-32 °C
Interventions	All natural fluoridation Group 1: 3.7 ppm Grpup 2: 0.62 ppm
Outcomes	Outcome: fluorosis prevalence (Deans Index); caries data collected but not presented in this review due to study design Age at assessment: 12-13 years
Funding	Not stated
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	All available subjects were included in the study population. Insufficent information was reported on the sampling frame
Confounding	Low risk	SES was similar across groups and there was virtually no dental care or fluoride therapy in the population at the time
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information. Examinations were made at the children's schools but no mention of blind assessment

Grobler 1986 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	High risk	Examinations were done by a single examiner but no mention of intra-examiner calibration

Grobler 2001

Methods	**FLUOROSIS STUDY** Country of study: South Africa Geographic location: Leeu Gamka, Kuboes and Sanddrif Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: continuous residence since birth; having virtually no dental care or fluoride therapy including the use of fluoride-containing toothpaste; absence of any obvious under-nutrition and no dietary habits that could significantly contribute to the ingestion of fluorine Exclusion criteria: not stated Other sources of fluoride: participants had virtually no dental care or fluoride therapy, including the use of fluoride-containing toothpaste Social class: similarly low socioeconomic status across groups reflected in the fact that they all lived in sub-economic housing units Ethnicity: mixed ethnic origin from Khoi, Caucasian and Negroid roots which over hundreds of years have developed into a homogenous ethnic group Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.19 ppm Group 2: 0.48 ppm Group 3: 3 ppm
Outcomes	Outcome: fluorosis prevalence (Deans Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 10-15 years
Funding	Not stated
Notes	
Risk of bias	

Grobler 2001 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All available children in the specified study areas were examined
Confounding	Low risk	SES was similar across groups and there was virtually no exposure to fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Guo 1984

Methods	**CARIES STUDY** Country of study: Taiwan Geographic location: Chung-Hsing New Village (F); Tsao-Tun (non-F) Year of study: 1971 Year study ended: 1984 Year of change in fluoridation status: 1971 Study design: CBA
Participants	Inclusion criteria: lifetime residents of study areas Exclusion criteria: children who migrated from other areas during study period Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: similar climate with mean daily air temperature of 24 °C
Interventions	**Initiation of water fluoridation** Group 1 baseline: 0.07 ppm (natural fluoridation) Group 1 post intervention: 0.6 ppm (artificial fluoridation) Group 2: 0.08 ppm (natural fluoridation)
Outcomes	dmft, DMFT, % caries free (deciduous), % caries free (permanent) Age at baseline measure: 5, 8, 12 and 15 years

Guo 1984 *(Continued)*

	Age at final measure: 5, 8, 12 and 15 years
Funding	Not stated
Notes	Data extracted from Guo 1984 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children in the study areas were included in the study
Confounding	High risk	Did not account for the use of other fluoride sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	Examinations were carried out by the dentists from the University hospital and recorded on the same type of record forms but there is no mention of examiner calibration

Haavikko 1974

Methods	**FLUOROSIS STUDY** Country of study: Finland Geographic location: Espoo (low F); Elimaki (high F); Hanko (optimal F); Lohja (low F) Year of study: 1969 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children who had been resident in study areas for the first 6 years of life; children aged 10-11 years Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: continuous residence for the first 6 years Other confounding factors: food sources of fluoride
Interventions	All natural fluoridation

Haavikko 1974 *(Continued)*

	Group 1: 1.08 ppm Group 2: 0.41 ppm Group 3: 0.11 ppm Group 4: 0.05 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 10-11 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Eligible children were selected at random from the health records. No further details regarding the sampling frame were reported
Confounding	High risk	SES and the use of fluoride from other sources were not reported on
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	High risk	Both dentists carried out the diagnosis of enamel defects but there was no mention of examiner calibration

Harding 2005

Methods	**FLUOROSIS STUDY** Country of study: Ireland Geographic location: Cork city (F); Cork county (non-F) Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: age 5 years; location of the school attended and fluoridation status of water supply Exclusion criteria: absence on the day of examination; too apprehensive to participate or < 5 years; incorrectly received a form; incomplete form; existing medical condition Other sources of fluoride: fluoride prevalence of children with different nutritional and brushing habits were reported: breast-fed = 30 (28%) vs not breast-fed = 38 (21%); brushing before 12 months: F = 47 (22.6%) vs non-F = 19 (22.1%); started brushing with toothpaste between 12 and 18 months: F =

Harding 2005 *(Continued)*

	79 (38%) vs non-F = 25 (29.1%); started brushing with toothpaste between 19 and 24 months: F = 37 (17.8%) vs non-F = 21 (24.4%); started brushing with toothpaste after 24 months: F = 41 (19.7%) vs non-F = 18 (20.9%) Social class: schools were chosen to provide a socioeconomic spread; 7 urban and 10 rural schools Ethnicity: not stated Residential history: lifetime residents Other confounding factors: food sources of fluoride
Interventions	Group 1: 0.8-1 ppm (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (TSIF) Age at assessment: 5 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A stratified sample for 5-year olds was drawn from study areas on the basis of age, location, school attended and fluoridation status. Schools were chosen to provide a socioeconomic spread
Confounding	Low risk	SES range (by school) was sampled. There were similar levels of toothpaste use across the groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Of the 311 participants examined, outcome data were not presented for 17 participants due to partial fluoride history; unlikely to influence the results
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	Clinical examination was carried out by one examiner trained extensively by a gold standard but no report of calibration nor intra-examiner reliability tests

Hardwick 1982

Methods	**CARIES STUDY** Country of study: England Geographic location: Alsager, Middlewich, Nantwich (F), Northwich (non-F) Year study started: 1974 Year study ended: 1978

Hardwick 1982 *(Continued)*

	Year of change in fluoridation status: 1975 Study design: prospective cohort
Participants	Inclusion criteria: 12-year-old children living in study area. Consent from relevant country authorities and teachers at schools included in the study Exclusion criteria: none stated Other sources of fluoride: Fluoride group (n = 152): 142 (94%) used only fluoride dentifrices; 125 (83%) used at least once a day Control group (n = 194): 185 (95%) used only fluoride dentifrices; 147 (76%) used at least once a day 2 children in fluoride group and 4 children in control had used fluoride tablets Social class: control and experimental groups matched on urban and rural characteristics Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1 baseline: < 0.1 ppm (natural fluoridation) Group 1 post intervention: 1.0 ppm (artificial fluoridation) Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	DMFT, DMSF Age at baseline measure: 12 years Age at final measure: 16 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were invited to participate
Confounding	High risk	Use of fluoride from other sources was broadly equal between the groups. The groups were matched on SES however, no information was reported on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The children were transported to a central examination centre in small numbers and were then randomly mixed with children from the other group. Furthermore, the children were requested not to wear school uniform and, in case they forgot, donned a large operating gown to hide their clothes"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants

Hardwick 1982 *(Continued)*

Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Heifetz 1988

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: 7 rural towns within 75 miles of each other in Illinois Year of study: 1980-1985 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 8-10 and 13-15 years; continuous residence in study community Exclusion criteria: not stated Other sources of fluoride: food and drinks produced in fluoride areas Social class: study areas shared similar socioeconomic characteristics Ethnicity: not stated Residential history: continuous residence Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 3.8-4.1 ppm Group 2: 2.8-3.8 ppm Group 3: 2.1 ppm Group 4: 1.1 ppm
Outcomes	Dental fluorosis (TSIF); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 13-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Participants consumed food and drinks produced in fluoride areas, however, it is not clear whether there was a difference in consumption among different areas. Insufficient detail is provided regarding use of fluoride from other sources

Heifetz 1988 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Heintze 1998

Methods	**FLUOROSIS STUDY** Country of study: Brazil Geographic location: Garca (F); Itrapolis (non-F), Sao Paulo state Year of study: 1995 Year of change in fluoridation status: 1973 and 1975 Study design: cross-sectional
Participants	Inclusion criteria: subjects aged 5-24 years; from all social strata; used tap water; took urine samples from all 3 daytime periods Exclusion criteria: usbjects that used tap water, otherwise not stated Other sources of fluoride: subjects asked about use of toothpaste or mouth rinses containing fluoride. 98% used toothpaste containing fluoride and 16.5% used a fluoride mouth rinse daily or weekly Social class: cities similar in socioeconomic and sociodemographic conditions, subjects from all social strata included Ethnicity: not stated Residential history: not stated Other confounding factors: Garca altitude = 526 m, mean temp = 22 °C, population = 41,351; Itapolis: altitude = 491 m, mean temp = 23 °C, population = 30, 111
Interventions	Group 1: 0.9 ppm (artificial fluoridation) Group 2: 0.02 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TF Index) Age at assessment: 5-24 years
Funding	Not stated
Notes	
Risk of bias	

Heintze 1998 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Participants were accessed via health centres, schools and factories and all eligible participants were included in the study
Confounding	High risk	Study areas were matched for SES. Information was collected on the use of fluoride paste and mouth rinse, however this was not reported according to exposure of water fluoridation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data presented as percentages making it difficult to determine if all participants are accounted for
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Unclear risk	Dental fluorosis was recorded by a trained and calibrated examiner, however, details of intra-examiner reliability not provided

Heller 1997

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: national survey of oral health of US school children Year of study: 1986 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; aged 7-17 years; ompletion of survey by parents Exclusion criteria: none stated Other sources of fluoride: written questionnaire included question regarding child's use of fluoride drops, fluoride tablets, professional topical fluoride treatments and school fluoride rinses Social class: not stated Ethnicity: not stated Residential history: continuous residency Other confounding factors: results standardised to age and sex distribution of US schoolchildren who participated in survey
Interventions	Group 1: > 1.2 ppm (natural fluoridation) Group 2: 0.7-1.2 ppm (artificial fluoridation) Group 3: 0.3-0.7 ppm (natural fluoridation) Group 4: < 0.3 ppm (natural fluoridation)

Heller 1997 *(Continued)*

Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 7-17 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Stratified sampling was carried out and oral examination was conducted for 78% of all sampled students
Confounding	High risk	Results were not adjusted for SES and the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Hernandez-Montoya 2003

Methods	**FLUOROSIS STUDY** Country of study: Mexico Geographic location: not stated Year of study started: 2001 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: having at least 1 year residence in the study area Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: ≥ 1 year residence in study area Other confounding factors: in all study areas, parents reported the use of fluoride toothpaste

Hernandez-Montoya 2003 *(Continued)*

Interventions	All natural fluoridation Group 1: 0.74 ppm Group 2: 1.3 ppm Group 3: 3.56 ppm Group 4: 4.07 ppm Group 5: 5.19 ppm Group 6: 5.57 ppm Group 7: 7.59 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 9-11 years
Funding	Financial and logistical support from the Health Institute of the State of Aguascalientes, Institute Tecnologico de Aguascalientes and COSNET
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Random sampling was performed and considered the total population exposed to fluoridated water at each study area
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some participants were excluded from the analysis but no reason was provided
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Unclear risk	Outcome was assessed by a working group previously trained and calibrated. Insufficient information on reliability testing

Holdcroft 1999

Methods	**CARIES STUDY** Country of study: England Geographic location: north Birmingham and Sandwell (F), North Staffordshire, Herefordshire and Shropshire (non-F) Year study started: 1985/6 Year of change in fluoridation status: 1986 Study design: CBA

Holdcroft 1999 *(Continued)*

Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not Stated Social class: measured using Jarman scores Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1: not stated Group 2: not stated
Outcomes	dmft Age at baseline measure: not stated Age at final measure: not stated
Funding	Not stated
Notes	Data from original CRD review (unverified data)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Unable to make a judgement as study was unavailable
Confounding	High risk	Data does not appear to have been controlled for SES and use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unable to make a judgement as study was unavailable
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unable to make a judgement as study was unavailable
Selective reporting (reporting bias)	Unclear risk	Unable to make a judgement as study was unavailable
Other bias	Unclear risk	Unable to make a judgement as study was unavailable

Hong 1990

Methods	**FLUOROSIS STUDY** Country of study: Taiwan Geographic location: Chung-hsing New village (F) and Tsao-tun (non-F)

Hong 1990 *(Continued)*

	Year of study: not stated Year of change in fluoridation status: 1978 Study design: cross sectional
Participants	Inclusion criteria: children aged 6-15 years: resident in village since initiation of fluoridation Exclusion criteria: children who migrated from other areas during study period Other sources of fluoride: not stated Social class: 2 communities alike in social and living customs Ethnicity: not stated Residential history: resident since fluoride initiation Other confounding factors: 2 areas have virtually identical climates, only 3 km apart
Interventions	Group 1: 0.6 ppm (artificial fluoridation) Group 2: 0.08 ppm (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 6-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	The participating sample consisted of children from 6-15 years in the study areas. No other information was provided on sample selection
Confounding	High risk	Did not account for the use of other fluoride sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest was fully reported on and balanced across groups
Other bias	Low risk	No other apparent bias

Ibrahim 1995

Methods	**FLUOROSIS STUDY** Country of study: Sudan

Ibrahim 1995 *(Continued)*

	Geographic location: Abu Gronn (F); Treit El Biga (low F) Year of study: 1992 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: at least 1 erupted permanent maxillary incisor; lifetime residents of study areas; age 7-16 years Exclusion criteria: not stated Other sources of fluoride: not stated Social class: author stated that areas had more or less the same socioeconomic background Ethnicity: author stated that areas had more or less the same ethnic background Residential history: lifetime residents Other confounding factors: altitude= 300m for both areas; mean temperature = 25-35 °C. In low F area boys had significantly more fluorosis than girls
Interventions	All natural fluoridation Group 1: 2.56 ppm Group 2: 0.25 ppm
Outcomes	Dental fluorosis (Community Fluorosis Index) Age at assessment: 7-16 years
Funding	Norwegian Universities Committee for Development Research and Education
Notes	Data extracted from Ibrahim 1995 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient information was reported on sampling; the sampling frame was unspecified
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	No mention of calibration of examiners and reliability testing

Indermitte 2007

Methods	**FLUOROSIS STUDY** Country of study: Estonia Geographic location: Tartu city Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: 12-year-old children; continuous residence; only districts supplied by definite tube wells of known fluoride concentration were selected Exclusion criteria: not stated Social class: selected districts were of same eco-environmental, ethnic as well as socioeconomic standards Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.2 ppm Group 2: 0.3 ppm Group 3: 1.2 ppm Group 4: 1.6 ppm Group 5: 2.4 ppm Group 6 3.9 ppm
Outcomes	Dental fluorosis (index not reported) Age at assessment: 12 years
Funding	The study was supported by the Target Funding Projects no. 0180052s07 and no. 0182648s04 of the Ministry of Education and Science of Estonia and by Estonian Society of Stomatololgy
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Areas of study were sampled purposively and limited information was reported on the selection of individuals
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants

Indermitte 2007 *(Continued)*

Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	Examination carried out by a trained examiner with an assistant, but no mention of calibration and reliability testing

Indermitte 2009

Methods	**FLUOROSIS STUDY** Country of study: Estonia Geographic location: not stated Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: < 1 ppm Group 2: 1-1.5 ppm Group 3: 1.51-2 ppm Group 4: 2.1-3 ppm Group 5: 3.1-4 ppm Group 6: > 4 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 7-15 years
Funding	The study was supported by the Estonian Society of Stomatology and Estonian Science Foundation grant number 7403
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Sampling was partly based on data from 2 previous studies which provide insufficient sampling information while the sub-sample was selected from town

Indermitte 2009 *(Continued)*

		of Tartu, where the fluoride content in drinking water varied significantly between regions
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	Clinical examination by a 'trained' dentist. Insufficient information on intra-examiner reliability testing

Ismail 1990

Methods	**FLUOROSIS STUDY** Country of study: Canada Geographic location: public and private schools in Trois Rivieres (F) and Sherbrooke (non-F), Quebec Year of study: 1987 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children randomly selected from private and public schools separately; children aged 11-17 years; resident in study areas for first 6 years Exclusion criteria: none stated Other sources of fluoride: fluoride tablet use around 13% in F areas and 67% in non-F area Social class: stratified on school type: private or public (authors state private school likely to have been higher social class) Ethnicity: not stated Residential history: resident from 0-6 years Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.0 ppm Group 2: < 0.1 ppm
Outcomes	Dental fluorosis prevalence (TSIF); caries data collected, however, not presented in this review due to study design Age at assessment: 11-17 years
Funding	National Health Research and Development Program, Health and Welfare (6605-1316-53)

Ismail 1990 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A 2-stage stratified sample was selected from each city. In the first stage, private and public schools were randomly selected. In the second stage, students were randomly selected from the private and public schools separately
Confounding	High risk	There was an imbalance of the use of fluoride supplements between groups with more supplements being consumed by those living in the non-fluoridated area
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Examiners were blind to the content of questionnaire" and by implication, fluoridation status of participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	No other apparent bias

Jackson 1975

Methods	**FLUOROSIS STUDY** Country of study: Wales Geographic location: Anglesey (F); Bangor and Caernarfon (non-F) Year of study: 1974 Year of change in fluoridation status: 1955 Study design: unclear
Participants	Inclusion criteria: lifetime residents of study areas; continuous use of public water supply; school children aged 15 years; parental consent Exclusion criteria: children who had ever received fluoride tablets; left the study area; did not consume piped water supply for entire life; unavailable at time of sampling Other sources of fluoride: children who had received fluoride tablets excluded Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 0.9 ppm (artificial fluoridation)

Jackson 1975 *(Continued)*

	Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	Mottling; caries data collected, however, not presented in this review due to study design Age at assessment: 15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Stated that children were randomly sampled, however information on sampling was insufficient
Confounding	High risk	Children who had received fluoride tablets were excluded, however SES was not taken into account
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants were taken to a central examination centre by taxi and examiners were unaware of the area from which a child came
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data presented for approximately 30% of participants sampled from each study area (Anglesey 28%; Bangor 32%)
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	High risk	Even though the examiners carried out their investigations independently, no sort of calibration seemed to have been carried out

Jackson 1999

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Connersville (non-F); Brownsburg (optimal-F); Lowell (high-F), Indiana Year of study: 1992 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; consumed public water from birth or supply with comparable water level;cChildren aged 7-14; parental and personal consent Exclusion criteria: factors in medical history that would contraindicate a dental examination; full mouth fixed orthodontic appliance Other sources of fluoride: use of fluoride supplements: non-F areas = 58%; optimal-F area = 20%; high-F area = 9%. Also fluoride from mouth rinses, gels, other topical applications Social class: not stated

Jackson 1999 *(Continued)*

	Ethnicity: approximately 2% non-white (stated for baseline survey) Residential history: lifetime residents Other confounding factors: areas all in same climatic zone
Interventions	All natural fluoridation Group 1: 4.0 ppm Group 2: 1.0 ppm Group 3: 0.2 ppm
Outcomes	Dental fluorosis (TSIF) Age at assessment: 7-10 years and 11-14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Information on the use of other fluoride sources was collected, however, the results were not adjusted for this factor. Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The examiner was unaware of the residency status of the participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Jolly 1971

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: the Punjab Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children Exclusion criteria: none stated

Jolly 1971 *(Continued)*

	Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All naturally fluoridated Group 1: 0.7 ppm Group 2: 1.4 ppm Group 3: 2.4 ppm Group 4: 2.4 ppm Group 5: 2.5 ppm Group 6: 3.0 ppm Group 7: 3.0 ppm Group 8: 3.3 ppm Group 9: 3.3 ppm Group 10: 3.6 ppm Group 11: 4.3 ppm Group 12: 5.0 ppm Group 13: 5.09 ppm Group 14: 5.49 ppm Group 15: 7.02 ppm Group 16: 8.5 ppm Group 17: 9.5 ppm
Outcomes	Mottled enamel Age at assessment: 5-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of participants examined was not reported and the outcome was reported as a proportion
Selective reporting (reporting bias)	High risk	The outcome of interest was reported as a proportion; and without absolute numbers or the number of participants examined (n) it is unclear what the proportion represents. Data not in suitable format for analysis
Other bias	High risk	No mention of examiner calibration

Kanagaratnam 2009

Methods	**FLUOROSIS STUDY** Country of study: New Zealand Geographic location: Auckland Year of study: not stated Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: only children who returned signed consent form and questionnaire completed by parents Exclusion criteria: schools with fewer than 5 9-year-old children were excluded because of resource, time and efficiency constraints Other sources of fluoride: data presented on fluoride tablet supplementation, brushing with toothpaste frequency, amount of toothpaste used and toothpaste swallowed, however, the use of other sources of fluoride had no effect on the proportion of children with diffuse opacities Social class: high (deciles 8–10) = 40% (F), 19% (non-F); middle (deciles 4–7) = 141% (F) , 44% (non-F); low (deciles 1–3) = 19% (F), 37% (non-F) (a schools decile indicates the extent to which it includes students from low socioeconomic communities) Ethnicity: more children of European descent and fewer children of Asian descent attended schools within non-fluoridated areas compared with fluoridated areas Residential history: lifetime residents and intermittent residents, however, data on lifetime residents alone presented in this review due to confounding Other confounding factors: not stated
Interventions	Group 1: 0.1-0.3 ppm (natural fluoridation) Group 2: 0.7-1 ppm (artificial fluoridation)
Outcomes	Dental fluorosis (Dean's Index); caries data collected, however, not presented in this review due to study design Age at assessment: 7-15 years
Funding	Funded by AUT University, Counties Manukau District Health Board and New Zealand Dental Research Foundation
Notes	Fluoride concentrations were not reported in the study but deduced from discussion section and anecdotal evidence

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	The number of schools and students from each school were probabilistically sampled to reflect the overall decile and school size distribution representative of Auckland schools yet produce a sample that was balanced between fluoridated and non-fluoridated regions.
Confounding	Unclear risk	While the sample included participants from a range of SES, the numbers in these groups were not equal. There were significantly fewer children in

Kanagaratnam 2009 *(Continued)*

		high-decile schools in non-fluoridated areas and fewer children in low-decile schools in fluoridated areas
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	No other apparent bias

Kotecha 2012

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: not stated Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: all age groups Exclusion criteria: those who could not be studied in the second visit Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: < 1.5 ppm Group 2: > 1.5 ppm
Outcomes	Dental fluorosis (index not reported); caries data also evaluated within the study but excluded from review due to study design Age at assessment: all age groups
Funding	Not stated
Notes	
Risk of bias	

Kotecha 2012 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	11 out of 261 villages with high fluoride content in the drinking water and 11 out of 1490 villages with normal fluoride drinking water were randomly selected for water sampling
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Data for 75% of population of the study areas presented and attrition was not balanced across groups
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	High risk	Measurement done by trained tutors and assistant professors, however, it is not clear whether the personnel measuring the outcome were calibrated

Kumar 1999

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Newburgh City (F); Newburgh Town (F 1984); New Windsor (non-F); Kingston (non-F) Year study started: 1986 Year study ended: 1995 Year of change in fluoridation status: 1984 Study design: CBA
Participants	Inclusion criteria: children aged 7-14 years; lifetime residents of study areas Exclusion criteria: not stated Other sources of fluoride: fluoridation plus early brushing or tablet use, fluoride tablet plus early brushing, early brushing, and fluoride tablets all associated with an increased risk of fluorosis scored very mild to severe compared to children exposed to none of these additional sources Social class: not stated Ethnicity: no difference in odds of fluorosis in African-Americans compared to white and other races Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: 1 ppm (artificial fluoridation) Group 3: 'low' level - ppm not stated (natural fluoridation)

Kumar 1999 *(Continued)*

	Group 4: 'low' level - ppm not stated (natural fluoridation)
	Group 5: 'low' level - ppm not stated (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design
	Age at baseline measure: 7-14 years
	Age at final measure: 7-14 years
Funding	Supported by a grant from the National Institute of Dental Research (R01 DE 1088801)
Notes	Group 1 (Newburgh City) had been fluoridated since 1945; Group 2 (Newburgh Town) was fluoridated in 1984. Data for 1995 only were available for Group 5 (Ulster)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place
Confounding	Unclear risk	While the authors reported that SES was considered, this information was not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	There were great methodological differences between the before- and after-study in questionnaire design and examiner and the examiners were not reported to have been calibrated

Kumar 2007

Methods	**FLUOROSIS STUDY**
	Country of study: India
	Geographic location: not stated
	Year study started: 1999-2000
	Year of change in fluoridation status: NA
	Study design: cross-sectional
Participants	Inclusion criteria: not stated
	Exclusion criteria: not stated
	Other sources of fluoride: not stated

Kumar 2007 *(Continued)*

	Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.6 ppm Group 2: 1.1 ppm Group 3: 1.1 ppm Group 4: 1.1 ppm Group 5: 1.2 ppm Group 6: 1.3 ppm Group 7: 1.7 ppm Group 8: 1.7 ppm Group 9: 1.8 ppm Group 10: 1.9 ppm Group 11: 2.1 ppm Group 12: 2.9 ppm Group 13: 4.6 ppm
Outcomes	Dental fluorosis (Smith's classification) Age at assessment: 5-14 years
Funding	Indian Council of Medical Research
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A stratified random sampling procedure was adopted for selection of water sources and villages
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interested reported
Other bias	High risk	Examiner calibration was not mentioned

Kunzel 1976

Methods	**FLUOROSIS STUDY** Country of study: Cuba

Kunzel 1976 *(Continued)*

	Geographic location: La Salud (low F); Mir (medium F); San Augustin and Blanqizal (high F) Year of study: 1973 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children resident in study areas. Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated however, most of the children were born in the area Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 2.3-3.6 ppm Group 2: 1.1-1.6 ppm Group 3: 0.6-0.8 ppm Group 4: 0.1 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 9-10 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The dental examinations were carried out while the fluoride content of the water consumed was unknown"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcome reported
Other bias	Low risk	No other apparent biases

Kunzel 1997

Methods	**CARIES STUDY** Country of study: Germany Geographic location: Chemnitz (F); Plauen (non-F) Year study started: 1959 Year study ended: 1971 Year of change in fluoridation status: 1959 Study design: CBA
Participants	Inclusion criteria: children born in study areas Exclusion criteria: children who had moved into the 2 study areas; disabled children Other sources of fluoride: number of topical applications of fluoride toothpastes; solutions and gel was low - water fluoridation was the only preventive measure Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: increasing annual sugar consumption in both areas
Interventions	**Initiation of water fluoridation** Group 1 baseline: 0.2 ppm (natural fluoridation) Group 1 post intervention: 1 ppm (artificial fluoridation) Group 2: 0.2 ppm (natural fluoridation)
Outcomes	dmft, DMFT, % caries free (deciduous dentition), % caries free (permanent dentition) Age at baseline measure: 6-15 years Age at final measure: 6-15 years
Funding	Supported by the German Federal Ministry of Education, Science, Research and Technology, grant 01 ZZ 9502
Notes	Data extracted from Kunzel 1997 differs from that presented in CRD review (additional data extracted) Study presents data on both initiation and cessation of water fluoridation, but cessation data excluded from this review due to unsuitable control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Sampling details had previously been published (Kunzel 1980), however, the exclusion of disabled children as stated in this study, puts the representativeness of the sample in doubt
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias)	High risk	Insufficient information

Kunzel 1997 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	Standard deviation was not reported
Other bias	Low risk	No other biases apparent

Leverett 1986

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Rochester, NY and several surrounding towns (F); 4 towns in western New York state (non-F) Year of study: 1981 Year of change in fluoridation status: 1963 Study design: cross sectional
Participants	Inclusion criteria: children resident in study areas; children aged 7-17 years Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: children in both non-F and F areas were "not necessarily lifetime residents of their communities" Other confounding factors: none stated
Interventions	Group 1: 1.0 ppm (artificial fluoridation) Group 2: ≤0.3 ppm (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 7-17 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection of children within schools took place

Leverett 1986 *(Continued)*

Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	The examiners do not seem to have been calibrated

Levine 1989

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: Birmingham (F); Leeds (non-F) Year of study: 1987 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas (children only); schools with catchment areas inside study areas; children aged 9-10 years Exclusion criteria: Asian and West Indian children; non-continuous residents; teeth with fractures or restorations; children who had received fluoride supplements at any time Other sources of fluoride: children who had received fluoride supplements at any time excluded Social class: schools selected that served similar socioeconomic populations (social class groups 3,4,5) Ethnicity: Asian and West Indian children excluded Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: < 0.1 ppm (natural fluoridation)
Outcomes	Enamel defect-hypoplasia (TSIF) Age at assessment: 9-10 years
Funding	Not stated
Notes	Data extracted from Levine 1989 differs from that presented in CRD review
Risk of bias	

Levine 1989 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	Low risk	Children using fluoride supplements were excluded and sampling ensured that groups were comparable in terms of SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Photographic examination was blinded Quote: "The colour transparencies were coded and placed in a random sequence before being projected and viewed"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition was balanced across groups as results for 18 (2.9%) and 12 (2.4%) children from the non-F and F area respectively were not available for photographic assessment
Selective reporting (reporting bias)	Unclear risk	There was selective reporting on the central incisor and the reason was not stated
Other bias	Low risk	No other apparent bias

Lin 1991

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: Xinyuan (F); Langan and Jiayi (non-F) Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children aged 7-14 years Exclusion criteria: not stated Other sources of fluoride: not stated Social class: low socioeconomic status, mean annual income of about 200 yuan Ethnicity: not stated Residential history: not reported Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.88 ppm Group 2: 0.34 ppm
Outcomes	Dental fluorosis Age at assessment: 7-14 years
Funding	Not stated

Lin 1991 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Used rRandom stratified sampling
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unclear whether data presented for all participants assessed for dental fluorosis
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	The examiners do not seem to have been calibrated

Loh 1996

Methods	**CARIES STUDY** Country of study: Singapore and Malacca (West Malaysia) Geographic location: Singapore (F); Malacca (non-F) Year study started: 1957 Year study ended: 1966 Year of change in fluoridation status: 1958 Study design: CBA
Participants	Inclusion criteria: Chinese and Malay children aged 7-9 years Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: Chinese and Malay children - results presented separately Residential history: unclear Other confounding factors: not stated
Interventions	**Initiation of water fluoridation** Group 1: 0.7 ppm (artificial fluoridation) Group 2: 'low' level - ppm not stated (natural fluoridation)
Outcomes	DMFT

Loh 1996 *(Continued)*

	Age at baseline measure: 7-9 years Age at final measure: 7-9 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection of schools and children within those schools took place
Confounding	High risk	No details were reported on the use of fluoride from other sources, SES or on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding was not undertaken
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers of children examined at each time point are approximate
Selective reporting (reporting bias)	High risk	The outcomes of interest were not clearly stated a priori and while dental caries was reported (not fully), dental fluorosis appears to have been measured on a different age group, but not reported in useful format
Other bias	Low risk	No other bias detected

Louw 2002

Methods	**FLUOROSIS STUDY** Country of study: South Africa Geographic location: Sanddrif, Williston, Kuboes, Fraserburg, Brandvlei, Kenhardt, and Leeu Gamka Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: aged 11-13 years, similar nutrition and dietary habits, similar ethnic and socioeconomic status Exclusion criteria: not stated Other sources of fluoride: no dental care or fluoride therapy, including the use of fluoride containing toothpaste Social class: similarly low SES reflected in living in subeconomic housing units Ethnicity: mixed with Khoi, Caucasian and Negroid roots that developed into a homogenous ethnic group

Louw 2002 *(Continued)*

	Residential history: lifetime residents Other confounding factors: similar nutrition and dietary habits - mostly bread and potatoes with sporadic intake of vegetables and meat, all located in arid rural sections of South Africa
Interventions	All natural fluoridation Group 1: 0.19 ppm Group 2: 0.36 ppm Group 3: 0.48 ppm Group 4: 1 ppm Group 5: 1.66 ppm Group 6: 2.64 ppm Group 7: 3 ppm
Outcomes	Dental fluorosis prevalence (Dean's Index) Age at assessment: 11-13 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place
Confounding	Low risk	SES was reported as comparable and the participants were not in receipt of dental care, fluoride supplements or toothpaste
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all (99%) participants
Selective reporting (reporting bias)	Low risk	Expected outcome reported
Other bias	Low risk	No other apparent bias

Machiulskiene 2009

Methods	**FLUOROSIS STUDY** Country of study: Lithuania Geographic location: Vilkaviskis and Jonuciai Year of study: 2004 Year of change in fluoridation status: NA Study design: cross-sectional

Machiulskiene 2009 *(Continued)*

Participants	Inclusion criteria: never having taken part in any caries preventive programme; lifetime residency in the area; informed consent to participate Exclusion criteria: 1 school in Vilkaviskis was not eligible to participate in the study as a result of current caries prevention programmes, involving fluoride rinses and fissure sealants; tooth surfaces from which recordings could not be made because of the presence of fixed orthodontic appliances Other sources of fluoride: not stated Social class: children affected by parental unemployment: 1.1 ppm fluoride group = 39%; 0.3ppm fluoride group = 23%. More children in the 1.1 ppm fluoride group reported parental unemployment, however, the 2 towns were initially considered similar from a socioeconomic point of view Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.3 ppm Group 2: 1.1 ppm
Outcomes	Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 13 years (mean)
Funding	Funded by Unrestricted grant from Colgate Palmolive (USA)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible secondary schools and students within them were invited to participate
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information. The measurement and recording of outcome were by different personnel, but they were not reported to have been blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcome reported
Other bias	Low risk	No other apparent bias

Mackay 2005

Methods	**FLUOROSIS STUDY**

Mackay 2005 *(Continued)*

	Country of study: New Zealand Geographic location: not stated Year of study: 2002 Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: ingestion of toothpaste before the age of three = 40%; use of fluoride tablets up to (and including) age three = 49 (11.2%) Ethnicity: not stated Social class: high SES school (deciles 8-10) = 192 (44%); medium SES school (deciles 4-7) = 121 (27.8%); low SES school (deciles 1-3) = 128 (28.2%) Residential history: the study included both continuous and intermittent residents, however, only data from continuous residents included in analysis Other confounding factors: not stated
Interventions	Group 1: 0.1-0.3 ppm (natural fluoridation) Group 2: 0.8 ppm (artificial fluoridation)
Outcomes	Enamel defects (DDE); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 8.7-11.1 years
Funding	New Zealand Dental Research Foundation
Notes	Fluoride concentration deduced from discussion section and anecdotal evidence

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A random sample of 600 Year 5 children enrolled with the Southland District Health Board's school dental service was invited to participate in the study
Confounding	High risk	A statistical model used showed that hypoplastic defects were influenced by ingestion of toothpaste before age four but the results were not adjusted for this factor
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	436 (74.5%) of the 600 children invited to the study were examined
Selective reporting (reporting bias)	Low risk	All expected outcome reported

Mackay 2005 *(Continued)*

Other bias	Low risk	No other apparent bias

Macpherson 2007

Methods	**FLUOROSIS STUDY** Country of study: Sweden Geographic location: Kungsbacken (F); Halmsted (non-F) Year of study: 2002-2003 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: presence of 2 individual anterior labial-view photographs of any upper anterior teeth present; similar date of birth (difference in age due to undertaking fieldwork in study areas a year apart) Exclusion criteria: not stated Other sources of fluoride: Age at which started brushing: 6-12 months vs 12 months (P value 0.99) Frequency of brushing: ≤ 1/day vs ≥ 2/day (P value 0.42) Toothpaste F < 1000 ppm vs ≥ 1000 ppm (P value 0.49) Amount of toothpaste ≤ pea size vs > pea size (P value 0.09) Fluoride tablets previously: 'No' vs 'Yes' (P value 0.001) Fluoride tablets now: 'No' vs 'Yes' (P value 0.001) Ethnicity: not stated Social class: low education: F = 47, non-F = 56; high education: F = 64, nonF = 73. Both groups were similar with respect to parents' education attainment (P value 0.87) Residential history: children from Kungsbacka were generally exposed to fluoridated water in early childhood, while those from Halmstad were not exposed to fluoridated water during infancy (discussion section) Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.1 ppm Group 2: 1.3 ppm
Outcomes	Dental fluorosis (TF Index; photographic assessment) Age at assessment: 7-10 years
Funding	Not stated
Notes	
Risk of bias	

Macpherson 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Cluster random sample of parents of eligible children aged 7-10 years from the same birth cohort
Confounding	High risk	Use of fluoride toothpaste and frequency of brushing was similar across groups, however, current use of fluoride supplements as well as past use was significantly higher in the control group. This information is used to provide adjusted odds ratios however, for the purposes of this review only the raw data has been used which remains subject to confounding factors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blind to the source area of each slide
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Unclear risk	Photographic assessment as well as TF Index of dental fluorosis were measured but only photographic assessment reported
Other bias	Low risk	No other apparent bias

Mandinic 2009

Methods	**FLUOROSIS STUDY** Country of study: Serbia Geographic location: Valjevo and Vranjska Banja Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: used the fluoride concentration database and consumption database to determine fluoride exposure Ethnicity: not stated Social class: not stated Residential history: used the fluoride concentration database and consumption database to determine fluoride exposure Other confounding factors: dietary sources of fluoride – potato, beans
Interventions	All natural fluoridation Group 1: 0.1 ppm Group 2: 11 ppm
Outcomes	Dental fluorosis (Dean's Index)

Mandinic 2009 *(Continued)*

	Age at assessment: 12 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place - sampling frame was unspecified
Confounding	High risk	Fluoride exposure and consumption were measured but not reported. Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Expected outcome reported
Other bias	Low risk	No other apparent bias

Mandinic 2010

Methods	**FLUOROSIS STUDY** Country of study: Serbia Geographic location: Valjevo, Veliko Gradiste, Kacarevo and Vranjska Banja Year of study: 2006 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: healthy 12-year-old school children, both genders, lifetime residents of the same municipality Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: there were no addition sources of exposure, i.e. industries that could pollute the environment by fluoride emission
Interventions	All natural fluoridation Wells

Mandinic 2010 *(Continued)*

	Group 1: 0.79 ppm Group 2: 0.1 ppm Group 3: 0.15 ppm Group 4: 11 ppm Tap water Group 1: 0.17 ppm Group 2: 0.07 ppm Group 3: 0.1 ppm Group 4: 0.15 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 12 years
Funding	Ministry of Science and Technological Development of the Republic of Serbia
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient information on sampling
Confounding	High risk	The use of other fluoride sources and SES were not considered
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome data for all participants was reported
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other bias apparent

Marya 2010

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: 30 villages from district Gurgaon and district Hissar Year of study: not stated Year of change in fluoridation status: NA

Marya 2010 *(Continued)*

	Study design: cross-sectional
Participants	Inclusion criteria: only continuous residents; selected individuals had to have all their permanent teeth (except third molars) erupted Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: not stated Social class: environmental factors such as eating habits, nutritional status, consumption of water, living conditions were almost uniform in all 7 groups studied Residential history: continuous residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.5 ppm Group 2: 0.87 ppm Group 3: 1.51 ppm Group 4: 2.45 ppm Group 5: 5.27 ppm Group 6: 8.5 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 12-16 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place
Confounding	Unclear risk	Environmental factors such as eating habits, nutritional status, consumption of water, and living conditions were almost uniform in all 7 groups studied, however, it was unclear whether this extended to exposure to fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Expected outcome reported
Other bias	Low risk	No other apparent bias

Masztalerz 1990

Methods	**FLUOROSIS STUDY** Country of study: Poland Geographic location: Neisse (high-F), Breslau (F), Militsch and Gryfów (non-F) Year of study: not stated Year of change in fluoridation status: not stated Study design: cross sectional
Participants	Inclusion criteria: none stated Exclusion criteria: children who were not lifetime residents and had those who did not yet have permanent canine teeth Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifelong residents Other confounding factors: fluoride in the air was high in Greifenberg
Interventions	Appeared to be natural fluoridation, however this was not clear Group 1: 4-7 ppm Group 2: 0.7-0.9 ppm Group 3: < 0.2 ppm
Outcomes	Dental fluorosis (index unclear) Age at time of measurement: 12 years
Funding	Not stated
Notes	Paper translated from German

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	The authors report that all eligible children were to be studies however, the sampling frame was not specified
Confounding	High risk	Did not account for SES or the use of fluoride from other sources (except from air pollution though this is unclear)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information. No details on blinding were reported, no standard index for measurement of fluorosis appears to have been used
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for 88% of participants
Selective reporting (reporting bias)	Low risk	Data appears present

Masztalerz 1990 *(Continued)*

Other bias	Low risk	No other bias detected

Maupome 2001

Methods	**CARIES STUDY** Country of study: Canada Geographic location: British Columbia Year study started: 1993-1994 Year study ended: 1996-1997 Year of change in fluoridation status: 1992 Study design: CBA
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: data on oral hygiene and exposure to diverse fluoride technologies were collected but not reported. However, the authors stated that British Columbia had relatively homogeneous exposure to fluorides, widespread use of fluoride toothpastes. good adherence to oral hygiene regimens and good access to oral health care Social class: participants showed similar SES at baseline Ethnicity: not stated Residential history: information about the regression analysis suggests that both lifetime and non-lifetime residents might have been included Other confounding factors: not reported
Interventions	**Fluoride cessation** Group 1: 'optimal' level - ppm not stated (artificial fluoridation) to non-fluoridated Group 2: 'optimal' level - ppm not stated (artificial fluoridation)
Outcomes	DMFS Age at baseline: Grades 2, 3, 8 and 9 Age at final measurement: Grades 2, 3, 8 and 9
Funding	NHRDP operating grant 6610-2225-002 supported this study
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	Study was a multi-site study and also both a repeated cross-sectional prevalence survey and a longitudinal investigation. Children were examined in their schools but no other sampling details reported

Maupome 2001 *(Continued)*

Confounding	High risk	At baseline data for lifetime and non-lifetime residents were reported; information on diet (snacks) and other fluoride sources were collected but the results were not adjusted for these factors
Blinding of outcome assessment (detection bias) All outcomes	High risk	Used different examiners for different study sites who where not blinded to fluoridation status
Incomplete outcome data (attrition bias) All outcomes	High risk	About 90% of all eligible children were examined at baseline; 64.2% at follow-up with variation across groups
Selective reporting (reporting bias)	Low risk	Expected outcome was presented
Other bias	Unclear risk	Baseline data were collected 14-19 months after cessation of fluoridation. This gap between the actual cessation of fluoridation and the beginning of data collection might be a source of bias, towards the null, since the exposure had been modified from fluoridated to non-fluoridated water

Mazzotti 1939

Methods	**FLUOROSIS STUDY** Country of study: Mexico Geographic location: all areas in Mexico, 11 states, 107 cities Year of study: 1938 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	Groups: 0-4 unclear ppm
Outcomes	Dental fluorosis (index unclear) Age at assessment: not stated
Funding	Not stated
Notes	Paper translated from Spanish

Mazzotti 1939 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	No details were reported on SES or fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information to determine whether there was attrition
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Unclear risk	Overall reporting on any information too poor to permit thorough assessment of any risk of bias

McGrady 2012

Methods	**FLUOROSIS STUDY** Country of study: Thailand Geographic location: Chiang Mai Year of study: 2007 Year study ended: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: life long residency; good general health with both maxillary incisors fully erupted; free from fixed orthodontic appliances Exclusion criteria: non-lifetime residents; unsuitable dentition Other sources of fluoride: • Non-fluorosed breast and formula: 88/305 (28.8%) • Formula only: 14/57 (24.6%) • F content paste: < 1000 ppm = 13/59 (22%); 1000 ppmF = 150/501 (29.9%) • Toothbrushing frequency: once/day = 45/130 (34.6%); twice/day = 99/360 (27.5%); > 3 times/day =19/70 (27.1%) • Age toothbrushing started: 4 years+ = 20/76 (26.3%); 3-4 years = 43/138 (31.2%); 2-3 years = 48/178 (27%); 1-2 years = 35/126 (27.8%); 0-1 year = 8/23 (34.8%) Ethnicity: not stated Social class: not stated Residential history: continuous residents

McGrady 2012 *(Continued)*

	Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: < 0.2 ppm Group 2: 0.2-0.59 ppm Group 3: 0.6 -0.89 ppm Group 4: ≥ 0.9 ppm
Outcomes	Dental fluorosis (TF Index) Age at assessment: 8-13 years
Funding	One author was funded by a Clinician Scientist Award from the National Institute for Health Research (UK). The Colgate Palmolive Dental Health Unit was funded by an unrestricted grant from Colgate Palmolive Possible conflicts of interest: RPE is an employee of a manufacturer of oral care products
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	High risk	The study was based on a convenience sample population with varying exposures to fluoride
Confounding	High risk	The data on fluoride from other sources was not presented in a usable format and outcome data were not adjusted for it. Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The examiners were blinded to the probable fluoride exposure and the images were presented for examination in a randomised order
Incomplete outcome data (attrition bias) All outcomes	High risk	Data for 148 (21%) examined participants not analysed
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other bias apparent

McInnes 1982

Methods	**FLUOROSIS STUDY** Country of study: South Africa Geographic location: Kenhardt (F); Keimoes (non-F); North-western Cape Province Year of study: not stated Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: lifetime residents of study area; pre-school children aged 1-5 years

McInnes 1982 *(Continued)*

	Exclusion criteria: none stated Other sources of fluoride: majority of babies were breastfed so would not be exposed to fluoride from water used in preparation of infant formula Social class: reported as being the same across groups; experimental and control groups reported as being similar (parents were land or railway labourers) Ethnicity: all children same ethnic origin i.e. European-African-Malay origin Residential history: lifetime residents Other confounding factors: same climatic conditions in both areas
Interventions	All natural fluoridation Group 1: 2.2-4.1 ppm Group 2: 0.2 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at time of measurement: 1-5 years
Funding	Part funded by South African Sugar Association
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place
Confounding	High risk	Malnutrition and SES were reported to be similar across groups but no supporting data provided Did not report any details about other sources of fluoride
Blinding of outcome assessment (detection bias) All outcomes	High risk	Did not undertake blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	All expected data appeared to be present
Other bias	Low risk	No other apparent bias

Mella 1992

Methods	**FLUOROSIS STUDY** Country of study: Chile Geographic location: students attending 2 boarding institutions in Santiago, who lived in areas throughout Chile Year of study: not stated

Mella 1992 *(Continued)*

	Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: students at boarding institution, exposure estimated from home fluoride level; lived for first 6 years in home town Exclusion criteria: students who could not remember the areas in which they spent the first 6 years of their life Other sources of fluoride: not stated Social class: distribution of subjects by high, moderate, low social class, but no significant differences between fluoride groups Ethnicity: not stated Residential history: first 6 years of life Other confounding factors: years lived in city of birth
Interventions	All natural fluoridation Group 1: > 0.3 ppm Group 2: ≤0.3 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 19 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	High risk	All subjects were selected from 2 boarding schools. Insufficient detail reported to determine how sampling took place
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Unclear risk	Unclear why only very mild, mild and moderate severities of dental fluorosis reported for both groups
Other bias	Low risk	No other apparent bias

Mella 1994

Methods	**FLUOROSIS STUDY**

Mella 1994 *(Continued)*

	Country of study: Chile Geographic location: Iquique (F); Santiago (non-F); Valparaiso-Vina (F); Temuco (low-F) Year of study: 1983 Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: 4 schools in study areas Exclusion criteria: not stated Other sources of fluoride: not stated Social class: 2 schools in each area, 1 from low social class, 1 from medium/high social class, results presented separately by social class Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	Group 1: 2.2 ppm (natural fluoridation) Group 2: 0.0 ppm (natural fluoridation) Group 3: 1.0 ppm (artificial fluoridation) Group 4: 0.3 ppm (natural fluoridation)
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 7 and 12 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place. 4 schools from a list of schools benefiting from school feeding programs were selected from each city, however it was not reported how these were chosen or how the children within the schools were chosen
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Meyer-Lueckel 2006

Methods	**FLUOROSIS STUDY** Country of study: Iran Geographic location: Youssefabad, Seman, Dibaj Year of study: 2003 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children aged 6-9 years who were lifetime residents Exclusion criteria: not stated Other sources of fluoride: not stated Social class: Youssefabad, Semnan were of upper middle and lower middle class, social class of the third community was not mentioned Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.2 ppm Group 2: 0.3 ppm Group 3: 1.3 ppm
Outcomes	Dental fluorosis (TSIF); caries data evaluated in study but excluded from review due to study design Age at assessment: 6-9 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	2 schools (one boys' and one girls') were randomly selected from 2 of the 3 study areas, and in the third study area the only school (coeducation) was selected and all participants were then examined
Confounding	High risk	2 study areas varied in social class, while there was no information on SES for the third study area; in addition the use of other fluoride sources was not considered
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Fluorosis outcome data were reported in bar charts making it difficult to assess whether there were incomplete outcome data or not.

Meyer-Lueckel 2006 *(Continued)*

Selective reporting (reporting bias)	High risk	Though outcome of interest was reported, fluorosis outcome was not reported for the Youssefabad area
Other bias	Unclear risk	The single examiner involved in the study was calibrated, and though the reliability of caries recording was assessed, it was not done for fluorosis outcome

Milsom 1990

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: Nantwich (F); Northwich (non-F) Year of study: 1988 Year of change in fluoridation status: 1975 Study design: cross-sectional
Participants	Inclusion criteria: children aged 8 years attending state-maintained schools; lifetime residents of study areas; parental consent Exclusion criteria: parishes not bounded on all sides by parishes with optimally fluoridated water for fluoride areas; exposure to fluoride supplements Other sources of fluoride: age at which tooth brushing first began Social class: measured by parental occupation; social class makeup of study areas almost identical (data presented in paper) Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: < 0.3 ppm (natural fluoridation)
Outcomes	Enamel defect (DDE) Age at assessment: 8 years
Funding	Financial support from the North Western Regional Health Authority
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	The study included all eligible children who lived in the non-fluoridated area and those in the fluoridated area were selected by a two-stage random sampling technique
Confounding	Low risk	There was no difference in SES across groups and children with exposure to fluoride supplements were excluded

Milsom 1990 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants were taken to the examination centre by bus, examiner was unaware of the schools in attendance and fluoridation status
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest appears present
Other bias	Unclear risk	Data were collected on age of commencement of tooth brushing but not reported

Mondal 2012

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Nalhati I (Nasipur, Vabanandapur, Deshnabagram) and Rampurhat II (Chalk Atla, Nowapara, Junitpur and Kamdebpur) Year of study: 2003 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 3.15 ppm Group 2: 3.83 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: < 10 years to > 50 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	High risk	"The recruitment of respondents was performed at seven primary schools in the study area with pupils in the age range of 4–10 years and the rest of the age

Mondal 2012 *(Continued)*

		group samples were collected from the respective villages". There was no indication that random sampling was carried out
Confounding	High risk	Participants were lifetime residents, however, SES and the use of other fluoride sources were not considered
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome data for all participants reported
Selective reporting (reporting bias)	Low risk	Outcome of interest fully reported
Other bias	Unclear risk	Examination was done by a 'competent dentist', however, there was no mention of calibration

Montero 2007

Methods	**FLUOROSIS STUDY** Country of study: Venezuela Geographic location: Maria May, Roscio and Madre Emilia Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: not stated Social class: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.13 ppm Group 2: 0.31 ppm Group 3: 1.58 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated in study but excluded from review due to study design Age at assessment: 8-12 years
Funding	Not stated

Montero 2007 *(Continued)*

Notes	Paper translated from Spanish

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Random sampling was used
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcome presented
Other bias	Low risk	No other apparent bias

Nanda 1974

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: 23 villages in Lucknow (North Central India) Year of study: not stated Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: lifetime residents of study areas; children from 103 urban and 66 rural schools; all permanent teeth (excluding third molars) present Exclusion criteria: none stated Other sources of fluoride: dietary fluoride intake Social class: not stated Ethnicity: not stated Residential history: lifelong residents Other confounding factors: climate
Interventions	All natural fluoridation Group 1: > 1.21 ppm Group 2: 0.81-1.2 ppm Group 3: 0.41-0.8 ppm Group 4: 0-0.4 ppm
Outcomes	Dental fluorosis (Dean's Index)

Nanda 1974 *(Continued)*

	Age at time of measurement: 6-17 years
Funding	Supported by PL-480 grants from the Bureau of Health Manpower Education, Division of Dental Health Public Health Service under the aegis of the Indian Council of Medical Research, New Delhi
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding was not undertaken
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear due to poor reporting of participant numbers and data
Selective reporting (reporting bias)	High risk	Poor reporting of outcome data
Other bias	High risk	No other bias detected

Narbutaite 2007

Methods	**FLUOROSIS STUDY** Country of study: Lithuania Geographic location: Klaipeda and Kaunas Year of study: 1997 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: not stated Social class: Klaipeda and Kaunas said to be the 2 largest cities in Lithuania and to be of a similar size and socioeconomic structure Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.22 ppm

Narbutaite 2007 *(Continued)*

	Group 2: 1.7-2.2 ppm
Outcomes	Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 12 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	8 out of 23 ordinary secondary schools in Klaipeda (the high-F area) and 8 out of 30 in Kaunas (the low-F area), were selected to cover the regions. However, it is not clear how these schools were selected
Confounding	High risk	No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	High risk	All examinations were carried out by 1 examiner who was a specialist with additional training in dental fluorosis diagnosis but no mention of reliability testing; water was taken from 3 sampling sites in the high-F area and 1 in the low-F area, no explanation was provided for the inconsistency

Narwaria 2013

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Dumduma, Bangama, Hazinager, Sillarpur, Sirsod, Nichroli, Toda Karera, Toda Rampur, Kali Pahadi and Zuzai in Karera Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: primary school children; mostly 5-12 years Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: not stated

Narwaria 2013 *(Continued)*

	Social class: not stated. Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.65 ppm Group 2: 1.84 ppm Group 3: 1.84 ppm Group 4: 1.88 ppm Group 5: 1.91 ppm Group 6: 2.15 ppm Group 7: 2.22 ppm Group 8: 2.53 ppm Group 9: 3.91 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 5-12 years
Funding	Funding for travelling and laboratory facilities provided by Special Assistance Program (SAP)-I UGC, New Delhi
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	10 villages were selected for study using the eligibility criteria. Within these villages, all government schools were included and children were randomly selected from each class
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interested reported
Other bias	High risk	Examination was performed by 2 trained dentists. No mention of calibration or of reliability testing

Nunn 1992

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: Hartlepool, Newcastle and Middlesborough

Nunn 1992 *(Continued)*

	Year of study: 1989 Year of change in fluoridation status: NA Study design: cross-sectional study
Participants	Inclusion criteria: lifetime residents of study areas; children in selected schools aged 15-16 years Exclusion criteria: children with fractured incisor teeth, orthodontic bracket or surface otherwise obscured Other sources of fluoride: not stated Social class: occupation of head of household recorded; participants of low and high SES were recruited when possible Ethnicity: ethnicity recorded but no expansion on variable Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1-1.3 ppm Group 2: 1 ppm Group 3: 0.2 ppm
Outcomes	Enamel defect Age at assessment: 12 years
Funding	Financial assistance from the British Council
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for the use of fluoride from other sources. Balance of SES between groups was unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Photographs of the maxillary central incisors of participants were cut out from the print and identified with a code which would prevent identification by the examiners
Incomplete outcome data (attrition bias) All outcomes	High risk	In England, data for 68% of examined participants were reported due to camera failure in a school of SES
Selective reporting (reporting bias)	Low risk	Expected outcome appeared to be present
Other bias	Low risk	No other apparent bias

Nunn 1994a

Methods	**FLUOROSIS STUDY** Country of study: England Geographic location: north-east England Year of study: 1990-1991 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas (England only); children aged 12 years; parental consent (England only) Exclusion criteria: none stated Other sources of fluoride: not stated, but expected higher use of toothpaste in higher SES groups Social class: children divided into high and low social class Ethnicity: not stated Residential history: UK participants were lifetime residents. Other confounding factors: not stated
Interventions	Group 1: 0.1 ppm Group 2: 0.5 ppm Group 3: 1.0 ppm
Outcomes	Enamel defect (DDE) Age at assessment: 12 years
Funding	Not stated
Notes	Two study centres: England Sri Lanka. Different methodology used in England and Sri Lankan study centres, therefore reported under different study ID's (England - Nunn 1994a and Sri Lankan - Nunn 1994b)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Schools were selected by the district dental officer in order to achieve a target of about 150 eligible 12 year old children in each sub-group. Insufficient information provided regarding how the children were selected within the schools
Confounding	High risk	Higher reported use of toothpaste in the higher SES groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The examiner was largely unaware of fluoride and socioeconomic status of the children
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participants sampled were < 80% in the study areas and not balanced across groups, however, data presented for all recruited participants

Nunn 1994a *(Continued)*

Selective reporting (reporting bias)	Low risk	Expected outcome was presented
Other bias	Low risk	No other apparent bias

Nunn 1994b

Methods	**FLUOROSIS STUDY** Country of study: Sri-Lanka Geographic location: Sri Lanka Year of study: 1990-1991 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 12. Exclusion criteria: none stated Other sources of fluoride: not stated, but expected higher use of toothpaste in higher SE groups Social class: children divided into high and low social class Ethnicity: not stated Residential history: Sri Lankan populations were non-mobile and confirmed continuous residence when asked at the time of examination Other confounding factors: not stated
Interventions	Group 1: 0.1 ppm Group 2: 0.5 ppm Group 3: 1.0 ppm
Outcomes	Enamel defect (DDE) Age at assessment: 12 years
Funding	Not stated
Notes	Two study centres: England Sri Lanka. Different methodology used in England and Sri Lankan study centres, therefore reported under different study ID's (England - Nunn 1994a and Sri Lankan - Nunn 1994b)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Schools were selected by the district dental officer in order to achieve a target of about 150 eligible 12-year-old children in each sub-group. Insufficient information provided regarding how the children within the schools were selected

Nunn 1994b *(Continued)*

Confounding	High risk	Imbalance of SES between groups. Two of the three study areas recruited only children of low SES and one area recruited both low and high SES children
Blinding of outcome assessment (detection bias) All outcomes	High risk	The examiner was aware of the fluoride and socioeconomic status of the children
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participants sampled were < 80% in the study areas and not balanced across groups, however, data presented for all recruited participants
Selective reporting (reporting bias)	Low risk	Expected outcome was presented
Other bias	Low risk	No other apparent bias

Ockerse 1941

Methods	**FLUOROSIS STUDY** Country of study: South Africa Geographic location: Upington, Kenhardt and Pofadder Year of study: 1939 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children attending schools in study areas; children aged 6-17 years Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: participants were born and lived up to the age of 8 in the study areas Other confounding factors: sStudy areas at same altitude, same climate, similar countryside and vegetation, differences in drinking water composition discussed
Interventions	All natural fluoridation Group 1: 2.46 ppm (average) Group 2: 6.8 ppm Group 3: 0.38 ppm
Outcomes	Mottled enamel; caries data also evaluated within the study but excluded from review due to study design Age at assessment: 6-17 years
Funding	Not stated
Notes	

Ockerse 1941 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	High risk	Areas thought to be most affected by caries and mottling were selected and visited. Selection of 'at risk' population is likely to have introduced bias
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Caries data reporting may have been a post-hoc decision
Other bias	High risk	Data were collected on age of commencement of tooth brushing but not reported. There was no mention of examiner training or calibration

Pontigo-Loyola 2008

Methods	**FLUOROSIS STUDY** Country of study: Mexico Geographic location: urban - Tula Centro and San Marcos; rural – El Llano Year of study: 1999 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: having fixed orthodontic appliances; metal crowns; refusal to be examined; unavailable for oral examination Other sources of fluoride: not stated Ethnicity: not stated Social class: not stated. Residential history: birth to ≥ 6 years Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.38 ppm Group 2: 1.42 ppm Group 3: 3.07 ppm
Outcomes	Dental fluorosis (modified Dean's Index)

Pontigo-Loyola 2008 *(Continued)*

	Age at assessment: 12 and 15 years
Funding	Data collection by the Universidad Autonoma del Estado de Hidalgo and data analysis was partially supported by a grant from the National Council of Science and Technology of Mexico
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible participants were included in the study
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Only 66.6% of the included participants were in the final study population. The reason for withdrawal was not reported
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Pot 1974

Methods	**CARIES STUDY** Country of study: Holland Geographic location: Tiel (F); Culemborg (non-F) Year study started: 1950 Year study ended: 1970 Year of change in fluoridation status: 1953 Study design: CBA
Participants	Inclusion criteria: residents of study areas born between 1896 and 1945; lifelong residents of study areas Exclusion criteria: subjects who left the study areas for more than 3 months after fluoridation was introduced Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents

Pot 1974 *(Continued)*

	Other confounding factors: age: results for final survey presented in 5-year age groups and showed that higher proportion of younger subjects had prosthetic teeth in Culemborg than in Tiel
Interventions	Group 1: 1.1 ppm (artificial fluoridation) Group 2: 0.1 ppm (natural fluoridation)
Outcomes	Outcome: % with false teeth Age at baseline measure: 5-55 Age at final measure: 25-75
Funding	Not stated
Notes	Paper translated from Dutch

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Participants were selected by random sampling from the city population registers
Confounding	High risk	Did not report on SES or the use of other fluoride sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Study reports on % false teeth; no caries data
Other bias	High risk	There was no mention of examiner calibration or of reliability testing

Ray 1982

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Rustampur and Ledhupur, 2 adjacent village in Varanasi District Year of study: not stated Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: none stated Exclusion criteria: none stated Other sources of fluoride: not stated

Ray 1982 *(Continued)*

	Social class: study areas similar with respect to demographic and socioeconomic characteristics Ethnicity: not stated Residential history: not stated Other confounding factors: villages similar with respect to geoclimatic characteristics
Interventions	All natural fluoridation Group 1: > 2 ppm Group 2: 1-2 ppm Group 3: < 1 ppm
Outcomes	Dental fluorosis (index not stated) Age at assessment: not stated
Funding	Funded by the Indian Council of Medical Research
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible participants were included in the study
Confounding	High risk	Did not report on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of participants recruited not stated
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	High risk	No mention of how examination was conducted or whether the examiner was calibrated

Riordan 1991

Methods	**FLUOROSIS STUDY** Country of study: Australia Geographic location: Perth (F); Bunbury (non-F), Western Australia Year of study: 1989 Year of change in fluoridation status: 1968 Study design: cross-sectional

Riordan 1991 *(Continued)*

Participants	Inclusion criteria: children born in 1978; children attending government schools in study areas; parental consent Exclusion criteria: subjects with amelogenesis imperfecta or orthodontic banding Other sources of fluoride: questionnaire investigated periods and duration of use of fluoride supplements, use of fluoride toothpaste, included age at which use of toothpaste commenced, whether child swallowed toothpaste Social class: schools assigned socioeconomic score - no significant difference in scores between study areas Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	Group 1: 0.8 ppm (artificial fluoridation) Group 2: < 0.2 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TF Index) Age at assessment: 12 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Random selection of 14 Dental Therapy Centres; selection of 1 class/centre of children born in 1978
Confounding	High risk	Insufficient information to determine whether use of other fluoride sources was balanced across groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blind outcome assessment (with regard to residency) was not undertaken
Incomplete outcome data (attrition bias) All outcomes	Low risk	7/376 and 3/338 not available for evaluation; unlikely to influence results
Selective reporting (reporting bias)	Low risk	All relevant outcome data reported
Other bias	Low risk	No other apparent bias

Riordan 2002

Methods	FLUOROSIS STUDY Country of study: Australia Geographic location: Western Australia Year of study: 2000

Riordan 2002 *(Continued)*

	Year of change in fluoridation status: NA Study design: Cross-sectional
Participants	Inclusion criteria: Children born around 1990 (10 yrs old) who had lived in Australia/New Zealand for most of their lives (so as to ensure life time exposure to water fluoridation) Exclusion criteria: Migrants from outside Australia and New Zealand, refusal to consent, not present at school at the time of exam Other sources of fluoride: Information was collected on use of infant formula, age at which toothpaste was introduced and the use of fluoride supplements. Fluoride supplement use was almost exclusive to residents of the non-fluoridated areas Social class: Not specified Ethnicity: Not specified Residential history: Participants were categorised as having been exposed to water fluoridation if they had spent more than half their life between the ages of 0-5 in a water fluoridated area Other confounding factors: Not specified
Interventions	Group 1: 0.8ppm (artificial fluoridation) Group 2: 0.2-0.3 ppm (naturally fluoridated)
Outcomes	Dental fluorosis (TF index) Age at assessment: 10 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	The sampling frame was made up of children registered with the School dental service and children were accessed via schools. All eligible children were invited to take part in the study
Confounding	High risk	Information on other sources of fluoride was collected and more children in the non-fluoridated area took fluoride supplements. SES was not stated.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Ruan 2005

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: urban - Bao Ji and Jing Bian

Ruan 2005 *(Continued)*

	Year of study: 2002 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: absent or unavailable; non-permanent residents Other sources of fluoride: no fluoride supply was provided by dental service and no fluoride supplement program was implemented in any of the communities Ethnicity: not stated Social class: the selected schools served rural communities where socioeconomic standards were comparable Residential history: permanent residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.4ppm Group 2: 1.0 ppm Group 3: 1.8 ppm Group 4: 3.5 ppm Group 5: 5.6 ppm
Outcomes	Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 12 and 13 years
Funding	The study was supported by the Norwegian State Educational Loan Fund
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	13 schools were contacted and all children were invited to participate. The sampling frame for schools was not specified
Confounding	High risk	Even though fluoride supplement and fluoride supply by dental service were taken into account, the use of fluoride toothpaste (a common source) was not mentioned. It is not clear why it was not acknowledged or investigated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The fluoride concentration of the local drinking-water supplies was unknown to the examiner at the time of the clinical examinations, which took place with the students seated on ordinary chairs outside the school building
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Partial reporting of outcome - only reported prevalence of fluorosis with TF score ≥ 3 (fluorosis of aesthetic concern)

Ruan 2005 *(Continued)*

Other bias	Low risk	No other apparent bias

Rugg-Gunn 1997

Methods	**FLUOROSIS STUDY** Country of study: Saudi Arabia Geographic location: Jeddah (low F); Riyadh (moderate F); and Quassim (high F) Year of study: 1992 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; boys aged 14 years; parental consent Exclusion criteria: photographs that failed to show whole buccal surface; out of focus photographs Other sources of fluoride: not stated Social class: schools grouped according to the socioeconomic status of residential areas in the urban community; family income and parental education measured using questionnaire Ethnicity: not stated Residential history: lifetime residents Other confounding factors: nutritional status
Interventions	All natural fluoridation Group 1: 2.7 ppm Group 2: 0.8 ppm Group 3: < 0.3 ppm
Outcomes	Dental fluorosis (index unclear) Age at assessment: 14 years
Funding	Not stated
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Low risk	Quote: "All school were grouped according to SES of the residential area in the urban community only and schools sampled randomly"
Confounding	High risk	Schools were grouped according to the SES of residential areas however it is not clear whether the study areas were balanced in this regard. No detail was reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information

Rugg-Gunn 1997 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appears to have been presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	No other apparent bias

Russell 1951

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Colorado Springs (F); Boulder (non-F), Colorado Year of study: 1950 Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: white native residents listed in school census record for 1920, 1930 or 1940 and as resident in current city directory; mothers living in study area at time of birth; age 20-44 years; residence and usage of local water unbroken except for periods not exceeding 60 days during calcification and eruption of permanent teeth Exclusion criteria: none stated Other sources of fluoride: not stated Social class: workers in 2 communities followed similar occupations and had similar average salaries Ethnicity: native born white = 98% of Boulder population, and 96% of Colorado Springs population. This study only reports upon white participants (not clear if this was coincidence or purpose) Residential history: lifetime residents Other confounding factors: Colorado Springs 3 times size of Bolder, similar altitude and climate, neither population ageing nor young, both were highly literate, water systems similar
Interventions	All natural fluoridation Group 1: 2.5 ppm Group 2: < 0.1 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design Age at time of measurement: 20-44 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Russell 1951 *(Continued)*

Sampling	Low risk	Samples came from official registries in the areas (school, electoral, marriage etc). Authors estimate 5/6ths of eligible people participated
Confounding	Unclear risk	Considering the age of the study, other sources of fluoride are unlikely to affect the results. Although no measure of SES was provided, populations are reported as homogenous.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding was not undertaken
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants appeared to be present.
Selective reporting (reporting bias)	High risk	Only data on fluorosis of aesthetic concern reported as opposed to all severities
Other bias	High risk	All examinations were made by the senior author, however, there was no mention of examiner calibration

Rwenyonyi 1998

Methods	**FLUOROSIS STUDY** Country of study: Uganda Geographic location: 4 areas of Uganda located at different altitudes Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: mothers interviewed about water intake and food habits of child during early childhood; altitude
Interventions	All natural fluoridation Group 1: 2.5 ppm (low altitude) Group 2: 2.5 ppm (high altitude) Group 3: 0.5 ppm (low altitude) Control: 0.5 ppm (high altitude)
Outcomes	Dental fluorosis (index not stated) Age at assessment: 10-14 years

Rwenyonyi 1998 *(Continued)*

Funding	The Norwegian Universities' Committee for Development Research and Education and the Committee for Research and Postgraduate Training, University of Bergen
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Children were selected from schools for study in a quasi-random way
Confounding	High risk	While SES and use of fluoride toothpaste were reported as being similar across groups, there appeared to be a higher intake of tea (and therefore fluoride from water) among the participants in Kasese (0.5 ppm) than Kisoro (2.5 ppm)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to have been presented for all participants
Selective reporting (reporting bias)	Unclear risk	Outcome of interest was reported mainly in graphic form and was unclear
Other bias	Low risk	Examinations were carried out by a single examiner. Intra-rater reliability was tested (kappa > 0.8)

Rwenyonyi 1999

Methods	**FLUOROSIS STUDY** Country of study: Uganda Geographic location: Kasese (low F); Kisoro (high F) Year of study: 1996-1997 Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: children aged 10-14 years (born between 1982 and 1987); lifetime residents of study areas; consumed drinking water from same source for first 6 years of life; parental consent Exclusion criteria: absence from the village for more than 1 month per year Other sources of fluoride: fluoride exposure from liquid estimated by daily liquid intake - subjects from high fluoride area had higher intake of water, consumed more boiled water and consumed less tea than subjects from control area, higher consumption of fluoride from Trona in control group Social class: most families were small scale farmers and all appeared to be of similar social class Ethnicity: all children were ethnic Bantu Africans from the Bafumbria and Bakonjo tribes Residential history: lifelong residents

Rwenyonyi 1999 *(Continued)*

	Other confounding factors: vegetarianism (associated with fluorosis); altitude (results presented separately for different altitudes) - no association found between altitude and fluorosis
Interventions	All natural fluoridation Group 1: 2.5 (altitude = 2800 m) Group 2: 2.5 (altitude = 1750 m) Group 3: 0.5 (altitude = 2200 m) Group 4: 0.5 (altitude = 900 m)
Outcomes	Dental fluorosis (TF Index) Age at time of measurement: mean age 12.2 years (SD 1.3)
Funding	Norwegian Universities Committee for Development Research and Education and the Committee for Research and Postgraduate Trianing, University of Bergen
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Quasi-random stratified sample of all eligible children
Confounding	High risk	SES was broadly similar, however, multivariate analysis revealed that factors that were not accounted for were associated with fluorosis. These included: daily intake of water (amount), altitude, water storage, vegetarianism and infant formula use
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Examiners were blind to fluoride concentrations at the start of the study and tests were carried out on the water after the children's teeth were examined
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	All data appears to have been reported
Other bias	Low risk	No other bias was detected

Saravanan 2008

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Tamil Nadu Year of study: not stated Year of change of fluoridation status: NA Study design: cross-sectional

Saravanan 2008 *(Continued)*

Participants	Inclusion criteria: the coverage of children was confined only to primary schools as each village had a primary school and 99% of the children of primary school age group in the study area were attending schools Exclusion criteria: high school children were not included as only 85% of the children of high school age group (11-16 years) in the study area were attending schools Other sources of fluoride: not stated Ethnicity: not stated Social class: the majority of people in the study setting were of lower socioeconomic class Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: < 0.1 ppm Group 2: < 0.1 ppm Group 3: 0.25 ppm Group 4: 0.56 ppm Group 5: 0.66 ppm Group 6: 0.67 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 5-10 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were invited to participate
Confounding	High risk	No details were reported on the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Around 1.1% of the school children were eventually excluded because of absenteeism. It is not clear which fluoride areas they belonged to, however, these participants are unlikely to have been systematically different from those that completed the study
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Unclear risk	High school children were not included as only 85% of the children of high school age group (11-16 years) in the study area were attending schools; examiners were calibrated and intra-and inter-examiner reliability assessed, however, Kappa scores not reported

Scheinin 1964

Methods	**FLUOROSIS STUDY** Country of study: Finland Geographic location: Artjarvi, Askola, Elimaki, Litti, Myrskyla, Parikkala, Taipalsaari, Valkeala, Vehkalahti Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 11 Exclusion criteria: children resident in area for < 6 years; fluoride concentration of drinking water unknown Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: residence for < 6 years Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0-0.1 ppm Group 2: 0.11-0.39 ppm Group 3: 0.40-0.99 ppm Group 4: 1.0-1.59 ppm Group 5: 1.6-ppm
Outcomes	Dental fluorosis (community fluorosis index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 11 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were invited to participate
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The dental examinations were carried out as a blind study, the examiners having no information of the preliminary fluoride determinations"
Incomplete outcome data (attrition bias)	Low risk	Data presented for all participants

Scheinin 1964 *(Continued)*
All outcomes

Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	No mention of examiner calibration

Segreto 1984

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: 16 Texas communities Year of study: 1978-1981 Year of change in fluoridation status: Unclear Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents who may have resided at several different addresses in the same community; absence from community for no more than 3 months during any calendar year; grades 2-6, aged 7-12 years and grades 9-12, aged 14-18 years; city water supply as principal source of drinking water throughout lifetime; non-usage of water treatment systems that result in defluoridation of water Exclusion criteria: subjects with staining attributable to medication such as tetracycline Other sources of fluoride: not stated Social class: not stated Ethnicity: subjects were primarily those with Spanish surnames or white Residential history: lifetime residents Other confounding factors: not stated
Interventions	Unclear if natural or artificial fluoridation Group 1: 0.3 ppm Group 2: 0.3 ppm Group 3: 0.4 ppm Group 4: 1.0 ppm Group 5: 1.3 ppm Group 6: 1.3 ppm Group 7: 1.4 ppm Group 8: 2.3 ppm Group 9: 2.3 ppm Group 10: 2.5 ppm Group 11: 2.7 ppm Group 12: 2.7 ppm Group 13: 2.7 ppm Group 14: 2.9 ppm Group 15: 3.1 ppm Group 16: 4.3 ppm
Outcomes	Mottled enamel (Dean's Index) Age at assessment: 7-12 years and 14-18 years

Segreto 1984 *(Continued)*

Funding	Not stated
Notes	Data extracted from Segreto 1984 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	16 study sites that had a central well as main water supply and sufficient school population were selected
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	No mention of examiner calibration

Sellman 1957

Methods	**FLUOROSIS STUDY** Country of study: Sweden Geographic location: Malmo (low F); Simirshamn, Astorp and Nyvang (High F) Year of study: 1953 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 11-14 years Exclusion criteria: children missed due to illness; children under 11½ and over 14½ Other sources of fluoride: all children received yearly systematic treatment by the School Dental Service Social class: socioeconomic distribution of lifetime residents was similar in all study areas, however distribution was different for non-continuous residents compared to continuous residents Ethnicity: not stated Residential history: only results of lifetime residents were presented Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.0 ppm

Sellman 1957 *(Continued)*

	Group 2: 1.0-1.3 ppm Group 3: 1.3 ppm Control: 0.3-0.5 ppm
Outcomes	Outcome: dental fluorosis (Dean's Index) Age at assessment: 12-14 years
Funding	Not stated
Notes	Data extracted from Sellman 1957 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	All children received yearly systematic treatment by the School Dental Service, however, it is not clear whether the use of other fluoride sources was balanced across groups
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data appear to be presented for all participants
Selective reporting (reporting bias)	Low risk	All expected outcome reported
Other bias	High risk	No mention of examiner calibration and reliability testing

Selwitz 1995

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Kewanee (optimal), Monmouth (2 x optimal), Abingdon, Elmwood (3 x optimal), Bushneell, Ipava, Table Grove (4 x optimal), Illinois Year of study: 1980 Year study ended: 1990 Year of change in fluoridation status: unclear Study design: repeated cross-sectional
Participants	Inclusion criteria: children aged 8-10 years and 14-16 years; written parental consent; lifetime residents of study areas; continuous use of community water supply Exclusion criteria: none stated

Selwitz 1995 *(Continued)*

	Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Unclear whether all was natural fluoridation, parts of the optimally fluoridated area may have been artificially adjusted Group 1: 4 ppm Group 2: 3 ppm Group 3: 2 ppm Group 4: 1 ppm
Outcomes	Dental fluorosis (% fluorosed surfaces (TSIF); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 8-10 years and 13-15 years
Funding	Not stated
Notes	Data extracted from Selwitz 1995 differs from that presented in CRD review

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place. Reference was made to a previous study (Leverett 1986) for further information on sampling, however this study also reported insufficient information on sampling
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Selwitz 1998

Methods	**FLUOROSIS STUDY** Country of study: USA

Selwitz 1998 *(Continued)*

	Geographic location: Kewanee (F); Holdrege and Broken Bow (non-F) Year of study: 1990-1998 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; parental consent Exclusion criteria: none stated Other sources of fluoride: type of toothpaste currently used and used before age 6; use of dietary fluoride supplements; receipt of professionally applied fluoride treatments Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: use of private well-water
Interventions	All natural fluoridation Group 1: 1 ppm Group 2: < 0.3 ppm
Outcomes	Dental fluorosis (TSIF); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 8-10 years and 13-16 years
Funding	Not stated
Notes	Data extracted from Selwitz 1998 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for SES, and there was a difference between groups in the use of fluoride supplements
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Shanthi 2014

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: 3 strata (according to fluoride concentration) Khammam district, Andhra Pradesh Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children, aged 9-12 years irrespective of sex, race, and socioeconomic status, who were residents of that particular region and using the same source of drinking water; more than 50% of the crown erupted and no fillings on the facial surface of anterior teeth; co-operative parental consent Exclusion criteria: children who obtained their drinking water from more than one source; those with orthodontic brackets; children with severe extrinsic stains on their teeth; children with any communicable or systemic diseases and fractured anterior teeth Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: the consumption of sugar in the study population was about 61.3% in boys and 38.7% in girls (not specified by group)
Interventions	All natural fluoridation Group 1: < 0.7 ppm Group 2: 0.7-1.2 ppm Group 3: 1.3-3.5 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 9-12 years
Funding	Stated no funding
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Quote: "A stratified random sampling technique was used"
Confounding	Unclear risk	Insufficient information on characteristics of the groups compared
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding not specified
Incomplete outcome data (attrition bias)	Unclear risk	Number of children in each strata not specified; unclear whether all those sampled were evaluated

Shanthi 2014 *(Continued)*

All outcomes

Selective reporting (reporting bias)	High risk	Fluorosis data not presented by strata
Other bias	Low risk	No other apparent bias

Shekar 2012

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Nalgonda district Year of study: 2008 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: continuous residency; availability on the day of examination. Exclusion criteria: not stated Other sources of fluoride: information on oral hygiene practices, dietary habits, source of drinking water, and amount of liquid consumed in a day, use of fluoridated tooth paste was collected but not reported Ethnicity: not stated Social class: the majority of people in the study setting were from lower socioeconomic class Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: < 0.7 ppm Group 2: 0.7-1.2 ppm Group 3: 1.2-2 ppm Group 4: 2.1-4 ppm Group 5: > 4 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 12 and 15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Schools were selected for study using simple random sampling. All children within those schools were invited to participate

Shekar 2012 *(Continued)*

Confounding	High risk	SES was broadly similar across groups as was the use of fluoride toothpaste, however, no details were reported regarding use of fluoride supplements
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Skinner 2013

Methods	**FLUOROSIS STUDY** Country of study: Australia Geographic location: New South Wales Year of study: 2010 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school students aged 14-15 years under the jurisdiction of the NSW Department of Education and Training, the Catholic Education Commission and Independent Schools Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: aboriginal status was coded from parental responses (not reported by fluoridation status) Social class: self-reported family income data were provided by parents or guardians and was used as a measure of SES (not reported by fluoridation status) Residential history: not stated Other confounding factors: not stated
Interventions	Group 1: fluoridated (artificial; ppm not specified) Group 2: non-fluoridated
Outcomes	Dental fluorosis (TF); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 14 and 15 years
Funding	The Centre for Oral Health Strategy NSW
Notes	

Skinner 2013 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Quote: "random sample"
Confounding	Low risk	Quote: "initial weights were adjusted to ensure the distribution of the sample reflected the regional population distribution of 14-15-year-olds in NSW"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Particpation rate low (23%). Did not account for all participants in analysis
Selective reporting (reporting bias)	Unclear risk	Observed enamel fluorosis/defects were recorded for both the central incisors; not all data reported
Other bias	Unclear risk	No other apparent bias

Skotowski 1995

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Iowa Year of study: 1991 Year of change in fluoridation status: NA Study design: case-control study
Participants	Inclusion criteria: children aged 8-17 years; patients attending Iowa College of Dentistry's Paediatric clinic; all permanent incisors and first molars present and erupted; parent who could provide consent and details of fluoride exposure accompanied child Exclusion criteria: children with fixed orthodontic appliances; all permanent incisors and first molars present and erupted Other sources of fluoride: dietary fluoride supplement use; age began brushing with toothpaste; toothpaste usage in 8 years; mouth rinse usage; professional fluoride treatments Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 3.1 ppm Group 2: 5.6 ppm

Skotowski 1995 *(Continued)*

Outcomes	Dental fluorosis (TSIF) Age at assessment: 8-17 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	High risk	The study population was a convenience sample of children receiving treatment at the clinic
Confounding	High risk	Did not account for SES. When analysed for effect of duration of residence and use of other fluoride sources, the results were found to have been influenced by duration of exposure and toothpaste usage in 8 years, however the results were not adjusted for these factors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The examiner had no previous knowledge of subjects' dental fluorosis status or fluoride exposures"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Fluorosis prevalence was not reported according to fluoridation status or fluoride concentration
Other bias	High risk	The examiner was not calibrated. Quote: "Because of the burden that replicated examination would cause for the children and their parents, formal reliability assessments were not conducted"

Spadaro 1955

Methods	**FLUOROSIS STUDY** Country of study: Italy Geographic location: Barcelona, Pozzo di Gotto, Sicily Year of study: 1954 Year of change in fluoridation status: unclear Study design: cross-sectional
Participants	Inclusion criteria: children attending schools in study areas Exclusion criteria: none stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated

Spadaro 1955 *(Continued)*

	Residential history: not stated Other confounding factors: not stated
Interventions	Unclear if natural or artificial fluoridation Group 1: 0.4 ppm Group 2: 1.9 ppm
Outcomes	Dental fluorosis (index not stated); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 6-11 years
Funding	Not stated
Notes	Data from original CRD review (data unverified)

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Unable to make a judgement as study was unavailable
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unable to make a judgement as study was unavailable
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unable to make a judgement as study was unavailable
Selective reporting (reporting bias)	Unclear risk	Unable to make a judgement as study was unavailable
Other bias	Unclear risk	Unable to make a judgement as study was unavailable

Stephen 2002

Methods	**FLUOROSIS STUDY** Country of study: Scotland Geographic location: Burghead, Kinloss and Findhorn Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: information on the use of fluoridated tooth paste was collected but not reported

Stephen 2002 *(Continued)*

	Ethnicity: not stated Social class: the socioeconomic analyses showed that 17% of F subjects were in the 'high' SES groups I or II, 75% in 'non-manual' group III, and 8% in 'manual' groups IV or V. For non-F children, the corresponding percentages were 23%, 60% and 17%, thus revealing a higher percentage of non-F subjects at either end of the SES scale Residential history: the participants were either lifetime or school-lifetime (i.e. permanently present therein since commencing full-time schooling at approximately 5 years of age) residents Other confounding factors: information about oral hygiene practices, dietary habits, source of drinking water, and amount of liquid consumed in a day
Interventions	All natural fluoridation Group 1: 1-2.4 ppm Group 2: 0.03 ppm
Outcomes	Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 5-6 years (caries only) and 8-12 years (caries and fluorosis)
Funding	Supported by a Scottish Office Department of Health grant
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	There was insufficient detail reported to determine how selection took place, however it was reported that about one-fifth (21.9%) of the eligible participants were not examined because of non-consent (9.4%) and unavailability for examination (12.6%)
Confounding	Unclear risk	Matched by SES, details on the use of fluoride sources show that fluorosis prevalence was not influenced by the use of other fluoride sources. Similar use of fluoride supplements across groups. The age at which brushing with fluoridated paste began did not appear to affect the prevalence of fluorosis, however information on brushing history was only available for the parents who were able to recall
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants were examined without knowledge of their fluoridation status. Slides were viewed blind and scored randomly under standardised projection conditions by the assessors with a 10% random reviewing for inter and intra-observer agreement calculations
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Only lifetime residents between 8 and 12 years were assessed for fluorosis and data for all of them presented
Other bias	Unclear risk	The study involved children between the age of 5-6 years and 8-12 years, but the investigators only conducted fluorosis assessments on 8- to 12-year olds so data have been extracted for only children for whom fluorosis assessment was conducted

Sudhir 2009

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: Andhra Pradesh Year of study: 2006-2007 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: school children aged 13-15 years; lifelong residence of the region; use of the same source of drinking water from birth to 10 years of age; having permanent teeth with at least > 50% of the crown erupted and no fillings on facial surface Exclusion criteria: migration from some other place; change of source of drinking water; drinking water from more than 1 source; having orthodontic brackets; having teeth with severe extrinsic stains Other sources of fluoride: information was collected on aids used for oral hygiene maintenance (fluoridated or non-fluoridated); no data on aids used for oral hygiene maintenance reported Ethnicity: not stated Social class: not stated Residential history: lifetime residents Other confounding factors: the questionnaire consisted of information in 2 parts: the first part consisted of information on demographic data, permanent residential address, source of drinking water, duration of use of present source of drinking water, staple food, liquids routinely consumed
Interventions	All natural fluoridation Group 1: < 0.7 ppm Group 2: 0.7-1.2 ppm Group 3: 1.3-4 ppm Group 4: > 4 ppm
Outcomes	Outcome: fluorosis prevalence (TF Index); Age at assessment: 13-15 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Used a stratified random sampling technique. The entire geographical area of Nalgonda district was divided into 4 strata based on different levels of naturally occurring fluoride in drinking water supply. So in each stratum, or for each level, several villages were involved. Sample size was divided equally among all the 4 strata, and representation from both the sexes was included in the sampling
Confounding	High risk	Data were collected on aids used for oral hygiene maintenance (fluoridated or non-fluoridated) but not reported

Sudhir 2009 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Szpunar 1988

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Hudson, Redford, Richmond (F); Cadillac (non-F), Michigan Year of study: not stated Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; children aged 6-12 years Exclusion criteria: none stated Other sources of fluoride: use of fluoride supplements; dental attendance; time interval since last dental visit; age began brushing (parent & child); age at start of F rinsing; feeding method in 1st year of life. Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1.2 ppm (artificial fluoridation) Group 2: 1.0 ppm (artificial fluoridation) Group 3: 0.8 ppm (artificial fluoridation) Group 4: 0.0 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TSIF); caries data also evaluated in the study but not included in the review due to study design Age at assessment: 6-12 years
Funding	NIH National Research Service Award
Notes	Data extracted from Szpunar 1988 differs from that presented in CRD review
Risk of bias	

Szpunar 1988 *(Continued)*

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Classroom teachers distributed and collected permission slips
Confounding	High risk	Did not appear to account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data collected for 1103 participants but only lifetime resident data (n = 556) presented
Selective reporting (reporting bias)	Low risk	Relevant fluorosis outcome data
Other bias	Low risk	No other apparent risk of bias

Tabari 2000

Methods	**FLUOROSIS STUDY** Country of study: UK Geographic location: Northumberland and Newcastle upon Tyne Year of study: 1998 Year of change in fluoridation status: 1969 Study design: cross-sectional
Participants	Inclusion criteria: parental consent; lifetime residency Exclusion criteria: not stated Ethnicity: not stated Other sources of fluoride: data on the use of fluoride drops and tablets collected but not presented. Data on toothbrushing habit/frequency presented in detail and appeared to be similar in F and non-F areas Social class: the subjects from Newcastle tended to reside in more underprivileged areas than those in Northumberland. The mean Jarman UPA8 score was 16.3 (SD = 19.1) for subjects in Newcastle and 7.3 (SD = 15.0) for Northumberland (P value < 0.001). However, the authors were reported to have chosen schools to provide children from a spectrum of SES backgrounds Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 1 ppm (artificial fluoridation) Group 2: 0.1 ppm (natural fluoridation)
Outcomes	Dental fluorosis (TF Index); Age at assessment: 8-9 years

Tabari 2000 *(Continued)*

Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	In Newcastle and Northumberland, 14 and 15 schools respectively were chosen. However, there was insufficient information on how the selection was done
Confounding	High risk	There was a significant difference in measure of deprivation between the 2 study areas
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessment was by the use of photographs in order to allow examination of teeth of children without the examiner being aware of which area the child was from
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	In the 2 groups, 78% and 79% of the eligible children had complete data. It was not clear whether those whose photographs were unacceptable (examined but not analysed) were systematically different from those who remained in the study
Selective reporting (reporting bias)	Low risk	Outcome of interested reported
Other bias	Low risk	No other apparent bias

Tessier 1987

Methods	**CARIES STUDY** Country of study: Canada (province of Québec) Geographic location: Windsor (F) and Richmond (non-F) Year study started: 1977 Year study ended: 1986 Year of change in fluoridation status: 1978 Study design: CBA
Participants	Inclusion criteria: All 6- and 7-year-old schoolchildren Exclusion criteria: children living too far from the fluoridated water supply; or drinking fluoridated water 3 years or less Other sources of fluoride: mouthwash and toothpaste; participants underwent similar fluoride rinse programmes Social class: comparable study areas with similar socioeconomic status and lifestyles Ethnicity: not stated Residential history: not stated

Tessier 1987 *(Continued)*

	Other confounding factors: similar access to dental care, oral hygiene and levels of dental plaque
Interventions	Group 1: 'optimal' level - ppm not stated (artificial fluoridation) Control: 'low' level - ppm not stated (natural fluoridation)
Outcomes	DMFT; % caries prevalence Age at baseline measure: 6 and 7 years Age at final measure: 6 and 7 years
Funding	Not stated
Notes	Translated from French

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All children aged 6 and 7 years in both study areas were selected
Confounding	High risk	Participants might have had varied exposures to fluoridated water. No details were reported on the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Standard deviation not reported
Other bias	High risk	No mention of examiner calibration and reliability testing

Tsutsui 2000

Methods	**FLUOROSIS STUDY** Country of study: Japan Geographic location: not stated Year of study: 1987 Year of change in fluoridation status: naturally occurring fluoride Study design: cross-sectional
Participants	Inclusion criteria: use of municipal water supply and lifelong residency of study area; difference of ≤ 0.2 ppm where home and school were located in different water supply areas Exclusion criteria: failure to meet any of the inclusion criteria; other reasons for exclusion were incomplete questionnaire and periodic application of topical fluoride

Tsutsui 2000 *(Continued)*

	Other sources of fluoride: children that had received periodic applications of topical fluoride were excluded; no children had used fluoride mouth rinses; use of fluoride-containing toothpaste was not determined as the market share was only 12% and thus not commonly used by children at the time Ethnicity: not stated Social class: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0-0.2 ppm Group 2: 0.2-0.4 ppm Group 3: 0.4-0.6 ppm Group 4: 0.6-0.8 ppm Group 5: 0.8-1 ppm Group 6: 1-1.4 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 10-12 years
Funding	Niigata University
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were invited to participate
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The examiners had no knowledge of the concentration of fluoride in the drinking water where they carried out the examinations
Incomplete outcome data (attrition bias) All outcomes	High risk	Out of the 1967 children that were examined, data for 907 (46.1%) were not presented
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Venkateswarlu 1952

Methods	**FLUOROSIS STUDY**

Venkateswarlu 1952 *(Continued)*

	Country of study: India and Switzerland
	Geographic location: villages in the Visakhapatnam area (India), and 3 villages in Switzerland
	Year of study: not stated
	Year of change in fluoridation study: NA
	Study design: cross-sectional
Participants	Inclusion criteria: children aged 3-14 years; areas with ≤ 2 ppm F in water supplies
	Exclusion criteria: none stated
	Other sources of fluoride: not stated
	Social class: not stated
	Ethnicity: not stated
	Residential history: not stated
	Other confounding factors: not stated
Interventions	All natural fluoridation
	Group 1: 0.3 ppm
	Group 2: 0.5 ppm
	Group 3: 0.5 ppm
	Group 4: 0.9 ppm
	Group 5: 0.9 ppm
	Group 6: 0.9 ppm
	Group 7: 0.9 ppm
	Group 8: 1 ppm
	Group 9: 1.3 ppm
	Group 10: 1.4 ppm
	Group 11: 0.5-0.8 ppm
	Group 12: 0.4-1.6 ppm
Outcomes	Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design
	Age at assessment: 3-14 years
Funding	Not stated
Notes	
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**

Venkateswarlu 1952 *(Continued)*

Sampling	Unclear risk	Children aged 3-14 years belonging to the study areas were examined; as far as possible, at least 100 children per village. It was not clear how exactly these children were selected
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	12 Indian villages were involved in the study; data from 1 village (Malkapuram) with 102 participants not presented
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	High risk	Calibration of examiners not mentioned

Vignarajah 1993

Methods	**FLUOROSIS STUDY** Country of study: Antigua Geographic location: urban and rural areas in Antigua Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged 12-14 years; lifetime residents of study areas Exclusion criteria: restored or fractured tooth surfaces Other sources of fluoride: toothpaste swallowing when younger; consumption of mixed sources of water; fluoride mouth rinses Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.6-1 ppm Group 2: 0.1-0.3 ppm
Outcomes	Dental fluorosis (TSIF) Age at assessment: 12-14 years
Funding	Not stated

Vignarajah 1993 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	A stratified random technique using random number tables was used to select schools and children. Quote: "All the schools were first listed and then divided into two groups, urban and rural…"
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of participants recruited not stated
Selective reporting (reporting bias)	Low risk	Outcome of interest presented
Other bias	Low risk	No other apparent bias

Vilasrao 2014

Methods	**FLUOROSIS STUDY** Country of study: India Geographic location: 7 districts of the Chhattisgarh State Year of study: 2013-2014 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: none stated Exclusion criteria: none stated Other sources of fluoride: not stated Ethnicity: not stated Social class: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 3.8 ppm Group 2: 2.5 ppm

Vilasrao 2014 *(Continued)*

	Group 3: 2.0 ppm Group 4: 3.0 ppm Group 5: 2.2 ppm Group 6: 2.8 ppm Group 7: 3.3 ppm
Outcomes	Dental fluorosis (assessed using: mottled enamel, chalk white, yellowish brown or brownish black, horizontal streaks over teeth); bowing of legs/spine also evaluated
Funding	Ministry of Health and Family Welfare
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Quote: "door-to-door survey .... randomly selected"
Confounding	High risk	Did not acount for potential confounding factors
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insuffieicnt information
Selective reporting (reporting bias)	High risk	Number of participants by district not reported
Other bias	Unclear risk	No other apparent bias

Villa 1998

Methods	**FLUOROSIS STUDY** Country of study: Chile Geographic location: Rancagua (non-F), Santiago (low-F), La Serena (medium-F), San Felipe and Iquique (high-F) Year of study: 1996 Year of change in fluoridation status: fluoride was naturally occurring Study design: cross-sectional study
Participants	Inclusion criteria: lifetime residents of study areas; children aged 7,12 and 15 years in selected schools in study areas Exclusion criteria: none stated Other sources of fluoride: not stated

Villa 1998 *(Continued)*

	Social class: children selected from schools graded according to socioeconomic status to give similar socioeconomic distribution in each study area Ethnicity: not stated Residential history: lifetime residents Other confounding factors: temperature
Interventions	All natural fluoridation Group 1: 0.07 ppm Group 2: 0.21 ppm Group 3: 0.55 ppm Group 4: 0.93 ppm Group 5: 1.10 ppm
Outcomes	Dental fluorosis (Deans Index); caries data also evaluated within the study but excluded from review due to study design Age at assessment: 15 years
Funding	Study was supported by the Chilean Council for Scientific and Technological Research (FONDECYT) through grant no. 1960993
Notes	Data extracted Villa 1998 differs from that presented in CRD review

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Selection of schools for each community was made at random from the complete list of private schools and publicly supported elementary schools. All eligible children were invited to participate
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Data not in suitable format for analysis
Other bias	High risk	There may have been misclassification bias as fluorosis prevalence was reported without taking 'questionable' fluorosis prevalence into account

Vuhahula 2009

Methods	**FLUOROSIS STUDY**

Vuhahula 2009 *(Continued)*

	Country of study: Tanzania Geographic location: Arusha, Shinyanga, Manyara, Dodoma, Singida and Tabora Year of study: not stated Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: aged 12-18 years; lifelong residence Exclusion criteria: in order to avoid over-scoring, teeth that were tempered with by grinding or other forms of mutilations were excluded Other sources of fluoride: not stated Ethnicity: not stated Social class: not stated Residential history: mostly lifelong residents Other confounding factors: information on 'magadi' consumption was collected, however, participants seemed to be accessing 'magadi' from different sources making the correlation of fluoride in 'magadi' versus dental fluorosis complicated
Interventions	All natural fluoridation Group 1: 2.2 ppm Group 2: 2.4 ppm Group 3: 2.5 ppm Group 4: 4.2 ppm Group 5: 4.7 ppm Group 6: 5.6 ppm
Outcomes	Dental fluorosis (Dean's Index) Age at assessment: 12-18 years
Funding	Funded by the Japanese International Cooperation Agency (JICA) of Tanzania
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Regions were randomly chosen and then schools within them. Children were quota sampled from these schools
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information

Vuhahula 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	High risk	Data not in suitable format for analysis
Other bias	Low risk	No other apparent bias

Wang 1993

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: Hotan, Kaxgar and Aksu, in south Xinjiang Year of study: 1991 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: children aged from 8-15 years living around the water source Exclusion criteria: not stated Other sources of fluoride: not stated Social class: farmers and herdsmen in south Xinjiang Ethnicity: Minority, mainly Uygur ethnic group Residential history: living in study area for a long time ("since many years ago") Other confounding factors: the combined effects of iodine deficiency and high fluorine; the habit of tea drinking
Interventions	All natural fluoridation Group 1: 1.58 ppm Group 2: 1.85-2.00 ppm Group 3: 0.48 ppm Group 4: 2.55 ppm Group 5: 0.43 ppm Group 6: 0.46 ppm Group 7: 0.43 ppm
Outcomes	Dental fluorosis (index not stated) Age at assessment: 15 years
Funding	Not stated in translation

Wang 1993 *(Continued)*

Notes	Paper translated from Chinese

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Children aged 8-15 living in the vicinity of the water sources were included. Insufficient sampling information
Confounding	High risk	Did not account for the use of fluoride from other sources, residential history not clearly stated
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants reported
Selective reporting (reporting bias)	Low risk	Outcome of interest presented
Other bias	Unclear risk	Unable to identify information pertaining to the training/reliability of outcome assessors

Wang 1999

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: Xindiliang Village (high F), Shiligetu Village (lower F) Year of study: 1999 Year of change in fluoridation status: NA Study design: cross sectional study
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: not stated Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.3 ppm Group 2: 2-4 ppm

Wang 1999 *(Continued)*

Outcomes	Dental fluorosis and skeletal fluorosis (3 grade classification for both) Age at assessment: all ages
Funding	Japan International Cooperation Agency
Notes	Removal of fluoride from the water in these areas was attempted in the 1980s but failed to be applied continuously

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Households in the villages of study were arbitrarily chosen so that 25% were included in the study
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest presented
Other bias	High risk	There was no mention of examiner calibration

Wang 2012

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: not stated Year of study: 2008-2009 Year of change in fluoridation status: NA Study design: cross sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Social class: not stated Ethnicity: not stated Residential history: in the mild, moderate and severe endemic areas, the authors made reference to native-born residents, but it is not clear what proportion of them constituted the entire population

Wang 2012 *(Continued)*

	Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 1.3 ppm Group 2: 2-4 ppm
Outcomes	Dental fluorosis (Dean's Index); skeletal fluorosis Age at assessment: 8-12 years for dental fluorosis and > 16 years for skeletal fluorosis
Funding	Supported by the Chinese government for Endemic Disease Control in 2008-2009
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	Villages were selected at random, and in the selected villages, all eligible children were invited to participate
Confounding	High risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Unclear risk	Outcome of interest reported
Other bias	High risk	No mention of examiner calibration

Warnakulasuriya 1992

Methods	**FLUOROSIS STUDY** Country of study: Sri Lanka Geographic location: 4 geographic areas at same altitude and temperature from 4 districts in Sri Lanka (Galewala, Wariyapola, Kekirawa and Rambukkana) Year of study: 1986 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; children aged 14 years Exclusion criteria: children who lived more than 15 miles from school; children absent on day of examination

Warnakulasuriya 1992 *(Continued)*

	Other sources of fluoride: fluoride containing toothpaste or other fluoride therapies had not been used by or on these children during time of development of primary dentition; tea consumption high Social class: wide ranges of socioeconomic differences not expected Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: <0.39 ppm Group 2: 0.4-0.59 ppm Group 3: 0.6-0.79 ppm Group 4: 0.8-0.99 ppm Group 5: >1.0 ppm
Outcomes	Fluorosis (Dean's Index); caries data evaluated in study but not included in review due to study design Age at assessment: 14 years
Funding	National Water Supply, Sri Lanka
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children in each school were invited to participate
Confounding	Unclear risk	The study authors considered that fluoride supplements or paste were not widely used among the study population and that SES was broadly similar across groups, however no supporting information was provided
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data presented for all participants
Selective reporting (reporting bias)	Low risk	Outcome of interest presented
Other bias	Low risk	No other apparent bias

Warren 2001

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Iowa Year of study: 1997-2000

Warren 2001 *(Continued)*

	Year of change in fluoridation status: unclear Study design: cross-sectional data from within cohort study
Participants	Inclusion criteria: not stated Exclusion criteria: not stated. Other sources of fluoride: fluoride dentifrice use = 159/637 (25%); dietary fluoride supplement use = 131/637 (20.6%). There was no difference in fluorosis prevalence between those who used other sources of fluoride and those who did not Ethnicity: not stated Social class: not stated Residential history: mostly lifelong residents Other confounding factors: not stated
Interventions	Group 1: < 0.7 ppm (natural fluoridation) Group 2: 0.7-1.2 ppm (artificial fluoridation) Group 3: > 1.2 ppm (natural fluoridation)
Outcomes	Fluorosis prevalence (TSIF) Age at assessment: 4.5-5 years
Funding	Supported by NIH grants 2ROl-DE09551, 2P30-10126, and CRC-RROOO5
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Children included in the present study were part of the Iowa Fluoride Study cohort, which had been followed prospectively since birth. Full details were not reported
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome data available for 559 out of the 637 (87.8%) participants due to lack of information on water fluoride concentration
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Wenzel 1982

Methods	**FLUOROSIS STUDY** Country of study: Denmark Geographic location: Naestved (F); Greve (F); Ry (non-F) Year of study: not stated Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; girls aged 12-15 years Exclusion criteria: children with orthodontic appliances; history of additional fluoride use Other sources of fluoride: only children without fluoride use were included; no attempt was made to distinguish between users and non-users of fluoridated dentifrice Social class: not stated Ethnicity: not stated Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: < 0.2 ppm Group 2: 1.0 ppm Group 3: 2.4 ppm
Outcomes	Fluorosis (TF Index); skeletal maturity Age at assessment: 12-14 years
Funding	Sponsored by Colgate Palmolive, Denmark
Notes	Data extracted Wenzel 1982 differs from that presented in CRD review

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Unclear risk	Insufficient detail reported to determine how selection took place
Confounding	High risk	Did not account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants presented
Selective reporting (reporting bias)	Low risk	Outcome of interest presented
Other bias	High risk	No information on examiner calibration

Whelton 2004

Methods	**FLUOROSIS STUDY** Country of study: Republic of Ireland (RoI) Geographic location: not stated Year of study: 2001/2002 Year of change in fluoridation status: 1964 Study design: cross-sectional
Participants	Inclusion criteria: children in Junior Infants, Second Class, Sixth Class, and Junior Certificate Exclusion criteria: not stated. Other sources of fluoride: participants in the fluoridated group may have had additional exposure to fluoride tablets and fluoride mouth rinses Ethnicity: not stated Social class: possesion of a medical card was used in this study as a surrogate for disadvantage; RoI medical card vs no medical card = 24% vs 75% (full F = 25.2% vs 74.4%; non-F = 20.3% vs 79.4%); figures do not add up to 100%, however, authors reported that figures included children for whom medical card details were missing Residential history: fluoridated group subjects' home water supply had to have been fluoridated continuously since birth, and the non-fluoridated group subjects' home water supply had never to have been fluoridated. No further details reported Other confounding factors: not stated
Interventions	Group 1: 0.8-1 ppm (artificial fluoridation) Group 2: 'non-fluoridated'
Outcomes	Fluorosis prevalence (Dean's Index); caries data (dmft/DMFT) evaluated in study but not included in review due to study design Age at assessment: 5, 8, 12 and 15 years
Funding	Funded by the Department of Health and Children and the Health Boards in Ireland
Notes	The authors carried out and reported power calculation for the primary outcome (DMFT) but not for the fluorosis outcome

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	National survey using a cluster sampling technique with schools as the clustering unit and children in Junior Infants, Second Class, Sixth Class and Junior Certificate were selected
Confounding	High risk	SES accounted for in caries analysis; did not account for the use of fluoride from other sources or the dietary habits of the children
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Fluoride codes ascribed after examinations; unlikely to be systematic bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome data presented as a percentage; unclear if accounted for all participants

Whelton 2004 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Fluorosis outcomes presented as percentages; unclear if accounted for all participants
Other bias	Low risk	No other apparent bias

Whelton 2006

Methods	FLUOROSIS STUDY Country of study: Republic of Ireland (RoI) and Northern Ireland (NI) Geographic location: not stated Year of study: 2001/2002 Year of change in fluoridation status:1964 Study design: cross-sectional
Participants	Inclusion criteria: Junior Infants, Second Class, Sixth Class and Junior Certificate in RoI and Primary 1, Primary 4, Year 1 and Year 4 in NI Exclusion criteria: not stated Other sources of fluoride: participants in the fluoridated group may have had additional exposure to fluoride tablets and fluoride mouth rinses Ethnicity: not stated Social class: possession of a medical card (MC) was used in this study as a surrogate for disadvantage in RoI, whilst receipt of low-income benefits (LIB) was used as a surrogate for disadvantage in NI. RoI full-F: MC vs no MC = 25.2% vs 74.4%; NI non-F LIB vs no LIB = 37.3% vs 61.3%; figures do not add up to 100%, however, authors reported that figures included children for whom MC/LIB details were missing Residential history: fluoridated group subjects' home water supply had to have been fluoridated continuously since birth and the non-fluoridation group subjects' home water supply had never to have been fluoridated. No further details reported Other confounding factors: not stated
Interventions	Group 1 (RoI): 0.8-1 ppm (artificial fluoridation) Group 2 (NI): 'non-fluoridated' - ppm not reported
Outcomes	Fluorosis prevalence (Dean's Index); caries data (dmft/DMFT) evaluated in study but not included in review due to study design Age at assessment: 5, 8, 12 and 15 years
Funding	Funded by the Department of Health and Children and the Health Boards in Ireland
Notes	The authors carried out and reported power calculation for the primary outcome (DMFT), but not for the fluorosis outcome

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Sampling	Low risk	National survey using a cluster sampling technique with schools as the clustering unit and children in Junior Infants, Second Class, Sixth Class and Junior Certificate in RoI and Primary 1, Primary 4, Year 1 and Year 4 in NI

Whelton 2006 *(Continued)*

Confounding	High risk	SES accounted for in caries analysis; did not account for the use of fluoride from other sources or the dietary habits of the children; used different measures for assessing SES
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Fluoride codes ascribed after examinations; unlikely to be systematic bias
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome data presented as a percentage; unclear if accounted for all participants
Selective reporting (reporting bias)	Unclear risk	Fluorosis outcomes presented as percentages; unclear if accounted for all participants
Other bias	Low risk	No other apparent bias

Wondwossen 2004

Methods	**FLUOROSIS STUDY** Country of study: Ethiopia Geographic location: not stated Year of study: 1997 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: not stated Exclusion criteria: not stated Other sources of fluoride: not stated Ethnicity: not stated Social class: the villages were of approximately the same size and socioeconomic standards and were selected purposively for the study. Residential history: fluoridated group subjects' home water supply had to have been fluoridated continuously since birth and the non-fluoridation group subjects' home water supply had to have never been fluoridated. No further details reported Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.3-2.2 ppm Group 2: 10-14 ppm
Outcomes	Fluorosis prevalence (TF Index); caries data evaluated in study but not included in review due to study design Age at assessment: 12-15 years
Funding	Supported by the Norwegian State Educational Loan Fund, NUFU Project 61/96 and the Committee for Research and Postgraduate Training, Faculty of Dentistry, University of Bergen, Norway and the Faculty of Medicine (Fluoride Project), University of Addis Ababa, Ethiopia
Notes	

Wondwossen 2004 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Participants were chosen from a census, however, insufficient detail was reported on individual selection
Confounding	High risk	Did not account for the use of fluoride from other sources
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Intra-oral examination was conducted at the health centers of the areas by two examiners" Blinding not undertaken
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants presented
Selective reporting (reporting bias)	Low risk	Outcome of interest reported
Other bias	Low risk	No other apparent bias

Zheng 1986

Methods	**FLUOROSIS STUDY** Country of study: China Geographic location: Guangzhou and Fangcun (F); Fushan and Zhaoqing (non-F) Year of study: not stated Year of change in fluoridation status: not stated Study design: cross-sectional
Participants	Inclusion criteria: students who were 7-, 9-, 12-, 15-, and 17-years old Exclusion criteria: not stated Other sources of fluoride: not stated, but time point of 1975 in Guangdong province of China would be mean that exposure to fluoridated toothpaste could be assumed Social class: not stated Ethnicity: chinese Residential history: lifetime residents Other confounding factors: not stated
Interventions	Group 1: 0.6-1.2 ppm (artificial fluoridation) Group 2: 0.4-1.2 ppm (artificial fluoridation) Group 3: 0.2 ppm (natural fluoridation) Group 4: 0.2 ppm (natural fluoridation)
Outcomes	Outcome: fluorosis prevalence (Dean's Index) Age at assessment: 12-17 years

Zheng 1986 *(Continued)*

Funding	Not stated
Notes	Data extracted from Zheng 1986 differs from that presented in CRD review Translated from Chinese

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Unclear risk	Insufficent information to make a judgement
Confounding	High risk	Did not appear to account for SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Fluorosis data for all participants reported
Selective reporting (reporting bias)	High risk	The authors seem to have collected caries data at baseline, but reported only the follow-up data
Other bias	Unclear risk	Unable to identify information pertaining to the training/reliability of outcome assessors

Zimmermann 1954

Methods	**FLUOROSIS STUDY** Country of study: USA Geographic location: Aurora, Illinois (F); Montgomery and Prince Georges counties, Maryland (non-F) Year of study: 1953 Year of change in fluoridation status: NA Study design: cross-sectional
Participants	Inclusion criteria: lifetime residents of study areas; white children aged 12-14 years Exclusion criteria: children who had left study areas for periods of time other than for holidays Other sources of fluoride: not stated Social class: not stated Ethnicity: white children only Residential history: continuous residents Other confounding factors: not stated
Interventions	All natural fluoridation Group 1: 0.2 ppm Group 2: 1.2 ppm
Outcomes	Fluorosis (Deans Index); caries data evaluated in study but not included in review due to study design

Zimmermann 1954 *(Continued)*

	Age at assessment: 12-14 years
Funding	Not stated
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Sampling	Low risk	All eligible children were invited to participate
Confounding	Low risk	Did not account for the use of fluoride from other sources or SES
Blinding of outcome assessment (detection bias) All outcomes	High risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data for all participants presented
Selective reporting (reporting bias)	Low risk	Outcome of interest presented
Other bias	High risk	There was no mention of examiner calibration

Abbreviations
CBA: controlled before-and-after study
CFI: Community Fluorosis Index
CRD: Centre for Reviews and Dissemination
DDE: developmental defects of tooth enamel
dmft: decayed, missing and filled deciduous teeth
DMFT: decayed, missing and filled permanent teeth
F: fluoride/fluoridated
ITS: interrupted time series study
LIB: low-income benefits
NA: not applicable
NI: Northern Ireland
non-F: non-fluoridated
NUFU: Norwegian Programme for Development, Research and Education
RoI: Republic of Ireland
SD: standard deviation
SE: standard error
SES: socioeconomic status
TF Index: Thylstrup-Fejerskov Index
TSIF: Tooth Surface Index of Fluorosis
UPA8: under privileged area 8

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Acharya 2003	Evaluated caries in a single time point cross-sectional study
Agarwal 2014	Evaluated fluorosis levels in single area

Study	Reason for exclusion
Ajayi 2008	Evaluated caries in a single time point cross-sectional study
Akosu 2008	No direct comparison of different fluoride concentrations
Aldosari 2004	Evaluated caries in a single time point cross-sectional study
Aleksejuniene 2004	Naturally high fluoride area was compared to a low fluoride area, however, there was no change in concentration at the 2 time points reported
Alimskii 2000	Unable to locate study
Antunes 2004	Evaluated caries in a single time point cross-sectional study
Anuradha 2002	Evaluation of periodontal disease in relation to fluoride concentration
Archila 2003	Evaluated caries in a single time point cross-sectional study
ARCPOH 2008	Evaluated caries in a single time point cross-sectional study
Armfield 2004	Evaluated caries in a single time point cross-sectional study
Armfield 2005	Evaluated caries in a single time point cross-sectional study
Armfield 2007	Evaluated caries in a single time point cross-sectional study
Armfield 2010	Evaluated caries in a single time point cross-sectional study
Arora 2010	Evaluated caries in a single time point cross-sectional study
Attwood 1988	Inappropriate design for studying cessation of water fluoridation
Bailie 2009	Evaluated caries in a single time point cross-sectional study
Baldani 2002	Evaluated caries in a single time point cross-sectional study
Baldani 2004	Evaluated caries in a single time point cross-sectional study
Bihari 2008	No fluorosis data
Binbin 2005	Evaluated caries in a single time point cross-sectional study
Blagojevic 2004	Evaluated caries in a single time point cross-sectional study
Blayney 1960	Data measured at different time points for fluoridated and non-fluoridated areas
Bo 2003	Evaluation of skeletal/dental fluorosis
Bottenberg 2004	No distinct comparison between areas
Bradnock 1984	Evaluated caries in a single time point cross-sectional study
Buchel 2011	Comparison of water fluoridation and salt fluoridation
Burt 2000	Assesses effect of break in water fluoridation in single area

Study	Reason for exclusion
Buscariolo 2006	Evaluated fluorosis levels in single area
Buzalaf 2004	Assessed effect of break in water fluoridation in single area
Campain 2010	Evaluated cost savings from community water fluoridation in Australia
Carmichael 1980	Evaluated caries in a single time point cross-sectional study
Carmichael 1984	Evaluated caries in a single time point cross-sectional study
Carmichael 1989	Evaluated caries in a single time point cross-sectional study
Carvalho 2007	Assessed fluorosis prior to commencing water fluoridation
Catani 2007	Compared areas with 'one with homogenous fluoride concentration and oscillating concentration'
Chen 2009	No direct comparison of different fluoride concentrations
Chen 2012	No distinct comparison between areas
Cheng 2000	Compared different ethnic populations receiving similar water fluoride levels
Ciketic 2010	Cost-effectiveness study
Clark 2006	Assessed fluorosis after cessation of water fluoridation
de Lourdes Azpeitia-Valadez 2009	Compared areas but no mention of differing fluoride concentrations
Dini 2000	Comparison of areas with different duration of water fluoridation
Do 2007	Evaluated risk-benefit balance of several fluoride exposures
Dobaradaran 2008	No concurrent control
Evans 1995	Evaluated caries in a single time point cross-sectional study
Evans 2009	Evaluated the effect of a water fluoridation programme in the single area
Faye 2008	Evaluated fluorosis in single city following change in water supply
Gillcrist 2001	Evaluated caries in a single time point cross-sectional study
Gushi 2005	Evaluated caries in a single time point cross-sectional study
Han 2011	Evaluated caries in a single time point cross-sectional study
Hobbs 1994	Inappropriate design for studying cessation of water fluoridation
Hoffmann 2004	Evaluated dental caries between children attending public and private schools in fluoridated city
Hopcraft 2003	Cross-sectional study evaluating caries experience; no comparison of fluoride concentrations and no fluorosis data
Hussain 2013	Focused on evaluation of groundwater concentrations

Study	Reason for exclusion
Ito 2007	Thesis - unable to access
Jones 1997	Evaluated caries in a single time point cross-sectional study
Jones 2000a	Evaluated caries in a single time point cross-sectional study
Jones 2000b	Evaluated caries in a single time point cross-sectional study
Kalsbeek 1993	Inappropriate design for studying cessation of water fluoridation
Khan 2004	Evaluated dose-response relationship between the prevalence of dental caries; did not compare fluorosis levels by fluoride concentration
Kirkeskov 2010	Evaluated caries in a single time point cross-sectional study
Kozlowski 2002	Abstract only
Kukleva 2007	Evaluated fluorosis levels in single area (with high use of bottled water)
Kumar 2001	Evaluated caries in a single time point cross-sectional study
Kunzel 2000	Data measured at different time points for fluoridated and non-fluoridated areas
Kunzel 2000a	No concurrent control group
Lee 2004	Evaluated caries in a single time point cross-sectional study
Liu 2006	Evaluated fluorosis with regard to improvement in water supply
Liu 2009	Evaluated fluorosis with regard to improvement in water supply
Murray 1984	Evaluated caries in a single time point cross-sectional study
Murray 1991	Evaluated caries in a single time point cross-sectional study
Nayak 2009	No comparison made
Ncube 2005	Evaluated fluorosis with regard to improvement in water supply
Nirgude 2010	Evaluated fluorosis levels in single area
Niu 2012	Evaluated fluorosis with regard to improvement in water supply
Pandey 2002	Evaluated fluorosis with regard to improvement in water supply
Pandey 2005	Evaluated fluorosis with regard to improvement in water supply
Pandey 2010	Evaluated fluorosis with regard to improvement in water supply
Peres 2006	Evaluated caries in a single time point cross-sectional study
Provart 1995	Evaluated caries in a single time point cross-sectional study
Rihs 2008	Evaluated caries in a single time point cross-sectional study

Study	Reason for exclusion
Riley 1999	Evaluated caries in a single time point cross-sectional study
Ruan 2004	Evaluated fluorosis with regard to improvement in water supply
Rugg-Gun 1977	Evaluated caries in a single time point cross-sectional study
Sagheri 2007	Evaluated caries in a single time point cross-sectional study
Sales-Peres 2002	Evaluated caries in a single time point cross-sectional study
Saliba 2008	Evaluated caries in a single time point cross-sectional study
Sampaio 2000	Evaluated caries in a single time point cross-sectional study
Seppa 1998	Inappropriate design for studying cessation of water fluoridation
Shitumbanuma 2007	Evaluated fluorosis levels associated with drinking water from hot springs
Slade 2013	Evaluated caries in a cross-sectional study; no fluorosis data
Sohu 2007	No clear comparison of fluorosis across different fluoride concentrations
Spencer 2008	Mixed fluoridation status of study areas
Sun 2007	Evaluated fluorosis with regard to improvement in water supply
Tagliaferro 2004	Evaluated caries in a single time point cross-sectional study
Tiano 2009	Evaluated caries in a single time point cross-sectional study
Tickle 2003	Evaluated caries in a single time point cross-sectional study
Vuhahula 2008	Evaluated fluorosis with regard to improvement in water supply
Wang 2005	Evaluated fluorosis with regard to improvement in water supply
Wang 2008	Evaluated fluorosis with regard to improvement in water supply
Wei 2010	Evaluated fluorosis with regard to improvement in water supply
Wong 2006	No concurrent control
Wong 2014	Evaluated fluorosis but no concurrent comparison groups
Wongdem 2001	Focus on measurement of fluoride concentration
Wragg 1999	Inappropriate design for studying cessation of water fluoridation
Wu 2006	Evaluated fluorosis with regard to improvement in water supply
Wu 2008	Evaluated fluorosis with regard to improvement in water supply
Zhu 2009	Evaluated fluorosis with regard to improvement in water supply
Zietsman 2003	Thesis – unable to access

Study	Reason for exclusion
Zimmermann 2002	Evaluated caries in a single time point cross-sectional study

Characteristics of studies awaiting assessment *[ordered by study ID]*

Wang 2014

Methods	
Participants	
Interventions	
Outcomes	
Notes	We are in the process of attempting to access this study report

Characteristics of ongoing studies *[ordered by study ID]*

Pretty (ongoing)

Trial name or title	An evaluation of a water fluoridation scheme in Cumbria
Methods	Cohort The study design aims to assess the topical effects of water fluoridation by recruiting groups of children and following them over 6 years
Participants	All children in their first school year in 2013
Interventions	Re-introduction of fluoridated water compared with non-fluoridated area
Outcomes	Caries Age at assessment: 5, 7 and 11 years
Starting date	2013
Contact information	michaela.goodwin@manchester.ac.uk
Notes	

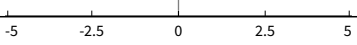
DATA AND ANALYSES

Comparison 1. Initiation of water fluoridation compared with low/non-fluoridated water

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in decayed, missing or filled deciduous teeth (dmft)	9	22134	Mean Difference (IV, Random, 95% CI)	1.81 [1.31, 2.31]
1.1 Studies conducted in 1975 or earlier	7	17039	Mean Difference (IV, Random, 95% CI)	1.82 [1.53, 2.11]
1.2 Studies conducted after 1975	2	5095	Mean Difference (IV, Random, 95% CI)	1.56 [-0.67, 3.80]
2 Change in decayed, missing or filled permanent teeth (DMFT)	10	39382	Mean Difference (IV, Random, 95% CI)	1.16 [0.72, 1.61]
2.1 Studies conducted in 1975 or earlier	7	30499	Mean Difference (IV, Random, 95% CI)	1.41 [0.84, 1.98]
2.2 Studies conducted after 1975	3	8883	Mean Difference (IV, Random, 95% CI)	0.64 [-0.27, 1.55]
3 Change in proportion of caries free children (deciduous teeth)	10	19983	Mean Difference (IV, Random, 95% CI)	-0.15 [-0.19, -0.11]
3.1 Studies conducted in 1975 or earlier	7	11902	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.19, -0.15]
3.2 Studies conducted after 1975	3	8081	Mean Difference (IV, Random, 95% CI)	-0.12 [-0.24, -0.01]
4 Change in proportion of caries free children (permanent teeth)	8	26769	Mean Difference (IV, Random, 95% CI)	-0.14 [-0.23, -0.05]
4.1 Studies conducted in 1975 or earlier	6	17459	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.24, -0.03]
4.2 Studies conducted after 1975	2	9310	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.43, 0.10]

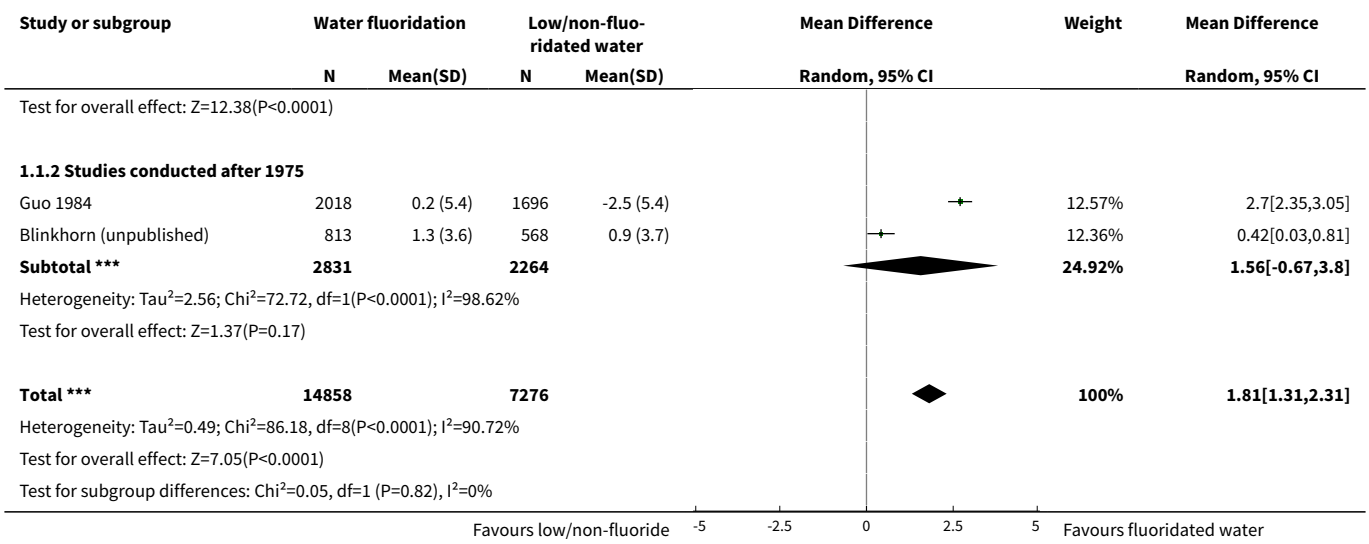
Analysis 1.1. Comparison 1 Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 1 Change in decayed, missing or filled deciduous teeth (dmft).

Study or subgroup	Water fluoridation N	Water fluoridation Mean(SD)	Low/non-fluoridated water N	Low/non-fluoridated water Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Studies conducted in 1975 or earlier							
Arnold 1956	4931	2.8 (5)	1437	1.2 (5.8)		12.63%	1.57[1.24,1.9]
Adriasola 1959	263	2.5 (7)	157	0.3 (6.7)		6.79%	2.2[0.85,3.55]
DHSS Wales 1969	1910	2.9 (4.7)	959	0.6 (5.5)		12.28%	2.23[1.82,2.64]
DHSS England 1969	654	3.1 (4.3)	557	1 (4.2)		11.91%	2.05[1.57,2.53]
Beal 1971	182	2.5 (5.8)	223	-0.1 (6.3)		7.71%	2.58[1.4,3.76]
Kunzel 1997	3726	1.7 (4.1)	1312	0.1 (5)		12.76%	1.52[1.22,1.82]
Beal 1981	361	2 (4.2)	367	0.6 (4.6)		11%	1.45[0.81,2.09]
Subtotal ***	**12027**		**5012**			**75.08%**	**1.82[1.53,2.11]**
Heterogeneity: Tau²=0.07; Chi²=13.37, df=6(P=0.04); I²=55.12%							

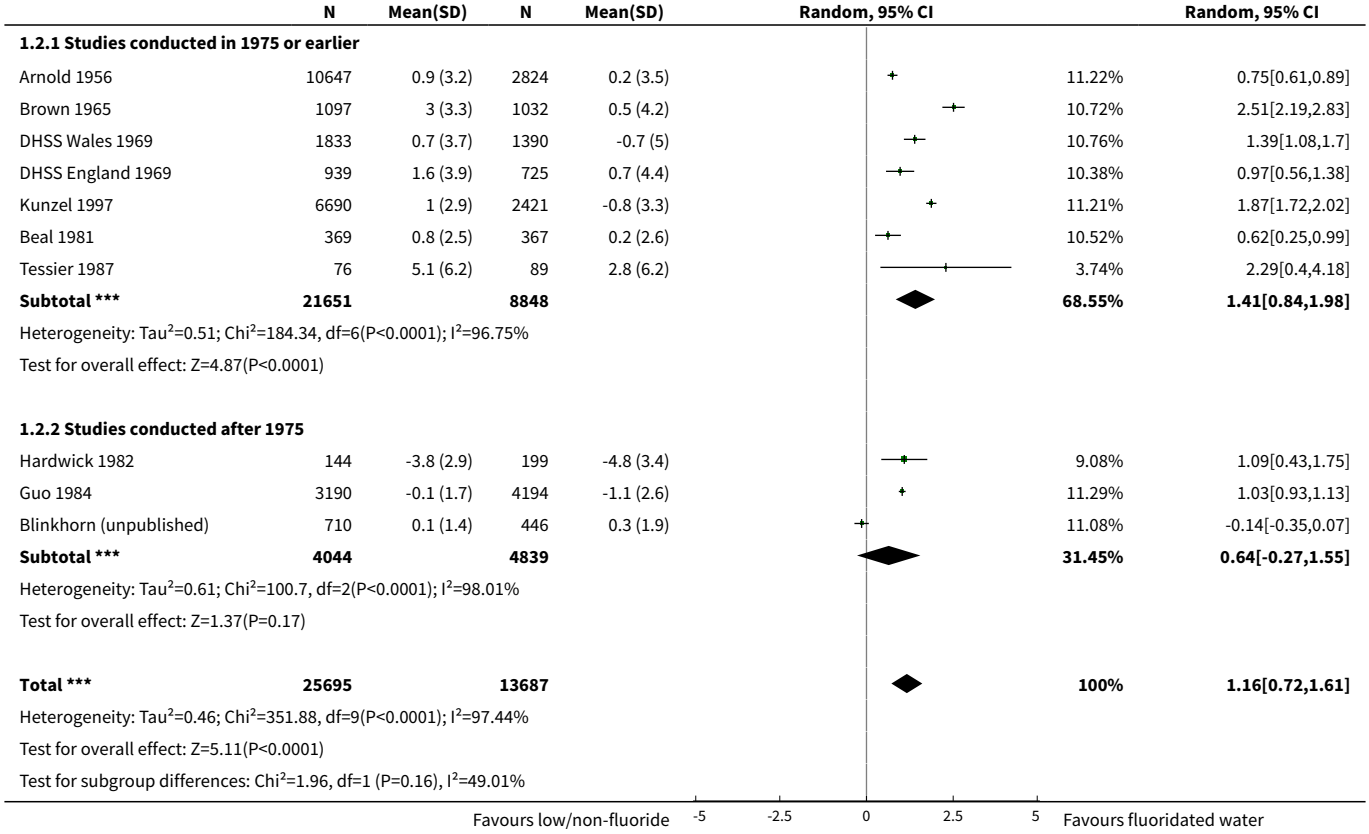


Favours low/non-fluoride

Favours fluoridated water

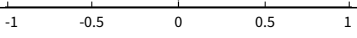


Analysis 1.2. Comparison 1 Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 2 Change in decayed, missing or filled permanent teeth (DMFT).



Analysis 1.3. Comparison 1 Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 3 Change in proportion of caries free children (deciduous teeth).

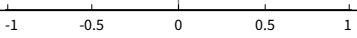
Study or subgroup	Water fluoridation N	Water fluoridation Mean(SD)	Low/non-fluoridated water N	Low/non-fluoridated water Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.3.1 Studies conducted in 1975 or earlier							
Ast 1951	246	-0.3 (0.6)	292	-0 (0.6)		7.24%	-0.22[-0.33,-0.11]
Adriasola 1959	633	-0.2 (1.2)	356	-0 (0.4)		7.64%	-0.12[-0.22,-0.02]
DHSS Wales 1969	1910	-0.2 (0.7)	959	-0 (0.5)		11.96%	-0.19[-0.23,-0.15]
DHSS England 1969	654	-0.3 (0.7)	557	-0.1 (0.5)		10.33%	-0.16[-0.22,-0.1]
Beal 1971	306	-0.2 (0.6)	223	-0.1 (0.5)		7.7%	-0.15[-0.25,-0.05]
Kunzel 1997	3726	-0.2 (0.3)	1312	-0 (0.4)		13.13%	-0.17[-0.19,-0.15]
Beal 1981	361	-0.2 (0.6)	367	-0.1 (0.5)		9.1%	-0.11[-0.19,-0.03]
Subtotal ***	**7836**		**4066**			**67.1%**	**-0.17[-0.19,-0.15]**
Heterogeneity: Tau^2=0; Chi^2=5.06, df=6(P=0.54); I^2=0%							
Test for overall effect: Z=18.89(P<0.0001)							
1.3.2 Studies conducted after 1975							
Guo 1984	2068	-0 (0.5)	1696	0.1 (0.4)		12.84%	-0.07[-0.1,-0.04]
Gray 2001	2493	-0.2 (0.5)	443	0.1 (0.6)		10.39%	-0.25[-0.31,-0.19]
Blinkhorn (unpublished)	813	-0.2 (0.7)	568	-0.2 (0.7)		9.67%	-0.05[-0.12,0.02]
Subtotal ***	**5374**		**2707**			**32.9%**	**-0.12[-0.24,-0.01]**
Heterogeneity: Tau^2=0.01; Chi^2=27.58, df=2(P<0.0001); I^2=92.75%							
Test for overall effect: Z=2.1(P=0.04)							
Total ***	**13210**		**6773**			**100%**	**-0.15[-0.19,-0.11]**
Heterogeneity: Tau^2=0; Chi^2=56.44, df=9(P<0.0001); I^2=84.05%							
Test for overall effect: Z=6.95(P<0.0001)							
Test for subgroup differences: Chi^2=0.62, df=1 (P=0.43), I^2=0%							



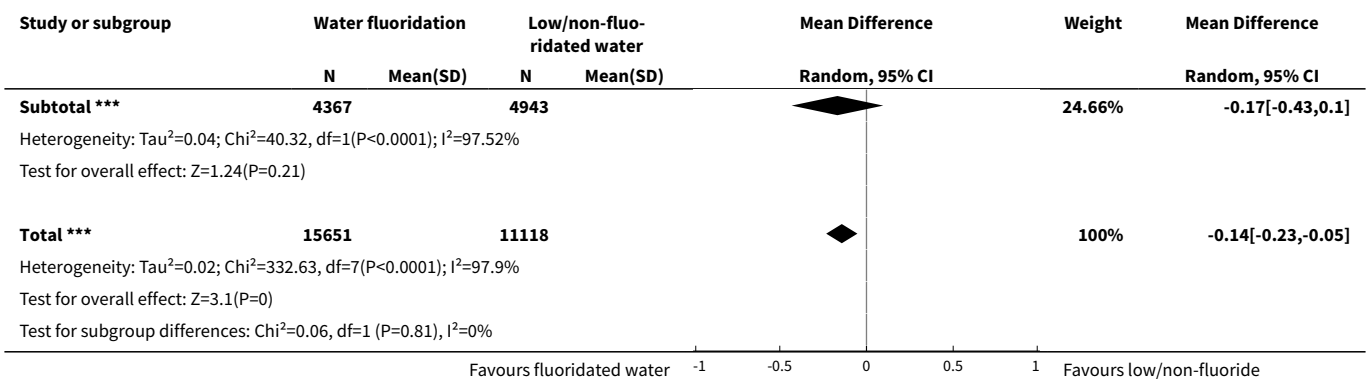
Favours fluoridated water — Favours low/non-fluoride

Analysis 1.4. Comparison 1 Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 4 Change in proportion of caries free children (permanent teeth).

Study or subgroup	Water fluoridation N	Water fluoridation Mean(SD)	Low/non-fluoridated water N	Low/non-fluoridated water Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.4.1 Studies conducted in 1975 or earlier							
Adriasola 1959	356	0 (0.2)	204	-0 (0.2)		12.73%	0.03[-0.01,0.07]
Brown 1965	1097	-0.3 (0.5)	1032	-0 (0.3)		12.73%	-0.26[-0.3,-0.22]
DHSS Wales 1969	1833	-0.1 (0.7)	1390	0.1 (0.4)		12.73%	-0.13[-0.17,-0.09]
DHSS England 1969	939	-0.2 (0.5)	761	-0.1 (0.4)		12.63%	-0.09[-0.13,-0.05]
Kunzel 1997	6690	-0.2 (0.4)	2421	0.1 (0.5)		12.89%	-0.28[-0.3,-0.26]
Beal 1981	369	-0.1 (0.7)	367	-0 (0.5)		11.62%	-0.06[-0.15,0.03]
Subtotal ***	**11284**		**6175**			**75.34%**	**-0.13[-0.24,-0.03]**
Heterogeneity: Tau^2=0.02; Chi^2=258.15, df=5(P<0.0001); I^2=98.06%							
Test for overall effect: Z=2.43(P=0.02)							
1.4.2 Studies conducted after 1975							
Guo 1984	3657	0.1 (0.6)	4497	0.4 (0.7)		12.83%	-0.3[-0.33,-0.27]
Blinkhorn (unpublished)	710	-0.1 (0.6)	446	-0 (0.7)		11.83%	-0.03[-0.11,0.05]



Favours fluoridated water — Favours low/non-fluoride



ADDITIONAL TABLES

Table 1. dmft data and underlying calculations *(Continued)*

Study ID	Age	Fluoridated area						Non/low fluoridated area					
		Baseline (before/at initiation)			Follow-up			Baseline			Follow-up		
		MEAN	SD	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	N
ADRIASOLA 1959	5	8.9	5.03	186	6.4	4.18	340	8.1	4.77	174	7.8	4.67	140
	5	**Mean (SD) change in dmft: 2.5 (7.04)**						**Mean (SD) change in dmft: 0.3 (6.72)**					
ARNOLD 1956[a]	4	4.19	3.30	323	2.13	2.26	168	5.05	3.66	20	4.46	3.42	63
	5	5.37	3.79	1633	2.27	2.34	853	6.82	4.33	402	5.25	3.74	351
	6	6.43	4.19	1789	2.98	2.73	750	7.17	4.46	462	5.67	3.91	294
	7	6.29	4.14	1806	4.03	3.23	423	6.66	4.28	408	5.77	3.95	223
	8	5.78	3.95	1647	4.12	3.27	470	6.06	4.06	376	5.32	3.77	275
	4-8	**Mean (SD) change in dmft: 2.75 (4.99)**						**Mean (SD) change in dmft: 1.18 (5.8)**					
BEAL 1971	5	4.91	4.86	182	2.45	3.24	182	4.97	4.12	217	5.09	4.84	229
	5	**Mean (SD) change in dmft: 2.46 (5.8)**						**Mean (SD) change in dmft: -0.12 (6.27)**					
BEAL 1981	5	4.29	3.50	196	1.8	2.48	170	4.28	3.58	205	3.49	3.62	180
	8	5	2.89	189	3.42	2.84	167	5.36	3.06	163	4.97	3.00	186
	5/8	**Mean (SD) change in dmft: 2.02 (4.18)**						**Mean (SD) change in dmft: 0.57 (4.6)**					
BLINKHORN 2015	5-7	2.02	3.13	781	0.72	1.63	844	2.09	2.91	523	1.21	2.27	612
	5-7	**Mean (SD) change in dmft: 1.3 (3.56)**						**Mean (SD) change in dmft: 0.88 (3.74)**					
DHSS 1969 (Eng)[a]	3	2.7	2.58	43	0.6	1.11	133	1.4	1.79	44	1.2	1.64	144
	4	3.6	3.03	66	1.3	1.71	131	2.6	2.53	47	1.8	2.06	162

Table 1. dmft data and underlying calculations *(Continued)*

	5	5.4	3.80	148	1.6	1.92	111	5	3.64	110	2.8	2.63	119
	6	5.7	3.92	182	2.5	2.47	130	5.4	3.80	127	4.1	3.26	107
	7	6.4	4.18	192	2.7	2.58	172	6	4.03	121	4.3	3.35	133
	3-7	**Mean (SD) change in dmft: 3.09 (4.3)**						**Mean (SD) change in dmft: 1.04 (4.22)**					
DHSS 1969 (Wales)[a,b]	3	3.9	3.17	310	1.4	1.79	171	4	3.21	146	3.3	2.89	105
	4	5.54	3.86	413	2.6	2.53	267	5.8	3.96	210	4.8	3.56	122
	5	5.5	3.84	556	2.9	2.69	284	5.5	3.84	256	4.8	3.56	138
	6	6.3	4.15	603	3.1	2.79	310	6.2	4.11	331	5.9	4.00	133
	7	6.85	4.35	640	3.65	3.05	266	7.3	4.50	346	6.8	4.33	130
	3-7	**Mean (SD) change in dmft: 2.87 (4.68)**						**Mean (SD) change in dmft: 0.64 (5.54)**					
GUO 1984	3	3	3.4	202	2.6	3.3	79	1.3	3.2	205	3.7	3.9	128
	4	4.6	4	354	4.5	4.7	164	5.6	4.6	246	7.1	4.6	164
	5	6.5	4.4	589	5.5	4.3	345	6.4	4.2	218	8.5	4.6	387
	6	6.7	4.4	695	6.2	4.8	297	5.8	4.2	309	9	4.3	354
	7	5.5	3.7	399	5.6	3.7	240	5.4	3.7	335	7.9	3.6	352
	8	4.2	3	392	4.4	2.9	279	3.5	2.7	343	6	3.1	350
	3-8	**Mean (SD) change in dmft: 0.23 (5.39)**						**Mean (SD) change in dmft: -2.47 (5.35)**					
KUNZEL 1992[a]	5	2.4	2.415006452	688	1.4	1.7857954	1306	3.3	2.886475039	172	2.9	2.684991275	597
	8	4.9	3.601718817	2438	2.8	2.632743187	3020	4.9	3.601718817	777	4.9	3.601718817	1078
	5-8	**Mean (SD) change in dmft: 2.1 (5.01)**						**Mean (SD) change in dmft: 0.13 (5.0)**					

Note: Only data up to the age of 8 years included for the deciduous dentition
a. Imputed standard deviation

b. 2 fluoridated areas combined

Table 2. DMFT data and underlying calculations *(Continued)*

Study ID	Age	FLuoridated area						Non/low fluoridated area					
		Baseline (before/at initiation)			Follow-up			Baseline			Follow-up		
		MEAN	SD	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	N
ARNOLD 1956[a]	6	0.78	1.29	1789	0.26	0.70	750	0.81	1.31	462	0.8	1.31	294
	7	1.89	2.11	1806	0.84	1.34	423	1.99	2.17	408	1.88	2.11	223
	8	2.95	2.71	1647	1.58	1.91	470	2.81	2.64	376	2.63	2.54	275
	9	3.9	3.17	1639	2.04	2.21	582	3.81	3.13	357	3.52	2.99	277
	10	4.92	3.61	1626	2.93	2.70	141	4.91	3.61	359	4.32	3.36	62
	11	6.41	4.19	1556	3.67	3.06	151	6.32	4.15	293	5.34	3.78	139
	12	8.07	4.76	1685	5.89	3.99	176	8.66	4.95	328	7.71	4.64	48
	13	9.73	5.29	1668	6.6	4.26	497	9.98	5.36	377	9.36	5.18	225
	14	10.95	5.65	1690	8.21	4.81	128	12	5.95	369	11.36	5.77	59
	15	12.48	6.08	1511	8.91	5.03	53	12.86	6.18	292	12.38	6.05	21
	16	13.5	6.35	1107	11.06	5.68	198	14.07	6.50	248	13.16	6.26	155
	6-16	**Mean (SD) change in DMFT: 0.90 (3.20)**						**Mean (SD) change in DMFT: 0.15 (3.51)**					
BEAL 1981	8	1.48	1.51	189	0.65	1.16	167	1.55	1.40	163	1.34	1.50	186
	12	3.53	3.32	192	2.74	2.33	189	4.28	2.47	188	4.11	2.95	197
	8/12	**Mean (SD) change in DMFT: 0.82 (2.50)**						**Mean (SD) change in DMFT: 0.20 (2.64)**					
BLINKHORN 2015[a]		0.59	1.10	777	0.45	0.95	642	0.99	1.47	436	0.72	1.23	455

Table 2. DMFT data and underlying calculations *(Continued)*

		Mean (SD) change in DMFT: 0.14 (1.44)						**Mean (SD) change in DMFT: 0.28 (1.92)**					
BROWN 1960	9-11	4.07	2.20	595	1.52	1.80	502	4.21	2.63	571	3.68	2.35	521
	12-14	7.68	3.90	593	3.23	2.92	503	7.94	4.41	486	7.46	4.40	485
	9-14	**Mean (SD) change in DMFT: 3.03 (3.31)**						**Mean (SD) change in DMFT: 0.52 (4.18)**					
DHSS 1969 (Eng)[a]	8	2.4	2.42	199	1.08	1.54	95	2.4	2.42	148	1.85	2.09	79
	9	3.1	2.79	227	1.5	1.86	135	2.9	2.68	166	2.4	2.42	95
	10	3.6	3.03	134	2	2.18	115	3.8	3.12	160	3.1	2.79	80
	11	4.6	3.48	145	3	2.74	200	4.7	3.52	126	3.9	3.17	122
	12	5.6	3.88	111	3.52	2.99	134	6.1	4.07	51	4.99	3.64	99
	13	7.1	4.43	91	4.9	3.60	132	6.6	4.26	52	6.1	4.07	127
	14	8.4	4.87	70	5.77	3.95	90	7.9	4.71	36	6.74	4.31	108
	8-14	**Mean (SD) change in DMFT: 1.62 (3.92)**						**Mean (SD) change in DMFT: 0.65 (4.39)**					
DHSS 1969 (Wales)[agb]	8	2.00	2.18	607	1.31	1.72	283	1.95	2.15	351	2.16	2.28	125
	9	2.65	2.55	553	1.98	2.17	260	2.6	2.53	325	2.9	2.68	134
	10	3.35	2.91	502	2.59	2.52	241	3.2	2.84	308	3.6	3.03	133
	11	3.83	3.14	278	2.99	2.73	126	3.3	2.89	270	4.1	3.26	42
	12	4.65	3.50	186	4.38	3.38	108	3.95	3.19	265	6.16	4.09	108
	13	6	4.03	178	5.9	4.00	93	5.2	3.72	274	7.6	4.61	105
	14	6.95	4.38	158	6.73	4.30	93	5.6	3.88	243	7.64	4.62	96
	8-14	**Mean (SD) change in DMFT: 0.66 (3.72)**						**Mean (SD) change in DMFT: -0.73 (4.95)**					
GUO 1984	6	0.2	0.6	695	0.2	0.5	297	0.1	0.4	309	0.5	0.9	354

Table 2. DMFT data and underlying calculations *(Continued)*

	7	0.4	0.8	399	0.4	0.9	240	0.3	0.7	335	1.2	1.4	352
	8	0.5	1	392	0.5	1	279	0.4	0.8	343	1.6	1.5	350
	9	0.7	1.1	388	0.8	1.4	275	0.7	1.1	310	2.2	2	352
	10	0.7	1.3	346	1.1	1.5	310	0.8	1.5	323	2.4	2	436
	11	0.8	1.5	330	1.6	1.9	307	0.9	1.4	451	3	2.7	365
	12	1.1	1.7	468	1.7	2.4	208	0.9	1.5	841	3.4	3	493
	13	1.4	2	469	2.1	2.9	232	1.2	1.6	801	3.8	3.3	504
	14	1.2	1.8	322	2.6	2.9	221	1	1.5	795	4.4	3.8	490
	15	1.7	2.5	164	2.2	2.3	38	1.2	1.7	121	4.2	4	63
	6-15	**Mean (SD) change in DMFT: -0.11 (1.69)**						**Mean (SD) change in DMFT: -1.14 (2.59)**					
HARDWICK 1982	**12**	**Mean (SD) increment in DMFT: -3.76 (2.86)**						**Mean (SD) increment in DMFT: -4.85 (3.39)**					
KUNZEL 1997[c,d]	6	0.3	0.7		0.2			0.5	0.8		0.4	0.89	
	7	0.7	1.1		0.3			0.9	1.2		1	1.48	
	8	1.3	1.4	2419	0.5	1.00	3016	1.3	1.4	777	1.8	2.06	1076
	9	1.9	1.5		0.9			1.8	1.6		2.4	2.42	
	10	2.4	1.8		1.2			2.4	1.8		3.2	2.84	
	11	3	2		1.6			2.8	1.8		3.9	3.17	
	12	3.7	2.3	1626	2	2.18	2426	3.5	2.1	563	4.8	3.56	925
	13	4.3	2.7		2.6			4.1	2.6		5.5	3.84	
	14	5.3	3.1		3.4			4.7	2.5		6.5	4.22	

Table 2. DMFT data and underlying calculations *(Continued)*

	15	5.8	3.5	1995	4	3.22	1897	5.2	3.1	744	7.4	4.54	756
	8/12/15	**Mean (SD) change in DMFT: 1.02 (2.94)**						**Mean (SD) change in DMFT: -0.85 (3.26)**					
LOH 1996		1.6	1.8		2			1.9			3.1		
		4.4			2.1			3.7			4.5		
	Insufficient data to include in further analysis												
TESSIER 1987[a]	6-7	8.28		56	3.16		96	8.23		85	5.4		93
	6-7	**Mean (SD) change in DMFT: 5.12 (6.16)**						**Mean (SD) change in DMFT: 2.83 (6.18)**					

a. Imputed standard deviation
b. 2 fluoridated areas combined
c. Imputed standard deviation for follow-up data only
d. N values only available for ages 8, 12 and 15 years

Table 3. Number of caries-free children: deciduous teeth *(Continued)*

Study ID	Age	Fluoridated area				Non/low fluoridated area			
		Baseline (before/at initiation)		Follow-up		Baseline		Follow-up	
		n	N	n	N	n	N	n	N
Adriasola 1959[a]	3	26	151	82	216	9	77	26	135
	4	12	156	55	216	11	76	11	110
	5	4	186	45	340	7	174	14	140
	8	21	493	11	458	17	223	2	226
Ast 1951	5	63	274	108	217	73	259	107	324
Beal 1971[b]	5	62	297	138	314	35	217	55	229
Beal 1981	5	41	196	78	170	43	205	54	180

Table 3. Number of caries-free children: deciduous teeth *(Continued)*

	8	18	189	31	167	12	163	18	186
Blinkhorn 2015	5-7	397	781	632	844	254	523	412	612
DHSS 1969 (Eng)	3	16	43	96	133	27	44	97	144
	4	23	66	84	131	16	47	89	162
	5	12	148	51	111	15	110	42	119
	6	16	182	47	130	13	127	18	107
	7	13	192	55	172	7	121	24	133
DHSS 1969 (Wales)	3	89	310	100	171	39	146	21	105
	4	78	413	114	267	32	210	27	122
	5	56	556	90	284	18	256	19	138
	6	29	603	78	310	20	331	15	133
	7	17	640	53	266	14	346	5	130
Gray 2001[b]	5	1465	2462	1903	2524	345	466	273	419
Guo 1984	3	67	202	31	79	54	205	39	128
	4	74	354	39	164	32	246	14	164
	5	61	589	47	345	18	218	19	387
	6	53	695	56	397	27	309	12	354
	7	41	399	21	240	29	335	11	352
	8	53	392	24	279	50	343	16	350
	8	278	392	204	279	273	343	104	350
Kunzel 1997	5	231	688	682	1306	39	172	192	597

Table 3. Number of caries-free children: deciduous teeth *(Continued)*

	8	117	2438	746	3020	40	777	61	1078

Note: Only data up to the age of 8 years included for the deciduous dentition
a. Baseline data not available for ages 6 and 7 years
b. Data from all fluoridated areas combined

Table 4. Number of caries-free children: permanent teeth *(Continued)*

Study ID	Age	Fluoridated area				Non/low fluoridated area			
		Baseline (before/at initiation)		Follow-up		Baseline		Follow-up	
		n	N	n	N	n	N	n	N
ADRIASOLA 1959[a]	8	21	493	11	458	17	223	2	226
	12	7	292	8	419	3	197	9	211
BEAL 1981	8	77	189	115	167	56	163	82	186
	12	51	192	41	189	13	188	14	197
BLINKHORN 2015	10 to 12	525	777	486	642	272	436	307	455
BROWN 1960[b]	9 to 11	34	595	220	502	35	571	42	521
	12 to 14	7	593	94	503	3	486	11	485
DHSS 1969 (Eng)	8	40	199	50	95	33	148	29	79
	9	25	227	57	135	20	166	20	95
	10	13	134	36	115	14	160	10	80
	11	12	145	12	200	3	126	12	122
	12	3	111	20	134	0	51	4	99

Table 4. Number of caries-free children: permanent teeth *(Continued)*

	13	3	91	9	132	2	52	8	127
	14	0	70	4	90	2	36	9	180
DHSS 1969 (Wales)	8	143	607	112	283	88	351	26	125
	9	73	553	78	260	49	325	15	134
	10	63	502	44	241	25	308	8	133
	11	30	278	15	126	35	270	0	42
	12	15	186	10	108	27	265	2	108
	13	7	178	0	93	14	274	1	105
	14	8	158	3	93	15	243	1	96
Guo 1984	5	575	589	338	345	214	218	358	387
	6	616	695	266	297	284	309	249	354
	7	305	399	189	240	272	335	162	352
	8	278	392	204	279	273	343	104	350
	9	242	388	167	275	195	310	98	352
	10	215	346	161	310	199	323	84	436
	11	213	330	133	307	245	451	65	365
	12	240	468	90	208	475	841	91	493
	13	227	469	88	232	434	801	77	504
	14	161	322	69	221	455	795	73	490
	15	78	164	11	38	66	121	11	63
Kunzel 1997	8	1021	2419	2147	3016	334	777	333	1076

Table 4. Number of caries-free children: permanent teeth *(Continued)*

12	120	1626	801	2426	42	563	50	925
15	118	1995	249	1897	27	744	18	756

a. Baseline data not available for ages 11 and 15 years
b. Data for 16-17-year olds presented but no N

Table 5. Harms: other

Study ID	Outcome	Age	Fluoride level	Assigned F level	Number of subjects	Proportion with outcome
Chen 1993	Skeletal fluorosis	16 to 65	5.5	5.5	28	82.1
			3.1	3.1	114	71.1
			0.4	0.4	50	46
			3.1	3.1	50	86
Wang 2012[a]	Skeletal fluorosis	≥16	2.2	2.2	406,298	10.8
			0.5	0.5	188,400	4.8
Wenzel 1982[b]	Skeletal maturity	12 to 14	2.4	2.4	122	0.59 (0.1)[c]
			< 0.2	0.1	113	0.59 (0.09)[c]
Alarcon-Herrera	Bone fracture	6 to 12	< 1.5	0.75	97	5.2
			1.51-4.99	3.25	112	8.9
			5-8.49	6.75	38	2.6
			8.5-11.99	10.25	27	11.1
			12-16	14	59	8.5
		13 to 60	< 1.5	0.75	192	3.1
			1.51-4.99	3.25	330	7.9
			5-8.49	6.75	146	8.9
			8.5-11.99	10.25	138	7.2
			12-16	14	96	6.3
Jolly 1971[b]	Skeletal fluorosis	Not stated	0.7	0.7	Not stated	3.6
			1.4	1.4	Not stated	2.4
			2.4	2.4	Not stated	17
			2.4	2.4	Not stated	23
			2.5	2.5	Not stated	33
			3	3	Not stated	19.6
			3	3	Not stated	42.2
			3.3	3.3	Not stated	10

Table 5. Harms: other *(Continued)*

	3.3	3.3	Not stated	45
	3.6	3.6	Not stated	33.1
	4.3	4.3	Not stated	19.4
	5	5	Not stated	60
	5.1	5.1	Not stated	44.5
	5.5	5.5	Not stated	31.3
	7	7	Not stated	47.4
	8.5	8.5	Not stated	58.9
	9.4	9.4	Not stated	70.1

a. Participants were diagnosed on the basis of diagnostic criteria for endemic skeletal fluorosis (WS 192-2008)
b. Participants were examined radiologically
c. Reported outcome was mean (standard error) skeletal maturity

Table 6. Disparities in caries across social class *(Continued)*

Study ID	Age	Group	Measure	Social class	Baseline				Final			
					F level	N	% caries free	dmft (SD)	F level	N	% caries free	dmft (SD)
Beal 1971[a]	5	Balsall Heath	Descriptive	Poor area	Low	115	9	5.16 (0.44)	1	132	48	1.94 (0.22)
		Northfield		Industrial area	Low	182	29	4.91 (0.36)	1	182	41	2.45 (0.24)
		Dudley		Industrial area	< 0.1	217	16	4.97 (0.28)	< 0.1	229	24	5.09 (0.32)
Gray 2000[b]	5	South east Staffordshire	Jarman score	-23.09	Low	3435	66	1.21 (0.59)	1	3120	75	0.64 (1.46)
		Sandwell		18.1	Low	3950	51	1.93 (2.88)	1	3598	69	0.83 (1.68)
		Walsall		1.67	Low	3120	54	1.85 (2.31)	1	363	67	0.94 (1.77)
		Dudley		-13.68	Low	3657	58	1.6 (2.54)	1	3474	73	0.78 (1.75)
		North Birmingham		21.57	Low	1965	72	0.88 (1.97)	1	1904	74	0.71 (1.65)
		North Staffordshire		-3.59	Low	464	47	2.24 (3.04)	Low	1947	59	1.49 (2.46)
		Herefordshire		-13.01	Low	406	57	1.61 (2.55)	Low	305	50	1.79 (2.68)
		Shropshire		-12.34	Low	366	61	1.29 (2.22)	Low	311	60	1.33 (2.33)
		Kidderminster		-13.13	Low	904	58	1.74 (2.81)	Low	1053	61	1.4 (2.52)
Holdcroft 1999[b]	Not stated	North Birmingham	Jarman score	-7.85	Not stated	Not stated		2.18	High	Not stated		0.68
		Sandwell		15.03	Not stated	Not stated		2.55	High	Not stated		1.13
		North Staffordshire		-4.07	Not stated	Not stated		2.24	Not stated	Not stated		1.48

Table 6. Disparities in caries across social class *(Continued)*

Shropshire	-11.73	Not stated	Not stated	1.76	Not stated	Not stated	1.29
Herefordshire	-11.97	Not stated	Not stated	2.56	Not stated	Not stated	1.53

a. Caries data reported as deft (SE)
b. Caries data reported as dmft (SD)

Table 7. WHO region-specific weighted DMFT among 12-year olds *(Continued)*

WHO regions	DMFT
	2011
Africa	1.19
Americas	2.35
Eastern Mediteranean	1.63
Europe	1.95
South East Asia	1.87
Western Pacific	1.39
GLOBAL	**1.67**

http://www.mah.se/CAPP/Country-Oral-Health-Profiles/According-to-Alphabetical/Global-DMFT-for-12-year-olds-2011/

APPENDICES

Appendix 1. Databases searched in the original systematic review (McDonagh 2000)

- MEDLINE
- EMBASE
- NTIS (National Technical Information Service)
- Biosis
- Current Contents Search (Science Citation Index and Social Science Citation Index)
- Healthstar (Health Service Technology, Administration and Research)
- HSRProj
- TOXLINE
- Chemical Abstracts
- OldMEDLINE
- CAB Health
- FSTA (Food Science and Technology Abstracts)
- JICST- E Plus (Japanese Science and Technology)
- Pascal
- EI Compendex (Engineering Index)
- Enviroline
- PAIS (Public Affairs Information Services)
- SIGLE (System for Information on Grey Literature in Europe)
- Conference Papers Index
- Water Resources Abstracts
- Agricola (Agricultural Online Access)
- Waternet
- AMED (Allied and Complementary Medicine Database)
- Psyclit
- LILACS (Latin American and Caribbean Health Sciences Literature)

Appendix 2. The Cochrane Oral Health Group Trials Register search strategy

#1 ((fluorid* or flurid* or fluorin* or flurin*))
#2 water*
#3 (#1 and #2)

Appendix 3. The Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 MeSH descriptor Fluoridation this term only
#2 MeSH descriptor Fluorides explode all trees
#3 MeSH descriptor Fluorine this term only
#4 (fluorid* in All Text or fluorin* in All Text or flurin* in All Text or flurid* in All Text)
#5 (#1 or #2 or #3 or #4)
#6 MeSH descriptor Dietary supplements this term only
#7 MeSH descriptor Water supply this term only
#8 water* in All Text
#9 (#6 or #7 or #8)
#10 MeSH descriptor Tooth demineralization explode all trees
#11 (caries in All Text or carious in All Text)
#12 (teeth in All Text and (cavit* in All Text or caries in All Text or carious in All Text or decay* in All Text or lesion* in All Text or demineral* in All Text or remineral* in All Text))
#13 (tooth in All Text and (cavit* in All Text or caries in All Text or carious in All Text or decay* in All Text or lesion* in All Text or demineral* in All Text or remineral* in All Text))
#14 (dental in All Text and (cavit* in All Text or caries in All Text or carious in All Text or decay* in All Text or lesion* in All Text or demineral* in All Text or remineral* in All Text))
#15 (enamel in All Text and (cavit* in All Text or caries in All Text or carious in All Text or decay* in All Text or lesion* in All Text or demineral* in All Text or remineral* in All Text))
#16 (dentin in All Text and (cavit* in All Text or caries in All Text or carious in All Text or decay* in All Text or lesion* in All Text or demineral* in All Text or remineral* in All Text))
#17 (root* in All Text and (cavit* in All Text or caries in All Text or carious in All Text or decay* in All Text or lesion* in All Text or demineral* in All Text or remineral* in All Text))
#18 MeSH descriptor Dental plaque this term only
#19 ((teeth in All Text or tooth in All Text or dental in All Text or enamel in All Text or dentin in All Text) and plaque in All Text)
#20 MeSH descriptor Dental health surveys explode all trees
#21 ("DMF Index" in All Text or "Dental Plaque Index" in All Text)
#22 (#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #21) #23 (#5 and #9 and #22)

Appendix 4. MEDLINE (OVID) search strategy

1. Fluoridation/
2. exp Fluorides/
3. Fluorine/
4. (fluorid$ or fluorin$ or flurin$ or flurid$).mp.
5. or/1-4
6. Dietary supplements/
7. Water supply/
8. water$.mp.
9. or/6-8
10. exp TOOTH DEMINERALIZATION/
11. (caries or carious).mp.
12. (teeth adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
13. (tooth adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
14. (dental adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
15. (enamel adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
16. (dentin$ adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
17. (root$ adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.
18. Dental plaque/
19. ((teeth or tooth or dental or enamel or dentin) and plaque).mp.
20. exp DENTAL HEALTH SURVEYS/
21. ("DMF Index" or "Dental Plaque Index").mp.
22. or/10-21
23. case reports.pt.
24. Comment/
25. Letter/

26.Editorial/
27.or/23-26
28.exp animals/ not humans.sh.
29.5 and 9 and 22
30.29 not (28 or 27)

Appendix 5. EMBASE (OVID) search strategy

1. Fluoridation/
2. exp Fluoride/
3. Fluorine/
4. (fluorid$ or fluorin$ or flurin$ or flurid$).ti,ab.
5. or/1-4
6. Diet supplementation/
7. Water supply/
8. water$.ti,ab.
9. or/6-8
10. exp Dental caries/
11. (caries or carious).ti,ab.
12. (teeth adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).ti,ab.
13. (tooth adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).ti,ab.
14. (dental adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).ti,ab.
15. (enamel adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).ti,ab.
16. (dentin$ adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).ti,ab.
17. (root$ adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or demineral$ or remineral$)).ti,ab
18. Tooth plaque/
19. ((teeth or tooth or dental or enamel or dentin) and plaque).ti,ab.
20. ("DMF Index" or "Dental Plaque Index" or "dental health survey*").ti,ab.
21. or/10-20
22. 9 and 21
23. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
24. 22 not 23

Appendix 6. Proquest search strategy

ab(fluorid*) AND ab(water*) AND ab(caries OR carious OR dental OR tooth OR teeth OR plaque)

Appendix 7. Web of Science Conference Proceedings search strategy

#1 TS=(fluorid* or fluorin* or flurin* or flurid*)
#2 TS=water*
#3 TS=(caries or carious)
#4 TS=(teeth and (cavit* or caries* or carious or decay* or lesion* or demineral* or remineral*))
#5 TS=(tooth and (cavit* or caries* or carious or decay* or lesion* or demineral* or remineral*))
#6 TS=(dental and (cavit* or caries* or carious or decay* or lesion* or demineral* or remineral*))
#7 TS=(enamel and (cavit* or caries* or carious or decay* or lesion* or demineral* or remineral*))
#8 TS=(dentin* and (cavit* or caries* or carious or decay* or lesion* or demineral* or remineral*))
#9 TS=(root* and (cavit* or caries* or carious or decay* or lesion* or demineral* or remineral*))
#10 TS=((teeth or tooth or dental or enamel or dentin) and plaque)
#11 TS=("DMF Index" or "Dental Plaque Index")
#12 #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13 #1 and #2 and #12

Appendix 8. ZETOC Conference Proceedings search strategy

fluoride AND water AND caries
fluoridation AND water AND caries
fluoride AND water AND carious
fluoridation AND water AND carious
fluoride AND water AND dental
fluoridation AND water AND dental
fluoride AND water AND tooth
fluoridation AND water AND tooth

fluoride AND water AND teeth
fluoridation AND water AND teeth

Appendix 9. US National Institutes of Health Trials Registry and WHO International Clinical Trials Registry Platform search strategy

fluoride and water and caries

Appendix 10. Imputation of standard deviations for caries data

Where standard deviations are missing for the DMFT, dmft data we used the equation: log(SD) = 0.17 + 0.56 x log(mean) to estimate the standard deviations for both before and after mean caries values. A sensitivity analysis was undertaken omitting all the data for studies/age groups where the standard deviation was imputed.

The equation we used was obtained from the data we had available to us from the other included studies in the review (102 mean and standard deviation data points). The equation had a similar regression coefficient to those developed by van Rijkom 1996 and Marinho 2003b shown below, although the intercept was smaller. This is probably because both these models had been developed on caries increments whereas the data we have used is cross-sectional caries severity data.

Equation from:

van Rijkom 1996 log(SD) = 0.54 + 0.58 x log(mean), (R^2 = 0.83)

Marinho 2003b log(SD) = 0.64 + 0.55 x log(mean), (R^2 = 0.77)

This review log(SD) = 0.17 + 0.55 x log(mean), (R^2 = 0.90)

Appendix 11. Fluorosis studies

Studies included in the analysis of all level of fluorosis:

Acharya 2005; Adair 1999; Al-Alousi 1975; Alarcon-Herrera 2001; Albrecht 2004; AlDosari 2010; Angelillo 1999; Arif 2013; Azcurra 1995; Beltran-Aguilar 2002; Booth 1991; Brothwell 1999; Chandrashekar 2004; Chen 1989; Chen 1993; Clark 1993; Clarkson 1989; Cochran 2004a; Correia Sampaio 1999; Cutress 1985; Driscoll 1983; Ekanayake 2002; Eklund 1987; Ellwood 1995; Ellwood 1996; Firempong 2013; Forrest 1965; Garcia-Perez 2013; Gaspar 1995; Grimaldo 1995; Grobler 1986; Grobler 2001; Haavikko 1974; Heintze 1998; Heller 1997; Hernandez-Montoya 2003; Hong 1990; Ibrahim 1995; Indermitte 2007; Indermitte 2009; Ismail 1990; Jackson 1975; Jackson 1999; Kanagaratnam 2009; Kotecha 2012; Kumar 2007; Kunzel 1976; Leverett 1986; Levine 1989; Lin 1991; Louw 2002; Machiulskiene 2009; Mackay 2005; Macpherson 2007; Mandinic 2009; Marya 2010; Masztalerz 1990; McGrady 2012; McInnes 1982; Mella 1992; Mella 1994; Milsom 1990; Montero 2007; Nanda 1974; Narbutaite 2007; Narwaria 2013; Nunn 1994a; Ockerse 1941; Pontigo-Loyola 2008; Ray 1982; Riordan 1991; Riordan 2002; Rwenyonyi 1998; Rwenyonyi 1999; Saravanan 2008; Sellman 1957; Shekar 2012; Stephen 2002; Szpunar 1988; Tabari 2000; Tsutsui 2000; Wang 1993; Wang 1999; Wang 2012; Warnakulasuriya 1992; Warren 2001; Wenzel 1982; Wondwossen 2004; Zheng 1986; Zimmermann 1954

Studies included in the analysis of fluorosis of aesthetic concern:

Acharya 2005; Alarcon-Herrera 2001; AlDosari 2010; Angelillo 1999; Arif 2013; Beltran-Aguilar 2002; Chen 1989; Clark 1993; Correia Sampaio 1999; Driscoll 1983; Eklund 1987; Forrest 1965; Gaspar 1995; Grimaldo 1995; Grobler 1986; Grobler 2001; Haavikko 1974; Heller 1997; Hernandez-Montoya 2003; Hong 1990; Ibrahim 1995; Jackson 1999; Kunzel 1976; Leverett 1986; Louw 2002; Macpherson 2007; McGrady 2012; Mella 1992; Mella 1994; Montero 2007; Nanda 1974; Pontigo-Loyola 2008; Ray 1982; Riordan 1991; Riordan 2002; Ruan 2005; Russell 1951; Sellman 1957; Stephen 2002; Tabari 2000; Zheng 1986; Zimmermann 1954

Studies that could not be included in analysis:

Awadia 2000; Bao 2007; Baskaradoss 2008; Birkeland 2005; Butler 1985; Chen 1993; Clarkson 1992; Colquhoun 1984; Cypriano 2003; de Crousaz 1982; Downer 1994; Driscoll 1983; Ermis 2003; Forrest 1956; Franzolin 2008; Harding 2005; Heifetz 1988; Jolly 1971; Kumar 1999; Mandinic 2010; Mazzotti 1939; Rugg-Gunn 1997; Scheinin 1964; Segreto 1984; Selwitz 1995; Selwitz 1998; Shanthi 2014; Skinner 2013; Skotowski 1995; Spadaro 1955; Sudhir 2009; Venkateswarlu 1952; Vilasrao 2014; Villa 1998; Vignarajah 1993; Vuhahula 2009; Whelton 2004; Whelton 2006

WHAT'S NEW

Date	Event	Description
7 September 2015	Amended	Plain Language Summary amended for simplification.

HISTORY

Protocol first published: Issue 12, 2013
Review first published: Issue 6, 2015

Date	Event	Description
19 June 2015	Amended	Minor edit to Plain Language Summary for clarification. Missing referee name added to Acknowledgements.
2 February 2015	Amended	Background updated to justify the need for the review. Change to risk of bias domains, incorporating an item on 'sampling' Change to the handling of missing data; imputation of missing standard deviations for DMFT and dmft data

CONTRIBUTIONS OF AUTHORS

All authors contributed equally to the writing of the protocol in the published format. Authors contributed at different stages of the review process:

- Co-ordinating the review (ZIE, AMG)
- Data collection for the review (RA, ZIE, AMG, LO'M, TW, HW)
- Data management for the review (ZIE, AMG, LO'M, TW, HW)
- Analysis of data (AMG, HW, TW)
- Interpretation of data (JC, ZIE, AMG, LO'M, TW, HW)
- Writing the review (JC, ZIE, AMG, TW, HW)
- Providing general advice on the review (PT, VW)
- Performing previous work that was the foundation of the current review (RA, ZIE, AMG, RM, LO'M, PT, TW, HW, VW)

DECLARATIONS OF INTEREST

Authors on this review have also been involved in the evaluation of the evidence using different methodology for the CDC Task Force Recommendation on Water Fluoridation

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- Types of studies: additional clarification on difference between initiation and cessation studies added; the fact that randomised controlled trials are unfeasible is highlighted.
- Types of outcome measures: added sentence regarding disparities in dental caries across different groups of people. Changed 'fluorosis' to 'dental fluorosis'. Defined what is meant by adverse effects. Highlighted the fact that this review did not aim to provide a comprehensive systematic review of adverse effects other than dental fluorosis.
- Search methods for identification of studies: additional sources added,
- Assessment of risk of bias in included studies: 'sampling' was assessed while 'sequence generation' and 'allocation concealment' were not assessed.
- Measures of treatment effect: dmft and DMFT analyses calculated the difference in mean change scores between fluoridated and control groups. For the proportion caries free we calculated the difference in the proportion caries free between the fluoridated and control groups. For dental fluorosis data we calculated the log odds and presented as probabilities for interpretation.
- Protocol stated that adjusted and unadjusted results were to be presented for non-randomised studies and the unadjusted value used for analysis. Adjusted values were not available,
- Unit of analysis section deleted.
- Addition to Dealing with missing data: where standard deviations were missing for DMFT and dmft data we used the equation:
- log(SD) = 0.17 + 0.56 x log(mean) to estimate the standard deviations for both the before and after mean caries values. This equation was estimated from available data where the standard deviations were given ($R^2 = 0.91$). We undertook no other imputations. We undertook sensitivity analyses to determine the effect of the imputed standard deviations.
- Data synthesis: the following text has been deleted (to reflect changes in effect estimate): "Risk ratios will be combined for dichotomous data and mean differences combined for continuous data. Meta-analytic fixed-effect and random-effects models (with or without moderators) will be obtained via the linear (mixed-effects) model. In the case of random-effects, the DerSimonian-Laird estimator for the amount of (residual) heterogeneity will be utilised. Appropriate adjustments to the test statistics and confidence intervals due to the uncertainty in the estimate of the (residual) heterogeneity will be undertaken by application of the method by Knapp and Hartung (Knapp 2003).Tables indicating the general effect of fluoridation found in each study will be created for each outcome, and where possible, the point estimate and a measure of statistical significance (using the 95% confidence interval or P value) of the finding will also be included."
- Analysed dmft data only for children 8 years and younger.
- Approach to dental fluorosis data amended (although cut-offs regarding definition of dental fluorosis of aesthetic concern and decision to use data on 5 ppm or lower as primary analysis remain).
- Subgroup analysis and investigation of heterogeneity: we deleted the following text: "The heterogeneity among fluorosis studies will be explored by including variables that may account for the observed heterogeneity in the regression model. Since fluoride concentrations of control (non-fluoridated) groups across studies has been highlighted as a potential source of heterogeneity, a subgroup analysis of studies where the control group has fluoride concentration of 0.2 ppm or less will be undertaken".

INDEX TERMS

Medical Subject Headings (MeSH)

DMF Index; Dental Caries [*prevention & control]; Fluoridation [adverse effects] [*methods]; Fluorosis, Dental [epidemiology] [etiology]; Observational Studies as Topic; Prospective Studies; Selection Bias

MeSH check words

Adolescent; Child; Child, Preschool; Humans