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# Water fluoridation for the prevention of dental caries

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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 (CWF) is currently practised in about 25 countries; health authorities consider it to be a key strategy for preventing dental caries. CWF is of interest to health professionals, policymakers and the public. This is an update of a Cochrane review first published in 2015, focusing on contemporary evidence about the effects of CWF on dental caries.

## Objectives

To evaluate the effects of initiation or cessation of CWF programmes for the prevention of dental caries.

To evaluate the association of water fluoridation (artificial or natural) with dental fluorosis.

## Search methods

We searched CENTRAL, MEDLINE, Embase and four other databases up to 16 August 2023. We also searched two clinical trials registers and conducted backward citation searches.

## Selection criteria

We included populations of all ages.

For our first objective (effects of initiation or cessation of CWF programmes on dental caries), we included prospective controlled studies comparing populations receiving fluoridated water with those receiving non-fluoridated or naturally low-fluoridated water. To evaluate change in caries status, studies measured caries both within three years of a change in fluoridation status and at the end of study follow-up.

For our second objective (association of water fluoridation with dental fluorosis), we included any study design, with concurrent control, comparing populations exposed to different water fluoride concentrations. In this update, we did not search for or include new evidence for this objective.

## Data collection and analysis

We used standard methodological procedures expected by Cochrane.

For our first objective, we included the following outcomes as change from baseline: decayed, missing or filled teeth (‘dmft’ for primary and ‘DMFT’ for permanent teeth); decayed, missing or filled tooth surfaces ('dmfs' for primary and 'DMFS' for permanent teeth); proportion of caries-free participants for both primary and permanent dentition; adverse events. We stratified the results of the meta-analyses according to whether data were collected before or after the widespread use of fluoride toothpaste in 1975.

For our second objective, we included dental fluorosis (of aesthetic concern, or any level of fluorosis), and any other adverse events reported by the included studies.

## Main results

We included 157 studies. All used non-randomised designs. Given the inherent risks of bias in these designs, particularly related to management of confounding factors and blinding of outcome assessors, we downgraded the certainty of all evidence for these risks. We downgraded some evidence for imprecision, inconsistency or both. Evidence from older studies may not be applicable to contemporary societies, and we downgraded older evidence for indirectness.

#### Water fluoridation initiation (21 studies)

Based on contemporary evidence (after 1975), the initiation of CWF may lead to a slightly greater change in dmft over time (mean difference (MD) 0.24, 95% confidence interval (CI) -0.03 to 0.52; P = 0.09; 2 studies, 2908 children; low-certainty evidence). This equates to a difference in dmft of approximately one-quarter of a tooth in favour of CWF; this effect estimate includes the possibility of benefit and no benefit. Contemporary evidence (after 1975) was also available for change in DMFT (4 studies, 2856 children) and change in DMFS (1 study, 343 children); we were very uncertain of these findings.

CWF may lead to a slightly greater change over time in the proportion of caries-free children with primary dentition (MD -0.04, 95% CI -0.09 to 0.01; P = 0.12; 2 studies, 2908 children), and permanent dentition (MD -0.03, 95% CI -0.07 to 0.01; P = 0.14; 2 studies, 2348 children). These low-certainty findings (a 4 percentage point difference and 3 percentage point difference for primary and permanent dentition, respectively) favoured CWF. These effect estimates include the possibility of benefit and no benefit. No contemporary data were available for adverse effects.

Because of very low-certainty evidence, we were unsure of the size of effects of CWF when using older evidence (from 1975 or earlier) on all outcomes: change in dmft (5 studies, 5709 children), change in DMFT (3 studies, 5623 children), change in proportion of caries-free children with primary dentition (5 studies, 6278 children) or permanent dentition (4 studies, 6219 children), or adverse effects (2 studies, 7800 children).

Only one study, conducted after 1975, reported disparities according to socioeconomic status, with no evidence that deprivation influenced the relationship between water exposure and caries status.

#### Water fluoridation cessation (1 study)

Because of very low-certainty evidence, we could not determine if the cessation of CWF affected DMFS (1 study conducted after 1975; 2994 children). Data were not available for other review outcomes for this comparison.

#### Association of water fluoridation with dental fluorosis (135 studies)

The previous version of this review found low-certainty evidence that fluoridated water may be associated with dental fluorosis. With a fluoride level of 0.7 parts per million (ppm), approximately 12% of participants had fluorosis of aesthetic concern (95% CI 8% to 17%; 40 studies, 59,630 participants), and approximately 40% had fluorosis of any level (95% CI 35% to 44%; 90 studies, 180,530 participants). Because of very low-certainty evidence, we were unsure of other adverse effects (including skeletal fluorosis, bone fractures and skeletal maturity; 5 studies, incomplete participant numbers).

## Authors' conclusions

Contemporary studies indicate that initiation of CWF may lead to a slightly greater reduction in dmft and may lead to a slightly greater increase in the proportion of caries-free children, but with smaller effect sizes than pre-1975 studies. There is insufficient evidence to determine the effect of cessation of CWF on caries and whether water fluoridation results in a change in disparities in caries according to socioeconomic status. We found no eligible studies that report caries outcomes in adults.

The implementation or cessation of CWF requires careful consideration of this current evidence, in the broader context of a population's oral health, diet and consumption of tap water, movement or migration, and the availability and uptake of other caries-prevention strategies. Acceptability, cost-effectiveness and feasibility of the implementation and monitoring of a CWF programme should also be taken into account.

# Plain language summary

# Does adding fluoride to water supplies prevent tooth decay?

**Key messages**

- Adding fluoride to water supplies may lead to slightly less tooth decay in children's baby teeth.

- It may also lead to slightly more children being free of tooth decay.

- The benefits of fluoride in water supplies may be smaller than they were before the widespread addition of fluoride to toothpaste.

**Tooth decay and the use of fluoride**

Tooth decay is a worldwide problem affecting most adults and children. Untreated decay may cause pain and lead to teeth having to be removed.

Fluoride is a mineral which occurs naturally in water at different concentrations. It prevents tooth decay. Since 1975, fluoride has been an ingredient in most toothpastes. It is available in some mouth-rinses, and dentists use treatments that contain fluoride. It is possible to add fluoride to the local water supply. In this case, everyone in a community will have access to fluoride.

If young children swallow too much fluoride while their permanent teeth are forming, marks may develop on those teeth – this is called dental fluorosis. This can be very mild, with barely noticeable white lines or streaks. Rarely, some fluorosis is more noticeable, and people can dislike how their teeth look.

**What did we want to find out?**

We wanted to find out if water with added fluoride in the local water supply is better than water without added fluoride at:

- reducing the number of teeth, or tooth surfaces, with signs of decay;

- increasing the number of people who have no tooth decay.

We also wanted to find out about unwanted effects.

**What did we do?**

We searched for studies comparing communities that had fluoride added to their water supplies with communities that had no additional fluoride in their water.

The last time we published this Cochrane review, we also searched for studies that reported dental fluorosis and the concentration of fluoride in the water. Because the association of fluoridated water with dental fluorosis is widely accepted, we did not update the evidence on this occasion.

**What did we find?**

We found 21 studies that assessed the effects of adding fluoride to a water supply. We also found one study that assessed the effects of stopping artificially-added fluoride in a water supply. Studies only measured tooth decay in children.

In the last version of the review – not updated on this occasion – we found 135 studies that assessed the association of fluoridated water with dental fluorosis.

**Main results**

Studies conducted after 1975 showed that adding fluoride to water may lead to slightly less tooth decay in children's baby teeth. We could not be sure whether adding fluoride to water reduced tooth decay in children's permanent teeth or decay on the surfaces of permanent teeth.

Adding fluoride to water may slightly increase the number of children who have no tooth decay in either their baby teeth or permanent teeth. However, these results also included the possibility of little or no difference in tooth decay.

Studies conducted in 1975 or earlier showed a clear and important effect on prevention of tooth decay in children. However, due to the increased availability of fluoride in toothpaste since 1975, it is unlikely that we will see this effect in all populations today.

We were unsure whether there were any effects on tooth decay when fluoride is removed from a water supply.

We were unsure if fluoride reduces differences in tooth decay between richer and poorer people.

In the last version of the review, we found that adding fluoride to water supplies increases the number of people with dental fluorosis. If water contains 0.7 mg/L of fluoride, about 12% of people may have dental fluorosis that causes them to be bothered about how their teeth look, and about 40% of people may have dental fluorosis of any level. We were unsure whether fluoride in water leads to other unwanted effects.

**What are the limitations of the evidence?**

Our confidence in the evidence is limited because this review included studies in which communities were deliberately selected to have changes to fluoride levels in the water supply. Although a common study approach for this topic, it can mean that there are differences between communities that might affect the results. In addition, the

findings in some studies were different from others, and some results included the possibility of benefit and no benefit.

Older studies were conducted before the widespread use of fluoride toothpaste and other improvements in tooth decay prevention. This meant we could not tell if these results were applicable to current times. However, they may still be relevant to countries in which tooth decay is very high and people don't have easy access to fluoride toothpaste and other prevention strategies.

**How current is this evidence?**

For the effects of water fluoridation on tooth decay, this review updates our previous review and the evidence is current to August 2023.

For the association of fluoridated water with dental fluorosis, the review evidence is current to February 2015.

# Summary of findings

**Summary of findings 1**

## The initiation of community water fluoridation programmes on the prevention of dental caries

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

**Population:** people of all ages included in the review (although no studies on the effect of water fluoridation in adults met the inclusion criteria)

**Settings:** community setting

**Intervention:** initiation of water fluoridation

**Comparison:** low-/non-fluoridated water

| Outcomes | Impact of initiation of water fluoridation | | No. of participants (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|
| | Effect in area with low-/non-fluoridated water | Comparative effect; mean difference (95% CI) | | | |
| **Change in number of decayed, missing and filled teeth in the primary dentition (dmft)**<br>Scale from 0 to 20 (greater reduction = better)[a]<br>Follow-up: range from 3 to 12 years | **Contemporary evidence (after 1975) with lower burden of disease[b]** | | | | |
| | The change in the mean dmft from baseline to follow-up in the control group ranged from 0.44 to 0.88. | In the areas with water fluoridation, there was a greater reduction (change) in mean dmft from baseline to follow-up of 0.24 (-0.03 to 0.52). | 2908[c]<br>(2 NRSI) | Low[d]<br>⊕⊕⊖⊖ | The mean dmft at baseline in the non-/low-fluoridated areas ranged from 1.18 to 2.09.<br>One study reported data according to disparities, and found no evidence that deprivation influences the relationship between water fluoridation and the severity of caries (as measured by dmft counts). |
| | **Data from 1975 or earlier with higher burden of disease[b]** | | | | |
| | The change in the mean dmft from baseline to follow-up in the control group ranged from 0.3 to 1.04. | In the areas with water fluoridation, there was a greater reduction (change) in mean dmft from baseline to follow-up of 2.10 (1.71 to 2.49). | 5709[c]<br>(5 NRSI) | Very low<br>⊕⊖⊖⊖[e] | The mean dmft at baseline in the non-/low-fluoridated areas ranged from 4.76 to 8.1.<br>We downgraded the certainty of the evidence for indirectness (i.e. inapplicability of the evidence to contemporary settings). We acknowledge that in some countries, caries levels remain high and access to fluoridated toothpaste and other caries prevention strategies may remain limited. |
| **Change in number of decayed, missing and filled teeth in the permanent dentition (DMFT)**<br>Scale from 0 to 32 (greater reduction = better)[a]<br>Follow-up: range from 4 to 11 years | **Contemporary evidence (after 1975) with lower burden of disease[b]** | | | | |
| | The change in the mean DMFT from baseline to follow-up in the control group ranged from 0.27 to 2.83; caries increments ranged from -0.4 to -4.85. | In the areas with water fluoridation, there was a greater reduction (change) in mean DMFT from baseline to follow-up of 0.27 (-0.11 to 0.66). | 2856[c]<br>(4 NRSI) | Very low[f]<br>⊕⊖⊖⊖ | The mean DMFT at baseline in the non-/low-fluoridated areas ranged from 0.99 to 8.23, where reported.<br>One study reported data according to disparities, and found no evidence that deprivation influences the relationship between water fluoridation and the severity of caries (as measured by DMFT counts). |
| | **Data from 1975 or earlier with higher burden of disease[b]** | | | | |
| | The change in the mean DMFT from baseline to follow-up in the control group ranged from -0.73 to 0.65. | In the areas with water fluoridation, there was a greater reduction (change) in mean DMFT from baseline to follow-up of 1.00 (0.54 to 1.47). | 5623[c]<br>(3 NRSI) | Very low<br>⊕⊖⊖⊖[g] | The mean DMFT at baseline in the non-/low-fluoridated areas ranged from 3.01 to 4.03.<br>We downgraded the certainty of the evidence for inapplicability to contemporary settings. We acknowledge that in some countries, caries levels remain high and access |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | to fluoridated toothpaste and other caries prevention strategies may remain limited. |
| **Change in number of decayed, missing and filled tooth surfaces in the primary dentition (dmfs)** | - | - | - | - | There were no data for dmfs reported in the included studies conducted before or after 1975. |
| **Change in number of decayed, missing and filled tooth surfaces in the permanent dentition (DMFS)**<br>Scale from 0 to 128 (lower values indicate reduction in caries)<br>Follow-up: 4 years | **Contemporary evidence (after 1975) with lower burden of disease[b]** | | | | |
| | The mean DMFS increment was 9.19. | The mean DMFS increment was 2.46 lower (1.11 lower to 3.81 lower). | 343 (1 NRSI) | Very low[h] ⊕⊝⊝⊝ | There were no data for DMFS reported in the included studies conducted in 1975 or earlier. |
| **Change in proportion of caries-free participants (primary teeth)**<br>Scale: 0 to 1 (greater increase = better)[i]<br>Follow-up: range 3 to 11 years | **Contemporary evidence (after 1975) with lower burden of disease[b]** | | | | |
| | The change in the proportion of caries-free children from baseline to follow-up in the control group ranged from -0.19 to -0.11. | In the areas with water fluoridation, there was a greater increase (change) in the proportion of caries-free children from baseline to follow-up of -0.04 (-0.09 to 0.01). | 2908[c] (2 NRSI) | Low[d] ⊕⊕⊝⊝ | The proportion of caries-free children at baseline in the non-/low-fluoridated areas ranged from 0.49 to 0.68.<br>One study reported data according to disparities, and found no evidence that deprivation influences the relationship between water fluoridation and the presence or absence of caries in the primary dentition. |
| | **Data from 1975 or earlier with higher burden of disease[b]** | | | | |
| | The change in the proportion of caries-free children from baseline to follow-up in the control group ranged from -0.14 to 0.02. | In the areas with water fluoridation, there was a greater increase (change) in the proportion of caries-free children from baseline to follow-up of -0.17 (-0.20 to -0.13). | 6278[c] (5 NRSI) | Very low ⊕⊝⊝⊝[e] | The proportion of caries-free children at baseline in the non-/low-fluoridated areas ranged from 0.08 to 0.20.<br>We downgraded the certainty of the evidence for inapplicability to contemporary settings. We acknowledge that in some countries, caries levels remain high and access to fluoridated toothpaste and other caries prevention strategies may remain limited. |
| **Change in proportion of caries-free participants (permanent teeth)**<br>Scale: 0 to 1 (greater increase = better)[i]<br>Follow-up: range 3 to 11 years | **Contemporary evidence (after 1975) with lower burden of disease[b]** | | | | |
| | The change in the proportion of caries-free children from baseline to follow-up in the control group ranged from -0.78 to -0.05. | In the areas with water fluoridation, there was a greater increase (change) in the proportion of caries-free children from baseline to follow-up of -0.03 (-0.07 to 0.01). | 2348[c] (2 NRSI) | Low[d] ⊕⊕⊝⊝ | The proportion of caries-free children at baseline in the non-/low-fluoridated areas was 0.62, where reported.<br>One study reported data according to disparities, and found no evidence that deprivation influences the relationship between water fluoridation and the presence or absence of caries in the primary dentition. |
| | **Data from 1975 or earlier with higher burden of disease[b]** | | | | |
| | The change in the proportion of caries-free children from baseline to follow-up in the control group ranged from -0.07 to 0.05. | In the areas with water fluoridation, there was a greater increase (change) in the proportion of caries-free children from baseline to follow-up of -0.06 (-0.14 to 0.02). | 6219[c] (4 NRSI) | Very low ⊕⊝⊝⊝[g] | The proportion of caries-free children at baseline in the non-/low-fluoridated areas ranged from 0.05 to to 0.12.<br>We downgraded the certainty of the evidence for inapplicability to contemporary settings. We acknowledge that in some countries, caries levels remain high and access to fluoridated toothpaste and other caries prevention strategies may remain limited. |
| **Adverse effects** (including dental fluorosis, skeletal fluorosis, hip fractures, cancer, congenital malformations, mortality) | **Contemporary evidence (after 1975) with lower burden of disease[b]** | | | | |
| | - | | - | - | No studies reported data for this outcome. |
| | **Data from 1975 or earlier with higher burden of disease[b]** | | | | |
| | In one study, there was a small increase in the number of children with mild fluorosis (0.12% increase).<br>In another study, there were no cases of "unsightly mottling". | | 7800 participants (2 NRSI) | Very low ⊕⊝⊝⊝[j] | |

**CI:** confidence interval; **NRSI:** non-randomised studies of interventions

**GRADE Working Group grades of evidence**

**High certainty**: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty**: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty**: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

**Very low certainty**: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]A positive value represents a greater reduction in mean dmft/DMFT from baseline to follow-up in the water fluoridation group; a negative value represents a greater reduction in mean dmft/DMFT from baseline to follow-up in the non-fluoridated group.

[b]Summary statistics for severity of caries were much higher in studies conducted in 1975 or earlier.

[c]Because data were collected from a different sample of participants at baseline and follow-up, overall sample sizes differed at each time point. Therefore, we conducted analysis using an average number of participants of the baseline and follow-up sample sizes in each study. Only two studies (for permanent dentition) used the same sample of participants, and we did not need to calculate an average sample size for these studies.

[d]Downgraded by only one level for risk of bias because both included studies were at low risk of confounding and selection bias. Also downgraded by one level for imprecision.

[e]Downgraded by two levels due to the inherent risk of bias in the design of the included studies, and by one level due to indirectness (applicability) of evidence (findings from studies conducted prior to 1975 may not be applicable to contemporary settings; 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).

[f]Downgraded by two levels due to the inherent risk of bias in the design of some of the included studies, and by one level due to considerable statistical heterogeneity and imprecision.

[g]Downgraded by two levels due to the inherent risk of bias in the design of the included studies, and by one level due to indirectness (applicability) of evidence (findings from studies conducted prior to 1975 may not be applicable to contemporary settings; 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). We also noted that the effect estimate included considerable statistical heterogeneity.

[h]Downgraded by two levels because of the inherent risk of bias in the design of the included study, and by one level for imprecision (owing to the very small sample size).

[i]A negative value represents a greater increase in the proportion of caries-free children from baseline to follow-up in the water fluoridation group; a positive value represents a greater increase in the proportion of caries-free children from baseline to follow-up in the non-fluoridated group.

[j]Downgraded by two levels due to the inherent risk of bias in the design of the included studies, and one level for indirectness (applicability of the evidence, because the evidence was only available in studies conducted prior to 1975 and may not be applicable to contemporary settings). This evidence was also limited by the small number of studies that contributed data (relative to the overall number of studies in this comparison); both of these studies had an overall critical risk of bias.

**Summary of findings 2**

## The cessation of community water fluoridation programmes on the prevention of dental caries

**Population:** people of all ages included in the review (although no studies on the effect of water fluoridation in adults met the inclusion criteria)

**Settings:** community setting

**Intervention:** cessation of water fluoridation

**Comparison:** fluoridated water

| Outcomes | Impact of cessation of water fluoridation | | No of participants (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|
| | Effect in area with continuously fluoridated water | Comparative effect; mean difference (95% confidence interval) | | | |
| **Change in number of decayed, missing and filled teeth in the primary dentition (dmft)** | No evidence to determine the effect of the cessation of water fluoridation on dmft | | | | |
| **Change in number of decayed, missing and filled teeth in the permanent dentition (DMFT)** | No evidence to determine the effect of the cessation of water fluoridation on DMFT | | | | |
| **Change in number of decayed, missing and filled tooth surfaces in the primary dentition (dmfs)** | No evidence to determine the effect of the cessation of water fluoridation on dmfs | | | | |
| **Change in number of decayed, missing and filled tooth surfaces in the permanent dentition (DMFS)**<br>Scale from: 0 to 128 (lower = better)<br>Follow-up: 3 years | | | 2994[a]<br>(1 observational study) | Very low[b]<br>⊕⊝⊝⊝ | Insufficient evidence to determine the effect of the cessation of water fluoridation on caries |
| **Change in proportion of caries-free participants** (primary teeth) | No evidence to determine the effect of the cessation of water fluoridation on proportion of caries-free participants (primary teeth) | | | | |
| **Change in proportion of caries-free participants** (permanent teeth) | No evidence to determine the effect of the cessation of water fluoridation on proportion of caries-free participants (permanent teeth) | | | | |

| | |
|---|---|
| **Adverse effects** | No evidence to determine whether cessation of a water fluoridation programme is associated with any harms |

**GRADE Working Group grades of evidence**

**High certainty**: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty**: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty**: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

**Very low certainty**: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Total number of participants measured

[b]Downgraded by two levels because of inherent risk of bias in the design of the included study, and by one level for imprecision

**Summary of findings 3**

## The association of water fluoridation (artificial or natural) with dental fluorosis

The association of water fluoridation (artificial or natural) with dental fluorosis

**Population:** people of all ages

**Settings:** community settings

**Intervention:** water with any concentration of fluoride from either natural sources or artificially added

**Comparison:** n/a

| Outcomes | Impact | No. of participants (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|
| **Dental fluorosis of aesthetic concern**[a] (measured by Dean's Index, TFI, TSIF) | 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%).<br>Controlling for study effects, we would expect the odds of dental fluorosis of aesthetic concern 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 NRSI) | ⊕⊕⊖⊖ Low[b] | |
| **Dental fluorosis of any level**[a] - including dental fluorosis that can only be detected under normal clinical conditions and other enamel defects (measured by Dean's Index, TFI, TSIF) | For a fluoride level of 0.7 ppm, the percentage of participants with any level of dental fluorosis was estimated to be 40% (95% CI 35% to 44%).<br>Controlling for study effects, we would expect the odds of dental fluorosis of any level to increase by a factor of 3.60 (95% CI 2.86 to 4.53) for each one unit increase in fluoride level (1 ppm F) | 180,530 (90 NRSI) | ⊕⊕⊖⊖ Low[b] | |
| **Other adverse effects** | - | 596,410[c] (5 NRSI) | ⊕⊖⊖⊖ Very low[d] | Only a small number of studies reported other types of adverse effects (including skeletal fluorosis, bone fracture and skeletal maturity). We did not analyse the data, and we were unable to draw conclusions from data reported by individual study authors. |

**CI:** confidence interval; **n/a:** not applicable (because the studies assessed the association of an effect, a comparison group was not necessary for this objective); **NRSI:** non-randomised studies of interventions; **ppm:** parts per million; **TFI:** Thylstrup and Fejerskov index; **TSIF:** Tooth Surface Index of Fluorosis

**GRADE Working Group grades of evidence**

**High certainty**: we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty**: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty**: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

**Very low certainty**: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Dental fluorosis of aesthetic concern only with levels of reported fluoride exposure of 5 ppm or less

[b]The certainty of the evidence starts at low because of the risk of bias in these study designs. From visual observation of the data, we also noted the possibility of inconsistency. We did not downgrade by further levels.

[c]One of the included studies did not report participant numbers and, therefore, this is an approximate number of participants based on the data in the remaining four studies.

[d]The certainty of the evidence starts at low because of the risk of bias in these study designs. We also downgraded by one level due to indirectness because the concentrations of fluoride in many of the data groups were much higher than optimal levels.

# 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 microorganisms 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 (Lagerweij 2015), inequalities in dental health persist (WHO 2021), with significant numbers of individuals and communities having a clinically significant burden of preventable dental disease. Dental caries are 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 poor school performance (Rebelo 2019), restricted activity days, as well as problems with 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 its widespread prevalence in adulthood, most children are at risk of dental caries.

Dental caries is a major public health problem in low-, middle- and high-income countries. The estimated prevalence of caries in primary teeth ranges from 18.7% to 53.2%, with children living in low-income countries being most impacted (WHO 2021). It has been estimated that, in the USA, 37% of children aged between two and eight years have caries experience in their primary teeth, and 58% of those aged 12 to 19 years have caries experience in their permanent teeth (Dye 2015). 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 low- and middle-income countries, especially those where community-based preventive oral care programmes are not established (WHO 2021). 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 (Frencken 2017). This has major implications, especially in high-income countries experiencing an increase in life expectancy.

## Description of the intervention

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.

Water can be artificially fluoridated (also known as community water fluoridation (CWF)) 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 part per million (ppm) (Dean 1941). World Health Organization (WHO) Guidelines and the European Union water quality directive specify 1.5 ppm as the maximum level for human consumption (European Union 1998; WHO 2017). In 2015, the USA updated the 'optimum' level of fluoride in water to 0.7 ppm, replacing the previous stated optimum range of 0.7 to 1.2 ppm, in recognition that people now receive fluoride from other sources (HHS 2015).

Community water fluoridation was initiated in the USA in 1945 and is currently practised in about 25 countries around the world (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 72.7% of the population on public water systems receive fluoridated water, with the aim of increasing the number of people whose water systems have the recommended amount of fluoride to 77% by 2030 (CDC 2023). In Australia, all states and territories provide fluoridated drinking water, but with the coverage in each jurisdiction varying from 76% to 100% (NHMRC 2017). 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, potentially reducing oral health inequalities. 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 a 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 groundwater 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.

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).

## 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 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 or time of exposure, or a combination of these factors (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; NHMRC 2017).

## Why it is important to do this review

The use of water fluoridation as a means of improving dental health has been endorsed by many national and international health institutions. It has been hailed by the US Surgeon General as "the best method for delivering fluoride to all members of the community, regardless of age, education, income level or access to routine dental care" (ADA 2016). Opponents have raised concerns about ethical issues of mass intervention, and potential harms associated with fluoride (Cheng 2007). As a result, community water fluoridation remains controversial. Over the years, numerous systematic reviews of water fluoridation have been undertaken, employing different inclusion criteria and different methods of assessment and analysis (Griffin 2007; McDonagh 2000; Moynihan 2019; NHMRC 2017; Truman 2002). One of the first systematic reviews of water fluoridation, also known as the York review, was published by McDonagh and colleagues (McDonagh 2000). The review findings have often been misinterpreted and have been used to support arguments on both sides of the water fluoridation debate (Cheng 2007). McDonagh 2000 showed that fluoridation programmes reduce caries as well as increase the risk of dental fluorosis. However, the review authors found insufficient evidence to draw conclusions regarding other potential harms or health disparities. Indeed, they stated that "the evidence about reducing inequalities in dental health was of poor quality, contradictory and unreliable" (McDonagh 2000). Despite this, the review is often used to support the statement that water fluoridation reduces oral health inequalities.

Our 2015 Cochrane review highlighted the lack of contemporary evidence evaluating the effectiveness of water fluoridation for the prevention of caries (Iheozor-Ejiofor 2015). The caries data included in the review came predominantly from studies conducted prior to the widespread use of fluoride toothpastes. Whilst the review showed that water fluoridation is effective at reducing caries levels in both primary and permanent dentition in children, our confidence in the effect estimates was 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 review called for more contemporary studies evaluating the effectiveness of water fluoridation for the prevention of caries.

Since the publication of Iheozor-Ejiofor 2015, new studies evaluating the effect of community water fluoridation initiation programmes have been published. Given the continued interest in this topic from health professionals, policymakers and the public, it is important to update and maintain a robust systematic review to reflect emerging, contemporary evidence.

This review update focuses on updating the caries data only; we undertook no update of the fluorosis data. In Iheozor-Ejiofor 2015, we included 135 studies evaluating the association between water fluoridation and fluorosis, with 90% (122/135) of the studies conducted after 1975 and, thus, after the advent of the widespread use of fluoride toothpaste. We consider the evidence from these studies to be applicable to current settings.

In addition to updating the data on the effectiveness of water fluoridation programmes for preventing dental caries, this review update aims to address concerns raised in a critique of the review (Rugg-Gunn 2016), where valid. Changes to the methods are listed in Differences between protocol and review.

# Objectives

To evaluate the effects of initiation or cessation of community water fluoridation (CWF) programmes for the prevention of dental caries.

To evaluate the association of water fluoridation (artificial or natural) with dental fluorosis.

# Methods

# Criteria for considering studies for this review

## Types of studies

The criteria for including studies in the review and the subsequent methods differed according to the objectives evaluated.

### Evaluation of initiation or cessation of community water fluoridation programmes for the prevention of dental caries

In this review update, our primary objective was to evaluate the most up-to-date evidence evaluating the impact of the initiation or cessation of a community water fluoridation (CWF) programme on the prevention of dental caries. We only searched for studies that measured and reported our primary outcomes, and for this purpose we used the criteria in Iheozor-Ejiofor 2015. We recognise that randomised controlled trials are logistically unfeasible for this topic, and we included non-randomised studies of interventions (NRSI) in this review. Therefore, we included prospective studies with a concurrent control comparing a fluoridated water community with a non-fluoridated water community as we judged that this was the most robust study design for this topic.

Because we intended to measure the change in dental caries as a consequence of a CWF programme, we included studies that measured caries at a minimum of two time points: at baseline before initiation or cessation of a CWF programme and at the end of the study follow-up. Groups had to be comparable in terms of fluoridated water at baseline. To measure the impact of initiating a CWF programme on dental caries, we included studies in which study communities had comparable non-fluoridated/low-fluoridated water (less than 0.4 ppm fluoride concentration) at baseline (before fluoride was artificially added to the water system in one of the study groups). To measure the impact of stopping a CWF programme on dental caries, we included studies in which both study communities had comparable fluoridation programmes at baseline before artificial fluoride was removed from the water system in one of the study groups.

We acknowledge that single time point, cross-sectional studies may provide context in terms of demonstrating the association between water fluoridation and dental caries. These studies may be important in terms of exploring the wider picture beyond the scope of the present review question. However, such study designs are limited in their ability to account for unobservable confounding (Reeves 2017), and are not appropriate for answering the review question regarding the impact of initiation or cessation of a CWF programme to prevent dental caries. Although we did not include single time point studies that measured the association between water fluoridation and dental caries in this review, we made a note of any such studies that we identified in the screening process (see Searching other resources) and presented their findings for reference.

### Evaluation of the association of water fluoridation (artificial or natural) with dental fluorosis

In order to assess the association of water fluoridation (artificial or natural) with dental fluorosis, we included any study design, with concurrent control, comparing populations exposed to different water fluoride concentrations. We included studies with single time points because these types of studies are suited to answer questions of association.

**We did not update the evidence for fluorosis in this version of the review.** We judged that the evidence for dental fluorosis was sufficiently summarised in Iheozor-Ejiofor 2015; no new studies evaluating the association of water fluoridation and dental fluorosis have been included in this review update. The methods used specifically for studies that measured fluorosis outcomes are summarised in Appendix 1.

## Types of participants

We included populations of all ages that received fluoridated water and populations that received non-fluoridated/low-fluoridated water. We included populations of any size.

## Types of interventions

### Evaluation of initiation or cessation of community water fluoridation for the prevention of dental caries

We included studies that evaluated the effects of 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/low-fluoridated water (less than 0.4 ppm) could be in conjunction with other sources of fluoride (e.g. fluoridated toothpaste), where the other sources could be assumed to be similar across study areas. Where specific information on the use of other sources of fluoride was not reported, we assumed that populations in studies conducted after 1975 in industrialised countries had been exposed to fluoridated toothpaste.

### Evaluation of the association of water fluoridation (artificial or natural) with dental fluorosis

We included studies that evaluated fluoride at any concentration present in drinking water.

## Types of outcome measures

### Evaluation of initiation or cessation of community water fluoridation for the prevention of dental caries

We collected data for the following outcomes.

- Change in the number of decayed, missing and filled primary and permanent teeth (dmft and DMFT, respectively). We reported this outcome separately according to dentition type.
- Change in the number of decayed, missing and filled primary and permanent tooth surfaces (dmfs and DMFS, respectively). We reported this outcome separately according to dentition type.
- Change in the proportion of caries-free participants. Where feasible, we reported this outcome separately according to dentition type (primary and permanent).
- Adverse effects. We included dental fluorosis (using any measurement instrument reported below), or other possible adverse effects, including skeletal fluorosis, hip fractures, cancer, congenital malformations, mortality.

Within the context of this review, we refer to dental fluorosis 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 reported disparities in dental caries across different groups of people.

In their Cochrane review exploring fluoride varnishes for caries prevention, Marinho and colleagues developed an a priori set of rules for prioritising the various caries outcome measures they expected studies would use (Marinho 2013). We would have adopted these rules if the data had required it.

#### Evaluation of the association of water fluoridation (artificial or natural) with dental fluorosis

We collected data for the following.

- Dental fluorosis of aesthetic concern, measured using Dean's Fluorosis Index, Tooth Surface Index of Fluorosis (TSIF), Thylstrup and Fejerskov Index (TFI) or the modified Developmental Defects of Enamel (DDE).
- Any level of dental fluorosis (measured using any of the above measurement instruments).
- Other possible adverse effects, including skeletal fluorosis, hip fractures, cancer, congenital malformations and mortality, as reported in the included studies.

We reported fluorosis outcome data according to fluoride levels: fluoride levels below 5 ppm; or all fluoride levels.

## Search methods for identification of studies

### Electronic searches

In this review update, we searched the following databases.

- Cochrane Oral Health's Trials Register (searched 12 July 2022; database no longer being updated)
- Cochrane Central Register of Controlled Trials (CENTRAL; 2023, Issue 8), in the Cochrane Library
- MEDLINE Ovid (1946 to 16 August 2023)
- Embase Ovid (1980 to 16 August 2023)
- ProQuest (all databases; to 16 August 2023)
- Web of Science (Clarivate Analytics) Conference Proceedings (1990 to 23 August 2023)
- ZETOC Conference Proceedings (1993 to 12 July 2022; unable to access this database in August 2023)

Subject strategies were modelled on the search strategy designed for MEDLINE Ovid. There were no language, publication year or publication status restrictions. See Appendix 2 for search strategies.

### Searching other resources

We searched the following trials registries for ongoing trials (see Appendix 2).

- US National Institutes of Health Ongoing Trials Register, ClinicalTrials.gov (clinicaltrials.gov; searched 23 August 2023)
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; searched 23 August 2023)

We searched the reference lists of included studies and relevant systematic reviews for further studies.

We checked that none of the studies included in this review were retracted due to error or fraud, using Retraction Watch (https://retractionwatch.com).

We did not perform a separate search for adverse effects of interventions; we only considered adverse effects described in the study reports of included studies.

In order to address feedback on the previous version of this review, we also noted any single time point studies that measured caries data. We sourced these studies from the results of database searches, backward citation searching of relevant systematic reviews or other sources, as well as from the reference list of previously excluded

studies in Iheozor-Ejiofor 2015. These studies were not eligible for this review, and we did not use systematic methods to identify these studies (for example, using two independent review authors). We included references and data for these studies in additional figures in order to provide a wider context for the interpretation of the review findings (see Discussion).

## Data collection and analysis

The following methods relate only to our primary objective of evaluating the most up-to-date evidence on the effects of the initiation or cessation of a CWF programme for the prevention of dental caries. The methods used specifically for studies that measured fluorosis outcomes are summarised in Appendix 1.

### Selection of studies

Working independently, two review authors screened the titles and abstracts (when available) of all reports identified through the electronic search update (see Contributions of authors). 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 the studies met the inclusion criteria. We resolved any disagreements through discussion. Where resolution was not possible, we consulted a third review author. We recorded any studies rejected at this or subsequent stages in the Characteristics of excluded studies table, and gave reasons for their exclusion.

### Data extraction and management

Working independently, two review authors extracted data using specially designed data extraction forms (produced in Excel) (see Contributions of authors). We piloted the data extraction forms on several papers and modified them as required before use. Where translations were required, this was either done by colleagues fluent in the relevant language who completed the data extraction form, or through the use of Google Translate. We discussed any disagreements and consulted a third review author where necessary.

For each study, we aimed to record details for the following data.

- Year of publication, country of origin and source of study funding
- Participants, including demographic characteristics (socioeconomic status (SES), ethnicity), age, gender, primary/permanent dentition, residential history, and criteria for inclusion and exclusion
- Type of intervention and comparator
- Reported outcomes, including method of assessment, and time intervals; unadjusted and adjusted effect estimates
- Confounding factors and methods used to control for confounding. We noted information reported by study authors for socioeconomic status. We also noted variables that predict the consumption of water (e.g. ethnicity, age); these may provide context regarding the impact of the programme but are not related to bias (Assessment of risk of bias in included studies).
- Co-interventions (e.g. fissure sealant programmes; other sources of fluoride)

### Assessment of risk of bias in included studies

In the 2015 review (Iheozor-Ejiofor 2015), we assessed all included studies for risk of bias using the Cochrane risk of bias assessment tool adapted for non-randomised controlled studies (Higgins 2011). In this update, we assessed all relevant results of studies evaluating the effects of CWF programmes on the prevention of dental caries using an updated ROBINS-I tool which was in development at the time of the production of this review (Glenny 2022 [pers comm]). The ROBINS-I tool reflects the developments in assessing the risk of bias in NRSI (www.riskofbias.info/welcome). During this process, we carried out a re-assessment of studies that evaluated our first review objective and had been assessed using the previous tool in 2015. Working independently, three review authors (AMG, LO, TW) carried out the risk of bias assessments. We resolved disagreements through group discussion. We did not re-assess studies evaluating the association of water fluoridation and dental fluorosis.

The ROBINS-I tool assesses material bias associated with:

- domain 1: risk of bias due to confounding;
- domain 2: risk of bias in classification of interventions;
- domain 3: risk of bias in selection of participants into the study (or into the analysis);
- domain 4: risk of bias due to deviations from intended interventions;
- domain 5: risk of bias due to missing data;
- domain 6: risk of bias arising from measurement of the outcome;
- domain 7: risk of bias in selection of the reported result.

In this review, we considered socioeconomic status to be the only relevant confounder as we were only interested in prognostic factors that predict the implementation of the water fluoridation programme and caries. In the context

of this review, socioeconomic status may predict whether an area has CWF implemented or not (i.e. it may be more likely to be implemented in areas of greater deprivation); it may also predict caries levels.

We used the preliminary questions from the ROBINS-I tool for each study (i.e. Did the authors make any attempts to control for confounding? If not, is there sufficient potential for confounding that an unadjusted result should not be considered further? Was the method of measuring the outcome inappropriate?). We automatically assessed any study that failed these preliminary questions as being at critical risk of bias, and we undertook no further assessment.

We made a risk of bias assessment for each domain, and subsequently, an overall judgement of risk of bias across the seven domains. We present details about how we arrived at our judgements, and their interpretation, in Appendix 3.

We tabulated judgements of low, moderate, serious and critical risk of bias for each study, and presented supporting information for these judgements in the Characteristics of included studies tables.

## Measures of treatment effect

We planned to include the following caries indices in the analyses: dmft, DMFT, dmfs, DMFS and the proportion of caries-free participants. For dmft/DMFT and dmfs/DMFS analyses, we calculated the difference in mean change scores (baseline and follow-up) between fluoridated and control groups. For the proportion of caries-free participants, we calculated the difference in the change in the proportion of caries-free participants (baseline to follow-up) between the fluoridated and control groups.

We report data on both adjusted and unadjusted results where available and noted the reason for adjustment.

## Unit of analysis issues

We did not anticipate, or identify during the review process, any unit of analysis issues.

## Dealing with missing data

Where outcome data were missing from the published report, or could not be calculated from the information presented in a study report, we attempted to contact the study authors to obtain the data and clarify any uncertainty. The analyses generally included only the available data (ignoring missing data). If studies did not report the number of participants evaluated, we did not include their outcome data in the analyses. Where standard deviations (SDs) were missing for dmft(s) and DMFT(S) data, we used the equation: log(SD) = 0.17 + 0.56 x log(mean) to estimate the SDs for both the before and after mean caries values. We estimated this equation from available data where the SDs were given ($R^2$ = 0.91; Appendix 4). We undertook no other imputations.

## Assessment of heterogeneity

We assessed clinical heterogeneity by examining the type of participants, interventions and outcomes of each study. We assessed statistical heterogeneity by visual inspection of the point estimates and CIs in forest plots; lack of overlap of CIs may indicate heterogeneity. We also assessed statistical heterogeneity using Cochran's test for heterogeneity and the $I^2$ statistic. For the interpretation of statistical heterogeneity, we used the methods outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2021). For Cochran's Q test for heterogeneity, we considered heterogeneity to be evident if P values were less than 0.1. We interpreted the $I^2$ statistic as follows:

- 0% to 40% might not be important;
- 30% to 60% may represent moderate heterogeneity;
- 50% to 90% may represent substantial heterogeneity;
- 75% to 100% considerable heterogeneity.

## Assessment of reporting biases

We planned to assess publication bias according to the recommendations described in the *Cochrane Handbook for Systematic Reviews of Interventions* if we included at least 10 studies in any meta-analysis of the outcomes regarding prevention of caries (Page 2022). Had we identified asymmetry in the contour-enhanced funnel plots, we would have investigated possible causes. However, none of the meta-analyses included at least 10 studies.

## Data synthesis

### Initiation or cessation of community water fluoridation for the prevention of dental caries

We did not include studies assessed at critical risk of bias in the primary analysis (see Assessment of risk of bias in included studies and Sensitivity analysis). We used a random-effects model for all analyses.

For the analysis of change in dmft/DMFT and dmfs/DMFS, we calculated mean change scores (change from baseline to follow-up) for both the water fluoridation and control groups. We tabulated the raw data and mean change scores. We weighted the mean change scores for age when studies presented data by different age groups. For dmft, we only analysed data for children aged eight years and younger. Using these mean change

scores, we calculated a mean difference in change scores between the water fluoridation and control groups for the review. As different populations and sample sizes were evaluated at baseline and follow-up, we calculated an average sample size using the samples from the baseline and follow-up time points in each study.

For the proportion of caries-free participants, we calculated the risk differences between baseline and follow-up measurements separately for the water fluoridation and control groups. We used a meta-analytical approach to pool data across age groups within each study. For information, we presented in the review tabulated available raw data from each study reported for each age group. In order to calculate the change in the proportion of caries-free participants in each group, we subsequently combined these summary effect estimates and SDs in a meta-analysis as continuous data. Once again, we calculated an average sample size to give an indication of the size of the studies.

We managed data separately for initiation and cessation studies, and for primary and permanent dentition. We used RevMan 2024 for all calculations.

We stratified the results of the meta-analyses according to whether data were collected after the widespread use of fluoride toothpaste (after 1975) or in 1975 and earlier.

We reported data on disparities and adverse effects (other than fluorosis) narratively.

Methods for the analysis of fluorosis data are presented in Appendix 1.

## Subgroup analysis and investigation of heterogeneity

For studies that evaluated the effects of initiation or cessation of community water fluoridation for the prevention of dental caries, we undertook subgroup analyses according to whether data were collected after the widespread use of fluoride toothpaste, or before. We planned to include the following caries indices in the subgroup analyses: dmft, DMFT, dmfs, DMFS and the proportion of caries-free participants. We used a threshold of 1975 for this purpose (≤ 1975 or > 1975). We did not use the results of formal tests of subgroup interactions to inform our decision on whether to pool data across subgroups; we stratified data separately according to these subgroups.

## Sensitivity analysis

We planned to include the following caries indices in all sensitivity analyses: dmft, DMFT, dmfs, DMFS and the proportion of caries-free participants.

ROBINS-I guidance suggests excluding from meta-analysis those studies deemed to be at critical risk of bias. We used this approach for our primary analysis. However, given the limited evidence available within the review, we conducted a sensitivity analysis including studies assessed as being at overall critical risk of bias.

In addition, we undertook sensitivity analysis based upon the analytical approach used for the prospective cohort studies, analysing them as either cohort studies with the same individuals at baseline and follow-up or as controlled before-and-after (CBA) studies with different individuals at different time points.

We also undertook sensitivity analyses to determine the effect of removing studies with imputed SDs.

We had planned to undertake further sensitivity analyses to determine if the results of the meta-analysis were influenced by the timing of the baseline measurement, as appropriate. However, there was little variation in the timing of the baseline measurement, and so we did not undertake this sensitivity analysis.

## Summary of findings and assessment of the certainty of the evidence

We assessed the certainty of the evidence for the outcomes in this review using GRADE methods (gdt.guidelinedevelopment.org), with assessment undertaken for risk of bias, indirectness, inconsistency, imprecision and publication bias. We used a collaborative approach to the GRADE assessments through discussion with team members (JC, AMG, SL, LO, PR, TW, HW).

We presented the results and certainty of evidence for each outcome in three summary of findings tables, according to our review objectives:

- the initiation of community water fluoridation programmes for the prevention of dental caries (Summary of findings table 1);
- the cessation of community water fluoridation programmes for the prevention of dental caries (Summary of findings table 2);
- the association of water fluoridation (artificial or natural) with dental fluorosis (Summary of findings table 3).

As outlined in the *Cochrane Handbook* (Schünemann 2023), all studies assessed using ROBINS-I start as high-certainty evidence. Typically, a body of evidence from NRSI is then downgraded by two levels due to the inherent risk of bias (due to confounding and selection bias) associated with the lack of randomisation. We used this approach when assessing the certainty of the evidence for the initiation or cessation of water fluoridation in our first two summary of findings tables. When we judged that studies did not require downgrading from high to low certainty due to risk of bias, we provided justification for this decision in the review. We also reported and justified all downgrading decisions for other GRADE criteria.

For the initiation of water fluoridation, we presented outcome data in the summary of findings table according to whether data were collected after the widespread use of fluoride toothpaste, or before; we used a threshold of 1975

for this purpose (≤ 1975 or > 1975). For studies conducted in 1975 or before, we downgraded the certainty of the evidence for indirectness (applicability), as their findings may not be applicable to contemporary settings. In addition to the advent of fluoridated toothpaste use, we assumed that 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 since 1975. We did not separate the data according to study dates for cessation of water fluoridation because this comparison included data from only one study.

This review did not include an update of the evidence for the association of water fluoridation with dental fluorosis. We presented this summary of findings table, using GRADE judgements supported by previous risk of bias judgements, as reported in Iheozor-Ejiofor 2015.

# Results

## Description of studies

### Results of the search

After removal of duplicates from the search results, we screened 2057 titles and abstracts, which included backward citation searches and searches of clinical trials registers. We reviewed the full texts of 17 records and selected two new studies (with two records) for inclusion in the review, and two additional records for two already included studies. During this selection process, we excluded nine studies (13 records). We also included 155 studies previously reported in Iheozor-Ejiofor 2015, and thus included a total of 157 studies (171 records) in this update.

The full details of the search results, screening and selection of included studies is illustrated in the PRISMA flow diagram (Figure 1).

### Included studies

We included 157 studies in the review (see Characteristics of included studies).

#### Evaluation of the effects of initiation or cessation of community water fluoridation on dental caries

Overall, twenty-two prospective NRSI (24 records) published between 1951 and 2022 met the inclusion criteria for this review objective.

##### Initiation of water fluoridation

Twenty-one of these studies looked at the effect of the initiation of a water fluoridation programme on dental caries (Adriasola 1959; Arnold 1956; Ast 1951; Backer-Dirks 1961; Beal 1971; Beal 1981; Blinkhorn 2015; Brown 1965; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Goodwin 2022; Gray 2001; Guo 1984; Hardwick 1982; Holdcroft 1999; Kim 2019; Kunzel 1997; Loh 1996; Pot 1974; Tessier 1987). All studies included an intervention group in which a population had initially been exposed to water with naturally low fluoride or no fluoride, followed by the initiation of a community-wide water fluoridation programme. Studies also included a prospective control group in which populations were exposed to water with naturally low fluoride or no fluoride throughout the study period. These studies measured dental caries in both the intervention and control groups before the initiation of a CWF programme (within three years of initiation) and at a later follow-up. This allowed us to measure and compare the change in caries status between fluoridated areas and naturally low- (or non-) fluoridated areas.

The studies were conducted in multiple locations in Europe (Backer-Dirks 1961; Beal 1971; Beal 1981; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Goodwin 2022; Gray 2001; Hardwick 1982; Holdcroft 1999; Kunzel 1997; Pot 1974), North America (Arnold 1956; Ast 1951; Brown 1965; Tessier 1987), South America (Adriasola 1959), Australia (Blinkhorn 2015), and Asia (Guo 1984; Kim 2019; Loh 1996).

Studies evaluated dental caries in a sample of children in both intervention and control populations. Only three studies followed the same participants over time (Goodwin 2022; Hardwick 1982; Pot 1974). All other studies evaluated specific age groups during a baseline measurement and then, using a different sample of participants in the same specific age groups, at a later follow-up. These studies cannot be used to establish change over time, but rather change at a group or population level. Except for Pot 1974, participants in all studies evaluating the effects of the initiation of a CWF programme were aged from three to 16 years, and were mostly recruited from schools. In Pot 1974, which involved a 20-year follow-up period and followed up the same sample of study participants, adults and children were included in assessments (aged five to 55 years at baseline measurement).

In the intervention groups, in which populations were exposed to fluoridated water, reported concentrations of fluoride ranged from 0.6 ppm to 1.2 ppm; however, most studies reported the concentration of fluoride to be 1 ppm. In studies with incomplete reporting of fluoride concentration, we classed descriptions of 'high' or 'fluoridated' as the intervention group and 'low' or 'non-fluoridated' as the control group.

Measures of dental caries reported in the included studies were: decayed, missing and filled primary teeth (dmft); decayed, missing and filled permanent teeth (DMFT); decayed, missing and filled surfaces in permanent teeth (DMFS); and the proportion of caries-free children (primary or permanent dentition). The period of time between baseline and final measurement ranged from two to 20 years.

Four studies reported disparities in their study populations (Beal 1971; Goodwin 2022; Gray 2001; Holdcroft 1999). These studies were all conducted in the UK and assessed caries outcomes in different socioeconomic groups. The methods used to categorise socioeconomic status (SES) differed between studies, using area descriptive measures of "poor" or "industrial" (Beal 1971), scores according to Jarman 1984 (Gray 2001; Holdcroft 1999), or Index of Multiple Deprivation scores (Goodwin 2022). Caries measures reported in these studies according to socioeconomic status were: decayed, extracted and filled primary teeth (deft; Beal 1971), dmft (Gray 2001; Goodwin 2022; Holdcroft 1999), DMFT (Goodwin 2022), and percentage of caries-free children (Beal 1971; Goodwin 2022; Gray 2001).

Five studies were funded by research grants from research organisations, health authorities and government organisations (Beal 1971; Blinkhorn 2015; Booth 1991; Goodwin 2022; Kunzel 1997); we assumed no conflicts of interest regarding these funding sources. One study was funded in collaboration with members of the "pro-fluoridation committee" (Adriasola 1959), while the other studies did not state their funding sources.

We contacted the authors of two studies for further information and both responded: we contacted authors of Blinkhorn 2015 for the original review, and Goodwin 2022 for this update.

#### Cessation of water fluoridation

One study, conducted in Canada, focused on the effect of cessation of fluoridation on caries (Maupome 2001). In this prospective controlled before-and-after study, the artificial fluoridation of water was stopped in one area of British Columbia, Canada; in the control area, artificial fluoridation of water continued. The concentration of fluoride in the control area was not stated but was described as "optimal". Caries were measured in a sample of children (school grades 2 and 3, and 8 and 9) before cessation of water fluoridation and after three years in both the intervention and control areas; a different sample of children of the same ages were used at each time point. In this study, caries were measured as DMFS. Disparities in caries between different population groups were not reported.

Maupome 2001 was funded by a research grant; we assumed no conflicts of interest regarding this funding source.

### Evaluation of the association of water fluoridation (artificial or natural) with dental fluorosis

In this update, we did not search for new studies or update the evidence for this review objective. Here, we summarise studies as previously reported in Iheozor-Ejiofor 2015.

In Iheozor-Ejiofor 2015, we included 135 eligible studies that used observational methods to collect fluorosis data in populations that had artificial or natural concentrations of fluoride in their water. Studies 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 studies reported sufficient data for inclusion in the analysis for fluorosis of aesthetic concern, and 90 studies were included in the analysis for all severities of dental fluorosis. The remaining studies reported insufficient data for inclusion in the analysis, typically because of failure to indicate water fluoride concentration in the study areas or reporting inappropriate measures 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 Fluorosis 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, Thylstrup and Fejerskov Index (TFI), Tooth Surface Index of Fluorosis (TSIF) and the Developmental Defects of Enamel (DDE) were reported in 41%, 19%, 10% and 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.

In addition to reporting dental fluorosis, five studies also reported other adverse effects associated with water fluoridation (Alarcon-Herrera 2001; Chen 1993; Jolly 1971; Wang 2012; Wenzel 1982). Where stated, adverse effects were measured using radiographs or the diagnostic criteria of endemic skeletal fluorosis.

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; we assumed no conflicts of interest regarding these funding sources. 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).

## Excluded studies

We excluded nine studies in this updated review (see Characteristics of excluded studies). Most studies did not include an appropriate comparison group with a non-fluoridated population or report caries data according to fluoridation status, and were therefore not eligible for this review (Armfield 2013; Do 2014; Hawew 1996; Kämppi 2013; Koh 2015; Zander 2013). We excluded two studies because caries measurements were not taken within three years of the cessation of a fluoridation programme (Lee 2015; McLaren 2022). In the previous version of the review, we had listed Wang 2014 as 'awaiting classification'. We were unable to source the full text of the publication in this update, and we have therefore now excluded this study.

For studies excluded in the previous version of this review, see Iheozor-Ejiofor 2015.

# Risk of bias in included studies

## Evaluation of the effects of initiation or cessation of community water fluoridation on dental caries

ROBINS-I assessments were the same for all results within each study; therefore, we present only one summary assessment per study. See Table 1 for details of the risk of bias assessment for caries prevention studies.

Of the 22 studies, we judged 10 studies to be at critical risk of bias because they did not report any attempt to control for socioeconomic status (prespecified as an important confounding factor for the intervention-outcome relationship) (Arnold 1956; Ast 1951; Beal 1971; Brown 1965; Gray 2001; Guo 1984; Kim 2019; Kunzel 1997; Loh 1996; Pot 1974). Because we judged these studies to be at critical risk of bias, we undertook no further assessment.

We fully assessed 11 studies with the ROBINS-I tool. We rated 10 studies to be at serious risk of bias (Adriasola 1959; Backer-Dirks 1961; Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Hardwick 1982; Maupome 2001; Tessier 1987), and one study to be at moderate risk of bias (Goodwin 2022). It was not possible to fully assess the risk of bias in the remaining study as we were unable to access the original study report (Holdcroft 1999). However, based on the information available in McDonagh 2000, it was possible to assess the domain of risk of bias due to missing data; therefore, we judged this study to be at serious risk of bias overall. It is unclear from the studies whether the bias would overestimate or underestimate the effect.

### Risk of bias due to confounding

We considered that socioeconomic status was the only important confounding factor relevant for this intervention. We judged studies to be at low risk for this domain if there was an attempt to control for socioeconomic status by design (i.e. matching test and control areas for socioeconomic status) and we considered that socioeconomic status was measured in a valid and reliable way. We judged only two studies to be at low risk of bias for this domain, as they reported detailed data for socioeconomic status of the populations involved in the studies (Blinkhorn 2015; Goodwin 2022). Where studies reported that socioeconomic status had been controlled for by design but there was less assurance of the accuracy of the data related to socioeconomic status (i.e. approximate population level data were provided), we judged studies to be at moderate risk of bias for this domain (Adriasola 1959; Hardwick 1982; Maupome 2001; Tessier 1987). Five studies were at serious risk of bias; for these, study authors reported that the populations being compared were comparable in terms of socioeconomic status, but they provided no data or further assurance (Backer-Dirks 1961; Beal 1981; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969).

### Risk of bias in classification of interventions

We judged all studies that underwent full assessment to be at low risk of bias with regard to classification of interventions.

### Risk of bias in selection of participants into the study (or into the analysis)

We judged all but one of the studies that underwent full assessment to be at low risk of bias with regard to selection of participants. We judged Maupome 2001 to be at moderate risk of bias due to baseline imbalance with regard to caries measures.

### Risk of bias due to deviations from intended interventions

We judged all studies that underwent full assessment to be at low risk of bias with regard to deviations from the intended intervention.

### Risk of bias due to missing data

Ten of the included studies were at serious risk of bias due to missing data (Adriasola 1959; Backer-Dirks 1961; Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Scotland 1969; Hardwick 1982; Holdcroft 1999; Maupome 2001; Tessier 1987). Although we were not able to fully assess Holdcroft 1999 for risk of bias due to the report being unavailable, we were able to assess this domain as being at serious risk of bias based on the information reported in McDonagh 2000. We judged DHSS Wales 1969 to be at moderate risk of bias due to missing data, and we judged Goodwin 2022 to be at low risk of bias due to missing data.

### Risk of bias arising from measurement of the outcome

We judged 10 of the studies that underwent full assessment to be at moderate risk of bias arising from measurement of the outcome (Adriasola 1959; Backer-Dirks 1961; Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969; Goodwin 2022; Maupome 2001; Tessier 1987). This was largely due to the practical difficulties involved in blind examination of children owing to the nature of the intervention. However, in Hardwick 1982, the study team had arranged to examine the children involved in the study in a central facility where children from fluoridated and non-fluoridated areas were mixed, such that examiners could not determine where they resided. We judged this study to be at low risk of bias for this domain.

### Risk of bias in selection of the reported result

We judged all studies that underwent full assessment to be at low risk of bias with regard to selection of reported results.

### Evaluation of the association of water fluoridation (artificial or natural) with dental fluorosis

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

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

## Effects of interventions

We describe the results of our review according to our review objectives. We did not include studies assessed at critical risk of bias in the primary analysis. Of the 12 studies included in the primary analysis, seven were conducted after 1975 (Beal 1981; Blinkhorn 2015; Goodwin 2022; Hardwick 1982; Holdcroft 1999; Maupome 2001; Tessier 1987); these were conducted in multiple locations across the UK, North America and Australia.

### Evaluation of the effects of initiation or cessation of community water fluoridation for the prevention of dental caries

#### Initiation of water fluoridation

See Summary of findings table 1.

Twenty-one studies met the inclusion criteria, evaluating the effects of initiation of community water fluoridation. All except Pot 1974 included children and adolescents. Four studies provided insufficient information to be included in a meta-analysis: one study reported data on caries by tooth surface but no overall measure of caries (Backer-Dirks 1961); one study provided data on edentulous (i.e. toothless) individuals only (Pot 1974); and two studies did not report the number of participants examined (Holdcroft 1999; Loh 1996).

The results of the studies reporting the caries primary outcomes are presented in forest plots, stratified according to when they were conducted (those conducted after 1975 (n = 8; Guo 1984 commenced in 1971, but final analysis occurred in 1981) and those conducted in 1975 or before (n = 13)). Studies assessed at critical risk of bias were not included in the primary analysis that follows.

Four studies reported data according to socioeconomic status. We assessed two of these studies to be at critical risk of bias and therefore did not further analyse the data for disparities in these studies (Beal 1971; Gray 2001). In another study, data for disparities were reported without the number of participants (Holdcroft 1999). For completeness, we include the available data for these three studies in Appendix 5. We included disparities findings for the remaining study alongside data for the relevant outcome (Goodwin 2022).

##### Change in the number of decayed, missing or filled primary teeth (dmft)

Seven studies, with data from 17,230 participants, reported data for dmft; six had an overall serious risk of bias (Adriasola 1959; Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969), and one, moderate risk of bias overall (Goodwin 2022). In these studies, final follow-up data were collected between three and 12 years after the initiation of water fluoridation. We did not include in our primary analysis other studies with available data because we judged them to have an overall critical risk of bias (Arnold 1956; Beal 1971; Guo 1984; Kunzel 1997); see results of sensitivity analysis below.

There were significant subgroup differences between studies conducted after 1975 and conducted in 1975 or earlier ($Chi^2$ = 57.81, degrees of freedom (df) = 1; P < 0.001, $I^2$ = 98%). We undertook no overall pooling.

It should be noted that a positive value represents a greater reduction in mean dmft from baseline to follow-up in the water fluoridation group; a negative value represents a greater reduction in mean dmft from baseline to follow-up in the non-fluoridated group.

###### Studies conducted after 1975

Two studies were conducted after 1975, with baseline data collection in 2008 (Blinkhorn 2015) and 2013 (Goodwin 2022).

We calculated the change in mean dmft from baseline to follow-up for the fluoridated and the non-fluoridated/low-fluoridated groups. We noted that the mean dmft decreased over time (baseline to follow-up) in both groups (Table 2). Using these data, the difference in the change in mean dmft between groups shows that initiation of water fluoridation may lead to a slightly greater reduction in dmft (mean difference (MD) 0.24, 95% confidence interval (CI) -0.03 to 0.52; P = 0.09, $I^2$ = 26%; 2 studies, 2908 participants (average n); low-certainty evidence; Analysis 1.1). We downgraded the certainty of the evidence by only one level for risk of bias, as both studies were at low risk of bias for confounding and selection bias. We also downgraded by one level due to imprecision.

Goodwin 2022 reported adjusted and unadjusted data. We used the unadjusted data from this study in Analysis 1.1, due to the variation in the analytical approach for dmft. For completeness, we report the adjusted data in Appendix 6. Goodwin 2022 also reported disparities and analysed these data in order to determine whether there was an effect on dmft reduction. In this study, there was no evidence that deprivation influenced the relationship between water fluoridation and the severity of caries (as measured by dmft counts).

At the baseline measurement, the mean dmft in the non-/low-fluoridated areas ranged from 1.18 to 2.09 (averaged across ages per study).

#### Studies conducted in 1975 or earlier

Five studies were conducted (or reported data from) 1975 or earlier (Adriasola 1959; Beal 1981; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969).

We calculated the change in mean dmft from baseline to follow-up for the fluoridated and the non-fluoridated/low-fluoridated groups. We noted that the mean dmft decreased over time (baseline to follow-up) in both groups (Table 2). Using these data, the difference in the change in mean dmft between groups shows that initiation of water fluoridation may reduce dmft but the applicability of the evidence to a contemporary setting is very uncertain (MD 2.10, 95% CI 1.71 to 2.49; P < 0.001, $I^2$ = 44%; 5 studies, 5709 participants (average n); very low-certainty evidence; Analysis 1.1). We downgraded the evidence by two levels due to the inherent risk of bias in the design of the included studies, and further downgraded by one level due to indirectness (applicability) of evidence (findings from studies conducted prior to 1975 may not be applicable to contemporary settings).

At the baseline measurement, the mean dmft in the non-/low-fluoridated areas ranged from 4.76 to 8.1 (averaged across ages per study).

### Change in the number of decayed, missing or filled permanent teeth (DMFT)

Seven studies, with data from 15,418 participants, reported data for DMFT; six had an overall serious risk of bias (Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Wales 1969; Hardwick 1982; Tessier 1987), and one, an overall moderate risk of bias (Goodwin 2022). In these studies, final follow-up data were collected between four and 11 years after the initiation of water fluoridation. We did not include in our primary analysis other studies with available data because we judged them to have an overall critical risk of bias (Arnold 1956; Brown 1965; Guo 1984; Kim 2019; Kunzel 1997); see results of sensitivity analysis below.

The Blinkhorn 2015 data for DMFT that we used in the analysis was unpublished and supplied by the study authors whilst we prepared the previous version of this review.

There were significant subgroup differences between studies conducted post-1975 and those conducted in 1975 or earlier ($Chi^2$ = 5.60, df = 1; P = 0.02, $I^2$ = 82%). We undertook no overall pooling.

It should be noted that a positive value represents a greater reduction in mean DMFT from baseline to follow-up in the water fluoridation group; a negative value represents a greater reduction in mean DMFT from baseline to follow-up in the non-fluoridated group.

#### Studies conducted after 1975

Four studies were conducted after 1975 (Blinkhorn 2015; Goodwin 2022; Hardwick 1982; Tessier 1987). Two studies were prospective cohort studies following the same children over time (Goodwin 2022; Hardwick 1982). We used data as reported in the study reports for the caries increments from these studies, which we entered into the meta-analysis as negative values. The mean caries increments in these studies were lower for the fluoridated group than the non-fluoridated/low-fluoridated group. For the other two studies (Blinkhorn 2015; Tessier 1987), we calculated the change in mean DMFT from baseline to follow-up for the fluoridated and the non-fluoridated/low-fluoridated groups. In Tessier 1987, we noted a greater change in DMFT in the fluoridated group. However, in Blinkhorn 2015, the reduction was greater in the non-fluoridated/low-fluoridated group. Goodwin 2022 reported adjusted and unadjusted data. We used the unadjusted data for this study in Analysis 1.2 due to a different estimate of effect being presented for adjusted data (i.e. incidence rate ratio rather than mean difference). For completeness, we report the adjusted data in Appendix 6.

Using these data, the difference in the change in mean DMFT between groups shows that initiation of water fluoridation may lead to a slightly greater reduction in DMFT, but the evidence is very uncertain (MD 0.27, 95% CI -0.11 to 0.66; P = 0.16, $I^2$ = 83%; 4 studies, 2856 participants (average n); very low-certainty evidence; Analysis 1.2). We downgraded by two levels for the inherent risks of bias in the design of some of the included studies, and by one level due to considerable statistical heterogeneity and imprecision. Although we did not further explore the statistical heterogeneity in this effect estimate, we note that the direction of effect in Blinkhorn 2015 differed from the other studies in this meta-analysis.

Goodwin 2022 reported disparities and analysed their data in order to determine whether there was an effect on DMFT reduction. In this study, there was no evidence that deprivation influenced the relationship between water fluoridation and the severity of caries (as measured by DMFT counts).

At the baseline measurement, the mean DMFT in the non-/low-fluoridated areas ranged from 0.99 to 8.23 (averaged across ages per study), where reported.

#### Studies conducted in 1975 or earlier

Three studies were conducted pre-1975 (Beal 1981; DHSS England 1969; DHSS Wales 1969).

We calculated the change in mean dmft from baseline to follow-up for the fluoridated and the non-fluoridated/low-fluoridated groups (data for each age group in each included study are presented in Table 3). We noted that the mean DMFT decreased over time in the fluoridated and non-fluoridated/low-fluoridated groups in Beal 1981 and DHSS England 1969. However, in DHSS Wales 1969, the mean DMFT decreased in the fluoridated group but increased in the non-fluoridated/low-fluoridated group (Table 3). The difference in the change in mean DMFT between groups shows that initiation of water fluoridation may reduce DMFT but the applicability of the evidence to a contemporary setting is very uncertain (MD 1.00, 95% CI 0.54 to 1.47; P < 0.001, $I^2$ = 80%; 3 studies, 5623 participants (average n); very low-certainty evidence; Analysis 1.2). We downgraded the certainty of the evidence by two levels due to the inherent risk of bias in the included studies, and one level due to indirectness (applicability) of evidence (findings from studies conducted prior to 1975 may not be applicable to contemporary settings). We also note that this effect estimate included considerable statistical heterogeneity.

At the baseline measurement, the mean DMFT in the non-/low-fluoridated areas ranged from 3.01 to 4.03 (averaged across ages per study).

#### Change in the number of dmfs

There were no data for dmfs reported in any of the included studies (i.e. both those conducted in 1975 or earlier, or after 1975).

#### Change in the number of DMFS

##### Studies conducted after 1975

One study, with data from 343 participants, reported data on DMFS increment (Hardwick 1982). We judged this study to be at serious risk of bias.

A smaller caries increment was observed for the water fluoridation group (6.73) than for the control group (9.19). Initiation of community water fluoridation may lead to a lower DMFS increment, but the evidence is very uncertain (MD 2.46, 95% CI 1.11 to 3.81; 1 study, 343 participants; very low-certainty evidence; Analysis 1.3). We downgraded the certainty of the evidence by two levels due to the inherent risk of bias in the design of the included study, and one level for imprecision owing to the very small sample size.

##### Studies conducted in 1975 or earlier

There were no data for DMFS reported in the included studies conducted in 1975 or earlier.

#### Change in the proportion of caries-free participants (primary dentition)

Seven studies, with data from 19,767 children, reported data for the change in the proportion of children that were caries-free in their primary dentition. Six studies had an overall serious risk of bias (Adriasola 1959; Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969), and one an overall moderate risk of bias (Goodwin 2022). In these studies, final follow-up data were collected between three and 11 years after the initiation of water fluoridation. We did not include in our primary analysis other studies with available data because we judged them to have an overall critical risk of bias (Ast 1951; Beal 1971; Gray 2001; Guo 1984; Kunzel 1997); see results of sensitivity analysis below.

There were significant subgroup differences between studies conducted after 1975 and those conducted in 1975 or earlier ($Chi^2$ = 18.03, df = 1; P < 0.001, $I^2$ = 95%). We undertook no overall pooling.

##### Studies conducted after 1975

Two studies were conducted after 1975 (Blinkhorn 2015; Goodwin 2022), one of which was a prospective cohort study following the same children over time (Goodwin 2022).

We calculated the risk difference between baseline and follow-up measurements separately for the fluoridated water and control groups, using raw data in Table 4, and we pooled summary estimates across age groups in each study (not shown). We noted that the proportion of caries-free children increased over time in both the fluoridated and non-fluoridated/low-fluoridated groups.

Using these pooled summary estimates, the difference in the change in the proportion of caries-free children between groups shows that the initiation of water fluoridation may lead to a slightly greater increase in the proportion of caries-free children (MD -0.04, 95% CI -0.09 to 0.01; P = 0.12, $I^2$ = 0%; 2 studies, 2908 participants (average n); low-certainty evidence; Analysis 1.4). This absolute increase of 0.04 in the proportion of caries-free children in fluoridated areas may be considered a small but important effect. We downgraded the certainty of the evidence by only one level for risk of bias as both studies were at low risk for confounding and selection bias. We also downgraded by one level due to imprecision.

Goodwin 2022 reported adjusted and unadjusted data. We used the unadjusted data from this study in Analysis 1.4 due to the variation in the analytical approach for primary dentition. For completeness, we report the adjusted data in Appendix 6. Goodwin 2022 also reported disparities and analysed these data in order to determine whether there was an effect on caries. In this study, there was no evidence that deprivation influenced the relationship between water fluoridation and the presence or absence of caries in primary dentition.

At the baseline measurement, the proportion of caries-free children in the non-fluoridated/low-fluoridated areas ranged from 0.49 to 0.68.

#### Studies conducted in 1975 or earlier

Five studies were conducted in 1975 or earlier (Adriasola 1959; Beal 1981; DHSS England 1969; DHSS Scotland 1969; DHSS Wales 1969).

We calculated the risk difference between baseline and follow-up measurements separately for the fluoridated water and control groups, using raw data in Table 4, and we pooled summary estimates across age groups in each study (not shown). We noted that the proportion of caries-free children increased over time or remained similar in both the fluoridated and non-fluoridated/low-fluoridated groups.

Using these pooled summary estimates, the difference in the change in the proportion of caries-free children between groups shows that the initiation of water fluoridation may increase the proportion of caries-free children, but the applicability of the evidence to a contemporary setting is very uncertain (MD -0.17, 95% CI -0.20 to -0.13; P < 0.001, $I^2$ = 13%; 5 studies, 6278 participants (average n); very low-certainty evidence; Analysis 1.4). We downgraded the certainty of the evidence by two levels due to the inherent risk of bias in the design of the included studies, and by one level due to indirectness (applicability) of evidence (findings from studies conducted prior to 1975 may not be applicable to contemporary settings).

At the baseline measurement, the proportion of caries-free children in the non-fluoridated/low-fluoridated areas ranged from 0.08 to 0.20.

#### Change in the proportion of caries-free participants (permanent dentition)

Six studies, with data from 17,336 participants, reported data for the change in the proportion of children that were caries-free in their permanent dentition. Five studies had an overall serious risk of bias (Adriasola 1959; Beal 1981; Blinkhorn 2015; DHSS England 1969; DHSS Wales 1969), and one an overall moderate risk (Goodwin 2022). In these studies, final follow-up data were collected between three and 11 years after the initiation of water fluoridation. We did not include in our primary analysis other studies with available data because we judged them to have an overall critical risk of bias (Brown 1965; Guo 1984; Kunzel 1997); see results of sensitivity analysis below.

There were no significant subgroup differences between studies conducted post-1975 and those conducted in 1975 or earlier ($Chi^2$ = 0.49, df = 1; P = 0.48, $I^2$ = 0%). We undertook no overall pooling.

#### Studies conducted after 1975

Two studies were conducted after 1975 (Blinkhorn 2015; Goodwin 2022), one of which was a prospective cohort study following the same children over time (Goodwin 2022).

We calculated the risk difference between baseline and follow-up measurements separately for the fluoridated water and control groups, using data in Table 5, and we pooled summary estimates across age groups in each study (not shown). We noted that the proportion of caries-free children increased over time in both the fluoridated and non-fluoridated/low-fluoridated groups.

Using these pooled summary estimates, the difference in the change in the proportion of caries-free children between groups shows that the initiation of water fluoridation may lead to a slightly greater increase in the proportion of caries-free children (MD -0.03, 95% CI -0.07 to 0.01; P = 0.14, $I^2$ = 0%; 2 studies, 2348 participants (average n); low-certainty evidence; Analysis 1.5). This absolute increase of 0.03 in the proportion of caries-free children in fluoridated areas may be considered a small but important effect. We downgraded the certainty of the evidence by only one level for risk of bias, as both studies were at low risk of bias for confounding and selection bias. We also downgraded by one level due to imprecision.

Goodwin 2022 reported adjusted and unadjusted data. We used unadjusted data in Analysis 1.5 due to a different outcome being presented for the adjusted data. For completeness, we report the adjusted data in Appendix 6. Goodwin 2022 also reported disparities and analysed these data in order to determine whether there was an effect on caries. In this study, there was no evidence that deprivation influenced the relationship between water fluoridation and the presence or absence of caries in permanent dentition.

At the baseline measurement, the proportion of caries-free children in the non-fluoridated/low-fluoridated areas was 0.62, where reported.

#### Studies conducted in 1975 or earlier

Four studies were conducted (or used data from) 1975 or earlier (Adriasola 1959; Beal 1981; DHSS England 1969; DHSS Wales 1969).

We calculated the risk difference between baseline and follow-up measurements separately for the fluoridated water and control groups, using raw data in Table 5, and we pooled summary estimates across age groups in each study (not shown).

Using these pooled summary estimates, the difference in the change in the proportion of caries-free children between groups shows that the initiation of water fluoridation may increase the proportion of caries-free children, but the applicability of the evidence to a contemporary setting is very uncertain (MD -0.06, 95% CI -0.14 to 0.02; P = 0.13, $I^2$ = 93%; 4 studies, 6219 participants (average n); very low-certainty evidence; Analysis 1.5). We downgraded the certainty of the evidence by two levels for the inherent risk of bias in the design of all included studies, and by one level due to indirectness (applicability) of evidence (findings from studies conducted prior to 1975 may not be applicable to contemporary settings). We also noted that this effect estimate included considerable statistical heterogeneity.

At the baseline measurement, the proportion of caries-free children in the non-fluoridated/low-fluoridated areas ranged from 0.05 to 0.12.

#### Adverse effects

Arnold 1956 reported a small increase in the number of children with mild fluorosis: "0.24 percent in 1944; 0.36 percent in 1954". Brown 1965 reported no cases of "unsightly mottling". No other studies evaluating the effects of initiation of a community water fluoridation programme reported outcome data for fluorosis or any other adverse effect. We judged the certainty of the evidence to be very low. We downgraded by two levels due to the inherent risk of bias in the design of the included studies, and one level for indirectness (the available evidence came from studies conducted prior to 1975 and may not be applicable to contemporary settings). In addition, we note that this evidence came from only two studies (a small number relative to the overall number of studies in this comparison), and that both of these studies had an overall critical risk of bias.

### Sensitivity analyses – caries outcomes

In sensitivity analyses, we: included studies at critical risk of bias in meta-analyses; used an alternative analytical approach for managing data from Goodwin 2022; and excluded studies in which we had imputed missing standard deviations (SDs). Although these sensitivity analyses sometimes increased or decreased the size of the effect, we did not consider the results of the sensitivity analyses to introduce any important changes to our interpretation of the review findings. We noted that the effect estimate was no longer imprecise when we used a different analytical approach to manage dmft data in Goodwin 2022. The results of all sensitivity analyses are summarised in Appendix 7.

### Cessation of water fluoridation

One study, with data for 2994 participants, evaluated the effects of cessation of water fluoridation on DMFS during a three-year period (Maupome 2001). The study was conducted in a population with "generally low caries experience, living in an affluent setting with widely accessible dental services". We assessed the overall risk of bias in this study to be serious.

This study reported no data for change in the number of dmft or DMFT, change in the number of dmfs, proportion of caries-free participants (in either dentition type), or adverse effects. In addition, the study did not include any data regarding disparities across social class.

See Summary of findings table 2.

#### Change in the number of DMFS

The study authors reported that "Caries incidence (assessed in 2994 life-long residents, grades 5, 6, 11, 12) expressed in terms of D1D2MFS was not different between the still-fluoridating and fluoridation-ended communities" (Maupome 2001). However, it should be noted that there was a baseline imbalance in D1D2MFS between the two groups. The results of the study did not demonstrate an increase in caries in the children in the fluoridation-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. We did not analyse these data in the review owing to the baseline imbalance in D1D2MFS between the groups. We downgraded the certainty of the evidence by two levels due to the inherent risk of bias in the design of the included studies, and by one level due to imprecision.

## Evaluation of the association of water fluoridation (artificial or natural) with dental fluorosis

We did not update the evidence for dental fluorosis in this updated review. Here, we summarise the results of findings for this objective as previously described in Iheozor-Ejiofor 2015. 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 8).

See Summary of findings table 3.

### Dental fluorosis of 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 (SD) of 0.80 (0.90) ppm.

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. We used the reported fluoride level as a predictor rather than the log of reported fluoride exposure. We then centred this predictor 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; a higher prevalence of dental fluorosis is associated with increased fluoride exposure (odds

ratio (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 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 2).

The marginal probabilities of dental fluorosis of aesthetic concern at different fluoride levels are given below. We judged the certainty of the evidence for dental fluorosis of aesthetic concern to be low. Because of the risk of bias in these study designs, the certainty of the evidence starts at low; we did not further downgrade the evidence. From visual observation of Figure 2, we noted the possibility of inconsistency.

| 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 (SD) of 0.85 (1.03) ppm. 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 level of 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 exposure.

The relationship between the log odds of dental fluorosis and fluoride level and log fluoride level were both approximately linear. Consequently, we used the reported fluoride exposure as a predictor rather than the log of reported fluoride exposure. We then centred this predictor 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 3).

The marginal probabilities of any dental fluorosis are presented in the table below. We judged the certainty of the evidence for dental fluorosis of any level to be low. Because of the risk of bias in these study designs, the certainty of the evidence starts at low; we did not further downgrade the evidence. From visual observation of Figure 3, we noted the possibility of inconsistency.

| 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 (SD) fluoride level of 1.28 (1.11) ppm. There was little change in the pooled estimates when we included all fluoride levels 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 the source of fluoride and its interaction with fluoride concentration by including them as fixed covariates in the models above. We classified the source of fluoride as natural or artificial. We excluded from the analysis studies that reported mixed sources of fluoridation, or where the source of fluoridation was not reported. We carried out separate analyses for the outcomes of fluorosis of aesthetic concern and any level of fluorosis, and for studies reporting fluoride concentrations restricted to 5 ppm or less and concentrations at any level.

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 adverse effects

Only five of 135 studies reported other adverse effects. These adverse effects were: skeletal fluorosis (Chen 1993; Jolly 1971; Wang 2012), bone fracture (Alarcon-Herrera 2001), and skeletal maturity (Wenzel 1982). Data were available for participants aged between 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 Jolly 1971 did not include the number of participants. Fluoride concentration in all studies ranged from less than 0.2 ppm to 14 ppm. All studies were at high risk of bias. We did not analyse the data from these studies, and we were unable to draw conclusions from the available data; we present the individual study data in Table 6. We judged the certainty of the evidence for other adverse effects to be very low. Because of the risk of bias in these study designs, the certainty of the evidence starts at low certainty. We also downgraded by one level for indirectness because very high concentrations of natural fluoride in some groups were unlikely to be applicable to all settings.

# Discussion

## Summary of main results

We included 157 non-randomised studies in the review. These studies evaluated two objectives: the effect of initiation or cessation of a water fluoridation programme on dental caries, and the association of a water fluoridation programme with dental fluorosis. We did not update the evidence for the association of water fluoridation with dental fluorosis, and the results reported here are the same as those described in Iheozor-Ejiofor 2015.

For our primary objective, we reported data separately according to whether studies evaluated the initiation or the cessation of a community water fluoridation programme.

We included 21 studies that evaluated the initiation of water fluoridation. The contemporary evidence, which was derived from studies conducted after 1975, was mostly of low certainty, and came from studies conducted in multiple locations across the UK, North America and Australia. We found that water fluoridation may lead to a slightly greater reduction in decayed, missing or filled primary teeth (dmft). Although pooled data from contemporary studies also indicated a slightly greater reduction in decayed, missing or filled teeth or surfaces in the permanent dentition (DMFT/DMFS), we were very uncertain of this effect (because of very low-certainty evidence).

Water fluoridation may lead to a slightly greater increase in change in the proportion of children who are caries-free (in their primary dentition and permanent dentition) in favour of water fluoridation. The difference in the change in the proportion of caries-free children in areas with fluoridated water may be considered a small but important effect.

Other evidence for the initiation of water fluoridation came from studies conducted before 1975, and although the effect estimates indicated a positive benefit of water fluoridation in caries reduction, we judged this evidence to be of very low certainty. These very low-certainty judgements were partly informed by the limited applicability of the evidence specifically to a contemporary environment, with ready access to fluoridated toothpastes and other caries prevention strategies, in contrast to settings that continue to have poor access to these resources.

Only one study, in Canada, evaluated the cessation of a water fluoridation programme, and only had data available for one of our review outcomes. Although this study found no difference in the caries incidence measured in terms of DMFS between the still-fluoridating and fluoridation-ended communities, we were very uncertain of this effect (because of very low-certainty evidence).

We did not update the evidence for the association of water fluoridation with dental fluorosis in this review. As previously reported, we found low-certainty evidence of a positive association with fluoridated water and dental fluorosis of aesthetic concern as well as dental fluorosis of any level of severity.

### Disparities in dental caries

Only four studies reported dental caries according to socioeconomic group disparities. We judged the data for two studies to be at a critical risk of bias, and a third study reported insufficient data for us to report disparities meaningfully. One recent study, with socioeconomic status data measured according to the Index of Multiple Deprivation, found that there was no evidence that deprivation influenced the relationship between water exposure and caries status (as measured by dmft/DMFT counts or proportion of caries-free participants).

## Overall completeness and applicability of evidence

Despite the scope of the review including both adults and children, there was no available evidence on the effect of initiation/cessation of water fluoridation on caries outcomes in adults. Therefore, the evidence meeting the review's inclusion criteria pertains to caries in children only.

Our primary analysis focuses on data from studies conducted post-1975 with the most recent studies being conducted in 2015 and onwards. Approximately 60% of the studies that evaluated the initiation of water fluoridation were conducted in 1975 or earlier. The applicability of 50- to 75-year-old evidence to today's lifestyles 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). For example, in many parts of the world, people consume more industrially-processed foods, and prepare and cook less food at 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, through beverages and foods prepared with tap water, to provide a benefit to their oral health.

In public health research, some have argued that a 'halo effect' may reduce the expected effect size of interventions in studies that compare effects in populations in two geographic areas in close proximity. In relation to community water fluoridation (CWF), the halo effect refers to the diffusion of fluoride beyond the geographical locations receiving CWF to those areas not receiving CWF; for example, when food and beverages are produced in an area with fluoridated water and then transported and consumed in non-fluoridated areas, and vice versa. In the UK, approximately 46% of the food consumed is imported (DEFRA 2021); 'home-grown' food is also transported widely within the UK. We are unaware of any evidence to quantify the potential impact of the halo effect, or to suggest this is greater in areas evaluated that are in close proximity. Similarly, there is little evidence to suggest more recent studies are at greater 'risk' of the halo effect than older studies.

Globally, caries levels have been decreasing, although there is variation by World Health Organization region (Table 7). Figure 4 shows the estimated prevalence of untreated caries of permanent teeth in people aged five years and older. 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, 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 a relatively high distribution of water fluoridation and moderate caries levels (e.g. Brazil).

In countries where the widespread use of fluoride toothpastes has increased 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), the benefit of water fluoridation may be diluted.

Most research evaluating water fluoridation and its association with dental caries has been undertaken using single time point, cross-sectional studies with concurrent control. There have been concerns regarding the exclusion of these studies from the previous version of this review (Rugg-Gunn 2016). We did not include these studies in our review because they do not allow a measure of change in caries status over time and therefore do not address the review's research question with regard to evaluating the initiation/cessation of water fluoridation. However, the single time point studies do provide context in terms of demonstrating the association between water fluoridation

and dental caries and may therefore be helpful in terms of interpreting the wider picture beyond the scope of the present review question. For this reason, we collected data from single time point studies found during our database searches and used these data to plot the mean difference in caries outcomes between populations with and without fluoridated water. This task was not part of our formal review process and therefore, we did not use systematic approaches for study identification. In terms of dmft, most identified single time point studies were conducted in the UK. Data from these UK single time point studies, alongside the results of the review, show a clear reduction in the size of effect with regard to caries measures over time (Figure 5), with the most recent single time point studies showing a mean difference of 0.16 to 0.21 dmft between fluoridated and low-fluoridated/non-fluoridated areas (PHE 2014; PHE 2018; PHE 2022). A similar pattern was seen in terms of DMFT (Figure 6). With regard to the difference in proportion of caries-free participants between fluoridated and low-fluoridated/non-fluoridated areas, a smaller effect size was seen in the more recent studies across most countries (Figure 7). Comparison between studies evaluating the effectiveness of CWF and single time point studies evaluating association is not strictly appropriate due to variation in study design and measurement of the caries outcome (point estimate or change over time). However, the findings from the evaluation of the effectiveness of CWF in this review do not contradict the evidence from the contemporary single time point studies.

We did not update the evidence for the association of dental fluorosis in this review. We have no concerns regarding the applicability of the findings for dental fluorosis from our previous review, owing to the large number of included studies across a wide range of settings that provided data for this outcome (Iheozor-Ejiofor 2015).

There was limited reporting of adverse effects, other than dental fluorosis, in the studies included in this review. The broader literature speculates about harms associated with higher levels of fluoride in water (e.g. cancer, lowered intelligence, endocrine dysfunction) (Solanki 2022). However, there has been insufficient evidence to draw conclusions. A recent evidence summary evaluated the impact of fluoridated water on the systemic health of the human population (Lambe 2022). The review found no conclusive evidence for an association between CWF and most conditions evaluated, including bone health, cancer, kidney stones, birth and infant abnormalities, and death rates. The authors acknowledge that the evidence was typically of low quality.

It should be noted that the impact of water fluoridation may be affected by inconsistencies in the delivery of artificially fluoridated water supplies at the desired, optimal dose. An evaluation of long-term variability in artificially and naturally fluoridated water supplies in England reported that artificially fluoridated samples showed wide variation in fluoride dose control: "Mean fluoride concentrations in the artificially fluoridated supplies ranged from 0.53 (SD 0.47) to 0.93 (SD 0.22) mg F/L and were within the optimal range of 0.7-1.0 mg F/L in 27.7%-77.8% of samples" (Moore 2019). This variability in fluoride concentrations in CWF programmes, over time and geography, was confirmed in a subsequent study which called for greater access and collation of fluoride concentration data to allow for "essential monitoring, surveillance and research" (Nyakutsikwa 2022). The challenge of consistent delivery at an optimal concentration is not just confined to the UK. For example, monitoring reports from the USA have also demonstrated variability in dosing outside the target range (Boehmer 2023).

#### Brief economic commentary

Our review did not evaluate the cost-effectiveness of water fluoridation. However, we undertook a brief economic commentary on this topic. From literature searches, we identified 437 reports from which we identified 56 potentially eligible reports. We assessed the full texts of these 56 reports and found 25 eligible reports for 24 studies. For the full details of this search and our summary of the eligible reports, see oralhealth.cochrane.org/our-evidence/brief-economic-commentaries.

In general, across the studies, some clear findings emerge. CWF appears to offer good value for money due to its low per capita intervention delivery costs, potential to reduce caries, even at low magnitudes of effect size, and the related impact on dental treatment costs averted. However, the magnitude of cost-effectiveness (or net cost-savings) is shown to be sensitive to the size of the fluoridated population, the magnitude of water fluoride's effectiveness observed in more recent studies, and the underlying caries risk in the treated population. Therefore, whilst in general water fluoridation appears to offer good value for money, this is context-dependent, and each proposed scheme should be considered on a case-by-case basis according to population size, magnitude of benefit and underlying caries prevalence in the population served.

#### Sustainability of the intervention

When considering the implementation of any intervention, the environmental impact should be considered; promoting oral health and disease prevention is the most impactful route to environmental sustainability in dentistry. Following Cochrane Oral Health policy (https://oralhealth.cochrane.org/about-us/sustainability), we conducted a brief search for healthcare sustainability science research for community water fluoridation using the search strategy in Appendix 9. One review author (SL) screened the results of this search. We identified one life-cycle analysis of water fluoridation (Duane 2022), comparing the environmental impact of community water fluoridation to data for school-based fluoride varnish programmes, supervised toothbrushing or the provision of toothbrushes and toothpaste. The analysis was undertaken for a five-year-old child over a one-year period. The life-cycle analysis model was based on an existing water fluoridation scheme in Ireland and the return on investment measures from PHE 2016 were used to map against the environmental impacts. Water fluoridation was shown to have the lowest environmental impact and the lowest disability-adjusted life-years impact. We note, however, that the PHE 2016 calculations were based on a pooled effect estimate from studies conducted predominantly over 50 years ago and do not consider set-up costs for new initiatives. The applicability of the findings of the life-cycle analysis to other water fluoridation schemes needs consideration; any future life-cycle analysis should include return-on-investment

data from more contemporary studies and include set-up and ongoing monitoring costs. We encourage people to explore other resources on this topic to understand, learn and promote sustainable actions in oral health.

### Certainty of the evidence

We used the GRADE approach to assess the certainty of the evidence within the review. As outlined in the *Cochrane Handbook* (Higgins 2021), all studies assessed using ROBINS-I start with high certainty of evidence when applying GRADE criteria. Typically, we downgraded the body of evidence from the caries studies by two levels due to the inherent risk of bias in non-randomised studies of interventions (NRSI; due to confounding and selection bias). We downgraded evidence from Blinkhorn 2015 and Goodwin 2022 by only one level for risk of bias, as we considered both studies to be at low risk of bias with regard to confounding and selection bias.

In our review protocol (Iheozor-Ejiofor 2013), we stated that we would produce summary of findings tables, applying the GRADE criteria. We have attempted to be transparent in our decisions regarding the downgrading of the certainty of the evidence, and feel our decisions are justified. With regard to the caries outcomes, we judged the certainty of the contemporary evidence (from studies conducted after 1975) to be either low or very low. We downgraded the certainty of the evidence owing to the inherent risks of bias in the designs of included studies, as identified during our risk of bias assessments using ROBINS-I. We downgraded the evidence for imprecision when effect estimates included the possibility of benefit and no benefit (change in the number of dmft and DMFT, and changes in the proportion of caries-free participants with primary and permanent dentition). We also downgraded the evidence for change in the number of DMFT for inconsistency, because the effect estimate included considerable statistical heterogeneity.

We assessed the evidence from studies conducted in 1975 or earlier as being at very low certainty, due to all studies being at serious risk of bias and for concerns regarding the applicability of the evidence to today's societies (see Overall completeness and applicability of evidence). Present day reductions in caries may be of a smaller magnitude in regions with access to other sources of fluoride.

With regard to our second objective (evaluating the association of water fluoridation with dental fluorosis), we deemed the evidence to be stable, and we made no changes to the risk of bias assessment and GRADE assessment in this review. With regard to the fluorosis outcomes, we judged the certainty of the evidence to be low, downgraded due to an overall high risk of bias. We also note inconsistency in the findings due to substantial between-study variation.

We did not downgrade any of the evidence for publication bias. We expected that publication bias was less likely for studies evaluating the initiation and cessation of water fluoridation programmes because these were often large-scale prospective studies. However, we could not rule out the possibility of publication bias in the evidence for dental fluorosis, which was sometimes evaluated in small studies.

## Potential biases in the review process

In this updated review, we conducted a thorough search and independently assessed study eligibility, extracted data and assessed the risk of bias in the included studies before reaching consensus together or with one other review author.

We did not update the evidence for the association of water fluoridation with dental fluorosis, which included data from 90 studies. We reached this decision through discussion with the review team and the wider Cochrane editorial team.

During the review process, we made decisions to classify studies according to thresholds for fluoride concentration, participant age for primary and permanent dentition (if not specified by study authors), and contemporary and early studies. We acknowledge that these cut-offs were arbitrary.

We classified water with a fluoride concentration of 0.4 ppm or less as low- or non-fluoridated, based on a priori clinical judgement, and it is possible that this cut-off might be high for equivalence of non-fluoridation in hot climates. In practice, almost half of the studies evaluating the initiation of a water fluoridation programme did not include the fluoride concentration for the low- or non-fluoridated areas, and in this case, we used the study authors' classification of areas as low- or non-fluoridated. Only one of the 21 studies reported a fluoride concentration greater than 0.2 ppm in the non-fluoridated area (Beal 1981).

When analysing the dental fluorosis data, our primary analysis focused on fluoride concentrations of 5 ppm or less. However, there was little difference in the results obtained when we examined all fluoride concentrations.

As in our earlier review (Iheozor-Ejiofor 2015), we only reported on dmft in children eight years old and younger, which was based on clinical judgement. This cut-off is unlikely to alter the review's findings as very little data were excluded due to this cut-off.

We used a cut-off date of 1975 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 was true in their study populations. We note that the systematic review by Griffin 2007 used a cut-off date of 1979. In this review, we included three studies in the contemporary group with a study duration that included a threshold between 1975 and 1979: in Guo 1984, the change in fluoridation was in 1971, with a final assessment in 1981; in Hardwick 1982, the study was carried out between 1974 and 1978; and in Tessier 1987, the study was carried out between 1978 and 1986. We did not include Guo 1984 in the analysis (because it had an overall critical risk of bias). We did not further explore the impact of including Hardwick 1982 and Tessier 1987 in the analysis of contemporary studies.

We used sensitivity analysis to explore the impact of decisions made during our primary analysis. We imputed the standard deviation (SD) for five studies included in the analysis measuring change in caries (dmft and DMFT). We had not prespecified the decision to impute SDs in the original protocol (Iheozor-Ejiofor 2013), but this decision allowed us to include more data in the analyses. We assessed the impact of this decision through sensitivity analyses, and found that although effect sizes were larger in the contemporary evidence and smaller in the earlier evidence, our overall interpretation of the results was the same.

We undertook a post hoc sensitivity analysis regarding the analytical approach of longitudinal studies. In the primary analysis, we used a controlled before-and-after study design approach for Goodwin 2022. This study also reported dmft caries increment, and we used these data in sensitivity analysis. Using the caries increment from the longitudinal analysis resulted in a very similar pooled effect estimate to the primary analysis, although imprecision in the estimate was no longer a concern using the longitudinal analysis.

## Agreements and disagreements with other studies or reviews

Multiple systematic reviews have explored the effectiveness of water fluoridation programmes or the association between fluoridated water and caries, dental fluorosis and harms, including Griffin 2007, McDonagh 2000, Moynihan 2019, NHMRC 2017, Rugg-Gunn 2012 and Truman 2002. The scope of the reviews and the methods used vary. However, findings across the reviews are broadly consistent with regard to caries and fluorosis. Older studies (conducted in 1975 or earlier) provide consistent evidence that water fluoridation reduced the incidence of dental caries and increased the proportion of caries-free children; contemporary studies conducted after 1975 show smaller effect sizes. There is insufficient/inconsistent evidence from the current review and other reviews with regard to the impact of water fluoridation on disparities in caries (McDonagh 2000; NHMRC 2017).

#### Evaluating the initiation of community water fluoridation programmes for the prevention of dental caries

Whilst the most widely recognised systematic review of water fluoridation remains the York review published in 2000 (McDonagh 2000), it should be recognised that over 80% of the studies in McDonagh 2000 evaluating the initiation of water fluoridation were conducted before 1975. Like the current review, for the evaluation of the initiation or cessation of water fluoridation programmes, McDonagh 2000 included prospective studies comparing at least two populations, one receiving fluoridated water and the other non-fluoridated water, with at least two time points evaluated. A change in the level of fluoride in the water supply of at least one of the study areas had to have occurred within three years of the baseline survey. McDonagh 2000 excluded single time point cross-sectional studies, and did not pool any study data. The mean difference in change in dmft/DMFT and increase in proportion of caries-free children were presented for selected ages/age groups. The 2015 version of this review and the current update differ from the York review in that we did undertake statistical pooling, imputing SDs 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 primary teeth for children aged eight years and younger, and all available data for permanent teeth. The analyses showed mean reductions of 0.24 in dmft and 0.27 in DMFT for studies undertaken post-1975, 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 a reduction in the proportion of caries-free children of −0.05 to an increase of 0.64. The pooled estimate obtained in our review demonstrates an increase in the proportion of caries-free children in the areas with water fluoridation of 0.04 for primary teeth and 0.03 for permanent teeth, based on studies conducted since 1975.

In Truman 2002, five studies with before-and-after measurements showed that starting (or continuing) water fluoridation decreased dental caries experience among children aged four to 17 years by a median of 29.1% during three to 12 years of follow-up. Two studies with before-and-after measurements showed increased dental caries with continuation of water fluoridation; inadequate control of confounding is suggested to be the cause of these inconsistencies. If the studies with negative findings are excluded from the analysis, then starting water fluoridation decreased dental caries experience by a median of 41.2% (range from 14.5% to 110%). If all studies are included, then water fluoridation decreased dental caries experience by a median of 29.1% (range from 66.8% increase to 110% decrease).

The National Health and Medical Research Council (Australia) undertook a comprehensive overview of reviews (NHMRC 2017). It evaluated systematic reviews published between 1 October 2006 and 12 November 2015 which evaluated evidence for the effect of water fluoridation on dental caries. Three systematic reviews were included (Griffin 2007; Iheozor-Ejiofor 2015; Rugg-Gunn 2012). The reviews were assessed using AMSTAR and found to range from high quality (Iheozor-Ejiofor 2015) to low quality (Rugg-Gunn 2012). The overview of reviews supplemented evidence from the three systematic reviews with evidence from 25 primary studies published between 1 October 2006 and 17 November 2015. Evidence statements, based on both the systematic reviews and primary studies, showed consistent evidence that water fluoridation at current Australian levels is associated with a decreased prevalence of dental caries in both primary teeth of children and permanent teeth of children, adolescents and adults (assessed using measures of dmft/DMFT, dmfs/DMFS, proportion of caries-free teeth and caries prevalence). The authors conclude that water fluoridation reduces the incidence of dental caries in the primary and permanent teeth of children by approximately 35% compared to non-fluoridated water, and increases the proportion of children who have no dental caries by approximately 15%. The values presented in the report's conclusion (35% and 15%) are illustrative proportions from Iheozor-Ejiofor 2015; no overall effect estimates for adults were presented.

None of the reviews by Iheozor-Ejiofor 2015, McDonagh 2000, Truman 2002, or this current Cochrane review update, included studies evaluating 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 review is included in the NHMRC 2017 overview (above). 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, and hence fell outside the scope of both the McDonagh 2000 review and this one. In their 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 two of these more recent studies was not reported, 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 findings. However, as discussed above, the NHMRC 2017 review found consistent evidence from Griffin 2007 and additional primary studies that water fluoridation at current Australian levels is associated with a decreased prevalence of dental caries in the permanent teeth of adults.

A systematic review published in 2015 addressed the question “Does an optimum concentration of fluoride in water reduce the risk of [early childhood caries] (ECC)?” (Moynihan 2019). Thirty-two studies (13 described as cohort studies, 15 cross-sectional studies and four ecologic studies), including infants and children younger than 72 months, were identified. The authors state that the highest level evidence comes from cohort studies that reported ECC in children who had resided in fluoridated areas from birth compared with those residing in non-fluoridated areas. Most of the studies were described as being at moderate risk of bias, although the authors reported no details regarding the ROBINS-I assessments. The findings for Moynihan 2019 are based on these 13 cohort studies (excluding the cross-sectional studies from the analysis), stating, “All studies showed lower development of ECC in children exposed to fluoridated water, and there was evidence of a large effect size in individual studies.” Only four of the studies were deemed suitable for meta-analysis, showing a mean difference in mean dmft of −1.25 (95% CI −2.14 to −0.36; P = 0.006, $I^2$ = 94%). There is significant unexplained statistical heterogeneity. Given that data from less than 30% of the available cohort studies are available for analysis, caution should be used in interpreting the findings.

A more recent systematic review has evaluated children's dental health surveys at national, regional and county levels conducted in the Republic of Ireland from 1950 to 2021, and compares the dental caries experience in children living in areas with and without community water fluoridation (Sharma 2023). The review did not evaluate the initiation of water fluoridation but the association between fluoridation and caries. In line with most reviews, large reductions in the prevalence of dental caries were seen over time. Whilst greater reductions in dental caries were reported in areas with fluoridation than without, the authors report that a quantitative assessment of the evidence was not feasible due to the frequent lack of data on the SDs of the mean dmft/DMFT. Sharma 2023 presented no effect estimate.

**Evaluating the cessation of community water fluoridation programmes on the prevention of dental caries**

With regard to the cessation of water fluoridation programmes, the McDonagh 2000 review included eight studies, whereas our review included only one study (Maupome 2001). This variation is due to differences in criteria for the control group in this comparison. 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 most of the cessation studies in McDonagh 2000, 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 (“of 22 analyses of stopping water fluoridation, 14 found… that stopping water fluoridation led to an increase in caries in the previously fluoridated area compared to the never-fluoridated area”), this result was not confirmed in the study included in our review.

In the review by Truman 2002, three studies with before-and-after measurements showed that stopping water fluoridation was associated with an increase in dental caries experience by a median of 17.9% with a range from 31.7% increase to a 42.2% decrease in caries. One study showing a negative estimate of effectiveness was subsequently excluded from the analysis due to post hoc concerns regarding potential confounding, resulting in a revised increase in dental caries experience by a median of 29.1% (range from 17.9% to 31.7%). One study with post-exposure measurements only also showed an increased dental caries experience following the stopping of water fluoridation. All the study populations involved children aged four to 17 years.

**Impact of water fluoridation on disparities in caries**

Our 2015 Cochrane review was criticised for reporting that there was insufficient evidence regarding the effectiveness of CWF for reducing social disparities in oral health, suggesting that the review may be “inadvertently, or deliberately, misinterpreted” as reporting that water fluoridation is ineffective in these regards (Rugg-Gunn 2016). It is not our intention to cause confusion or promote misinterpretation of our findings. None of the identified systematic reviews have identified consistent, robust evidence that water fluoridation reduces dental health inequalities. We would stress, however, that a lack of evidence to demonstrate an effect does not equate to lack of effect.

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." The review findings continue to be misrepresented. For example, its findings have been used to infer that the effect includes a broader age group than the two age categories specified (children aged five and 12), or is applicable to all caries outcome measures, as in the following quotation: “The York review, in England, reported ‘some evidence that water fluoridation reduces the inequalities in dental health across social classes in 5- to 12-year olds’” (Do 2019). Due to concerns regarding the misinterpretation of their findings, the review authors put out a statement in 2003, stating “The evidence about reducing inequalities in dental health was of poor quality, contradictory and unreliable” (McDonagh 2000). There were no data for disparities in caries levels among adults.

On this issue, the Australian National Health and Medical Research Council overview of reviews stated, “The evidence evaluation identified one review and three ecological studies which provided insufficient evidence to reach a conclusion about any association between water fluoridation at current Australian levels and disparities in dental caries experience” (NHMRC 2017).

A review by Shen 2021 evaluated a range of interventions aimed at reducing inequality in dental caries in children. They conclude that "whole population interventions such as water fluoridation are more likely to reduce inequalities". However, there were no quantitative data to support this and three-quarters of the included studies were assessed as at low risk of bias for random sequence generation, despite all four studies being non-randomised studies of interventions.

Griffin 2007, Moynihan 2019 and Truman 2002 did not aim to evaluate the association between water fluoridation and oral health disparities. Truman 2002 does highlight important research questions that remain unanswered, including “what is the effectiveness of CWF in reducing socioeconomic or racial and ethnic disparities in caries burden?”

#### Evaluating the association of water fluoridation (artificial or natural) with dental fluorosis

We have not updated the evidence for dental fluorosis reported in Iheozor-Ejiofor 2015; the analysis of dental fluorosis in 2015 was, itself, an update of the analysis presented in the McDonagh 2000 review. The results from our review of the dental fluorosis data are fairly comparable with those of the McDonagh 2000 review. In the analysis of fluorosis in the McDonagh 2000 review, areas with natural fluoride levels above 5 ppm were excluded. It was acknowledged that this is significantly above the level recommended for artificial fluoridation. However, the range of concentrations from 0 ppm to 5 ppm allowed exploration of a dose-response relationship. In Iheozor-Ejiofor 2015, we also conducted analyses of studies of fluoride concentrations of 5 ppm or lower, in addition to an analysis 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 a 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.

#### Other adverse effects

The broader literature speculates about harms associated with higher levels of fluoride in water (e.g. cancer, lowered intelligence, endocrine dysfunction) (Solanki 2022). These harms have not been systematically evaluated in this review, as these outcomes were rarely reported in the included studies. However, previous reviews suggest there is no conclusive evidence for an association between CWF and most conditions evaluated (Lambe 2022; MRC 2002; NHMRC 2017).

# Authors' conclusions

### Implications for practice

Contemporary studies indicate that initiation of community water fluoridation may lead to a slightly greater reduction in decayed, missing or filled primary teeth (dmft) and may lead to a slightly greater increase in the proportion of caries-free children, but with smaller effect sizes than earlier studies. This evidence was of low certainty. There is insufficient evidence to determine the effect of cessation of community water fluoridation on caries and whether water fluoridation results in a change in disparities in caries according to socioeconomic status. There are no studies evaluating the effect of initiation/cessation of water fluoridation on the prevention of caries outcomes in adults.

There is a significant association between dental fluorosis (of aesthetic concern or all levels of dental fluorosis) and fluoride level. The certainty of the evidence is limited due to a high risk of bias within the studies. From visual observation of the data, we also noted the possibility of inconsistency.

The implementation or cessation of community water fluoridation requires careful consideration of the current evidence alongside the broader context of a population's oral health, oral health behaviours, diet and consumption of tap water, movement or migration, and the availability and uptake of other caries-prevention strategies. In addition, factors such as acceptability, cost-effectiveness and the feasibility of the implementation and monitoring of a community water fluoridation programme should be taken into account.

### Implications for research

Any initiation or cessation of a community water fluoridation programme should be fully evaluated using robust methods to address confounding, and should collect cost data to inform economic evaluation. These studies should include a concurrent control with comparable fluoridation status at baseline. Measures of caries outcomes should therefore be taken at a minimum of two time points (i.e. baseline and follow-up).

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

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

If one of the key aims of community water fluoridation is to reduce oral health disparities, then full evaluations of the effects of community water fluoridation by socioeconomic status should be undertaken and fully reported whenever schemes are introduced or removed.

# Acknowledgements

We thank Richard Macey, Rahul Alam, Vivien Welch and Peter Tugwell for their contributions as authors on the previous version of this review.

Acknowledgements for the previous version of the review are in Iheozor-Ejiofor 2015.

We would like to thank the editors and all those providing written referee comments on this review.

**Editorial contributions**

Cochrane Oral Health Group supported the authors in the development of this systematic review. The following people conducted the editorial process for this article:

**Sign-off Editors** (final editorial decision): Robert Boyle, Imperial College London, UK, and Alonso Carrasco-Labra, Cochrane Oral Health Collaborating Center and Center for Integrative Global Oral Health, University of Pennsylvania, School of Dental Medicine; **Managing Editor** (edited the article, collated peer-reviewer comments, and provided editorial guidance to authors): Marwah Anas El-Wegoud, Cochrane Central Editorial Service; **Editorial Assistant** (selected peer reviewers, conducted editorial policy checks and supported editorial team): Jacob Hester, Cochrane Central Editorial Service; **Copy Editor** (copy editing and production): Faith Armitage and Denise Mitchell, Cochrane Central Production Service.

Peer-reviewers (provided comments and recommended an editorial decision): Jennifer Hilgart, Cochrane Evidence Production and Methods Directorate (**methods review**); Jo Platt, Central Editorial Information Specialist (**search review**); Brian Duncan (**consumer review**). Two additional peer reviewers provided clinical peer-review but chose not to be publicly acknowledged.

# 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 |
|---|---|---|---|---|
| 1.1 Change in the number of decayed, missing or filled primary teeth (dmft) | 7 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.1.1 Studies conducted after 1975 | 2 | 2908 | Mean Difference (IV, Random, 95% CI) | 0.24 [-0.03, 0.52] |
| 1.1.2 Studies conducted in 1975 or earlier | 5 | 5709 | Mean Difference (IV, Random, 95% CI) | 2.10 [1.71, 2.49] |
| 1.2 Change in the number of decayed, | 7 | | Mean Difference (IV, | Subtotals only |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| missing or filled permanent teeth (DMFT) | | | Random, 95% CI) | |
| 1.2.1 Studies conducted after 1975 | 4 | 2856 | Mean Difference (IV, Random, 95% CI) | 0.27 [-0.11, 0.66] |
| 1.2.2 Studies conducted in 1975 or earlier | 3 | 5623 | Mean Difference (IV, Random, 95% CI) | 1.00 [0.54, 1.47] |
| 1.3 Change in the number of decayed, missing or filled permanent surfaces (DMFS) | 1 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 1.4 Change in the proportion of caries-free participants (primary teeth) | 7 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.4.1 Studies conducted after 1975 | 2 | 2908 | Mean Difference (IV, Random, 95% CI) | -0.04 [-0.09, 0.01] |
| 1.4.2 Studies conducted in 1975 or earlier | 5 | 6278 | Mean Difference (IV, Random, 95% CI) | -0.17 [-0.20, -0.13] |
| 1.5 Change in the proportion of caries-free participants (permanent teeth) | 6 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.5.1 Studies conducted after 1975 | 2 | 2348 | Mean Difference (IV, Random, 95% CI) | -0.03 [-0.07, 0.01] |
| 1.5.2 Studies conducted in 1975 or earlier | 4 | 6219 | Mean Difference (IV, Random, 95% CI) | -0.06 [-0.14, 0.02] |
| 1.6 Sensitivity analysis - all included studies: change in the number of decayed, missing or filled primary teeth (dmft) | 11 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.6.1 Studies | 3 | 6622 | Mean Difference (IV, | 1.08 [-0.53, 2.70] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| conducted after 1975 | | | Random, 95% CI) | |
| 1.6.2 Studies conducted in 1975 or earlier | 8 | 17520 | Mean Difference (IV, Random, 95% CI) | 1.91 [1.60, 2.23] |
| 1.7 Sensitivity analysis - all included studies: change in the number of decayed, missing or filled permanent teeth (DMFT) | 12 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.7.1 Studies conducted after 1975 | 6 | 12906 | Mean Difference (IV, Random, 95% CI) | 0.53 [0.00, 1.06] |
| 1.7.2 Studies conducted in 1975 or earlier | 6 | 30334 | Mean Difference (IV, Random, 95% CI) | 1.35 [0.77, 1.94] |
| 1.8 Sensitivity analysis - all included studies: change in the proportion of caries-free participants (primary teeth) | 12 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.8.1 Studies conducted after 1975 | 4 | 9608 | Mean Difference (IV, Random, 95% CI) | -0.10 [-0.19, -0.01] |
| 1.8.2 Studies conducted in 1975 or earlier | 8 | 12383 | Mean Difference (IV, Random, 95% CI) | -0.17 [-0.19, -0.15] |
| 1.9 Sensitivity analysis - all included studies: change in the proportion of caries-free participants (permanent teeth) | 9 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.9.1 Studies conducted after 1975 | 3 | 10502 | Mean Difference (IV, Random, 95% CI) | -0.12 [-0.33, 0.09] |
| 1.9.2 Studies conducted | 6 | 17459 | Mean Difference (IV, | -0.13 [-0.24, -0.03] |

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| in 1975 or earlier | | | Random, 95% CI) | |
| 1.10 Sensitivity analysis - change in analytical approach: change in the number of decayed, missing or filled primary teeth (dmft) | 2 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.10.1 Studies conducted after 1975 | 2 | 2825 | Mean Difference (IV, Random, 95% CI) | 0.28 [0.12, 0.43] |
| 1.11 Sensitivity analysis - excluding studies with imputed standard deviations: change in the number of decayed, missing or filled primary teeth (dmft) | 4 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.11.1 Studies conducted after 1975 | 2 | 2908 | Mean Difference (IV, Random, 95% CI) | 0.24 [-0.03, 0.52] |
| 1.11.2 Studies conducted in 1975 or earlier | 2 | 1148 | Mean Difference (IV, Random, 95% CI) | 1.59 [1.01, 2.16] |
| 1.12 Sensitivity analysis - excluding studies with imputed standard deviations: change in the number of decayed, missing or filled permanent teeth (DMFT) | 3 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 1.12.1 Studies conducted after 1975 | 2 | 1535 | Mean Difference (IV, Random, 95% CI) | 0.53 [-0.45, 1.51] |
| 1.12.2 Studies conducted in 1975 or earlier | 1 | 736 | Mean Difference (IV, Random, 95% CI) | 0.62 [0.25, 0.99] |

# What's new

| Date | Event | Description |
|---|---|---|
| 22 September 2023 | New citation required and conclusions have changed | The conclusions of the review reflect contemporary evidence of greater certainty. |
| 22 September 2023 | New search has been performed | Update of objective 1: To evaluate the initiation or cessation of community water fluoridation programmes for the prevention of dental caries.<br>Two new studies added (average number of particpants used in analysis 4193); risk of bias updated to reflect advances in methods (ROBINS-I used); single-time point studies provided to provide context<br>Objective 2 was not updated: To evaluate the association of water fluoridation (artificial or natural) with dental fluorosis.<br>Two additional review authors (PR and SL) contributed to this review update. Four review authors (RM, RA, VW, PT) did not contribute to this review update (see Acknowledgements). |

# History

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

| Date | Event | Description |
|---|---|---|
| 7 September 2015 | Amended | Plain Language Summary amended for simplification. |
| 19 June 2015 | Amended | Minor edit to Plain Language Summary for clarification.<br>Missing referee name added to Acknowledgements. |
| 2 February 2015 | Amended | Background updated to justify the need for the review.<br>Change to risk of bias domains, incorporating an item on 'sampling'<br>Change to the handling of missing data; imputation of missing standard deviations for DMFT and dmft data |

# Contributions of authors

Review authors' contributions to the previous version of this review are listed in Iheozor-Ejiofor 2015.

Authors' contributions to the current version:

- Co-ordinating the review: AMG
- Screening of studies: AMG, LO, PR, SL, ZIE
- ROBINS-I assessments: AMG, LO, TW
- Data extraction for the review: AMG, LO, TW, HW, PR, SL
- Analysis of data: AMG, TW, HW
- Interpretation of data: AMG, LO, TW, JC, HW, PR, SL
- Writing the review: AMG, LO, TW, HW, JC, SL, DB
- Providing general advice/comments on the review: JC, ZIE

# Declarations of interest

ZIE has declared that they have no conflict of interest.

TW is a co-author on Goodwin 2022 and Co-Director (since July 2023) of the Colgate-Palmolive Dental Health Unit based at The University of Manchester. She has been Statistical Editor for Cochrane Oral Health. TW did not participate in the assessment of Goodwin 2022.

SL is a former Deputy Co-ordinating Editor for the Bone, Joint and Muscle Trauma group; she has had no role in the editorial process for the review.

PR is Deputy Co-ordinating Editor for Cochrane Oral Health; he has had no role in the editorial process for this review.

DB has declared that they have no conflict of interest.

JC is Joint Co-ordinating Editor for Cochrane Oral Health; she has had no role in the editorial process for this review.

HW was previously Joint Co-ordinating Editor for Cochrane Oral Health/Statistical Editor; she has had no role in the editorial process for this review.

AMG is Joint Co-ordinating Editor for Cochrane Oral Health; she has had no role in the editorial process for this review.

LO'M has declared that they have no conflict of interest.

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  The views and opinions expressed therein are those of the authors and do not necessarily reflect those of either The University of Pennsylvania or The University of Manchester.
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  The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health.

# Differences between protocol and review

Here, we note differences between this review update and the previous version of the review (Iheozor-Ejiofor 2015).

**Review authors:** two additional review authors (PR and SL) contributed to this review update. Four review authors (RM, RA, VW, PT) did not contribute to this review update (see Acknowledgements).

**Objectives**

- We reworded the objectives of the review in order to improve clarity, in particular to distinguish between studies designed to measure change in caries and studies designed to measure the association of water fluoridation with dental fluorosis. We used these new objectives as subheadings throughout the review.
- We did not update the evidence for our second review objective (association of water fluoridation with dental fluorosis) in this review update. We believed that the evidence for this association was stable. We discussed this decision with the author team and the Cochrane Editorial team. In order to improve readability, we moved some methods, relating specifically to the management of these studies, to an appendix. We did not alter any methods for the management of these studies in this review update.

**Types of studies**: following feedback on the previous version of the review, we provided more detail about the types of study designs and reasons for choosing these designs to evaluate different types of objectives.

**Types of outcome measures:** rather than using primary and secondary outcome descriptors, we separated the outcomes according to the two review objectives.

**Searching other resources**

- We checked whether any eligible studies had been retracted from journals.

- In response to previous feedback, we carried out an additional search for single time point cross-sectional studies evaluating caries measures. This was not part of the formal review process, but provided important context in the Discussion; hence, we noted this in the methods section of the review.

**Risk of bias:** we used a different risk of bias tool in this update. We re-assessed all studies that were eligible for our first review objective using a new version of ROBINS-I. The decision to use a different risk of bias tool was driven by methodological developments in risk of bias assessment of non-randomised trials.

**Data synthesis:** in the previous version of the review, we included all studies in the analysis, regardless of risk of bias assessment. However, guided by recommendations for ROBINS-I, we did not include studies that we had assessed as having a critical risk of bias in the primary analysis. We explored this decision in sensitivity analysis.

**Subgroup analysis:** we did not further explore sources of heterogeneity (as described in the review protocol; Iheozor-Ejiofor 2013) because we had insufficient data.

**Sensitivity analysis:** we conducted sensitivity analysis related to the exclusion of studies at critical risk of bias. We also explored other decisions made during the review process; in particular, those related to the analytical approach used in analysis of the cohort studies.

**Summary of findings and assessment of the certainty of the evidence**

- Because we presented the review and outcome measures according to two distinct objectives, we presented separate summary of findings tables in this update (one each for the initiation and the cessation of water fluoridation programmes; and one for association of water fluoridation with dental fluorosis). Although we did not update the evidence for this latter objective, the presentation of the certainty of the evidence in the summary of findings table differs from the previous version of the review; these changes are minor and reflect changes in methodological standards expected by Cochrane, rather than changes in the overall certainty of the evidence.
- In the previous version of the review, we had analysed data separately according to the year that the study was conducted (after 1975, or earlier). This approach was not reflected in the presentation of the summary of findings table. In this update, we presented the data for initiation of water fluoridation programmes according to these date thresholds, in order to highlight the more relevant contemporary evidence.

# Notes

Responses to ROBINS-I signalling questions are available on request.

# Characteristics of studies

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

**Acharya 2005**

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

| | |
|---|---|
| cessation of CWF for prevention of dental caries | |
| 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 in order to determine how selection took place |
| Confounding | High risk | Did not account for use of other fluoride sources |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Warren County, Georgia<br>Year of study: not stated<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children attending sole elementary and middle schools in study area<br>Exclusion criteria: children whose homes were served with well-water<br>Other sources of fluoride: parents completed questionnaire regarding dentifrice use, home water source and current use of systemic fluoride supplements; all children received school water fluoridated at 0.5 ppm<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not considered<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.5 to 1.2 ppm (both natural and artifical fluoridation)<br>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<br>Age at assessment: 8 to 10 years, and 11 to13 years |
| Funding | NIDR Grant DE-06113 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 in order to determine how selection took place |
| Confounding | High risk | SES was not accounted for |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 |
| 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

***Study characteristics***

| | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Chile<br>Geographic location: Group 1: Curico (F); Group 2: San Fernando (non-F). Total population sizes in each location not stated<br>Year study started: 1953 |

| | |
|---|---|
| | Year study ended: 1956<br>Year of change in fluoridation status: 1953<br>Study design: CBA. A different sample of children was assessed at baseline and at end of study |
| Participants | Inclusion criteria: children aged 3 to 15 years; children from 2 primary schools in the study areas<br>Exclusion criteria: none stated<br>Sample size at baseline: Group 1: 1279 children; Group 2: 748 children<br>Sample size at final assessment: Group 1: 3060 children; Group 2: 1680 children<br>SES: based on author's knowledge of the demographics, culture and social economy of the intervention and control areas, it was assumed that the study areas were comparable<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: distribution was similar across groups<br>Residential history: not stated |
| Interventions | **Initiation of water fluoridation**<br>Group 1: 1 ppm (artificial fluoridation)<br>Group 2: ppm not stated (natural fluoridation) |
| Outcomes | % caries-free participants<br>Age at baseline assessment: 3 to 8 years and 11, 12 and 15 years<br>Age at final assessment: 3 to 8 years, and 11, 12 and 15 years |
| Funding | In collaboration with members of the committee Pro-Fluoridation |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Efforts were made to control for confounding through design. The groups were considered to be comparable by the author team owing to the areas being neighbouring cities. "The comparison is based on the knowledge of their demographics, culture and social economy". While data were not collected on SES as part of the study, existing data were used to provide reassurance of comparability on SES proxies including infant mortality rate and illiteracy rates. These rates were reported in the paper to allow readers to judge that the areas were comparable across these characteristics.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** All eligible children in the cities were invited to the study<br>**Deviations from intended interventions.** No deviations from intended intervention<br>**Missing data.** No missing outcome data, however, no data regarding the confounder. The study reported on existing data only at baseline rather than collecting data with regard to the confounder directly from study participants.<br>**Measurement of the outcome.** Outcome assessment was conducted by unblinded assessors<br>**Selection of the reported result.** Outcome of interest reported |
| Notes | Data extracted from Adriasola 1959 differs from that presented in McDonagh 2000 (additional data extracted)<br>Paper translated from Spanish |

### Al-Alousi 1975

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: UK<br>Geographic location: Anglesey (F); Leeds (non-F)<br>Year of study: 1973<br>Year of change in fluoridation status: 1955<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; children aged 12 to 16 years<br>Exclusion criteria: missing, fractured or crowned teeth; refusal to participate (1 school in Leeds)<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.9 ppm (artificial fluoridation)<br>Group 2: < 0.01 ppm (natural fluoridation) |
| Outcomes | Dental fluorosis<br>Age at assessment: 12 to 16 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Al-Alousi 1975 differs from that presented in McDonagh 2000 |

| ***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 Anglesey were selected from schools randomly |
| Confounding | High risk | Did not account for use of other fluoride sources or SES |
| Blinding of outcome assessment (detection bias)<br>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)<br>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 2 examiners and there was no mention of any sort of calibration of the examiners. This may have resulted in measurement bias |

**Alarcon-Herrera 2001**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Mexico<br>Geographic location: Durango<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 6 to 12 years who had established permanent residence in the area<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: permanent residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: non-detectable to 1.5 ppm<br>Group 2: 1.51 to 4.99 ppm<br>Group 3: 5.0 to 8.49 ppm<br>Group 4: 8.5 to 11.9 ppm<br>Group 5: > 12 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Adverse effects (bone fracture)<br>Age at assessment: 6 to 12 years |
| Funding | Project grant from the Mexican National Council of Science and Technology Conacyt-Sivilla, Project 9502160 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Low risk | Through a polystage conglomerate random sampling, 380 families were selected and prorated into 77 to 80 families per concentration area zone. The division yielded a total of 1437 individuals from the 5 different areas |
| Confounding | High risk | Did not account for use of other fluoride sources or SES |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Hungary<br>Geographic location: Bár and Dunaszekcső<br>Year of study: 2004<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | |

| | |
|---|---|
| | Inclusion criteria: healthy schoolchildren, aged 6 to 18 years; lifelong residents in the communities Bár or Dunaszekcső; only permanent teeth were investigated<br>Exclusion criteria: any systemic disease<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 1.7 ppm<br>Group 2: 2 ppm |
| Outcomes | Dental fluorosis (Dean's Index and TSIF)<br>Age at assessment: 6 to 18 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Paper translated from Hungarian |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Saudi Arabia<br>Geographic location: Riyadh<br>Year of study: 2010<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: Saudi nationality; lifetime residence in the area<br>Exclusion criteria: non-Saudi nationality; absence from school on the day of dental examination<br>Other sources of fluoride: not stated<br>SES: both schools from urban and rural areas were included in the sample frame<br>Ethnicity: Saudi nationals, no further details<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0 to 0.3 ppm<br>Group 2: 0.31 to 0.6 ppm<br>Group 3: 0.61 to 1 ppm<br>Group 4: 1.01 to 1.5 ppm<br>Group 5: 1.51 to 2 ppm<br>Group 6: 2.01 to 2.5 ppm<br>Group 7: ≥ 2.51 ppm |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 6 to 18 years |
| Funding | Supported by a grant from King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 ≥ 1 school were surveyed. However, there was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 study authors did not report or justify not presenting fluorosis data for the age group 15 to 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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Italy<br>Geographic location: areas around Naples (F); Catanzaro (non-F)<br>Year of study: 1997<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: partially erupted teeth; orthodontic banding<br>Other sources of fluoride: tooth brushing habits (frequency of tooth brushing); fluoride tablets; fluoride dentifrices<br>SES: parents' employment status<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: sweet consumption; climate | |
| Interventions | All natural fluoridation<br>Group 1: ≥ 2.5 ppm<br>Group 2: ≤ 0.3 ppm | |
| Outcomes | Dental fluorosis; caries data evaluated in study but not included in review due to study design<br>Age at assessment: 12 years | |
| Funding | Partially supported by a grant of Acquedotto Vesuviano S.p.A. | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Nagaur district<br>Year of study: 2013<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: not stated |

| | |
|---|---|
| | Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | 54 villages receiving water with different natural fluoride concentrations ranging from 0.9 to 5.8 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: not stated |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 study authors via email |
| Other bias | High risk | Fluoride concentration for the different villages overlapped making the data impossible to interpret |

## Arnold 1956

***Study characteristics***

| | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: USA<br>Geographic location: Group 1: Grand Rapids (F); Group 2: Muskegon (non-F). Total population sizes for each location not stated<br>Year study started: 1944<br>Year study ended: 1951 (after which time the control group became fluoridated; evaluated until 1954)<br>Year of change in fluoridation status: 1945<br>Study design: CBA. A different sample of children was assessed at each time point, according to age at last birthday. |
| Participants | Inclusion criteria: children aged 4 to 16 years; used city water supplies since birth<br>Exclusion criteria: children who lived outside study areas for more than 3 months of any 1 year<br>Sample size at baseline: Group 1: 19,680; Group 2: 4291 (all school children)<br>Sample size at final assessment: Group 1: 4590; Group 2: 2192 (sample of school children in 1951)<br>SES: not stated<br>Co-interventions: study 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<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: lifetime residents |
| Interventions | **Initiation of water fluoridation**<br>Group 1: 1 ppm (artificial fluoridation)<br>Group 2: < 0.2 ppm (natural fluoridation) |
| Outcomes | DMFT; dmft<br>Age at baseline assessment: 5 to 13 years (primary dentition); 6 to 16 years (permanent dentition)<br>Age at final assessment: 5 to 13 years (primary dentition); 6 to 16 years (permanent dentition) |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of | See Table 1 for ROBINS-I assessment. |

| | |
|---|---|
| dental caries | **Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of particpants into the study/analysis.** Children were selected through schools. Almost all eligible children in the areas of study were examined<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** "samples consist of all available children in certain grades (or in sections of the grades)"<br>Number of children examined each year presented, however, numbers varied across each age group and each year (not a continuous study sample).<br>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, SD not reported.<br>**Measurement of the outcome.** No blinding of assessors<br>**Selection of the reported result.** 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, SD not reported |
| Notes | Data extracted from Arnold 1956 differed from that presented in McDonagh 2000 (additional data extracted) |

**Ast 1951**

| *Study characteristics* | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: USA<br>Geographic location: Group 1: Newburgh (F); Group 2: Kingston (non-F). Total population sizes for each location not stated.<br>Year study started: 1945<br>Year study ended: 1952<br>Year of change in fluoridation status: 1945<br>Study design: CBA. A different sample of children was assessed at baseline and time points throughout the study, according to age groups at the time of assessment. |
| Participants | Inclusion criteria: all 5- to 12-year-old children present at school on days of examination; lifetime residents of study areas<br>Exclusion criteria: none stated<br>Sample size at baseline: Group 1: approximately 3400 children; Group 2: approximately 2800 children<br>Sample size at final assessment: Group 1: 3200 children; Group 2: 3100 children<br>SES: not stated<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: most were lifetime residents. Study authors note that small transient community in the study area was unlikely to impact the outcome data |
| Interventions | **Initiation of water fluoridation**<br>Group 1 baseline: < 0.1 ppm (natural fluoridation)<br>Group 1 post intervention: 1 to 1.2 ppm (artificial fluoridation)<br>Group 2: < 0.1 ppm (natural fluoridation) |
| Outcomes | DMFT rate per 100 erupted permanent teeth; % caries-free children (primary dentition)<br>Age at baseline assessment: 5 years (primary dentition); 6 to 12 years (permanent dentition)<br>Age at final assessment: 5 years (primary dentition); 6 to 12 years (permanent dentition) |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of particpants into the study/analysis.** 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<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** The number of participants for whom outcome data were 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) |

| | |
|---|---|
| | **Measurement of the outcome.** Insufficient information regarding blinding of assessors<br>**Selection of the reported result.** No apparent selective reporting, however, it should be noted that baseline dates of children in the intervention (1944 to 1945) and control (1945 to 1946) groups varied |
| Notes | Data extracted from Ast 1951 differs from that presented in McDonagh 2000 (additional data extracted) |

### Awadia 2000

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Tanzania<br>Geographic location: Arusha and Moshi<br>Year of study: 1996<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: age 9 to 14 years; lifelong residence in respective towns or villages<br>Exclusion criteria: not stated<br>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%)<br>SES: 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%)<br>Ethnicity: Arusha area (Arusha and Arusha Meru) – mainly ethnic Asians; Kilimanjaro region (Moshi and Kibosho) - Africans<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.2 ppm<br>Group 2: 0.3 ppm<br>Group 3: 3.6 ppm | |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 9 to 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 | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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, including the school in Arusha Meru, all the registered schoolchildren 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 1 examiner was involved; no testing for intra-rater reliability with regard to detection of the outcome variable. |

### Azcurra 1995

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Argentina<br>Geographic location: Sampacho (F); Porteña (non-F) in the Cordoba province<br>Year of study: 1993<br>Year of change in fluoridation status: NA |

| | |
|---|---|
| | Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 6 to 7 years (1st grade) and 12 to 13 years (7th grade) at primary school<br>Exclusion criteria: none stated<br>Other sources of fluoride: frequency of tooth brushing<br>Group 1 (aged 6-7): 56% brushed at least once a day (28/50)<br>Group 1 (aged 12-13): 74% brushed at least once a day (37/50)<br>Group 2 (aged 6-7): 46% brushed at least once a day (23/50)<br>Group 2 (aged 12-13): 50% brushed at least once a day (25/50)<br>SES: determined by occupation and highest attained level of schooling attained by main breadwinner in family (classified as high, medium, and low social class)<br>Group 1 (aged 6-7): 80% low SES (40/50)<br>Group 1 (aged 12-13): 82% low SES (41/50)<br>Control (aged 6-7): 74% low SES (37/50)<br>Control (aged 12-13) 80% low SES (40/50)<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 9.05 ppm<br>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<br>Age at assessment: 6 to 7 years and 12 to 13 years |
| Funding | Part of this work was subsidised by the Ministry of Science and Technology of the National University of Córdoba, Córdoba, Argentina |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Blinding not stated, however the two calibrated operators, as study authors, were likely to have knowledge of the study areas |
| Incomplete outcome data (attrition bias)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Holland<br>Geographic location: Group 1: Tiel (F); Group 2: Culemborg (non-F). Total population sizes for each location not stated<br>Year study started: 1952<br>Year study ended: 1959<br>Year of change in fluoridation status: 1953<br>Study design: CBA. A different sample of children was assessed at baseline and time points throughout the study, according to age at the time of assessment. |
| Participants | Inclusion criteria: children aged 11 to 15 years; lifelong residents of the study areas; used the piped water supply; 100 children of each age examined<br>Exclusion criteria: not stated<br>Sample size at baseline: Group 1: not specified but assumed to be 100 participants per year of age from the information in the study report (i.e. 500 children); Group 2: not specified but assumed to be 100 participants per year of age (i.e. 500 children)<br>Sample size at final assessment: Group 1: as above, assumed to be 500 participants ; Group 2: as above, assumed to be 500 participants<br>SES: areas similar in social class structure and proportional numbers of children selected from each school type<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: equally balanced |

| | |
|---|---|
| | Residential history: lifetime residents |
| Interventions | **Initiation of water fluoridation**<br>Group 1: 1.1 ppm (artificial fluoridation)<br>Group 2: 0.1 ppm (natural fluoridation) |
| Outcomes | Carious approximal surfaces per child; approximal surfaces with caries of the dentine; pit and fissure caries per child; pit and fissure caries with cavitation; carious lesions of smooth surfaces. No totals for all surfaces<br>Age at baseline assessment: 11 to 15 years (permanent dentition)<br>Age at final assessment: 11 to 15 years (permanent dentition) |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** "Attention was given to population structure, site, size (above 15,000 inhabitants), migration and water composition, and two cities were selected which were as equal as possible". Areas similar in social class structure and proportional numbers of participants selected from each school type, although no details on how SES was measured or distributed. Study authors therefore provided some reassurance that the areas were comparable in terms of characteristics which are proxy measures of SES, but these data were not reported for the reader to make this judgement on compatibility for themselves.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** A proportion of children were chosen at random from different types of schools (public school, Roman Catholic, Protestant)<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** No missing outcome data, however, no data regarding confounder. Authors commented on the populations being equal at baseline but did not collect data directly from participants regarding the confounder.<br>**Measurement of the outcome.** No blinding regarding assessment of pit and fissure lesions. For aproximal caries: "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.<br>**Selection of the reported result.** Outcome of interest reported, however, SDs missing |
| Notes | |

**Bao 2007**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: 3 cities (Harbin, Mudanjiang, Zhaodong) and 3 rural areas (Zhaoyuan, Shuangcheng, Linkou) in the Heilongjiang province<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: 12-year-old children in Heilongjiang<br>Exclusion criteria: not reported<br>Other sources of fluoride: not reported<br>SES: 396 (198 male; 198 female) from cities; 396 (198 male; 198 female) from rural areas<br>Ethnicity: Chinese<br>Residential history: not reported<br>Other confounding factors: not reported | |
| Interventions | All natural fluoridation<br>Group 1 (Linkou): 0.29 ppm<br>Group 2 (Mudanjiang): 0.40 ppm<br>Group 3 (Shuangcheng): 0.68 ppm<br>Group 4 (Harbin): 0.77 ppm<br>Group 5 (Zhaoyuan): 0.80 ppm<br>Group 6 (Zhaodong): 1.14 ppm | |
| Outcomes | Dental fluorosis (CFI); caries data evaluated in study, but excluded from review due to study design<br>Age at assessment: 12 years | |
| Funding | Research Fund of Bureau of Health of Heilongjiang Province (grant no.2005[122]) | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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 study 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | The study 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 | Quote: "Dean's Index was used to classify fluorosis."<br>Comment: data not presented in a format that allowed for further evaluation. The study 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) |
| Other bias | Low risk | No other apparent bias |

**Baskaradoss 2008**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: 9 villages (Munchirai, Thovalai, Melpuram, Rajakkamangalam, Kurunthencode, Thiruvattar, Agasteeswaram, Thuckalay, Killiyoor) in Kanyakumari district<br>Year of study: 2006<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: brushing pattern (toothbrush) = 84.6%; toothpaste (Colgate) = 92.2%; frequency (once daily) = 80.7%; age of starting to brush (< 2 years) = 69.2%<br>SES: low SES (46.1%); urban residence (44.2%)<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: Information was collected on diet, seafood intake and tea | |
| Interventions | All natural fluoridation<br>Groups 1 to 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)<br>Age at assessment: 10 to 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Outcome data for all participants reported |
| Selective reporting (reporting bias) | High risk | Data not in suitable format for analysis |
| Other bias | Unclear risk | No mention of calibration |

**Beal 1971**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: England<br>Geographic location: Group 1: Balsall Heath and Northfield, Birmingham (F); Group 2: Dudley (non-F). Total population sizes for each location not stated<br>Year study started: 1967<br>Year study ended: 1970 |

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|---|---|
| | Year of change in fluoridation status: 1964<br>Study design: CBA. A different sample of children was assessed at baseline and time points throughout the study, according to age at the time of assessment. |
| Participants | Inclusion criteria: children aged 5 years attending schools that participated in each year of the study<br>Exclusion criteria: none stated<br>Sample size at baseline: Group 1: 297 children; Group 2: 217 children<br>Sample size at final assessment: Group 1: 314 children; Group 2: 229 children<br>SES: 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.<br>Co-interventions: not stated<br>Ethnicity: all areas have some proportion of immigrants<br>Gender: not stated, but study authors describe results for boys and girls as "not significantly different".<br>Residential history: no attempt was made to select continuously resident children from the samples. |
| Interventions | Initiation of water fluoridation<br>Group 1 and Group 2: 1 ppm (artificial fluoridation)<br>Group 3: < 0.1 ppm (natural fluoridation) |
| Outcomes | dmft; % caries-free children<br>Age at baseline assessment: 5 years (primary dentition)<br>Age at final assessment: 5 years (primary dentition) |
| Funding | MRC grant-funded trial |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to one area being reported as a poor area of the city with a higher proportion of immigrants in the population. No further assessment<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Insufficient information<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** Given lack of information on sampling, proportion of missing data at each time point unknown<br>**Measurement of the outcome.** Examination undertaken in mobile clinic at each school; blinding unlikely<br>**Selection of the reported result.** No apparent selective reporting |
| 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." |

**Beal 1981**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: England<br>Geographic location: Group 1: Scunthorpe (F) - population size of 70,000 residents; Group 2: Corby (non-F) - population size of 52,000. Study authors state that despite differences in size, both towns are similar in other respects.<br>Year study started: 1969<br>Year study ended: 1975<br>Year of change in fluoridation status: 1968<br>Study design: CBA. A different sample of children was assessed at baseline and time points throughout the study, according to age at the time of assessment. |
| Participants | Inclusion criteria: lifetime residents in study areas; children aged 5, 8 and 12 years<br>Exclusion criteria: teeth extracted for orthodontic purposes<br>Sample size at baseline: Group 1: 196 children; Group 2: 205 children<br>Sample size at final assessment: Group 1: 170 children; Group 2: 180 children<br>SES: both areas had iron/steel as main industry-socioeconomic; composition of the 2 areas was similar<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: lifetime residents |
| Interventions | **Fluoride initiation**<br>Group 1: 0.9 ppm (artificial fluoridation)<br>Group 2: 0.35 ppm (natural fluoridation) |
| Outcomes | dmft; DMFT; % caries-free children (primary teeth); % caries-free subjects (permanent teeth)<br>Age at baseline assessment: 5, 8 and 12 years |

| | |
|---|---|
| | Age at final assessment: 5, 8 and 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** The SES composition of the 2 towns was stated as being similar, although no details on how SES was measured or distributed<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Schools were chosen by random selection and every child of eligible age in these schools was examined.<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** The study reports that "every child of eligible age in these schools was examined", suggesting outcome data for all participants are presented although not explicitly stated. No data on confounding variable for participants reported<br>**Measurement of the outcome.** Insufficient information regarding blinding of assessors<br>**Selection of the reported result.** No apparent selection of reporting |
| Notes | |

**Beltran-Aguilar 2002**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: not stated<br>Year of study: 1986<br>Year study ended: 1987<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: aged 12 to 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<br>Other fluoride sources: tablets = 623 (14.9%); drops = 627 (14.5%); tablets and drops = 317 (8.4%).<br>Suboptimal fluoride: drops only = 507 (23.0); tablets only = 512 (22.5); tablets and drops = 279 (13.2).<br>Optimal fluoride:drops only = 103 (6.8); tablets only = 98 (6.0); tablets and drops = 32 (2.2)<br>Natural fluoride: drops only = 13 (5.5); tablets only = 17 (7.5); tablets and drops = 6 (2.5)<br>Exclusion criteria: any criterion in discord with the inclusion criteria<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: all the children were continuous residents of areas with the reported water systems<br>Other confounding factors: not stated | |
| Interventions | Group 1: < 0.7 ppm (natural fluoridation)<br>Group 2: 0.7 to 1.2 ppm (artificial fluoridation)<br>Group 3: 0.7 to 4 ppm (natural fluoridation) | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 12 to 14 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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 > 4 million schoolchildren. There is no evidence that any eligible children were excluded |
| Confounding | High risk | The use of other fluoride sources was similar in those who 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias) | Unclear risk | Children with missing outcome data were excluded. It is not clear whether there was an imbalance across groups in excluded children |

| | | |
|---|---|---|
| All outcomes | | |
| 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 to 1.2 ppm and 0.7 to 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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Namibia<br>Geographic location: Ombili, Ondera, Vryheid, Kakuse<br>Year of study: October 2004<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: aged 8 to 21 years<br>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)<br>Exclusion criteria: not stated<br>SES: not stated<br>Ethnicity: !Kung (45%); Heikum (35%); Damara (13%); Bantu (7%)<br>Residential history: residents of Ombili had been resident since 1991 and the residents of the other farms were lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.28 ppm<br>Group 2: 0.38 ppm<br>Group 3: 1.06 ppm<br>Group 4: 1.43 ppm |
| Outcomes | Dental fluorosis (Dean's Index; CFI)<br>Age at assessment: 8 to 21 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Sampling | Unclear risk | Children selected from Ombili Primary School and divided into groups according to 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All participants accounted for in analysis |
| Selective reporting (reporting bias) | Low risk | Outcome data fully reported |
| Other bias | Low risk | No other apparent bias |

**Birkeland 2005**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sudan<br>Geographic location: Triet el Biga, Abu Delaig and Abu Groon<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: residence in the village from the age of 1 year<br>Exclusion criteria: not stated |

| | |
|---|---|
| | Other fluoride sources: not stated<br>SES: similar socioeconomic conditions<br>Ethnicity: similar ethnicity<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.3 to 1.4 ppm<br>Group 2: 0.8 to 2.2 ppm<br>Group 3: 2 to 4.2 ppm |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 11 to 13 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data presented for all participants |
| 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 2015**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Australia<br>Geographic location: Group 1: Wyong Shire (population size of 142,724 residents); Group 2: Gosford city (population size of 162,017 residents); Group 3: Ballina and Byron (population sizes of 40,266 residents and 30,635 residents, respectively).<br>Year study started: 2008<br>Year study ended: 2012<br>Year of change in fluoridation status: 2008<br>Study design: ITS. A different sample of children was assessed at baseline and time points throughout the study, according to age at the time of assessment. |
| Participants | Inclusion criteria: children aged 5 to 7 years (data for 10- to 12-year-olds also provided)<br>Exclusion criteria: not stated<br>Sample size at baseline: Group 1: 825 children; Group 2: 781 children; Group 2: 523 children<br>Sample size at final assessment: Group 1: 811 children; Group 2: 844 children: Group 3: 612 children<br>SES: shires of Ballina and Byron were more rural and less industrialised than Wyong Shire and Gosford City. Information on parent's educational attainment and cardholder status was recorded, but not reported in detail.<br>Co-interventions: information on toothbrushing habit and sugary drink consumption was collected, but not reported in detail.<br>Ethnicity: aboriginal status was recorded, but not reported in detail.<br>Gender in baseline sample: equally balanced<br>Residential history: not stated |
| Interventions | Group 1: fluoridated for over 40 years (data not included in review)<br>Group 2: newly fluoridated (ppm not stated)<br>Group 3: non-fluoridated (ppm not stated) |
| Outcomes | dmft; DMFT; % caries-free (primary dentition); % caries-free (permanent dentition)<br>Age at baseline assessment: 5 to 7 years; 10 to 12 years<br>Age at final assessment: 5 to 7 years; 10 to 12 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 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** SES accounted for in analysis. Measured using cardholder status and highest educational attainment; details provided<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** 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 to 7 years added up to around 900.<br>**Deviations from intended interventions.** No deviations from intended interventions reported<br>**Missing data.** Imbalance across study areas with regard to response rates (e.g 55% vs 80% in 2008 for non-fluoridated vs newly fluoridated)<br>**Measurement of the outcome.** Children evaluated in school; examiners likely to know fluoridation status<br>**Selection of the reported result.** No apparent selection of reporting |
| Notes | Published and unpublished data. DMFT data only available in unpublished report. |

**Booth 1991**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>Geographic location: Huddersfield (F); Dewsbury (non-F)<br>Year of study: 1989<br>Year of change in fluoridation status: 1989<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: all 3-year-old white children; lifetime residents of study areas; positive informed consent<br>Exclusion criteria: children who had moved out of the area; children who were ill; children taking fluoride tablets<br>Other sources of fluoride: children taking fluoride tablets excluded from study<br>SES: areas matched using socioeconomic data from the 1981 census and recent unemployment data; parents asked about occupation of head of household during interview<br>Ethnicity: white children only<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: < 0.3 ppm (natural fluoridation) | |
| Outcomes | Dental fluorosis (modified developmental defects of enamel index), caries data evaluated in study but excluded from review due to study design<br>Age at assessment: 3 years | |
| Funding | North Western Regional Health Authority | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Canada |

| | |
|---|---|
| | Geographic location: Wellington and Dufferin (neighbouring counties), South-Western Ontario<br>Year of study: 1996 to 1997 (academic year)<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children resident in Wellington-Dufferin-Guelph Health Unit area; parental consent; children aged 7 to 8 years<br>Exclusion criteria: children with non-erupted or insufficiently erupted central incisors; children absent on day of examination<br>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<br>SES: 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 subgroup affects the estimates of prevalence is unknown; however, it is unlikely to be a major source of bias."<br>Ethnicity: not stated<br>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)<br>Other confounding factors: breast-feeding duration |
| Interventions | Group 1: ≥ 0.7 ppm (natural fluoridation)<br>Group 2: < 0.7 ppm (natural fluoridation) |
| Outcomes | Dental fluorosis (TSIF score > 1)<br>Age at assessment: 7 to 8 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Brothwell 1999 differs from that presented in McDonagh 2000 |

***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)<br>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)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Canada<br>Geographic location: Group 1: Brantford (F) - total population size in 1951 was 36,727 residents; Group 2: Stratford (natural F) - total population size in 1951 was 18,785 residents; Group 3: Sarnia (non-F), Ontario - total population size in 1951 was 34,697 residents<br>Year study started: 1948<br>Year study ended: 1959<br>Year of change in fluoridation status: 1945<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age groups at the time of assessment. |
| Participants | Inclusion criteria: children aged 9 to 14 years; lifetime residents (absence of < 6 weeks since birth); all primary and secondary schools in study areas<br>Exclusion criteria: none stated<br>Sample size at baseline (children aged 9 to 14 years): Group 1: 1188 children; Group 2: 803 children; Group 3: 1057 children<br>Sample size at final assessment (children aged 9 to 14 years): Group 1: 1005 children; Group 2: 1007 children; Group 3: 1006 children |

| | |
|---|---|
| | SES: not stated<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: lifetime residents |
| Interventions | **Initiation of water fluoridation**<br>Group 1: artificial fluoridation - ppm not stated<br>Group 2: natural fluoridation - ppm not stated<br>Group 3: 'negligible' - ppm not stated (natural fluoridation) |
| Outcomes | DMFT, % caries-free children (permanent teeth)<br>Age at baseline assessment: 9 to 11 years and 12 to 14 years<br>Age at final assessment: 9 to 11 years and 12 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** 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)<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** Children 6 to 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.<br>**Measurement of the outcome.** Insufficient information regarding blinding; examiners likely to know fluoridation status<br>**Selection of the reported result.** No apparent selective reporting |
| Notes | |

### Budipramana 2002

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

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Low risk | The study 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)<br>All outcomes | High risk | Not reported |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Outcome data for all participants were reported. |
| Selective reporting (reporting bias) | Low risk | All expected outcomes were reported. |
| Other bias | High risk | No mention of examiner calibration |

**Butler 1985**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: 16 Texas communities (selected to reflect a wide range of fluoride levels in drinking water)<br>Year of study: 1980<br>Year study ended: 1981<br>Year of change in fluoridation status: unclear if natural or artifical fluoridation<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: lifetime residents of study areas; enroled in grades 2 to 6 (aged 7 to 13 years) and 9 to 12 (aged 14 to 19 years) in public schools<br>Exclusion criteria: none stated<br>Other sources of fluoride: fluoride toothpaste, fluoride drops, number of fluoride treatments<br>SES: mother's education<br>Ethnicity: white/Spanish/black (ethnicity judged by surname?)<br>Residential history: lifetime residents<br>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 whether the fluoridation was natural in all areas<br>Group 1: 0.2 ppm<br>Group 2: 0.2 ppm<br>Group 3: 0.3 ppm<br>Group 4: 0.7 ppm<br>Group 5: 1.0 ppm<br>Group 6: 1.0 ppm<br>Group 7: 1.1 ppm<br>Group 8: 1.8 ppm<br>Group 9: 1.9 ppm<br>Group 10: 1.9 ppm<br>Group 11: 2.1 ppm<br>Group 12: 2.1 ppm<br>Group 13: 2.3 ppm<br>Group 14: 2.3 ppm<br>Group 15: 2.4 ppm<br>Group 16: 3.3 ppm | |
| Outcomes | Dental fluorosis (CFI score; prevalence of observed mottling (moderate))<br>Age at assessment: 7 to 19 years | |
| Funding | Supported by grants from the US Environmental Protection Agency | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Data extracted from Butler 1985 differs from that presented in McDonagh 2000 | |

| ***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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 were 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 study authors, however, calibration was not mentioned |

## Chandrashekar 2004

| *Study characteristics* | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Davangere district<br>Year of study: 2002<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: lifetime residency; age 12 to 15 years<br>Exclusion criteria: not stated<br>Other fluoride sources: not stated<br>SES: similar socioeconomic conditions<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.22 ppm<br>Group 2: 0.43 ppm<br>Group 3: 0.74 ppm<br>Group 4 0.93 ppm<br>Group 5: 1.1 ppm<br>Group 6: 1.22 ppm<br>Group 7: 1.63 ppm<br>Group 8: 2.08 ppm<br>Group 9: 2.33 ppm<br>Group 10: 2.64 ppm<br>Group 11: 2.91 ppm<br>Group 12: 3.41 ppm | |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 12 to 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Taiwan<br>Geographic location: Shenkang Hsiang, Changwa<br>Year of study: 1987 to 1988<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 6 to 16 years; lifetime residents of study areas; always used water wells as primary source of drinking water<br>Exclusion criteria: not stated<br>Other fluoride sources: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents |

| | |
|---|---|
| | Other confounding factors: study author states that project communities had approximately the same location, climate, diet, food habits and customs, mean average daily temperature (range) = 25 $^{o}$C (13 $^{o}$C to 37 $^{o}$C) |
| Interventions | All natural fluoridation<br>Group 1: 4.2 to 4.9 ppm<br>Group 2: 2.1 to 2.8 ppm<br>Group 3: 1.4 to 2.1 ppm<br>Group 4: 0.7 to 1.4 ppm<br>Group 5: 0.4 to 0.7 ppm<br>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<br>Age at assessment: 6 to 16 years |
| Funding | National Science Council, Taiwan, ROC (NSC-77-0412-B-039-05) |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 use of other fluoride sources or SES |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: Anquan village (low F); Hubei village (high F), Fenshun county, Guangdong Province<br>Year of study: 1984<br>Year study ended: 1991<br>Year of change in fluoridation status: 1984 Hubei, 1986 Anquan<br>Study design: before-and-after |
| Participants | Inclusion criteria: native born children aged 8 to 12 years for dental fluorosis<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: author stated that economic and living habits were similar in all study areas<br>Ethnicity: not stated<br>Residential history: only native-born children were assessed.<br>Other confounding factors: not stated |
| Interventions | Water source from wells changed to river water<br>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)<br>* 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<br>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<br>Age at baseline measure: 8 to 12 years (dental fluorosis) and 16 to 65 years (skeletal fluorosis)<br>Age at final measure: 8 to 12 years (dental fluorosis) and 16 to 65 years (skeletal fluorosis) |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Chen 1993 differs from that presented in McDonagh 2000<br>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 to 65 years were randomly sampled to have roentgenograms taken in pelvis |
| Confounding | High risk | Did not account for use of other fluoride sources |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Ireland and England<br>Geographic location: Cork (low and high F; 2 separate areas) and Manchester (low F)<br>Year of study: not stated |

| | |
|---|---|
| | Year of change in fluoridation status: not stated<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 8 and 15 years<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | Group 1: 'optimal' level - ppm not stated (artificial fluoridation)<br>Group 2: 'low' level - ppm not stated (natural fluoridation)<br>Group 3: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | Enamel defects (DDE)<br>Age at assessment: 8 and 15 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Clarkson 1989 differs from that presented in McDonagh 2000 |

***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)<br>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)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Ireland<br>Geographic location: Ireland<br>Year of study: 1984<br>Year of change in fluoridation status: 1964<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 8 and 15 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: increase in use of fluoride-containing toothpaste and infant formula made with fluoridated water<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>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)<br>Group 2: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | Dental fluorosis (Deans Index); enamel defects (DDE)<br>Age at assessment: 8 and 15 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Ireland, England, Greece, Netherlands, Finland, Iceland, and Portugal<br>Geographic location: Cork, Haarlem, Athens, Reykjavík, Oulu, Knowsley, Almada/Setubal<br>Year of study: 1997 to 1998<br>Year of change in fluoridation status: varies<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>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.<br>SES: the sampling ensured a wide socioeconomic spread of participants.<br>Ethnicity: not stated<br>Residential history: parents were given questionnaires to supply information on history of living a fluoridated area. No further details reported<br>Other confounding factors: not stated | |
| Interventions | Group 1: < 0.01 ppm (natural fluoridation)<br>Group 2: 0.05 ppm (natural fluoridation)<br>Group 3: 0.08 ppm (natural fluoridation)<br>Group 4: < 0.1 ppm (natural fluoridation)<br>Group 5: 0.13 ppm (natural fluoridation)<br>Group 6: 1 ppm (artificial fluoridation) | |
| Outcomes | Dental fluorosis (TF Index); enamel defects (DDE)<br>Age at assessment: 8 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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% to 23%) is representative |
| Confounding | High risk | Data were collected on the use of fluoride from other sources but not reported |
| Blinding of outcome assessment (detection bias)<br>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)<br>All outcomes | Low risk | Quote: "A total of 5250 transparencies was taken, of which 114 (2.2%) were not suitable for analysis"<br>Comment: unlikely to influence results |
| Selective reporting (reporting bias) | Unclear risk | Outcome of interest fully reported, however data relating to confounding variables were 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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: New Zealand<br>Geographic location: Auckland |

| | |
|---|---|
| | Year of study: 1983<br>Year of change in fluoridation status: 1953<br>Study design: cross-sectional |
| Participants | Inclusion criteria: schoolchildren aged 7 to 12 years<br>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.<br>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 towards a greater severity of dental fluorosis among younger children.<br>SES: 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<br>Ethnicity: ethnic composition of study areas was similar except for higher proportion of Maori and Pacific Island people in the lower SES areas<br>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.<br>Other confounding factors: not stated |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | Dental fluorosis (diffuse opacities)<br>Age at baseline measure: 7 to 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Colquhoun 1984 differs from that presented in McDonagh 2000 |

***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 study 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 who were of low, middle and high SES while the non-fluoridated area had only participants of low SES. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Brazil<br>Geographic location: rural areas of Paraiba<br>Year of study: 1997<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; children attending public schools (aged 6 to 11 years)<br>Exclusion criteria: children who refused to be examined; those without permanent teeth; undetermined place of birth<br>Other sources of fluoride: no topical or systemic fluoride programme implemented in schools; children interviewed about oral health habits and use of toothpaste<br>SES: all study areas were of low SES<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: nutritional status |
| Interventions | Group 1: > 1.0 ppm (natural fluoridation)<br>Group 2: 0.7 to 1.0 ppm (natural fluoridation)<br>Control: < 0.7 ppm (natural fluoridation) |

| | |
|---|---|
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 6 to 11 years |
| Funding | Brazilian Ministry of Education CAPES (1666/95-4) |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 biases |

**Cutress 1985**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: New Zealand<br>Geographic location: Auckland, Frankton and Rodney<br>Year of study: not stated<br>Year of change in fluoridation: 1953<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children returning parental consent forms and completed questionnaires; lifetime residents of study areas; children aged 9 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: ingestion of fluoride tablets<br>SES: not stated<br>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).<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 1.0 ppm (artificial fluoridation)<br>Group 2: < 0.3 ppm (natural fluoridation) |
| Outcomes | Any enamel defect<br>Age at assessment: 9 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | Low risk | Children were taken to the examination centre by bus to prevent the examiner from identifying residence or fluoridation status. |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Brazil<br>Geographic location: Porto Feliz, Ipero, Itaoca and Barra do Chapeu (F); Bom Sucesso do Itarare and Itapirapua Paulista (non-F)<br>Year of study: 2003<br>Year of change in fluoridation status: 1981<br>Study design: cross-sectional |
| Participants | Inclusion criteria: pre-school children aged 5 to 6 years and students aged 7 to 12 years<br>Exclusion criteria: individuals outside the 5-to-12-years age bracket<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | Group 1: 'optimal' level - ppm not stated (artificial fluoridation)<br>Group 2: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | Dental fluorosis (CFI)<br>Age at assessment: 5 to 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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. |
| Confounding | High risk | Did not account for the use of other fluoride sources or SES. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data for all participants appear 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

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

| | | |
|---|---|---|
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Data extracted from de Crousaz 1982 differs from that presented in McDonagh 2000 | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| 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)<br>All outcomes | Low risk | Examiners worked independently without knowledge of the origin of the children. |
| Incomplete outcome data (attrition bias)<br>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 study 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

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: England<br>Geographic location: Watford (F); Sutton (non-F). Total population in each location was approximately 70,000 to 80,000 residents<br>Year of study: 1956<br>Year study ended: 1967<br>Year of change in fluoridation status: 1956<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment. |
| Participants | Inclusion criteria: lifetime residents of study areas; consumed piped water at home and at school<br>Exclusion criteria: children who were not continuous residents<br>Sample size at baseline: Group 1: 1608 children; Group 2: 1188 children<br>Sample size at final assessment: Group 1: 1578 children; Group 2: 1375 children<br>SES: 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)<br>Co-interventions: not stated (information on oral hygiene was recorded)<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: lifetime residents |
| Interventions | **Initiation of water fluoridation**<br>Group 1 at baseline: 'low' level - ppm not stated (natural fluoridation)<br>Group 1 post intervention: 0.89 ppm to 0.99 ppm (artificial fluoridation)<br>Group 2: 'low level' - ppm not stated (natural fluoridation) |
| Outcomes | dmft, DMFT, % caries-free children (primary teeth), % caries-free children (permanent teeth)<br>Age at baseline assessment: 3 to 14 years<br>Age at final assessment: 3 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Quote: "an area with broadly similar characteristics was selected as a control", although no reporting on how SES was measured or distributed<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Quote: "representative cross-sections of children attending school were selected"<br>**Deviations from intended interventions.** No deviations from intended intervention<br>**Missing data.** It is reported that representative cross-sections of children were examined at each time point. There is no information to make a judgement about the numbers examined versus the numbers reported. No data on confounding variables for participants is reported.<br>**Measurement of the outcome.** No blinding of assessment<br>**Selection of the reported result.** Outcome of interest reported, however, standard deviations missing |
| Notes | Data extracted from DHSS England 1969 differs from that presented in McDonagh 2000 (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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data for all participants appear 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; SD not reported |
| Other bias | High risk | No mention of calibration and reliability testing of the examiners |

**DHSS Scotland 1969**

| *Study characteristics* | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Scotland<br>Geographic location: Group 1: Kilmarnock (F); Group 2: Ayr (non-F). Total population size in each location approximately 43,000 residents<br>Year study started: 1956<br>Year study ended: 1968<br>Year of change in fluoridation status: 1956. Fluoridation stopped in 1962.<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment |
| Participants | Inclusion criteria: lifetime residents of study areas; consumed piped water at home and at school<br>Exclusion criteria: not stated<br>Sample size at baseline: Group 1. 209, Group 2. 184<br>Sample size at final assessment: Group 1. 306, Group 2. 262<br>SES: not stated<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: continuous residents |
| Interventions | **Initiation of fluoridation**<br>Group 1: 1 ppm (artificial fluoridation)<br>Group 2: 'low' level - ppm not reported (natural fluoridation) |
| Outcomes | dmft, % caries-free children (primary teeth)<br>Age at baseline assessment: 3 to 4 years<br>Age at final assessment: 3 to 4 years<br>DMFT data are reported, but without numbers per group or SDs, and only for baseline and 6 years after fluoridation ceased. |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Quote: "an area with broadly similar characteristics was selected as a control", although no reporting on how SES was measured or distributed.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Quote: "representative cross-sections of children attending school were selected"<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** It is reported that representative cross-sections of children were examined at each time point. There is no information to make a judgement about the numbers examined versus the numbers reported. No data on confounding variables for participants is reported.<br>**Measurement of the outcome.** No blinding of assessment<br>**Selection of the reported result.** Outcome of interest reported, however, SDs missing and it is stated in the 1962 report that examinations of nursery age children were taken but not reported. |
| Notes | Study evaluated children 3 to 7 years old; only 3- and 4-year-old data included in the review as full dentition not available for other age groups. |

**DHSS Wales 1969**

| *Study characteristics* | |
|---|---|
| Methods | |

| | |
|---|---|
| | **CARIES STUDY**<br>Country of study: Wales<br>Geographic location: Group 1 and Group 2: Gwalchmai zone (F); Holyhead (mainly F - gets most water from Gwalchmai, but occasionally also receives water from Bodafon); Group 3: Bodafon zone (non-F). Total population in Anglesey region was 50,000 residents<br>Year study started: 1956<br>Year study ended: 1965<br>Year of change in fluoridation status: 1955<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment. |
| 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)<br>Exclusion criteria: not stated<br>Sample size at baseline: Group 1: 3004 children; Group 2: 1980 children; Group 3: 3325 children<br>Sample size at final assessment: Group 1: 1525 children; Group 2: 977 children; Group 3: 1371 children<br>Other sources of fluoride: not stated<br>SES: not stated, however, study areas and associated control area had be situated near to each other and be of the same character (e.g. rural).<br>Co-interventions: not stated (information on oral hygiene was recorded)<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: continuous residents |
| Interventions | **Initiation of water fluoridation**<br>Group 1 baseline: 'low' level - ppm not stated (natural fluoridation)<br>Group 1 post intervention: 0.8 to 0.9 ppm (artificial fluoridation)<br>Group 2 baseline: 'low' level - ppm not stated (natural fluoridation)<br>Group 2 post intervention: 0.8 to 0.9 ppm (artificial fluoridation)<br>Group 3: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | dmft, DMFT, % caries-free children (primary teeth), % caries-free children (permanent teeth)<br>Age at baseline assessment: 3 to 14 years<br>Age at final assessment: 3 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Quote: "an area with broadly similar characteristics was selected as a control", although no reporting on how SES was measured or distributed<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** All eligible school children (those with lifetime residency) examined<br>**Deviations from intended interventions.** No deviations from intended intervention. The dose in the intervention area was found to vary from 0.71-0.96 ppm due to supplementation of water supplies locally however this is within the range for what is considered to be optimal dose.<br>**Missing data.** The study reports that "All eligible school children were examined", suggesting outcome data for all participants are presented although not explicitly stated. No data on confounding variables for participants are reported.<br>**Measurement of the outcome.** No blinding of assessment<br>**Selection of the reported result.** Outcome of interest reported, however, SDs missing |
| Notes | Data extracted from DHSS Wales 1969 differs from that presented in McDonagh 2000 (additional data extracted) |

**Downer 1994**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England, Scotland and Ireland<br>Geographic location: Dublin (F); north London, Edinburgh and Glasgow (non-F)<br>Year of study: not stated<br>Year of change in fluoridation status: 1965<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 12 years; lifetime residents of study areas<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated, however, sampling in the fluoridated areas was done to achieve a mix of participants from different SES<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |

| | |
|---|---|
| Interventions | Group 1: 0.9 ppm (artificial fluoridation)<br>Group 2: 'low' level - ppm not stated (natural fluoridation)<br>Group 3: 'low' level - ppm not stated (natural fluoridation)<br>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<br>Age at assessment: 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | 25% of the secondary schools in Glasgow and Dublin were 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 study authors state that this was "unlikely to have caused sampling bias".<br>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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 |

**Driscoll 1983**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: 7 rural Illinois communities within 75 miles of each other<br>Year of study: 1980<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children in grades 3-10 (age 8 to 16 years); lifetime residents of study areas; consumed public water; parental consent<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: relatively small, rural communities chosen because they shared several similar characteristics<br>Ethnicity: < 5% non-white<br>Residential history: lifetime residents<br>Other confounding factors: same climatic zone |
| Interventions | Group 1: 3.84 to 4.07 ppm (natural fluoridation)<br>Group 2: 2.84 to 3.77 ppm (natural fluoridation)<br>Group 3: 2.08 ppm (natural fluoridation)<br>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<br>Age at assessment: 8 to 16 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 in order 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)<br>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. |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All findings were based only on those children assessed for both fluorosis and caries; 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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sri Lanka<br>Geographic location: Uda Walawe<br>Year of study: 2001<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: almost all belonged to the low socioeconomic group<br>Ethnicity: not stated<br>Residential history: resident at present address since birth<br>Other confounding factors: no details reported; nearly 75% of the chldren had used fluoride toothpaste from the age of about 9 to 12 months (discussion section) | |
| Interventions | All natural fluoridation<br>Group 1: ≤ 0.3 ppm<br>Group 2: 0.31 to 0.49 ppm<br>Group 3: 0.5 to 0.7 ppm<br>Group 4: > 0.7 ppm | |
| Outcomes | Enamel defect (DDE)<br>Age at assessment: 14 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | 6.25% of the children examined were not included in the analysis. The study 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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Lordsburg (high-F); Deming (lower-F), New Mexico<br>Year of study: not stated<br>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; participants aged approximately 30 to 60 years old; consumed city water supplies<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: areas similar for education and income level; number of years of education similar between areas<br>Ethnicity: Lordsburg: 89.6% = Hispanic; Deming: 74.2% = Hispanic<br>Residential history: residence for the first 6 years of life<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 3.5 ppm<br>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<br>Age at assessment: 27 to 65 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Eklund 1987 differs from that presented in McDonagh 2000 |

***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% to 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)<br>All outcomes | Unclear risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England, Ireland and Wales<br>Geographic location: Chester (non-F); Bala (non-F); Anglesey (F); Cork (F)<br>Year of study: 1991<br>Year study ended: not reported<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional study |
| Participants | Inclusion criteria: lifetime residents of study areas (children only); agreement to participate<br>Exclusion criteria: fixed orthodontic appliances<br>Other sources of fluoride: tooth brushing behaviour - age started brushing; weekly tooth brushing frequency<br>SES: children from all 3 groups were from schools with a similar social profile<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.7 ppm (artificial fluoridation)<br>Group 2: 0.9 ppm (artificial fluoridation)<br>Group 3: < 0.1 ppm (natural fluoridation) |
| Outcomes | Enamel defect (DDE)<br>Age at assessment: 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | |

| | | |
|---|---|---|
| | | There was insufficient detail reported in order 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)<br>All outcomes | Low risk | Photographs were taken, identified randomly and examined without reference to participant details. |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England and Wales<br>Geographic location: Anglesey (F); Chester and Bala (non-F)<br>Year of study: 1991<br>Year of change in fluoridation status: 1955<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children in their 3rd year of secondary education; lifelong residents of study areas<br>Exclusion criteria: children with fixed orthodontic appliances; absence at the time of examination<br>Other sources of fluoride: not stated<br>SES: not stated, however, the schools in the non-fluoridated areas had similar catchment areas to those from the fluoridated area. No further details reported<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.7 (artificial fluoridation)<br>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<br>Age at assessment: 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | Low risk | Photographs were taken, randomly mixed and scored without reference to participant details. |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Turkey<br>Geographic location: Izmir and Isparta<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: the selected schools were public secondary schools<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>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<br>Group 1: 0.3 to 0.4 ppm<br>Group 2: 1.42 to 1.54 ppm<br>Group 3: 1.55 to 1.66 ppm |
| Outcomes | Dental fluorosis prevalence (TSIF); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 12 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Ghana<br>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)<br>Year of study: 2008-2009<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: medically confirmed dental problem different from dental fluorosis; history of tobacco or kola use<br>Other sources of fluoride: information on frequency of toothbrushing (P = 0.101) and type of oral health product (P = 0.179) were collected and there was no difference between the 4 zones<br>SES: the children had similar educational backgrounds<br>Ethnicity: not stated<br>Residential history: lifetime residents for first 7 years of childhood<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.95 ppm<br>Group 2: 1 ppm<br>Group 3: 1.86 ppm<br>Group 4: 2.36 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 7 to 18 years |
| Funding | Supported by the Regional Laboratory of the Ghana Water Company/Aqua Viten Rands Limited in Tamale, Ghana |

| | |
|---|---|
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data presented for all participants |
| 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 ..."<br>Comment: intra-examiner reliability test not reported and may not have been conducted |

**Forrest 1956**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>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)<br>Year of study: 1954<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; children aged 12 to 14 years<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 5.8 ppm<br>Group 2: 3.5 ppm<br>Group 3: 2.0 ppm<br>Group 4: 0.9 ppm<br>Group 5: 0.1 to 0.2 ppm<br>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<br>Age at assessment: 12 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Forrest 1956 differs from that presented in McDonagh 2000 |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Wales<br>Geographic location: Gwalchmai (F); Bodafon (non-F), Anglesey<br>Year of study: 1963<br>Year of change in fluoridation status: 1955<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: children aged 8 years from a selection of schools<br>Exclusion criteria: schools in Holyhead; schools in Llangefni and Beaumaris, as changed supply from fluoridated to non-fluoridated in 1961<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not clearly stated, however, the participants were chosen for being the only ones who had received fluoride for most of their lives.<br>Other confounding factors: not stated | |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: ≤ 0.2 ppm (natural fluoridation) | |
| Outcomes | Outcome: enamel defects<br>Age at assessment: 8 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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. |
| Blinding of outcome assessment (detection bias)<br>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)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Brazil<br>Geographic location: São Paulo<br>Year of study: not stated<br>Year of change in fluoridation status: 1975<br>Study design: cross-sectional |
| Participants | Inclusion criteria: residence in the same geographical area as the school since birth<br>Exclusion criteria: not stated<br>SES: homogeneous population comprising entirely of public school students<br>Ethnicity: white = 243 (67.5%); black = 41 (11.4%); admixture = 73 (20.3%); Asian = 3 (0.8%)<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 'optimal' level - ppm not stated (artificial fluoridation via water treatment station)<br>Group 2: 'optimal' level - ppm not stated (artificial fluoridation via direct fluoridation in well)<br>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 |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>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)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Mexico<br>Geographic location: Morelos<br>Year of study: 2013<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: systemic diseases requiring premedication; absence on the days of the oral examination; children who had brackets<br>Other sources of fluoride: bottled water often containing 0.3 to 0.6 ppm fluoride levels; dentifrice use; number of times brushing teeth per day<br>SES: both communities had a low socioeconomic level<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.56 to 0.76 ppm<br>Group 2: 1.45 to 1.61 ppm |
| Outcomes | Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design<br>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) |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | Unclear risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Brazil<br>Geographic location: Piracicaba (F); Iracemapolis (non-F)<br>Year of study: not stated<br>Year of change in fluoridation status: 1974<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 10-14; lifetime residents of study areas<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: < 0.2 ppm (natural fluoridation)<br>Group 2: 0.7 ppm (artificial fluoridation) |
| Outcomes | Dental fluorosis prevalence (TF Index)<br>Age at assessment: 10 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data from McDonagh 2000; unable to obtain original unpublished study (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)<br>All outcomes | Unclear risk | Unable to make a judgement as study was unavailable |
| Incomplete outcome data (attrition bias)<br>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 |

## Goodwin 2022

***Study characteristics***

| | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: UK<br>Geographic location: West Cumbria (F) - population size 132,134 residents; East Cumbria (non-F) - population size 333,909 residents<br>Year study started: 2013. We note that this area had previously been served by a water fluoridation programme since the 1960s, but the scheme was paused in 2006 owing to a refurbishment project. The start of the study in 2013 was a recommencement of a water fluoridation programme.<br>Year study ended: 2019<br>Year of change in fluoridation status: 2013<br>Study design: CBA. The same cohort of children was followed up from baseline to final assessment. |
| Participants | Inclusion criteria: children living in the study areas. For the older school cohort - attending state school, in first year of study at time of recruitment, had been lifetime residents of predefined areas of Cumbria<br>Exclusion criteria: people planning to move from the area during the study period; lack of consent; individuals with life-threatening conditions (including maternal and foetal, for birth cohort) at time of recruitment<br>Sample size at baseline: Group 1: 786 children; Group 2: 1249 children<br>Sample size at final assessment: Group 1: 609 children; Group 2: 835 children.<br>SES: higher levels of deprivation in fluoridated water locations<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: equally balanced<br>Residential history: lifetime residents |
| Interventions | Initiation of water fluoridation<br>Group 1: 1 ppm fluoride (artificial fluoridation) |

| | |
|---|---|
| | Group 2: 'non-WF', ppm not stated (natural fluoridation) |
| Outcomes | DMFT; dmft; health inequalities<br>Age at baseline assessment: birth cohort (born in first year of study); older school cohort - 5 years of age<br>Age at final assessment: birth cohort - 5 years; older school cohort - 11 years |
| Funding | NIHR Public Health Research programme |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Quote: "In both cohorts, the primary outcome and secondary outcomes (dmft/DMFT) were compared across exposed and non-exposed groups by quintile of deprivation"<br>**Classification of interventions.** Quote: "The fluoridated area in Cumbria covers a population of approximately 132,134 people in the areas of Allerdale and Copeland (but not all residents in Allerdale and Copeland receive WF)." The proportion of those not receiving WF is unclear.<br>**Selection of participants into the study/analysis.** Birth cohort - quote: "All new parents were approached during pregnancy and postnatally"; Older cohort - quote: "all primary schools in West Cumbria and a comparable group across North Cumbria"<br>**Deviations from intended interventions.** Quote: "there was substantial interruption to the dosing of water supplies caused, in part, by a series of major flooding events that hit Cumbria at the end of 2015 and start of 2016, as well as the innate fragility of the plants themselves". It is noted that such variations in dosing is common within water fluoridation programmes.<br>**Missing data.** No concerns<br>**Measurement of the outcome.** Quote: "The difference in the proportion of participants with decay between test and control groups assessed using blinded photographs was compared with the difference in the proportion of participants with decay between test and control groups assessed using traditional unblinded clinical examinations to identify any systematic bias". For birth cohort a kappa score of 0.71 was shown; no kappa score presented for older cohort<br>**Selection of the reported result.** No concerns |
| Notes | |

## Goward 1982

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>Geographic location: 2 adjacent districts of Leeds with different fluoride levels<br>Year of study: 1979<br>Year of change in fluoridation status: 1968<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas (children only); children aged 5<br>Exclusion criteria: not clear, though children using systemic or topical fluoride supplements were excluded from the study<br>Other sources of fluoride: children using systemic or topical fluoride supplements excluded from the study<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: difference in breastfed vs bottle-fed children |
| Interventions | Group 1: 0.9 ppm (artificial fluoridation)<br>Group 2: < 0.1 ppm (natural fluoridation) |
| Outcomes | Dental fluorosis (defined by Al-Alousi)<br>Age at time of measurement: 5 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order to determine how selection took place. |
| Confounding | High risk | Did not account for SES |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: England<br>Geographic location: Group 1: Sedgeley and Coseley (F), Group 2: Dudley town (F), Group 3: Brierley Hill and Kingswinford (F), Group 4: Halesowen (F); Group 5: Stourbridge (non-F). Total population sizes for each location not stated<br>Year study started: 1988<br>Year study ended: 1997<br>Year of change in fluoridation status: 1987<br>Study design: CBA. A different sample of children was assessed at baseline and time points during the study, according to age at the time of assessment. |
| Participants | Inclusion criteria: children living in study area since 1988<br>Exclusion criteria: not stated<br>Sample size at baseline: Group 1: 537 children; Group 2: 552 children: Group 3: 826 children; Group 4: 547 children; Group 5: 466 children<br>Sample size at final assessment: Group 1: 475 children; Group 2: 594 children; Group 3: 891 children; Group 4: 564 children; Group 5: 419 children<br>SES: participants were all from state-funded primary schools and might have been socioeconomically similar<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: not stated<br>Residential history: lifetime residents |
| Interventions | **Initiation of water fluoridation**<br>Group 1: 1 ppm (artificial fluoridation)<br>Group 2: 1 ppm (artificial fluoridation)<br>Group 3: 1 ppm (artificial fluoridation)<br>Group 4: 1 ppm (artificial fluoridation)<br>Group 5: 0.3 ppm (natural fluoridation) |
| Outcomes | % caries free (primary teeth)<br>Age at baseline assessment: 5 years<br>Age at final assessment: 5 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment.<br>**Classification of interventions.** Quote: "the location of the school attended by children, was used in the 1988/89 and the 1992/93 studies as the basis for allocating children to each of the towns. This is not an ideal basis, as children may live in one area and attend school in a neighbouring area and there will be some cross boundary flow in the two earlier studies."<br>**Selection of participants into the study/analysis.** According to Pitts 1997, representative samples were drawn from a whole population of Dudley health authority<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** Insufficient information<br>**Measurement of the outcome.** No blinding of assessors<br>**Selection of the reported result.** No evidence of selective reporting |
| Notes | Data extracted from Gray 2001 differs from that from Gray 2000 (unpublished) which was originally presented in McDonagh 2000 |

### Grimaldo 1995

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Mexico<br>Geographic location: San Luis Potasi<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents at same address; children aged 11 to 13 years in selected schools; parental consent |

| | |
|---|---|
| | Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: local diet rich in calcium, reduces fluoride absorption |
| Interventions | All natural fluoridation<br>Group 1: > 2.0 ppm<br>Group 2: 1.2 to 2.0 ppm<br>Group 3: 0.7 to 1.2 ppm<br>Group 4: < 0.7 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 11 to 13 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | The study 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | There was a variation in the number 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 |
| Other bias | High risk | No indication that the examiners were calibrated |

### Grobler 1986

***Study characteristics***

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

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | All available participants were included in the study population. Insufficient 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)<br>All outcomes | High risk | Insufficient information. Examinations were made at the children's schools but no mention of blind assessment |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: South Africa<br>Geographic location: Leeu Gamka, Kuboes and Sanddrif<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: not stated<br>Other sources of fluoride: participants had virtually no dental care or fluoride therapy, including the use of fluoride-containing toothpaste<br>SES: similarly low socioeconomic status across groups reflected in the fact that they all lived in subeconomic housing units<br>Ethnicity: mixed ethnic origin from Khoi, Caucasian and Negroid roots which over hundreds of years have developed into a homogeneous ethnic group<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.19 ppm<br>Group 2: 0.48 ppm<br>Group 3: 3 ppm | |
| Outcomes | Outcome: fluorosis prevalence (Dean's Index); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 10 to 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Taiwan<br>Geographic location: Group 1: Chung-Hsing New Village (F); Group 2: Tsao-Tun (non-F). Total population size of each location not stated<br>Year of study: 1971<br>Year study ended: 1981<br>Year of change in fluoridation status: 1971 |

| | |
|---|---|
| | Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment. |
| Participants | Inclusion criteria: lifetime residents of study areas<br>Exclusion criteria: children who migrated from other areas during study period<br>Sample size at baseline: not stated<br>Sample size at final assessment: Group 1: 2995 children; Group 2: 4438 children<br>SES: not stated<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: equally balanced<br>Residential history: lifetime residents<br>Other: similar climate with mean daily air temperature of 24 °C |
| Interventions | **Initiation of water fluoridation**<br>Group 1 baseline: 0.07 ppm (natural fluoridation)<br>Group 1 post-intervention: 0.6 ppm (artificial fluoridation)<br>Group 2: 0.08 ppm (natural fluoridation) |
| Outcomes | dmft, DMFT, % caries-free (primary), % caries-free (permanent)<br>Age at baseline assessment: 5, 8, 12 and 15 years<br>Age at final assessment: 5, 8, 12 and 15 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** All children studied were either born in the area or had continuous residence<br>**Deviations from intended interventions.** No deviations from intended intervention<br>**Missing data.** Unclear<br>**Measurement of the outcome.** Insufficient information regarding blinding; examiners likely to know fluoridation status<br>**Selection of the reported result.** No apparent selection of reporting |
| Notes | Data extracted from Guo 1984 differs from that presented in McDonagh 2000 |

### Haavikko 1974

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Finland<br>Geographic location: Espoo (low F); Elimaki (high F); Hanko (optimal F); Lohja (low F)<br>Year of study: 1969<br>Year of change in fluoridation status: NA<br>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 to 11 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: continuous residence for the first 6 years<br>Other confounding factors: food sources of fluoride |
| Interventions | All natural fluoridation<br>Group 1: 1.08 ppm<br>Group 2: 0.41 ppm<br>Group 3: 0.11 ppm<br>Group 4: 0.05 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 10 to 11 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Ireland<br>Geographic location: Cork city (F); Cork county (non-F)<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: age 5 years; location of the school attended and fluoridation status of water supply<br>Exclusion criteria: absence on the day of examination; too apprehensive to participate or < 5 years; incorrectly received a form; incomplete form; existing medical condition<br>Other sources of fluoride: fluoride prevalence of children with different nutritional and brushing habits were reported: breastfed = 30 (28%) vs not breastfed = 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 = 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%)<br>SES: schools were chosen to provide a socioeconomic spread; 7 urban and 10 rural schools<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: food sources of fluoride |
| Interventions | Group 1: 0.8 to 1 ppm (artificial fluoridation)<br>Group 2: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | Dental fluorosis (TSIF)<br>Age at assessment: 5 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 examiner but no report of calibration nor intra-examiner reliability tests |

## Hardwick 1982

| *Study characteristics* |
|---|

| | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: England<br>Geographic location: Group 1: Alsager, Middlewich, Nantwich (F), Group 2: Northwich (non-F). Total population size in each location not stated<br>Year study started: 1974<br>Year study ended: 1978<br>Year of change in fluoridation status: 1975<br>Study design: prospective cohort. The same cohort of children was followed from baseline to end of study |
| Participants | Inclusion criteria: 12-year-old children living in study area. Consent from relevant country authorities and teachers at schools included in the study<br>Exclusion criteria: none stated<br>Sample size at baseline: Group 1: 305 children; Group 2: 343 children<br>Sample size at final assessment: Group 1: 144 children; Group 2: 199 children<br>SES: control and experimental groups matched on urban and rural characteristics<br>Co-interventions: fluoridation 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<br>Ethnicity: not stated<br>Gender: quote: "close agreement between the two groups of children in...sex ratios..."<br>Residential history: not stated |
| Interventions | **Initiation of water fluoridation**<br>Group 1 baseline: < 0.1 ppm (natural fluoridation)<br>Group 1 post intervention: 1.0 ppm (artificial fluoridation)<br>Group 2: < 0.1 ppm (natural fluoridation) |
| Outcomes | DMFT, DMFS<br>Age at baseline assessment: 12 years<br>Age at final assessment: 16 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** SES not accounted for in analysis. Non-fluoridated area comprised "a mix of small urban and rural communities similar to those of the fluoridated area".<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Census approach taken in order to obtain the required numbers for the study. All schools in the area were involved in the study.<br>**Deviations from intended interventions.** No deviations from intended intervention<br>**Missing data.** Baseline examination of 677 children (ns not reported by group). 343 children examined at 4th annual re-examination (199 non-F, 144 F), 49% attrition. One large school in the fluoridated area withdrew from the study due to exams and so two "similar" schools in the non-fluoridated area were withdrawn from the study.<br>**Measurement of the outcome.** Dental examiner was blind to fluoridation status as central examination centre was used for assessment. Calibrated for clinical and radiographic assessment.<br>**Selection of the reported result.** No apparent selection of reporting |
| Notes | |

**Heifetz 1988**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: 7 rural towns within 75 miles of each other in Illinois<br>Year of study: 1980 to 1985<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 8 to 10 years and 13 to 15 years; continuous residence in study community<br>Exclusion criteria: not stated<br>Other sources of fluoride: food and drinks produced in fluoride areas<br>SES: study areas shared similar socioeconomic characteristics<br>Ethnicity: not stated<br>Residential history: continuous residence<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 3.8 to 4.1 ppm |

| | | |
|---|---|---|
| | Group 2: 2.8 to 3.8 ppm<br>Group 3: 2.1 ppm<br>Group 4: 1.1 ppm | |
| Outcomes | Dental fluorosis (TSIF); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 13 to 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | There was insufficient detail reported in order 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. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| | | |
|---|---|---|
| ***Study characteristics*** | | |
| Methods | **FLUOROSIS STUDY**<br>Country of study: Brazil<br>Geographic location: Garca (F); Itrapolis (non-F), São Paulo state<br>Year of study: 1995<br>Year of change in fluoridation status: 1973 and 1975<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: children aged 5 to 24 years; from all social strata; used tap water; took urine samples from all 3 daytime periods<br>Exclusion criteria: children that used tap water, otherwise not stated<br>Other sources of fluoride: children 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<br>SES: cities similar in socioeconomic and socio-demographic conditions, children from all social strata included<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: Garca altitude = 526 m, mean temperature = 22 °C, population = 41,351; Itapolis: altitude = 491 m, mean temperature = 23 °C, population = 30,111 | |
| Interventions | Group 1: 0.9 ppm (artificial fluoridation)<br>Group 2: 0.02 ppm (natural fluoridation) | |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 5 to 24 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: national survey of oral health of US school children<br>Year of study: 1986<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; aged 7 to 17 years; completion of survey by parents<br>Exclusion criteria: none stated<br>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<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: continuous residency<br>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)<br>Group 2: 0.7 to 1.2 ppm (artificial fluoridation)<br>Group 3: 0.3 to 0.7 ppm (natural fluoridation)<br>Group 4: < 0.3 ppm (natural fluoridation) |
| Outcomes | Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 7 to 17 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Mexico<br>Geographic location: not stated<br>Year of study started: 2001<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: having at least 1 year residence in the study area<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: ≥ 1 year residence in study area |

| | |
|---|---|
| | Other confounding factors: in all study areas, parents reported the use of fluoride toothpaste |
| Interventions | All natural fluoridation<br>Group 1: 0.74 ppm<br>Group 2: 1.3 ppm<br>Group 3: 3.56 ppm<br>Group 4: 4.07 ppm<br>Group 5: 5.19 ppm<br>Group 6: 5.57 ppm<br>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<br>Age at assessment: 9 to 11 years |
| Funding | Financial and logistical support from the Health Institute of the State of Aguascalientes, Institute Tecnologico de Aguascalientes and COSNET |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: England<br>Geographic location: north Birmingham and Sandwell (F), North Staffordshire, Herefordshire and Shropshire (non-F)<br>Year study started: 1985/6<br>Year of change in fluoridation status: 1986<br>Study design: CBA |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>SES: measured using Jarman scores<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: N/A<br>Residential history: not stated |
| Interventions | **Initiation of water fluoridation**<br>Group 1: not stated<br>Group 2: not stated |
| Outcomes | dmft<br>Age at baseline assessment: not stated<br>Age at final assessment: not stated |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | We could not conduct a complete assessment of the risk of bias because we did not have the full text. Judgements on risk of bias due to missing data (as reported in the main text and Table 1) have been taken from McDonagh 2000. |
| Notes | Data from original McDonagh 2000; unable to obtain original unpublished study (unverified data) |

## Hong 1990

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Taiwan<br>Geographic location: Chung-hsing New village (F) and Tsao-tun (non-F) |

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

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | The participating sample consisted of children from 6 to 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sudan<br>Geographic location: Abu Gronn (F); Treit El Biga (low F)<br>Year of study: 1992<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: at least 1 erupted permanent maxillary incisor; lifetime residents of study areas; age 7 to 16 years<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: author stated that areas had more or less the same socioeconomic background<br>Ethnicity: author stated that areas had more or less the same ethnic background<br>Residential history: lifetime residents<br>Other confounding factors: altitude = 300 m for both areas; mean temperature = 25 °C to 35 °C. In low F area, boys had significantly more fluorosis than girls |
| Interventions | All natural fluoridation<br>Group 1: 2.56 ppm<br>Group 2: 0.25 ppm |
| Outcomes | Dental fluorosis (CFI)<br>Age at assessment: 7 to 16 years |
| Funding | Norwegian Universities Committee for Development Research and Education |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Ibrahim 1995 differs from that presented in McDonagh 2000 |

***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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Estonia<br>Geographic location: Tartu city<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: not stated<br>SES: selected districts were of same eco-environmental, ethnic as well as socio-economic standards<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.2 ppm<br>Group 2: 0.3 ppm<br>Group 3: 1.2 ppm<br>Group 4: 1.6 ppm<br>Group 5: 2.4 ppm<br>Group 6 3.9 ppm |
| Outcomes | Dental fluorosis (index not reported)<br>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 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data presented for all participants |
| 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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Estonia<br>Geographic location: not stated<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated |

| | |
|---|---|
| | SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: < 1 ppm<br>Group 2: 1 to 1.5 ppm<br>Group 3: 1.51 to 2 ppm<br>Group 4: 2.1 to 3 ppm<br>Group 5: 3.1 to 4 ppm<br>Group 6: > 4 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 7 to 15 years |
| Funding | The study was supported by the Estonian Society of Stomatology and Estonian Science Foundation grant number 7403 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 subsample was selected from town 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Wales<br>Geographic location: Anglesey (F); Bangor and Caernarfon (non-F)<br>Year of study: 1974<br>Year of change in fluoridation status: 1955<br>Study design: unclear | |
| Participants | Inclusion criteria: lifetime residents of study areas; continuous use of public water supply; school children aged 15 years; parental consent<br>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<br>Other sources of fluoride: children who had received fluoride tablets excluded<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | Group 1: 0.9 ppm (artificial fluoridation)<br>Group 2: < 0.1 ppm (natural fluoridation) | |
| Outcomes | Mottling; caries data collected, however, not presented in this review due to study design<br>Age at assessment: 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>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)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Connersville (non-F); Brownsburg (optimal-F); Lowell (high-F), Indiana<br>Year of study: 1992<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |

| | |
|---|---|
| Participants | Inclusion criteria: lifetime residents of study areas; consumed public water from birth or supply with comparable water level; children aged 7 to 14 years; parental and personal consent<br>Exclusion criteria: factors in medical history that would contraindicate a dental examination; full mouth fixed orthodontic appliance<br>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<br>SES: not stated<br>Ethnicity: approximately 2% non-white (stated for baseline survey)<br>Residential history: lifetime residents<br>Other confounding factors: areas all in same climatic zone |
| Interventions | All natural fluoridation<br>Group 1: 4.0 ppm<br>Group 2: 1.0 ppm<br>Group 3: 0.2 ppm |
| Outcomes | Dental fluorosis (TSIF)<br>Age at assessment: 7 to 10 years and 11 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: the Punjab<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: school children<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All naturally fluoridated<br>Group 1: 0.7 ppm<br>Group 2: 1.4 ppm<br>Group 3: 2.4 ppm<br>Group 4: 2.4 ppm<br>Group 5: 2.5 ppm<br>Group 6: 3.0 ppm<br>Group 7: 3.0 ppm<br>Group 8: 3.3 ppm<br>Group 9: 3.3 ppm<br>Group 10: 3.6 ppm<br>Group 11: 4.3 ppm<br>Group 12: 5.0 ppm<br>Group 13: 5.09 ppm<br>Group 14: 5.49 ppm<br>Group 15: 7.02 ppm |

| | |
|---|---|
| | Group 16: 8.5 ppm<br>Group 17: 9.5 ppm |
| Outcomes | Mottled enamel; skeletal fluorosis<br>Age at assessment: 5 to 15 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: New Zealand<br>Geographic location: Auckland<br>Year of study: not stated<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional |
| Participants | Inclusion criteria: only children who returned signed consent form and questionnaire completed by parents<br>Exclusion criteria: schools with fewer than five 9-year-old children were excluded because of resource, time and efficiency constraints<br>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<br>SES: high (deciles 8 to 10) = 40% (F), 19% (non-F); middle (deciles 4 to 7) = 141% (F), 44% (non-F); low (deciles 1 to 3) = 19% (F), 37% (non-F) (a school's decile indicates the extent to which it includes students from low socioeconomic communities)<br>Ethnicity: more children of European descent and fewer children of Asian descent attended schools within non-fluoridated areas compared with fluoridated areas<br>Residential history: lifetime residents and intermittent residents, however, data on lifetime residents alone presented in this review due to confounding<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.1 to 0.3 ppm (natural fluoridation)<br>Group 2: 0.7 to 1 ppm (artificial fluoridation) |
| Outcomes | Dental fluorosis (Dean's Index); caries data collected, however, not presented in this review due to study design<br>Age at assessment: 7 to 15 years |
| Funding | Funded by AUT University, Counties Manukau District Health Board and New Zealand Dental Research Foundation |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 high-decile schools |

| | | |
|---|---|---|
| | | in non-fluoridated areas and fewer children in low-decile schools in fluoridated areas |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 |

**Kim 2019**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: South Korea<br>Geographic location: Group 1: Hapcheon (F); Group 2: National (non-F). Total population sizes for each location not stated<br>Year study started: 2000<br>Year study ended: 2015<br>Year of change in fluoridation status: 2000<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment. |
| Participants | Inclusion criteria: children aged 8, 10 and 12 in the intervention area (Hapcheon) attending 2 primary and 2 middle schools selected for study (reason for selection of each of the schools in unclear). For the control group, data were taken from the KNHANES survey for children aged 8, 10 and 12.<br>Sample size at baseline: Group 1: 671 children; Group 2: 3603 children<br>Sample size at final assessment: Group 1: 498 children; Group 2: 952 children<br>Exclusion criteria: none stated<br>SES: not stated<br>Co-interventions: there was a difference in the proportion of dental sealants placed in children across the groups. There was a greater proportion of sealants placed in the children in the intervention group at baseline compared with the national control group.<br>Ethnicity: not stated<br>Gender: distribution was broadly similar across groups<br>Residential history: not stated |
| Interventions | **Initiation of water fluoridation**<br>Group 1: Community water fluoridation programme (ppm not reported; artificial fluoridation)<br>Group 2: low or no fluoride content (ppm not reported; natural fluoridation) |
| Outcomes | % caries-free participants<br>Age at baseline assessment: 8, 10, 12 years (permanent dentition)<br>Age at final assessment: 8, 10, 12 years (permanent dentition) |
| Funding | Unfunded research |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Eligible children attending 2 primary and 2 middle schools in the intervention area were included in the study; it is not clear how the schools were selected. National data was used for the control group.<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** No apparent missing data though there are greater numbers at baseline, particularly in the control group. There are no data pertaining to the confounder.<br>**Measurement of the outcome.** Insufficient information regarding blinding of assessors<br>**Selection of the reported result.** No apparent selective reporting |
| Notes | |

**Kotecha 2012**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: not stated<br>Year of study: not stated<br>Year of change in fluoridation status: NA |

| | |
|---|---|
| | Study design: cross-sectional |
| Participants | Inclusion criteria: all age groups<br>Exclusion criteria: those who could not be studied in the second visit<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: < 1.5 ppm<br>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<br>Age at assessment: all age groups |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Newburgh City (F); Newburgh Town (F 1984); New Windsor (non-F); Kingston (non-F)<br>Year study started: 1986<br>Year study ended: 1995<br>Year of change in fluoridation status: 1984<br>Study design: CBA |
| Participants | Inclusion criteria: children aged 7 to 14 years; lifetime residents of study areas<br>Exclusion criteria: not stated<br>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<br>SES: not stated<br>Ethnicity: no difference in odds of fluorosis in African-Americans compared to white and other races<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: 1 ppm (artificial fluoridation)<br>Group 3: 'low' level - ppm not stated (natural fluoridation)<br>Group 4: 'low' level - ppm not stated (natural fluoridation)<br>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<br>Age at baseline measure: 7 to 14 years<br>Age at final measure: 7 to 14 years |
| Funding | Supported by a grant from the National Institute of Dental Research (R01 DE 1088801) |

| | | |
|---|---|---|
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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 in order to determine how selection took place. |
| Confounding | Unclear risk | While the study authors reported that SES was considered, this information was not reported. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 large 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**

| | | |
|---|---|---|
| ***Study characteristics*** | | |
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: not stated<br>Year study started: 1999 to 2000<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.6 ppm<br>Group 2: 1.1 ppm<br>Group 3: 1.1 ppm<br>Group 4: 1.1 ppm<br>Group 5: 1.2 ppm<br>Group 6: 1.3 ppm<br>Group 7: 1.7 ppm<br>Group 8: 1.7 ppm<br>Group 9: 1.8 ppm<br>Group 10: 1.9 ppm<br>Group 11: 2.1 ppm<br>Group 12: 2.9 ppm<br>Group 13: 4.6 ppm | |
| Outcomes | Dental fluorosis (Smith's classification)<br>Age at assessment: 5 to 14 years | |
| Funding | Indian Council of Medical Research | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Cuba<br>Geographic location: La Salud (low F); Mir (medium F); San Augustin and Blanqizal (high F)<br>Year of study: 1973<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: children resident in study areas<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated however, most of the children were born in the area<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 2.3 to 3.6 ppm<br>Group 2: 1.1 to 1.6 ppm<br>Group 3: 0.6 to 0.8 ppm<br>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<br>Age at assessment: 9 to 10 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>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)<br>All outcomes | Low risk | Data presented for all participants |
| Selective reporting (reporting bias) | Low risk | All expected outcomes reported |
| Other bias | Low risk | No other apparent biases |

**Kunzel 1997**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Germany<br>Geographic location: Group 1: Chemnitz (F), population size of 300,000 residents; Group 2: Plauen (non-F), population size of 95,000 residents<br>Year study started: 1959<br>Year study ended: 1971<br>Year of change in fluoridation status: 1959<br>Study design: CBA |
| Participants | Inclusion criteria: children born in study areas<br>Exclusion criteria: children who had moved into the 2 study areas; disabled children<br>Sample size at baseline: Group 1: 17,906 children; Group 2: 5241 children<br>Sample size at final assessment (1971): 24,317 children; Group 2: 8882 children<br>SES: not stated<br>Co-interventions: number of topical applications of fluoride toothpastes; solutions and gel was low - water fluoridation was the only preventive measure.<br>Ethnicity: not stated |

| | |
|---|---|
| | Gender: not stated<br>Residential history: lifetime residents<br>Other: increasing annual sugar consumption in both areas |
| Interventions | **Initiation of water fluoridation**<br>Group 1 baseline: 0.2 ppm (natural fluoridation)<br>Group 1 post intervention: 1 ppm (artificial fluoridation)<br>Group 2: 0.2 ppm (natural fluoridation) |
| Outcomes | dmft, DMFT, % caries-free (primary dentition), % caries-free (permanent dentition)<br>Age at baseline assessment: 6 to 15 years<br>Age at final assessment: 6 to 15 years |
| Funding | Supported by the German Federal Ministry of Education, Science, Research and Technology, grant 01 ZZ 9502 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** School children born in either of the two study areas.<br>**Deviations from intended interventions.** There were deviations from the intervention reported in the paper but not covering the time period of the data extracted for this review. Fluoride concentration was suboptimal for 1973-1977, and was switched off due to technical error for 22 months in 1971. Only data up to 1971 have been used in this review and the dose is reported to be stable for this period (1959-1971).<br>**Missing data.** Unclear<br>**Measurement of the outcome.** Examinations took place in schoolrooms; examiners likely to know fluoridation status<br>**Selection of the reported result.** No apparent selection of reporting |
| Notes | Data extracted from Kunzel 1997 differs from that presented in McDonagh 2000 (additional data extracted)<br>Study presents data on both initiation and cessation of water fluoridation, but cessation data excluded from this review due to unsuitable control group. Data for Period 1 (1959 to 1971) used; fluoridation interrupted/suboptimal post 1971. |

**Leverett 1986**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Rochester, NY and several surrounding towns (F); 4 towns in western New York state (non-F)<br>Year of study: 1981<br>Year of change in fluoridation status: 1963<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: children resident in study areas; children aged 7 to 17 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: children in both non-F and F areas were "not necessarily lifetime residents of their communities"<br>Other confounding factors: none stated | |
| Interventions | Group 1: 1.0 ppm (artificial fluoridation)<br>Group 2: ≤ 0.3 ppm (natural fluoridation) | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 7 to 17 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | There was insufficient detail reported in order to determine how selection of children within schools took place. |
| Confounding | High risk | Did not account for the use of fluoride from other sources or SES |

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>Geographic location: Birmingham (F); Leeds (non-F)<br>Year of study: 1987<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: lifetime residents of study areas (children only); schools with catchment areas inside study areas; children aged 9 to 10 years<br>Exclusion criteria: Asian and West Indian children; non-continuous residents; teeth with fractures or restorations; children who had received fluoride supplements at any time<br>Other sources of fluoride: children who had received fluoride supplements at any time excluded<br>SES: schools selected that served similar socioeconomic populations (social class groups 3, 4, 5)<br>Ethnicity: Asian and West Indian children excluded<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: < 0.1 ppm (natural fluoridation) | |
| Outcomes | Enamel defect-hypoplasia (TSIF)<br>Age at assessment: 9 to 10 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Data extracted from Levine 1989 differs from that presented in McDonagh 2000 | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | Low risk | Photographic examination was blinded.<br>Quote: "The colour transparencies were coded and placed in a random sequence before being projected and viewed" |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: Xinyuan (F); Langan and Jiayi (non-F)<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: school children aged 7 to 14 years<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: low SES, mean annual income of about 200 yuan |

| | |
|---|---|
| | Ethnicity: not stated<br>Residential history: not reported<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.88 ppm<br>Group 2: 0.34 ppm |
| Outcomes | Dental fluorosis<br>Age at assessment: 7 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Sampling | Low risk | Used random stratified sampling |
| Confounding | High risk | Did not account for the use of fluoride from other sources |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Singapore and West Malaysia<br>Geographic location: Singapore (F), population size approximately 2.9 million residents; Malacca (non-F), town in West Malaysia, population size not stated<br>Year study started: 1957<br>Year study ended: 1966<br>Year of change in fluoridation status: 1958<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment. |
| Participants | Inclusion criteria: Chinese and Malay children aged 7 to 9 years<br>Exclusion criteria: not stated<br>Sample size at baseline: overall, approximately 2200 children (not reported by group)<br>Sample size at final assessment: overall, approximately 2200 children (not reported by group)<br>SES: not stated<br>Co-interventions: not stated<br>Ethnicity: Chinese and Malay children - results presented separately<br>Gender: not stated<br>Residential history: unclear |
| Interventions | **Initiation of water fluoridation**<br>Group 1: 0.7 ppm (artificial fluoridation)<br>Group 2: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | DMFT<br>Age at baseline assessment: 7 to 9 years<br>Age at final assessment: 7 to 9 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment.<br>**Classification of interventions.** Intervention status classified correctly for SIngapore; limited information on fluoridation status for Malacca (Malyasia)<br>**Selection of participants into the study/analysis.** Insufficient detail reported in order to determine how selection of schools and children within those schools took place<br>**Deviations from intended interventions.** It is reported in the paper that due to technical issues there was variation in the dosing of fluoride in the water in the 'earlier years'. It is not reported what the variation range was or for how long this lasted<br>**Missing data.** Unclear<br>**Measurement of the outcome.** Examinations took place in mobile dental clinics in each country; examiners likely to know fluoridation status |

| | |
|---|---|
| | **Selection of the reported result.** No apparent selection of reporting |
| Notes | |

### Louw 2002

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: South Africa<br>Geographic location: Sanddrif, Williston, Kuboes, Fraserburg, Brandvlei, Kenhardt, and Leeu Gamka<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: aged 11 to 13 years, similar nutrition and dietary habits, similar ethnic and SES<br>Exclusion criteria: not stated<br>Other sources of fluoride: no dental care or fluoride therapy, including the use of fluoride-containing toothpaste<br>SES: similarly low SES reflected in living in sub-economic housing units<br>Ethnicity: mixed with Khoi, Caucasian and Negroid roots that developed into a homogeneous ethnic group<br>Residential history: lifetime residents<br>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<br>Group 1: 0.19 ppm<br>Group 2: 0.36 ppm<br>Group 3: 0.48 ppm<br>Group 4: 1 ppm<br>Group 5: 1.66 ppm<br>Group 6: 2.64 ppm<br>Group 7: 3 ppm |
| Outcomes | Dental fluorosis prevalence (Dean's Index)<br>Age at assessment: 11 to 13 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | Insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Lithuania<br>Geographic location: Vilkaviskis and Jonuciai<br>Year of study: 2004<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: never having taken part in any caries preventive programme; lifetime residency in the area; informed consent to participate<br>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<br>SES: 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<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.3 ppm<br>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<br>Age at assessment: 13 years (mean) |
| Funding | Funded by Unrestricted grant from Colgate Palmolive (USA) |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information. The measurement and recording of outcomes were by different personnel, but they were not reported to have been blinded. |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: New Zealand<br>Geographic location: not stated<br>Year of study: 2002<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: ingestion of toothpaste before the age of 3 years = 40%; use of fluoride tablets up to (and including) age 3 years = 49 (11.2%)<br>Ethnicity: not stated<br>SES: high SES school (deciles 8 to 10) = 192 (44%); medium SES school (deciles 4 to 7) = 121 (27.8%); low SES school (deciles 1 to 3) = 128 (28.2%)<br>Residential history: the study included both continuous and intermittent residents, however, only data from continuous residents included in analysis<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.1 to 0.3 ppm (natural fluoridation)<br>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<br>Age at assessment: 8.7 to 11.1 years |
| Funding | New Zealand Dental Research Foundation |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 enroled 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 4 years of age, but the results were not adjusted for this factor |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 outcomes reported |
| Other bias | Low risk | No other apparent bias |

**Macpherson 2007**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sweden<br>Geographic location: Kungsbacken (F); Halmsted (non-F)<br>Year of study: 2002 to 2003<br>Year of change in fluoridation status: NA<br>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)<br>Exclusion criteria: not stated<br>Other sources of fluoride<br>• Age at which started brushing: 6 to 12 months vs 12 months (P = 0.99)<br>• Frequency of brushing: ≤ 1/day vs ≥ 2/day (P = 0.42)<br>• Toothpaste F < 1000 ppm vs ≥ 1000 ppm (P = 0.49)<br>• Amount of toothpaste ≤ pea size vs > pea size (P = 0.09)<br>• Fluoride tablets previously: 'No' vs 'Yes' (P = 0.001)<br>• Fluoride tablets now: 'No' vs 'Yes' (P = 0.001)<br>Ethnicity: not stated<br>SES: low education: F = 47, non-F = 56; high education: F = 64, non-F = 73. Both groups were similar with respect to parents' education attainment (P = 0.87)<br>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)<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.1 ppm<br>Group 2: 1.3 ppm | |
| Outcomes | Dental fluorosis (TF Index; photographic assessment)<br>Age at assessment: 7 to 10 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |

| ***Risk of bias*** | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Low risk | Cluster random sample of parents of eligible children aged 7 to 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 have been used which remains subject to confounding factors. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Assessors were blind to the source area of each slide. |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Serbia<br>Geographic location: Valjevo and Vranjska Banja<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: used the fluoride concentration database and consumption database to determine fluoride exposure<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: used the fluoride concentration database and consumption database to determine fluoride exposure<br>Other confounding factors: dietary sources of fluoride – potato, beans |
| Interventions | All natural fluoridation<br>Group 1: 0.1 ppm<br>Group 2: 11 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

| *Risk of bias* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | Insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Serbia<br>Geographic location: Valjevo, Veliko Gradiste, Kacarevo and Vranjska Banja<br>Year of study: 2006<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: healthy 12-year-old school children, both genders, lifetime residents of the same municipality<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: there were no additional sources of exposure, i.e. industries that could pollute the environment by fluoride emission |
| Interventions | All natural fluoridation<br>Wells<br>Group 1: 0.79 ppm<br>Group 2: 0.1 ppm<br>Group 3: 0.15 ppm<br>Group 4: 11 ppm<br>Tap water<br>Group 1: 0.17 ppm |

| | |
|---|---|
| | Group 2: 0.07 ppm<br>Group 3: 0.1 ppm<br>Group 4: 0.15 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 12 years |
| Funding | Ministry of Science and Technological Development of the Republic of Serbia |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: 30 villages from district Gurgaon and district Hissar<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: only continuous residents; selected individuals had to have all their permanent teeth (except third molars) erupted<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: environmental factors such as eating habits, nutritional status, consumption of water**,** living conditions were almost uniform in all 7 groups studied<br>Residential history: continuous residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.5 ppm<br>Group 2: 0.87 ppm<br>Group 3: 1.51 ppm<br>Group 4: 2.45 ppm<br>Group 5: 5.27 ppm<br>Group 6: 8.5 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 12 to 16 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Sampling | Unclear risk | Insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

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

| *Risk of bias* | | |
|---|---|---|
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | The study authors report that all eligible children were to be studied 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)<br>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)<br>All outcomes | Low risk | Data presented for 88% of participants |
| Selective reporting (reporting bias) | Low risk | Data appear present |
| Other bias | Low risk | No other bias detected |

## Maupome 2001

| *Study characteristics* | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Canada<br>Geographic location: Group 1: Comox-Courtenay and Campbell River, British Columbia; Group 2: Kamloops, British Columbia. Total population sizes in each location not stated<br>Year study started: 1993 to 1994<br>Year study ended: 1996 to 1997<br>Year of change in fluoridation status: 1992<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age (school grade) at the time of assessment. |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Sample size at baseline: Group 1: 3184 children; Group 2: 2743 children<br>Sample size at final assessment: Group 1: 2211 children; Group 2: 1719 children<br>SES: participants showed similar SES at baseline<br>Co-interventions: data on oral hygiene and exposure to diverse fluoride technologies were collected but not reported. However, the study 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<br>Ethnicity: not stated<br>Gender: not stated |

| | |
|---|---|
| | Residential history: information about the regression analysis suggests that both lifetime and non-lifetime residents might have been included. |
| Interventions | **Fluoride cessation**<br>Group 1: 'optimal' level - ppm not stated (artificial fluoridation) to non-fluoridated<br>Group 2: 'optimal' level - ppm not stated (artificial fluoridation) |
| Outcomes | DMFS<br>Age at baseline assessment: Grades 2, 3, 8 and 9<br>Age at final assessment: Grades 2, 3, 8 and 9 |
| Funding | NHRDP operating grant 6610-2225-002 supported this study |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** SES measured through questionnaire response indicated that children "showed similar SES"; no further details provided<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Study was a multi-site study and also both a repeated cross-sectional prevalence survey and a longitudinal investigation. All children and adolescents in specified communities and grades were invited to participate. Almost 90% of eligible children were examined at baseline (negative consent). There were substantial baseline imbalances in caries measures between areas being compared<br>**Deviations from intended interventions.** No reported deviations from intended intervention<br>**Missing data.** About 90% of all eligible children were examined at baseline; 64.2% at follow-up with variation across groups. Data on SES (parental educational attainment of head of household) was only available for 3022 participants<br>**Measurement of the outcome.** Used different examiners for different study sites who where not blinded to fluoridation status<br>**Selection of the reported result.** No apparent selection of reporting |
| Notes | |

### Mazzotti 1939

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Mexico<br>Geographic location: all areas in Mexico, 11 states, 107 cities<br>Year of study: 1938<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated | |
| Interventions | Groups: 0-4 unclear ppm | |
| Outcomes | Dental fluorosis (index unclear)<br>Age at assessment: not stated | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Paper translated from Spanish | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Thailand<br>Geographic location: Chiang Mai<br>Year of study: 2007<br>Year study ended: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifelong residency; good general health with both maxillary incisors fully erupted; free from fixed orthodontic appliances<br>Exclusion criteria: non-lifetime residents; unsuitable dentition<br>Other sources of fluoride:<br>• Non-fluorosed breast and formula: 88/305 (28.8%)<br>• Formula only: 14/57 (24.6%)<br>• F content paste: < 1000 ppm = 13/59 (22%); 1000 ppm F = 150/501 (29.9%)<br>• Toothbrushing frequency: once/day = 45/130 (34.6%); twice/day = 99/360 (27.5%); > 3 times/day =19/70 (27.1%)<br>• Age toothbrushing started: 4 years+ = 20/76 (26.3%); 3 to 4 years = 43/138 (31.2%); 2 to 3 years = 48/178 (27%); 1 to 2 years = 35/126 (27.8%); 0 to 1 year = 8/23 (34.8%)<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: continuous residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: < 0.2 ppm<br>Group 2: 0.2 to 0.59 ppm<br>Group 3: 0.6 to 0.89 ppm<br>Group 4: ≥ 0.9 ppm |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 8 to 13 years |
| Funding | 1 study author was funded by a Clinician Scientist Award from the NIHR (UK). The Colgate Palmolive Dental Health Unit was funded by an unrestricted grant from Colgate Palmolive<br>Possible conflicts of interest: 1 study author (RPE) is an employee of a manufacturer of oral care products |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 were 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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: South Africa<br>Geographic location: Kenhardt (F); Keimoes (non-F); North-western Cape Province<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |

| | | |
|---|---|---|
| Participants | Inclusion criteria: lifetime residents of study area; pre-school children aged 1 to 5 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: the majority of babies were breastfed so would not be exposed to fluoride from water used in preparation of infant formula.<br>SES: reported as being the same across groups; experimental and control groups reported as being similar (parents were land or railway labourers)<br>Ethnicity: all children same ethnic origin i.e. European-African-Malay origin<br>Residential history: lifetime residents<br>Other confounding factors: same climatic conditions in both areas | |
| Interventions | All natural fluoridation<br>Group 1: 2.2 to 4.1 ppm<br>Group 2: 0.2 ppm | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at time of measurement: 1 to 5 years | |
| Funding | Part funded by South African Sugar Association | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | Insufficient detail reported in order to determine how selection took place |
| Confounding | High risk | Malnutrition and SES were reported to be similar across groups but no supporting data provided<br>Did not report any details about other sources of fluoride |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Did not undertake blinding |
| Incomplete outcome data (attrition bias)<br>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**

| | | |
|---|---|---|
| ***Study characteristics*** | | |
| Methods | **FLUOROSIS STUDY**<br>Country of study: Chile<br>Geographic location: students attending 2 boarding institutions in Santiago, who lived in areas throughout Chile<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: students who could not remember the areas in which they spent the first 6 years of their life<br>Other sources of fluoride: not stated<br>SES: distribution of participants by high, moderate, low social class, but no significant differences between fluoride groups<br>Ethnicity: not stated<br>Residential history: first 6 years of life<br>Other confounding factors: years lived in city of birth | |
| Interventions | All natural fluoridation<br>Group 1: > 0.3 ppm<br>Group 2: ≤ 0.3 ppm | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 19 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | High risk | All children were selected from 2 boarding schools. Insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Chile<br>Geographic location: Iquique (F); Santiago (non-F); Valparaiso-Vina (F); Temuco (low-F)<br>Year of study: 1983<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: 4 schools in study areas<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: 2 schools in each area, 1 from low social class, 1 from medium/high social class, results presented separately by social class<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated | |
| Interventions | Group 1: 2.2 ppm (natural fluoridation)<br>Group 2: 0.0 ppm (natural fluoridation)<br>Group 3: 1.0 ppm (artificial fluoridation)<br>Group 4: 0.3 ppm (natural fluoridation) | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 7 and 12 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | Insufficient detail reported in order to determine how selection took place. 4 schools from a list of schools benefiting from school feeding programmes 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Iran<br>Geographic location: Youssefabad, Seman, Dibaj<br>Year of study: 2003<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: school children aged 6 to 9 years who were lifetime residents<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: Youssefabad, Semnan were of upper-middle and lower-middle class, social class of the third community was not mentioned |

| | |
|---|---|
| | Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.2 ppm<br>Group 2: 0.3 ppm<br>Group 3: 1.3 ppm |
| Outcomes | Dental fluorosis (TSIF); caries data evaluated in study but excluded from review due to study design<br>Age at assessment: 6 to 9 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 (co-education) 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)<br>All outcomes | High risk | Not reported |
| Incomplete outcome data (attrition bias)<br>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. |
| 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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>Geographic location: Nantwich (F); Northwich (non-F)<br>Year of study: 1988<br>Year of change in fluoridation status: 1975<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 8 years attending state-maintained schools; lifetime residents of study areas; parental consent<br>Exclusion criteria: parishes not bounded on all sides by parishes with optimally fluoridated water for fluoride areas; exposure to fluoride supplements<br>Other sources of fluoride: age at which tooth brushing first began<br>SES: measured by parental occupation; social class makeup of study areas almost identical (data presented in paper)<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: < 0.3 ppm (natural fluoridation) |
| Outcomes | Enamel defect (DDE)<br>Age at assessment: 8 years |
| Funding | Financial support from the North Western Regional Health Authority |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 2-stage random sampling technique. |
| Confounding | Low risk | There was no difference in SES across groups and children with exposure to fluoride supplements were excluded. |
| Blinding of outcome assessment (detection bias)<br>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)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Nalhati I (Nasipur, Vabanandapur, Deshnabagram) and Rampurhat II (Chalk Atla, Nowapara, Junitpur and Kamdebpur)<br>Year of study: 2003<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 3.15 ppm<br>Group 2: 3.83 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: < 10 years to > 50 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Venezuela<br>Geographic location: Maria May, Roscio and Madre Emilia<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |

| | |
|---|---|
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.13 ppm<br>Group 2: 0.31 ppm<br>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<br>Age at assessment: 8 to 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data appear to be presented for all participants |
| Selective reporting (reporting bias) | Low risk | All expected outcomes presented |
| Other bias | Low risk | No other apparent bias |

**Nanda 1974**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: 23 villages in Lucknow (North Central India)<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>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<br>Exclusion criteria: none stated<br>Other sources of fluoride: dietary fluoride intake<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifelong residents<br>Other confounding factors: climate |
| Interventions | All natural fluoridation<br>Group 1: > 1.21 ppm<br>Group 2: 0.81 to 1.2 ppm<br>Group 3: 0.41 to 0.8 ppm<br>Group 4: 0 to 0.4 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at time of measurement: 6 to 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 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | Insufficient detail reported in order to determine how selection took place |
| Confounding | High risk | Did not account for SES |

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding was not undertaken |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Lithuania<br>Geographic location: Klaipeda and Kaunas<br>Year of study: 1997<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: Klaipeda and Kaunas said to be the 2 largest cities in Lithuania and to be of a similar size and socioeconomic structure<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.22 ppm<br>Group 2: 1.7 to 2.2 ppm | |
| Outcomes | Dental fluorosis (TF Index); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 12 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

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

| | |
|---|---|
| | Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 1.65 ppm<br>Group 2: 1.84 ppm<br>Group 3: 1.84 ppm<br>Group 4: 1.88 ppm<br>Group 5: 1.91 ppm<br>Group 6: 2.15 ppm<br>Group 7: 2.22 ppm<br>Group 8: 2.53 ppm<br>Group 9: 3.91 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 5 to 12 years |
| Funding | Funding for travelling and laboratory facilities provided by Special Assistance Program (SAP)-I UGC, New Delhi |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>Geographic location: Hartlepool, Newcastle and Middlesborough<br>Year of study: 1989<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional study |
| Participants | Inclusion criteria: lifetime residents of study areas; children in selected schools aged 15 to 16 years<br>Exclusion criteria: children with fractured incisor teeth, orthodontic bracket or surface otherwise obscured<br>Other sources of fluoride: not stated<br>SES: occupation of head of household recorded; participants of low and high SES were recruited when possible<br>Ethnicity: ethnicity recorded but no expansion on variable<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 1 tp 1.3 ppm<br>Group 2: 1 ppm<br>Group 3: 0.2 ppm |
| Outcomes | Enamel defect<br>Age at assessment: 12 years |
| Funding | Financial assistance from the British Council |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>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)<br>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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: England<br>Geographic location: north-east England<br>Year of study: 1990 to 1991<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: lifetime residents of study areas (England only); children aged 12 years; parental consent (England only)<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated, but expected higher use of toothpaste in higher SES groups<br>SES: children divided into high and low social class<br>Ethnicity: not stated<br>Residential history: UK participants were lifetime residents.<br>Other confounding factors: not stated | |
| Interventions | Group 1: 0.1 ppm<br>Group 2: 0.5 ppm<br>Group 3: 1.0 ppm | |
| Outcomes | Enamel defect (DDE)<br>Age at assessment: 12 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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 subgroup. 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)<br>All outcomes | Low risk | The examiner was largely unaware of fluoride and socioeconomic status of the children |
| Incomplete outcome data (attrition bias)<br>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 |

**Nunn 1994b**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sri Lanka<br>Geographic location: Sri Lanka<br>Year of study: 1990 to 1991<br>Year of change in fluoridation status: NA |

| | |
|---|---|
| | Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 12 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated, but expected higher use of toothpaste in higher SE groups<br>SES: children divided into high and low social class<br>Ethnicity: not stated<br>Residential history: Sri Lankan populations were non-mobile and confirmed continuous residence when asked at the time of examination<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.1 ppm<br>Group 2: 0.5 ppm<br>Group 3: 1.0 ppm |
| Outcomes | Enamel defect (DDE)<br>Age at assessment: 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 subgroup. Insufficient information provided regarding how the children within the schools were selected |
| Confounding | High risk | Imbalance of SES between groups; 2 of the 3 study areas recruited only children of low SES and one area recruited both low- and high-SES children. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | The examiner was aware of the fluoride and socioeconomic status of the children. |
| Incomplete outcome data (attrition bias)<br>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

***Study characteristics***

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

| | | |
|---|---|---|
| Notes | | |
| ***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**

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

| | |
|---|---|
| ***Study characteristics*** | |
| Methods | **CARIES STUDY**<br>Country of study: Holland<br>Geographic location: Group 1: Tiel (F); Group 2: Culemborg (non-F). Total population sizes in each location not stated<br>Year study started: 1950<br>Year study ended: 1970 |

| | |
|---|---|
| | Year of change in fluoridation status: 1953<br>Study design: prospective cohort. The same cohort of adults was followed from baseline to end of study |
| Participants | Inclusion criteria: residents of study areas born between 1896 and 1945; lifelong residents of study areas<br>Exclusion criteria: participants who left the study areas for more than 3 months after fluoridation was introduced<br>Sample size at baseline: not stated<br>Sample size at final assessment: Group 1: 521 participants; Group 2: 507 participants<br>Other sources of fluoride: not stated<br>SES: not stated<br>Co-interventions: not stated<br>Ethnicity: not stated<br>Gender: equally balanced<br>Residential history: lifetime residents |
| Interventions | Group 1: 1.1 ppm (artificial fluoridation)*<br>Group 2: 0.1 ppm (natural fluoridation)* |
| Outcomes | Outcome: % with false teeth<br>Age at baseline assessment: 5 to 55 years<br>Age at final assessment: 25 to 75 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Study assessed as at critical risk for confounding due to lack of details regarding SES. No further assessment<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** Participants were selected by random sampling from the city population registers<br>**Deviations from intended interventions.** No reported deviations from the intervention<br>**Missing data.** Data presented for all participants<br>**Measurement of the outcome.** Insufficient information regarding blinding; examiners likely to know fluoridation status<br>**Selection of the reported result.** No apparent selection of reporting with regard to chosen outcome (study reports on percentage of false teeth; no caries data) |
| Notes | Paper translated from Dutch<br>*Information about fluoride dose sourced from Backerdirks et al, 1961 (secondary reference under Pot 1974). |

**Ray 1982**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Rustampur and Ledhupur, 2 adjacent village in Varanasi District<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: none stated<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: study areas similar with respect to demographic and socioeconomic characteristics<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: villages similar with respect to geoclimatic characteristics |
| Interventions | All natural fluoridation<br>Group 1: > 2 ppm<br>Group 2: 1 to 2 ppm<br>Group 3: < 1 ppm |
| Outcomes | Dental fluorosis (index not stated)<br>Age at assessment: not stated |

| | |
|---|---|
| Funding | Funded by the Indian Council of Medical Research |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Australia<br>Geographic location: Perth (F); Bunbury (non-F), Western Australia<br>Year of study: 1989<br>Year of change in fluoridation status: 1968<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children born in 1978; children attending government schools in study areas; parental consent<br>Exclusion criteria: children with amelogenesis imperfecta or orthodontic banding<br>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<br>SES: schools assigned socioeconomic score - no significant difference in scores between study areas<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.8 ppm (artificial fluoridation)<br>Group 2: < 0.2 ppm (natural fluoridation) |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 12 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Blind outcome assessment (with regard to residency) was not undertaken |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Australia<br>Geographic location: Western Australia<br>Year of study: 2000 |

| | |
|---|---|
| | Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children born around 1990 (10-year-olds) who had lived in Australia/New Zealand for most of their lives (to ensure lifetime exposure to water fluoridation)<br>Exclusion criteria: migrants from outside Australia and New Zealand, refusal to consent, not present at school at the time of exam<br>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<br>SES: not stated<br>Ethnicity: not stated<br>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 to 5 years in water fluoridated area<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.8ppm (artificial fluoridation)<br>Group 2: 0.2-0.3 ppm (naturally fluoridated) |
| Outcomes | Dental fluorosis (TF index)<br>Age at assessment: 10 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: urban - Bao Ji and Jing Bian<br>Year of study: 2002<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: absent or unavailable; non-permanent residents<br>Other sources of fluoride: no fluoride supply was provided by dental service and no fluoride supplement programme was implemented in any of the communities<br>Ethnicity: not stated<br>SES: the selected schools served rural communities where socioeconomic standards were comparable<br>Residential history: permanent residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.4ppm<br>Group 2: 1.0 ppm<br>Group 3: 1.8 ppm<br>Group 4: 3.5 ppm<br>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<br>Age at assessment: 12 and 13 years |
| Funding | The study was supported by the Norwegian State Educational Loan Fund |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |

| | | |
|---|---|---|
| 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)<br>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)<br>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) |
| Other bias | Low risk | No other apparent bias |

**Rugg-Gunn 1997**

| | | |
|---|---|---|
| ***Study characteristics*** | | |
| Methods | **FLUOROSIS STUDY**<br>Country of study: Saudi Arabia<br>Geographic location: Jeddah (low F); Riyadh (moderate F); and Quassim (high F)<br>Year of study: 1992<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: lifetime residents of study areas; boys aged 14 years; parental consent<br>Exclusion criteria: photographs that failed to show whole buccal surface; out of focus photographs<br>Other sources of fluoride: not stated<br>SES: schools grouped according to the socioeconomic status of residential areas in the urban community; family income and parental education measured using questionnaire<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: nutritional status | |
| Interventions | All natural fluoridation<br>Group 1: 2.7 ppm<br>Group 2: 0.8 ppm<br>Group 3: < 0.3 ppm | |
| Outcomes | Dental fluorosis (index unclear)<br>Age at assessment: 14 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Low risk | Quote: "All schools 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)<br>All outcomes | Unclear risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data appear 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**

| | |
|---|---|
| ***Study characteristics*** | |
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA |

| | |
|---|---|
| | Geographic location: Colorado Springs (F); Boulder (non-F), Colorado<br>Year of study: 1950<br>Year of change in fluoridation status: NA<br>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 to 44 years; residence and usage of local water unbroken except for periods not exceeding 60 days during calcification and eruption of permanent teeth<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: workers in 2 communities followed similar occupations and had similar average salaries<br>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)<br>Residential history: lifetime residents<br>Other confounding factors: Colorado Springs 3 times size of Boulder, similar altitude and climate, neither population ageing nor young, both were highly literate, water systems similar |
| Interventions | All natural fluoridation<br>Group 1: 2.5 ppm<br>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<br>Age at time of measurement: 20 to 44 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| 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 homogeneous. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Blinding was not undertaken |
| Incomplete outcome data (attrition bias)<br>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 study author, however, there was no mention of examiner calibration |

**Rwenyonyi 1998**

***Study characteristics***

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

| | |
|---|---|
| Outcomes | Dental fluorosis (index not stated)<br>Age at assessment: 10 to 14 years |
| Funding | The Norwegian Universities' Committee for Development Research and Education and the Committee for Research and Postgraduate Training, University of Bergen |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Uganda<br>Geographic location: Kasese (low F); Kisoro (high F)<br>Year of study: 1996 to 1997<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 10 to 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<br>Exclusion criteria: absence from the village for more than 1 month per year<br>Other sources of fluoride: fluoride exposure from liquid estimated by daily liquid intake - children from high fluoride area had higher intake of water, consumed more boiled water and consumed less tea than those from control area, higher consumption of fluoride from Trona in control group<br>SES: most families were small scale farmers and all appeared to be of similar social class<br>Ethnicity: all children were ethnic Bantu Africans from the Bafumbria and Bakonjo tribes<br>Residential history: lifelong residents<br>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<br>Group 1: 2.5 (altitude = 2800 m)<br>Group 2: 2.5 (altitude = 1750 m)<br>Group 3: 0.5 (altitude = 2200 m)<br>Group 4: 0.5 (altitude = 900 m) |
| Outcomes | Dental fluorosis (TF Index)<br>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 Training, University of Bergen |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>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)<br>All outcomes | Low risk | Data appear to be presented for all participants. |

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Low risk | All data appear to have been reported. |
| Other bias | Low risk | No other bias was detected |

### Saravanan 2008

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Tamil Nadu<br>Year of study: not stated<br>Year of change of fluoridation status: NA<br>Study design: cross-sectional | |
| 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<br>Exclusion criteria: high school children were not included as only 85% of the children of high school age group (11 to 16 years) in the study area were attending schools<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: the majority of people in the study setting were of lower SES<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: < 0.1 ppm<br>Group 2: < 0.1 ppm<br>Group 3: 0.25 ppm<br>Group 4: 0.56 ppm<br>Group 5: 0.66 ppm<br>Group 6: 0.67 ppm | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 5 to 10 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 who 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 to 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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Finland<br>Geographic location: Artjarvi, Askola, Elimaki, Litti, Myrskyla, Parikkala, Taipalsaari, Valkeala, Vehkalahti<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 11<br>Exclusion criteria: children resident in area for < 6 years; fluoride concentration of drinking water unknown |

| | |
|---|---|
| | Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: residence for < 6 years<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0 to 0.1 ppm<br>Group 2: 0.11 to 0.39 ppm<br>Group 3: 0.40 to 0.99 ppm<br>Group 4: 1.0 to 1.59 ppm<br>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<br>Age at assessment: 11 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>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)<br>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 |

## Segreto 1984

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: 16 Texas communities<br>Year of study: 1978 to 1981<br>Year of change in fluoridation status: unclear<br>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 to 6, aged 7 to 12 years and grades 9 to 12, aged 14 to 18 years; city water supply as principal source of drinking water throughout lifetime; non-usage of water treatment systems that result in de-fluoridation of water<br>Exclusion criteria: children with staining attributable to medication such as tetracycline<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: children were primarily those with Spanish surnames or white<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Unclear if natural or artificial fluoridation<br>Group 1: 0.3 ppm<br>Group 2: 0.3 ppm<br>Group 3: 0.4 ppm<br>Group 4: 1.0 ppm<br>Group 5: 1.3 ppm<br>Group 6: 1.3 ppm<br>Group 7: 1.4 ppm<br>Group 8: 2.3 ppm<br>Group 9: 2.3 ppm<br>Group 10: 2.5 ppm<br>Group 11: 2.7 ppm<br>Group 12: 2.7 ppm<br>Group 13: 2.7 ppm<br>Group 14: 2.9 ppm<br>Group 15: 3.1 ppm<br>Group 16: 4.3 ppm |

| | |
|---|---|
| Outcomes | Mottled enamel (Dean's Index)<br>Age at assessment: 7 to 12 years and 14 to 18 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Segreto 1984 differs from that presented in McDonagh 2000 |

***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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sweden<br>Geographic location: Malmo (low F); Simirshamn, Astorp and Nyvang (High F)<br>Year of study: 1953<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children aged 11 to 14 years<br>Exclusion criteria: children missed due to illness; children < 11.5 years and > 14.5 years<br>Other sources of fluoride: all children received yearly systematic treatment by the School Dental Service<br>SES: socioeconomic distribution of lifetime residents was similar in all study areas, however distribution was different for non-continuous residents compared to continuous residents<br>Ethnicity: not stated<br>Residential history: only results of lifetime residents were presented<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 1.0 ppm<br>Group 2: 1.0 to 1.3 ppm<br>Group 3: 1.3 ppm<br>Control: 0.3 to 0.5 ppm |
| Outcomes | Outcome: dental fluorosis (Dean's Index)<br>Age at assessment: 12 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Sellman 1957 differs from that presented in McDonagh 2000 |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data appear to be presented for all participants. |
| Selective reporting (reporting bias) | Low risk | All expected outcomes reported |

| | | |
|---|---|---|
| Other bias | High risk | No mention of examiner calibration and reliability testing |

### Selwitz 1995

| *Study characteristics* | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Kewanee (optimal), Monmouth (2 x optimal), Abingdon, Elmwood (3 x optimal), Bushneell, Ipava, Table Grove (4 x optimal), Illinois<br>Year of study: 1980<br>Year study ended: 1990<br>Year of change in fluoridation status: unclear<br>Study design: repeated cross-sectional | |
| Participants | Inclusion criteria: children aged 8 to 10 years and 14 to 16 years; written parental consent; lifetime residents of study areas; continuous use of community water supply<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | Unclear whether all was natural fluoridation, parts of the optimally fluoridated area may have been artificially adjusted<br>Group 1: 4 ppm<br>Group 2: 3 ppm<br>Group 3: 2 ppm<br>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<br>Age at assessment: 8 to 10 years and 13 to 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Data extracted from Selwitz 1995 differs from that presented in McDonagh 2000 | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Kewanee (F); Holdrege and Broken Bow (non-F)<br>Year of study: 1990-1998<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; parental consent<br>Exclusion criteria: none stated<br>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 |

| | |
|---|---|
| | SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: use of private well-water |
| Interventions | All natural fluoridation<br>Group 1: 1 ppm<br>Group 2: < 0.3 ppm |
| Outcomes | Dental fluorosis (TSIF); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 8 to 10 years and 13 to 16 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Selwitz 1998 differs from that presented in McDonagh 2000 |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: 3 strata (according to fluoride concentration) Khammam district, Andhra Pradesh<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: school children, aged 9 to 12 years irrespective of sex, race, and SES, 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<br>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<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>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<br>Group 1: < 0.7 ppm<br>Group 2: 0.7 to 1.2 ppm<br>Group 3: 1.3 to 3.5 ppm |
| Outcomes | Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 9 to 12 years |
| Funding | Stated no funding |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Blinding not specified |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Number of children in each stratum not specified; unclear whether all those sampled were evaluated |
| Selective reporting (reporting bias) | High risk | Fluorosis data not presented by strata |
| Other bias | Low risk | No other apparent bias |

### Shekar 2012

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Nalgonda district<br>Year of study: 2008<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: continuous residency; availability on the day of examination<br>Exclusion criteria: not stated<br>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 toothpaste was collected but not reported<br>Ethnicity: not stated<br>SES: the majority of people in the study setting were from lower socioeconomic class<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: < 0.7 ppm<br>Group 2: 0.7 to 1.2 ppm<br>Group 3: 1.2 to 2 ppm<br>Group 4: 2.1 to 4 ppm<br>Group 5: > 4 ppm | |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 12 and 15 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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. |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Australia<br>Geographic location: New South Wales<br>Year of study: 2010<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: school students aged 14 to 15 years under the jurisdiction of the NSW Department of Education and Training, the Catholic Education Commission and Independent Schools |

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|---|---|
| | Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>Ethnicity: aboriginal status was coded from parental responses (not reported by fluoridation status)<br>SES: self-reported family income data were provided by parents or guardians and was used as a measure of SES (not reported by fluoridation status)<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | Group 1: fluoridated (artificial; ppm not specified)<br>Group 2: non-fluoridated |
| Outcomes | Dental fluorosis (TF); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 14 and 15 years |
| Funding | The Centre for Oral Health Strategy NSW |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Participation 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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Iowa<br>Year of study: 1991<br>Year of change in fluoridation status: NA<br>Study design: case-control study |
| Participants | Inclusion criteria: children aged 8 to 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<br>Exclusion criteria: children with fixed orthodontic appliances; all permanent incisors and first molars present and erupted<br>Other sources of fluoride: dietary fluoride supplement use; age began brushing with toothpaste; toothpaste usage in 8 years; mouth rinse usage; professional fluoride treatments<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 3.1 ppm<br>Group 2: 5.6 ppm |
| Outcomes | Dental fluorosis (TSIF)<br>Age at assessment: 8 to 17 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | Low risk | Quote: "The examiner had no previous knowledge of subjects' dental fluorosis status or fluoride exposures" |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Italy<br>Geographic location: Barcelona, Pozzo di Gotto, Sicily<br>Year of study: 1954<br>Year of change in fluoridation status: unclear<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: children attending schools in study areas<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated | |
| Interventions | Unclear if natural or artificial fluoridation<br>Group 1: 0.4 ppm<br>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<br>Age at assessment: 6 to 11 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Data from McDonagh 2000 (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)<br>All outcomes | Unclear risk | Unable to make a judgement as study was unavailable |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Scotland<br>Geographic location: Burghead, Kinloss and Findhorn<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated |

| | |
|---|---|
| | Other sources of fluoride: information on the use of fluoridated toothpaste was collected but not reported<br>Ethnicity: not stated<br>SES: 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<br>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<br>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<br>Group 1: 1 to 2.4 ppm<br>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<br>Age at assessment: 5 to 6 years (caries only) and 8 to 12 years (caries and fluorosis) |
| Funding | Supported by a Scottish Office Department of Health grant |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | There was insufficient detail reported in order 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<br>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)<br>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)<br>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 to 6 years and 8 to 12 years, but the investigators only conducted fluorosis assessments on 8- to 12-year-olds. Therefore, the data have been extracted for only children for whom fluorosis assessment was conducted. |

**Sudhir 2009**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: Andhra Pradesh<br>Year of study: 2006-2007<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: school children aged 13 to 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<br>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<br>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<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: lifetime residents<br>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<br>Group 1: < 0.7 ppm<br>Group 2: 0.7 to 1.2 ppm<br>Group 3: 1.3 to 4 ppm<br>Group 4: > 4 ppm |
| Outcomes | Outcome: fluorosis prevalence (TF Index);<br>Age at assessment: 13 to 15 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 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. |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Hudson, Redford, Richmond (F); Cadillac (non-F), Michigan<br>Year of study: not stated<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; children aged 6 to 12 years<br>Exclusion criteria: none stated<br>Other sources of fluoride: use of fluoride supplements; dental attendance; time interval since last dental visit; age began brushing (parent and child); age at start of F rinsing; feeding method in 1st year of life.<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 1.2 ppm (artificial fluoridation)<br>Group 2: 1.0 ppm (artificial fluoridation)<br>Group 3: 0.8 ppm (artificial fluoridation)<br>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<br>Age at assessment: 6 to 12 years |
| Funding | NIH National Research Service Award |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Szpunar 1988 differs from that presented in McDonagh 2000 |

***Risk of bias***

| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: UK<br>Geographic location: Northumberland and Newcastle upon Tyne<br>Year of study: 1998<br>Year of change in fluoridation status: 1969<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: parental consent; lifetime residency<br>Exclusion criteria: not stated<br>Ethnicity: not stated<br>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<br>SES: the children 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 children in Newcastle and 7.3 (SD = 15.0) for Northumberland (P value < 0.001). However, the study authors were reported to have chosen schools to provide children from a spectrum of SES backgrounds.<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | Group 1: 1 ppm (artificial fluoridation)<br>Group 2: 0.1 ppm (natural fluoridation) | |
| Outcomes | Dental fluorosis (TF Index)<br>Age at assessment: 8 to 9 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>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)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **CARIES STUDY**<br>Country of study: Canada<br>Geographic location: Group 1: Windsor (F), population size of 6000 residents; Group 2: Richmond (non-F), population size of 4000 residents<br>Year study started: 1977<br>Year study ended: 1986<br>Year of change in fluoridation status: 1978<br>Study design: CBA. A different sample of children was assessed at baseline and end of study, according to age at the time of assessment. |
| 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<br>Sample size at baseline: Group 1: 96 children; Group 2: 93 children<br>Sample size at final assessment: Group 1: 89 children; Group 2: 86 children<br>SES: comparable study areas with similar SES and lifestyles<br>Co-interventions: mouthwash and toothpaste; participants underwent similar fluoride rinse programmes and had similar access to dental care<br>Ethnicity: not stated<br>Gender: broadly balanced across groups<br>Residential history: not stated |
| Interventions | Group 1: 'optimal' level - ppm not stated (artificial fluoridation)<br>Control: 'low' level - ppm not stated (natural fluoridation) |
| Outcomes | DMFT; % caries prevalence<br>Age at baseline assessment: 6 and 7 years<br>Age at final assessment: 6 and 7 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | See Table 1 for ROBINS-I assessment<br>**Confounding.** Efforts were made to control for confounding through design. The groups were considered to be comparable by the study author team but no data were provided.<br>**Classification of interventions.** Intervention status classified correctly<br>**Selection of participants into the study/analysis.** A school in each area was selected (reason for selection is unclear); all eligible children in each school were invited to participate<br>**Deviations from intended interventions.** No deviations from intended intervention reported<br>**Missing data.** No missing outcome data, however, no data regarding confounder<br>**Measurement of the outcome.** Outcome assessment was conducted by unblinded assessors<br>**Selection of the reported result.** Outcome of interest reported |
| Notes | Translated from French |

**Tsutsui 2000**

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Japan<br>Geographic location: not stated<br>Year of study: 1987<br>Year of change in fluoridation status: naturally occurring fluoride<br>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<br>Exclusion criteria: failure to meet any of the inclusion criteria; other reasons for exclusion were incomplete questionnaire and periodic application of topical fluoride<br>Other sources of fluoride: children who 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.<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0 to 0.2 ppm<br>Group 2: 0.2 to 0.4 ppm<br>Group 3: 0.4 to 0.6 ppm<br>Group 4: 0.6 to 0.8 ppm<br>Group 5: 0.8 to 1 ppm<br>Group 6: 1 to 1.4 ppm |
| Outcomes | Dental fluorosis (Dean's Index); caries data also evaluated within the study but excluded from review due to study design<br>Age at assessment: 10 to 12 years |
| Funding | Niigata University |

| | |
|---|---|
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>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)<br>All outcomes | High risk | Out of the 1967 children who 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**

***Study characteristics***

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

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | Children aged 3 to 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)<br>All outcomes | High risk | Insufficient information |

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Antigua<br>Geographic location: urban and rural areas in Antigua<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: children aged 12 to 14 years; lifetime residents of study areas<br>Exclusion criteria: restored or fractured tooth surfaces<br>Other sources of fluoride: toothpaste swallowing when younger; consumption of mixed sources of water; fluoride mouth rinses<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | All natural fluoridation<br>Group 1: 0.6 to 1 ppm<br>Group 2: 0.1-0.3 ppm | |
| Outcomes | Dental fluorosis (TSIF)<br>Age at assessment: 12 to 14 years | |
| Funding | Not stated | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: India<br>Geographic location: 7 districts of the Chhattisgarh State<br>Year of study: 2013 to 2014<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: none stated<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation |

| | |
|---|---|
| | Group 1: 3.8 ppm<br>Group 2: 2.5 ppm<br>Group 3: 2.0 ppm<br>Group 4: 3.0 ppm<br>Group 5: 2.2 ppm<br>Group 6: 2.8 ppm<br>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 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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 account for potential confounding factors |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Insufficient information |
| Selective reporting (reporting bias) | High risk | Number of participants by district not reported |
| Other bias | Unclear risk | No other apparent bias |

**Villa 1998**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Chile<br>Geographic location: Rancagua (non-F), Santiago (low-F), La Serena (medium-F), San Felipe and Iquique (high-F)<br>Year of study: 1996<br>Year of change in fluoridation status: fluoride was naturally occurring<br>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<br>Exclusion criteria: none stated<br>Other sources of fluoride: not stated<br>SES: children selected from schools graded according to SES to give similar socioeconomic distribution in each study area<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: temperature |
| Interventions | All natural fluoridation<br>Group 1: 0.07 ppm<br>Group 2: 0.21 ppm<br>Group 3: 0.55 ppm<br>Group 4: 0.93 ppm<br>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<br>Age at assessment: 15 years |
| Funding | Study was supported by the Chilean Council for Scientific and Technological Research (FONDECYT) through grant no. 1960993 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted Villa 1998 differs from that presented in McDonagh 2000 |

***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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Tanzania<br>Geographic location: Arusha, Shinyanga, Manyara, Dodoma, Singida and Tabora<br>Year of study: not stated<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: aged 12 to 18 years; lifelong residence<br>Exclusion criteria: in order to avoid over-scoring, teeth that were tempered with by grinding or other forms of mutilations were excluded<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: mostly lifelong residents<br>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<br>Group 1: 2.2 ppm<br>Group 2: 2.4 ppm<br>Group 3: 2.5 ppm<br>Group 4: 4.2 ppm<br>Group 5: 4.7 ppm<br>Group 6: 5.6 ppm |
| Outcomes | Dental fluorosis (Dean's Index)<br>Age at assessment: 12 to 18 years |
| Funding | Funded by the Japanese International Cooperation Agency (JICA) of Tanzania |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: Hotan, Kaxgar and Aksu, in south Xinjiang<br>Year of study: 1991<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |

| | |
|---|---|
| Participants | Inclusion criteria: children aged from 8 to 15 years living around the water source<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: farmers and herdsmen in south Xinjiang<br>Ethnicity: Minority, mainly Uygur ethnic group<br>Residential history: living in study area for a long time ("since many years ago")<br>Other confounding factors: the combined effects of iodine deficiency and high fluorine; the habit of tea drinking |
| Interventions | All natural fluoridation<br>Group 1: 1.58 ppm<br>Group 2: 1.85 to 2.00 ppm<br>Group 3: 0.48 ppm<br>Group 4: 2.55 ppm<br>Group 5: 0.43 ppm<br>Group 6: 0.46 ppm<br>Group 7: 0.43 ppm |
| Outcomes | Dental fluorosis (index not stated)<br>Age at assessment: 15 years |
| Funding | Not stated in translation |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Paper translated from Chinese |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Sampling | Unclear risk | Children aged 8 to 15 years 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)<br>All outcomes | High risk | Not reported |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: Xindiliang Village (high F), Shiligetu Village (lower F)<br>Year of study: 1999<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: not stated<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 1.3 ppm<br>Group 2: 2 to 4 ppm |
| Outcomes | Dental fluorosis and skeletal fluorosis (3 grade classification for both)<br>Age at assessment: all ages |
| Funding | Japan International Cooperation Agency |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China<br>Geographic location: not stated<br>Year of study: 2008 to 2009<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: not stated<br>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.<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 1.3 ppm<br>Group 2: 2 to 4 ppm |
| Outcomes | Dental fluorosis (Dean's Index); skeletal fluorosis<br>Age at assessment: 8 to 12 years for dental fluorosis and > 16 years for skeletal fluorosis |
| Funding | Supported by the Chinese government for Endemic Disease Control in 2008 to 2009. |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Sri Lanka<br>Geographic location: 4 geographic areas at same altitude and temperature from 4 districts in Sri Lanka (Galewala, Wariyapola, Kekirawa and Rambukkana)<br>Year of study: 1986<br>Year of change in fluoridation status: NA<br>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<br>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<br>SES: wide ranges of socioeconomic differences not expected<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: < 0.39 ppm<br>Group 2: 0.4 to 0.59 ppm<br>Group 3: 0.6 to 0.79 ppm<br>Group 4: 0.8 to 0.99 ppm<br>Group 5: >1.0 ppm |
| Outcomes | Fluorosis (Dean's Index); caries data evaluated in study but not included in review due to study design<br>Age at assessment: 14 years |
| Funding | National Water Supply, Sri Lanka |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Iowa<br>Year of study: 1997 to 2000<br>Year of change in fluoridation status: unclear<br>Study design: cross-sectional data from within cohort study |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>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<br>Ethnicity: not stated<br>SES: not stated<br>Residential history: mostly lifelong residents<br>Other confounding factors: not stated |
| Interventions | Group 1: < 0.7 ppm (natural fluoridation)<br>Group 2: 0.7 to 1.2 ppm (artificial fluoridation)<br>Group 3: > 1.2 ppm (natural fluoridation) |
| Outcomes | Fluorosis prevalence (TSIF)<br>Age at assessment: 4.5 to 5 years |
| Funding | Supported by NIH grants 2ROI-DE09551, 2P30-10126, and CRC-RROOO5 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| *Study characteristics* | | |
|---|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Denmark<br>Geographic location: Naestved (F); Greve (F); Ry (non-F)<br>Year of study: not stated<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional | |
| Participants | Inclusion criteria: lifetime residents of study areas; girls aged 12 to 15 years<br>Exclusion criteria: children with orthodontic appliances; history of additional fluoride use<br>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<br>SES: not stated<br>Ethnicity: not stated<br>Residential history: lifetime residents<br>Other confounding factors: not stated | |
| Interventions | Group 1: < 0.2 ppm<br>Group 2: 1.0 ppm<br>Group 3: 2.4 ppm | |
| Outcomes | Fluorosis (TF Index); skeletal maturity<br>Age at assessment: 12 to 14 years | |
| Funding | Sponsored by Colgate Palmolive, Denmark | |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | | |
| Notes | Data extracted Wenzel 1982 differs from that presented in McDonagh 2000 | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Sampling | Unclear risk | Insufficient detail reported in order to determine how selection took place. |
| Confounding | High risk | Did not account for SES |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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**

| *Study characteristics* | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Republic of Ireland (RoI)<br>Geographic location: not stated<br>Year of study: 2001/2002<br>Year of change in fluoridation status: 1964<br>Study design: cross-sectional |
| Participants | Inclusion criteria: children in Junior Infants, Second Class, Sixth Class, and Junior Certificate<br>Exclusion criteria: not stated<br>Other sources of fluoride: participants in the fluoridated group may have had additional exposure to fluoride tablets and fluoride mouth rinses<br>Ethnicity: not stated |

| | |
|---|---|
| | SES: possession 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, study authors reported that figures included children for whom medical card details were missing.<br>Residential history: fluoridated group participants' home water supply had to have been fluoridated continuously since birth, and the non-fluoridated group participants' home water supply had never to have been fluoridated. No further details reported<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.8 to 1 ppm (artificial fluoridation)<br>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<br>Age at assessment: 5, 8, 12 and 15 years |
| Funding | Funded by the Department of Health and Children and the Health Boards in Ireland |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | The study 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)<br>All outcomes | Low risk | Fluoride codes ascribed after examinations; unlikely to be systematic bias |
| Incomplete outcome data (attrition bias)<br>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 |

**Whelton 2006**

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Republic of Ireland (RoI) and Northern Ireland (NI)<br>Geographic location: not stated<br>Year of study: 2001/2002<br>Year of change in fluoridation status:1964<br>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<br>Exclusion criteria: not stated<br>Other sources of fluoride: participants in the fluoridated group may have had additional exposure to fluoride tablets and fluoride mouth rinses<br>Ethnicity: not stated<br>SES: 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, study authors reported that figures included children for whom MC/LIB details were missing.<br>Residential history: fluoridated group participants' home water supply had to have been fluoridated continuously since birth and the non-fluoridation group participants' home water supply had never to have been fluoridated. No further details reported<br>Other confounding factors: not stated |
| Interventions | Group 1 (RoI): 0.8 to 1 ppm (artificial fluoridation)<br>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<br>Age at assessment: 5, 8, 12 and 15 years |
| Funding | Funded by the Department of Health and Children and the Health Boards in Ireland |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

| | |
|---|---|
| | The study 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 |
| 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)<br>All outcomes | Low risk | Fluoride codes ascribed after examinations; unlikely to be systematic bias |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: Ethiopia<br>Geographic location: not stated<br>Year of study: 1997<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: not stated<br>Exclusion criteria: not stated<br>Other sources of fluoride: not stated<br>Ethnicity: not stated<br>SES: the villages were of approximately the same size and socioeconomic standards and were selected purposively for the study.<br>Residential history: fluoridated group participants' home water supply had to have been fluoridated continuously since birth and the non-fluoridation group participants' home water supply had to have never been fluoridated. No further details reported<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.3 to 2.2 ppm<br>Group 2: 10 to 14 ppm |
| Outcomes | Fluorosis prevalence (TF Index); caries data evaluated in study but not included in review due to study design<br>Age at assessment: 12 to 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 |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | |

***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)<br>All outcomes | High risk | Quote: "Intra-oral examination was conducted at the health centers of the areas by two examiners"<br>Comment: blinding not undertaken |
| Incomplete outcome data (attrition bias)<br>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**

***Study characteristics***

| | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: China |

| | |
|---|---|
| | Geographic location: Guangzhou and Fangcun (F); Fushan and Zhaoqing (non-F)<br>Year of study: not stated<br>Year of change in fluoridation status: not stated<br>Study design: cross-sectional |
| Participants | Inclusion criteria: students who were 7, 9, 12, 15, and 17 years old<br>Exclusion criteria: not stated<br>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<br>SES: not stated<br>Ethnicity: Chinese<br>Residential history: lifetime residents<br>Other confounding factors: not stated |
| Interventions | Group 1: 0.6 to 1.2 ppm (artificial fluoridation)<br>Group 2: 0.4 to 1.2 ppm (artificial fluoridation)<br>Group 3: 0.2 ppm (natural fluoridation)<br>Group 4: 0.2 ppm (natural fluoridation) |
| Outcomes | Outcome: fluorosis prevalence (Dean's Index)<br>Age at assessment: 12 to 17 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| Notes | Data extracted from Zheng 1986 differs from that presented in McDonagh 2000<br>Translated from Chinese |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Sampling | Unclear risk | Insufficient information to make a judgement |
| Confounding | High risk | Did not appear to account for SES |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Not reported |
| Incomplete outcome data (attrition bias)<br>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

| ***Study characteristics*** | |
|---|---|
| Methods | **FLUOROSIS STUDY**<br>Country of study: USA<br>Geographic location: Aurora, Illinois (F); Montgomery and Prince Georges counties, Maryland (non-F)<br>Year of study: 1953<br>Year of change in fluoridation status: NA<br>Study design: cross-sectional |
| Participants | Inclusion criteria: lifetime residents of study areas; white children aged 12 to 14 years<br>Exclusion criteria: children who had left study areas for periods of time other than for holidays<br>Other sources of fluoride: not stated<br>SES: not stated<br>Ethnicity: white children only<br>Residential history: continuous residents<br>Other confounding factors: not stated |
| Interventions | All natural fluoridation<br>Group 1: 0.2 ppm<br>Group 2: 1.2 ppm |
| Outcomes | Fluorosis (Deans Index); caries data evaluated in study but not included in review due to study design<br>Age at assessment: 12 to 14 years |
| Funding | Not stated |
| ROBINS-I comments for studies evaluating initiation or cessation of CWF for prevention of dental caries | |
| 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)<br>All outcomes | High risk | Insufficient information |
| Incomplete outcome data (attrition bias)<br>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 |

**CBA:** controlled before-and-after study; **CFI:** Community Fluorosis Index; **CRD:** Centre for Reviews and Dissemination; **CWF:** community water fluoridation; **DDE:** Developmental Defects of Enamel; **DHSS:** Department of Health and Social Security; **dmft:** decayed, missing and filled primary teeth; **DMFT:** decayed, missing and filled permanent teeth; **dmfs:** decayed, missing or filled primary tooth surfaces; **DMFS:** decayed, missing or filled permanent tooth surfaces; **F:** fluoride/fluoridated; **ITS:** interrupted time series study; **KNHANES:** Korean National Health and Nutrition Examination Survey; **LIB:** low-income benefits; **MRC:** Medical Research Council; **NA:** not applicable; **NHRDP:** National Health Research and Development Program; **NI:** Northern Ireland; **NIHR:** National Institute for Health and Care Research; **non-F:** non-fluoridated; **NUFU:** Norwegian Programme for Development, Research and Education; **MRC:** Medical Research Council; **ppm:** parts per million; **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 |
|---|---|
| Armfield 2013 | Study focused on sugar consumption; exposure to water fluoridation was reported in a way that did not provide a non-fluoridated control group |
| Do 2014 | Not a longitudinal study; no direct comparison of fluoridated versus non-fluoridated areas |
| Hawew 1996 | Compared different levels of fluoride rather than fluoride/non-fluoride comparison |
| Koh 2015 | No concurrent control group: assessments pre-fluoridation compared with assessments post-fluoridation |
| Kämppi 2013 | Geographical distribution of dental caries prevalence and associated factors |
| Lee 2015 | No baseline measurement within 3 years of a change in fluoridation status |
| McLaren 2022 | No baseline measurement within 3 years of a change in fluoridation status |
| Wang 2014 | Unable to locate a full text publication; previously listed as awaiting assessment |
| Zander 2013 | Does not provide data on caries by fluoridation status |

# Appendices

## Appendix 1. Methods for evaluating the association of water fluoridation (artificial or natural) with dental fluorosis

In this updated review, we did not search for studies that evaluated the association of water fluoridation with dental fluorosis. Therefore, the Methods for managing these studies are consistent with those described in Iheozor-Ejiofor 2015. Here, we summarise the methods that are specific to the management of these types of studies.

### Types of studies

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

Due to the nature of the research question, randomised controlled trials are unfeasible.

### Types of participants

Fluoride at any concentration present in drinking water.

### Types of outcomes

Percentage of children with fluorosis (any level of fluorosis, or fluorosis of aesthetic concern), measured using any of the following instruments:

- 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 index 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.

### Search methods for identification of studies

We searched for studies that measured fluorosis on 19 February 2015. We used the search methods described in the main text of this review.

### Assessment of risk of bias in the included studies

We used 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 identified the following factors as important confounders for the primary and secondary outcomes: sugar consumption/dietary habits, socioeconomic status (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 across domains (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 calculated the log odds and presented them as probabilities for interpretation.

### Data synthesis

We carried out the primary analysis 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 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.

We planned to explore differences in fluoride concentration, outcome measurement index and technique as possible sources of heterogeneity.

### Presentation of the results

We assessed the certainty 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 certainty of the body of evidence starts at 'low'. We considered subsequent downgrading of the certainty 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 certainty of the evidence on the basis of an assessment of the risk of publication bias, the magnitude of the effect and whether there was evidence of a dose response.

We presented the results and certainty of evidence for each outcome in a summary of findings table.

## Appendix 2. Search strategies

**Cochrane Oral Health's Trial Register** (via Cochrane Register of Studies)

For information on how the register is compiled, see https://oralhealth.cochrane.org/trials.

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

**CENTRAL**

#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 deminerali* in All Text or reminerali* 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 deminerali* in All Text or reminerali* 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 deminerali* in All Text or reminerali* 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 deminerali* in All Text or reminerali* 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 deminerali* in All Text or reminerali* 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 deminerali* in All Text or reminerali* 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)

**MEDLINE (via OVID)**

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 deminerali$ or reminerali$)).mp.

13. (tooth adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or deminerali$ or reminerali$)).mp.

14. (dental adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or deminerali$ or reminerali$)).mp.

15. (enamel adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or deminerali$ or reminerali$)).mp.

16. (dentin$ adj5 (cavit$ or caries$ or carious or decay$ or lesion$ or deminerali$ or reminerali$)).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)

**Embase (via OVID)**

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. 5 and 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

**ProQuest**

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

**Web of Science Conference Proceedings (Clarivate Analytics)**

#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 deminerali* or reminerali*))

#8 TS=(dentin* and (cavit* or caries* or carious or decay* or lesion* or deminerali* or reminerali*))

#9 TS=(root* and (cavit* or caries* or carious or decay* or lesion* or deminerali* or reminerali*))

#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

**ZETOC Conference Proceedings**

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

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**US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) and World Health Organization International Clinical Trials Registry Platform search strategy**

fluoride and water and caries

## Appendix 3. Descriptors of risk of bias judgements and their interpretation using ROBINS-I

**Risk of bias judgements for each of the seven domains**

| Judgement | Interpretation |
|---|---|
| Low risk of bias | There is little or no concern about bias with regard to this domain. |
| Moderate risk of bias | There is some concern about bias with regard to this domain, although it is not clear that there is an important risk of bias. |
| Serious risk of bias | The study has some important problems in this domain: characteristics of the study give rise to a serious risk of bias. |
| Critical risk of bias | The study is very problematic in this domain: characteristics of the study give rise to a critical risk of bias, such that the result should generally be excluded from evidence synthesis. |

**Overall assessment of risk of bias across domains**

| Judgement | Interpretation | How reached |
|---|---|---|
| Low risk of bias except for concerns about uncontrolled confounding | There is the possibility of uncontrolled confounding that has not been controlled for (given the observational nature of the study), but otherwise little or no concern about bias in the result. | Low risk of bias except for concerns about uncontrolled confounding in Domain 1, and low risk of bias in all other domains. |
| Moderate risk of bias | There is some concern about bias in the result, although it is not clear that there is an important risk of bias. | At least one domain is at moderate risk of bias, but no domains are at serious or critical risk of bias. |
| Serious risk of bias | The study has some important problems: characteristics of the study give rise to a serious risk of bias in the result. | At least one domain is at serious risk of bias, but no domains are at critical risk of bias.<br>OR<br>Several domains are at moderate risk of bias, leading to an additive judgement of serious risk of bias. |
| Critical risk of bias | The study is very problematic: characteristics of the study give rise to a critical risk of bias in the result, such that the result should generally be excluded from evidence synthesis. | At least one domain is at critical risk of bias.<br>OR<br>Several domains are at serious risk of bias, leading to an additive judgement of critical risk of bias. |

## Appendix 4. Imputation of standard deviations for caries data

Where standard deviations were missing for the DMFT and 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. We undertook a sensitivity analysis omitting all the data for studies/age groups where we imputed the standard deviation.

The equation we used was obtained from the data we had available to us from the other studies included 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 2003 shown below, although the intercept was smaller. This is probably because both these models were 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 2003: 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 5. Disparities in caries across socioeconomic status

| Study ID | Age | Group | Measure | Socioeconomic status | Baseline | | | | Final follow-up | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 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 | Southeast Staffordshire | Jarman 1984 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 1984 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 |
| | | 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 |

**deft:** decayed, extracted or filled teeth (primary dentition); **dmft:** decayed, missing or filled teeth (primary dentition); **F:** fluoride; **SD:** standard deviation; **SE:** standard error

[a]Caries data reported as deft (SE)

[b]Caries data reported as dmft (SD)

## Appendix 6. Adjusted caries data

Goodwin 2022 reports the results of both unadjusted and adjusted analyses for caries outcomes. The primary meta-analyses in this review included data from the unadjusted analysis. For completeness, the results of the adjusted analyses reported in the study publication are presented below.

- **Change in the number of dmft.** The caries outcome in the adjusted analysis was the incidence of decay expressed as dmft count. Results from a negative binomial regression indicated that the incidence rate ratio of dmft for children in a fluoridated area was 0.61 times that of children living in a non-fluoridated area,

conditional on the values of the covariates deprivation quintile, age and sex (Incidence rate ratio 0.61, 95% CI 0.44 to 0.86; 1333 participants).

- **Change in the number of DMFT**. The caries outcome in the adjusted analysis was the incidence of decay expressed as DMFT count. Results from a negative binomial regression indicated that the incidence rate ratio of DMFT for children in a fluoridated area was 0.69 times that of children living in a non-fluoridated area, conditional on the values of the covariates deprivation quintile, age, sex and dmft at baseline (Incidence rate ratio 0.69, 95% CI 0.52 to 0.93; 1127 participants).
- **Change in the proportion of caries-free participants (primary dentition).** The caries outcome in the adjusted analysis was the development of decay. The study authors report that the odds of developing decay for children from a fluoridated area were 74% of the odds of decay for children from a non-fluoridated area, conditional on the values of the covariates deprivation quintile, age and sex (OR 0.74, 95% CI 0.56 to 0.98; 1333 participants).
- **Change in the proportion of caries-free participants (permanent dentition).** The caries outcome in the adjusted analysis was the development of decay. The study authors report that the odds of developing decay for children from a fluoridated area were 80% of the odds of decay for children from a non-fluoridated area, conditional on the values of the covariates deprivation quintile, age, sex and dmft at baseline (OR 0.80, 95% CI 0.58 to 1.09; 1089 participants).

## Appendix 7. Sensitivity analyses

| Including studies assessed as having a critical risk of bias | | | | |
|---|---|---|---|---|
| **Outcome** | **Year of study** | **Effect estimate in primary analysis[a]** | **Effect estimate in sensitivity analysis[a]** | **Interpretation** |
| **Change in number of dmft** | After 1975 | MD 0.24, 95% CI -0.03 to 0.52; $I^2$ = 26%; 2 studies, 2908 participants; Analysis 1.1 | MD 1.08, 95% CI -0.53 to 2.70; $I^2$ = 99%; 3 studies, 6622 participants; Analysis 1.6 | The sensitivity analysis includes a larger effect size than the primary analysis, and has higher levels of statistical heterogeneity. |
| | 1975 or earlier | MD 2.10, 95% CI 1.71 to 2.49; $I^2$ = 44%; 5 studies, 5709 participants; Analysis 1.1 | MD 1.91, 95% CI 1.60 to 2.23; $I^2$ = 63%; 8 studies, 17,520 participants; Analysis 1.6 | The sensitivity analysis includes a smaller effect size than the primary analysis. |
| **Change in number of DMFT** | After 1975 | MD 0.27, 95% CI -0.11 to 0.66; $I^2$ = 83%; 4 studies, 2856 participants; Analysis 1.2 | MD 0.53, 95% CI 0.00 to 1.06; $I^2$ = 98%; 6 studies, 12,906 participants; Analysis 1.7 | The sensitivity analysis includes a larger effect size than the primary analysis.[b] |
| | 1975 or earlier | MD 1.00, 95% CI 0.54 to 1.47; $I^2$ = 80%; 3 studies, 5623 participants; Analysis 1.2 | MD 1.35, 95% CI 0.77 to 1.94; $I^2$ = 97%; 6 studies, 30,334 participants; Analysis 1.7 | The sensitivity analysis includes a larger effect size than the primary analysis. |
| **Change in the proportion of caries-free participants (primary dentition)** | After 1975 | MD -0.04, 95% CI -0.09 to 0.01; $I^2$ = 0%; 2 studies, 2908 participants; Analysis 1.4 | MD -0.10, 95% CI -0.19 to -0.01; $I^2$ = 90%; 4 studies, 9608 participants; Analysis 1.8 | The sensitivity analysis includes a larger effect size than the primary analysis. |
| | 1975 or earlier | MD -0.17, 95% CI -0.20 to -0.13; $I^2$ = 13%; 5 studies, 6278 participants; Analysis 1.4 | MD -0.17, 95% CI -0.19 to -0.15; $I^2$ = 0%; 8 studies, 12,383 participants; Analysis 1.8 | The sensitivity analysis has a very similar effect to the primary analysis. |
| **Change in the proportion of caries-free participants (permanent dentition)** | After 1975 | MD -0.03, 95% CI -0.07 to 0.01; $I^2$ = 0%; 2 studies, 2368 participants; Analysis 1.5 | MD -0.12, 95% CI -0.33 to 0.09; $I^2$ = 98%; 3 studies, 10,502 participants, Analysis 1.9 | The sensitivity analysis includes a larger effect size than the primary analysis.[c] |
| | 1975 or earlier | MD -0.06, 95% CI -0.14 to 0.02; $I^2$ = 93%; 4 studies, 6278 participants; Analysis 1.5 | MD -0.13, 95% CI -0.24 to -0.03; $I^2$ = 98%; 6 studies, 17,459 participants; Analysis 1.9 | The sensitivity analysis includes a larger effect size than the primary analysis.[d] |
| **Change of analytical approach[d]** | | | | |
| **Outcome** | **Year of studies** | **Effect estimate in primary analysis** | **Effect estimate in sensitivity analysis** | **Interpretation** |
| Change in number of dmft | After 1975 | MD 0.24, 95% CI -0.03 to 0.52; $I^2$ = 26%; 2 studies, 2908 participants; Analysis 1.1 | MD 0.28, 95% CI 0.12 to 0.43; $I^2$ = 0%; 2 studies, 2825 participants; Analysis 1.10 | Using the caries increment from the longitudinal analysis[e] resulted in a very similar pooled effect estimate to the primary analysis. However, imprecision is no longer a concern using the longitudinal analysis. |
| **Excluding studies in which missing standard deviations were imputed** | | | | |
| **Outcome** | **Year of studies** | **Effect estimate in primary analysis** | **Effect estimate in sensitivity analysis** | **Interpretation** |
| Change in number of dmft | 1975 or earlier | MD 2.10, 95% CI 1.71 to 2.49; $I^2$ = 44%; 5 studies, 5709 participants; Analysis 1.1 | MD 1.59, 95% CI 1.01 to 2.16; $I^2$ = 0%; 2 studies, 1148 participants; Analysis 1.11 | The sensitivity analysis includes a smaller effect size than the primary analysis. |

| | | | | |
|---|---|---|---|---|
| Change in number of DMFT | After 1975 | MD 0.27, 95% CI -0.11 to 0.66; $I^2$ = 83%; 4 studies, 2856 participants; Analysis 1.2 | MD 0.53, 95% CI -0.45 to 1.51; $I^2$ = 89%; 2 studies, 1535 participants; Analysis 1.12 | The sensitivity analysis includes a larger effect size than the primary analysis. |
| | 1975 or earlier | MD 1.00, 95% CI 0.54 to 1.47; $I^2$ = 80%; 3 studies, 5623 participants; Analysis 1.2 | MD 0.62, 95% CI 0.25 to 0.99; 1 study, 736 participants; Analysis 1.12 | The sensitivity analysis includes a smaller effect size than the primary analysis. |

**CI:** confidence interval; **dmft:** decayed, missing or filled teeth (primary dentition); **DMFT:** decayed, missing or filled teeth (permanent dentition); **MD:** mean difference

[a]Because measurements were taken from different population samples at baseline and follow-up, we reported the average number of participants alongside the effect estimates.

[b]It should be noted that in Guo 1984, the mean DMFT values at baseline for both the control and water fluoridation groups were low at 0.8, and this increased in both groups. However, the increase was greatest for the control group. This explains why the changes are both negative.

[c]We did not include Loh 1996 in the sensitivity analysis because the number of participants was unknown.

[d]We did not include Pot 1974 in the sensitivity analysis because the data were only available for the edentulous (i.e. toothless) participants.

[e]In the primary analysis, we used a controlled before-and-after study design approach for Goodwin 2022. This study also reported dmft caries increment, and we used these data in sensitivity analysis.

## Appendix 8. Fluorosis studies

**Studies included in the analysis of all levels 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

## Appendix 9. Sustainability of the intervention: search strategy

**MEDLINE (via Ovid; 1946 to 15 May 2024)**

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. 4 and 9
11. exp Sustainable Development/
12. Environmental Monitoring/
13. Carbon Footprint/
14. "Conservation of Natural Resources"/
15. Waste Management/
16. Air Pollution/
17. Climate Change/
18. (life cycle adj3 (assess* or analys*)).mp.
19. "cradle to grave".mp.
20. sustainab*.mp.
21. (environment* adj3 impact).mp.
22. carbon footprint.mp.
23. sustainable development.mp.
24. waste management.mp.
25. climate change.mp.
26. circular economy.mp.
27. or/11-26
28. 10 and 27

# References

## References to studies included in this review


### Acharya 2005 {published data only}

Acharya S. Dental caries, its surface susceptibility and dental fluorosis in South India. International Dental Journal 2005;55(6):359-64.

### Adair 1999 {published data only}

Adair S, Hanes C, Russell C, Whitford G. Dental caries and fluorosis among children in a rural Georgia area. Pediatric Dentistry 1999;21(2):81-5.

### Adriasola 1959 {published data only}

* Adriasola G. First evaluation of the program of fluoridation of drinking water in Curico-San Fernando, Chile, 1956. Boletin de la Oficina Sanitaria Panamericana 1959;47:412-20.

Alvarez-Ubilla A. Primera evaluación del programa de fluoacion del agua potable Curico-San Fernando. Odontologica Chilena 1959;41:1277-83.

### Al-Alousi 1975 {published data only}

Al-Alousi W, Jackson D, Compton G, Jenkins OC. Enamel mottling in a fluoride and a non-fluoride community. A study. British Dental Journal 1975;138(1):9-15.

### Alarcon-Herrera 2001 {published data only}

Alarcon-Herrera M, Martin-Dominguez I, Trejo-Vazquez R, Rodriguez-Dozal S. Well water fluoride, dental fluorosis, and bone fractures in the Guadiana Valley of Mexico. Fluoride 2001;34(2):139-49.

### Albrecht 2004 {published data only}

Albrecht M, Maros E. [Dental fluorosis in children in Bár and Dunaszekcsó in the 6-18 age group]. Orvosi Hetilap 2004;145(5):229-32.

### AlDosari 2010 {published data only}

AlDosari A, Akpata E, Khan N. Associations among dental caries experience, fluorosis, and fluoride exposure from drinking water sources in Saudi Arabia. Journal of Public Health Dentistry 2010;70(3):220-6.

### Angelillo 1999 {published data only}

Angelillo I, Torre I, Nobile C, Villari P. Caries and fluorosis prevalence in communities with different concentrations of fluoride in the water. Caries Research 1999;33(2):114-22.

### Arif 2013 {published data only}

Arif M, Hussain J, Kumar S. Assessment of fluoride level in groundwater and prevalence of dental fluorosis in Didwana block of Nagaur district, central Rajasthan, India. International Journal of Occupational and Environmental Medicine 2013;4(4):178-84.

### Arnold 1956 {published data only}

Arnold F, Dean H, Jay P, Knutson J. Effect of fluoridated public water supply on dental caries prevalence. Public Health Reports 1956;71:652-8.

### Ast 1951 {published data only}

Ast DB, Finn SB, Chase HC. Newburgh-Kingston caries fluorine study. III. Further analysis of dental findings including the permanent and deciduous dentitions after four years of water fluoridation. Journal of the American Dental Association (1939) 1951;42:188-95.

### Awadia 2000 {published data only}

* Awadia A, Birkeland J, Haugejorden O, Bjorvatn K. An attempt to explain why Tanzanian children drinking water containing 0.2 or 3.6 mg fluoride per liter exhibit a similar level of dental fluorosis. Clinical Oral Investigations 2000;4(4):238-44.

Awadia A, Birkeland J, Haugejorden O, Bjorvatn K. Caries experience and caries predictors--a study of Tanzanian children consuming drinking water with different fluoride concentrations. Clinical Oral Investigations 2002;6(2):98-103.

### Azcurra 1995 {published data only}

Azcurra A, Battellino L, Calamari S, de Cattoni S, Kremer M, Lamberghini F. Dental health status of students living in places supplied with drinking water of very high and very low levels of fluorides. Revista de Saude Publica 1995;29(5):367-75.

### Backer-Dirks 1961 {published data only}

Backer-Dirks O, Houwink B, Kwant G. The results of 6½ years of artificial fluoridation of drinking water in the Netherlands. The Tiel-Culemborg experiment. Archives of Oral Biology 1961;5:284-300.

### Bao 2007 {published data only}

Bao LL, Li YY, Zhang YY. Dental caries and fluorosis among 12-year-old children with different fluoride exposure in Heilongjiang province. Shanghai Journal of Stomatology 2007;16(6):574-7.

### Baskaradoss 2008 {published data only}

Baskaradoss JK, Clement RB, Narayanan A. Prevalence of dental fluorosis and associated risk factors in 11-15 year old school children of Kanyakumari District, Tamilnadu, India: a cross sectional survey. Indian Journal of Dental Research 2008;19(4):297-303.

### Beal 1971 {published data only}

Beal J, James P. Dental caries prevalence in 5 year old children following five and a half years of water fluoridation in Birmingham. British Dental Journal 1971;130(7):284-8.

### Beal 1981 {published data only}

Beal J, Clayton M. Fluoridation a clinical survey in Corby and Scunthorpe England UK. Public Health 1981;95(3):152-60.

### Beltran-Aguilar 2002 {published data only}

Beltran-Aguilar E, Griffin S, Lockwood S. Prevalence and trends in enamel fluorosis in the United States from the 1930s to the 1980s. Journal of the American Dental Association 2002;133(2):157-65.

### Berndt 2010 {published data only}

Berndt Ch, Meller Ch, Poppe D, Splieth ChH. Fluorosis, caries and oral hygiene in schoolchildren on the Ombili Foundation in Namibia. Oral Health & Preventive Dentistry 2010;8:269-75.

### Birkeland 2005 {published data only}

Birkeland J, Ibrahim Y, Ghandour I, Haugejorden O. Severity of dental caries among 12-year-old Sudanese children with different fluoride exposure. Clinical Oral Investigations 2005;9(1):46-51.

### Blinkhorn 2015 {published and unpublished data}

Blinkhorn A, Byun R, Metha P, Kay M. A four year assessment of a new water fluoridation scheme in New South Wales, Australia (unpublished). (Personal communication with study author) 2015.

* Blinkhorn AS, Byun R, Johnson G, Metha P, Kay M, Lewis P. The dental health of primary school children living in fluoridated, pre-fluoridated and non-fluoridated communities in New South Wales, Australia. BMC Oral Health 2015;15(9):no pagination. [PMID: 25604625]

### Booth 1991 {published data only}

Booth I, Mitropoulos C, Worthington H. A comparison between the dental health of 3-year old children living in fluoridated Huddersfield and non-fluoridated Dewsbury in 1989. Community Dental Health 1991;9:151-7.

### Brothwell 1999 {published data only}

Brothwell DJ, Limeback H. Fluorosis risk in grade 2 students residing in a rural area with widely varying natural fluoride. Community Dentistry and Oral Epidemiology 1999;27(2):130-6.

### Brown 1965 {published data only}

* Brown H, McLaren H, Poplove M. The Brantford-Sarnia-Stratford Fluoridation Caries Study - 1959 Report. Journal of the Canadian Dental Association 1960;26(3):131-42.

Brown H, Poplove M. The Brantford-Sarnia-Stratford Fluoridation Caries Study: Final Survey 1963. Canadian Journal of Public Health. Revue Canadienne de Sante Publique 1965;56(8):319-24.

### Budipramana 2002 {published data only}

Budipramana ES, Hapsoro A, Irmawati ES, Kuntari S. Dental fluorosis and caries prevalence in the fluorosis endemic area of Asembagus, Indonesia. International Journal of Paediatric Dentistry 2002;12(6):415-22.

### Butler 1985 {published data only}

Butler WJ, Segreto V, Collins E. Prevalence of dental mottling in school-aged lifetime residents of 16 Texas communities. American Journal of Public Health 1985;75(12):1408-12.

### Chandrashekar 2004 {published data only}

Chandrashekar J, Anuradha K. Prevalence of dental fluorosis in rural areas of Davangere, India. International Dental Journal 2004;54(5):235-9.

### Chen 1989 {published data only}

Chen B. An epidemiological study on dental fluorosis and dental caries prevalence in communities with negligible, optimal and above-optimal fluoride concentrations in drinking water supplies. Chinese Journal of Dental Research 1989;8:117-27.

### Chen 1993 {published data only}

Chen W, Xu R, Chen G, Zao J, Chen J. Institution: Health and Epidemic Prevention Station of Guangdong Province. Changes in the prevalence of endemic fluorosis after changing water sources in two villages in Guangdong, China. Bulletin of Environmental Contamination and Toxicology 1993;51(4):479-82.

### Clark 1993 {published data only}

Clark D, Hann H, Williamson M, Berkowitz J. Aesthetic concerns of children and parents in relation to different classifications of the tooth surface index of fluorosis. Community Dentistry and Oral Epidemiology 1993;21(6):360-4.

### Clarkson 1989 {published data only}

Clarkson J, O'Mullane D. A modified DDE index for use in epidemiological studies of enamel defects. Journal of Dental Research 1989;68(3):445-50.

### Clarkson 1992 {published data only}

Clarkson J, O'Mullane D. Prevalence of enamel defects-fluorosis in fluoridated and non-fluoridated areas in Ireland. Community Dentistry and Oral Epidemiology 1992;20(4):196-9.

### Cochran 2004a {published data only}

Cochran J, Ketley C, Arnadóttir I, Fernandes B, Koletsi-Kounari H, Oila A-M, et al. A comparison of the prevalence of fluorosis in 8-year-old children from seven European study sites using a standardized methodology. Community Dentistry and Oral Epidemiology 2004;32 Suppl 1:28-33.

### Colquhoun 1984 {published data only}

Colquhoun J. Disfiguring dental fluorosis in Aukland, New Zealand. Fluoride 1984;17:234-42.

### Correia Sampaio 1999 {published data only}

Correia Sampaio F, Ramm von der Fehr F, Arneberg P, Petrucci Gigante D, Hatloy A. Dental fluorosis and nutritional status of 6- to 11-year-old children living in rural areas of Paraiba, Brazil. Caries Research 1999;33(1):66-73.

### Cutress 1985 {published data only}

Cutress T, Suckling G, Pearce E. Defects in tooth enamel in children in fluoridated and non-fluoridated water areas of the Auckland Region. New Zealand Dental Journal 1985;81:12-9.

### Cypriano 2003 {published data only}

Cypriano S, Pecharki GD, de Sousa Mda L, Wada RS. [Oral health of schoolchildren residing in areas with or without water fluoridation in Sorocaba, Sao Paulo State, Brazil] [Portuguese]. Cadernos de Saude Publica 2003;19(4):1063-71.

### de Crousaz 1982 {published data only}

de Crousaz P. Observations on enamel opacities in Switzerland in relation to water or salt fluoridation. SSO Schweiz Monatsschr Zahnheilkd 1982;92(4):332-44.

### DHSS England 1969 {published data only}

Department of Health and Social Security, Scottish Office, Welsh Office. The fluoridation studies in the United Kingdom and results achieved after 11 years. A report of the Committee on Research into Fluoridation. London: Her Majesty's Stationary Office. Reports on Public Health Medical Subjects 1969;No. 122.

* Ministry of Health, Scottish Office and Ministry of Housing and Local Government. The Conduct of the Fluoridation Studies and the Results Achieved after Five Years. Reports on Public Health and Medical Subjects 1962;105(London, HMSO).

### DHSS Scotland 1969 {published data only}

Department of Health and Social Security, Scottish Office, Welsh Office. The fluoridation studies in the United Kingdom and results achieved after 11 years. A report of the Committee on Research into Fluoridation. London: Her Majesty's Stationary Office. Reports on Public Health Medical Subjects 1969;No. 122.

* Ministry of Health, Scottish Office and Ministry of Housing and Local Government. The Conduct of the Fluoridation Studies and the Results Achieved after Five Years. Reports on Public Health and Medical Subjects 1962;105(London, HMSO).

### DHSS Wales 1969 {published data only}

Department of Health and Social Security, Scottish Office, Welsh Office. The fluoridation studies in the United Kingdom and results achieved after 11 years. A report of the Committee on Research into Fluoridation. London: Her Majesty's Stationary Office. Reports on Public Health Medical Subjects 1969;No. 122.

* Ministry of Health, Scottish Office and Ministry of Housing and Local Government. The Conduct of the Fluoridation Studies and the Results Achieved after Five Years. Reports on Public Health and Medical Subjects 1962;105(London, HMSO).

### Downer 1994 {published data only}

Blinkhorn A, Attwood D, Gavin G, O'Hickey S. Joint epidemiological survey on dental health of 12-year-old school children in Dublin and Glasgow. Community Dentistry and Oral Epidemiology 1992 Oct;20(5):307-8.

* Downer M, Blinkhorn A, Holt R, Wight C, Attwood D. Dental caries experience and defects of dental enamel among 12-year-old children in north London, Edinburgh, Glasgow and Dublin. Community Dentistry and Oral Epidemiology 1994;22(Pt1):283-5.

### Driscoll 1983 {published data only}

Driscoll W, Horowitz H, Meyers R, Heifetz S, Kingman A, Zimmerman E. Prevalence of dental caries and dental fluorosis in areas with optimal and above-optimal water fluoride concentrations. Journal of the American

Dental Association (1939) 1983;107(1):42-7.

### Ekanayake 2002 {published data only}

Ekanayake L, van der Hoek W. Dental caries and developmental defects of enamel in relation to fluoride levels in drinking water in an arid area of Sri Lanka. Caries Research 2002;36(6):398-404.

### Eklund 1987 {published data only}

Eklund S, Ismail A, Burt B, Calderon J. High-fluoridated drinking water, fluorosis and dental caries in adults. Journal of the American Dental Association (1939) 1987;114(March):324-8.

### Ellwood 1995 {published data only}

Ellwood R, O'Mullane D. Dental enamel opacities in three groups with varying levels of fluoride in their drinking water. Caries Research 1995;29(2):137-42.

### Ellwood 1996 {published data only}

Ellwood R, O'mullane D. The association between developmental enamel defects and caries in populations with and without fluoride in their drinking water. Journal of Public Health Dentistry 1996;56(2):76-80.

### Ermis 2003 {published data only}

Ermis R, Koray F, Akdeniz B. Dental caries and fluorosis in low- and high-fluoride areas in Turkey. Quintessence International 2003;34(5):354-60.

### Firempong 2013 {published data only}

Firempong C, Nsiah K, Awunyo-Vitor D, Dongsogo J. Soluble fluoride levels in drinking water - a major risk factor of dental fluorosis among children in Bongo community of Ghana. Ghana Medical Journal 2013;47(1):16-23.

### Forrest 1956 {published data only}

Forrest J. Caries incidence and enamel defects in areas with different levels of fluoride in drinking water. British Dental Journal 1956;100:195-200.

### Forrest 1965 {published data only}

Forrest J, James P. A blind study of enamel opacities and dental caries prevalence after eight years of fluoridation of water. British Dental Journal 1965;119(7):319-22.

### Franzolin 2008 {published data only}

Franzolin Sde O, Goncalves A, Padovani C, Francischone L, Marta S. Epidemiology of fluorosis and dental caries according to different types of water supplies. Ciencia & Saude Coletiva 2008;15(Suppl 1):1841-7.

### Garcia-Perez 2013 {published data only}

Garcia-Perez A, Borges-Yanez A. Fluorosis and dental caries in Mexican schoolchildren residing in areas with different water fluoride concentrations and receiving fluoridated salt. Caries Research 2013;47(4):299-308.

### Gaspar 1995 {published data only}

Gaspar M, Pereira A, Moreira B. Non-fluorosis and dental fluorosis opacities in areas with lower (0.2 ppm F) and optimum (0.7 ppm F) fluoride concentration in drinking water [Opacidades de esmalte de origem não fluorótica e fluorose dentária em áreas com baixa (0,2 ppm F) e ótima (0,7 ppm F) concentrações de flúor nas águas de abastecimento público]. Revista Brasileira de Odontologia 1995;52(2):13-8.

### Goodwin 2022 {published and unpublished data}

Goodwin M, Emsley R, Kelly MP, Sutton M, Tickle M, Walsh T, et al. Evaluation of water fluoridation scheme in Cumbria: the CATFISH prospective longitudinal cohort study. Public Health Research 2022;10(11):1-228. [DOI: 10.3310/SHMX1584]

### Goward 1982 {published data only}

Goward P. Mottling on deciduous incisor teeth. A study of 5-year-old Yorkshire children from districts with and without fluoridation. British Dental Journal 1982;153(10):367-9.

### Gray 2001 {published data only}

Gray M, Davies-Slowik J. Changes in the percentage of 5-year-old children with no experience of decay in Dudley towns since the implementation of fluoridation schemes in 1987. British Dental Journal

2001;190(1):30-2.
* Gray M, Langford K. Notes on the results of the studies of 5 year old children conducted in the West Midlands since 1985. Unpublished report 2000.

### Grimaldo 1995 {published data only}

Grimaldo M, Borja Aburto VH, Ramirez AL, Ponce M, Rosas M, Diaz Barriga F. Endemic fluorosis in San Luis Potosi, Mexico. I. Identification of risk factors associated with human exposure to fluoride. Environmental Research 1965;68(1):25-30.

### Grobler 1986 {published data only}

Grobler S, Vanwyk C, Kotze D. Relationship between enamel fluoride levels, degree of fluorosis and caries experience in communities with a nearly optimal and a high fluoride level in the drinking water. Caries Research 1986;20(3):284-8.

### Grobler 2001 {published data only}

Grobler S, Louw A, van Kotze T. Dental fluorosis and caries experience in relation to three different drinking water fluoride levels in South Africa. International Journal of Paediatric Dentistry 2001;11(5):372-9.

### Guo 1984 {published data only}

Guo M, Hsieh C, Hong Y, Chen R. Effect of water fluoridation on prevalence of dental caries in Chung-Hsing New Village Taiwan after 9 years. Journal of the Formosan Medical Association 1984;83(10):1035-43.

### Haavikko 1974 {published data only}

Haavikko K, Helle A. The prevalence and distribution of enamel defects in with different fluoride contents in the drinking water. Proceedings of the Finnish Dental Society 1974;70(5):178-85.

### Harding 2005 {published data only}

Harding M, Whelton H, O'Mullane D, Cronin M, Warren J. Primary tooth fluorosis in 5-year-old school children in Ireland. European Journal of Paediatric Dentistry 2005;6(3):155-61.

### Hardwick 1982 {published data only}

Hardwick J, Teasdale J, Bloodworth G. Caries increments over 4 years in children aged 12 at the start of water fluoridation. British Dental Journal 1982;153(6):217-22.

### Heifetz 1988 {published data only}

Heifetz S, Driscoll W, Horowitz H, Kingman A. Prevalence of dental caries and dental fluorosis in areas with optimal and above-optimal water-fluoride concentrations: a 5-year follow-up survey. Journal of the American Dental Association (1939) 1988;116(4):490-5.

### Heintze 1998 {published data only}

Heintze s, Bastos J, Bastos R. Urinary fluoride levels and prevalence of dental fluorosis in three Brazilian cities with different fluoride concentrations in the drinking water. Community Dentistry and Oral Epidemiology 1998;26:316-23.

### Heller 1997 {published data only}

Heller K, Eklund S, Burt B. Dental caries and dental fluorosis at varying water fluoride concentrations. Journal of Public Health Dentistry 1997;57(3):136-43.

### Hernandez-Montoya 2003 {published data only}

Hernandez-Montoya V, Bueno-Lopez JI, Sanchez-Ruelas AM, Garcia-Servin J, Trejo-Vazquez R, Bonilla-Petriciolet A, et al. [Fluorosis and dental decay in children aged 9 to 11 years in the State of Aguascalientes, Mexico]. Revista Internacional de Contaminacion Ambiental 2003;19(4):197-204.

### Holdcroft 1999 {published data only}

Holdcroft C. Five year old dental health in England, 1993-94. Unpublished report 1999.

### Hong 1990 {published data only}

Hong C, Hong Y, Guo M, Hsieh C, Chen R. Prevalence of mottled enamel after 12 years of water fluoridation in Chung-Hsing New Village (Taiwan). Journal of the Formosan Medical Association 1990;89(3):225-30.

### Ibrahim 1995 {published data only}

Ibrahim Y, Affan A, Bjorvatn K. Prevalence of dental fluorosis in Sudanese children from two villages with 0.25 and 2.56 ppm fluoride in the drinking water. International Journal of Paediatric Dentistry 1995;5(4):223-9.

### Indermitte 2007 {published data only}

Indermitte E, Saava A, Russak S, Kull A. The contribution of drinking water fluoride to the risk of dental fluorosis in Estonia. In: Environmental Health Risk IV. Vol. 11. WIT Press, 2007:161-70. [DOI: 10.2495/EHR070171]

### Indermitte 2009 {published data only}

Indermitte EE, Saava AA, Karro EE. Exposure to high fluoride drinking water and risk of dental fluorosis in Estonia. International Journal of Environmental Research and Public Health 2009;6(2):710-21.

### Ismail 1990 {published data only}

Ismail A, Brodeur J-M, Kavanagh M, Boisclair G, Tessier C, Picotte L. Prevalence of dental caries and dental fluorosis in students, 11-17 years of age, in fluoridated and non-fluoridated cities in Quebec (Canada). Caries Research 1990;24(2):290-7.

### Jackson 1975 {published data only}

Jackson D, James PM, Wolfe WB. Fluoridation in Anglesey. A clinical study. British Dental Journal 1975;138(5):165-71.

### Jackson 1999 {published data only}

Jackson R. Dental fluorosis in children residing in communities with different water fluoride levels: 33-month follow-up. Pediatric Dentistry 1999;21(4):248-54.

### Jolly 1971 {published data only}

Jolly S, Prasad S, Sharma R, Rai B. Human fluoride intoxication in Punjab. Flouride 1971;4(2):64-79.

### Kanagaratnam 2009 {published data only}

Kanagaratnam S, Schluter P, Durward C, Mahood R, Mackay T. Enamel defects and dental caries in 9-year-old children living in fluoridated and nonfluoridated areas of Auckland, New Zealand. Community Dentistry & Oral Epidemiology 2009;37(3):250-9.

### Kim 2019 {published data only}

* Kim H-N, Kong W-S, Lee J-H, Kim J-B. Reduction of dental caries among children and adolescents from a 15-year community water fluoridation program in a township area, Korea. International Journal of Environmental Research and Public Health 2019;16(1306):1-13. [DOI: 10.3390/ijerph16071306]

### Kotecha 2012 {published data only}

Kotecha P, Patel S, Bhalani K, Shah D, Shah V, Mehta K. Prevalence of dental fluorosis & dental caries in association with high levels of drinking water fluoride content in a district of Gujarat, India. The Indian Journal of Medical Research 2012;135(6):873-7.

### Kumar 1999 {published data only}

Kumar J, Swango P. Fluoride exposure and dental fluorosis in Newburgh and Kingston, New York: policy implications. Community Dentistry and Oral Epidemiology 1999;27(3):171-80.

### Kumar 2007 {published data only}

Kumar R, Khandare A, Brahmam G, Venkiah K, Reddy C, Sivakumar B. Assessment of current status of fluorosis in north-western districts of Tamil Nadu using community index for dental fluorosis. Journal of Human Ecology 2007;21(1):27-32.

### Kunzel 1976 {published data only}

Kunzel W, Padron F. Caries and dental fluorosis in Cuban children. Caries Research 1976;10(2):104-12.

### Kunzel 1997 {published data only}

Kunzel W, Fischer T. Rise and fall of caries prevalence in German towns with different F concentrations in drinking water. Caries Research 1997;31(3):166-73.

### Leverett 1986 {published data only}

Leverett D. Prevalence of dental fluorosis in fluoridated and nonfluoridated communities--a preliminary investigation. Journal of Public Health Dentistry 1986;46(4):184-7.

### Levine 1989 {published data only}

Levine R, Beal J, Flemming C. A photographically recorded assessment of enamel hypoplasia in fluoridated and non fluoridated areas. British Dental Journal 1989;166:249-52.

### Lin 1991 {published data only}

Lin F-F, Zhao H-X, Lin J, Jian J-Y. The relationship of a low-iodine an high-fluoride environment to subclinical cretinism in Xinjiang. 1991 Xinjiang Institute for Endemic Disease Control and Research, Office of Leading Group for Endemic Disease Control of Hetian Prefectural Committee of the Communist Party of China and County Health and Endemic Prevention Station, Yutian, Xinjiang. Unpublished report submitted through NHS CRD website 1991.

### Loh 1996 {published data only}

Loh T. Thirty-eight years of water fluoridation – the Singapore scenario. Community Dental Health 1996;13(2):47-50.

### Louw 2002 {published data only}

Louw AJ, Grobler SR, van WKTJ. Degree of fluorosis in areas of South Africa with differing levels of fluoride in drinking water. General Dentistry 2002;50(4):352-6.

### Machiulskiene 2009 {published data only}

Machiulskiene V, Baelum V, Fejerskov O, Nyvad B. Prevalence and extent of dental caries, dental fluorosis, and developmental enamel defects in Lithuanian teenage populations with different fluoride exposures. European Journal of Oral Sciences 2009;117(2):154-60.

### Mackay 2005 {published data only}

Mackay T, Thomson W. Enamel defects and dental caries among Southland children. New Zealand Dental Journal 2005;101(2):35-43.

### Macpherson 2007 {published data only}

Macpherson L, Conway D, Gilmour W, Petersson L, Stephen K. Photographic assessment of fluorosis in children from naturally fluoridated Kungsbacka and non-fluoridated Halmstad, Sweden. Acta Odontologica Scandinavica 2007;65(3):149-55.

### Mandinic 2009 {published data only}

Mandinic Z, Curcic M, Antonijevic B, Lekic C, Carevic M. Relationship between fluoride intake in Serbian children living in two areas with different natural levels of fluorides and occurrence of dental fluorosis. Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association 2009;47(6):1080-4.

### Mandinic 2010 {published data only}

Mandinic Z, Curcic M, Antonijevic B, Carevic M, Mandic J, Djukic-Cosic D, et al. Fluoride in drinking water and dental fluorosis. Science of the Total Environment 2010;408(17):3507-12.

### Marya 2010 {published data only}

Marya C, Ashokkumar B, Dhingra S, Dahiya V, Gupta A. Exposure to high-fluoride drinking water and risk of dental caries and dental fluorosis in Haryana, India. Asia-Pacific Journal of Public Health/Asia-Pacific Academic Consortium for Public Health 2014;26(3):295-303.

* Marya C, Dahiya V, Gupta A. Prevalence and severity of dental fluorosis in endemic fluoride areas of Haryana, India: an epidemiologic study [Croatian, English]. Acta Stomatologica Croatica 2010;44(3):152-8.

### Masztalerz 1990 {published data only}

Masztalerz A, Masztalerzowa Z, Szymanska M, Tomelka J. Fluoride and dentition. Epidemiologische Untersuchung 1990;51(4):234-7.

### Maupome 2001 {published data only}

Maupome G, Clark D, Levy S, Berkowitz J. Patterns of dental caries following the cessation of water fluoridation. Community Dentistry & Oral Epidemiology 2001;29(1):37-47.

### Mazzotti 1939 {published data only}

Mazzotti L, Gonzalez Rivera M. Dental fluorosis in Mexico. Revista del Instituto de Salubridad y Enfermedades Tropicales 1939;1:105-21.

### McGrady 2012 {published data only}

* McGrady M, Ellwood R, Srisilapanan P, Korwanich N, Worthington H, Pretty I. Dental fluorosis in populations from Chiang Mai, Thailand with different fluoride exposures - Paper 1: assessing fluorosis risk, predictors of fluorosis and the potential role of food preparation. BMC Oral Health 2012 Jun;21(12):16. [DOI: 10.1186/1472-6831-12-16]

McGrady MG, Ellwood RP, Srisilapanan P, Korwanich N, Taylor A, Goodwin M, et al. Dental fluorosis in populations from Chiang Mai, Thailand with different fluoride exposures - Paper 2: The ability of fluorescence imaging to detect differences in fluorosis prevalence and severity for different fluoride intakes from water. BMC Oral Health 2012;12:33.

### McInnes 1982 {published data only}

McInnes P, Richarson B, Cleaton-Jones P. Comparison of dental fluorosis and caries in primary teeth of preschool-children living in arid high and low fluoride villages. Community Dentistry and Oral Epidemiology 1982;10:182-6.

### Mella 1992 {published data only}

Mella S, Atalah E, Aranda W, Montagna R. Prevalence of dental fluorosis in Chile - a pilot-study. Revista Medica De Chile 1992;120(8):866-71.

### Mella 1994 {published data only}

Mella S, Molina X, Atalah E. Prevalence of dental fluorosis and its relation with fluoride content of communal drinking-water [Prevalencia de fluorosis dental endemica en relacion alcontenido de fluoruros en las aguas de abasto publico]. Revista Medica De Chile 1994;122(11):1263-70.

### Meyer-Lueckel 2006 {published data only}

Meyer-Lueckel H, Paris S, Shirkhani B, Hopfenmuller W, Kielbassa AM. Caries and fluorosis in 6- and 9-year-old children residing in three communities in Iran. Community Dentistry and Oral Epidemiology 2006;34(1):63-70.

### Milsom 1990 {published data only}

Milsom K, Mitropoulos C. Enamel defects in 8 year old children in fluoridated and non-fluoridated parts of Cheshire. Caries Research 1990;1990(24):286-9.

### Mondal 2012 {published data only}

Mondal NK, Pal KC, Kabi S. Prevalence and severity of dental fluorosis in relation to fluoride in ground water in the villages of Birbhum district, West Bengal, India. Environmentalist 2012;32(1):70-84.

### Montero 2007 {published data only}

Montero M, Rojas-Sanchez F, Socorro M, Torres J, Acevedo AM. Dental caries and fluorosis in children consuming water with different fluoride concentrations in Maiquetia, Vargas State, Venezuela [Spanish]. Investigacion Clinica 2007;48(1):5-19.

### Nanda 1974 {published data only}

Nanda R, Zipkin I, Doyle J, Horowitz H. Factors affecting the prevalence of dental fluorosis in Lucknow, India. Archives of Oral Biology 1974;19:781-92.

### Narbutaite 2007 {published data only}

Narbutaite J, Vehkalahti M, Milciuviene S. Dental fluorosis and dental caries among 12-yr-old children from high- and low-fluoride areas in Lithuania. European Journal of Oral Sciences 2007;115(2):137-42.

### Narwaria 2013 {published data only}

* Narwaria Y, Saksena D. Incidence of dental fluorosis in domestic animals of Shivpuri, Madhya Pradesh, India. Journal of Environmental Research and Development July-September 2012;7(1A):426-30.

Narwaria Y, Saksena D. Prevalence of dental fluorosis among primary school children in rural areas of Karera Block, Madhya Pradesh. Indian Journal of Pediatrics 2013;80(9):718-20.

### Nunn 1992 {published data only}

Nunn J, Murray J, Reynolds P, Tabari D, Breckon J. The prevalence of developmental defects of enamel in 15-16-year-old children residing in three districts (natural fluoride, adjusted fluoride, low fluoride) in the north east of England. Community Dental Health 1992;9(3):235-47.

### Nunn 1994a {published data only}

Nunn J, Rugg-Gunn A, Ekanayake L, Saparamandu K. Prevalence of developmental defects of enamel with different fluoride and socio-economic groups. International Dental Journal 1994;44:165- 73.

### Nunn 1994b {published data only}

Nunn J, Murray J, Reynolds P, Tabari D, Breckon J. The prevalence of developmental defects of enamel in 15-16-year-old children residing in three districts (natural fluoride, adjusted fluoride, low fluoride) in the north east of England. Community Dental Health 1992;9(3):235-47.

### Ockerse 1941 {published data only}

Ockerse T. Fluorosis in Kenhardt and Gordonia districts Cape Province, South Africa. Journal of the American Dental Association (1939) 1941;28:936-41.

### Pontigo-Loyola 2008 {published data only}

Pontigo-Loyola A, Islas-Marquez A, Loyola-Rodriguez J, Maupome G, Marquez-Corona M, Medina-Solis C. Dental fluorosis in 12- and 15-year-olds at high altitudes in above-optimal fluoridated communities in Mexico. Journal of Public Health Dentistry 2008;68(3):163-6.

### Pot 1974 {published data only}

Backerdirks O, Houwink B, Kwant GW. The results of 6.5 years of artificial fluoridation of drinking water in The Netherlands: The tiel—Culemborg experiment. Archives of Oral Biology 1961;5:284-300. [DOI: https://doi.org/10.1016/0003-9969(61)90065-6]

Pot T, Purdell-Lewis D, Groeneveld A. The influence of 17 years of water fluoridation upon the dentition of adults [De invloed van 17 jaren drinkwater-fluoirdering op het gebit van volwassenen]. Nederlands Tijdschrift voor Tandheelkunde 1974;81(1):5-12.

### Ray 1982 {published data only}

Ray S, Ghosh S, Tiwari I, Nagchaudhuri J, Kaur P, Reddy D. Prevalence of dental fluorosis in relation to fluoride in drinking water in two villages of Varanasi (U.P.). Indian Journal of Public Health 1982;26(3):173-8.

### Riordan 1991 {published data only}

Riordan P, Banks J. Dental fluorosis and fluoride exposure in Western Australia. Journal of Dental Research 1991;70(7):1022-8.

### Riordan 2002 {published data only}

Riordan P. Dental fluorosis decline after changes to supplement and toothpaste regimens. Community Dentistry and Oral Epidemiology 2002;30(3):233-40.

### Ruan 2005 {published data only}

Ruan J, Yang Z, Wang Z, Astrom A, Bardsen A, Bjorvatn K. Dental fluorosis and dental caries in permanent teeth: rural schoolchildren in high-fluoride areas in the Shaanxi province, China. Acta Odontologica Scandinavica 2005;63(5):258-65.

### Rugg-Gunn 1997 {published data only}

Rugg-Gunn A, Al Mohammadi S, Butler T. Effects of fluoride level in drinking water, nutritional status, and socio-economic status on the prevalence of developmental defects of dental enamel in permanent teeth in Saudi 14-year-old boys. Caries Research 1997;31(4):259-67.

### Russell 1951 {published data only}

Russell A, Elvove E. Domestic Water and Dental Caries. A study of the fluoride-dental caries relationship in an adult population. Public Health Reports 1951;66(43):1389-401.

### Rwenyonyi 1998 {published data only}

Rwenyonyi M, Birkeland J, Bjorvatn K, Haugejorden O. Dental fluorosis in Ugandans related to fluoride in drinking water and altitude. Journal of Dental Research 1998;77:1299.

### Rwenyonyi 1999 {published data only}

Rwenyoyi C, Bjorvatn K, Birkeland J, Haugejorden O. Altitude as a risk Indicator of dental fluorosis in children residing in areas with 0.5 and 2.5 mg fluoride per litre in drinking water. Caries Research 1999;33:267-74.

### Saravanan 2008 {published data only}

Saravanan S, Kalyani C, Vijayarani M, Jayakodi P, Felix A, Nagarajan S, et al. Prevalence of dental fluorosis among primary school children in rural areas of Chidambaram Taluk, Cuddalore district, Tamil Nadu, India. Indian Journal of Community Medicine: official publication of Indian Association of Preventive & Social Medicine 2008;33(3):146-50.

### Scheinin 1964 {published data only}

Scheinin A, Kalijaervi E, Harjola O, Heikkinen K. Prevalence of dental caries and dental health in relation to variable concentration of fluorides in drinking water; a clinical study on Finnish school-children. Acta Odontologica Scandinavica 1964;22:229-54.

### Segreto 1984 {published data only}

Segreto V, Collins E, Camann D, Smith C. A current study of mottled enamel in Texas. Journal of the American Dental Association (1939) 1984;108(1):56-9.

### Sellman 1957 {published data only}

Sellman S, Syrrist A, Gustafson G. Fluorine and dental health in southern Sweden. Odontologisk Tidskrift 1957;65:61-93.

### Selwitz 1995 {published data only}

Selwitz R, Nowjack Raymer R, Kingman A, Driscoll W. Prevalence of dental caries and dental fluorosis in areas with optimal and above-optimal water fluoride concentrations: a 10-year follow-up survey. Journal of Public Health Dentistry 1995;55(2):85-93.

### Selwitz 1998 {published data only}

Selwitz R, Nowjack Raymer R, Kingman A, Driscoll W. Dental caries and dental fluorosis among schoolchildren who were lifelong residents of communities having either low or optimal levels of fluoride in drinking water. Journal of Public Health Dentistry 1998;58(1):28-35.

### Shanthi 2014 {published data only}

Shanthi M, Reddy B, Venkataramana V, Gowrisankar S, Reddy B, Chennupati S. Relationship between drinking water fluoride levels, dental fluorosis, dental caries and associated risk factors in 9-12 years old school children of Nelakondapally Mandal of Khammam district, Andhra Pradesh, India: a cross-sectional survey. Journal of International Oral Health 2014;6(3):106-10.

### Shekar 2012 {published data only}

* Shekar C, Cheluvaiah M, Namile D. Prevalence of dental caries and dental fluorosis among 12 and 15 years old school children in relation to fluoride concentration in drinking water in an endemic fluoride belt of Andhra Pradesh. Indian Journal of Public Health 2012;56(2):122-8.

Sukhabogi J, Parthasarathi P, Anjum S, Shekar B, Padma C, Rani A. Dental fluorosis and dental caries prevalence among 12 and 15-year-old school children in Nalgonda district, Andhra Pradesh, India. Anals of Medical and Health Sciences Research Sep-Oct 2014;4(3):245-52.

### Skinner 2013 {published data only}

Skinner J, Johnson G, Phelan C, Blinkhorn A. Dental caries in 14- and 15-year-olds in New South Wales, Australia. BMC Public Health 2013;13:1060.

### Skotowski 1995 {published data only}

Skotowski M, Hunt R, Levy S. Risk-factors for dental fluorosis in pediatric dental patients. Journal of Public Health Dentistry 1995;55(3):154-9.

### Spadaro 1955 {published data only}

Spadaro O, Pagano V. Fluorosis and dental caries in the community of Barcellona Pozzo di Gotto. Igiene e Sanita Pubblica 1955;11(7-8):403-10.

### Stephen 2002 {published data only}

Stephen K, Macpherson L, Gilmour W, Stuart R, Merrett M. A blind caries and fluorosis prevalence study of school-children in naturally fluoridated and nonfluoridated townships of Morayshire, Scotland. Community Dentistry and Oral Epidemiology 2002;30(1):70-9.

### Sudhir 2009 {published data only}

Sudhir K, Prashant G, Subba Reddy V, Mohandas U, Chandu G. Prevalence and severity of dental fluorosis among 13- to 15-year-old school children of an area known for endemic fluorosis: Nalgonda district of

Andhra Pradesh. Journal of the Indian Society of Pedodontics and Preventive Dentistry 2009;27(4):190-6.

### Szpunar 1988 {published data only}

Szpunar S, Burt B. Dental caries, fluorosis and fluoride exposure in Michigan schoolchildren. Journal of Dental Research 1988;67(5):802-6.

### Tabari 2000 {published data only}

Tabari E, Ellwood R, Rugg-Gunn A, Evans D, Davies R. Dental fluorosis in permanent incisor teeth in relation to water fluoridation, social deprivation and toothpaste use in infancy. British Dental Journal 2000;189(4):216-20.

### Tessier 1987 {published data only}

Tessier C. Effets de la fluoruration de l'eau a Windsor, Que. depuis 7 ans sur les enfants de 6 a 7 ans. Journal Dentaire du Quebec 1987;XXIV:17-23.

### Tsutsui 2000 {published data only}

Tsutsui A, Yagi M, Horowitz AM. The prevalence of dental caries and fluorosis in Japanese communities with up to 1.4 ppm of naturally occurring fluoride. Journal of Public Health Dentistry 2000;60(3):147-53.

### Venkateswarlu 1952 {published data only}

Venkateswarlu P, Narayanu Rao D, Ranganatha Rao K. Endemic fluorosis: Visakhaptnam and suburban areas; fluorine, mottled enamel and dental caries. The Indian journal of Medical Research 1952;40(October):535-48.

### Vignarajah 1993 {published data only}

Vignarajah S. Dental caries experience and enamel opacities in children residing in urban and rural areas of Antigua with different levels of natural fluoride in drinking water. Community Dental Health 1993;10(2):159-66.

### Vilasrao 2014 {published data only}

Vilasrao G, Kamble K, Sabat R. Child fluorosis in Chhattisgarh, India: a community-based survey. Indian Pediatrics November 15, 2014;51:903-5.

### Villa 1998 {published data only}

Villa A, Guerrero S, Villalobos J. Estimation of optimal concentration of fluoride in drinking water under conditions prevailing in Chile. Community Dentistry and Oral Epidemiology 1998;26(4):249-55.

### Vuhahula 2009 {published data only}

Vuhahula E, Masalu J, Mabelya L, Wandwi W. Dental fluorosis in Tanzania Great Rift Valley in relation to fluoride levels in water and in 'Magadi' (Trona). Desalination 2009;248(1-3):610-5.

### Wang 1993 {published data only}

Wang. An investigation on the fluoride level in drinking water sources and the condition of fluorosis in some part of South Xinjiang. Endemic Diseases Bulletin 1993;8(3):57-60.

### Wang 1999 {published data only}

Wang X, Kawahara K, Guo X. Fluoride contamination of groundwater and its impacts on human health in Inner Mongolia area. Journal of Water Services Research and Technology-Aqua 1999;48(4):146-53.

### Wang 2012 {published data only}

Wang C, Gao Y, Wang W, Zhao L, Zhang W, Han H, et al. A national cross-sectional study on effects of fluoride-safe water supply on the prevalence of fluorosis in China. BMJ Open 2012;2(5):e001564.

### Warnakulasuriya 1992 {published data only}

Warnakulasuriya K, Balasuriya S, Perera P, Peiris L. Determining optimal levels of fluoride in drinking-water for hot, dry climates - a case-study in Sri-Lanka. Community Dentistry and Oral Epidemiology 1992;20(6):364-7.

### Warren 2001 {published data only}

Warren J, Levy S, Kanellis M. Prevalence of dental fluorosis in the primary dentition. Journal of Public Health Dentistry 2001;61(2):87-91.

### Wenzel 1982 {published data only}

Wenzel A, Thylstrup A, Melsen B. Skeletal development and dental fluorosis in 12- -14-year-old Danish girls from a fluoride and a non-fluoride community. Scandinavian Journal of Dental Research 1982;90(2):83-8.

### Whelton 2004 {published data only}

Whelton H, Crowley E, O'Mullane D, Donaldson M, Kelleher V, Cronin M. Dental caries and enamel fluorosis among the fluoridated and non-fluoridated populations in the Republic of Ireland in 2002. Community Dental Health 2004;21(1):37-44.

### Whelton 2006 {published data only}

Whelton H, Crowley E, O'Mullane D, Donaldson M, Cronin M, Kelleher V. Dental caries and enamel fluorosis among the fluoridated population in the Republic of Ireland and non fluoridated population in Northern Ireland in 2002. Community Dental Health 2006;23(1):37-43.

### Wondwossen 2004 {published data only}

Wondwossen F, Astrom A, Bjorvatn K, Bardsen A. The relationship between dental caries and dental fluorosis in areas with moderate- and high-fluoride drinking water in Ethiopia. Community Dentistry and Oral Epidemiology 2004;32(5):337-44.

### Zheng 1986 {published data only}

Zheng CL. A survey of dental caries in Guangzhou China after 18 years of community water fluoridation. Chinese Journal of Preventive Medicine 1986;20(2):79-82.

### Zimmermann 1954 {published data only}

Zimmermann ER. Fluoride and nonfluoride enamel opacities involving fluorosis. Public Health Reports 1954;69:1115-20.

## References to studies excluded from this review

### Armfield 2013 {published data only}

Armfield JM, Spencer AJ, Roberts-Thomson KF, Plastow K. Water fluoridation and the association of sugar-sweetened beverage consumption and dental caries in Australian children. American Journal of Public Health 2013;103(3):494-500. [PMID: 23327241]

### Do 2014 {published data only}

Do LG, Miller J, Phelan C, Sivaneswaran S, Spencer AJ, Wright C. Dental caries and fluorosis experience of 8-12-year-old children by early-life exposure to fluoride. Community Dentistry and Oral Epidemiology 2014;42(6):553-62. [PMID: 24738787]

### Hawew 1996 {published data only}

Hawew RM, Ellwood RP, Hawley GM, Worthington HV, Blinkhorn AS. Dental caries in children from two Libyan cities with different levels of fluoride in their drinking water. Community Dental Health 1996;13(3):175-7. [PMID: 8897743]

### Kämppi 2013 {published data only}

Kämppi A, Tanner T, Päkkilä J, Patinen P, Järvelin MR, Tjäderhane L, et al. Geographical distribution of dental caries prevalence and associated factors in young adults in Finland. Caries Research 2013;47:346-54. [PMID: 23548873]

### Koh 2015 {published data only}

Koh R, Pukallus ML, Newman B, Foley M, Walsh LJ, Seow WK. Effects of water fluoridation on caries experience in the primary dentition in a high caries risk community in Queensland, Australia. Caries Research 2015;49(2):184-91. [PMID: 25661315]

### Lee 2015 {published data only}

Lee H-J, Han D-H. Exploring the determinants of secular decreases in dental caries among Korean children. Community Dentistry and Oral Epidemiology 2015;42(4):357-65. [PMID: 25753788]

### McLaren 2022 {published data only}

McLaren L, McNeil DA, Potestio M, Patterson S, Thawer S, Faris P, et al. Equity in children's dental caries before and after cessation of community water fluoridation: differential impact by dental insurance status

and geographic material deprivation. International Journal for Equity in Health 2016;15:24. [PMID: 26864565]

McLaren L, Patterson S, Thawer S, Faris P, McNeil D, Potestio M, et al. Measuring the short-term impact of fluoridation cessation on dental caries in Grade 2 children using tooth surface indices. Community Dentistry and Oral Epidemiology 2016;44(3):274-82. [PMID: 26888380]

McLaren L, Patterson S, Thawer S, Faris P, McNeil D, Potestio ML, et al. Exploring the short-term impact of community water fluoridation cessation on children's dental caries: a natural experiment in Alberta, Canada. Public Health 2017;146:56-64. [PMID: 28404475]

McLaren L, Patterson SK, Faris P, Chen G, Thawer S, Figueiredo R, et al. Fluoridation cessation and children's dental caries: a 7-year follow-up evaluation of Grade 2 schoolchildren in Calgary and Edmonton, Canada. Community Dentistry and Oral Epidemiology 2022;50(5):391-403. [PMID: 34309045]

* McLaren L, Patterson SK, Faris P, Chen G, Thawer S, Figueiredo R, et al. Fluoridation cessation and oral health equity: a 7-year post-cessation study of Grade 2 schoolchildren in Alberta, Canada. Canadian Journal of Public Health 2022;113(6):955-68. [PMID: 35799095]

### Wang 2014 {published data only}

Wang Y, Wang C-S, Xia Y-T, Wang P-H. Investigation on drinking water-borne endemic fluorosis in Jiangsu, 2013. Journal of Environment and Health 2014;31(6):516-8.

### Zander 2013 {published data only}

Zander A, Sivaneswaran S, Skinner J, Byun R, Jalaludin B. Risk factors for dental caries in small rural and regional Australian communities. Rural Remote Health 2013;13(3):2492. [PMID: 23937258]

## Additional references

### ADA 2016

American Dental Association. Surgeon General Endorses Fluoridation. www.ada.org/en/resources/community-initiatives/fluoride-in-water/fluoridation-resources#:~:text=Water%20fluoridation%20is%20the%20best,-%20and%20less%20severe%20-%20cavities (accessed September 2023).

### Ahovuo-Saloranta 2013

Ahovuo-Saloranta A, Forss H, Walsh T, Hiiri A, Nordblad A, Mäkelä M, et al. Sealants for preventing dental decay in the permanent teeth. Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No: CD001830. [DOI: 10.1002/14651858.CD001830.pub4]

### Antunes 2004

Antunes JL, Narvai PC, Nugent ZJ. Measuring inequalities in the distribution of dental caries. Community Dentistry and Oral Epidemiology 2004;32(1):41-8.

### Armfield 2010

Armfield JM. Community effectiveness of public water fluoridation in reducing children's dental disease. Public Health Reports 2010;125(5):655-64.

### Arora 2010

Arora A, Evans RW. Dental caries in children: a comparison of one non-fluoridated and two fluoridated communities in NSW. New South Wales Public Health Bulletin 2010;21(11-12):257-62.

### Bagramian 2009

Bagramian RA, Garcia-Godoy F, Volpe AR. The global increase in dental caries. A pending public health crisis. American Journal of Dentistry 2009;22(1):3-8.

### Bailie 2009

Bailie RS, Stevens M, Armfield JM, Ehsani JP, Beneforti M, Spencer J. Association of natural fluoride in community water supplies with dental health of children in remote indigenous communities - implications for policy. Australian and New Zealand Journal of Public Health 2009;33(3):205-11.

### Blinkhorn 1981

Blinkhorn A, Brown M, Attwood D, Downer M. The effect of fluoridation on the dental health of urban Scottish school children. Journal of Epidemiology and Community Health 1981;35:98-101.

### Boehmer 2023

Boehmer T, Lesaja S, Espinoza L, Ladva C. Community water fluoridation levels to promote effectiveness and safety in oral health — United States, 2016–2021. Center for Disease Control and Prevention Morbidity and Mortality Weekly Report 2023;72(22):593-6.

### Bomfirm 2022

Bomfirm RA, Frazao P. Impact of water fluoridation on dental caries decline across racial and income subgroups of Brazilian adolescents. Epidemiology and Health 2022;44:e2022007.

### Booth 1992

Booth IM, Mitropoulos CM, Worthington HV. A comparison between the dental health of 3-year-old children living in fluoridated Huddersfield and non-fluoridated Dewsbury in 1989. Community Dental Health 1992;9:151-7.

### British Fluoridation Society 2012

British Fluoridation Society. One in a million: the facts about water fluoridation. bfsweb.org/one-in-a-million/#1344-1344-wpfd-one-in-a-million-p1 (accessed 21 August 2023).

### Brown 1990

Brown LP, Mulqueen TF, Storey E. The effect of fluoride consumption and social class on dental caries in 8-year-old children. Australian Dental Journal 1990;35(a):61-8.

### Browne 2005

Browne D, Whelton H, O'Mullane D. Fluoride metabolism and fluorosis. Journal of Dentistry 2005;33(3):177-86.

### Burt 1999

Burt BA, Eklund SA. Dentistry, Dental Practice and the Community. Philadelphia, Pennsylvania: WB Saunders Company, 1999.

### Carmichael 1980

Carmichael C, Rugg-Gunn A, French A, Cranage J. The effect of fluoridation upon the relationship between caries experience and social class in 5-year-old children in Newcastle and Northumberland. British Dental Journal 1980;149(6):163-7.

### Carmichael 1989

Carmichael C, Rugg-Gunn A, Ferrell R. The relationship between fluoridation, social class and caries experience in 5 year old children in Newcastle and Northumberland in 1987. British Dental Journal 1989;167:57-61.

### CDC 2023

Centers for Disease Control and Prevention (CDC). Water Fluoridation Data & Statistics. www.cdc.gov/fluoridation/statistics/index.htm (accessed September 2023).

### Cheng 2007

Cheng KK, Chalmers I, Sheldon TA. Adding fluoride to water supplies. BMJ 2007;335(7622):699-702.

### Cochran 2004b

Cochran J, Ketley C, Sanches L, Mamai-Homata E, Oila A-M, Arnadottir I, et al. A standardized photographic method for evaluating enamel opacities including fluorosis. Community Dentistry and Oral Epidemiology 2004;32(Suppl 1):19-27.

### Cortes 1996

Cortes DF, Ellwood R, O'Mullane DM, Bastos JR. Drinking water fluoride levels, dental fluorosis, and caries experience in Brazil. Journal of Public Health Dentistry 1996;56:226-8.

### Cruz 2018

Cruz MG, Narvai PC. Caries and fluoridated water in two Brazilian municipalities with low prevalence of the disease. Revista de Saude Publica 2018;52:28. [PMID: 29641653]

### Dean 1941

Dean T, Jay P, Arnold F, Elvove E. Domestic water and dental caries. II. A study of 2832 white children, aged 12-14 years, of 8 suburban communities, including Lactobacillus acidophilus studies of 1761 children. Public Health Reports 1941;56(15):761-92.

### DEFRA 2021

Department for Environment, Food and Rural Affairs. United Kingdom Food Security Report 2021: Theme 2: UK Food Supply Sources. www.gov.uk/government/statistics/united-kingdom-food-security-report-2021/united-kingdom-food-security-report-2021-theme-2-uk-food-supply-sources#:~:text=About%2054%25%20of%20food%20on,subsequent%20indicators%20will%20set%20out. (Accessed 13 May 2024).

### Department of Health and Human Services 2000

Department of Health and Human Services, US Public Health Service. Oral Health in America: A Report of the Surgeon General. Rockville, MD: US Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health, 2000.

### Department of National Health and Welfare 1952

Dental Health Division and Research and Statistics Division. A suggested methodology for fluoridation surveys in Canada. Department of National Health and Welfare, Ottawa 1952.

### Do 2015

Do L, Spencer AJ. Contemporary multilevel analysis of the effectiveness of water fluoridation in Australia. Australian and New Zealand Journal of Public Health 2015;39(1):44-50.

### Do 2019

Do LG, Australian Research Centre for Population Oral Health. Guidelines for use of fluorides in Australia: update 2019. Australian Dental Journal 2020;65(1):30-8. [PMID: 31868926]

### Duane 2022

Duane B, Lyne A, Parle R, Ashley P. The environmental impact of community caries prevention - part 3: water fluoridation. British Dental Journal 2022;233(4):303-7. [PMID: 36028695]

### Dye 2015

Dye BA, Thornton-Evans G, Li X, Iafolla TJ. Dental caries and sealant prevalence in children and adolescents in the United States, 2011–2012. NCHS Data Brief, no191. Hyattsville, MD: National Center for Health Statistics 2015.

### European Union 1998

European Union 1998 Council Directive 98/83/EC. On the quality of water intended for human consumption. Official Journal of the European Communities 1998;L330/42.

### Evans 1995

Evans DJ, Rugg-Gunn AJ, Tabari ED. The effect of 25 years of water fluoridation in Newcastle assessed in four surveys of 5-year-old children over an 18-year period. British Dental Journal 1995;178:60-4.

### Feitosa 2005

Feitosa S, Colares V, Pinkham J. The psychosocial effects of severe caries in 4-year-old children in Recife, Pernambuco, Brazil. Cadernos de Saúde Pública 2005;21(5):1550-6.

### Freire 2013

Freire M, Reis SC, Figueiredo N, Peres KG, da Silveira Moreira R, Antunes JL. Individual and contextual determinants of dental caries in Brazilian 12-year-olds in 2010. Revista de Saude Publica 2013;47(Suppl 3):40-9. [PMID: 24626580]

### French 1984

French AD, Carmichael CL, Furness JA, Rugg-Gunn AJ. Relationship between social class and dental health in 5-year old children in the North and South of England. British Dental Journal 1984;156:83-6.

### Frencken 2017

Frencken J, Sharma P, Stenhouse L, Green D, Laverty D, Dietrich T. Global epidemiology of dental caries and severe periodontitis – a comprehensive review. Journal of Clinical Periodontology 2017;44(Suppl 18):S94–S105. [DOI: doi.org/10.1111/jcpe.12677]

### Frieden 2010

Frieden TR. A framework for public health action: the health impact pyramid. American Journal of Public Health 2010;100(4):590-5.

### Gillcrist 2001

Gillcrist JA, Brumley DE, Blackford JU. Community fluoridation status and caries experience in children. Journal of Public Health Dentistry 2001;61(3):168-71. [PMID: 11603320]

### Glenny 2022 [pers comm]

Glenny AM. Water fluoridation - confounders [personal communication]. Email to: J Sterne 13 April 2022.

### Griffin 2007

Griffin SO, Regnier E, Griffin PM, Huntley V. Effectiveness of fluoride in preventing caries in adults. Journal of Dental Research 2007;86(5):410-5.

### Gushi 2005

Gushi LL, da Candelária Soares M, Forni TI, Vieira V, Wada RS, da Luz Rosário de Sousa M. Dental caries in 15-to-19-year-old adolescents in Sao Paulo State, Brazil, 2002. Cadernos de Saude Publica 2005;21(5):1383-91.

### HHS 2015

US Department of Health and Human Services (HHS) Federal Panel on Community Water Fluoridation. U.S. Public Health Service recommendation for fluoride concentration in drinking water for the prevention of dental caries. Public Health Reports 2015;130(4):318-31. [DOI: 10.1177/003335491513000408]

### Higgins 2011

Higgins JP, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from https://training.cochrane.org/handbook/archive/v5.1/ (accessed September 2023).

### Higgins 2021

Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 6.2 (updated February 2021). Cochrane, 2021. Available from https://training.cochrane.org/handbook/archive/v6.2 (accessed September 2023).

### Hopcraft 2005

Hopcraft M, Morgan MV. Dental caries experience in Australian Army recruits 2002–2003. Australian Dental Journal 2005;50:16-20.

### Hopcraft 2009

Hopcraft MS, Yapp KE, Mahoney G, Morgan MV. Dental caries experience in young Australian Army recruits 2008. Australian Dental Journal 2009;54:316-22.

### Jackson 1980

Jackson D, Goward PE, Morrell GV. Fluoridation in Leeds. A clinical survey of 5-year-old children. British Dental Journal 1980;149(8):231-4.

### Jackson 1985

Jackson D, James PM, Thomas FD. Fluoridation in Anglesey 1983: a clinical study of dental caries. British Dental Journal 1985;158(2):45-9.

### James 2021

James P, Harding M, Beecher T, Browne D, Cronin M, Guiney H, et al. Impact of reducing water fluoride on dental caries and fluorosis. Journal of Dental Research 2021;100(5):507-14. [PMID: 33345672]

### Jarman 1984

Jarman B. Underprivileged areas: validation and distribution of scores. British Medical Journal 1984;289(6458):1587-92. [PMID: 6439333]

### Jones 1997

Jones CM, Taylor GO, Whittle JG, Evans D, Trotter DP. Water fluoridation, tooth decay in 5 year olds, and social deprivation measured by the Jarman score: analysis of data from British dental surveys. British Medical

Journal 1997;315:514-7.

### Kanagaratnam 2009

Kanagaratnam S, Schluter P, Durward C, Mahood R, Mackay T. Enamel defects and dental caries in 9-year-old children living in fluoridated and nonfluoridated areas of Auckland, New Zealand. Community Dentistry and Oral Epidemiology 2009;37:250-9.

### Kearney 2010

Kearney J. Food consumption trends and drivers. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences 2010;365:2793–807.

### Kelman 1996

Kelman AM. Fluoridation – the Israel experience. Community Dental Health 1996;13(Suppl 2):42-6.

### Kim 2017

Kim HN, Kim JH, Kim SY, Kim JB. Associations of community water fluoridation with caries prevalence and oral health inequality in children. International Journal of Environmental Research and Public Health 2017;14(6):631. [PMID: 28608827]

### Kumar 2001

Kumar JV, Green EL, Coluccio C, Davenport R. Oral health status of second grade school children in upstate New York. New York State Dental Journal 2001;67(2):26-31. [PMID: 11280142]

### Lagerweij 2015

Lagerweij MD, van Loveren C. Declining caries trends: are we satisfied? Current Oral Health Reports 2015;2(4):212-7. [DOI: 10.1007/s40496-015-0064-9]

### Lalloo 2015

Lalloo R, Jamieson LM, Ha D, Ellershaw A, Luzzi L. Does fluoride in the water close the dental caries gap between Indigenous and non-Indigenous children? Australian Dental Journal 2015;60(3):390-6.

### Lambe 2022

Lambe K, Farragher A, Moloney T, Sunday S, Long J. Impact of community water fluoridation on systemic health excluding oral health: an evidence review. www.hrb.ie/publications (accessed 22 August 2023).

### Lee 2004

Lee M, Dennison PJ. Water fluoridation and dental caries in 5- and 12-year-old children from Canterbury and Wellington. New Zealand Dental Journal 2004;100(1):10-5.

### Marinho 2003

Marinho VC, Higgins JP, Loga S, Sheiham A. Fluoride toothpastes for preventing dental caries in children and adolescents. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No: CD002278. [DOI: 10.1002/14651858.CD002278]

### Marinho 2013

Marinho VC, Worthington HV, Walsh T, Clarkson JE. Fluoride varnishes for preventing dental caries in children and adolescents. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No: CD002279. [DOI: 10.1002/14651858.CD002279.pub2]

### Marques 2022

Marques RB, Lima CC, de Abreu Costa ML, de Deus Moura de Lima M, de Fátima Almeida de Deus Moura L. Fluoridated water impact on tooth decay and fluorosis in 17-20-year-olds exposed to fluoride toothpaste. Journal of Public Health Dentistry 2022;82(4):385-94. [PMID: 34350986]

### McDonagh 2000

McDonagh M, Whiting P, Bradley M, Cooper J, Sutton A, Chestnutt I, et al. A systematic review of community water fluoridation. NHS Centre for Reviews and Dissemination, University of York 2000.

### McLaren 2012

McLaren L, Emery JC. Drinking water fluoridation and oral health inequities in Canadian children. Canadian Journal of Public Health 2012;103(7 Suppl 1):eS49-56.

### Moore 2019

Moore D, Goodwin M, Pretty IA. Long-term variability in artificially and naturally fluoridated water supplies in England. Community Dentistry and Oral Epidemiology 2020;48(1):49-55. [PMID: 31625207]

### Morgan 1992

Morgan MV, Stonnill A, Laslett AM. Dental caries amongst Royal Australian Navy recruits, 1988. Australian Dental Journal 1992;37:201-4.

### Moynihan 2019

Moynihan P, Tanner LM, Holmes RD, Hillier-Brown F, Mashayekhi A, Kelly SA, et al. Systematic review of evidence pertaining to factors that modify risk of early childhood caries. JDR Clinical and Translational Research 2019;4(3):202-16. [PMID: 30931717]

### MRC 2002

Medical Research Council (MRC). Working Group Report: Water Fluoridation and Health. www.mrc.ac.uk/pdf-publications-water_fluoridation_report.pdf (accessed February 2015).

### Murray 1991a

Murray J, Breckon J, Reynolds P, Tabari E, Nunn J. The effect of residence and social class on dental caries experience in 15-16 year old children living in three towns (natural fluoride, adjusted fluoride and low fluoride) in the North East of England. British Dental Journal 1991;171(10):319-22.

### NHMRC 2017

National Health and Medical Research Council (NHMRC). Information paper – Water fluoridation: dental and other human health outcomes, report prepared by the Clinical Trials Centre at University of Sydney, NHMRC; Canberra. www.nhmrc.gov.au/sites/default/files/documents/reports/fluoridation-info-paper.pdf (accessed September 2023). [ISBN ONLINE: 978-1-925129-83-0]

### Nyakutsikwa 2022

Nyakutsikwa B, Walsh T, Pretty I, Moore D. Water fluoride concentrations in England, 2009-2020. Community Dental Health 2022;39(2):106-12. [PMID: 34982862]

### NZ MoH 2010

Ministry of Health. Our oral health: key findings of the 2009 New Zealand oral health survey. Wellington: Ministry of Health 2010.

### O'Mullane 1996

O'Mullane D, Whelton HP, Costelloe P, Clarke D, McDermott S, McLoughlin J. The results of water fluoridation in Ireland. Journal of Public Health Dentistry 1996;56:259–64.

### Page 2022

Page MJ, Higgins JP, Sterne JA. Chapter 13: Assessing risk of bias due to missing results in a synthesis. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). Cochrane, 2022. Available from https://training.cochrane.org/handbook/archive/v6.3 (accessed September 2023).

### Pendrys 2001

Pendrys DG. Fluoride ingestion and oral health. Nutrition 2001;17(11-12):979-80.

### Peres 2006

Peres M, Antunes J, Peres K. Is water fluoridation effective in reducing inequalities in dental caries distribution in developing countries? Recent findings from Brazil. Sozial-und Praventivmedizin 2006;51(5):302-10.

### PHE 2014

Public Health England. Water fluoridation health monitoring report for England 2014. www.gov.uk/government/publications/water-fluoridation-health-monitoring-report-for-england-2014 (accessed 21 August 2023).

### PHE 2016

Public Health England. Return on investment of oral health improvement programmes for 0-5 year olds. assets.publishing.service.gov.uk/government/uploads/system/uploads/attach

ment_data/file/560973/ROI_oral_health_interventions.pdf (accessed 21 August 2023).

### PHE 2018

Public Health England. Water fluoridation: health monitoring report for England 2018. www.gov.uk/government/publications/water-fluoridation-health-monitoring-report-for-england-2018 (accessed 21 August 2023).

### PHE 2022

Public Health England. Water fluoridation: health monitoring report for England 2022. www.gov.uk/government/publications/water-fluoridation-health-monitoring-report-for-england-2022 (accessed 21 August 2023).

### Pitts 1997

Pitts NB, Evans DJ, Pine C. British Association for the Study of Community Dentistry (BASCD) diagnostic criteria for caries prevalence studies - 1996/7. Community Dental Health 1997;14(Suppl 1):6-9.

### Provart 1995

Provart S, Carmichael C. The relationship between caries, fluoridation and material deprivation in five year-old children in Country Durham. Community Dental Health 1995;12:200-3.

### Rebelo 2019

Rebelo MA, Vieira JM, Pereira JV, Quadros LN, Vettore MV. Does oral health influence school performance and school attendance? A systematic review and meta-analysis. International Journal of Peadiatric Dentistry 2019;29(2):138-48. [DOI: 10.1111/ipd.12441]

### Reeves 2017

Reeves BC, Wells GA, Waddington H. Quasi-experimental study designs series—paper 5: a checklist for classifying studies evaluating the effects on health interventions—a taxonomy without labels. Journal of Clinical Epidemiology 2017;89:30-42. [DOI: 10.1016/j.jclinepi.2017.02.016]

### RevMan 2024 [Computer program]

Review Manager (RevMan). Version 8.3.0. The Cochrane Collaboration, 2024. Available at revman.cochrane.org.

### Riley 1999

Riley J, Lennon M, Ellwood R. The effect of water fluoridation and social inequalities on dental caries in 5-year-old children. International Journal of Epidemiology 1999;28:300-5.

### Rozier 1994

Rozier RG. Epidemiologic indices for measuring the clinical manifestations of dental fluorosis: overview and critique. Advances in Dental Research 1994;8(1):39-55.

### Rugg-Gunn 1977a

Rugg-Gunn AJ, Carmichael CL, French AD, Furness JA. Fluoridation in Newcastle and Northumberland. A clinical study of five-year-old children. British Dental Journal 1977;142:395-402.

### Rugg-Gunn 1981a

Rugg-Gunn AJ, Nicholas KE, Cranage JD, Carmichael CL, French AD. Caries experience of 5-year-old children living in four communities in N.E. England receiving differing water fluoride levels. British Dental Journal 1981;150:9-12.

### Rugg-Gunn 2012

Rugg-Gunn AJ, Do L. Effectiveness of water fluoridation in caries prevention. Community Dentistry and Oral Epidemiology 2012;40(Suppl 2):55-64.

### Rugg-Gunn 2016

Rugg-Gunn AJ, Spencer AJ, Whelton HP, Jones C, Beal JF, Castle P, et al. Critique of the review of 'Water fluoridation for the prevention of dental caries' published by the Cochrane Collaboration in 2015. British Dental Journal 2016;220(7):335-40. [PMID: 27056513]

### Rugg-Gunn 1988

Rugg-Gunn AJ, Carmichael CL, Ferrell RS. Effect of fluoridation and secular trend in caries in 5-year-old children living in Newcastle and Northumberland. British Dental Journal 1988;165:359-64.

### Saliba 2008

Saliba NA, Moimaz SA, Casotti CA, Pagliari AV. Dental caries of lifetime residents in Baixo Guandu, Brazil, fluoridated since 1953 - a brief communication. Journal of Public Health Dentistry 2008;68(2):119-21.

### Schünemann 2023

Schünemann HJ, Vist GE, Higgins JP, Santesso N, Deeks JJ, Glasziou P, et al. Chapter 15: Interpreting results and drawing conclusions. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.

### Selwitz 2007

Selwitz RH, Ismail AI, Pitts NB. Dental caries. Lancet 2007;369(9555):51-9.

### Sharma 2023

Sharma V, Crowe M, Cassetti O, Winning L, O'Sullivan A, O'Sullivan M. Dental caries in children in Ireland: a systematic review. Community Dentistry and Oral Epidemiology 2023 Jul 29 [Epub ahead of print]. [DOI: 10.1111/cdoe.12897]

### Sheiham 2005

Sheiham A. Oral health, general health and quality of life. Bulletin of the World Health Organization 2005;83(9):644.

### Shen 2021

Shen A, Bernabé E, Sabbah W. Systematic review of intervention studies aiming at reducing inequality in dental caries among children. International Journal of Environmental Research and Public Health 2021;18(3):1300.

### Silva 2021

Silva MC, Lima CC, Lima MD, Moura LF, Tabchoury CP, Moura MS. Effect of fluoridated water on dental caries and fluorosis in schoolchildren who use fluoridated dentifrice. Brazilian Dental Journal 2021;32(3):75-83. [PMID: 34755792]

### Slimani 2009

Slimani N, Deharveng G, Southgate DA, Biessy C, Chajes V, van Bakkel MM, et al. Contribution of highly industrially processed foods to the nutrient intakes and patterns of middle-aged populations in the European Prospective Investigation into Cancer and Nutrition study. European Journal of Clinical Nutrition 2009;63:S206–25.

### Solanki 2022

Solanki YS, Agarwal M, Gupta AB, Gupta S, Shukla P. Fluoride occurrences, health problems, detection, and remediation methods for drinking water: a comprehensive review. Science of the Total Environment 2022;807(Pt 1):150601. [DOI: 10.1016/j.scitotenv.2021.150601] [PMID: 34597567]

### Stockwell 1990

Stockwell AJ, Medcalf GW, Rutledge GJ, Holman CDJ, Roberts M. Dental caries experience in schoolchildren in fluoridated and non-fluoridated communities in Western Australia. Community Dentistry and Oral Epidemiology 1990;18(4):184-9.

### Tagliaferro 2004

Tagliaferro EP, Cypriano S, da Luz Rosário de Sousa M, Wada RS. Caries experience among schoolchildren in relation to community fluoridation status and town size. Acta Odontologica Scandinavica 2004;62(3):124-8.

### Tank 1965

Tank G, Storvick CA. Caries experience of children one to six years old in two Oregon communities (Corvallis and Albany). Journal of the American Dental Association 1965;70(2):394-403.

### Ten Cate 1991

Ten Cate JM, Featherstone JD. Mechanistic aspects of the interactions between fluoride and dental enamel. Critical Reviews in Oral Biology and Medicine 1991;2(3):283-96.

### Thomas 1992

Thomas FD, Kassab JY. Fluoridation in Anglesey: a clinical study of dental caries in mothers at term. British Dental Journal 1992;173:136-40.

### Thomas 1995

Thomas FD, Kassab JY, Jones BM. Fluoridation in Anglesey: a clinical study of dental caries in in 5-year-old children who had experienced sub-optimal fluoridation. British Dental Journal 1995;178(2):55-9.

### Tiano 2009

Tiano AV, Moimaz SA, Saliba O, Saliba NA. Dental caries prevalence in children up to 36 months of age attending daycare centers in municipalities with different water fluoride content. Journal of Applied Oral Science 2009;17(1):39-44.

### Tickle 2003

Tickle M, Milsom KM, Jenner TM, Blinkhorn AS. The geodemographic distribution of caries experience in neighboring fluoridated and nonfluoridated populations. Journal of Public Health Dentistry 2003;63(2):92-8.

### Treasure 1994

Treasure ET, Dever JG. Relationship of caries with socioeconomic status in 14-year-old children from communities with different fluoride histories. Community Dentistry and Oral Epidemiology 1994;22:226-30.

### Truman 2002

Truman BI, Gooch BF, Sulemana I, Gift HC, Horowitz AM, Evans CA, et al. Reviews of evidence on interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. American Journal of Preventive Medicine 2002;23(1 Suppl):21-54.

### Van Rijkom 1996

Van Rijkom HM, Truin GJ, Van't Hof MA. A meta-analysis of clinical studies on the caries-inhibiting effect of chlorhexidine treatment. Journal of Dental Research 1996;75:790-5.

### Walsh 2010

Walsh T, Worthington HV, Glenny A-M, Appelbe P, Marinho VC, Shi X. Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No: CD007868. [DOI: 10.1002/14651858.CD007868.pub2]

### WHO 2017

World Health Organization. Guidelines for Drinking Water Quality. Fourth edition incorporating 1st addendum. Geneva: WHO, 2017. [ISBN: 978-92-4-154995-0]

### WHO 2021

World Health Organization. Global Oral Health Status Report: Towards Universal Health Coverage for Oral Health by 2030. Geneva: WHO, 2021. [ISBN: 978-92-4-006148-4]

### Zadik 1992

Zadik D, Zusman SP, Kelman AM. Caries prevalence in 5- and 12-year-old children in Israel. Community Dentistry and Oral Epidemiology 1992;20:54-5.

## References to other published versions of this review

### Iheozor-Ejiofor 2015

Iheozor-Ejiofor Z, Worthington HV, Walsh T, O'Malley L, Clarkson JE, Tugwell P, et al. Water fluoridation for the prevention of dental caries. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No: CD010856. [DOI: 10.1002/14651858.CD010856.pub2]

### Iheozor-Ejiofor 2013

Iheozor-Ejiofor Z, O'Malley LA, Glenny AM, Macey R, Alam R, Tugwell P, et al. Water fluoridation for the prevention of dental caries. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No: CD010856. [DOI: 10.1002/14651858.CD010856]

# Additional tables

**Table 1**

**ROBINS-I assessment for studies evaluating the initiation or cessation of community water fluoridation programmes on the prevention of dental caries**

| Study ID | Preliminary questions | Risk of bias due to confounding | Risk of bias in classification of interventions | Risk of bias in selection of participants into the study (or into the analysis) | Risk of bias due to deviations from intended interventions | Risk of bias due to missing data | Risk of bias arising from measurement of the outcome | Risk of bias in selection of the reported result | Overall risk of bias[a] |
|---|---|---|---|---|---|---|---|---|---|
| Adriasola 1959 | | Moderate | Low | Low | Low | Serious | Moderate | Low | SERIOUS |
| Arnold 1956 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Ast 1951 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Backer-Dirks 1961 | | Serious | Low | Low | Low | Serious | Moderate | Low | SERIOUS |
| Beal 1971 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Beal 1981 | | Serious | Low | Low | Low | Serious | Moderate | Low | SERIOUS |
| Blinkhorn 2015 | | Low | Low | Low | Low | Serious | Moderate | Low | SERIOUS |
| Brown 1965 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| DHSS England 1969 | | Serious | Low | Low | Low | Serious | Moderate | Low | SERIOUS |
| DHSS Scotland 1969 | | Serious | Low | Low | Low | Serious | Moderate | Low | SERIOUS |
| DHSS Wales 1969 | | Serious | Low | Low | Low | Moderate | Moderate | Low | SERIOUS |
| Goodwin 2022 | | Low | Low | Low | Low | Low | Moderate | Low | MODERATE |
| Gray 2001 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Guo 1984 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Hardwick 1982 | | Moderate | Low | Low | Low | Serious | Low | Low | SERIOUS |
| Holdcroft 1999[b] | | - | - | - | - | Serious | - | - | SERIOUS |
| Kim 2019 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Kunzel 1997 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Loh 1996 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Maupome 2001 | | Moderate | Low | Moderate | Low | Serious | Moderate | Low | SERIOUS |
| Pot 1974 | No further assessment | - | - | - | - | - | - | - | CRITICAL |
| Tessier 1987 | | Moderate | Low | Low | Low | Serious | Moderate | Low | SERIOUS |

[a]A brief summary to support the judgement for each signalling question is reported in the notes section of the Characteristics of included studies for the relevant study.

[b]We were unable to access the Holdcroft 1999 report and have based our assessment on information presented in McDonagh 2000. The only domain we are able to confidently assess is "Risk of bias due to missing data". Given the lack of information on the number of participants at baseline/follow-up, we assessed the study as being at serious risk of bias for this domain. Consequently, the best overall assessment this study could achieve was SERIOUS.

**Overall risk of bias judgements**

**Low risk of bias except for concerns about uncontrolled confounding:** there is the possibility of uncontrolled confounding that has not been controlled for (given the observational nature of the study); otherwise, little or no concern about bias in the result.

**Moderate risk of bias:** there is some concern about bias in the result, although it is not clear that there is an important risk of bias.

**Serious risk of bias:** the study has some important problems; characteristics of the study give rise to a serious risk of bias in the result.

**Critical risk of bias:** The study is very problematic; characteristics of the study give rise to a critical of bias in the result, such that the result should generally be excluded from evidence syntheses.

**Table 2**

**dmft data and underlying calculations**

| Study ID | Date | Age (years) | 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 |
| Blinkhorn 2015 | > 1975 | 5 to 7 | 2.02 | 3.13 | 781 | 0.72 | 1.63 | 844 | 2.09 | 2.91 | 523 | 1.21 | 2.27 | 612 |
| | | **5 to 7** | **Mean (SD) change in dmft: 1.3 (3.49), N = 813[a]** | | | | | | **Mean (SD) change in dmft: 0.88 (3.77), N = 568[a]** | | | | | |
| Goodwin 2022 | > 1975 | 5 | 1.06 | 2.16 | 699 | 0.49 | 1.40 | 609 | 1.18 | 2.41 | 911 | 0.74 | 1.96 | 835 |
| | | **5** | **Mean (SD) change in dmft: 0.57 (2.61), N = 654[a]** | | | | | | **Mean (SD) change in dmft: 0.44 (3.17), N = 873[a]** | | | | | |
| Adriasola 1959 | ≤ 1975 | 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), N = 263[a]** | | | | | | **Mean (SD) change in dmft: 0.3 (6.72), N = 157[a]** | | | | | |
| Arnold 1956[b] | ≤ 1975 | 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 to 8** | **Mean (SD) change in dmft: 2.75 (4.99), N = 4931[a]** | | | | | | **Mean (SD) change in dmft: 1.18 (5.8), N = 1437[a]** | | | | | |
| Beal 1971 | ≤ 1975 | 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), N = 182[a]** | | | | | | **Mean (SD) change in dmft: -0.12 (6.27), N = 223[a]** | | | | | |
| Beal 1981 | ≤ 1975 | 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 or 8** | **Mean (SD) change in dmft: 2.02 (4.18), N = 361[a]** | | | | | | **Mean (SD) change in dmft: 0.57 (4.6), N = 367[a]** | | | | | |
| DHSS England 1969[b] | ≤ 1975 | 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 |
| | | 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 to 7** | **Mean (SD) change in dmft: 3.09 (4.3), N = 654[a]** | | | | | | **Mean (SD) change in dmft: 1.04 (4.22), N = 557[a]** | | | | | |
| DHSS Scotland 1969[b] | ≤ 1975 | 3 | 4.87 | 3.6 | 97 | 1.88 | 2.11 | 135 | 5.2 | 3.72 | 107 | 4.45 | 3.44 | 130 |
| | | 4 | 7.12 | 4.43 | 112 | 2.97 | 2.71 | 171 | 7.16 | 4.47 | 77 | 6.86 | 4.35 | 132 |
| | | **3 to 4** | **Mean (SD) change in dmft: 3.49 (4.92), N = 258[a]** | | | | | | **Mean (SD) change in dmft: 0.59 (5.64), N = 223[a]** | | | | | |
| DHSS Wales 1969[b,c] | ≤ 1975 | 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 to 7** | **Mean (SD) change in dmft: 2.87 (4.68), N = 1910[a]** | | | | | | **Mean (SD) change in dmft: 0.64 (5.54), N = 959[a]** | | | | | |
| Guo 1984 | ≤ 1975 | 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 to 8** | **Mean (SD) change in dmft: 0.23 (5.39), N = 2018[a]** | | | | | | **Mean (SD) change in dmft: -2.47 (5.35), N = 1696[a]** | | | | | |
| Kunzel 1997[b,d] | ≤ 1975 | 5 | 2.4 | 2.42 | 688 | 1.4 | 1.79 | 1306 | 3.3 | 2.89 | 172 | 2.9 | 2.68 | 597 |
| | | 8 | 4.9 | 3.60 | 2438 | 2.8 | 2.63 | 3020 | 4.9 | 3.60 | 777 | 4.9 | 3.60 | 1078 |
| | | **5 to 8** | **Mean (SD) change in dmft: 2.1 (5.01), N = 3726[a]** | | | | | | **Mean (SD) change in dmft: 0.13 (5.0), N = 1313[a]** | | | | | |

**dmft:** decayed, missing or filled primary dentition; **SD:** standard deviation

**Note:** we only included data for children up to the age of 8 years for the primary dentition.

[a]Average number of participants

[b]Imputed SD

[c]We combined data from 2 fluoridated areas.

[d]Data from McDonagh 2000 review; not verified

**Table 3**

**DMFT data and underlying calculations**

| Study ID | Date | Age (years) | 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 |
| Blinkhorn 2015[a] | > 1975 | 10-12 | 0.59 | 1.10 | 777 | 0.45 | 0.95 | 642 | 0.99 | 1.47 | 436 | 0.72 | 1.23 | 455 |
| | | **10-12** | **Mean (SD) change in DMFT: 0.14 (1.50), N = 710[b]** | | | | | | **Mean (SD) change in DMFT: 0.27 (1.94), N = 446[b]** | | | | | |
| Goodwin 2022 | > 1975 | **11** | **Mean (SD) increment in DMFT:- 0.32 (0.77), N = 570** | | | | | | **Mean (SD) increment in DMFT: -0.40 (0.90), N = 622** | | | | | |
| Guo 1984 | > 1975 | 6 | 0.2 | 0.6 | 695 | 0.2 | 0.5 | 297 | 0.1 | 0.4 | 309 | 0.5 | 0.9 | 354 |
| | | 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 to 15** | **Mean (SD) change in DMFT: -0.11 (1.69), N = 3190[b]** | | | | | | **Mean (SD) change in DMFT: -1.14 (2.59), N = 4194[b]** | | | | | |
| Hardwick 1982 | > 1975 | **12** | **Mean (SD) increment in DMFT: -3.76 (2.86), N = 144** | | | | | | **Mean (SD) increment in DMFT: -4.85 (3.39), N = 199** | | | | | |
| Kim 2019 | > 1975 | 8 | 0.92 | 1.46 | 213 | 0.5 | 1.01 | 103 | 1 | 1.38 | 1194 | 0.44 | 0.94 | 243 |
| | | 10 | 1.75 | 2.53 | 198 | 0.5 | 1.29 | 116 | 1.59 | 2.08 | 1205 | 0.88 | 1.24 | 239 |
| | | 12 | 3.04 | 2.74 | 260 | 0.87 | 1.84 | 117 | 2.86 | 2.77 | 1203 | 1.38 | 1.86 | 239 |
| | | **8 to 12** | **Mean (SD) change in DMFT: 1.00 (2.5), N = 504[b]** | | | | | | **Mean (SD) change in DMFT: 0.81 (2.5), N = 2162[b]** | | | | | |
| Loh 1996 | > 1975 | 7 to 9 (Malay) | 2.9 | - | - | 2 | - | - | 1.9 | - | - | 3.1 | - | - |
| | | 7 to 9 (Chinese) | 4.4 | - | - | 2.1 | - | - | 3.7 | - | - | 4.5 | - | - |
| | | **Insufficient data to include in further analysis** | | | | | | | | | | | | |
| Tessier 1987[a] | > 1975 | 6 to 7 | 8.28 | - | 56 | 3.16 | - | 96 | 8.23 | - | 85 | 5.4 | - | 93 |
| | | **6 to 7** | **Mean (SD) change in DMFT: 5.12 (6.16), N = 76[b]** | | | | | | **Mean (SD) change in DMFT: 2.83 (6.18), N = 89[b]** | | | | | |
| Arnold 1956[a] | ≤ 1975 | 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 to 16** | **Mean (SD) change in DMFT: 0.90 (3.20), N = 10,647[b]** | | | | | | **Mean (SD) change in DMFT: 0.15 (3.51), N = 2824[b]** | | | | | |
| Beal 1981 | ≤ 1975 | 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), N = 369[b]** | | | | | | **Mean (SD) change in DMFT: 0.20 (2.64), N = 367[b]** | | | | | |
| Brown 1965 | ≤ 1975 | 9 to 11 | 4.07 | 2.20 | 595 | 1.52 | 1.80 | 502 | 4.21 | 2.63 | 571 | 3.68 | 2.35 | 521 |
| | | 12 to 14 | 7.68 | 3.90 | 593 | 3.23 | 2.92 | 503 | 7.94 | 4.41 | 486 | 7.46 | 4.40 | 485 |
| | | **9 to 14** | **Mean (SD) change in DMFT: 3.03 (3.31), N = 1097[b]** | | | | | | **Mean (SD) change in DMFT: 0.52 (4.18), N = 1032[b]** | | | | | |
| DHSS England 1969[a] | ≤ 1975 | 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 to 14** | **Mean (SD) change in DMFT: 1.62 (3.92), N = 939[b]** | | | | | | **Mean (SD) change in DMFT: 0.65 (4.39), N = 725[b]** | | | | | |
| DHSS Wales 1969[a,c] | ≤ 1975 | 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 to 14** | **Mean (SD) change in DMFT: 0.66 (3.72), N = 1833[b]** | | | | | | **Mean (SD) change in DMFT: -0.73 (4.95), N = 1390[b]** | | | | | |
| Kunzel 1997[d,e] | ≤ 1975 | 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 | - |
| | | 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), N = 6690[b]** | | | | | | **Mean (SD) change in DMFT: -0.85 (3.26), N = 2421[b]** | | | | | |

**DMFT:** decayed, missing or filled permanent teeth; **SD:** standard deviation

[a]Imputed SD

[b]Average number of participants

[c]Data combined from 2 fluoridated areas

[d]Imputed SD for follow-up data only

[e]N values only available for ages 8, 12 and 15 years

**Table 4**

**Number of caries-free children: primary teeth**

| | | | Fluoridated area | | | | Non-/low-fluoridated area | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline (before/at initiation) | | Follow-up | | Baseline | | Follow-up | |
| Study ID | Date | Age (years) | n | N | n | N | n | N | n | N |
| Blinkhorn 2015 | > 1975 | 5 to 7 | 397 | 781 | 632 | 844 | 254 | 523 | 412 | 612 |
| Goodwin 2022 | > 1975 | 5 | 478 | 699 | 503 | 609 | 620 | 911 | 656 | 835 |
| Gray 2001[a] | > 1975 | 5 | 1465 | 2462 | 1903 | 2524 | 345 | 466 | 273 | 419 |
| Guo 1984 | > 1975 | 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 |
| Adriasola 1959[b] | ≤ 1975 | 3 | 26 | 151 | 82 | 216 | 9 | 77 | 25 | 135 |
| | | 4 | 12 | 156 | 53 | 216 | 11 | 76 | 11 | 110 |
| | | 5 | 4 | 186 | 47 | 340 | 7 | 174 | 14 | 140 |
| Ast 1951 | ≤ 1975 | 5 | 63 | 274 | 108 | 217 | 73 | 259 | 107 | 324 |
| Beal 1971[a] | ≤ 1975 | 5 | 62 | 297 | 138 | 314 | 35 | 217 | 55 | 229 |
| Beal 1981 | ≤ 1975 | 5 | 41 | 196 | 78 | 170 | 43 | 205 | 54 | 180 |
| | | 8 | 18 | 189 | 31 | 167 | 12 | 163 | 18 | 186 |
| DHSS England 1969 | ≤ 1975 | 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 Scotland 1969[c] | ≤ 1975 | 3 | 30 | 97 | 69 | 135 | 27 | 107 | 29 | 130 |
| | | 4 | 14 | 112 | 51 | 171 | 10 | 77 | 15 | 132 |
| DHSS Wales 1969 | ≤ 1975 | 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 |
| Kunzel 1997 | ≤ 1975 | 5 | 231 | 688 | 682 | 1306 | 39 | 172 | 192 | 597 |
| | | 8 | 117 | 2438 | 746 | 3020 | 40 | 777 | 61 | 1078 |

Note: we only included data for children up to the age of 8 years for the primary dentition.

[a]Data from all fluoridated areas combined

[b]Baseline data not available for ages 6 and 7 years. Although data were available for children aged 8, we were uncertain whether these data were for primary or permanent dentition and did not include these data from this study.

[c]Baseline number of participants only available for first follow-up in 1961, when children up to 5 years of age would have received the full effect. Water fluoridation ceased in 1962.

**Table 5**

**Number of caries-free children: permanent teeth**

| Study ID | Date | Age (years) | Fluoridated area | | | | Non-/low-fluoridated area | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Baseline (before/at initiation) | | Follow-up | | Baseline | | Follow-up | |
| | | | n | N | n | N | n | N | n | N |
| Blinkhorn 2015 | > 1975 | 10 to 12 | 525 | 777 | 486 | 642 | 272 | 436 | 307 | 455 |
| Goodwin 2022 | > 1975 | 11 | N/A[a] | N/A[a] | 461 | 570 | N/A[a] | N/A[a] | 486 | 622 |
| Guo 1984 | > 1975 | 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 |
| Adriasola 1959[b] | ≤ 1975 | 12 | 7 | 292 | 8 | 419 | 3 | 197 | 9 | 211 |
| Beal 1981 | ≤ 1975 | 8 | 77 | 189 | 115 | 167 | 56 | 163 | 82 | 186 |
| | | 12 | 51 | 192 | 41 | 189 | 13 | 188 | 14 | 197 |
| Brown 1965[c] | ≤ 1975 | 9 to 11 | 34 | 595 | 220 | 502 | 35 | 571 | 42 | 521 |
| | | 12 to 14 | 7 | 593 | 94 | 503 | 3 | 486 | 11 | 485 |
| DHSS England 1969 | ≤ 1975 | 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 |
| | | 13 | 3 | 91 | 9 | 132 | 2 | 52 | 8 | 127 |
| | | 14 | 0 | 70 | 4 | 90 | 2 | 36 | 9 | 180 |
| DHSS Wales 1969 | ≤ 1975 | 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 |
| Kunzel 1997 | ≤ 1975 | 8 | 1021 | 2419 | 2147 | 3016 | 334 | 777 | 333 | 1076 |
| | | 12 | 120 | 1626 | 801 | 2426 | 42 | 563 | 50 | 925 |
| | | 15 | 118 | 1995 | 249 | 1897 | 27 | 744 | 18 | 756 |

**N/A:** not applicable

[a]Because this study reported increment data, following the same participants over time, there are no available data at baseline.

[b]Baseline data not available for ages 11 and 15 years. Although data were available for children aged 8 years, we were uncertain whether these data were for primary or permanent dentition and did not include these data from this study.

[c]Data for children aged 16 to 17 years presented in study report but without number of participants

**Table 6**

**Other adverse effects**

| Study ID | Type of adverse effect | Age (years) | Fluoride level (ppm) | Assigned fluoride level (ppm) | Number of participants | Proportion of participants 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 2001 | Bone fracture | 6 to 12 | < 1.5 | 0.75 | 97 | 5.2 |
| | | | 1.51 to 4.99 | 3.25 | 112 | 8.9 |
| | | | 5 to 8.49 | 6.75 | 38 | 2.6 |
| | | | 8.5 to 11.99 | 10.25 | 27 | 11.1 |
| | | | 12 to 16 | 14 | 59 | 8.5 |
| | | 13 to 60 | < 1.5 | 0.75 | 192 | 3.1 |
| | | | 1.51 to 4.99 | 3.25 | 330 | 7.9 |
| | | | 5 to 8.49 | 6.75 | 146 | 8.9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | 8.5 to 11.99 | 10.25 | 138 | 7.2 |
| | | | 12 to 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 |
| | | | 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 |

**ppm:** parts per million

[a]Participants were diagnosed on the basis of diagnostic criteria for endemic skeletal fluorosis (WS 192-2008)

[b]Participants were examined radiologically

[c]Reported data were mean (standard error) skeletal maturity

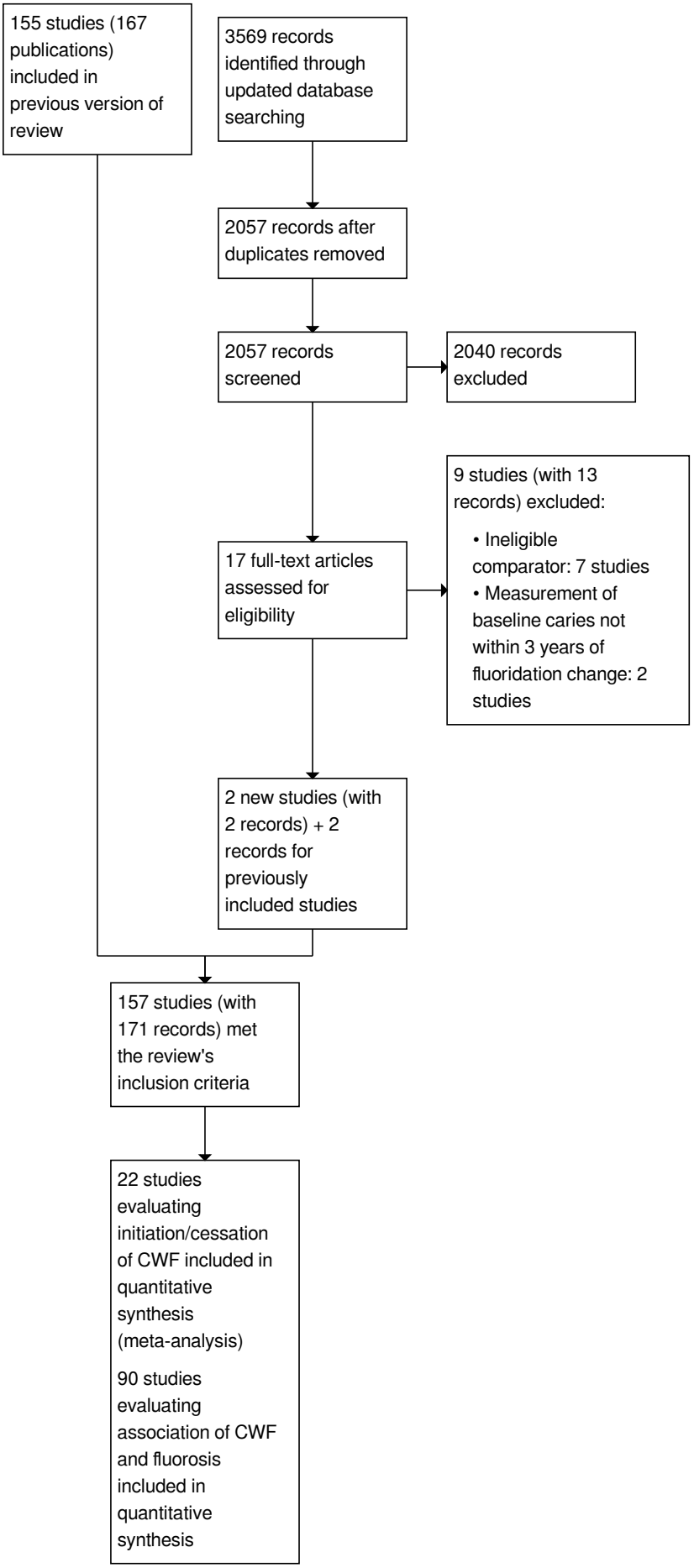
**Table 7**

**WHO region-specific estimated prevalence of caries in permanent teeth and the percentage change in prevalence**

| World Health Organization (WHO) region | Prevalence of caries 2019 | Percentage change in prevalence 1990 to 2019 |
|---|---|---|
| African Region | 28.50% | -1.66% |
| Eastern Mediterranean Region | 32.25% | -0.27% |
| European Region | 33.63% | -3.91% |
| Region of the Americas | 28.24% | -0.05% |
| South-East Asia Region | 28.69% | +0.67% |
| Western Pacific Region | 25.41% | -6.50% |
| **GLOBAL** | 28.70% | -2.59% |

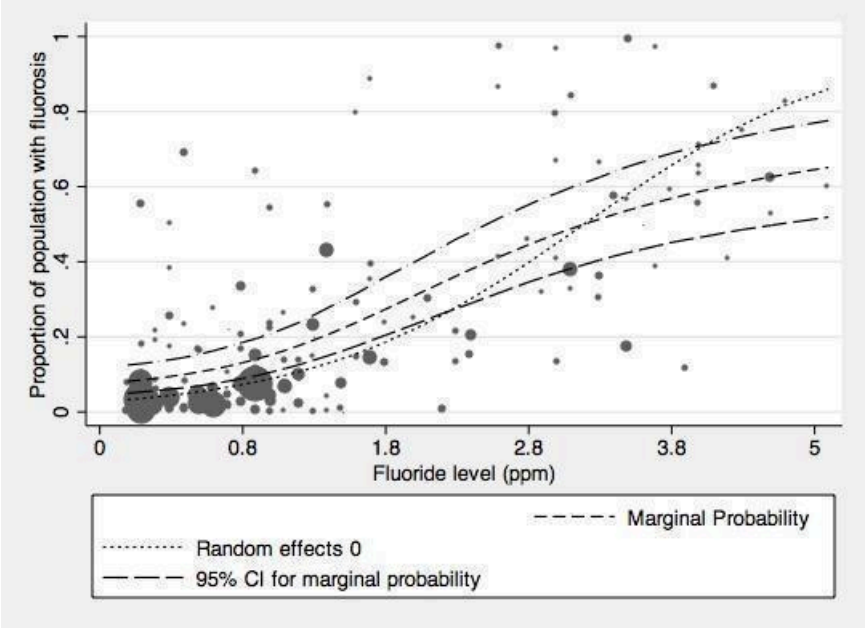
Table derived from a table in WHO 2021

**Figure 1**



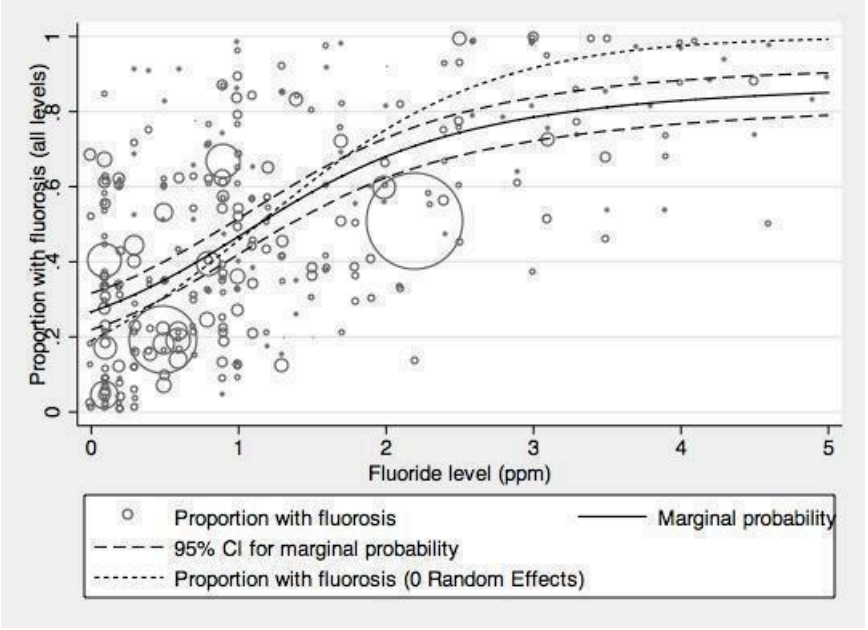

PRISMA flow diagram for the searches conducted in August 2023

**Figure 2**



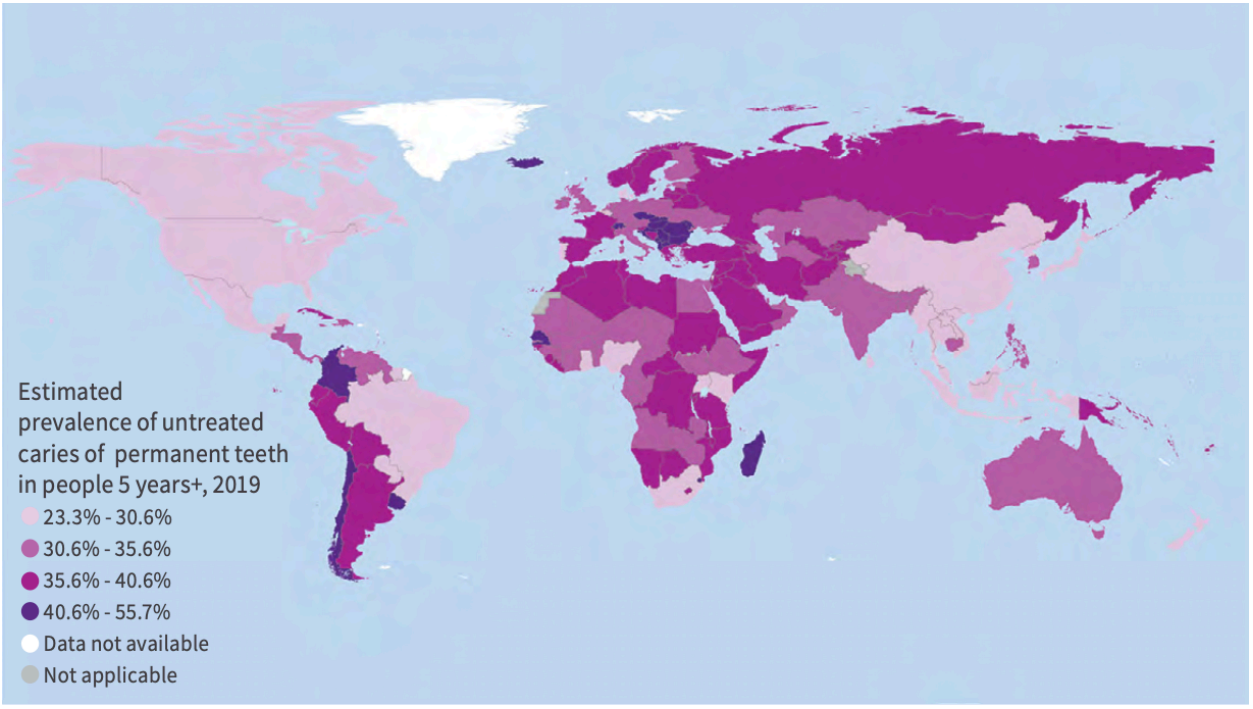

Proportion of the population with dental fluorosis of aesthetic concern by water fluoride level, together with 95% confidence interval for the proportion (studies reporting up to and including 5 ppm).

**Figure 3**



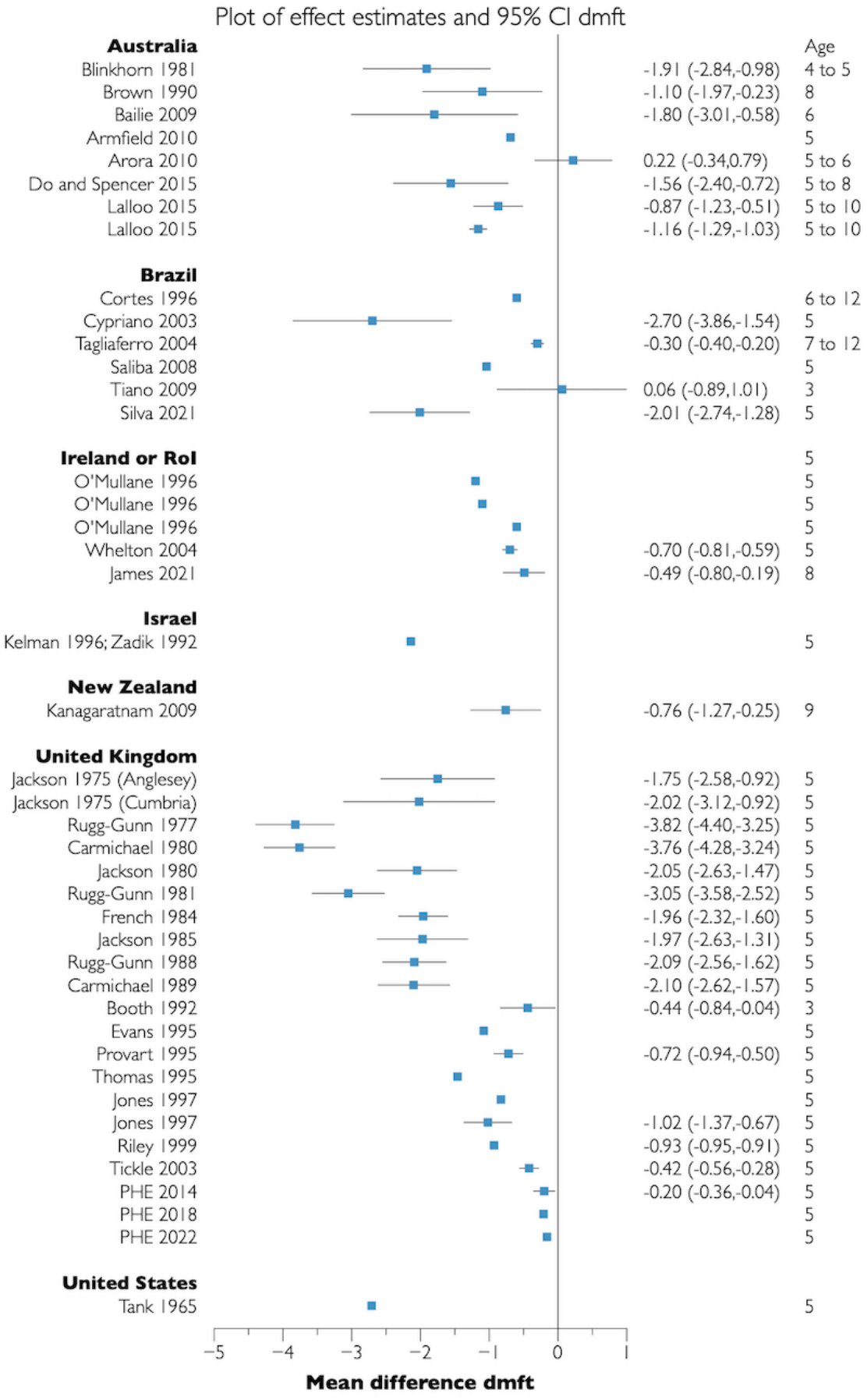

Proportion of the population with dental fluorosis of any level by water fluoride level, together with 95% confidence interval for the proportion (studies reporting up to and including 5 ppm fluoride concentration)

**Figure 4**



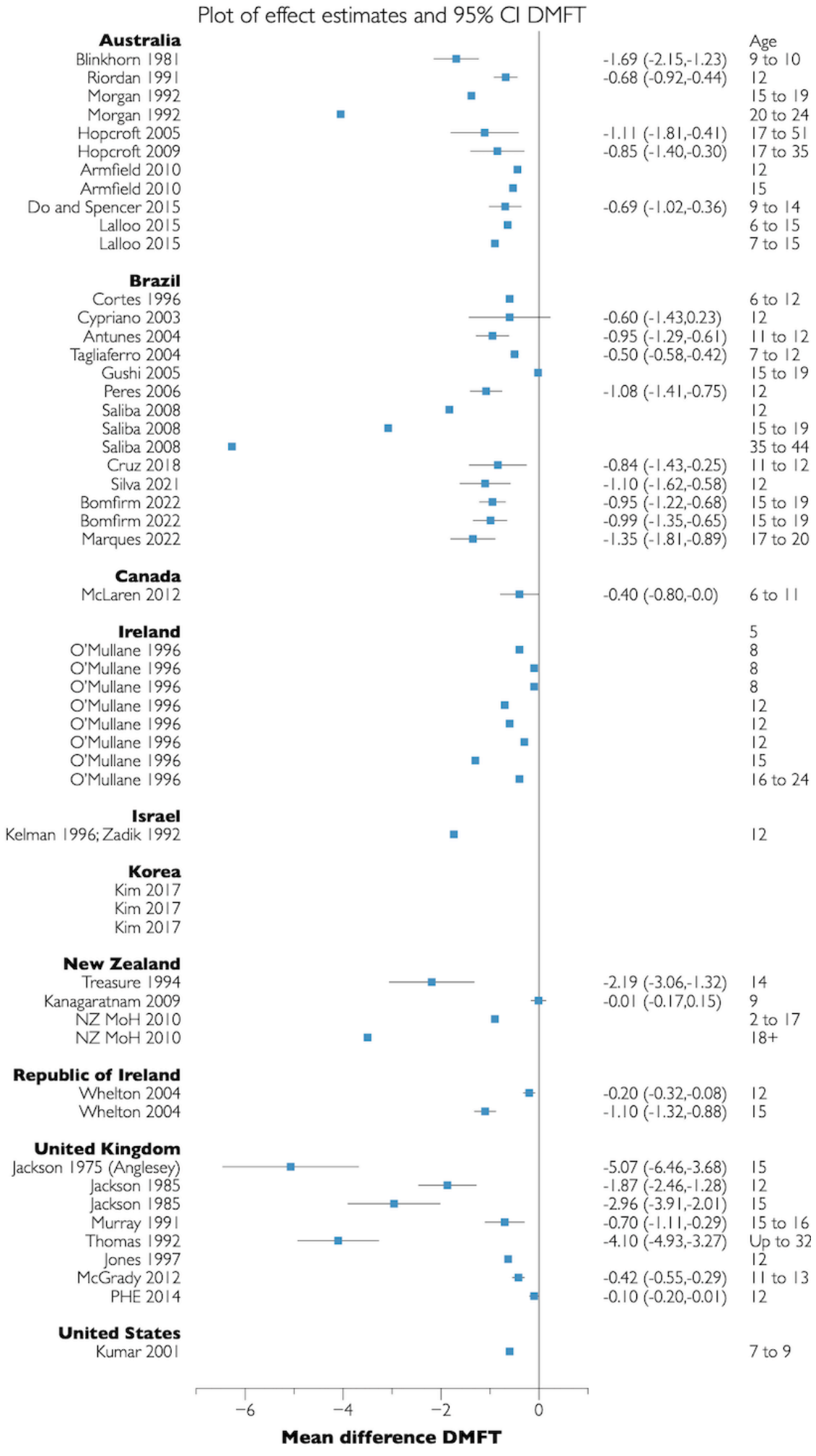

Source: WHO 2021. Datasource: Global Burden of Disease Collaborative Network. GBD 2019. Seattle:IHME;2020. Map Production: WHONCD/MNDunit. Map Creation Date: 30 August 2022. Note: N = 194 countries; data are age standardised, for ages > 5 years, both sexes, from GBD 2019.

**Figure 5**




Single time point cross-sectional studies: mean difference and 95% confidence interval (CI) in decayed, missing and filled teeth (dmft) in the primary dentition between fluoridated and low/non-fluoridated areas, with age (in years) at time of measurement (Armfield 2010; Arora 2010; Bailie 2009; Blinkhorn 1981; Booth 1992; Brown 1990; Carmichael 1980; Carmichael 1989; Cortes 1996; Cypriano 2003; Do 2015; Evans 1995; French 1984; Jackson 1975; Jackson 1980; Jackson 1985; James 2021; Jones 1997; Kanagaratnam 2009; Kelman 1996; Lalloo 2015; O'Mullane 1996; PHE 2014; PHE 2018; PHE 2022; Provart 1995; Riley 1999; Rugg-Gunn 1988; Rugg-Gunn 1977a; Rugg-Gunn 1981a; Saliba 2008; Silva 2021; Tagliaferro 2004; Tank 1965; Thomas 1995; Tiano 2009; Tickle 2003; Whelton 2004; Zadik 1992)

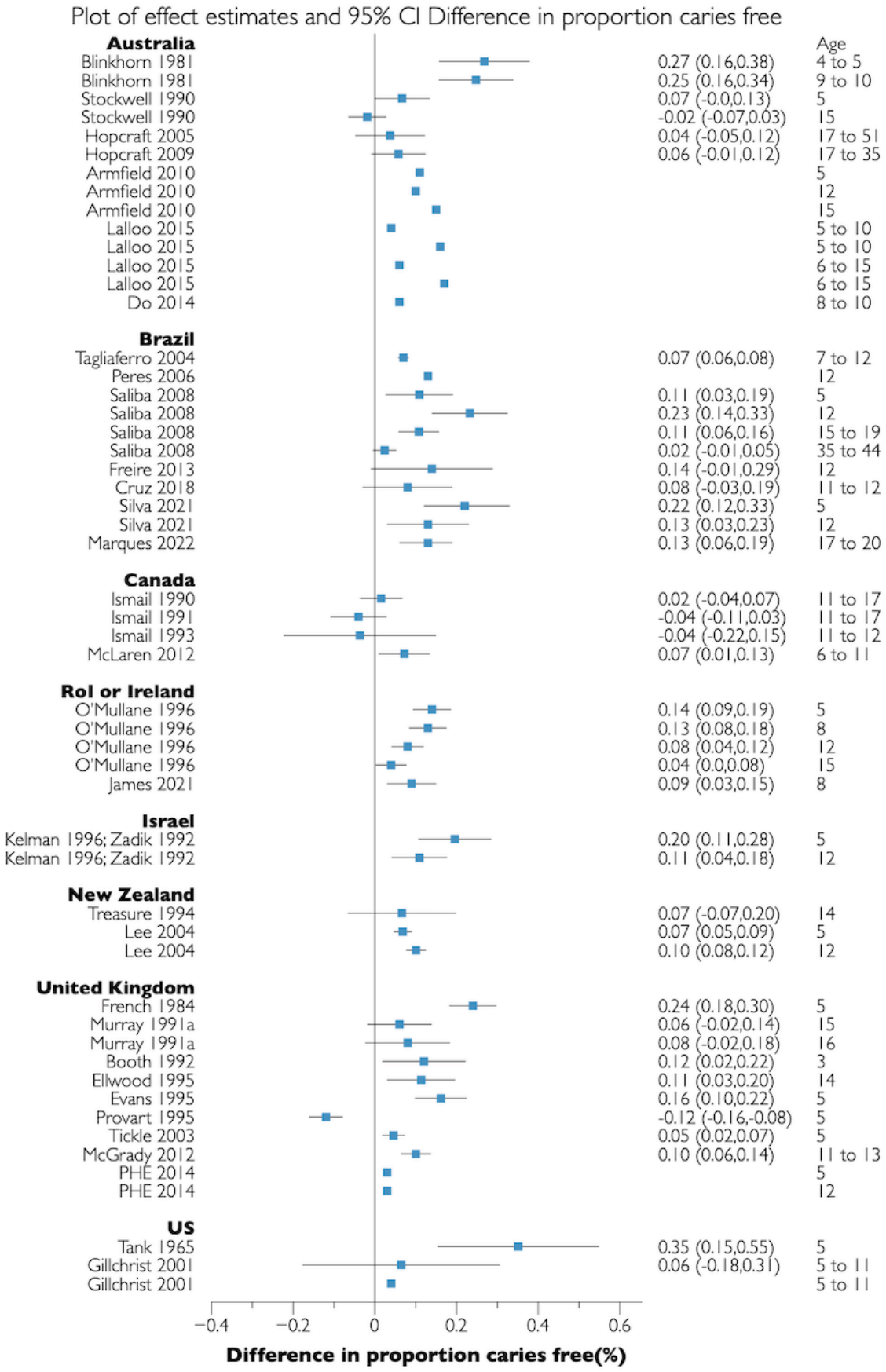
**Figure 6**




Single time point cross-sectional studies: mean difference and 95% confidence intervals (CI) in decayed, missing or filled teeth (DMFT) in the permanent dentition between fluoridated and low/non-fluoridated areas (Antunes 2004; Armfield 2010;

Blinkhorn 1981; Bomfirm 2022; Cortes 1996; Cruz 2018; Cypriano 2003; Do 2015; Gushi 2005; Hopcraft 2005; Jackson 1975; Jackson 1985; Jones 1997; Kanagaratnam 2009; Kelman 1996; Kim 2017; Kumar 2001; Lalloo 2015; Marques 2022; McGrady 2012; McLaren 2012; Morgan 1992; Murray 1991a; NZ MoH 2010; O'Mullane 1996; Peres 2006; PHE 2014; Riordan 1991; Saliba 2008; Silva 2021; Tagliaferro 2004; Thomas 1992; Treasure 1994; Whelton 2004; Zadik 1992)

**Figure 7**

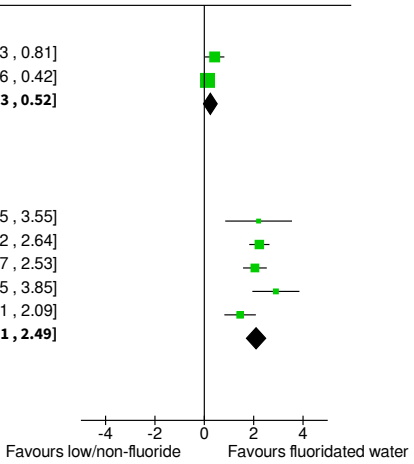



Single time point cross-sectional studies: mean difference and 95% confidence intervals (CI) in proportion of caries-free participants between fluoridated and low/non-fluoridated areas, with age (in years) at time of measurement (Armfield 2010; Blinkhorn 1981; Booth 1992; Cruz 2018; Do 2014; Ellwood 1995; Evans 1995; Freire 2013; French 1984; Gillcrist 2001; Hopcraft 2005; Hopcraft 2009; Ismail 1990; James 2021; Kelman 1996; Lalloo 2015; Lee 2004; Marques 2022; McGrady

2012; McLaren 2012; Murray 1991a; O'Mullane 1996; Peres 2006; PHE 2014; Provart 1995; Saliba 2008; Silva 2021; Stockwell 1990; Tagliaferro 2004; Tank 1965; Tickle 2003; Treasure 1994; Zadik 1992)

**Analysis 1.1**

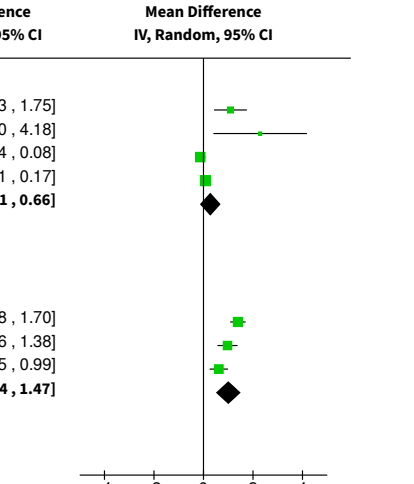
| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.1.1 Studies conducted after 1975** | | | | | | | | |
| Blinkhorn 2015 | 1.3 | 3.49 | 813 | 0.88 | 3.77 | 568 | 39.3% | 0.42 [0.03 , 0.81] |
| Goodwin 2022 | 0.57 | 2.61 | 654 | 0.44 | 3.17 | 873 | 60.7% | 0.13 [-0.16 , 0.42] |
| **Subtotal (95% CI)** | | | **1467** | | | **1441** | **100.0%** | **0.24 [-0.03 , 0.52]** |
| Heterogeneity: Tau² = 0.01; Chi² = 1.36, df = 1 (P = 0.24); I² = 26% | | | | | | | | |
| Test for overall effect: Z = 1.72 (P = 0.09) | | | | | | | | |
| **1.1.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Adriasola 1959 | 2.5 | 7.04 | 263 | 0.3 | 6.72 | 157 | 7.1% | 2.20 [0.85 , 3.55] |
| DHSS Wales 1969 | 2.87 | 4.68 | 1910 | 0.64 | 5.54 | 959 | 31.6% | 2.23 [1.82 , 2.64] |
| DHSS England 1969 | 3.09 | 4.3 | 654 | 1.04 | 4.22 | 557 | 27.9% | 2.05 [1.57 , 2.53] |
| DHSS Scotland 1969 | 3.49 | 4.92 | 258 | 0.59 | 5.64 | 223 | 12.4% | 2.90 [1.95 , 3.85] |
| Beal 1981 | 2.02 | 4.18 | 361 | 0.57 | 4.6 | 367 | 21.0% | 1.45 [0.81 , 2.09] |
| **Subtotal (95% CI)** | | | **3446** | | | **2263** | **100.0%** | **2.10 [1.71 , 2.49]** |
| Heterogeneity: Tau² = 0.08; Chi² = 7.14, df = 4 (P = 0.13); I² = 44% | | | | | | | | |
| Test for overall effect: Z = 10.57 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 57.81, df = 1 (P < 0.00001), I² = 98.3% | | | | | | | | |




Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 1: Change in the number of decayed, missing or filled primary teeth (dmft)

**Analysis 1.2**

| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.2.1 Studies conducted after 1975** | | | | | | | | |
| Hardwick 1982[a] | -3.76 | 2.86 | 144 | -4.85 | 3.39 | 199 | 18.6% | 1.09 [0.43 , 1.75] |
| Tessier 1987 | 5.12 | 6.16 | 76 | 2.83 | 6.18 | 89 | 3.8% | 2.29 [0.40 , 4.18] |
| Blinkhorn 2015 | 0.14 | 1.5 | 710 | 0.27 | 1.94 | 446 | 37.0% | -0.13 [-0.34 , 0.08] |
| Goodwin 2022 | -0.32 | 0.77 | 570 | -0.4 | 0.9 | 622 | 40.6% | 0.08 [-0.01 , 0.17] |
| **Subtotal (95% CI)** | | | **1500** | | | **1356** | **100.0%** | **0.27 [-0.11 , 0.66]** |
| Heterogeneity: Tau² = 0.09; Chi² = 17.87, df = 3 (P = 0.0005); I² = 83% | | | | | | | | |
| Test for overall effect: Z = 1.39 (P = 0.16) | | | | | | | | |
| **1.2.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| DHSS Wales 1969 | 0.66 | 3.72 | 1833 | -0.73 | 4.95 | 1390 | 35.3% | 1.39 [1.08 , 1.70] |
| DHSS England 1969 | 1.62 | 3.92 | 939 | 0.65 | 4.39 | 725 | 31.7% | 0.97 [0.56 , 1.38] |
| Beal 1981 | 0.82 | 2.5 | 369 | 0.2 | 2.64 | 367 | 33.0% | 0.62 [0.25 , 0.99] |
| **Subtotal (95% CI)** | | | **3141** | | | **2482** | **100.0%** | **1.00 [0.54 , 1.47]** |
| Heterogeneity: Tau² = 0.13; Chi² = 9.89, df = 2 (P = 0.007); I² = 80% | | | | | | | | |
| Test for overall effect: Z = 4.24 (P < 0.0001) | | | | | | | | |
| Test for subgroup differences: Chi² = 5.60, df = 1 (P = 0.02), I² = 82.1% | | | | | | | | |



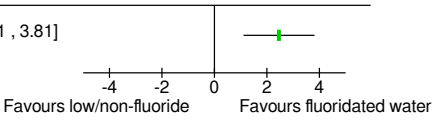

**Footnotes**

[a]Baseline examinations were completed by end of 1974, fluoridation started in 1975 with a possibility of fluoridated toothpaste being introduced during the study period.

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

**Analysis 1.3**

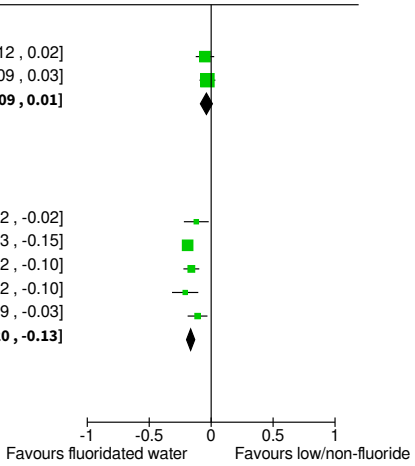
| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|
| Hardwick 1982 | -6.73 | 5.44 | 144 | -9.19 | 7.34 | 199 | 2.46 [1.11 , 3.81] |




Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 3: Change in the number of decayed, missing or filled permanent surfaces (DMFS)

**Analysis 1.4**

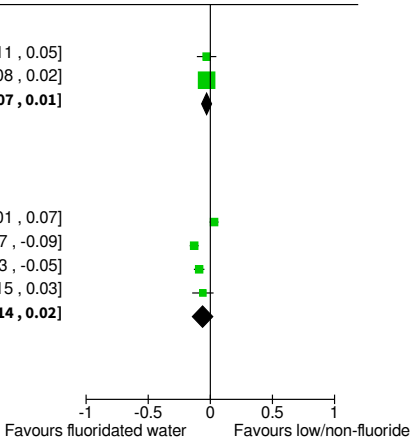
| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.4.1 Studies conducted after 1975** | | | | | | | | |
| Blinkhorn 2015 | -0.24 | 0.73 | 813 | -0.19 | 0.67 | 568 | 42.3% | -0.05 [-0.12 , 0.02] |
| Goodwin 2022 | -0.14 | 0.59 | 654 | -0.11 | 0.68 | 873 | 57.7% | -0.03 [-0.09 , 0.03] |
| **Subtotal (95% CI)** | | | **1467** | | | **1441** | **100.0%** | **-0.04 [-0.09 , 0.01]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 1.55 (P = 0.12) | | | | | | | | |
| **1.4.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Adriasola 1959 | -0.16 | 1.155 | 633 | -0.04 | 0.425 | 356 | 10.1% | -0.12 [-0.22 , -0.02] |
| DHSS Wales 1969 | -0.22 | 0.669 | 1910 | -0.03 | 0.474 | 959 | 42.8% | -0.19 [-0.23 , -0.15] |
| DHSS England 1969 | -0.3 | 0.652 | 654 | -0.14 | 0.481 | 557 | 22.6% | -0.16 [-0.22 , -0.10] |
| DHSS Scotland 1969 | -0.19 | 0.615 | 258 | 0.02 | 0.571 | 223 | 9.1% | -0.21 [-0.32 , -0.10] |
| Beal 1981 | -0.17 | 0.581 | 361 | -0.06 | 0.517 | 367 | 15.3% | -0.11 [-0.19 , -0.03] |
| **Subtotal (95% CI)** | | | **3816** | | | **2462** | **100.0%** | **-0.17 [-0.20 , -0.13]** |
| Heterogeneity: Tau² = 0.00; Chi² = 4.60, df = 4 (P = 0.33); I² = 13% | | | | | | | | |
| Test for overall effect: Z = 9.81 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 18.03, df = 1 (P < 0.0001), I² = 94.5% | | | | | | | | |




Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 4: Change in the proportion of caries-free participants (primary teeth)

**Analysis 1.5**

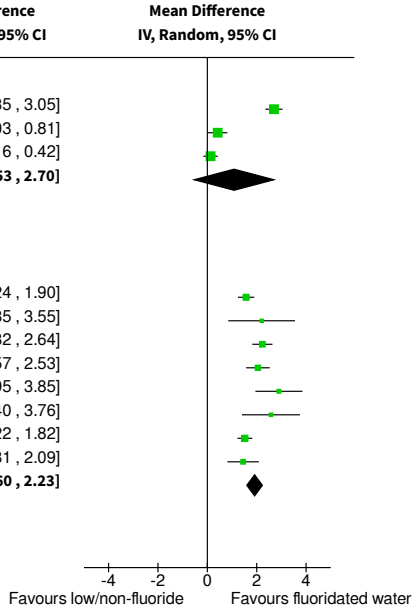
| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.5.1 Studies conducted after 1975** | | | | | | | | |
| Blinkhorn 2015 | -0.08 | 0.68 | 710 | -0.05 | 0.65 | 446 | 25.8% | -0.03 [-0.11 , 0.05] |
| Goodwin 2022 | -0.81 | 0.43 | 570 | -0.78 | 0.38 | 622 | 74.2% | -0.03 [-0.08 , 0.02] |
| **Subtotal (95% CI)** | | | **1280** | | | **1068** | **100.0%** | **-0.03 [-0.07 , 0.01]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 1.48 (P = 0.14) | | | | | | | | |
| **1.5.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Adriasola 1959 | 0 | 0.192 | 356 | -0.03 | 0.219 | 204 | 26.4% | 0.03 [-0.01 , 0.07] |
| DHSS Wales 1969 | -0.08 | 0.655 | 1833 | 0.05 | 0.38 | 1390 | 26.4% | -0.13 [-0.17 , -0.09] |
| DHSS England 1969 | -0.16 | 0.469 | 939 | -0.07 | 0.422 | 761 | 25.9% | -0.09 [-0.13 , -0.05] |
| Beal 1981 | -0.11 | 0.686 | 369 | -0.05 | 0.489 | 367 | 21.3% | -0.06 [-0.15 , 0.03] |
| **Subtotal (95% CI)** | | | **3497** | | | **2722** | **100.0%** | **-0.06 [-0.14 , 0.02]** |
| Heterogeneity: Tau² = 0.01; Chi² = 40.34, df = 3 (P < 0.00001); I² = 93% | | | | | | | | |
| Test for overall effect: Z = 1.50 (P = 0.13) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.49, df = 1 (P = 0.48), I² = 0% | | | | | | | | |




Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 5: Change in the proportion of caries-free participants (permanent teeth)

**Analysis 1.6**

| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.6.1 Studies conducted after 1975** | | | | | | | | |
| Guo 1984[a] | 0.23 | 5.39 | 2018 | -2.47 | 5.35 | 1696 | 33.3% | 2.70 [2.35 , 3.05] |
| Blinkhorn 2015 | 1.3 | 3.49 | 813 | 0.88 | 3.77 | 568 | 33.2% | 0.42 [0.03 , 0.81] |
| Goodwin 2022 | 0.57 | 2.61 | 654 | 0.44 | 3.17 | 873 | 33.5% | 0.13 [-0.16 , 0.42] |
| **Subtotal (95% CI)** | | | **3485** | | | **3137** | **100.0%** | **1.08 [-0.53 , 2.70]** |
| Heterogeneity: Tau² = 2.01; Chi² = 135.34, df = 2 (P < 0.00001); I² = 99% | | | | | | | | |
| Test for overall effect: Z = 1.31 (P = 0.19) | | | | | | | | |
| **1.6.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Arnold 1956 | 2.75 | 4.99 | 4931 | 1.18 | 5.8 | 1437 | 18.8% | 1.57 [1.24 , 1.90] |
| Adriasola 1959 | 2.5 | 7.04 | 263 | 0.3 | 6.72 | 157 | 4.4% | 2.20 [0.85 , 3.55] |
| DHSS Wales 1969 | 2.87 | 4.68 | 1910 | 0.64 | 5.54 | 959 | 16.9% | 2.23 [1.82 , 2.64] |
| DHSS England 1969 | 3.09 | 4.3 | 654 | 1.04 | 4.22 | 557 | 15.3% | 2.05 [1.57 , 2.53] |
| DHSS Scotland 1969 | 3.49 | 4.92 | 258 | 0.59 | 5.64 | 223 | 7.5% | 2.90 [1.95 , 3.85] |
| Beal 1971 | 2.46 | 5.8 | 182 | -0.12 | 6.27 | 223 | 5.5% | 2.58 [1.40 , 3.76] |
| Kunzel 1997 | 1.65 | 4.05 | 3726 | 0.13 | 5 | 1312 | 19.5% | 1.52 [1.22 , 1.82] |
| Beal 1981 | 2.02 | 4.18 | 361 | 0.57 | 4.6 | 367 | 12.0% | 1.45 [0.81 , 2.09] |
| **Subtotal (95% CI)** | | | **12285** | | | **5235** | **100.0%** | **1.91 [1.60 , 2.23]** |
| Heterogeneity: Tau² = 0.11; Chi² = 18.77, df = 7 (P = 0.009); I² = 63% | | | | | | | | |
| Test for overall effect: Z = 11.86 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.98, df = 1 (P = 0.32), I² = 0% | | | | | | | | |



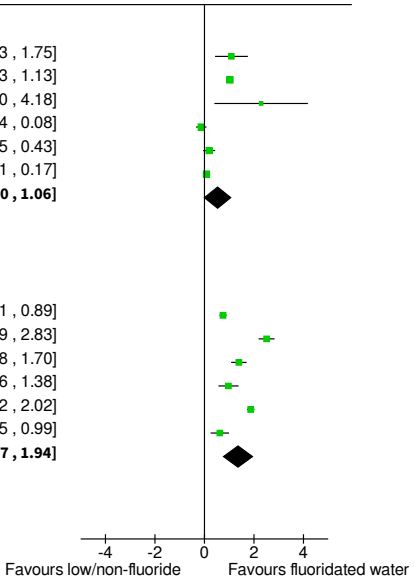

**Footnotes**

[a]Guo 1984 commenced in 1971; possibility of fluoridated toothpaste being introduced during study period

Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 6: Sensitivity analysis - all included studies: change in the number of decayed, missing or filled primary teeth (dmft)

**Analysis 1.7**

| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.7.1 Studies conducted after 1975** | | | | | | | | |
| Hardwick 1982[a] | -3.76 | 2.86 | 144 | -4.85 | 3.39 | 199 | 15.3% | 1.09 [0.43 , 1.75] |
| Guo 1984[b] | -0.11 | 1.69 | 3190 | -1.14 | 2.59 | 4194 | 20.0% | 1.03 [0.93 , 1.13] |
| Tessier 1987 | 5.12 | 6.16 | 76 | 2.83 | 6.18 | 89 | 5.7% | 2.29 [0.40 , 4.18] |
| Blinkhorn 2015 | 0.14 | 1.5 | 710 | 0.27 | 1.94 | 446 | 19.6% | -0.13 [-0.34 , 0.08] |
| Kim 2019 | 1 | 2.5 | 504 | 0.81 | 2.5 | 2162 | 19.4% | 0.19 [-0.05 , 0.43] |
| Goodwin 2022 | -0.32 | 0.77 | 570 | -0.4 | 0.9 | 622 | 20.0% | 0.08 [-0.01 , 0.17] |
| **Subtotal (95% CI)** | | | **5194** | | | **7712** | **100.0%** | **0.53 [0.00 , 1.06]** |
| Heterogeneity: Tau² = 0.36; Chi² = 233.68, df = 5 (P < 0.00001); I² = 98% | | | | | | | | |
| Test for overall effect: Z = 1.96 (P = 0.05) | | | | | | | | |
| **1.7.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Arnold 1956 | 0.9 | 3.2 | 10647 | 0.15 | 3.51 | 2824 | 17.2% | 0.75 [0.61 , 0.89] |
| Brown 1965 | 3.03 | 3.31 | 1097 | 0.52 | 4.18 | 1032 | 16.6% | 2.51 [2.19 , 2.83] |
| DHSS Wales 1969 | 0.66 | 3.72 | 1833 | -0.73 | 4.95 | 1390 | 16.6% | 1.39 [1.08 , 1.70] |
| DHSS England 1969 | 1.62 | 3.92 | 939 | 0.65 | 4.39 | 725 | 16.1% | 0.97 [0.56 , 1.38] |
| Kunzel 1997 | 1.02 | 2.94 | 6690 | -0.85 | 3.26 | 2421 | 17.2% | 1.87 [1.72 , 2.02] |
| Beal 1981 | 0.82 | 2.5 | 369 | 0.2 | 2.644 | 367 | 16.3% | 0.62 [0.25 , 0.99] |
| **Subtotal (95% CI)** | | | **21575** | | | **8759** | **100.0%** | **1.35 [0.77 , 1.94]** |
| Heterogeneity: Tau² = 0.51; Chi² = 183.36, df = 5 (P < 0.00001); I² = 97% | | | | | | | | |
| Test for overall effect: Z = 4.54 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 4.18, df = 1 (P = 0.04), I² = 76.1% | | | | | | | | |




**Footnotes**

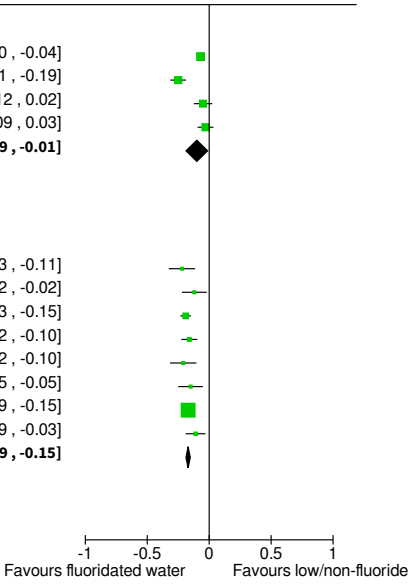
[a]Hardwick 1982 commenced in 1974; possibility of fluoridated toothpaste being introduced during study period

[b]Guo 1984 commenced in 1971; possibility of fluoridated toothpaste being introduced during study period

Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 7: Sensitivity analysis - all included studies: change in the number of decayed, missing or filled permanent teeth (DMFT)

**Analysis 1.8**

| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.8.1 Studies conducted after 1975** | | | | | | | | |
| Guo 1984[a] | -0.02 | 0.464 | 2068 | 0.05 | 0.42 | 1696 | 27.4% | -0.07 [-0.10 , -0.04] |
| Gray 2001 | -0.16 | 0.509 | 2493 | 0.09 | 0.644 | 443 | 24.6% | -0.25 [-0.31 , -0.19] |
| Blinkhorn 2015 | -0.24 | 0.73 | 813 | -0.19 | 0.67 | 568 | 23.4% | -0.05 [-0.12 , 0.02] |
| Goodwin 2022 | -0.14 | 0.59 | 654 | -0.11 | 0.68 | 873 | 24.5% | -0.03 [-0.09 , 0.03] |
| **Subtotal (95% CI)** | | | **6028** | | | **3580** | **100.0%** | **-0.10 [-0.19 , -0.01]** |
| Heterogeneity: Tau² = 0.01; Chi² = 30.94, df = 3 (P < 0.00001); I² = 90% | | | | | | | | |
| Test for overall effect: Z = 2.24 (P = 0.03) | | | | | | | | |
| **1.8.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Ast 1951 | -0.27 | 0.64 | 246 | -0.05 | 0.61 | 292 | 2.7% | -0.22 [-0.33 , -0.11] |
| Adriasola 1959 | -0.16 | 1.155 | 633 | -0.04 | 0.425 | 356 | 3.0% | -0.12 [-0.22 , -0.02] |
| DHSS Wales 1969 | -0.22 | 0.669 | 1910 | -0.03 | 0.474 | 959 | 16.6% | -0.19 [-0.23 , -0.15] |
| DHSS England 1969 | -0.3 | 0.652 | 654 | -0.14 | 0.481 | 557 | 7.3% | -0.16 [-0.22 , -0.10] |
| DHSS Scotland 1969 | -0.19 | 0.615 | 258 | 0.02 | 0.571 | 223 | 2.7% | -0.21 [-0.32 , -0.10] |
| Beal 1971 | -0.23 | 0.63 | 306 | -0.08 | 0.533 | 223 | 3.0% | -0.15 [-0.25 , -0.05] |
| Kunzel 1997 | -0.2 | 0.311 | 3726 | -0.03 | 0.369 | 1312 | 60.1% | -0.17 [-0.19 , -0.15] |
| Beal 1981 | -0.17 | 0.581 | 361 | -0.06 | 0.517 | 367 | 4.7% | -0.11 [-0.19 , -0.03] |
| **Subtotal (95% CI)** | | | **8094** | | | **4289** | **100.0%** | **-0.17 [-0.19 , -0.15]** |
| Heterogeneity: Tau² = 0.00; Chi² = 5.62, df = 7 (P = 0.58); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 19.27 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 2.39, df = 1 (P = 0.12), I² = 58.2% | | | | | | | | |



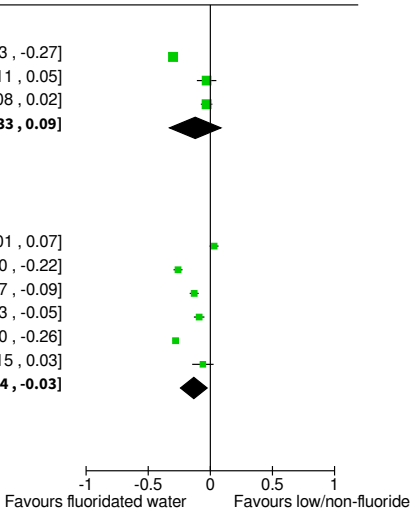

**Footnotes**

[a]Guo 1984 commenced in 1971; possibility of fluoridated toothpaste being introduced during study period

Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 8: Sensitivity analysis - all included studies: change in the proportion of caries-free participants (primary teeth)

**Analysis 1.9**

| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.9.1 Studies conducted after 1975** | | | | | | | | |
| Guo 1984[a] | 0.06 | 0.617 | 3657 | 0.36 | 0.684 | 4497 | 33.9% | -0.30 [-0.33 , -0.27] |
| Blinkhorn 2015 | -0.08 | 0.68 | 710 | -0.05 | 0.65 | 446 | 32.5% | -0.03 [-0.11 , 0.05] |
| Goodwin 2022 | -0.81 | 0.43 | 570 | -0.78 | 0.38 | 622 | 33.6% | -0.03 [-0.08 , 0.02] |
| **Subtotal (95% CI)** | | | **4937** | | | **5565** | **100.0%** | **-0.12 [-0.33 , 0.09]** |
| Heterogeneity: Tau² = 0.03; Chi² = 117.40, df = 2 (P < 0.00001); I² = 98% | | | | | | | | |
| Test for overall effect: Z = 1.15 (P = 0.25) | | | | | | | | |
| **1.9.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Adriasola 1959 | 0 | 0.192 | 356 | -0.03 | 0.219 | 204 | 16.9% | 0.03 [-0.01 , 0.07] |
| Brown 1965 | -0.28 | 0.507 | 1097 | -0.02 | 0.328 | 1032 | 16.9% | -0.26 [-0.30 , -0.22] |
| DHSS Wales 1969 | -0.08 | 0.655 | 1833 | 0.05 | 0.38 | 1390 | 16.9% | -0.13 [-0.17 , -0.09] |
| DHSS England 1969 | -0.16 | 0.469 | 939 | -0.07 | 0.422 | 761 | 16.8% | -0.09 [-0.13 , -0.05] |
| Kunzel 1997 | -0.22 | 0.417 | 6690 | 0.06 | 0.502 | 2421 | 17.1% | -0.28 [-0.30 , -0.26] |
| Beal 1981 | -0.11 | 0.686 | 369 | -0.05 | 0.489 | 367 | 15.5% | -0.06 [-0.15 , 0.03] |
| **Subtotal (95% CI)** | | | **11284** | | | **6175** | **100.0%** | **-0.13 [-0.24 , -0.03]** |
| Heterogeneity: Tau² = 0.02; Chi² = 258.15, df = 5 (P < 0.00001); I² = 98% | | | | | | | | |
| Test for overall effect: Z = 2.43 (P = 0.02) | | | | | | | | |
| Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0% | | | | | | | | |



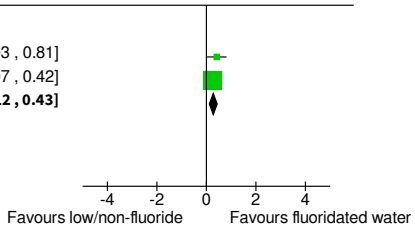

**Footnotes**

[a]Guo 1984 commenced in 1971; possibility of fluoridated toothpaste being introduced during study period

Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 9: Sensitivity analysis - all included studies: change in the proportion of caries-free participants (permanent teeth)

**Analysis 1.10**

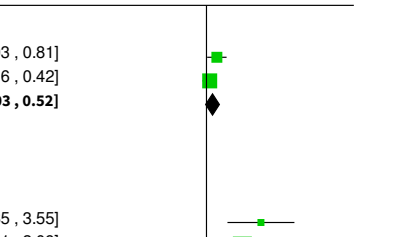
| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.10.1 Studies conducted after 1975** | | | | | | | | |
| Blinkhorn 2015 | 1.3 | 3.49 | 813 | 0.88 | 3.77 | 568 | 16.4% | 0.42 [0.03 , 0.81] |
| Goodwin 2022 | -0.489 | 1.402 | 609 | -0.737 | 1.964 | 835 | 83.6% | 0.25 [0.07 , 0.42] |
| **Subtotal (95% CI)** | | | **1422** | | | **1403** | **100.0%** | **0.28 [0.12 , 0.43]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 3.41 (P = 0.0006) | | | | | | | | |
| Test for subgroup differences: Not applicable | | | | | | | | |




Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 10: Sensitivity analysis - change in analytical approach: change in the number of decayed, missing or filled primary teeth (dmft)

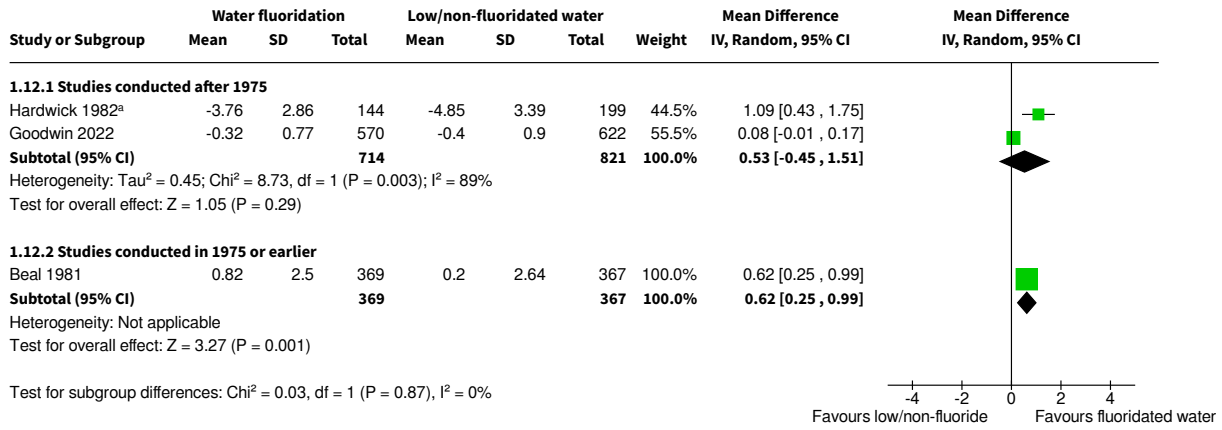
**Analysis 1.11**

| Study or Subgroup | Water fluoridation Mean | SD | Total | Low/non-fluoridated water Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **1.11.1 Studies conducted after 1975** | | | | | | | | |
| Blinkhorn 2015 | 1.3 | 3.49 | 813 | 0.88 | 3.77 | 568 | 39.3% | 0.42 [0.03 , 0.81] |
| Goodwin 2022 | 0.57 | 2.61 | 654 | 0.44 | 3.17 | 873 | 60.7% | 0.13 [-0.16 , 0.42] |
| **Subtotal (95% CI)** | | | **1467** | | | **1441** | **100.0%** | **0.24 [-0.03 , 0.52]** |
| Heterogeneity: Tau² = 0.01; Chi² = 1.36, df = 1 (P = 0.24); I² = 26% | | | | | | | | |
| Test for overall effect: Z = 1.72 (P = 0.09) | | | | | | | | |
| **1.11.2 Studies conducted in 1975 or earlier** | | | | | | | | |
| Adriasola 1959 | 2.5 | 7.04 | 263 | 0.3 | 6.72 | 157 | 18.2% | 2.20 [0.85 , 3.55] |
| Beal 1981 | 2.02 | 4.18 | 361 | 0.57 | 4.6 | 367 | 81.8% | 1.45 [0.81 , 2.09] |
| **Subtotal (95% CI)** | | | **624** | | | **524** | **100.0%** | **1.59 [1.01 , 2.16]** |
| Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 1 (P = 0.33); I² = 0% | | | | | | | | |
| Test for overall effect: Z = 5.39 (P < 0.00001) | | | | | | | | |
| Test for subgroup differences: Chi² = 16.89, df = 1 (P < 0.0001), I² = 94.1% | | | | | | | | |




Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 11: Sensitivity analysis - excluding studies with imputed standard deviations: change in the number of decayed, missing or filled primary teeth (dmft)

**Analysis 1.12**




**Footnotes**

[a]Baseline examinations were completed by end of 1974, fluoridation started in 1975 with a possibility of fluoridated toothpaste being introduced during the study period.

Comparison 1: Initiation of water fluoridation compared with low/non-fluoridated water, Outcome 12: Sensitivity analysis - excluding studies with imputed standard deviations: change in the number of decayed, missing or filled permanent teeth (DMFT)