

Water fluoridation for the prevention of dental caries (Protocol)

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[Intervention Protocol]

Water fluoridation for the prevention of dental caries

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

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

The original systematic review (McDonagh 2000) included five objectives. For the purposes of the current review, the original objectives 1 to 3 will be covered by objective 1 (above). The fourth objective will be covered by objective 2 (above) and the fifth objective which explored the differential effects of natural and artificial fluoridation is not covered in the current review.

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 (cavitated dental

caries), impairing its function (Ten Cate 1991). Despite reductions in the prevalence and severity of dental caries over time (CDC 2005), social inequalities in dental health persist (OECD 2011), with significant numbers of individuals and communities having a clinically significant burden of preventable dental disease. Dental caries is associated with pain, infection, tooth loss and reduced quality of life (Sheiham 2005). In children, the burden of dental disease also includes lost school time and restricted activity days, as well as problems in eating, speaking and learning. This especially affects those from lower income families owing to their higher prevalence of caries (Feitosa 2005). Given the progressive nature

of the condition and widespread prevalence in adulthood, most children are at risk of dental caries.

Clinical need and burden of disease

Dental caries is a major public health problem in most industrialised countries, affecting 60% to 90% of school children (Petersen 2003). It has been estimated that in the United States (US) 42% of children 2 to 11 years of age have caries experience in their primary teeth and 59% of those aged 12 to 19 years have caries experience in their permanent teeth (Dye 2007). Prevalence studies in South America, Asia and Europe have indicated that caries may affect between 20% and 100% of the population (Bagramian 2009). Increasing levels of dental caries are observed in some developing countries, especially those where community-based preventive oral care programmes are not established (Petersen 2004). Studies also suggest that the growing retention of teeth has also been accompanied by a rise in dental caries among ageing adults in different parts of the world (Selwitz 2007). This has major implications especially in high-income countries experiencing an increase in life expectancy.

Description of the intervention

Fluoride is 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 United States, ground waters have been found to contain particularly high concentrations of fluoride (up to 6.9 parts per million (ppm)) (WHO 2006). Water that is artificially fluoridated (also known as community water fluoridation) is set at the 'optimum level', considered to be around 1 ppm (Dean 1941; WHO 2011). The European Union water quality directive specifies 1.5 ppm as the maximum level for human consumption (European Union 1998). Community water fluoridation was initiated in the US in 1945 and is currently practiced in about 39 countries around the world (Browne 2005). It is considered 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 United States, over 70% of the population on public water systems receive fluoridated water (CDC 2008) as do a similar proportion of Australians (NHMRC 2007). The rationale behind the role of community water fluoridation is that it benefits both children and adults by effectively preventing caries, regardless of socioeconomic status or access to care. It is believed to have played an important role in the reductions in tooth decay (40% to 70% in children) and of tooth loss in adults (40% to 60%) in the US (Burt 1999). Fluoridation (natural or artificial) is an intervention occurring at the environmental level meaning individual compliance is not relied upon. Interventions at this level can have greater impact upon populations than those at the individual and clinical levels (Frieden 2010).

How the intervention might work

Fluoride impedes the demineralisation of the enamel and also enhances its remineralization (Ten Cate 1991). This function is very important in caries prevention as the progression of cavities depends on the balance of the demineralisation and remineralisation processes (Selwitz 2007). The presence of fluoride in drinking water therefore confers the advantage of providing a constant exposure to fluoride ions in the oral cavity. The effectiveness of fluoridated water (artificially or naturally) is well documented (McDonagh 2000; NHMRC 2007; Truman 2002) and alternative fluoride sources such as toothpastes and varnishes have also been proven to be effective (Marinho 2013; Walsh 2010). Some adverse effects of fluoridated water that have been explored are widely perceived to be dependent on dose, duration and/or time of exposure (Browne 2005). Supra-optimal levels of fluoride (occurring naturally) have been linked to severe dental fluorosis and skeletal fluorosis. 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 (Pendry 2001). It can appear on the teeth as white flecks, brown staining or pitting of the enamel and in severe cases could cause aesthetic concern. Other postulated harms such as thyroid cancer, goitre and Down's syndrome are supported by studies lacking in quality and have shown no evidence of strong association with water fluoridation (McDonagh 2000). The need for reduced incidence of adverse outcome due to high levels of fluoride exposure has resulted in recommendation of optimum water fluoride levels to minimise potential harms while maximising the benefits of fluoridation.

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, including the World Health Organization (MRC 2000). It has been hailed by the US Surgeon General as "one of the most effective choices communities can make to prevent health problems while actually improving the oral health of their citizens" (ADA 2013). Despite evidence of effectiveness, opponents have raised concerns about ethical issues and its potential harms (Cheng 2007), as a result of which the practice has remained controversial in some quarters. A comprehensive systematic review of water fluoridation has previously been published (McDonagh 2000). The review showed a benefit in terms of a reduction in caries as well as an increased risk of dental fluorosis. However, there was insufficient high quality evidence to draw conclusions with regard to other potential harms or health disparities. The review findings have often been misinterpreted and have been used to support arguments on both sides of the water fluoridation debate (Cheng 2007). Given the continued interest in this topic, from both health professionals, policy makers and the public, it is important to up-

date and maintain a systematic review of the available evidence. This review is being undertaken in collaboration with the Centre for Reviews and Dissemination of the University of York, United Kingdom as an update for their review published in 2000 (McDonagh 2000). It has also formed the development of a community guide, funded by the US Centers for Disease Control and Prevention (www.cdc.gov).

OBJECTIVES

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

The original systematic review (McDonagh 2000) included five objectives. For the purposes of the current review, the original objectives 1 to 3 will be covered by objective 1 (above). The fourth objective will be covered by objective 2 (above) and the fifth objective which explored the differential effects of natural and artificial fluoridation is not covered in the current review.

METHODS

Criteria for considering studies for this review

Types of studies

For objective 1

For caries data, only prospective studies with a concurrent control, comparing at least two populations, one receiving fluoridated the other non-fluoridated water and at least two points in time evaluated, will be included. For the purposes of this review, water with a fluoride concentration of less than 0.4 parts per million (ppm) or less (arbitrary cut-off) will be classified as non-fluoridated.

For objective 2

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

Types of participants

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

Types of interventions

For objective 1

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

For objective 2

Fluoride at any concentration present in drinking water.

Types of outcome measures

Primary outcomes

Any measure of dental caries including.

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

An a priori set of rules regarding the prioritisation of caries measures has been developed previously (Marinho 2013). These will be adopted for this review.

Secondary outcomes

Any measure of dental fluorosis including.

- Percentage of fluorosed children.
- Dean's Fluorosis Index.
- TSIF (Tooth Surface Index of Fluorosis).
- TFI (Thylstrup and Fejerskov index).
- Modified DDE (Developmental Defects of Enamel).

If available, we will record the prevalence of fluorosis for each tooth type. In measuring the percentage prevalence of fluorosis, all children with fluorosis according to the index used will be classified as 'fluorosed' as opposed to normal. As measured by the common epidemiologic indices for dental fluorosis (Rozier 1994), children with a DDE, TSIF, TFI score greater than zero or Dean's classification of 'questionable' or higher will be classified as fluorosed. If the other indices are used, the percentage prevalence of fluorosis as reported by the original investigators using other methods (e.g. photographic method or other index) will be considered

and adopted. Any fluorosed teeth scored ≥ 3 (TFI), ≥ 2 (TSIF) and 'mild' or worse (Dean's) will be considered to be of aesthetic concern. Analysis on dental fluorosis of aesthetic concern will be restricted to TFI, TSIF and Dean's indices as it is not easily determined from the modified DDE index.

Data on any other negative effects (e.g. skeletal fluorosis, hip fractures, cancer, congenital malformations, mortality) reported in the included studies will also be recorded. The above inclusion criteria are the same as the criteria stated in [McDonagh 2000](#) and have been adopted since this review is an update of [McDonagh 2000](#).

Search methods for identification of studies

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

For the identification of studies included or considered for this updated review, we will develop detailed search strategies combining controlled vocabulary and free text terms for each database searched. These will be based on the search strategy developed for MEDLINE ([Appendix 2](#)) but revised appropriately for each database to take account of differences in controlled vocabulary and syntax rules.

Electronic searches

We will search the following electronic databases.

- The Cochrane Oral Health Group's Trials Register (to date).
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, current issue).
- MEDLINE via OVID (1999 to date) ([Appendix 2](#)).
- EMBASE via OVID (1999 to date).
- Proquest (to date).
- Web of Science Conference Proceedings (1995 to date).
- ZETOC Conference Proceedings (1993 to date).

Searches will be conducted from the date of search in the original review (1999) for the databases which searched up to that date. Searches of Proquest, ZETOC and Web of Science Conference Proceedings will be conducted from database inception. There will be no restrictions on language of publication and non-English studies will be translated, unless a translator cannot be found through The Cochrane Collaboration.

Searching other resources

We will conduct handsearching as part of the Cochrane Worldwide Handsearching Programme (see the [Cochrane Masterlist](#) for the details of journals searched to date). In addition, we will review the reference lists of identified trials and review articles for additional appropriate studies.

Data collection and analysis

Selection of studies

Two review authors independently and in duplicate will screen the titles and abstracts (when available) of all reports identified through the electronic search update. For all studies appearing to meet the inclusion criteria, or for which there are insufficient data in the title and abstract to make a clear decision, we will obtain the full report. The full reports obtained from the electronic and other methods of searching will again be assessed independently by two review authors to establish whether the studies do meet the inclusion criteria or not. Disagreements will be resolved by discussion. Where resolution is not possible, a third review author will be consulted. Studies rejected at this or subsequent stages will be recorded in the 'Characteristics of excluded studies' table, and reasons for exclusion recorded.

Data extraction and management

Two review authors will extract data independently using specially designed data extraction forms (produced in Excel). The data extraction forms will be piloted on several papers and modified as required before use. Any disagreements will be discussed and a third review author consulted where necessary.

For each study the following data will be recorded.

- Year of publication, country of origin and source of study funding.
- Details of the participants including demographic characteristics (socio-economic status (SES), ethnicity), deciduous/permanent dentition and criteria for inclusion and exclusion.
- Details of the type of intervention, comparator and co-interventions.
- Details of the outcomes reported, including method of assessment, and time intervals.
- Details of confounding factors considered (potential confounders of relevance to this review include sealant use, life-time exposure to fluoridated water, sugar consumption, SES, ethnicity and the use of other fluoride sources).
- Details on comparability of groups with regard to confounding factors.
- Details on methods used to control for confounding.
- Details regarding both unadjusted and adjusted effect estimates.

Assessment of risk of bias in included studies

[McDonagh 2000](#) used specially designed validity assessment checklists, providing a 'validity score' and assigning a 'level of evidence' for each study. In this update, all included studies (including those from the previous review by [McDonagh 2000](#)) will be

assessed for risk of bias by two review authors using the Cochrane risk of bias assessment tool for non-randomised controlled studies (Higgins 2011). Domains assessed for each included study are: sequence generation, allocation concealment, confounding, blinding of outcome assessment, completeness of outcome data, risk of selective outcome reporting and risk of other potential sources of bias. For the primary outcome the following factors have been identified as important confounders: other sources of fluoride, social class, ethnicity and residential history, while the use of other fluoride sources is the only confounder considered to be relevant to the secondary outcome.

A description of the risk of bias domains will be tabulated for each included trial, along with a judgement of low, high or unclear risk of bias.

A summary assessment of the risk of bias for the primary outcome (across domains) across studies will be undertaken (Higgins 2011). Within a study, a summary assessment of low risk of bias will be given when there is a low risk of bias for all key domains, unclear risk of bias when there is an unclear risk of bias for one or more key domains, and high risk of bias when there is a high risk of bias for one or more key domains.

Measures of treatment effect

For dichotomous outcomes, we will calculate risk ratios for differences in the intervention and comparison groups, along with appropriate 95% confidence intervals for all prospective studies. For continuous outcomes, we will calculate the mean difference and 95% confidence intervals where means and standard deviations are presented or are calculable. Where a continuous outcome is measured using different scales, the standardised mean difference and standard deviations will be calculated.

Where both adjusted and unadjusted results are presented for non-randomised studies, the unadjusted value will be used for analysis. The particular (as well as number of) factors adjusted for will be recorded for each study.

Unit of analysis issues

Studies which allocate by 'cluster' will be assessed for unit of analysis error. If a unit of analysis error exists, and re-analysis is not possible, we will report only point estimates and no confidence intervals or P values. Where re-analysis is possible, we will follow the methods outlined in Chapter 16.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

Where outcome data are missing from the published report, or cannot be calculated from the information presented in the report of a trial, we will attempt to contact the authors to obtain the data and clarify any uncertainty. The analyses will generally include only the available data (ignoring missing data), however, we

will use methods for estimating missing standard deviations from section 7.7.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) if appropriate. Otherwise we will not undertake any imputations.

Assessment of heterogeneity

Differences in fluoridation technique, fluoride concentration, outcome measurement index and technique have all been identified as possible sources of heterogeneity. Initial consideration of heterogeneity will be via the DerSimonian-Laird model (commonly referred to as a random-effects meta-analysis). When between study variance is deemed to be both robustly estimated and substantial (judged as the estimate being larger than twice its standard error), the random-effects model will be favoured over a fixed-effect approach. Any heterogeneity will be further investigated via Baujat and normal quantile-quantile (Q-Q) plots, alongside influence diagnostics (for example DFFITS, Cook's distance, hat values and leave-one-out methods) as appropriate.

Assessment of reporting biases

If more than 10 trials are identified for any meta-analysis, publication bias will be assessed according to the recommendations as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Should asymmetry be identified in the contour enhanced funnel plots, possible causes will be investigated.

Data synthesis

Meta-analyses will be conducted when sufficient studies are identified. Risk ratios will be combined for dichotomous data and mean differences combined for continuous data. Meta-analytic fixed-effect and random-effects models (with or without moderators) will be obtained via the linear (mixed-effects) model. In the case of random-effects, the DerSimonian-Laird estimator for the amount of (residual) heterogeneity will be utilised. Appropriate adjustments to the test statistics and confidence intervals due to the uncertainty in the estimate of the (residual) heterogeneity will be undertaken by application of the method by Knapp and Hartung (Knapp 2003).

The primary analyses will be based on all included studies, irrespective of risk of bias (see 'Sensitivity analysis'). Tables indicating the general effect of fluoridation found in each study will be created for each outcome, and where possible, the point estimate and a measure of statistical significance (using the 95% confidence interval or P value) of the finding will also be included.

Subgroup analysis and investigation of heterogeneity

Since the data from non-randomised studies are more prone to bias and are often heterogeneous (Loke 2007), separate meta-analyses will be undertaken (where appropriate) and results presented according to different study designs. Where possible, meta-regression will be used to investigate and explain sources of heterogeneity among studies (potential confounders of relevance to this review include sealant use, life-time exposure to fluoridated water, sugar consumption, SES, ethnicity and the use of other fluoride sources). Dental caries results will be analysed using meta-regression in order to assess the impact of potential sources of heterogeneity and estimate the underlying effect of water fluoridation. The heterogeneity among fluorosis studies will be explored by including variables that may account for the observed heterogeneity in the regression model. Since fluoride concentrations of control (non-fluoridated) groups across studies has been highlighted as a potential source of heterogeneity, a subgroup analysis of studies where the control group has fluoride concentration of 0.2 ppm or less will be undertaken.

Sensitivity analysis

Provided sufficient trials are included, we will undertake sensitivity

analysis based on risk of bias. Further sensitivity analysis will be undertaken to determine if the results of the meta-analysis are influenced by the timing of baseline measurement, as appropriate.

Presentation of main results

A 'Summary of findings' table will be developed for the primary and secondary outcomes of this review using GRADEPro software. The quality of the body of evidence will be assessed with reference to the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates, the risk of publication bias, the magnitude of the effect and whether or not there is evidence of a dose response.

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* Indicates the major publication for the study

APPENDICES

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

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

Appendix 2. MEDLINE via OVID search strategy

1. Fluoridation/
2. exp Fluorides/
3. Fluorine/
4. (fluorid\$ or fluorin\$ or flurin\$ or fluid\$).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 deminerali\$ or reminerali\$)).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)

CONTRIBUTIONS OF AUTHORS

All authors contributed equally to the writing of the protocol and will complete the review.

DECLARATIONS OF INTEREST

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Disclaimer:

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