Canadian Agency for Drugs and Technologies in Health

HTA

HEALTH TECHNOLOGY INQUIRY SERVICE (HTIS)

TITLE: Fluoridated Water for Cavity Prevention: A Review of the Clinical-Effectiveness, Cost-Effectiveness, and Guidelines

DATE: 22 May 2009

CONTEXT AND POLICY ISSUES:

Water fluoridation has been used to reduce the incidence of tooth decay for sixty years.[1] It is endorsed by Health Canada, the World Health Organization, the US Centres for Disease Control and Prevention (CDC),[1] and over 90 other health agencies or professional associations.[2] Water fluoridation is considered by the scientific community to be safe, effective and economical however fluoridation continues to be met with resistance.[3]

Fluoride occurs naturally in air, soil, water, and food. Supplemental fluoride can be supplied at a population level in water, milk, or salt, or at an individual level as drops, tablets, rinses, varnish, or in toothpaste.[4] When provided at a population level, all socioeconomic sectors of the population can be reached, particularly those with limited access to preventative dentistry. The effectiveness of fluoride supplementation for cavity prevention at an individual level may be reduced by poor compliance or limited access.[4] Fluoride in dental plaque or saliva prevents the demineralization of tooth enamel and promotes remineralization.[1] Although the protective action of fluoride is thought to be mainly topical (after tooth eruption), there are also benefits from systemic exposure before tooth eruption.[1]

There are three compounds used to fluoridate water; sodium hexafluorosilicate, flurosilicic acid, and sodium fluoride.[4] The concentration of fluoride considered optimal for prevention of caries differs according to region and depends on the local climate and average water consumption volumes.[4] In Canada, the optimal fluoride concentration is 0.8 mg/L to 1.0 mg/L.[2] Fluoride is known to cause dental fluorosis, an opaque discoloring of the teeth. Mild fluorosis may be of little or no aesthetic concern to the patient. Severe fluorosis results in pitting and staining of the tooth surface.[4]

The cost of dental care in Canada was $9.9 billion in 2006.[1] A review of the costs, benefits, and safety of water fluoridation will help inform decisions to initiate or to continue with this public health intervention.

RESEARCH QUESTIONS:

1. What is the evidence for the clinical benefit and safety of fluoridated water for cavity prevention?
2. What is the cost-effectiveness of fluoridated water for cavity prevention?
3. What are the guidelines for methods to deliver fluoride for cavity prevention?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 2, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2004 and April, 2009 with exception of randomized controlled trials (RCTs). The search for RCTs was restricted to 2006 and April, 2009 publications dates. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, RCTs, economic studies, and guidelines.

Studies were selected if they assessed communities (adults or children) with fluoridated water compared to those with no or low levels of fluoridation. Relevant outcomes were dental caries, harms (for example, fluorosis, cancer, fractures) or cost-effectiveness. Study designs included were health technology assessments, systematic reviews, meta-analyses, RCTs, or economic studies. Reasons for study exclusion are listed in Appendix 1.

Measures of dental caries included the number of decayed missing or filled teeth (DMFT), decayed missing or filled tooth surfaces (DMFS), or percentage of caries free children. Other measures included the prevention fraction (defined as the mean increment in controls minus mean increment in treated group divided by the mean increment in control).

Evidence based guidelines were included if they assessed water fluoridation or other methods to deliver fluoride for cavity prevention and included a description of the methods used to search and evaluate the literature, and to develop recommendations.

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, systematic reviews, and meta-analyses are presented first. These are followed by economic evaluations, and evidence-based guidelines.

SUMMARY OF FINDINGS:

Two systematic reviews,[4,5] two economic evaluations[6,7] and one guideline[8] met the inclusion criteria. No relevant health technology assessments or RCTs were identified.

Systematic reviews and meta-analyses

A 2007 comprehensive review by Coleman et al. was commissioned by the Australian Government to evaluate the effectiveness and safety of topically applied fluoride or fluoride added to water, milk, or salt.[4] For this HTIS report, only the data regarding water fluoridation is summarized (Appendix 2, Table 1). The systematic review compared communities with water fluoridation to those with low or no fluoride in the water. Six systematic reviews were identified in the literature search. The systematic review by McDonagh et al. published in 2000 was

considered by Coleman et al. to be the most relevant, comprehensive, and of good methodological quality, and was used as the basis of 2007 systematic review. The literature search by McDonagh et al. was updated by Coleman et al. for each research question and any additional primary studies were summarized.[4]

For the prevention of dental caries, McDonagh et al. included 26 studies on fluoridated water (before-after, prospective cohort, and retrospective cohort). One additional study was found by Coleman et al. The results of this study did not change the conclusions in the McDonagh review. Separate analyses were conducted by tooth type (primary or permanent) and by age group. The percentage of caries-free children was statistically significantly higher in 20 of 30 analyses when water fluoridation was compared to no fluoridation. Seven of 30 analyses showed a non-significant increase and three showed a non-significant decrease in the percentage of caries-free children. The change in proportion of caries-free children was pooled. The mean difference was significantly different ($p<0.001$) favoring fluoridation [15.4% (95% confidence interval (CI) 10.8%, 20.1% unadjusted); 14.3% (95% CI 6.7%, 21.9%) adjusted for tooth type, setting, study duration, baseline % caries free, and validity score]. The number needed to treat (NNT) to prevent one additional person from developing caries was 6 (95% CI 5, 9). The mean difference in the DMFT score was 2.3 (95% CI 1.8, 2.8; $p<0.001$) suggesting that fluoridation is strongly associated with improvement in DMFT scores. This analysis however, did not take into account other sources of fluoridation such as toothpaste.[4]

McDonagh et al. also studied the impact on caries when fluoridation was discontinued. In 14 of 22 analyses, cessation of fluoridation resulted in a narrowing of differences in caries between groups. This difference was statistically significant in one analysis.[4]

The McDonagh report included 88 studies evaluating dental fluorosis (cross sectional, before and after, and case-control studies). Ten additional studies identified by Coleman et al. provided supplemental data. The results showed a statistically significant relationship between level of fluoride in water and the prevalence of fluorosis, with increasing prevalence as the fluoride concentration increased. The odds of any fluorosis (mild to severe) was two times higher in fluoridated compared to non-fluoridated areas [odds ratio (OR) 2.05, 95% CI 1.75, 2.39, $p<0.05$]. The OR for fluorosis of aesthetic concern in fluoridated versus non-fluoridated areas was 2.29 (95% CI 1.69, 3.12), $p<0.05$. An increase in water fluoride levels from 0.4 ppm to 1.0 ppm would lead to one addition person with fluorosis of aesthetic concern for every 22 people. The confidence intervals for the number needed to harm (NNH) analysis include zero so it is possible that there is no increase in risk. Data from the 10 additional studies showed a four fold increase in the risk of fluorosis of aesthetic concern with optimal fluoridation (0.8 ppm to 1.2 ppm) compared to suboptimal fluoridation (<0.4 ppm). The absolute difference in fluorosis increased by approximately 4% to 5%.[4]

In the McDonagh review, 29 studies were included in the assessment of fracture risk and fluoridation (ecological, retrospective and prospective cohort, and case-control studies). Three additional studies were identified by Coleman et al. Comparing fluoridation levels near 1 ppm to those with the lowest fluoride levels, the pooled estimate for hip fracture was 1.00 (95% CI 0.94, 1.06) indicating no difference between groups. Data for any fracture was similar with both levels of fluoridation, with no consistent evidence of harm or protective effects.[4]

The McDonagh review found no clear association between water fluoridation and overall cancer incidence or mortality, bone cancers, osteosarcoma, or thyroid cancer. The review included 26 studies (ecological, before and after, and case control studies) that compared areas with no fluoridation to those with natural or artificial fluoridation, including areas with fluoride levels

much higher than considered optimal for prevention of caries. The studies showed trends towards both increased and decreased risk of cancer however the studies were generally rated as poor quality and some failed to adjust for confounders. Four more recent studies were identified by Coleman et al. however these had methodological flaws. There was insufficient evidence to draw conclusions regarding other risks assessed (Down's syndrome, Alzheimer's disease, impaired mental function, or goitre).[4]

The systematic review by Griffin et al.[5] evaluated the effectiveness of water fluoridation and self- or professionally applied topical fluoride in preventing cavities in adults (Appendix 2 Table 2). Their report included 20 studies, nine of which addressed water fluoridation (n=7853). These nine studies compared communities with fluoridated water (0.7 to 3.5 ppm) to those without fluoridation in Canada (1), US (4), Europe (3) and Australia (1). One study was a prospective cohort and the others were cross sectional in design. When data was pooled, adults living in communities with water fluoridation had fewer coronal caries than controls ($p<0.001$). The relative risk of caries was 0.65 (95% CI 0.49, 0.87) for adults who were lifelong residents of fluoridated versus non-fluoridated communities. The prevented fraction for water fluoridation was 27% (95% CI 19%, 34%).[5]

Compared to controls, any fluoride intervention (water fluoridation, fluoride toothpaste, gel, varnish, or rinse) reduced the number of coronal caries among all adults (≥ 20 years) and those ≥ 40 years ($p<0.001$), and reduced the number of root caries among adults ≥ 40 years ($p<0.001$). When studies published after 1980 were pooled, any fluoride intervention averted 0.29 (95% CI 0.16, 0.42) coronal caries and 0.22 (95% CI 0.08, 0.37) root caries per year. The study's authors stated that these finding suggest fluoride reduces caries among adults.[5]

Economic evaluations

Goldsmith et al.[7] conducted a systematic review of economic evaluations of various public health interventions. Eleven economic evaluations (with 13 analyses) of water fluoridation published between 1973 and 2001 were included [Canada (1 study); Australia, New Zealand or Europe (7); US (3)]. Methodological quality varied, with more recent studies rated as higher quality. Analyses were conducted from both the payer and the societal perspective, and differed in design and effectiveness measures.[7]

All studies indicated that water fluoridation is a cost-saving intervention.[7] The eight cost-benefit analyses reported strong cost-savings with fluoridation. Savings were linked to community size with larger communities showing higher savings. One cost-utility and one cost-effectiveness analyses reported significant cost-savings and negative cost-utility or cost-effectiveness ratios (i.e., fluoridation was more effective and less costly than comparator). Three cost-effectiveness analyses showed small positive cost-effectiveness ratios (i.e., fluoridation more costly and more effective than comparator). The cost-utility ratio reported in the Canadian study was C$-20.64 per quality adjusted tooth-year, indicating that water fluoridation was cost-saving compared to no community water fluoridation.[7]

O'Connell et al.[6] developed a model to evaluate the costs and treatment savings of water fluoridation in Colorado US. Fluoridation costs included one-time fixed costs and annual operating costs to increase community water fluoride levels to those recommended by the CDC. Annual treatment savings included the costs of dental care avoided with fluoridation. Dental costs included the direct medical cost for restoration and the patient time spent for the dental visit. The estimate of dental decay avoided was obtained from the literature and was calculated for those aged 5 years and up, in permanent teeth only. Age-specific reductions in tooth decay

were matched to the Colorado population. Costs were calculated in 2003 US dollars and discounted at 3%. The analysis took a societal perspective. The authors did not include costs of any adverse events of fluoridation. Sensitivity analyses were conducted to test the model assumptions. The results showed that water fluoridation was associated with net savings of $60.78 per person (range $46.97 to $76.41). The ratio of benefits (savings) to costs varied from $21.82 for small water systems to $135.00 for large systems. The results were most sensitive to changes in the estimates of water fluoridation effectiveness.[6] The authors concluded that water fluoridation is cost saving to Colorado and additional savings and reductions in morbidity could be achieved if fluoridation was implemented in other communities with low natural fluoride levels.

Guidelines

The Scottish Intercollegiate Guidelines Network (SIGN) developed guidelines on the prevention and management of dental decay in pre-school children (Appendix 2, Table 3).[8] The guideline development group conducted a systematic review of the literature to evaluate the impact of diet and nutrition, tooth brushing and fluoride toothpaste, community and practice based prevention, and practice based management on dental decay. Draft guidelines under went internal and external peer review before publication in 2005.[8]

The guidelines endorse the use of fluoride toothpaste based on high levels of evidence (grade A) and topical fluoride varnish based on grade B evidence. The guidelines do not endorse the use of fluoride supplements (tablets, fluoride in salt or milk) in pregnant women (grade B) or as a public health measure (grade D). Fluoride supplements should be prescribed by dental practitioners on an individual bases (grade D).[8]

The guideline development group did not make a specific recommendation on water fluoridation but stated the review of the literature showed that water fluoridation increased the proportion of children without caries but increased the incidence of fluorosis. There was no clear evidence of other adverse effects. The guideline development group agreed that a study should be conducted in a community in Scotland to evaluate the benefits and risks of water fluoridation.[8]

Limitations

The most appropriate study design to answer questions of effectiveness for interventions implemented at an individual level (for example, fluoride drops, rinse or toothpaste) is the randomized controlled trial. For interventions implemented at a population level, however, prospective cohort studies are most suitable. It is preferable if the intervention (for example addition or removal of fluoride to water) is implemented within a short time of the beginning of the study, and the effect of the intervention is measured at different time points (baseline and at the end of follow up). Other study designs such as cross sectional or case-control studies may also provide useful information on effectiveness or harms, however these study designs are more prone to bias. The systematic reviews of water fluoridation used the highest level evidence available however there were relatively few prospective cohort studies. Not all of the studies included in the systematic reviews adjusted for confounders which may have a substantial impact on the results. These studies should be interpreted with caution. Confounders such as the use of fluoride toothpaste, fluoride supplements, or water consumption volumes are related to total fluoride exposure and therefore influence both effectiveness and adverse effects. In many of the meta-analyses conducted, statistical heterogeneity was detected.

Assessment of fluorosis is subjective. Not all studies blinded assessors to the patient's fluoride exposure. The fluorosis indices used also measure opacities that may not be caused by fluoride therefore overestimating the prevalence. The quality of the studies available was generally poor for the assessment of cancer risk, and insufficient to draw any conclusions for some other adverse effects.

Some of the studies were decades old. The overall incidence of dental caries has been declining in more recent studies,[1,7] thus the reductions in dental caries observed in older studies may not be generalizable to the current population.

The search identified only one economic evaluation conducted in Canada. Due to differences in costs and health systems, the generalizability of economic evaluations from other countries is limited.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

The studies identified showed that water fluoridation reduces the incidence of dental caries in adults and children. A relationship between level of fluoride in water and the prevalence of fluorosis was reported, with increasing prevalence as the fluoride concentration increases. No clear association could be detected between water fluoridation and fractures or cancer in the included systematic reviews. There is insufficient data to draw any conclusions regarding other adverse effects. The economic analyses indicated that water fluoridation may be cost saving from the payer or societal perspective. The one guideline that was identified endorsed the use of fluoride toothpaste, but did not make recommendations about water fluoridation. The information about benefits and harms that were identified, the limitations to the studies, as well as the economic information should be considered when making decisions about water fluoridation.

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8. *Prevention and management of dental decay in the pre-school child: a national clinical guideline*. Edinburgh: Scottish Intercollegiate Guidelines Network (SIGN); 2005. Available: http://www.sign.ac.uk/pdf/sign83.pdf (accessed 2009 May 11).

APPENDIX 1: Excluded Studies

Study	Reason for exclusion
Yeung CA. A systematic review of the efficacy and safety of fluoridation. *Evid Based Dent* 2008;9(2):39-43. PubMed: PM18584000	Commentary on systematic review by Coleman et al.
Splieth CH, Flessa S. Modelling lifelong costs of caries with and without fluoride use. *Eur J Oral Sci* 2008;116(2):164-9. PubMed: PM18353011	Water fluoridation was not evaluated. Interventions assessed included fluoridated salt, fluoride gel, fluoride toothpaste, or biannual professional application of fluoride.
Ehsani JP, Bailie R. Feasibility and costs of water fluoridation in remote Australian Aboriginal communities. *BMC Public Health* 2007;7:100. PubMed: PM17555604	Study assessed the cost of water fluoridation but not cost-effectiveness.
Health Canada. *Findings and recommendations of the fluoride expert panel (January 2007)*. Ottawa: Health Canada; 2008. Available: http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/water-eau/2008-fluoride-fluorure/2008-fluoride-fluorure-eng.pdf (accessed 2009 Apr 29).	Did not meet criteria for evidence-based guideline (no description of methods used to develop recommendations or review literature)
Levy M, Corbeil F. *Water fluoridation: an analysis of benefits and risks: scientific advisory.* Quebec City: Institut national de santé publique du Québec (INSPQ). Available: http://www.inspq.qc.ca/pdf/publications/705-WaterFluoration.pdf (accessed 2009 Apr 29).	Literature review. Did not meet criteria for systematic review or evidence-based guideline.
Department of Health: Dental and Ophthalmic Services Division. *Choosing better oral health: an oral health plan for England*. London (UK): The Department, 2005. Available: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4123253.pdf (accessed 2009 Apr 29).	Did not meet criteria for evidence-based guideline (no description of methods used to develop recommendations or review literature)

APPENDIX 2: Details of Included Systematic Reviews and Guidelines

Table 1. Summary of Systematic Review by Coleman[4]

Title	A systematic review of the efficacy and safety of fluoridation. Part A: review of methodology and results
Author, year	Coleman *et al*. 2007[4]
Design	Systematic review and meta-analysis
Methods	Search: Medline, Embase, Cochrane Clinical Trial databases from 1996 to 2006; English language only Population: adults and children Interventions: systematic fluoride (addition to water, salt, or milk) or topical fluoride (toothpaste, gel varnish or mouthrinse) Comparator: no systemic or topical fluoride Outcomes: prevention of caries, harms (dental fluorosis, cancer, fracture or osteoporosis, or other adverse events) Study design: systematic reviews, RCTs, pseudo-RCTs, observational studies, case reports. For each research question the highest level of evidence was selected and reported. Selection/extraction: conducted by 3 reviewers
Included studies*	Report based on systematic review by McDonagh *et al*. 2000. Additional studies updated the review: prevention of caries (1 study), fluorosis (10), fracture (3), cancer (4), other harms (3).
Results* Prevention of caries	*Mean difference in proportion of caries free children*: 15.4% (95% CI 10.8%, 20.1%, p<0.001 unadjusted); 14.3% (95% CI 6.7%, 21.9%, p<0.001, adjusted for tooth type, setting, study duration, baseline % caries free and validity score) *NNT to prevent 1 additional child from developing caries:* 6 (95% CI 5, 9) *Change in DMFT score*: 2.3 (95% CI 1.8, 2.8, p<0.001 unadjusted); 2.61 (95% CI 2.31, 2.91, p value NR, adjusted for baseline DMFT, age, validity score and setting)
Fluorosis	*OR of any fluorosis*: 2.05 (95% CI 1.75, 2.39, p<0.05 unadjusted) *OR of fluorosis of aesthetic concern*: 2.29 (95% CI 1.69, 3.12, p<0.05 unadjusted) RD of fluorosis of aesthetic concern: 4.5% (95% CI -4.5%, 13.6%, p=NS) Data from 10 additional studies *OR of any fluorosis*: 4.61 (95% CI 3.48, 6.11, p<0.001 unadjusted) *OR of fluorosis of aesthetic concern*: 4.58 (95% CI 3.54, 5.93, p<0.001 unadjusted) RD of fluorosis of aesthetic concern: 5% (95% CI 3%, 7%, p<0.001)
Fracture	Hip fracture: pooled effect 1.00 (95% CI 0.94, 1.06), p=NS
Cancer	No consistent increase or decrease in risk observed.
Other harms	Insufficient evidence regarding other risks assessed (Down's syndrome, Alzheimer's disease, impaired mental function, or goitre).
Author's conclusions*	The evidence strongly suggests that water fluoridation reduces dental caries. Water fluoridation increases the prevalence of dental fluorosis however the majority of fluorosis is mild and of little aesthetic concern. Optimal water fluoridation has little impact on the risk of fractures. There is no clear association between fluoridation and cancer incidence or mortality. There is insufficient evidence to determine if water fluoridation causes any other adverse effects.
Funding, conflicts of interest reported	National Health and Medical Research Council, Australian Government No conflict of interest declarations reported in the text

CI=confidence interval; DMFT= decayed, missing or filled teeth; NNT=number needed to treat; NS=not statistically significant; OR=odds ratio; RCT=randomized controlled trial; RD=risk difference * only data relevant to water fluoridation was extracted

Table 2. Summary of Systematic Review by Griffin[5]

Title	Effectiveness of fluoride in preventing caries in adults
Author, year	Griffin 2007[5]
Design	Systematic review and meta-analysis
Methods	Search: Medline, Embase and Cochrane databases up to 2004; reference lists searched; manufacturer, FDA and American Dental Association contacted to provide additional studies. Selection/extraction: two reviewers independently screened and extracted data Population: all adults (≥20 years) or ≥40 years Interventions: fluoridated water, or fluoride toothpaste, gel varnish, or rinse Comparator: no supplemental fluoride Outcomes: coronal caries (decayed missing or filled teeth or surfaces) or root caries Study design: systematic reviews or primary studies in English (randomized or non-randomized studies of a least 1 year in duration).
Included studies	All interventions: 20 studies (n=13,551)
	Self- or clinically applied fluoride: 11 studies (10 RCTs, 1 controlled trial) n=4809
	Water fluoridation: 9 studies (1 prospective cohort, 8 cross-sectional studies) published between 1962 and 1992 Number of adults: 7853 (median 595, range 104 to 3902) Fluoride concentration in water ranged from 0.7 ppm to 3.5 ppm in fluoridated communities and 0.1 ppm to 0.7 ppm in the control communities (not reported in 3 studies). Location: Canada (1), US (4), Australia (1), Sweden (1), UK (2)
Key results	Water fluoridation reduced coronal caries compared to control among adults of all ages ($p<0.001$). The relative risk of caries was 0.65 (95% CI 0.49, 0.87) (pooled data from 7 cross sectional studies of lifelong residents of communities with and without fluoridated water). Compared to controls, any fluoride intervention reduced the number of coronal caries among all adults ($p<0.001$), and among adults ≥40 years ($p<0.001$), and reduced root caries among adults ≥40 years ($p<0.001$). Among studies published after 1980, any fluoride intervention averted 0.29 (95% CI 0.16, 0.42) coronal caries and 0.22 (95% CI 0.08, 0.37 root caries per year.
Author's conclusions	The findings suggest that fluoride prevents caries in adults of all ages. The data available was scarce and further well-designed studies are needed in adults.
Funding, conflicts of interest reported	Funded by US government agencies No conflict of interest declarations reported in the text

CI=confidence interval; FDA=Food and Drug Administration; ppm=parts per million; RCT=randomized controlled trial

Table 3. Summary of SIGN Guidelines[8]

Author, year	SIGN 2005[8]
Objectives of the guideline	To address effective strategies for preventing and managing dental decay in the pre-school child.
Country	UK
Methodology	Systematic review of the literature according to SIGN methodology (details available from www.sign.ac.uk). Search: Embase and Medline search (1996 to 2004) and Cochrane library (1990 to 2004). Websites of relevant professional associations and health technology assessment agencies. Guidelines were developed by a multidisciplinary group, and reviewed by independent expert referees and SIGN editorial group. Draft guidelines were presented at a national open meeting and posted on the internet for a one month feedback period.
Recommendation regarding water fluoridation (grade)	No specific recommendation was issued. A review of the literature showed that water fluoridation increased the proportion of children without caries but increased the incidence of fluorosis. There was no clear evidence of other adverse effects. The guideline development group agreed that a study should be conducted in a community in Scotland to evaluate the benefits and risks of water fluoridation.
Recommendation regarding fluoride supplements (fluoride drops, salt, milk) (grade)	"Fluoride supplements are not recommended as a public health measure." (D) "Fluoride supplements should only be prescribed by dental practitioners on an individual basis." (D) "Pregnant women should be advised that there is no benefit to the child of taking fluoride supplements during pregnancy." (B)
Recommendations regarding topical fluoride (toothpaste, rinses, varnish, other) (grade)	"Children should have their teeth brushed with fluoride toothpaste containing 1,000 ppm fluoride ± 10%." (A) "Children should have their teeth brushed, or be assisted with toothbrushing by an adult, at least twice a day, with a smear or pea-sized amount of fluoride toothpaste."(C) "Topical fluoride varnish should be applied to the dentition at least twice yearly for pre-school children assessed as being at increased risk of dental caries."(B) "Community or home based oral health promotion interventions should use fluoride containing agents such as fluoride toothpaste." (A) "Community based toothbrushing programmes should include fluoride toothpaste with a concentration of 1000 ppm fluoride." (A)
Grading system used	(A) At least one meta-analysis, systematic review of RCTs, or RCTs rated as high quality and directly applicable to the target population, or a body of evidence consisting of studies rated as well conducted meta-analysis, systematic reviews of RCTs or RCTs with a low risk of bias (B) A body of evidence including high quality systematic reviews of case-control or cohort studies, or high quality case-control and cohort studies (very low risk of confounding or bias and a high probability that the relationship is causal) and are directly relevant to the target population. Extrapolated data from RCTs.

	(C) A body of evidence including high quality case control or cohort studies (low risk of confounding and a moderate probability that the relationship is causal) that is directly relevant to the target population and demonstrating overall consistency of results. Evidence extrapolated from studies described in grade B. (D) Non-analytic studies (case reports or series), or expert opinion. Extrapolated evidence from high quality case control or cohort studies described in grade C.
Funding source and potential conflicts of interest	UK National Health Service Conflicts of interest statements available from SIGN (not reported in document)

SIGN=Scottish Intercollegiate Guideline Network; ppm=parts per million; RCTs=randomized controlled trials