Caries-preventive effect of sodium fluoride mouthrinses: a systematic review of controlled clinical trials

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The Swedish Council on Technology Assessment in Health Care launched a project group in 1999 to systematically review and evaluate the existing literature on different caries-preventive methods. The aim of this article was to report the findings concerning the caries-preventive effect of fluoride mouthrinses (FMRs) in various age groups, with special reference to background fluorides. A systematic search in electronic databases for literature published between 1966 and August 2003 was conducted with the inclusion criteria of a randomized or controlled clinical trial, at least 2 years' follow-up, and caries increment in the permanent dentition (ΔDMFS/T) as endpoint. Out of 174 articles originally identified, 62 met the inclusion criteria. These studies were assessed independently by at least two reviewers and scored A–C according to predetermined criteria for methodology and performance. The measure of effect was the prevented fraction (PF) expressed as percent. The level of evidence was based on 25 articles. The results revealed limited evidence (evidence level 3) for the caries-preventive effect (PF 29%) of daily or weekly sodium fluoride rinses compared with placebo in permanent teeth of schoolchildren and adolescents with no additional fluoride exposure and for a caries-preventive effect on root caries in older adults. Inconclusive evidence (evidence level 4) was found regarding the effect of FMRs in schoolchildren and adolescents exposed to additional fluoride sources such as daily use of fluoride toothpaste. No firm support for the use of FMRs was disclosed in a small number of studies designed for patients at caries risk. Furthermore, no association between the frequency of the rinses and prevented fraction or saved surfaces per year was found. In conclusion, this systematic review suggests that sodium fluoride mouthrinses may have an anti-caries effect in children with limited background of fluoride exposure, while its additional effect in children with daily use of fluoride toothpaste could be questioned. The need for further clinical trials to elucidate the effect of FMRs in risk patients and older adults is emphasized. □ *Fluoride mouth rinsing; systematic review*

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Fluoride mouthrinses (FMRs) have frequently been used to prevent dental caries in school-based programs over the past 30 years (1, 2). Supervised and unsupervised FMRs were systematically investigated in Scandinavia in the 1960s with an estimated caries reduction of 20–50% (3, 4). The use of weekly or bi-weekly rinses thereafter became common in schools during the 1970s and 1980s and was thought to play an important part in the subsequent decline of dental caries. However, with decreasing caries prevalence, along with increased fluoride exposure from other sources, the effectiveness of FMRs as a population strategy came into question (5–8). The procedure was withdrawn from most schools in Sweden and the current concept is that FMRs are primarily indicated for young and adult individuals at increased caries risk or with high caries activity (9, 10). The generally advocated procedure is rinsing of the mouth daily with 10 mL of a 0.05% NaF (230 ppm F) solution or weekly with a solution containing 0.2% sodium fluoride (900 ppm F) for 1–2 min. Because of the risk of fluoride ingestion (11, 12), fluoride rinses are not recommended to children under the age of 6 years.

Recently, a systematic review and meta-analysis of the anti-caries effect of FMRs established a prevented fraction of 26%, but found no association with baseline caries prevalence, background fluoride exposure, or rinsing frequency (13). In 1999, the Swedish Council on Technology Assessment in Health Care (SBU) launched a project group to systematically review and evaluate the existing literature on various caries-preventive methods (14). The aim of this paper was to report the findings

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Table 1. Criteria for grading of assessed studies

Grade A (high value as evidence)	Grade B (moderate value as evidence)	Grade C (limited value as evidence)
All criteria should be met	All criteria should be met	One or more of conditions below
Randomization by subject	Randomization by subject, school or class	No or unclear randomization
Diagnostic reliability described	Diagnostic reliability described	Diagnostic reliability not described
Baseline value described	Baseline value described	Baseline value not described
Attrition explained	Attrition explained	Attrition not explained or
<10% per year	>10% per year	>10% per year
Blinded outcome assessment	Blinded outcome assessment	Non-blinded outcome assessment
Representative sample of population under study, results can be generalized	Population under study defined, results cannot fully be generalized	Population under study not defined, results cannot be generalized
Bias and confounders considered	Bias and confounders considered	Bias and confounders not considered

concerning the effect of FMRs in non-selected populations of all ages, with special reference to the background fluoride exposure.

Methods

Literature search

A search for relevant literature published in English, German, French, Spanish, and the Scandinavian languages was conducted in MEDLINE and the Cochrane Library databases from January 1966 to November 2001 with a later update in August 2003. The major search terms were 'fluoride mouthrinsing/rinses', 'fluoride mouthwashing/es' and 'dental caries'. The search was done with the cooperation of an information specialist at SBU and was limited to randomized controlled trials (RCT) or controlled clinical trials (CCT) with sodium fluoride solutions of at least 2 years' duration and which included coronal or root caries increment in the permanent teeth (ΔDMFS/T) as the main outcome measure. A total of 174 records were identified and printed out as abstracts or full-text articles (when an abstract was missing). In a second step, relevant papers were selected independently by two of the authors and papers of interest for the objective were ordered in full-text versions. Only original papers were considered and double publications, interim reports, abstracts, letters, short communications, and chapters in textbooks were ignored. If multiple reports of a trial had been published, only the latest publication based on the longest follow-up period was included. During the evaluation process, a hand-search of reference lists was made. At this stage it was decided not to include papers published prior to 1970 because of the significant caries decline, making any generalization to the caries situation of today questionable. Thus, a total of 62 papers were selected and subjected to further evaluation.

Evaluation of papers and levels of evidence

The selected papers were subjected to critical appraisal carried out independently by at least two members of the project group. Data were extracted using a pilot-tested form and each article was assessed with score A–C according to predetermined criteria for methodology and performance (as given in Table 1). In the event of disagreement among the examiners, the article was re-evaluated and discussed by the entire group until consensus was reached. If an ordered paper for some reason was found irrelevant for the research questions, the article was excluded. The assessed papers were compiled in tables and results were calculated. The primary measure of effect was the prevented fraction (PF), calculated as the difference in mean caries increment between the treatment and control groups expressed as the percentage of the increment in the control group. Correlations were calculated with Pearson correlation coefficient and statistically non-significant treatment effects were calculated as 'zero'. A P value less than 0.05 was considered statistically significant. Based on the evaluated literature, the level of evidence was judged within the entire project group according to the protocol of the Swedish Council on Technology Assessment in Health Care (15) as described in Table 2.

Results

Of the 62 papers critically assessed, 25 were included for the evaluation of evidence (presented in Tables 3–5) (16–40). None of the papers was graded as 'A'. The 37 reports that were excluded are listed in Table 6 along with the main reason for their exclusion (41–77). Most studies were published during the 1970s and 1980s, while five reports

Table 2. Definitions for level of evidence (15)

Evidence level	Definition
1 Strong evidence	At least two studies assessed with level 'A'
2 Moderate evidence	One study with level 'A' and at least two with level 'B'
3 Limited evidence	At least two studies with level 'B'
4 Inconclusive evidence	Less than two studies with level 'B'

Regarding levels 1–3: there should be no major study disclosing contradictory results.

Table 3. Clinical trials with fluoride mouthrinses in schoolchildren performed without any other assumed fluoride exposure

First author	Year	Ref.	Intervention	Control	Study design	Duration (years)	No. of subjects	Age (years)	Dropouts %	Effect/PF% ΔDMFS/T	Grading
van Wyk	1986	(16)	NaF [0.2] 1x/7d	Placebo	RCT/DB	3	925	12–13	38	4.6/7.5; 38%	C
Blinkhorn	1983	(17)	NaF [0.05] 1x/1d	Placebo	CCT/DB	3	826	11–12	9	4.7/6.3; 25%	B
Ringelberg	1979	(18)	NaF [0.025] 1x/1d	Placebo	CCT/DB	2.5	2,056	11	39	2.8/3.4; 18%	C
Ashley	1977	(19)	NaF [0.02] 1x/1d	Placebo	RCT/DB	2	1,135	12–14	12	4.8/5.6; 14 %	B
DePaola	1977	(20)	NaF [0.05] 1x/1d	Placebo	RCT/DB	2	200	10–12	>50	4.5/9.6; 53%	C
Gallagher	1974	(21)	NaF [0.4] 1x/7d	Placebo	CCT/DB	2	809	11–13	27	2.9/3.8; 33%	C
Heifetz	1973	(22)	NaF [0.3] 1x/7d	Placebo	RCT	2	947	10–12	56	4.7/7.1; 34%	C
Rugg-Gunn	1973	(23)	NaF [0.05] 1x/1d	Placebo	RCT/DB	3	434	11–12	12	6.6/10.2; 35%	B

PF = prevented fraction; RCT = randomized controlled trial; CCT = controlled clinical; trial DB = double blind; NaF = sodium fluoride; d = day; B = medium level of evidence; C = low level of evidence.

Table 4. Clinical trials with fluoride mouthrinsing in schoolchildren conducted versus other fluoride treatment or under conditions with other fluoride sources such as piped water or toothpaste

First author	Year	Ref.	Intervention	Control	Study design	Duration (years)	No. of subjects	Age (years)	Dropouts %	Effect/PF% ΔDMFS/T	Grading
Petersson	1998	(24)	NaF [0.05] 3dx2	Placebo	CCT/SB	3	139	13	0	2.8/3.2; NS	C
Driscoll	1992	(25)	NaF [0.2] 1x/7d	F-tabl & combination	RCT/SB	3	1,640	5–6	61	3.6/2.8/2.4;–33%	C
Heidmann	1992	(26)	NaF [0.2] 1x/14d	Placebo	RCT/DB	3	1,386	6–15	17	8.8/8.7; NS	B
deLiefde	1989	(27)	NaF [0.05] 1x/1d	Placebo	CCT/DB	5	273	5–8	13	2.9/2.7; NS	B
Axelsson	1987	(28)	NaF [0.05] 1x/7d	Placebo	RCT/DB	3	252	13–14	6	14.0/15.1: NS	B
Heifetz	1987	(29)	NaF [0.2] 1x/7d	F-tabl & combination	RCT/SB	2	1,154	5–6	30	0.9/0.8/0.8; NS	C
Ruiken	1987	(30)	NaF [0.2] 1x7d	Placebo	CCT/SB	3	501	8	59	3.6/3.1; NS	C
Bruun	1985	(31)	NaF [0.2] 1x/1d	Fp-varnish	CCT/DB	3	359	9–12	31	1.1/1.5; NS	B
Poulsen	1984	(32)	NaF [0.2] 1x/14d	Placebo	RCT/DB	3	365	8–10	8	1.8/1.8; NS	B
Blinkhorn	1983	(17)	NaF [0.05] 1x/1d	Placebo	CCT/DB	3	826	11–12	9	4.8/4.6; NS	B
Driscoll	1982	(33)	NaF [0.05] 1x/1d	Test 1x/7d & control	RCT/SB	2.5	966	13	46	1.9/2.0/2.6; 27%	C
Heifetz	1982	(34)	NaF [0.2] 1x/14d	Placebo	RCT/DB	3	824	10–12	27	3.3/4.7; 30%	B
Ringelberg	1982	(35)	NaF [0.05/0.2] 1x/1d/7d	Placebo	RCT/DB	2	1,238	12–13	39	2.8/2.8/3.4; 18%	C
DePaola	1980	(36)	NaF [0.23] 1x/7d	Placebo	RCT/DB	2	271	12–14	Not reported	7.1/9.1; 22%	C
Luoma	1978	(37)	NaF [0.05] 1x/d	Placebo	RCT/SB	2	82	11–15	12	4.3/5.1; NS	B

PF = prevented fraction; RCT = randomized controlled trial; CCT = controlled clinical trial; DB = double blind; SB = single blind; NaF = sodium fluoride; d = day; F-tabl = fluoride tablets; NS = not significant; B = medium level of evidence; C = low level of evidence.

Table 5. Clinical trials with fluoride mouthrinses in adults

First author	Year	Ref.	Intervention	Control	Study design	Duration (years)	No. of subjects	Age (years)	Dropouts %	Effect/PF%, root caries increment	Grading
Fure	1998	(38)	NaF [0.05] 2x/1d	Control	RCT/SB	2	164	>60	7	0.8/2.3; 65%	B
Wallace	1993	(39)	NaF [0.05] 1x/1d	F-gel/placebo	CCT/SB	4	603	>60	23	0.3/0.3/0.9; 67%	B
Ripa	1987	(40)	NaF [0.05] 1x/1d	Placebo	RCT/DB	3	1,006	18–65	27	0.4/0.4; NS	B

PF = prevented fraction; RCT = randomized controlled trial; CCT = controlled clinical trial; DB = double blind; SB = single blind; NaF = sodium fluoride; d = day; F-gel = fluoride gel; NS = not significant; B = medium level of evidence.

were from the 1990s. The included papers were subgrouped with regard to background fluoride and age. No general association was found between rinsing frequency and sodium fluoride concentration on the one hand and baseline caries prevalence, the prevented fraction, or saved DMF surfaces/year on the other.

Studies in younger individuals conducted without background fluoride exposure

The anti-caries effect of FMRs in young permanent teeth was compared with placebo rinses in 8 articles (16–23) from investigations covering around 7,000 children carried out in low-fluoride areas and with no assumed additional fluoride exposure (Table 3). The trials were conducted during the 1970s and 1980s and 3 were rated as 'B' and 5 as 'C'. All displayed a statistically significant reduction of caries following the FMR. The weighed mean prevented fraction was 29%, ranging from 14% to 53%. The average caries increment was fairly high, 2.44 DMFS per year, and the fluoride rinses saved a mean of 1.06 new decayed surfaces per year (range 0.40–2.55). As a whole, there was limited evidence (level 3) that mouthrinses containing sodium fluoride can prevent caries in schoolchildren and adolescents not exposed to other fluoride sources.

Studies in younger individuals conducted with background fluoride sources

Fifteen studies with approximately 10,000 subjects in which FMR was compared with placebo or other fluoride regimes and/or conducted in areas with fluoridated water or regular use of fluoride toothpaste were included (24–37). All were performed with sodium fluoride rinses on a daily or weekly basis, except in one case where an intensive rinsing schedule was utilized (24). The results are compiled in Table 4 and mixed and partly contrasting findings can be seen. Eight articles were scored as 'B' (26–28, 31, 32, 34, 37) and, of those, only one displayed a statistically significant effect on caries increment in schoolchildren (34). The seven articles rated as 'C included three studies with positive findings (33, 35, 36), three with non-significant outcomes (24, 29, 30), and one favored another fluoride regime (25). The average caries increment in the 15 included studies was 1.49 DMF surface per year, while the overall prevented fraction compared with placebo ranged from 0% to 30% (mean PF 6%), but the reduction was not statistically significant. Thus, the evidence for caries prevention by daily or weekly FMR in schoolchildren with additional background fluoride, such as regular use of fluoride toothpaste, was rated as inconclusive (evidence level 4).

Studies in adults

In adult subjects, three randomized clinical controlled trials (38–40) were included and evaluated for the

Table 6. Excluded papers

Main reason for exclusion	Ref.
Small study, selected subjects or teeth, short duration	41–45
Large dropout, confounders	46, 47
No or clear, controlled or actual clinical intervention(s) or agent(s)	48–50
Interactive or combined preventive program(s)	51–60
Retrospective, follow-up, cross-sectional, split-mouth	61, 62
No or lack of original or relevant data, data in other study	63–69
Thesis, meta-analysis, survey, review, post-intervention, guideline, repeated or other publication	70–74
Other reason(s)	75–77

preventive effect of FMR on root caries (as presented in Table 5). The three papers were rated as 'B' and displayed mixed but not contradictory results. While the study by Ripa et al. (40) showed a limited but statistically insignificant treatment effect on root caries in adults 18–65 years of age, the other 2 reported clearly significant caries protective findings in older adults over 60 years. Notably, in the study by Fure et al. (38), the subjects rinsed two times daily and fluoride toothpaste was used simultaneously. Thus, limited evidence (evidence level 3) was found for the ability of FMR to prevent root caries in older adults.

Discussion

The systematic search for literature with subsequent data extraction and quality assessment is today a well-established component of evidence-based medicine and dentistry, although the methods for this process differ slightly between various Health Technology Assessment organizations. The methodology used in this paper was adopted from the guidelines of the Swedish Council on Technology Assessment in Health Care. The primary object of this systematic review was to examine the caries-preventive effect of FMRs in non-selected populations of various age groups. Therefore, clinical trials of compromised or disabled patients were not taken into account; nor were studies in which FMR was part of a comprehensive preventive program. Furthermore, no attempts were made to evaluate possible differences between various fluoride salts or formulations and the evaluation was limited to interventions with NaF solutions. The selected literature was mainly focused on young permanent teeth in schoolchildren and adolescents and only a small number of trials dealt with coronal and root caries in the elderly. It was noted that almost all reviewed papers were carried out with a proper prospective design, caries scoring, and evaluation. The two factors that frequently contributed to downgrading and flawed evidence levels were (i) a significant attrition of participants, and (ii) an unclear randomization or randomization based on schools or school-classes rather than on individuals. The included studies exhibited an annual average dropout rate of 11%, an important fact that must be taken into account when considering the efficiency of FMRs. As stated by Stamm et al. (5), the problems associated with longer-term compliance are generally ignored. It is considered that FMRs are safe so long as the recommendations are followed (2, 10) and the evaluated papers did not unveil any contradictory or new information on the safety aspects.

The results of the present systematic evaluation were in fair agreement with previous reviews and systematic reviews (2, 10, 13) and in harmony with the beliefs of most experts (78). The prevented fraction of FMRs, based on clinical trials from the 1970s and 1980s, was calculated at 29% for daily or weekly rinses in the permanent teeth of schoolchildren and adolescents with no additional fluoride exposure. This was slightly higher than the meta-analysis of Marinho and co-workers (13), who found a caries-preventive fraction of 26%; the difference may be explained partly by the fact that they included (i) more studies and (ii) trials performed with varying background fluorides. In support of the Cochrane review (13), we found no significant association between the baseline caries prevalence or frequency of the mouthrinses and prevented fraction or the number of saved tooth surfaces per year. However, a finding in contrast to Marino et al. (13) was the clear tendency that the anti-caries effect of FMRs was dependent on the presence of background fluorides. In fact, we found no RCT, graded at least 'B', that demonstrated enhanced benefits of FMR over daily use of fluoride toothpaste. This was also clearly illustrated in two 'B'-rated RCTs by Blinkhorn et al. (17) and Ashly et al. (19) with four parallel arms covering combinations and simultaneous use of fluoride mouthrinses and fluoride toothpaste. On the other hand, additional fluorides could also result in enhanced caries protection, as exemplified by the study of Driscoll et al. (25) showing a superior caries reduction of a combination of daily FMRs and fluoride tablets compared with mouthrinses alone. Leverett concluded in 1989 (7) that FMRs were unlikely to save more than 0.4 surfaces annually, but according to the present review this too is an overestimation under current circumstances. As a comparison, the calculated mean number of saved surfaces per year from FMRs versus placebo in trials with fluoride backgrounds was 0.16 in the present study. Owing to the mixed and contrasting findings, we found inconclusive evidence for the anti-caries effect of daily, weekly, or intensive FMRs with NaF solutions in groups with additional exposure to fluoride. Although available in most countries, the regular use of fluoridated toothpaste varies from country to country and by socio-economic level (79). The results of this review thus reinforce the thinking that FMRs should still be considered as a school-based collective measure in vulnerable populations with irregular fluoride exposure in which epidemiological studies have identified dental caries as a public health problem.

In the vast majority of the included studies, FMR was

carried out in supervised programs monitored by teachers or dental personnel. However, fluoride rinses can also be self-applied and the findings of two trials (19, 23) indicated that supervised FMR was not superior to unsupervised rinsing. Two studies were included for evaluation in which daily fluoride rinses were compared with placebo in patients at caries risk (27, 37). Neither was able to demonstrate any significant caries reduction of note, especially in light of the present recommendations that FMR is indicated for high-risk and caries-active individuals. An obvious task for future research is to determine the efficacy and effectiveness of FMR in a study population selected at caries risk and/or with a proven caries activity, preferably in a multi-center setting in order to get sufficient power for conclusive results. Furthermore, additional studies on older adults are required to elucidate the effect of FMR on root caries control.

In conclusion, we found limited evidence that daily or weekly sodium FMRs had a significant caries-reducing effect in young permanent teeth compared with placebo when no additional background fluorides were present or used (evidence level 3). In contrast, the evidence for caries prevention by FMR in schoolchildren exposed to additional fluoride sources, such as regular use of fluoride toothpaste, was rated as inconclusive (evidence level 4). Moreover, no support for the use of FMRs in subjects at risk was disclosed, but we did reveal limited evidence (evidence level 3) for the prevention of root caries. Further studies should be carried out concerning elderly and selected groups of patients at risk.

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