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ABSTRACT

To date, no systematic reviews have found fluoride to be effective in preventing dental caries in adults. The objective of this meta-analysis was to examine the effectiveness of self- and professionally applied fluoride and water fluoridation among adults. We used a random-effects model to estimate the effect size of fluoride (absolute difference in annual caries increment or relative risk ratio) for all adults aged 20+ years and for adults aged 40+ years. Twenty studies were included in the final body of evidence. Among studies published after/during 1980, any fluoride (self- and professionally applied or water fluoridation) annually averted 0.29 (95%CI: 0.16-0.42) carious coronal and 0.22 (95%CI: 0.08-0.37) carious root surfaces. The prevented fraction for water fluoridation was 27% (95%CI: 19%-34%). These findings suggest that fluoride prevents caries among adults of all ages.

KEY WORDS: caries, fluoride, adults, meta-analysis.

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Effectiveness of Fluoride in Preventing Caries in Adults

INTRODUCTION

In systematic reviews on the effectiveness of fluoride in preventing/arresting caries, most of the studies included have been conducted among children (CDC, 2001; National Institutes of Health Consensus Development Conference Statement, 2001). For example, the National Institutes of Health Consensus Development Conference on Diagnosis and Management of Dental Caries Throughout Life noted that evidence on the effectiveness of fluoride in preventing dental caries was limited to studies involving populations of children between six and 15 yrs of age.

The reviews included in the consensus conference generally emphasized the professional application of fluorides (Treasure, 2001), and not self-applied fluoride or water fluoridation. Moreover, the Centers for Disease Control and Prevention's (CDC) 2001 Recommendations for Using Fluoride to Prevent and Control Dental Caries in the U.S. found that, "Few studies evaluating the effectiveness of fluoride toothpaste, gel, rinse, and varnish among adult populations are available", and called for further research on the effectiveness of different fluoride modalities on dental caries, including adults over 50 yrs old (CDC, 2001).

Documenting the effectiveness of fluoride in preventing/managing dental caries among adults is important. Although literature reviews suggest that the incidence of caries among adults is as high as that in children—about 1 new carious coronal tooth surface *per year* (Garcia, 1989; Griffin *et al.*, 2005)—with the exception of water fluoridation, virtually all primary preventive programs target children and youth (Association of State and Territorial Dental Directors, 2002). One possible reason for the lack of preventive programs for adults may be the lack of evidence on their effectiveness for this population. To compete successfully for resources to support primary prevention, programs must not only establish the importance of the problem, but also provide evidence that interventions are effective (Gooch *et al.*, 2006).

For this present study, we analyzed the topical effectiveness of fluoride (self- and professionally applied and in drinking water) in preventing/reversing caries in all adults (aged 20+ yrs) and in older adults (aged 40+ yrs). Because several clinical trials on the effectiveness of fluoride were conducted in the 1950s and 1960s, we expanded our search to include articles published before 1980, the earliest year in the National Institutes of Health search for systematic reviews (Rozier, 2001). We specifically addressed the following questions: (1) Is fluoride effective in preventing coronal caries in all adults and in older adults (≥ 40 yrs) and in preventing root caries in the older group? and (2) How effective are the different fluoride delivery modes in preventing caries?

METHODS

Search Strategy

We searched three electronic databases to locate primary studies and systematic reviews relating to the topical effectiveness of fluoride (*i.e.*, fluoridated water or fluoride-containing toothpaste, gel, varnish, or rinse) in preventing or arresting caries among adults:

- (1) MEDLINE from 1966 to week 42 of 2004 (Appendix Table 1) identified 1044 records;
- (2) EMBASE from 1988 to week 43 of 2004 (Appendix Table 2) identified 56 records; and
- (3) in the Cochrane Control Register of Controlled Trials (CENTRAL), we used MEDLINE search strategy to identify 148 records,

Two reviewers (VH and SG) independently reviewed the abstract and title of each record for relevant articles; records deemed relevant by at least one reviewer were examined. In addition, the references of each retrieved article were searched for relevant articles. In total, 489 articles were examined and screened with a form developed for this review (Appendix Table 3). We also contacted the American Dental Association, the Food and Drug Administration, and manufacturers of topical fluoride products for unpublished clinical trials (Appendix Table 4), but these inquiries did not yield additional studies.

Study Selection and Validity Assessment

A study was eligible for abstraction if it was published in English, lasted 1 yr or longer, and examined the association between fluoride and caries in intact human teeth in study populations that included adults. In all, we reviewed 50 studies (Appendix Fig. 1). Studies were excluded from the final body of evidence if the mean age of the study population was less than 20 yrs, they did not have a concurrent control group, or there was insufficient information to both extrapolate the benefits of fluoride to all 28 teeth and to calculate a standard error (Appendix Tables 5, 6).

We used an algorithm designed by the Guide to Community Preventive Services to determine the type of study design (Zaza *et al.*, 2000). To examine the effectiveness of self- or clinically applied fluoride, we included only longitudinal studies with random assignment of participants or of split-mouth design. For studies examining the effectiveness of water fluoridation, we included cross-sectional studies if their participants lived most of their lives (hereafter referred to as 'lifetime residency') in fluoridated/non-fluoridated communities, or they estimated the effect of exposure to water fluoridation controlling for potential confounding factors. Because water fluoridation is a community intervention, it is difficult to assign participants randomly to a treatment or control group, and thus other systematic reviews of the effectiveness of water fluoridation have not excluded non-randomized studies (McDonagh *et al.*, 2000). Other measures of validity (drop-out rate and examiner/participant blinding) were also examined and reported for included studies, but were not used to exclude studies.

Data Abstraction

All four authors pilot-tested an abstraction form developed for this project (Appendix Table 7). To calibrate the reviewers, all four reviewers abstracted the same five articles and then met to discuss and compare their completed abstraction forms. After a consensus had been reached on how the form should be completed, each article was randomly assigned to two reviewers. All four reviewers independently abstracted their assigned articles and then compared abstraction forms with the other reviewer to whom the article had been assigned; finally, the two reviewers completed a consensus abstraction form.

Outcome Measures

The primary outcome of interest was coronal caries increment, as measured by the number of teeth/surfaces becoming decayed or filled (DFT/S) or decayed, filled, or missing (DMFT/S). We examined this outcome in all adults (20+ yrs) and in adults (40+

yrs). We also estimated the root caries increment for adults, aged 40+ yrs. We chose 40 yrs as the cut-point age to balance age with the need to have a sufficient number of studies.

The reader should note that, for the cross-sectional studies with lifetime exposure to fluoridated/non-fluoridated water, DMFT/S prevalence measures lifetime caries increment or, if divided by the number of teeth/surfaces (assumed to be 28 teeth/128 surfaces), estimates the lifetime attack rate (% of teeth or surfaces attacked by caries).

Adjustment of Outcome Measures

When adjusting data, we used conservative methods that would bias the results against a statistical finding of a benefit of fluoride. For studies that reported the absolute difference in caries increment for the same population for different time intervals (*e.g.*, 12 and 30 mos), we used the results for the follow-up examination that was closest to, but at least 1 yr after, the first examination, so that the method used to annualize the variance would have minimal influence. For studies whose selected follow-up period exceeded 1 yr, we annualized the outcome measure by assuming that caries increment was constant, and therefore independent of the duration of the time since the first examination. Thus, we annualized the reported caries increment by dividing it by the number of yrs in the reported interval, and estimated the annual standard error by dividing the reported standard error for the interval by the square root of the number of years in the interval. If the caries increment were higher in the first year and the caries increment in the control group were higher than in the treatment group (as expected), the above method would underestimate the absolute difference in caries increment attributable to fluoride exposure.

Quantitative Data Synthesis

To examine if any fluoride is effective, we used Fisher's inverse chi-square method (Hedges and Olkin, 1985) to calculate whether combined p-values were statistically significant. This test statistic was calculated for studies examining the effectiveness of any mode of fluoride delivered to all and older adults. We also applied Fisher's test to the water fluoridation studies, because they also had different outcome measures and used different statistical methods.

To measure the size of the effect of water fluoridation, we calculated the relative risk ratio for each of the cross-sectional studies that excluded participants without continuous residency, where

$$\text{Relative risk} = \left(\frac{\% \text{ teeth or surfaces that are DMF}_{\text{Fluoridation}}}{\% \text{ teeth or surfaces that are DMF}_{\text{Control}}} \right)$$

We used the relative risk ratio because it is more invariant to differences in unit of measurement (teeth *vs.* surfaces), baseline caries risk status, and age (length of exposure), which were all possible confounding factors. To calculate the standard error for the relative risk ratio, we assumed perfect correlation among teeth (the most conservative assumption), and thus the effective sample size became the number of participants; we used this value in calculating the pooled standard error.

For the remaining studies, we used the absolute difference in annual caries increment between the control and the treatment groups to measure the effect size.

For those studies where the standard error had to be extracted from reported p-values, or it was necessary to pool standard errors to make comparisons similar across studies, we used standard statistical techniques, which are described in the Notes Section of

Table 1. Characteristics of Included Studies

Study	Design; Number of Subjects; Duration; Drop-out Rate	Location; Mean Age in Yrs (Range)	Mode of Fluoride Delivery
Burt <i>et al.</i> , 1986; Eklund <i>et al.</i> , 1987	Cross-sectional; 315; NA ^a ; NA	New Mexico; 41.6 (27-65)	Community water system (3.5 ppm ^b vs. 0.7 ppm)
DePaola, 1993	Randomized controlled trial; 71; 1 yr; 14%	Northeastern US; 71 (NR ^c)	Gel (1.2%) professionally applied for 2 min every 4 mos, and daily self-application of neutral sodium fluoride gel (0.5%)
Englander and Wallace, 1962	Cross-sectional; 1831; NA; NA	Illinois; 33 (18-59)	Community water system (1.2 ppm vs. 0.1 ppm)
Fure <i>et al.</i> , 1998	Randomized controlled trial; 81; 2 yrs; 6.8%	Sweden; 71.5 (NR)	Rinse (0.05%) twice daily
^a Not applicable. ^b Parts per million. ^c Not reported.			
Grembowski <i>et al.</i> , 1992	Cross-sectional; 595; NA; NA	Washington; 30.6 (20-34)	Community water system
Hunt <i>et al.</i> , 1989	Prospective cohort (random sample); 275; 1.5 yrs; 13%	Iowa; 75 (NR)	Community water system (0.7 to 1.5 ppm vs. < 0.5 ppm)
Jensen and Kohout, 1988	Randomized controlled trial; 810; 1 yr; 11%	Iowa; 68 (54-93)	Dentifrice (1.1%) used twice daily
Lu <i>et al.</i> , 1980	Randomized controlled trial; 1105; 1 yr; 17%	Oregon; 33 (18-78)	Dentifrice (stannous fluoride-calcium pyrophosphate, pH = 4.5; fluoride content NR)
Morgan <i>et al.</i> , 1992	Cross-sectional; 104; NA; NA	Australia; NR (20-24)	Community water system (fluoride content NR)
Muhler <i>et al.</i> , 1956	Randomized controlled trial; 322; 1 yr; 10%	Indiana; NR (17-36)	Dentifrice (4 mg stannous fluoride; frequency not reported ^a)
Muhler, 1958	Randomized controlled trial; 435; 1 yr; NR	Indiana; NR (17-38)	Aqueous solution professionally applied (10%), single application
^a Results stratified by good (≥ 3 times daily) or bad brushers (≤ 2 times daily), but numbers in each group not reported.			
Muhler <i>et al.</i> , 1967	Randomized controlled trial; 168; 1 yr; 17%	Indiana; NR (NR ^a)	Topical professionally applied every 6 mos preceded by prophylactic paste (% NR) and dentifrice (% NR)
Murray, 1971	Cross-sectional; 3902; NA; NA	Great Britain; findings presented by age group (20-60+)	Community water system (1.5-2.0 ppm vs. 0.2 ppm)
Rickles and Becks, 1951	Controlled trial (split-mouth); 25; 2 yrs; NR	USA; 27 (22-34)	Topical professionally applied (2%) every 3 mos
Ripa <i>et al.</i> , 1987	Randomized controlled trial; 731; 3 yrs; 27%	New York; 39.9 (20-65)	Rinse (0.05%) swished for 60 sec daily
Scola, 1970	Randomized controlled trial; 120; 2 yrs; NR	USA; 20.7 (18-22)	Topical (8.9%) professionally applied once yearly preceded by prophylaxis paste (8.9%) and dentifrice (0.4%)
^a Age was assumed to be greater than 20 yrs because participants were all dental students.			
Stamm <i>et al.</i> , 1990	Cross-sectional; 967; NA; NA	Canada; 41.5 (18-60+)	Community water system (1.6 ppm vs. 0.2 ppm)
Thomas and Kassab, 1992	Cross-sectional; 649; NA; NA	Great Britain; NR (20-32)	Community water system (0.9 ppm vs. NR)
Wallace <i>et al.</i> , 1993	Randomized controlled trial; 466; 4 yrs; 11.8% in year 1 and 22.7% in year 4	Alabama; NR (aged 60+)	Gel (1.2% in trays kept in place for 4 min) applied semi-annually or rinse (0.05%) used daily
Wiktorsson <i>et al.</i> , 1992	Cross-sectional; 496; NA; NA	Sweden; NR (30-40)	Community water system (fluoride content NR)

relevant studies in Appendix Table 6.

We estimated summary measures for the various modes of fluoride by age group if there were five or more studies for that mode. We used a random-effects model, which assumes that each study was randomly selected from a hypothetical population of studies (DerSimonian and Laird method, referenced in Normand, 1999). Because we included many studies published before 1980, we also estimated summary measures for studies conducted during or after 1980. We tested for homogeneity of effect size using a chi-

square test (Q_w) (Normand, 1999). Because we had a small number of studies in many cases, we estimated the quantity I^2 (Higgins and Thompson, 2002) for effect sizes that failed the heterogeneity test.

RESULTS

Quality Assessment

Twenty studies representing 13,551 participants were included in the final body of evidence (Table 1 and Appendix Table 6).

Eleven studies examined the effectiveness of self- or clinically applied fluoride. Of these studies, 10 were randomized clinical trials, and 1 was a controlled trial (split-mouth) that did not specify whether the treatment had been randomly assigned. Nine studies examined the effectiveness of water fluoridation—one was a prospective cohort trial that examined caries increment among randomly selected lifelong residents of fluoridated and non-fluoridated communities, and 8 were cross-sectional studies. In this last group, 7 compared caries prevalence between lifelong residents of fluoridated and non-fluoridated communities, and 1 used linear regression analysis to estimate averted caries increment attributable to 1 yr of exposure to water fluoridation. Among the 12 longitudinal studies, 9 reported the drop-out rate (mean drop-out rate for one yr [weighted by sample size] = 10.9%), 5 reported that examiners were blinded, and 8 reported using a placebo.

Is Any Fluoride Effective in Preventing Caries?

Eighteen studies (11,649 participants) compared coronal caries among adults of all ages by fluoride exposure (Table 2). Caries was always higher in the control group than in the treatment group. With Fisher's inverse chi-square method, the combined p-values were less than 0.001. Six studies (2290 participants) compared coronal caries among adults aged 40+ yrs. Again, caries was always higher in the control group than in the treatment group, and the combined p-values were less than 0.001. Finally, 7 studies (2112 participants) compared root caries among adults aged 40+ yrs by fluoride exposure (Table 2); in all studies, caries was higher in the non-fluoride than in the fluoride group, and the combined p-values were less than 0.001.

How Effective is Community Water Fluoridation in Preventing Caries?

The combined results of the 9 studies (7853 participants) examining the effectiveness of water fluoridation were significant at $p < 0.001$ (Table 2). Among the 7 studies including only lifelong residents of control or fluoridated-water communities (5409 participants; Appendix Table 8 and Appendix Fig. 2), the summary relative risk ratio was 0.654 (95% confidence interval [CI]: 0.490-0.874); this is equivalent to a prevented fraction of 34.6% (95%CI: 12.6%-51.0%). Heterogeneity was present. Heterogeneity was not an issue when we pooled the 5 fluoridation studies published after 1979 (2530 participants); the summary-prevented fraction was 27.2% (95%CI: 19.4%-34.3%).

How Effective are the Different Modes of Fluoride in Preventing Caries?

The difference in annual coronal caries increment between exposed and not-exposed adults of all ages for all modes of fluoride delivery ranged from 0.02 to 2.17 surfaces (11 studies

Table 2. P Values for Combined Results

Measure (Number of Studies; Number of Participants; References)	Combined p-value
Any fluoride, all adults, coronal caries (18 studies; 11,649 participants; Eklund <i>et al.</i> , 1987; Englander and Wallace, 1962; Fure <i>et al.</i> , 1998; Grembowski <i>et al.</i> , 1992; Hunt <i>et al.</i> , 1989; Jensen and Kohout, 1988; Lu <i>et al.</i> , 1980; Morgan <i>et al.</i> , 1992; Muhler, 1956; Muhler, 1958; Muhler <i>et al.</i> , 1967; Murray, 1971; Rickles and Becks, 1951; Ripa <i>et al.</i> , 1987; Scola, 1970; Stamm <i>et al.</i> , 1990; Thomas and Kassab, 1992; Wiktorsson <i>et al.</i> , 1992)	< 0.001
Any fluoride, older adults, coronal caries (6 studies; 2290 participants; Eklund <i>et al.</i> , 1987; Fure <i>et al.</i> , 1998; Hunt <i>et al.</i> , 1989; Jensen and Kohout, 1988; Murray, 1971; Stamm <i>et al.</i> , 1990)	< 0.001
Any fluoride, older adults, root caries (7 studies; 2112 participants; Burt <i>et al.</i> , 1986; De Paola, 1993; Fure <i>et al.</i> , 1998; Hunt <i>et al.</i> , 1989; Jensen and Kohout, 1988; Ripa <i>et al.</i> , 1987; Wallace <i>et al.</i> , 1993)	< 0.001
Water fluoridation, all adults, coronal caries (9 studies; 7853 participants; Eklund <i>et al.</i> , 1987; Englander and Wallace, 1962; Grembowski <i>et al.</i> , 1992; Hunt <i>et al.</i> , 1989; Morgan <i>et al.</i> , 1992; Murray, 1971; Stamm <i>et al.</i> , 1990; Thomas and Kassab, 1992; Wiktorsson <i>et al.</i> , 1992)	< 0.001

with 4809 participants; Fig. 1). The summary difference was 0.64 surfaces (95%CI: 0.35-0.94). Heterogeneity was present. There were enough studies to estimate an effect measure for studies published during/after 1980 (6 studies with 3573 participants). The summary difference in annual caries increment for these studies was 0.29 coronal surfaces (95%CI: 0.16-0.42). Both the chi-square test, $p > 0.05$, and the I^2 test, 0.38, indicated that heterogeneity was not an issue.

The difference in annual root caries increment by any fluoride exposure for adults aged 40+ ranged from 0.05 to 0.50 (5 studies all published after/during 1980, with 1894 participants; Fig. 2). The summary difference was 0.22 (95%CI: 0.08-0.37). Both the chi-square test, $p > 0.05$, and the quantity I^2 , equaling 0.15, indicated that heterogeneity was not significant.

For self-applied fluoride, the difference in annual coronal caries increment between exposed and not-exposed adults ranged from 0.02 to 2.17 (Appendix Fig. 3; 7 studies with 3503 participants). The summary difference was 0.72 (95%CI: 0.20-1.24). Heterogeneity was present. When we restricted the analysis to the 5 studies that included solely self-applied fluoride (3049 participants), the summary difference decreased to 0.30 surfaces (95%CI: 0.09 to 0.51). Although the chi-square test indicated that heterogeneity was not an issue, the quantity I^2 indicated that about 53% of the difference among studies was due to heterogeneity as opposed to random chance.

Because only 2 studies examined the effectiveness of professionally applied fluoride without another fluoride modality, we did not calculate summary measures for this mode of delivery.

DISCUSSION

One limitation of this review is the quality and the quantity of studies on fluoride effectiveness among adults. Recent meta-analyses of fluoride rinses and toothpastes among children

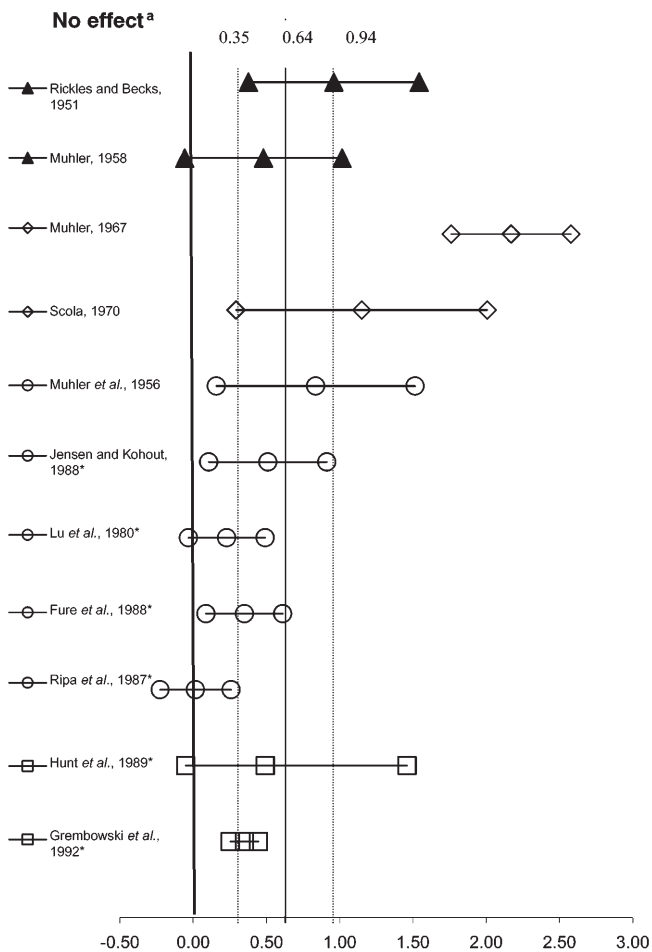


Figure 1. Absolute reduction in coronal caries increment that was attributed to fluoride exposure. *Indicates study published during or after 1980.

^a Values to the right of the 'no effect' line (difference in caries increment is positive) indicate fluoride effective, and values to the left (negative difference) indicate fluoride ineffective.

- Community water fluoridation.
- Self-applied fluoride.
- ◇ Combination of self-applied and professionally applied fluoride.
- ▲ Professionally applied fluoride.

included 36 and 74 randomized or *quasi*-randomized controlled trials (Marinho *et al.*, 2003a,b), respectively, whereas this review could locate only 8 such studies from which to estimate the size of the effect. Because of the paucity of studies, we were not able to exclude studies without blind outcome assessment, as was done in the recent meta-analysis for children. In addition, our findings on the effectiveness of self-applied fluoride may not be generalizable to the current generation of adults; there were only 4 studies published after 1979 (the summary measure, however, was significant). Finally, we also included cross-sectional studies to evaluate water fluoridation. Thus, there is a clear need for further well-designed studies on the effectiveness of fluoride among adults.

One interesting finding, however, was the consistency of the effect size for the various modes of fluoride delivery among adults, and their similarity to findings for children. Using findings from studies published after 1979, and assuming that the annual coronal caries increment among adults is 1 surface (Griffin *et al.*, 2005),

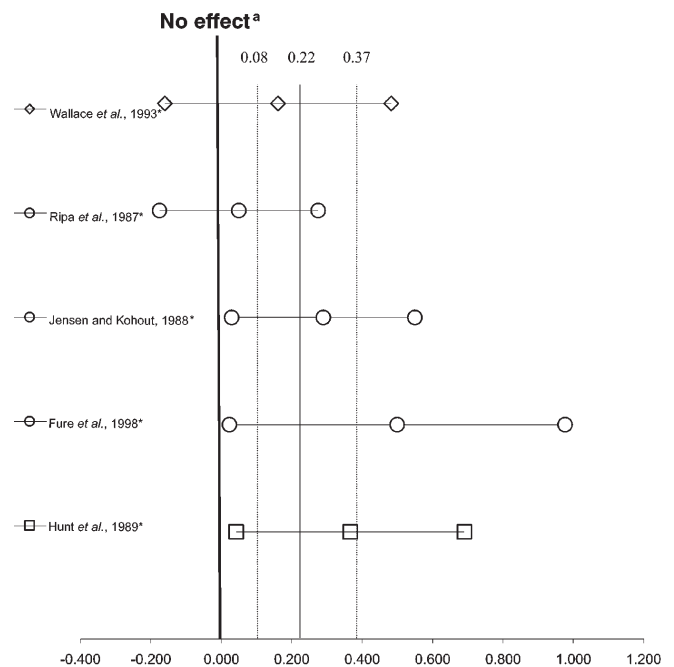


Figure 2. Absolute reduction in root caries increment attributed to fluoride exposure. *Indicates study published during or after 1980.

^a Values to the right of the 'no effect' line (difference in caries increment is positive) indicate fluoride effective, and values to the left (negative difference) indicate fluoride ineffective.

- Community water fluoridation.
- Self-applied fluoride.
- ◇ Combination of self-applied and professionally applied fluoride.

we found that exposure to any mode of fluoride reduced caries by about 25%. This value is similar to the prevented fraction for community water fluoridation. When we restricted the analysis of the effect of self-applied fluoride to 4 studies published after 1979, the prevented fraction again equaled 25% (data not shown). A recent meta-analysis conducted among children and youth also found preventive fractions of fluoride rinse (26%) and toothpaste (24%) close to 25% (Marinho *et al.*, 2003a,b).

On a population basis, caries is becoming a more important health issue among adults, especially older adults, because they are more likely to retain their natural teeth than in previous generations. A comparison of the National Health and Nutrition Examination Survey (NHANES III) conducted in 1988-1994 with that conducted in 1999-2002 indicates that the mean number of missing teeth among adults aged 40+ has decreased by 22% (Beltran-Aguilar *et al.*, 2005). In addition, the percentage of the population that is older is increasing. Thus, there are more at-risk teeth, making population-based efforts at prevention even more important.

Although adults are as likely to experience new caries as children, certain segments of the U.S. adult population—those with low incomes and the elderly—may have little or no access to restorative or preventive clinical care. At present, approximately 15% of state Medicaid programs provide no adult dental benefits at all, and approximately 45% cover only tooth extraction and emergency services (Oral Health America, 2003). Routine dental care is one of the few health areas not covered by Medicare. Limited access to restorative care increases the need for effective prevention; complications and

pain and suffering are more likely if caries remains untreated.

The proportion of the U.S. population comprised of older adults is increasing, most of these persons are likely to be dentate and at risk for dental caries, and many lower-income adults lack access to timely restorative care. Our finding that fluoride is effective among all adults supports the development and implementation of fluoride programs to serve this population.

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