

Burt and Eklund's Dentistry, Dental Practice, and the Community

SEVENTH EDITION

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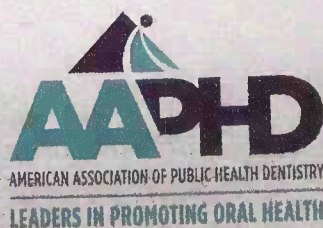
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time gave way to the simpler once-a-day ingestion of the tablet. Water, chewable tablets and lozenges were manufactured for older children, to be chewed or sucked 1 to 2 minutes before swallowing, the intent here being to obtain both topical and systemic effects. Most tablets contain neutral NaF, although acidulated phosphate fluoride (APF) tablets have been tested. There are also fluoride-tannin drops for infants, often prescribed by pediatricians.

Caries Prevention by Fluoride Supplementation

A systematic review¹³⁴ of fluoride supplement use to prevent caries in children examined evidence from trials that were at least 5 years in duration. Eleven studies provided sufficient evidence to demonstrate a 24% reduction in caries increment in permanent teeth. The effect of fluoride supplementation on primary teeth was unclear.

Dosing Schedules

To obtain fluoride supplements in the United States and Canada, a prescription from a dentist or physician is required. The ADA, the American Academy of Pediatric Dentistry (AAPD), and the American Academy of Pediatrics (AAP) maintain the same schedules of recommended doses of fluoride supplements.¹¹⁵

As the dosing schedules for fluoride supplements are revised periodically, the trend has been to make them ever more conservative. The current ADA-recommended schedule, based on the age of the child and the concentration of fluoride in the water supply, is shown in Table 25.3. It was updated in 2010 and continues to be reviewed periodically. When the recommended standard for drinking water was changed in 2015, the schedule was reviewed and deemed appropriate in light of the new recommendation of 0.7 ppm fluoride for public water systems. Drawbacks related to fluoride supplement use relate to compliance and cost. Since daily administration is required, compliance will vary from child to child. Cost may be a barrier for some families. Each situation should be evaluated including the water fluoride level tested before fluoride supplement is prescribed, and efforts to address these challenges should be discussed with parents and caregivers. It can also be questioned whether the emphasis should be on the use of fluoride dentifrice instead of fluoride supplements, although studies are required to determine which approach leads to better caries prevention outcomes.

TABLE 25.3 Recommended Dosage Levels of Supplemental Fluoride as Established by the American Dental Association in 2010 (in mg F/day)¹¹⁵

Age	CONCENTRATION OF FLUORIDE IN WATER (PPM)		
	<0.3	0.3–0.6	>0.6
6 mo to 3 yr	0.25	—	—
3–6 yr	0.50	0.25	—
6–16 yr	1.00	0.50	—

Prenatal Fluoride Supplementation

The question of whether to prescribe fluoride supplements for an expectant woman to increase caries resistance in the offspring has been debated for years. In light of the discussion on dietary fluoride supplements in general and fluoride's predominantly topical mechanism of action in preventing caries, it is not surprising that current views are that any enhanced resistance to caries will be only minor at best. The only prospective randomized trial of prenatal fluoride supplementation found no significant difference in the caries experience of the offspring.⁸³ Therefore, use of prenatal supplements is not recommended.

Clinical Guidance on Use of Fluoride Products

The ADA periodically provides clinical practice guidelines. The most recent guideline came out in 2013¹⁴² and is expected to be updated in 2020. The expert panel was convened by the ADA Council on Scientific Affairs and reviewed professionally applied and prescription-strength topical fluoride agents including mouth rinses, gels, foams, pastes, and varnishes.

The panel determined that sufficient evidence supports use of four different options to prevent dental caries in people at risk: 2.26% fluoride varnish; 1.23% APF gel; a prescription-strength, home-use 0.5% fluoride gel or paste; or 0.09% fluoride mouth rinse for individuals 6 years of age or older.¹⁴²

Fluoride Varnishes

Fluoride varnish is widely accepted as the treatment of choice for preventing caries in high-risk children.^{21,90,97} It is especially appropriate for children younger than age 6, due to concerns about fluoride ingestion related to gels and foams.¹⁴² Fluoride varnish is not intended to be as permanent as a fissure sealant (see Chapter 26); rather it is a vehicle for holding fluoride in close contact with the tooth for a period of time. An advantage of varnishes over other methods of professional fluoride application is that varnishes are adhesive and hence should maximize fluoride contact with the tooth surface. Varnishes are a way of using high fluoride concentrations in small amounts of material. Fluoride varnishes have a long history in Europe and Canada and were accepted for use in the United States in 1994 as a cavity liner, but they are used off label in caries prevention. In a systematic review of 22 trials of fluoride varnishes, evidence has clearly established caries reduction for both permanent and primary teeth.⁹⁰

Varnishes must be reapplied at regular intervals to maintain their cariostatic effect, and a dose-response pattern has been demonstrated.¹⁴¹ Innovative public health collaborative programs in the United States use fluoride varnish to bridge the gap between dental and medical practice. Efforts to bring appropriate use of fluoride varnish into the medical practice include training programs like Smiles for Life¹²⁴ and those offered for pediatricians through the AAP⁵ and in medical school.⁶⁴ In many states, physicians use fluoride varnish to prevent early childhood caries in their at-risk young patients and get reimbursed by the Medicaid program.⁷⁸ A recent review⁶¹ found evidence that supports collaborative medical-dental integration that makes use of topical fluoride varnish applications for children. The premise for integrating oral health into primary medical care is based on the fact that a much higher proportion of infants visit a physician's office than visit a dental office (see Chapter 5).

Fluoride Mouth Rinses

NaF formulations have been tested as a weekly rinse at 0.2% (200 ppm fluoride) and as a daily rinse at 0.05% (230 ppm fluoride). School-based programs have found the weekly regimen to be the most convenient, whereas daily rinsing is most appropriate for individual use. The caries reductions from daily rinsing are only slightly greater than those from weekly rinsing, and the slight differences do not compensate for the greater practicality and lower cost of weekly rinsing in a school-based program. A systematic review of 35 studies demonstrated a preventive fraction of 27% for DMFS increment for interventions of at least 1-year duration.⁸⁸ This finding was irrespective of background fluoride exposure from other sources and baseline caries status. For home use, dentists can advise patients to buy fluoride mouthrinse from the drugstore or supermarket. Products come and go; a list of current products with ADA approval can be found on the ADA's website. Fluoride mouthrinses in school-based programs used since the 1970s have come under some scrutiny, with decline of its use in public programs. Box 25.2 provides a discussion.

Fluoride Gel Applications

Professional fluoride gel-tray applications have long been considered not to be cost-effective for community-based health programs, but use of 1.23% APF gel in a clinical setting or a prescription-strength, home-use 0.5% fluoride gel or paste can be effective for high risk children older than age 6. Although the effectiveness of fluoride varnish compared to fluoride gel is inconclusive, the time savings for application of fluoride varnish make it a reasonable approach for highly susceptible special groups in targeted community programs.^{87,89}

Prophylaxis Pastes Containing Fluoride

Fluoride-containing prophylactic pastes are widely used in dentistry; the reasoning behind their development was that the prophylaxis and the professional fluoride application could be carried out at

the same time. However, results from systematic reviews do not demonstrate any benefit attributable to this procedure.¹⁴²

Estimating Fluoride Intake From Various Formulations

Table 25.4 lists the quantities and concentrations of the fluoride compounds most frequently used in dental practice and those self-applied by individuals. Box 25.3 is a guide to estimating the amounts of fluoride in dental products, and Box 25.4 brings together the information on toxic exposure to fluoride.

Fluoride Toothpastes

Toothpastes with a fluoride concentration of 1000 to 1500 ppm are proved effective in prevention of dental caries and supported internationally.^{45,55,143} Toothpastes without active ingredients, meaning those that contain abrasive and flavoring agents only and thus are intended for oral hygiene and cosmetic benefits, have no anticaries action by themselves. But because toothbrushing is a social norm in high-income countries, a variety of preventive and therapeutic agents (both known and hypothetical) have been added to toothpastes over the years. Early efforts to produce anticariogenic toothpastes included the addition of ammonia, antibiotics, chlorophyll, and various other agents to toothpastes. None of these agents was effective. To date, fluoride is the only nonprescription toothpaste additive that has been shown to prevent caries.

The earliest attempts to add fluoride to toothpaste were unsuccessful because of the incompatible abrasives used in the products, which bound the fluoride and thus made it biologically unavailable. The first successful clinical trials of an fluoride additive used SnF_2 with a calcium pyrophosphate abrasive.⁹⁹ These positive results were replicated during the 1960s in other American and British studies using the same formulation. Systematic reviews demonstrate caries reductions in children of 24% in studies of at least 1-year duration, and use of fluoride toothpastes in fluoridated

• BOX 25.2 Using Data to Inform Action—Fluoride Mouthrinsing as a Community-Based Preventive Intervention

The Association of State and Territorial Dental Directors (ASTDD) updated the *Best Practice Approach Report: Use of Fluoride in Schools* in 2018.¹³ This report noted that the number of states with school-based fluoride mouthrinse programs has dropped from 37 in 2002 to 14 in 2017. The ASTDD report identified recommendations from a 1986 American Public Health Association (APHA) technical report⁶ to shift focus and target "mouthrinse programs to at-risk populations in nonfluoridated communities and to primarily focus on dental sealants, reflecting the declining rate of decay on the smooth surfaces of teeth." The APHA report summarized the results of the National Preventive Dentistry Demonstration Program (NPDDP), a large program conducted in 10 US cities in 1976 to 1981 to compare the costs and effectiveness of a series of preventive mechanisms. The NPDDP raised serious doubts about fluoride mouthrinsing as an effective public health procedure.

The NPDDP found that the effectiveness of fluoride mouthrinsing was poor both in overall results⁷⁶ and in separate assessments of first-grade children with high and low caries increments.⁴² Earlier reviews by the NPDDP researchers had reported serious flaws in the conduct of many earlier studies that did not use concurrent control groups²⁶ and in some of the economic analyses that led to the assumption of cost-effectiveness.¹²⁰ Quite strong criticism was also leveled at the way in which the National Institute of Dental and Craniofacial Research had used its data to promote the use of fluoride mouthrinses in public health programs.⁴¹

At the same time, the NPDDP itself was criticized on the grounds of faulty design and analysis.⁵⁸ The atmosphere of uncertainty was dissipated to some extent at a workshop on the cost-effectiveness of preventive procedures in 1989, where it was concluded that fluoride mouthrinsing is a reasonable procedure to use in high-risk individuals or groups, though of questionable cost-effectiveness as a population-based strategy.⁸²

A question for consideration today is this: What should policy makers and program directors do when a large (and expensive) study reports findings that challenge the current practice and conventional wisdom? While systematic reviews to summarize evidence are a relatively newer phenomenon in public health, the number of studies that showed a benefit for a fluoride mouthrinse intervention in 1986 was sufficient to justify such programs in schools. Today, the summary of 35 published studies⁸⁰ stands in support of fluoride mouthrinse programs while one study stands in opposition.⁶

A way forward is to recognize the uncertainty and emphasize the importance of the use of data to drive program implementation and evaluation.²⁸ The costs for proper monitoring of a community program need to be included when planning a preventive intervention. Qualitative and quantitative data should be gathered to ensure smooth implementation and to guide quality improvement over the course of the intervention. Evaluation of the impact of the program serves to inform stakeholders and guide program expansion.

Concentration and Quantity of Fluoride in Commonly Used Topical Fluoride Compounds

• TABLE 25.4

Compound	Concentration (ppm)	Quantity
Topically Applied Agents		
5% NaF varnish (2.26% F)	22,600	9 mg in 0.4 mL unit dose ^a
1.23% APF gel, foam, or prophylactic paste	12,300	62 mg in 5 g
8% SnF ₂ solution	19,363	97 mg in 5 mL
2% NaF	9,050	44 mg in 5 mL
38% Silver diamine fluoride (5% F)	44,800	1.3 mg in 0.03 mL (1 drop)
Mouthrinses		
0.2% NaF—weekly	905	9 mg in 10 mL ^b
0.05% NaF—daily	226	2 mg in 10 mL
0.1% SnF—daily	242	2 mg in 10 mL
APF rinse (0.1% fluoride)—weekly	1,000	10 mg in 10 mL
APF rinse (0.022% fluoride)—daily	200	2 mg in 10 mL
Toothpastes		
0.76% Na ₂ FPO ₃	1,000	1 mg/g ^c
0.243% NaF	1,105	1.1 mg/g
1.1% NaF	5,000	5.0 mg/g
0.454% SnF ₂	1,100	1.1 mg/g

^aAmount of material varies by type of topical application.

^bAmounts of 5 and 10 mL are used in supervised mouthrinsing.

^cAn average load of toothpaste on the brush is about 1 g.

APF, Acidulated phosphate fluoride; F, fluoride.

Note: Some figures are rounded.

Serious marketing of fluoride toothpastes was underway by the early 1970s, and public acceptance was immediate in virtually all of the high-income nations. By the 1990s, fluoride toothpastes accounted for well over 90% of the toothpaste market in the United States, Canada, and many other countries. Their use in low-income countries, where fluoride toothpastes could potentially fill an important preventive role, is limited by their relatively high cost⁶³ and poor distribution.

Quality of the Fluoride Toothpaste Trials

It must be stated at this point that many of the clinical trials for fluoride toothpaste are among the most elegant trials to be found in dentistry—or in all of biomedicine for that matter—to demonstrate the efficacy of a product. All of the essential features of the best clinical trials (see Chapter 12) can be found in many of these studies: randomized groups, double-blind designs, placebo controls, and meticulous procedural protocols. Because the water fluoridation field trials have inherent design limitations as previously discussed, opponents of fluoridation can attack their validity. But if the issue is the efficacy of fluoride exposure, the fluoride toothpaste trials collectively include many studies that meet the gold standard for such trials. Taken together, the toothpaste trials provide the strongest evidence we have that fluoride exposure is efficacious in controlling caries.

Fluoride Concentrations in Toothpastes

The fluoride toothpastes that first became widely marketed contained about 1000 to 1100 ppm fluoride. When introduced into the oral cavity, fluoride in toothpaste is taken up directly by demineralized enamel,^{110,131} although its retention on sound enamel is thought to be of relatively minor importance. It also increases the fluoride concentration in dental plaque fluid,⁴⁹ thus leaving a store of fluoride available for remineralization.^{84,121} Salivary fluoride levels, normally low in resting saliva, rise 100- or even 1000-fold after toothbrushing with fluoride toothpaste.⁴⁹ This level drops over the next few hours. Postbrushing levels of intraoral fluoride are affected by the amount and vigor of water rinsing after brushing⁵⁰; the best advice for adults is to rinse gently after brushing or just spit and not rinse.

Because laboratory studies showed that the uptake of fluoride into demineralized enamel and into plaque was proportional to the concentration of fluoride in the toothpaste, a natural next step was the testing of toothpastes with higher concentrations. Toothpastes with 1500 ppm fluoride have been found slightly more efficacious than the 1000 ppm fluoride products.¹⁴⁵ Clinical trials have also been conducted with toothpastes of 2500 to 5000 ppm fluoride with mixed results. In general, systematic analyses conclude that caries reductions are proportional to the fluoride concentration in the toothpastes.¹⁴³ Prescription-strength toothpaste with 5000 ppm fluoride (1.1% NaF) is recommended for high-risk patients based on a systematic review.¹⁴²

At the other end of the spectrum, concerns about the fluorosis risk from the swallowing of toothpaste by children have led to the testing of toothpastes with lower than standard levels of fluoride. Children can swallow between 0.12 and 0.38 mg of toothpaste per brushing.¹⁹ In general, studies of 440 and 550 ppm fluoride products suggest a reduced risk for fluorosis compared with 1000 ppm fluoride toothpastes when used by young children. However, the systematic review of these levels showed that they are not sufficiently different from placebo for preventing caries. While toothpastes containing 400 ppm fluoride have been

areas has demonstrated an additive effect.^{86,135} There is some evidence that use of fluoride toothpaste prevents root caries in adults.⁶²

In all, more than 90 clinical trials have been conducted with various fluoride compounds as the active ingredient: SnF₂, NaF, sodium monofluorophosphate (MFP), and amine fluoride have all been successfully tested.⁹⁹ Even more compatible abrasives have been developed and tried: insoluble metaphosphate, sodium trimetaphosphate, hydrated silica gel, calcium carbonate, dicalcium dihydrate, and calcium pyrophosphate are the main ones. New formulations are constantly under investigation and are soon marketed when found effective.

There is some laboratory evidence that toothpastes with NaF are more efficacious than those with MFP, although clinical data on this subject are hard to interpret. Analyses of data available in the early 1990s were split on the issue, with discussion often becoming pedantic. Subsequent clinical trials that gave a slight edge to NaF required very large groups to show statistical significance,⁹¹ and another trial found no difference between NaF and MFP products.³⁹

Basic Information

1 oz = 28.4 g

"Percent" means g or mL per 100 g or mL; e.g., 2% NaF solution means 2 g NaF per 100 mL water

Atomic weights: Na = 23; F = 19, Sn = 119; P = 31; O = 16

Fluoride compounds most often used are NaF, SnF₂, Na₂FPO₃

Example 1: How much fluoride is in 10 mL of 0.05% NaF mouthrinse?

The mouthrinse has 0.05 g of NaF per 100 mL of rinse

= 50 mg of NaF, or 5 mg of NaF per 10 mL

Amount of fluoride = $5 \times 19/42 = 2.26$ mg

Example 2: How much fluoride is in a 6.4 oz tube of Colgate MFP toothpaste? (6.4 oz = 181.8 g)

Colgate with sodium monofluorophosphate (MFP) is 0.76% Na₂FPO₃, so it has 0.76 g of MFP per 100 mL of toothpaste

Grams of Na₂FPO₃ in a 6.4 oz tube = $0.76 \times 181.8/100 = 1.38$ g, which is 1380 mg Na₂FPO₃

Amount of fluoride in the tube = $1380 \times 19/144 = 182.1$ mg

Example 3: How much fluoride is in an 8.2 oz tube of Crest toothpaste? (8.2 oz = 232.9 g)

Crest contains 0.243% NaF, so it has 0.243 g of NaF per 100 mL of toothpaste

Grams of NaF in an 8.2 oz tube = $0.243 \times 232.9/100 = 0.566$ g, which is 566 mg NaF

Amount of fluoride in the tube = $566 \times 19/42 = 256$ mg

• BOX 25.4 Data on Toxic Fluoride Intake Levels in Humans^{30,68}

- Certainly lethal dose (CLD) = 32–64 mg fluoride/kg body weight
 - Death is likely in a child who ingests more than 15 mg fluoride/kg body weight
 - Probably toxic dose (PTD), defined as the minimum dose that could cause toxic signs and symptoms, including death, and the ingestion of which should trigger immediate intervention and hospitalization = 5 mg fluoride/kg body weight
- The 10th and 90th percentiles of weight for children at various ages are as follows:

Age	Weight
1 year	8–12 kg
2 years	10–15 kg
3 years	12–17 kg
4 years	14–20 kg
6 years	17–27 kg
8 years	22–34 kg

So for a child about 7 years of age, who would weight approximately 20 kg, the PTD would be around 100 mg fluoride.

available in Europe, Australia, and New Zealand for years, they have not been tested in clinical trials and are not approved for marketing in the United States and Canada.

The efficacy of fluoride toothpaste is mainly driven by three things: (1) the concentration of available fluoride; (2) the application to the tooth surface and biofilm; and (3) the retention of fluoride after brushing in saliva, plaque fluid, and other tissue reservoirs. However, the tendency to swallow toothpaste can lead to enamel fluorosis in children younger than age 6. Use of less toothpaste and brushing with adult supervision is advocated for this age group and *not* using an ineffective concentration of toothpaste. In 2014, the ADA published guidelines indicating that children under age 3 should be using no more than a smear of toothpaste that is the size of a grain of rice. For children 3 to 6 years old, caregivers should be dispensing no more than a pea-sized amount of fluoride toothpaste.³

Standards for Toothpaste Efficacy

The toothpaste market is a multibillion-dollar industry in the United States, so competition between major manufacturers is keen. Companies incur much research and development expense to secure the ADA's seal of approval for their products; the logo on the package improves marketing and is a guide for consumers as well. Because of the multitude of formulations of fluoride plus abrasive available, the ADA developed guidelines for use in judging applications for its seal of approval for fluoride toothpastes.¹ With newer formulations replacing earlier products and advertising claims being made of superiority over rival products, the ADA Council on Scientific Affairs periodically determines standards such as what evidence would be adequate to substantiate claims of equivalency or superiority of a particular formulation (i.e., fluoride ingredient with compatible abrasives) relative to other

formulations. Typically, manufacturer claims need to be backed by rigorous clinical trials in human populations and such trials require the use of the rival product as a positive control. The trials had to be designed to show a 10% difference in caries increment with a power of 80% (see Chapter 13). The ADA's seal of approval goes to particular formulations rather than to products. The list of toothpastes that carry the seal, which can be found on the ADA website, is now quite long and seems to be constantly growing.

Impact of Fluoride Toothpastes

The impact of fluoride toothpaste use on global caries experience has been profound. Fluoride exposure is accepted as the main reason for the decline of dental caries over recent years, and most authorities believe that fluoride toothpaste has been the most important fluoride vehicle on a global scale.²⁷ The caries reductions of 15% to 30% achieved in most clinical trials may appear modest compared to those attributed to water fluoridation, but it must be remembered that these were trials of 2 to 3 years' duration, whereas water fluoridation studies usually measured lifetime exposure. Because, as we know, fluoride works most effectively to prevent caries when small amounts are in the oral cavity at all times, there is no reason that regular lifetime use of fluoride toothpaste should not give results that are similar to those of lifetime use of fluoridated water.

Supervised brushing programs using fluoride toothpaste offer an approach for intervention in high-risk groups.⁴⁰ Efficacy of fluoride toothpaste appears to be enhanced in supervised settings^{86,135} and successful programs have been used in places such as Ireland.⁷³ However, some investigators find good evidence for supervised programs to be lacking.⁴⁴

Multiple Fluoride Exposures

The majority of clinical trials of fluoride products test only a single agent. In the modern world, however, exposure to multiple sources of fluoride is the rule rather than the exception. People who live in

fluoridated areas brush their teeth with fluoride toothpaste, and are periodically given professional fluoride applications by their dentists. Fluoride mouthrinsing is used in public health programs, and some mouthwashes contain fluoride. Then there are dietary supplements, whether used appropriately or not, as well as the fluoride exposures from food and drink. When these are added together, it becomes readily apparent that people in most high-income countries are being exposed to much more fluoride than in the past.

This phenomenon of multiple fluoride exposures can be viewed from several perspectives. In one way it is beneficial because with the several different anticaries actions of fluoride, fuller advantage is being taken of fluoride's potential. On the other hand, the increasing prevalence of fluorosis (see Chapter 19) is almost certain to be a product of these multiple and poorly controlled fluoride exposures. Dentistry's goal, though not an easy one to achieve for either an individual patient or the community, is to maximize the benefits from fluoride exposure while avoiding an unacceptable level of the undesirable side effects.

Multiple fluoride therapies, whether in fluoridated or non-fluoridated areas, are clearly beneficial for patients who are unusually susceptible to caries. For example, excellent results may be attained in preventing caries in patients with salivary disorders such as Sjögren disease or those who have had radiation treatment that can produce dysfunction of the salivary glands and hence loss of salivary caries-protective benefits. Based on a recent systematic review, only a generic recommendation can be made for the use of topical fluoride as the first line of defense in individuals with Sjögren disease due to the lack of sufficient evidence for specific types of fluoride or frequency of use.¹⁴⁹

Systematic reviews have found caries reductions above those expected from fluoridated water alone among children in studies of fluoride rinse⁸⁸ and studies of fluoride toothpaste.⁸⁶ In the context of cost-effectiveness, the data on the use of fluoride mouthrinses in fluoridated areas are worth examining in detail; Table 25.5 presents these data for four North American studies. A beneficial effect can be seen in each case, although even in the earlier studies the effects were limited in terms of absolute caries reductions. Cost-effectiveness issues arise given results such as

• **TABLE 25.5** Summarized Results of Studies of Fluoride Mouthrinses in Fluoridated Areas

Material	Age Groups	Duration	% Reduction	DMFS Reduction	Reference
0.1% SnF ₂ daily	8–13 yr	20 mo	33.1 ^a 43.3 ^b	1.00 1.22	Radake et al. ¹⁰⁸
0.05% NaF daily	12 yr	30 mo	27.9 ^a 49.7 ^a	0.72 0.94	Driscoll et al. ⁴⁶
0.2% NaF weekly	12 yr	30 mo	22.1 ^a 55.0 ^b	0.57 1.04	Driscoll et al. ⁴⁶
0.2% NaF weekly	Grades 1–2	48 mo	Not given ^c	0.29	Bell et al. ¹⁸
	Grade 5	24 mo	Not given ^c	0.03	

^aFirst of two examiners.

^bSecond of two examiners.

^cCould not be determined from the data provided.

DMFS, Decayed, missing, and filled tooth surfaces.

TABLE 25.6 Summarized Results of Studies of Additive Effects of Fluoride Mouthrinsing and Supervised Brushing With Fluoride Toothpastes DMFS Increments

Age Groups	Duration	F Rinse ^a	F Toothpaste ^b	Rinse + Toothpaste ^c	Placebo	Reference
Approximately 13 yr	24 mo	4.81 (13.1%) ^d	4.44 (17.9%) ^d	4.12 (22.7%) ^d		
11 yr	30 mo	4.79 (23.4%) ^d	5.14 (17.8%) ^d	5.30 (15.2%) ^d	5.61	Ashley et al. ⁹
11–12 yr	36 mo	4.72 (24.5%) ^d	4.60 (26.3%) ^d	4.76 (26.8%) ^d	6.51	Ringelberg et al. ¹¹²
					6.25	Blinkhorn et al. ²⁵

^a0.05% NaF daily at school.

^b0.76% Sodium monofluorophosphate except for Ringelberg et al.¹¹² (0.4% stannous fluoride, unsupervised).

^cAll conducted supervised rinse immediately after brushing.

^dPercentage reduction compared to placebo control.

DMFS, Decayed, missing, and filled tooth surfaces; F, fluoride.

these: When a new fluoride program is instituted among children who already have some fluoride exposure and low caries experience, is the additional benefit worth the cost?

The last two lines of Table 25.5 showing data from the NPDDP provoked the subsequent criticisms of fluoride mouthrinsing mentioned earlier in this chapter. Table 25.6 gives the results of studies in which supervised brushing with a fluoride toothpaste was combined with supervised daily fluoride mouthrinsing at school, and the results were compared with those for each procedure alone. The results for the combined procedures are, at best, only slightly superior to the use of either alone.

Because caries experience in North American children has generally reached lower levels than those at which the results in Tables 25.5 and 25.6 were produced, it is hard to argue for the cost-effectiveness of fluoride mouthrinsing in fluoridated areas, especially where frequent use of fluoride toothpaste is common, unless there is a way to target the intervention to individuals at high risk for caries. This conclusion was confirmed at the 1989 workshop on cost-effectiveness of preventive programs.⁸²

Cost-effectiveness is a less important issue for the private patient than for public health programs, but selection of a preventive regimen for an individual patient should still take into account the likely added benefit of multiple exposures. To illustrate, professional fluoride applications are of dubious additional value to the individual patient in a fluoridated area who brushes daily with fluoride toothpaste and who has little caries problem. However, even in a fluoridated area, more caries-susceptible patients may get reasonable additional benefit from professional fluoride applications or prescribed daily use of fluoride mouthrinses. In these decisions, the clinical judgment should always be guided by sound evidence and can be enhanced by attention to recommendations on fluoride use.¹⁴² The potential benefits of fluoride mouthrinses need to be weighed against the benefits of prescription high-concentration fluoride toothpaste for high caries-risk patients. As we have said already, however, broad exposure to multiple sources of fluoride is the norm in North America today. When introducing a new fluoride program in a community, therefore, a public health administrator must assess whether the program will produce benefits beyond those already being provided by other fluoride exposures. The evidence just cited shows that additional benefits will probably accrue, but the bigger public health question is whether the extra benefits will be worth the cost of the program.

Nonrestorative Caries Treatment-Arresting Advanced Carious Lesions With Fluoride

In 2018, the ADA Council on Scientific Affairs released the first in a series of clinical practice guidelines for caries management. It presents a viable role for silver diamine fluoride that may optimize patient care in some scenarios.¹²³

Silver Diamine Fluoride

Silver diamine fluoride (SDF) is not new, but around 2014 it re-emerged in the United States as a nonrestorative treatment that is effective for carious lesions.^{103,123} The 2018 ADA clinical practice guideline¹²³ summarizes and highlights the effectiveness of SDF for advanced cavitated coronal and root surface lesions. Application of 38% SDF biannually is shown to be more effective at arresting advanced cavitated lesions on primary teeth than 5% NaF varnish applied once per week for 3 weeks and more effective than a single application of 38% SDF annually. The ADA panel recommends use of 38% SDF biannually to arrest cavitated lesions on primary teeth as a first line of care. The panel was comfortable extrapolating the published research to date to go on and recommend biannual application of 38% SDF for advanced cavitated lesions on permanent teeth as well. Readers should be aware that ongoing research is likely to continue on use of SDF to better outline its comparative effectiveness in a range of settings.

Although the impact of SDF on cavitated lesions in primary teeth is well established, evidence that application of 38% SDF is effective for preventing new smooth surface lesions is building. A systematic review¹⁰³ of the beneficial impact of SDF on other teeth (beyond the ones treated with cavitated lesions) yielded only four studies that had data on primary teeth and followed the children at least 12 months. A key finding from a summarization of two studies that met the inclusion criteria was that 38% SDF provides a benefit to the entire primary dentition in children when they were followed at least 24 months. Compared to placebo, the prevented fraction was 77%.¹⁰³ More research will clarify these findings.

The formulation that has been approved for use in the United States is 38% SDF, which equates to 44,800 ppm fluoride. Clinical guidelines for treatment of cavitated lesions of coronal surfaces of primary and permanent teeth are for biannual applications of 38% SDF. The application of SDF arrests caries activity and forms a hard, blackened surface at the site. Use of SDF may be desired

in situations where traditional restorative options are not favored, such as in uncooperative patients whose parents or caregivers prefer not to undergo use of general anesthesia. The blackened surface that results from the use of SDF may unacceptable to some patients and/or caregivers. Proper informed consent procedures need to be followed when use of SDF is under consideration.

SDF arrests carious lesions and provides a therapeutic result via several complementary mechanisms.³³ First, the silver component has a direct bactericidal effect by affecting sulfhydryl groups and interfering with metabolism. Second, the silver salts that form on the dentin are very resistant to penetration and protect the dentin tubules from exposure, thereby reducing sensitivity. The fluoride component forms fluorapatite to increase the mineral content of the enamel and improve acid resistance.

Summary

Fluoride is an excellent model for examining preventive strategies in different contexts. However, in this chapter the focus is solely on fluoride in our efforts to prevent dental caries. Essentially, fluoride acts to raise the threshold of protection against injury to enamel from dietomicrobial acids. Injury prevention strategies⁶⁷ such as programs aimed to reduce traffic fatalities typically address factors beyond the occupants in the automobile and include efforts to improve the environmental substrate (i.e., the highway) and the factors that intensify the hazard, such as the velocity of the vehicle. It would be shortsighted to only focus on protecting the occupant when prevention of fatal crashes is the objective. Prevention strategies that aim further upstream to interrupt the cascade of factors that lead to the marshalling of the forces that produce the acid should also be deployed. Multiple avenues should be pursued to address biofilm composition¹⁰⁶ and accumulation as well as the role of dietary sugars^{98,120} for a more comprehensive approach to prevent dental caries. These aspects are addressed in other chapters of this volume (diet in Chapter 23 and sealants in Chapter 26).

References

1. ADA. *ADA Seal of Acceptance*. Available from: <https://www.ada.org/en/science-research/ada-seal-of-acceptance/how-to-earn-the-ada-seal/general-criteria-for-acceptance>; 2011.
2. ADA. *Fluoridation Facts 2018*. Chicago: American Dental Association; 2018.
3. ADA Council on Scientific Affairs. Fluoride toothpaste use for young children. *J Am Dent Assoc*. 2014;145(2):190–191.
4. Allukian M Jr, Carter-Pokras OD, Gooch BF, et al. Science, politics, and communication: the case of community water fluoridation in the US. *Ann Epidemiol*. 2018;28(6):401–410.
5. American Academy of Pediatrics. *Oral Health Education and Training*. Available from: <https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Oral-Health/Pages/Education-and-Training.aspx>. Accessed May 22, 2019.
6. APHA Technical Report. Review of the National Preventive Dentistry Demonstration Program. *Am J Public Health*. 1986;76(4):434–447.
7. Arnold FA Jr, Dean HT, Knutson JW. Effect of fluoridated public water supplies on dental caries prevalence: seventh year of Grand Rapids-Muskegon study. *Public Health Rep (1896–1970)*. 1953;68(2):141–148.
8. Arnold FA Jr, Likins RC, Russell AL, et al. Fifteenth year of the Grand Rapids fluoridation study. *J Am Dental Assoc*. 1962;65(6):780–785.
9. Ashley FP, Mainwaring PJ, Emslie RD, et al. Clinical testing of a mouthrinse and a dentifrice containing fluoride. A two-year supervised study in school children. *Br Dent J*. 1977;143(10):333–338.
10. Ast DB, Finn SB, McCaffrey I. The Newburgh-Kingston caries fluorine study. 1. Dental findings after three years of water fluoridation. *Am J Public Health Nations Health*. 1950;40(6):716–724.
11. Ast DB, Fitzgerald B. Effectiveness of water fluoridation. *J Am Dent Assoc*. 1962;65(5):581–587.
12. Ast DB, Smith DJ, Wachs B, Cantwell KT. The Newburgh-Kingston caries-fluorine study. XIV. Combined clinical and roentgenographic dental findings after ten years of fluoride experience. *J Am Dent Assoc*. 1956;52:314–325.
13. ASTDD. *Directors AoSaTD*. Best Practice Approach Report. Use of fluoride in schools. ASTDD; 2018.
14. Auerbach J. The 3 buckets of prevention. *J Public Health Manage Practice*. 2016;22(3):215–218.
15. Backer Dirks OHB, Kwant GW. The result of 6½ years of artificial drinking water in the Netherlands; the Tiel-Culemborg experiment. *Arch Oral Biol*. 1961;5:284–300.
16. Bailey W. Fluoridation Law. In: *NOHC 2009: National Oral Health Conference*; 2009.
17. Banoczy J, Rugg-Gunn AJ. Clinical Studies. In: Banoczy J, Petersen PE, Rugg-Gunn AJ, eds. *Milk fluoridation for the prevention of dental caries*. Geneva: World Health Organization; 2009.
18. Bell RM, Klein SP, Bohannon HM, Disney JA, Graves RC, Madison R. *Treatment effects in the National Preventive Dentistry Demonstration Program*. Santa Monica, CA: Rand Corporation; 1984.
19. Beltrán ED, Szpunar SM. Fluoride in toothpastes for children: suggestion for change. *Ped Dent*. 1988;10(3):185–188.
20. Beltrán-Aguilar ED, Barker L, Sohn W, Wei L. Water intake by outdoor temperature among children aged 1–10 years: implications for community water fluoridation in the U.S. *Public Health Rep*. 2015;130(4):362–371.
21. Beltrán-Aguilar ED, Goldstein JW, Lockwood SA. Fluoride varnishes: a review of their clinical use, cariostatic mechanism, efficacy and safety. *J Am Dent Assoc*. 2000;131(5):589–596.
22. Blayney JR, Hill IN. Fluorine and dental caries. *J Am Dent Assoc*. 1967;74(Special Issue):233–302.
23. Blayney JR, Hill IN, Wolf W. The Evanston dental caries study. XVI. Reduction in dental caries attack rates in children six to eight years old. *J Am Dent Assoc*. 1956;53(3):327–333.
24. Blayney JR, Tucker WH. The Evanston dental caries study: II. Purpose and mechanism of the study. *J Dent Res*. 1948;27(3):279–286.
25. Blinkhorn AS, Holloway PJ, Davies TGH. Combined effects of a fluoride dentifrice and mouthrinse on the incidence of dental caries. *Community Dent Oral Epidemiol*. 1983;11(1):7–11.
26. Bohannon HM, Graves RC, Disney JA, Stamm JW, Abernathy JB, Bader JD. Effect of secular decline in caries on the evaluation of preventive dentistry demonstrations. *J Public Health Dent*. 1985;45(2):83–89.
27. Bratthall D, Hansel-Petersson G, Sundberg H. Reasons for the caries decline: what do the experts believe? *Eur J Oral Sci*. 1996;104:416–422.
28. Brownson RC, Baker EA, Leet TL, Gillespie KN, True WR. *Evidence-Based Public Health*. 2nd ed. New York: Oxford University Press; 2011.
29. Buchalla W, Artin T, Schulte-Mönting J, Hellwig E. Fluoride uptake, retention, and remineralization efficacy of a highly concentrated fluoride solution on enamel lesions in situ. *J Dent Res*. 2002;81(5):329–333.
30. Burt BA. The changing patterns of systemic fluoride intake. *J Dent Res*. 1992;71:1228–1237.

31. Burt BA. Fluoridation and social equity. *J Public Health Dent.* 2002;62(4):195–200.
32. Burt BA, Eklund SA, Ismail AI. Root caries in an optimally fluoridated and a high-fluoride community. *J Dent Res.* 1986;65(9):1154–1158.
33. Chibinski AC, Wambier LM, Feltrin J, Loguercio AD, Wambier DS, Reis A. Silver diamine fluoride has efficacy in controlling caries progression in primary teeth: a systematic review and meta-analysis. *Caries Res.* 2017;51(5):527–541.
34. Dawes C. Salivary flow patterns and the health of hard and soft oral tissues. *J Am Dent Assoc.* 2008;139:18S–24S.
35. Dean HT. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. *Fluorine and dental health.* Washington DC: American Association for the Advancement of Science; 1942:23–31.
36. Dean HT, Arnold FA Jr, Jay P, et al. Studies on mass control of dental caries through fluoridation of the public water supply. *Public Health Rep.* 1950;65:1403–1408.
37. Dean HT, Arnold Francis A Jr, Elias E. Domestic Water and Dental Caries: V. Additional studies of the relation of fluoride domestic waters to dental caries experience in 4,425 white children, aged 12 to 14 years, of 13 cities in 4 states. *Public Health Rep (1896–1970).* 1942;57(32):1155–1179.
38. Dean HT, Jay P, Arnold FA Jr, et al. Domestic water and dental caries: II. A study of 2,832 white children, aged 12–14 years, of 8 suburban Chicago communities, including *Lactobacillus acidophilus* studies of 1,761 children. *Public Health Rep (1896–1970).* 1941;56(15):761–792.
39. DePaola PF, Soparkar PM, Triol C, et al. The relative anticaries effectiveness of sodium monofluorophosphate and sodium fluoride as contained in currently available dentifrice formulations. *Am J Dent.* 1993;S7–S12.
40. Dickson-Swift V, Kenny A, Gussy M, et al. Supervised toothbrushing programs in primary schools and early childhood settings: a scoping review. *Community Dent Health.* 2017;34(4):208–225.
41. Disney JA, Bohannon HM, Klein SP, et al. A case study in contesting the conventional wisdom: school-based fluoride mouthrinse programs in the USA. *Community Dent Oral Epidemiol.* 1990;18(1):46–56.
42. Disney JA, Graves RC, Stamm JW, et al. Comparative effects of a 4-year fluoride mouthrinse program on high and low caries forming grade 1 children. *Community Dent Oral Epidemiol.* 1989;17(3):139–143.
43. Do L, Ha D, Peres MA, Skinner J, et al. Effectiveness of water fluoridation in the prevention of dental caries across adult age groups. *Community Dent Oral Epidemiol.* 2017;45(3):225–232.
44. dos Santos APP, de Oliveira BH, Nadanovsky P. A systematic review of the effects of supervised toothbrushing on caries incidence in children and adolescents. *Int J Paed Dent.* 2018;28(1):3–11.
45. Dos Santos APP, Nadanovsky P, De Oliveira BH. A systematic review and meta-analysis of the effects of fluoride toothpastes on the prevention of dental caries in the primary dentition of preschool children. *Community Dent Oral Epidemiol.* 2013;41(1):1–12.
46. Driscoll WS, Swango PA, Horowitz AM. Caries-preventive effects of daily and weekly fluoride mouthrinsing in a fluoridated community: final results after 30 months. *J Am Dent Assoc.* (1939). 1982;105(6):1010–1013.
47. EPA. Drinking Water Regulations. Public Notifications. *Fed Reg.* 1987;52:41534–41550.
48. EPA. *National Primary Drinking Water Regulations; Announcement of the Results of EPA's Review of Existing Drinking Water Standards and Request for Public Comment and/or Information on Related Issues.* Washington, DC: National Archives; January 11, 2017.
49. Duckworth RM. Pharmacokinetics in the oral cavity: fluoride and other active ingredients. *Monographs in Oral Science.* 2013;23:125–139.
50. Duckworth RM, Knoop D, Stephen KW. Effect of mouthrinsing after toothbrushing with a fluoride dentifrice on human salivary fluoride levels. *Caries Res.* 1991;25(4):287–291.
51. EPA. Interim Primary Drinking Water Regulations. *Fed Reg.* 1980;45(168):57332–57357.
52. EPA. National Primary Drinking Water Regulations. *Fluoride Fed Reg.* 1985;50:20164–20175.
53. EPA. National Primary and Secondary Drinking Water Regulations. Fluoride; Final Rule. *Fed Reg.* 1986;51:11396–11412.
54. Featherstone JDB. Prevention and reversal of dental caries: role of low level fluoride. *Community Dent Oral Epidemiol.* 1999;27(1):31–40.
55. FDI World Dental Federation. *Promoting Dental Health Through Fluoride Toothpaste.* Geneva. 2018.
56. FDI World Dental Federation. *Promoting Oral Health Through Fluoride.* *Int Dent J.* 2018;68(1):16–17.
57. Fejerskov O. Concepts of dental caries and their consequences for understanding the disease. *Community Dent Oral Epidemiol.* 1997;25(1):5–12.
58. Fleiss JL. A dissenting opinion on the National Preventive Dentistry Demonstration Program. *Am J Public Health.* 1986;76(4):445–447.
59. Community Preventive Services Task Force. Available from: https://www.thecommunityguide.org/sites/default/files/assets/Oral-Health-Caries-Community-Water-Fluoridation_3.pdf.
60. Frieden TR. A framework for public health action: the health impact pyramid. *Am J Public Health.* 2010;100(4):590–595.
61. Gauger TL, Prosser LA, Fontana M, Polverini PJ. Integrative and collaborative care models between pediatric oral health and primary care providers: a scoping review of the literature. *J Public Health Dent.* 2018;78(3):246–256.
62. Gluzman R, Katz RV, Frey BJ, et al. Prevention of root caries: a literature review of primary and secondary preventive agents. *Spec Care Dentistry.* 2013;33(3):133–140.
63. Goldman AS, Yee R, Holmgren CJ, et al. *Global affordability of fluoride toothpaste.* 2008;4:7.
64. Graham E, Negron R, Domoto P, et al. Children's oral health in the medical curriculum: a collaborative intervention at a university-affiliated hospital. *J Dent Ed.* 2003;67(3):338–347.
65. Griffin SO, Gooch BF, Lockwood SA, et al. Quantifying the diffused benefit from water fluoridation in the United States. *Community Dent Oral Epidemiol.* 2001;29(2):120–129.
66. Groeneveld A, Van Eck AAMJ, Backer Dirks O. Fluoride in caries prevention: is the effect pre- or post-eruptive? *J Dent Res.* 1990;69 (Feb Spec Iss):751–755.
67. Haddon W Jr. On the escape of tigers: an ecologic note. *Am J Public Health Nat's Health.* 1970;60(12):2229–2234.
68. Heifetz SB, Horowitz HS. Amounts of fluoride in self administered dental products: safety considerations for children. *Pediatrics.* 1986;77:876–882.
69. Heller KE, Sohn W, Burt BA, Eklund SA. Water consumption in the United States in 1994–96 and implications for water fluoridation policy. *J Public Health Dent.* 1999;59(1):3–11.
70. Hutton WL, Linscott BW, Williams DB. The Brantford fluorine experiment: interim report after five years of water fluoridation. *Can J Public Health/Rev Can Sante Publique.* 1951;42(3):81–87.
71. Hutton WL, Linscott BW, Williams DB. Final report of local studies on water fluoridation in Brantford. *Can J Public Health/Rev Can Sante Publique.* 1956;47(3):89–92.
72. Iheozor-Ejiofor Z, Worthington HV, Walsh T, et al. Water fluoridation for the prevention of dental caries. *Cochrane DB Syst Rev* U6. 2015;(6). CD010856.
73. Irish Oral Health Services Guideline Initiative. *Topical fluorides: Evidence-based guidance on the use of topical fluorides for caries prevention in children and adolescents in Ireland.* University College Cork. 2008.
74. Ismail AI, Tellez M, Pitts NB, et al. Caries management pathways preserve dental tissues and promote oral health. *Community Dent Oral Epidemiol.* 2013;41(1):e12–e40.

75. Keyes PH. Recent advances in dental caries research. Bacteriology. Bacteriological findings and biological implications. *Int Dent J*. 1962;12(4):443-464.
76. Klein SP, Bohannon HM, Bell RM, et al. The cost and effectiveness of school-based preventive dental care. *Am J Public Health*. 1985; 75(4):382-391.
77. Koo H. Strategies to enhance the biological effects of fluoride on dental biofilms. *Adv Dent Res*. 2008;20(1):17-21.
78. Kranz AM, Preisser JS, Rozier RG. Effects of physician-based preventive oral health services on dental caries. *Pediatrics*. 2015;136(1):107.
79. Kumar JV. Is water fluoridation still necessary? *Adv Dent Res*. 2008;20(1):8-12.
80. Kumar JV, Adekugbe O, Melnik TA. Geographic variation in Medicaid claims for dental procedures in New York state: role of fluoridation under contemporary conditions. *Public Health Rep*. 2010;125(5):647-654.
81. Lamont RJ, Koo H, Hajishengallis G. The oral microbiota: dynamic communities and host interactions. *Nat Rev Microbiol*. 2018.
82. Leverett DH. Effectiveness of mouthrinsing with fluoride solutions in preventing coronal and root caries. *J Public Health Dent*. 1989; 49(5):310-316.
83. Leverett DH, Adair SM, Vaughan BW, et al. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res*. 1997;31(3):174-179.
84. Li X, Wang J, Joiner A, Chang J. The remineralisation of enamel: a review of the literature. *J Dent*. 2014;42:S12-S20.
85. Margolis HC, Moreno EC, Murphy BJ. Effect of low levels of fluoride in solution on enamel demineralization in vitro. *J Dent Res*. 1986;65(1):23-29.
86. Marinho VC, Higgins JP, Sheiham A, Logan S. Fluoride toothpastes for preventing dental caries in children and adolescents. *Cochrane DB Syst Rev (Online)*. 2003;(1).
87. Marinho VC, Higgins JP, Sheiham A, Logan S. One topical fluoride (toothpastes, or mouthrinses, or gels, or varnishes) versus another for preventing dental caries in children and adolescents. *Cochrane DB Syst Rev (Online)*. 2004;(1). Available from: <https://doi.org/10.1002/14651858.CD002780.pub2>.
88. Marinho VCC, Chong LY, Worthington HV, Walsh T. Fluoride mouthrinses for preventing dental caries in children and adolescents. *Cochrane DB Syst Rev*. 2016;2016(7).
89. Marinho VCC, Worthington HV, Walsh T, Chong LY. Fluoride gels for preventing dental caries in children and adolescents. *Cochrane DB Syst Rev*. 2015;2015(6).
90. Marinho VCC, Worthington HV, Walsh T, Clarkson JE. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane DB Syst Rev*. 2013;2013(7).
91. Marks RG, Conti AJ, Moorhead JE, et al. Results from a three-year caries clinical trial comparing NaF and SMFP fluoride formulations. *Int Dent J*. 1994;44(3 suppl 1):275-285.
92. Marquis RE, Clock SA, Mota-Meira M. Fluoride and organic weak acids as modulators of microbial physiology. *FEMS Microbiol Rev*. 2003;26(5):493-510.
93. Marshall TA, Levy SM, Broffitt B, et al. Patterns of beverage consumption during the transition stage of infant nutrition. *J Am Dietetic Assoc*. 2003;103(10):1350-1353.
94. Marthaler TM. Salt fluoridation and oral health. *Acta Med Academ*. 2013;42:140-155.
95. McDonagh MS, Kleijnen J, Whiting PF, et al. Systematic review of water fluoridation. *Br Med J*. 2000;321(7265):855-859.
96. McLaren L, Singhal S. Does cessation of community water fluoridation lead to an increase in tooth decay? A systematic review of published studies. *J Epidemiol Community Health*. 2016;70(9):934-940.
97. Moyer VA. Prevention of dental caries in children from birth through age 5 years: US Preventive Services Task Force recommendation statement. *Pediatrics*. 2014;133(6):1102-1111.
98. Moynihan PJ, Kelly SAM. Effect on caries of restricting sugars intake: systematic review to inform WHO guidelines. *J Dent Res*. 2014;93(1):8-18.
99. Muhler JC, Radake AW, Nebergall WH, Day HG. A comparison between the anticariogenic effects of dentifrices containing stannous fluoride and sodium fluoride. *J Am Dent Assoc*. (1939). 1955;51(5): 556-559.
100. National Research Council. *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*. Washington, DC: The National Academies Press; 2006.
101. O'Connell J, Rockell J, Ouellet J, et al. Costs and savings associated with community water fluoridation in the United States. *Health Affairs*. 2016;35(12):2224-2232.
102. O'Mullane DM, Bacz RJ, Jones S, et al. Fluoride and oral health. *Community Dent Health*. 2016;33(2):69-99.
103. Oliveira BH, Rajendra A, Veitz-Keenan A, et al. The effect of silver diamine fluoride in preventing caries in the primary dentition: a systematic review and meta-analysis. *Caries Res*. 2019;53(1):24-32.
104. Parnell C, Whelton H, O'Mullane D. Water fluoridation. *Eur Arch Paediatr Dent*. 2009;10(3):141-148.
105. Petersen PE, Ogawa H. Prevention of dental caries through the use of fluoride - the WHO approach. *Community Dent Health*. 2016;33:66-68.
106. Philip N, Suneja B, Walsh LJ. Ecological approaches to dental caries prevention: paradigm shift or shibboleth? *Caries Res*. 2018;52(1-2): 153-165.
107. Pitts NB, Zero DT, Marsh PD, et al. Dental caries. *Nat Rev Disease Primers*. 2017;3.
108. Radake AW, Gish CW, Peterson JK, et al. Clinical evaluation of stannous fluoride as an anticaries mouthrinse. *J Am Dent Assoc*. 1973;86(2):404-408.
109. Ran T, Chattopadhyay SK. Economic evaluation of community water fluoridation: a community guide systematic review. *Am J Prevent Med*. 2016;50(6):790-796.
110. Reintsema H, Schuthof J, Arends J. An in vivo investigation of the fluoride uptake in partially demineralized human enamel from several different dentifrices. *J Dent Res*. 1985;64(1):19-23.
111. Rihs LB, Da Luz Rosário De Sousa M, et al. Root caries in areas with and without fluoridated water at the southeast region of São Paulo State, Brazil. *J Appl Oral Sci*. 2008;16(1):70-74.
112. Ringelberg ML, Webster DB, Dixon DO, et al. The caries-preventive effect of amine fluorides and inorganic fluorides in a mouthrinse or dentifrice after 30 months of use. *J Am Dent Assoc*. (1939). 1979;98(2):202-208.
113. Rose G. Sick individuals and sick populations. *Int J Epidemiol*. 1985;14(1):32-38.
114. Rosier BT, Marsh PD, Mira A. Resilience of the oral microbiota in health: mechanisms that prevent dysbiosis. *J Dent Res*. 2018;97(4): 371-380.
115. Rozier RG, Adair S, Graham F, et al. Evidence-based clinical recommendations on the prescription of dietary fluoride supplements for caries prevention: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc*. 2010;141(12): 1480-1489.
116. Ruff JC, Herndon JB, Horton RA, et al. Developing a caries risk registry to support caries risk assessment and management for children: a quality improvement initiative. *J Public Health Dent*. 2018;78(2):134-143.
117. Rugg-Gunn AJ, Do L. Effectiveness of water fluoridation in caries prevention. *Community Dent Oral Epidemiol*. 2012;40(suppl 2):55-64.
118. Rugg-Gunn AJ, Spencer AJ, Whelton HP, et al. Critique of the review of "Water fluoridation for the prevention of dental caries" published by the Cochrane Collaboration in 2015. *Br Dent J*. 2016;220(7):335-340.
119. Russell AL. Dental fluorosis in Grand Rapids during the seventeenth year of fluoridation. *J Am Dent Assoc*. 1962;65(5): 608-612.
120. Sheiham A, James WPT. Diet and dental caries: the pivotal role of free sugars reemphasized. *J Dent Res*. 2015;94(10):1341-1347.
121. Shellis RP, Duckworth RM. Studies on the cariostatic mechanisms of fluoride. *Int Dent J*. 1994;44(3 suppl 1):263-273.

122. Slade GD, Grider WB, Maas WR, et al. Water fluoridation and dental caries in U.S. children and adolescents. *J Dent Res*. 2018;97(10):1122-1128.
123. Slayton RL, Urquhart O, Araujo MWB, et al. Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions. *J Am Dent Assoc*. 2018;149(10):837-849. e819.
124. Society of Teachers of Family Medicine. Caries risk assessment, fluoride varnish and counseling—Course 6. Smiles for Life. In: *A National Oral Health Curriculum*; 2017. Available from: <http://www.smilesforlifeoralhealth.org/buildcontent.aspx?tut=584&pagekey=64563&cbreceipt=0>.
125. Sohn W, Heller KE, Burt BA. Fluid consumption related to climate among children in the United States. *J Public Health Dent*. 2001;61(2):99-106.
126. Spencer AJ, Do LG, Ha DH. Contemporary evidence on the effectiveness of water fluoridation in the prevention of childhood caries. *Community Dent Oral Epidemiol*. 2018;46(4):407-415.
127. Spencer AJ, Liu P, Armfield JM, et al. Preventive benefit of access to fluoridated water for young adults. *J Public Health Dent*. 2017;77(3):263-271.
128. Stamm JW, Banting DW, Imrey PB. Adult root caries survey of two similar communities with contrasting natural water fluoride levels. *J Am Dent Assoc*. (1939). 1990;120(2):143-149.
129. Stamm JW, Bohannon HM, Graves RC, Disney JA. The efficiency of caries prevention with weekly fluoride mouthrinses. *J Dent Ed*. 1984;48(11):617-626.
130. Stoodley P, Sauer K, Davies DG, et al. Biofilms as complex differentiated communities. *Ann Rev Microbiol*. 2002;56:187-209.
131. Stookey GK, Schemehorn BR, Cheetham BL, et al. In situ fluoride uptake from fluoride dentifrices by carious enamel. *J Dent Res*. 1985;64(6):900-903.
132. Tank G, Storvick CA. Caries experience of children one to six years old in two Oregon communities (Corvallis and Albany). I. Effect of fluoride on caries experience and eruption of teeth. *J Am Dent Assoc*. (1939). 1964;69(6):749-757.
133. ten Cate JM, Featherstone JDB. Mechanistic aspects of the interactions between fluoride and dental enamel. *Crit Rev Oral Biol Med*. 1991;2(3):283-296.
134. Tubert-Jeannin S, Tramini P, Gerbaud L, et al. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. *Cochrane DB Syst Rev*. 2009;2009(1).
135. Twetman S, Axelsson S, Dahlgren H, et al. Caries-preventive effect of fluoride toothpaste: a systematic review. *Acta Odontol Scand*. 2003;61(6):347-355.
136. US Public Health Service Centers for Disease Control and Prevention. Ten great public health achievements: United States 1900-1999. *Morbidity Mortal Weekly Rep*. 1999;48(12):241-243.
137. US Public Health Service Centers for Disease Control and Prevention. Health Impact in 5 Years. Available from: <https://www.cdc.gov/policy/hst/his/index.html>; 2017.
138. US Public Health Service Centers for Disease Control and Prevention. *Fluoridation Statistics*. 2014; Revised July 2016. Available from: <https://www.cdc.gov/fluoridation/statistics/2014stats.htm>.
139. USDHHS Federal Panel on Community Water Fluoridation. US Public Health Service recommendation for fluoride concentration in drinking water for the prevention of dental caries. *Public Health Rep*. 2015;130(4):318-331.
140. Vogel GL. Oral fluoride reservoirs and the prevention of dental caries. *Monogr Oral Sci*. 2011;22:146-157.
141. Weintraub JA, Ramos-Gomez F, Jue B, et al. Fluoride varnish efficacy in preventing early childhood caries. *J Dent Res*. 2006;85(2):172-176.
142. Weyant RJ, Tracy SL, Anselmo T, et al. Topical fluoride for caries prevention. *J Am Dent Assoc*. 2013;144(11):1279-1291.
143. Wong MCM, Clarkson J, Glenny AM, et al. Cochrane reviews on the benefits/risks of fluoride toothpastes. *J Dent Res*. 2011;90(5):573-579.
144. Yeung CA, Chong LY, Glenny AM. Fluoridated milk for preventing dental caries. *Cochrane DB Syst Rev*. 2015;2015(9).
145. Zero DT. Adaptations in Dental Plaque. In: Bowen WH, Tabak L, eds. *Cariology for the Nineties*. Rochester, NY: University of Rochester Press; 1993:333-350.
146. Zero DT. Dental caries process. *Dent Clinics North Am*. 1999;43(4):635-664.
147. Zero DT. Sugars—the arch criminal? *Caries Res*. 2004;38(3):277-285.
148. Zero DT. Dentifrices, mouthwashes, and remineralization/caries arrestment strategies. *BMC Oral Health*. 2006;6(suppl 1):S9.
149. Zero DT, Brennan MT, Daniels TE, et al. Clinical practice guidelines for oral management of Sjögren disease: dental caries prevention. *J Am Dent Assoc*. 2016;147(4):295-305.
150. Zero DT, Raubertas RF, Pedersen AM, et al. Studies of fluoride retention by oral soft tissues after the application of home-use topical fluorides. *J Dent Res*. 1992;71(9):1546-1552.