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Topical fluoride for caries prevention

Executive summary of the updated clinical recommendations and supporting systematic review

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In 2006, the Council on Scientific Affairs (CSA) of the American Dental Association (ADA) published recommendations for the use of professionally applied topical fluorides for caries prevention.[1] It is ADA policy to start updating the evidence and clinical recommendations at five-year intervals. The objective of this report is to provide an update on professionally applied topical fluorides and address additional questions related to the use of prescription-strength, home-use topical fluorides for caries prevention. The panel evaluated sodium, stannous and acidulated phosphate fluoride (APF) for professional and prescription-strength home-use, including varnishes, gels, foams, mouthrinses and prophylaxis pastes. The panel did not include over-the-counter products, slow-release delivery devices, dental materials that release fluorides and products that contain sodium monofluorophosphate, silver diamine fluoride and titanium tetrafluoride in this report. Sodium monofluorophosphate is primarily a nonprescription, daily-use fluoride product. Silver diamine fluoride and titanium fluoride are not available in any products in the United States. For the remainder of this article, the term "topical fluoride agents" will be used to include professionally applied, as well as prescription-

ABSTRACT

Background. A panel of experts convened by the American Dental Association (ADA) Council on Scientific Affairs presents evidence-based clinical recommendations regarding professionally applied and prescription-strength, home-use topical fluoride agents for caries prevention. These recommendations are an update of the 2006 ADA recommendations regarding professionally applied topical fluoride and were developed by using a new process that includes conducting a systematic review of primary studies.

Types of Studies Reviewed. The authors conducted a search of MEDLINE and the Cochrane Library for clinical trials of professionally applied and prescription-strength topical fluoride agents—including mouthrinses, varnishes, gels, foams and pastes—with caries increment outcomes published in English through October 2012.

Results. The panel included 71 trials from 82 articles in its review and assessed the efficacy of various topical fluoride caries-preventive agents. The panel makes recommendations for further research.

Practical Implications. The panel recommends the following for people at risk of developing dental caries: 2.26 percent fluoride varnish or 1.23 percent fluoride (acidulated phosphate fluoride) gel, or a prescription-strength, home-use 0.05 percent fluoride gel or paste or 0.09 percent fluoride mouthrinse for patients 6 years or older. Only 2.26 percent fluoride varnish is recommended for children younger than 6 years. The strengths of the recommendations for the recommended products varied from "in favor" to "expert opinion for." As part of the evidence-based approach to care, these clinical recommendations should be integrated with the practitioner's professional judgment and the patient's needs and preferences.

Key Words. Caries prevention; caries; evidence-based dentistry; fluoride; practice guidelines; preventive dentistry.
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TABLE 1

Definitions for levels of certainty.*

LEVEL OF CERTAINTY	DEFINITION
High	This statement is strongly established by the best available evidence; the conclusion is unlikely to be affected strongly by the results of future studies.
Moderate	This statement is based on preliminary determination from the current best available evidence; as more information becomes available, the magnitude or direction of the observed effect could change, and this change could be large enough to alter the conclusion.
Low	The available evidence is insufficient to support the statement, or the statement is based on extrapolation from the best available evidence; more information could allow a reliable estimation of effects on health outcomes.

* For more details, see American Dental Association Center for Evidence-Based Dentistry.[2] Adapted from the U.S. Preventive Services Task Force system.[3]

strength, home-use products.

The grading system[2] used in this report was adapted from the U.S. Preventive Services Task Force (USPSTF) system,[3] and it differs markedly from the system the previous panel used for the 2006 clinical recommendations.[1] One difference is that the current clinical recommendations are based on a synthesis of primary evidence collected by means of a de novo systematic review, whereas the previous clinical recommendations were based primarily on published systematic reviews. Another difference is that the current recommendations are based on the net benefit of the intervention (that is, a balance of benefits with potential harm) in conjunction with the level of certainty in the evidence, whereas the 2006 clinical recommendations were based solely on the study design.[4] These changes have resulted in some modifications to the strengths assigned to the individual recommendations for products reviewed in this report compared with recommendations for the products reviewed in the 2006 clinical recommendations report.

The current grading system includes the use of expert opinion as a means of determining whether to make clinical recommendations when evidence is lacking, contradictory or judged to have a high risk of bias (that is, a reliable estimate of the net benefit of the intervention is not possible). Practitioners should note the strength of the recommendations and endeavor to understand the underlying evidence in terms of the level of certainty and the balance of benefits with potential harm. They should discuss uncertainties in evidence with their patients, providing awareness that there usually is some level of uncertainty in the evidence used for making clinical decisions, in part arising from lack of clinical data, changes in product formulations across time and the availability of a wide variety of products.

The panel prepared this report to help practitioners make decisions about the use of topical fluoride caries preventive agents. (The full report, which includes more details, is available at http://ebd.ada.org//ClinicalRecommendations.aspx.) The recommendations in this report are not intended to define a standard of care but rather should be integrated with each practitioner's professional judgment and each patient's needs and preferences.

METHODS

The ADA CSA convened the panel, which was multidisciplinary and comprised subject matter and methodology experts, as well as representatives from various stakeholder groups. They addressed two clinical questions:

- In primary and permanent teeth, does the use of a topical fluoride agent reduce the incidence of new lesions in coronal caries, root caries or both compared with no topical fluoride use?
- Does the use of prophylaxis before application of topical fluoride reduce the incidence of caries to a greater extent than the application of topical fluoride without prophylaxis?

In the first part of the process, the authors conducted a systematic review of the literature. They then developed evidence statements based on a statistical evaluation of the evidence, as well as an assessment of their level of certainty in the statement (high, moderate, low), according to a standardized grading system (Table 1[2,3]).

In the second part of the process, the panel developed clinical recommendations and graded the strength of the recommendations, according to a standardized process. The panel ascertained the net benefit rating by judging the balance of benefits with potential harm. For example, if a topical fluoride agent was found to be effective, and the benefit was judged to outweigh the potential harm, the net benefit was "benefit outweighs potential harm." The panel

ABBREVIATION KEY. ADA: American Dental Association. **APF:** Acidulated phosphate fluoride. **CSA:** Council on Scientific Affairs. **USPSTF:** U.S. Preventive Services Task Force.

used the information in Table 2[3] to combine the level of certainty with the net benefit rating to arrive at the strength of the recommendation (strong, in favor, weak, expert opinion for, expert opinion against or against) to determine the strength of the clinical recommendation as defined in Table 1.[2,3] Table 3[3] shows the definitions of these recommendation strengths.

The panel approved the clinical recommendations by a simple majority vote. The panel sought comments on this report from other subject matter experts, methodologists, epidemiologists and end-users before finalizing the recommendations. The ADA CSA approved the final report for publication.

TABLE 2

Balancing level of certainty and net benefit rating to arrive at recommendation strength.*

LEVEL OF CERTAINTY	NET BENEFIT RATING		
	Benefit Outweighs Potential Harm	Benefit Balanced With Potential Harm	No Benefit, Potential Harm Outweighs Benefit
High	Strong	In favor	Against
Moderate	In favor	Weak	Against
Low	Expert opinion for† or expert opinion against†		

* Adapted from the U.S. Preventive Services Task Force (USPSTF) system.[3]
† The USPSTF system defines this category of evidence as "insufficient"; "grade I indicates that the evidence is insufficient to determine the relationship between benefits and harms (i.e., net benefit)." The corresponding recommendation grade "I" is defined as follows: "The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined."

TABLE 3

Definitions for the strength of clinical recommendations.*

RECOMMENDATION STRENGTH	DEFINITION
Strong	Evidence strongly supports providing this intervention.
In Favor	Evidence favors providing this intervention.
Weak	Evidence suggests implementing this intervention after alternatives have been considered.
Expert Opinion For†	Evidence is lacking; the level of certainty is low. Expert opinion guides this recommendation
Expert Opinion Against†	Evidence is lacking; the level of certainty is low. Expert opinion suggests not implementing this intervention.
Against	Evidence suggests not implementing this intervention or discontinuing ineffective procedures.

* Adapted from the U.S. Preventive Services Task Force (USPSTF) system.[3]
† The USPSTF system defines this category of evidence as "insufficient"; "grade I indicates that the evidence is insufficient to determine the relationship between benefits and harms (i.e., net benefit)." The corresponding recommendation grade "I" is defined as follows: "The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined."

CLINICAL RECOMMENDATIONS: SUMMARY

For people who are at an elevated risk of developing dental caries, the panel makes clinical recommendations for the use of specific topical fluoride agents (Table 4); these recommendations are based on the evidence statements and the balance of benefits with potential harm (Table 5,[5,6] pages 1284-1285). The panel recommends topical fluoride agents only for people what are at elevated risk of developing dental caries.

The panel recommends the following for people at risk of developing dental caries: 2.26 percent fluoride varnish or 1.23 percent fluoride (APF) gel, or a prescription-strength, home-use 0.05 percent fluoride gel or paste or 0.09 percent fluoride mouthrinse for patients 6 years or older. Only 2.26 percent fluoride varnish is recommended for children younger than 6 years. The strengths of the recommendations for the recommended products varied from "in favor" to "expert opinion for."

The panel judged that the benefits outweighed the potential for harm for all professionally applied and prescription-strength, home-use topical fluoride agents and age groups except for children younger than 6 years. In these children, the risk of experiencing adverse events (particularly nausea and vomiting) associated with swallowing professionally applied topical fluoride agents outweighed the potential benefits of using all of the topical fluoride agents except for 2.26 percent fluoride varnish.

DISCUSSION OF EVIDENCE AND CLINICAL RECOMMENDATIONS

The panel included 71 trials in 82 published articles (some clinical studies were published in multiple articles) in its review and assessed the efficacy of various topical fluoride agents for preventing caries. Table 5[5,6] (pages 1284-1285) summarizes the expert panel's assessment of the evidence. There were some general considerations to take into account when reviewing the evidence. First, some of the studies were

TABLE 4

Clinical recommendations for use of professionally applied or prescription-strength, home-use topical fluorides for caries prevention in patients at elevated risk of developing caries.

Strength of recommendations: Each recommendation is based on the best available evidence. The level of evidence available to support each recommendation may differ.

Strong	In favor	Weak	Expert Opinion For	Expert Opinion Against	Against
Evidence strongly supports providing this intervention	Evidence favors providing this intervention	Evidence suggests implementing this intervention only after alternatives have been considered	Evidence is lacking; the level of certainty is low. Expert opinion guides this recommendation	Evidence is lacking; the level of certainty is low. Expert opinion suggests not implementing this intervention	Evidence suggests not implementing this intervention or discontinuing ineffective procedures

Age Group or Dentition Affected	Professionally Applied Topical Fluoride Agent	Prescription-Strength, Home-Use Topical Fluoride Agent
Younger Than 6 Years	2.26 percent fluoride varnish at least every three to six months ● In Favor	
6-18 Years	2.26 percent fluoride varnish at least every three to six months ● In Favor **OR** 1.23 percent fluoride (APF*) gel for four minutes at least every three to six months ● In Favor	0.09 percent fluoride mouthrinse at least weekly ● In Favor **OR** 0.5 percent fluoride gel or paste twice daily ● Expert Opinion For
Older Than 18 Years	2.26 percent fluoride varnish at least every three to six months ● Expert Opinion For **OR** 1.23 percent fluoride (APF) gel for four minutes at least every three to six months ● Expert Opinion For	0.09 percent fluoride mouthrinse at least weekly ● Expert Opinion For **OR** 0.5 percent fluoride gel or paste twice daily ● Expert Opinion For
Adult Root Caries	2.26 percent fluoride varnish at least every three to six months ● Expert Opinion For **OR** 1.23 percent fluoride (APF) gel for four minutes at least every three to six months ● Expert Opinion For	0.09 percent fluoride mouthrinse daily ● Expert Opinion For **OR** 0.5 percent fluoride gel or paste twice daily ● Expert Opinion For

Additional Information:

- 0.1 percent fluoride varnish, 1.23 percent fluoride (APF) foam or prophylaxis pastes are not recommended for preventing coronal caries in all age groups (● Expert Opinion Against or ● Against). The full report, which includes more details, is available at http://ebd.ada.org//ClinicalRecommendations.aspx.
- No prescription-strength or professionally applied topical fluoride agents except 2.26 percent fluoride varnish are recommended for children younger than 6 years (● Expert Opinion Against or ● Against), but practitioners may consider the use of these other agents on the basis of their assessment of individual patient factors that alter the benefit-to-harm relationship.
- Prophylaxis before to 1.23 percent fluoride (APF) gel application is not necessary for coronal caries prevention in all age groups (● Expert Opinion Against or ● Against). The full report, which includes more details, is available at http://ebd.ada.org//ClinicalRecommendations.aspx. No recommendation can be made for prophylaxis before application of other topical fluoride agents.

Patients at low risk of developing caries may not need additional topical fluorides other than over-the-counter fluoridated toothpaste and fluoridated water.

* APF: Acidulated phosphate fluoride.

conducted before the 1970s, when dental caries rates among children were higher,[7] the percentage of the population receiving fluoridated water was substantially lower,[8] and the percentage of people using fluoridated dentifrice was much lower.[9] Second, some studies were conducted in countries with different caries prevalence and different levels of background fluoride exposure and other caries prevention efforts. Third, the study populations often could not be categorized in terms of caries risk, and the panel could not assign risk categories to the populations as they are defined today. Therefore, caution is advised when extrapolating the results to today's high-risk populations, such as children at high risk of developing early childhood caries.

Table 6 (page 1286) presents the fluoride concentrations of each of topical fluoride agent evaluated, both as a concentration of fluoride ion and a concentration of sodium fluoride.

Varnish. There are more than 30 fluoride-containing varnish products on the market today, and they have varying compositions and delivery systems. These compositional differences lead to widely variable pharmacokinetics, the effects of which remain largely untested clinically. Through the literature search, the panel found clinical trials[10-38] regarding four brand-name products and decided to summarize the results of these trials on the basis of the percentage of fluoride, which was either 2.26 percent or 0.1 percent. Further research revealed that products identified with an identical brand name (Fluor Protector, Ivoclar Vivadent, Amherst, N.J.) underwent a compositional change in 1987 from 0.7 percent fluoride to 0.1 percent fluoride.[39] Because the 0.7 percent fluoride product no longer is available commercially, these trials[10-14] were not eligible for inclusion in this review. Therefore, the data are subdivided into 2.26 percent fluoride and 0.1 percent fluoride varnish categories.

2.26 percent fluoride varnish. The panel identified 17 randomized and five nonrandomized clinical trials that evaluated 2.26 percent fluoride varnish. There were six randomized[11-13,15-19] and two nonrandomized[20,21] clinical trials concerning the primary dentition, 11 randomized[11-13,22-32] and two nonrandomized[33,34] clinical trials concerning the permanent dentition and one controlled[35] clinical trial that combined results for both dentitions. The interventions for the control groups were no treatment, oral health counseling or placebo varnish. The studies were carried out in populations with various levels of dental caries. The studies were conducted in many countries (Brazil, Canada, Hong Kong, India, Kuwait, Netherlands, Poland, Spain, Sweden, United Kingdom and United States) in participants with and without additional fluoride use or other fluoride exposures (although most studies were conducted in low-fluoride areas) and with and without prior prophylaxis. The ages of the children at baseline varied from 6 months to 8 years for studies of the primary teeth; and from 5 to 15 years for studies of the permanent teeth. The panel identified two studies[30,31] of root caries. The age range in these two studies was 44 to 79 years. The varnish was applied professionally every three to 12 months; in most of studies, the varnish was applied every six months.

Because of the low risk of experiencing harm in children younger than 6 years, unit doses of 2.26 percent fluoride varnish are the only topical fluoride agents that are recommended for this age group, even though other topical fluorides may have some evidence of a benefit. The panel had a moderate level of certainty that there is a benefit of 2.26 percent fluoride varnish in the permanent teeth of children aged 6 through 18 years. Although there were no studies of coronal caries prevention in adults older than 18 years, the panel extrapolated the data from 6- through 18-year-olds to recommend using 2.26 percent varnish for this age group for both coronal and root caries. The benefits were judged to outweigh the potential for harm for all age groups.

0.1 percent fluoride varnish. The panel identified two nonrandomized clinical trials[36,37] in which investigators evaluated 0.1 percent fluoride varnish on the primary dentition and one randomized clinical trial[38] in which investigators evaluated 0.1 percent fluoride varnish in the permanent dentition. The control groups received oral hygiene instruction or no treatment. The studies were carried out in Germany and Sweden in populations with various baseline levels of dental caries. The ages of the children at baseline varied from 4 through 5 years for primary dentition and 9 through 12 years for permanent dentition. The varnish was applied professionally every six months in the primary dentition and every four months in the permanent dentition. Additional fluoride use or other fluoride exposure was variable, and all studies included prior prophylaxis.

The panel found evidence of no benefit from use of 0.1 percent fluoride varnish in children. Although there were no studies regarding coronal caries prevention in adults older than 18 years, the panel extrapolated the data from 6- through 18-year-olds that showed no benefit

TABLE 5

Evidence statements for professionally applied and prescription-strength, home-use topical fluorides used for caries prevention.

AGENT	AGE GROUP (YEARS) OR DENTITION AFFECTED	EVIDENCE STATEMENT
Varnish (2.26 Percent Fluoride)	Younger than 6	There is a benefit of 2.26 percent fluoride varnish application at least twice per year for caries prevention.
	6-18	There is a benefit of 2.26 percent fluoride varnish application at least twice per year for caries prevention.
	Adult root caries	There is a benefit of 2.26 percent fluoride varnish application at least twice per year for root caries prevention in adults.
Varnish (0.1 Percent Fluoride)	Younger than 6	There is no benefit of 0.1 percent fluoride varnish application twice per year for caries prevention.
	6-18	There is no benefit of applying 0.1 percent fluoride varnish three times per year for caries prevention.
APF* Gel (1.23 Percent Fluoride)	Younger than 6	There is a benefit of APF gel (1.23 percent fluoride) application up to every three months for four† minutes for caries prevention.
	6-18	There is a benefit of APF gel (1.23 percent fluoride) application up to every three months for four† minutes for caries.
	Adult root caries	There is a benefit of APF gel (1.23 percent fluoride) application twice per year for four† minutes to prevent root caries.
Prophylaxis Before APF Gel (1.23 Percent Fluoride) Application	Younger than 6	There is no benefit from conducting a prophylaxis prior to APF gel (1.23 percent fluoride) application for caries prevention.
	6-18	There is no benefit from conducting a prophylaxis prior to APF gel (1.23 percent fluoride) application for caries prevention.
APF Foam (1.23 Percent Fluoride)	Younger than 6	There is a benefit of APF foam (1.23 percent fluoride) application twice per year for four‡ minutes for caries prevention.
	6-18	There is no benefit of 1.23 percent APF foam application twice per year for four‡ minutes for caries prevention.
Prophylaxis Pastes Containing Fluoride	Younger than 6	There is no benefit of prophylaxis paste containing fluoride application for four minutes twice per year for caries prevention.
	6-18	There is no benefit of prophylaxis paste containing fluoride application for four minutes twice per year for caries prevention.
Prescription-Strength, Home-Use (0.5 Percent Fluoride) Gel or Paste	Younger than 6	There is a benefit of prescription-strength, home-use (0.5 percent fluoride) gel or paste application twice daily for caries prevention.
	6-18	There is a benefit of prescription-strength, home-use (0.5 percent fluoride) gel or paste application twice daily for caries prevention.
	Adult root caries	There is a benefit of prescription-strength, home-use (0.5 percent fluoride) gel or paste application twice daily in preventing root caries.
Prescription-Strength, Home-Use (0.09 Percent Fluoride) Mouthrinse	6-18	There is a benefit of using prescription-strength, home-use (0.09 percent fluoride) mouthrinse daily or weekly for caries prevention.
	Adult root caries	There is a benefit of using prescription-strength, home-use (0.09 percent fluoride) mouthrinse for root caries prevention among elderly people living in long-term care facilities.

* APF: Acidulated phosphate fluoride.
† No studies were found regarding professionally applied fluoride APF gels with an application time of less than three minutes.
‡ Two studies[5,6] regarding professionally applied fluoride (APF) foams used an application time of four minutes.

of 0.1 percent varnish for this age group. The panel was not comfortable extrapolating these results to root caries and gives no clinical recommendation for this form of the disease.

1.23 percent fluoride (APF) gel. The panel identified 11 randomized[5,40-50] and four nonrandomized[35,51-55] clinical trials that evaluated 1.23 percent fluoride (APF) gel quarterly, semiannually, annually or biannually (one application was observed after two years). The comparison groups received no treatment, a placebo, prophylaxis or a nonfluoride placebo gel. All studies except one[51] involved permanent teeth. In all of the studies, investigators applied fluoride gel for four minutes. All of the studies involved school-aged children (from 3 through 16 years) except for one.[49] This study involved noninstitutionalized adults who were at least 60 years of age, and investigators reported on root caries. Ten studies[40-45,48,49,51-55] were conducted in the United States and five elsewhere (India,[35,50] United Kingdom,[46] China[5] and Canada[47]).

TABLE 5 (CONTINUED)

LEVEL OF CERTAINTY	NET BENEFIT RATING
Moderate	Benefit outweighs potential harm
Moderate	Benefit outweighs potential harm
Low	Benefit outweighs potential harm
Moderate	No benefit
Low	No benefit
Low	Potential harm outweighs benefit
Moderate	Benefit outweighs potential harm
Low	Benefit outweighs potential harm
Low	No benefit
Moderate	No benefit
Low	Potential harm outweighs benefit
Low	No benefit
Low	No benefit
Moderate	No benefit
Low	Potential harm outweighs benefit
Low	Benefit outweighs potential harm
Low	Benefit outweighs potential harm
Moderate	Benefit outweighs potential harm
Low	Benefit outweighs potential harm

Although the panel had a low level of certainty that there was a benefit in using 1.23 percent fluoride (APF) gel in the primary dentition of children younger than 6 years, they judged that the potential for harm associated with swallowing APF gel could outweigh these benefits. The panel had a moderate level of certainty that there was a benefit of using 1.23 percent fluoride (APF) gel in the permanent teeth of children aged 6 through 18 years. The panel found no studies regarding the effect of 1.23 percent fluoride (APF) gel on coronal caries of adults older than 18 years, but they extrapolated the evidence from permanent teeth of children 6 through 18 years of age to recommend (at the strength of expert opinion) for this age group.

Prophylaxis before APF gel application. Although the panel searched the literature for prophylaxis before any topical fluoride application (per the second clinical question), it only found studies regarding prophylaxis before application of 1.23 percent fluoride (APF) gel. The panel identified two randomized[56-58] and one nonrandomized[59] clinical trials in which investigators assessed whether prophylaxis before professional application of APF gel affects its efficacy. Two studies were conducted in the United States,[57-59] and one was conducted in Canada.[56] All of the studies involved children aged 6 through 14 years at baseline. Investigators for both studies reported data regarding permanent teeth, and investigators for one[56] also reported data regarding primary teeth.

The panel found no benefit for performing prophylaxis before the application of 1.23 percent fluoride (APF) gel for the primary and permanent dentition of children. Although no studies were found in this category regarding adult populations, the panel extrapolated the evidence from the permanent teeth of children aged 6 through 18 years to coronal caries in adults, but it was not comfortable doing so for root caries and gives no clinical recommendation for this form of the disease.

1.23 percent fluoride (APF) foam. The panel identified two randomized clinical trials[5,6] that evaluated 1.23 percent fluoride (APF) foam in children aged 3 through 7 years at baseline. One study involved the primary dentition[6] and the other the permanent dentition.[5] The comparison groups received either no treatment or placebo. Both studies were conducted in China.

Although a benefit was found with using 1.23 percent fluoride (APF) foam in children younger than 6 years, the panel judged that the potential for harm—including swallowing APF foam—outweighed this benefit. The panel found no benefit regarding caries prevention in the permanent dentition of children. The panel extrapolated this finding to permanent teeth in adults and does not recommend foam use in adults older than 18 years. The panel was not comfortable extrapolating these results to root caries and gives no clinical recommendation for this form of the disease.

Prophylaxis pastes containing fluoride. The panel identified three randomized[60-62] and three nonrandomized[63-65] clinical trials in which investigators evaluated the annual or semiannual application of prophylaxis pastes, most of

TABLE 6

Fluoride ion and sodium fluoride concentrations in topical fluoride agents.

TOPICAL FLUORIDE AGENT	FLUORIDE ION, %	SODIUM FLUORIDE, %
Professionally Applied		
2.26 Percent fluoride varnish	2.26	5.0
APF* gel (with 0.1 molar phosphoric acid)	1.23	2.7
APF foam (with 0.1 M phosphoric acid)	1.23†	2.7†
Prophylaxis paste containing fluoride (most as APF)	1.23	2.7
0.1 Percent fluoride varnish	0.1‡	Not applicable
Prescription Strength, Home Use		
Prescription-strength gels or pastes with or without acidulation (0.1 M phosphoric acid)	0.5	1.1
Prescription-strength mouthrinses	0.09	0.2

* APF: Acidulated phosphate fluoride.
† Concentration of fluoride before being dispensed. When delivered as a foam by combining gel with air, the total amount of fluoride in the foam product is reduced.
‡ The fluoride ion form was 0.09 percent difluorsilane.

which contained 1.23 percent fluoride (APF), for caries prevention. These studies were conducted between 1966 and 1980. The comparison groups received placebo prophylaxis pastes. All studies except one[65] (regarding children aged 3-5 years at baseline) involved the permanent teeth of children aged 8 through 16 years at baseline.

The panel found no benefit of using prophylaxis pastes containing fluoride on the primary or permanent teeth of children. Although no studies were found regarding adult populations, the panel extrapolated the evidence of no benefit to coronal caries in adults but was not comfortable doing so for root caries and gives no clinical recommendation for this form of the disease.

Prescription-strength, home-use (0.5 percent fluoride) gels or pastes. The panel reviewed the data for prescription-strength, home-use gels and pastes together. The primary difference between gels and pastes is that pastes contain a small amount of an abrasive component. The panel noted that investigators in only one study[66] evaluated prescription-strength fluoride paste or gel (in this case, it was paste) in an unsupervised home environment, rather than by professional application in trays or with floss or in a supervised school setting. These products are often used at home and applied with a toothbrush.

The panel identified eight randomized[66-75] and one nonrandomized[76] clinical trials that met the inclusion criteria regarding prescription-strength (0.5 percent fluoride) paste or gel for home use. Six of the studies[66,69-73,75,76] involved permanent teeth, one[67] involved root caries, and two[71,72,74] involved primary teeth. The comparison group for all studies was either placebo, 0.125-0.145 percent fluoride paste or no treatment. The baseline age range of children was 2 through 15 years for most of the studies, and one study included participants older than 75 years.[67] The studies were performed in Denmark, French Polynesia, Netherlands, Sweden and the United States.

Although the panel found a benefit with 0.5 percent fluoride paste or gel treatment in children younger than 6 years, it judged that the potential for harm—including swallowing gels or pastes—outweighed this benefit. The panel had a low level of certainty regarding the benefit of 0.5 percent fluoride paste or gel on the permanent teeth of children and on root caries because there were few data on the home use of these products. However, the panel judged that the benefits outweighed potential harm. Although the panel found no studies in this category regarding permanent teeth in adults, the panel extrapolated the available evidence and judged that the benefits outweighed the potential for harm in this age group.

Prescription-strength, home-use (0.09 percent fluoride) mouthrinse. The panel identified 10 randomized[77-88] and two nonrandomized[89,90] clinical trials in which investigators evaluated 0.09 percent fluoride mouthrinse applications with daily, weekly or biweekly applications. Investigators in most of the studies compared the intervention with placebo mouthrinses, although some compared the intervention with no treatment[85,89] or oral hygiene instruction and prophylaxis.[79] All studies were conducted on permanent teeth. All of the studies but one[87] were conducted in school-aged children (5 through 12 years). No adult populations were studied except elderly people living in long-term care facilities (mean age, 83 years) in one study.[87] In most studies, the children's teachers supervised the use of the fluoride rinse. In only one study[88] were children enrolled on the basis of their caries risk status. Four of the studies[77,78,80-82,84] were conducted in the United States. The other studies were conducted in Canada,[87] Denmark,[83] New Zealand,[79-88] Philippines,[90] South Africa[86,89] and Sweden.[85]

The panel judged that the benefits outweighed the potential for harm in children 6 years or older and adults. Although there were

no studies regarding the effect of 0.09 percent fluoride mouthrinse on caries in children younger than 6 years, the panel judged that the risk of swallowing mouthrinse outweighed the potential for unknown benefits. Although there were no studies regarding coronal caries in adults older than 18 years, the panel extrapolated the results from children aged 6 through 18 years to arrive at a clinical recommendation based on expert opinion.

GENERAL REMARKS ON CLINICAL RECOMMENDATIONS

A practitioner should consider a patient's risk of experiencing disease when developing an optimal caries-prevention plan. Part of a patient's risk status includes whether the patient lives in an optimally fluoridated community and uses fluoridated toothpaste. Patients at low risk of developing caries may not need additional fluoride interventions, whereas caries in people at high risk of developing caries appears at times to be refractory to additional intensive preventive interventions.[91,92]

Professional judgment is required to interpret the clinical relevance of preventive measures for individual patients. The combination of evidence from clinical studies, the patient's caries risk status, the practitioner's professional judgment and the patient's needs and preferences should guide decision making. Patient education, assessment of readiness for change, dietary advice, other preventive modalities and periodic clinical examinations should be considered as a part of the caries-prevention plan. In public health care settings, additional considerations include the feasibility and cost of the proposed intervention. The panel did not consider these issues when providing its clinical recommendations.

The panel noted that clinical trials generally test the efficacy of an intervention, which results in the best possible outcome for the intervention because of the controlled nature of the trial and strict inclusion and exclusion criteria for participants. These results do not necessarily reflect the effectiveness of an intervention (that is, how the intervention works in routine practice), which typically includes patients with comorbidities who may be taking multiple medications. Under controlled study conditions, the efficacy is almost always higher than the effectiveness because of the presence of idealized conditions.

The panel has reported on several different topical fluoride agents, including those planned for home use. Practitioners can expect different compliance with treatment plans incorporating home-use products than with professionally applied products. Cost, efficacy or effectiveness related to the intended usage environment also may vary.

When considering any intervention, the practitioner and patient must balance the potential benefits with the potential harm. The panel considered harm reported by investigators of the included articles as well as known potential harm of fluoride use. Potential harm of topical fluorides includes, but may not be limited to, nausea and vomiting associated with the ingestion of topical fluorides[93] and dental fluorosis (an esthetic concern) while tooth enamel is developing (until about age 6 years) due to daily ingestion of topical fluoride, such as from toothpaste or from prescription-strength, home-use gels. There is less of a concern about professionally applied topical fluorides for which there are longer intervals between applications.[94] Fluoride varnish dispensed in unit doses has lower potential for harm than do other forms of high-concentration topical fluoride agents, because the amount of fluoride that is placed in the mouth by means of fluoride varnish is approximately one-tenth that of other professionally applied products.[95]

FUTURE RESEARCH

The panel recommends that multiple well-designed, appropriately powered, placebo-controlled randomized trials that follow the Consolidated Standards of Reporting Trials guidelines[96] with standardized reporting according to age, dentition and caries risk status be conducted in the United States. Standard methodologies for caries and fluoride randomized controlled trials should be developed. The panel recommends that future trials be registered with ClinicalTrials.gov or equivalent registries. Specific areas of research recommendations are as follows:

- **Mechanisms of fluoride action and effects.** Research is needed regarding various topical fluorides to determine their mechanism of action and caries-preventive effects when in use at the current level of background fluoride exposure (that is, fluoridated water and fluoride toothpaste) in the United States. Studies regarding strategies for using fluoride to induce arrest or reversal of caries progression, as well as topical fluoride's specific effect on erupting teeth, also are needed.
- **Populations.** Research is needed concerning the following subpopulations: adults aged 18 through 65 years, high-risk adults older than 65

(including those living in long-term care facilities) who are at high risk of developing caries, children and adults who are at extremely high risk of developing caries, U.S.-specific populations, special needs populations (for example, those with cognitive disabilities, compromised self-care abilities or physical disabilities) and populations with chronic diseases (such as Sjögren syndrome). Comparative effectiveness studies of different fluoride strategies in these populations, as well as studies regarding strategies to manage xerostomia-induced coronal and root caries also are needed.

- **Products and usage.** Research is needed concerning the effectiveness and risks of specific products in the following areas: self-applied, prescription-strength, home-use fluoride gels, toothpastes or drops; 2 percent professionally applied sodium fluoride gel; alternative delivery systems, such as foam; optimal application frequencies for fluoride varnish and gels; one-minute applications of APF gel; and combinations of products (home-use and professionally applied).
- **Measurement and outcomes.** Development of measurements to evaluate caries arrest and reversal are needed.
- **Economics.** Studies regarding caries prevention and the economic benefit of topical fluoride in different caries risk populations are needed.
- **Dissemination and implementation.** Research on the best ways to help practitioners incorporate clinical recommendations into practice are needed.

CONCLUSIONS

The panel recommends the following for people at risk of developing dental caries: 2.26 percent fluoride varnish or 1.23 percent fluoride (APF) gel; or prescription-strength, home-use 0.05 percent fluoride gel or paste or 0.09 percent fluoride mouthrinse for patients 6 years or older. Only 2.26 percent fluoride varnish is recommended for children younger than 6 years. The strengths of the recommendations for the recommended products varied from "in favor" to "expert opinion for." As part of the evidence-based approach to care, these clinical recommendations should be integrated with the practitioner's professional judgment and the patient's needs and preferences. ■

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