Cover Story

Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions

A report from the American Dental Association

Supplemental material is available online.

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ABSTRACT

Background. An expert panel convened by the American Dental Association Council on Scientific Affairs and the Center for Evidence-Based Dentistry conducted a systematic review and formulated evidence-based clinical recommendations for the arrest or reversal of noncavitated and cavitated dental caries using nonrestorative treatments in children and adults.

Types of Studies Reviewed. The authors conducted a systematic search of the literature in MEDLINE and Embase via Ovid, Cochrane CENTRAL, and Cochrane database of systematic reviews to identify randomized controlled trials reporting on nonrestorative treatments for noncavitated and cavitated carious lesions. The authors used the Grading of Recommendations Assessment, Development and Evaluation approach to assess the certainty in the evidence and move from the evidence to the decisions.

Results. The expert panel formulated 11 clinical recommendations, each specific to lesion type, tooth surface, and dentition. Of the most effective interventions, the panel provided recommendations for the use of 38% silver diamine fluoride, sealants, 5% sodium fluoride varnish, 1.23% acidulated phosphate fluoride gel, and 5,000 parts per million fluoride (1.1% sodium fluoride) toothpaste or gel, among others. The panel also provided a recommendation against the use of 10% casein phosphopeptide—amorphous calcium phosphate.

Conclusions and Practical Implications. Although the recommended interventions are often used for caries prevention, or in conjunction with restorative treatment options, these approaches have shown to be effective in arresting or reversing carious lesions. Clinicians are encouraged to prioritize use of these interventions based on effectiveness, safety, and feasibility.

Key Words. Carious lesion; American Dental Association; practice guidelines; evidence-based dentistry; decision making; general practice; clinical recommendations; nonrestorative treatments; caries.

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Dental caries is a chronic noncommunicable disease that affects people of all ages worldwide. From 2015 through 2016, approximately 4 of 10 young children[1] and from 2011 through 2012 9 of 10 adults[2] were affected by caries in the United States. Although in the past decade overall caries prevalence has stabilized in both children and adults, these rates remain at a constant high for specific subgroups. According to the 2011-2012 National Health and Nutrition Examination Survey, non-Hispanic white adults aged 20 through 64 years have the highest caries prevalence rates (94%) compared with those of Hispanic, non-Hispanic black, and non-Hispanic Asian adults.[2] The 2015-2016 National Health and Nutrition Examination Survey data show

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that Hispanic youth aged 2 through 19 years also have the highest prevalence rate (52%) compared with non-Hispanic black, non-Hispanic Asian, and non-Hispanic white youth.[1] In addition, there are income-related disparities in caries prevalence in which low-income groups have a higher prevalence of untreated caries than do high-income groups.[1] Worldwide, the direct costs of treatment because of dental disease were estimated to be approximately $298 billion yearly in 2010, with $120 billion attributed to the United States alone.[3]

Caries is caused by frequent acid production from the metabolism of dietary carbohydrates. This mechanism results in the emergence of acid-producing and acid-tolerant organisms in supragingival oral biofilms, altered pH, shift in the demineralization-remineralization equilibrium, and loss of tooth minerals. When there is a balance between protective factors (for example, fluoride, calcium, phosphate, adequate salivary flow, composition) and pathologic factors (for example, cariogenic bacteria, fermentable carbohydrates), demineralization and remineralization of enamel are relatively equal, and oral health is maintained.[4-6]

Preventing the onset of caries across the life span should be the primary goal of a caries management plan. However, once the disease is present, clinicians deal with the challenge of determining the appropriate approach to stop the consequences of the cariogenic process, which can be achieved by applying interventions at the patient level and managing the manifestation of the disease at the lesion level. Patient-level interventions aim to reestablish the mineralization balance. These interventions usually require adequate patient adherence for success and include, but are not limited to, diet counseling (for example, reducing sugar consumption[7]) and oral hygiene instructions and reinforcement[8] (for example, interdental cleaning, toothbrushing with fluoridated toothpaste). Patient-level interventions will be discussed further in a subsequent American Dental Association (ADA) guideline for caries prevention. Lesion-level interventions include nonrestorative or nonsurgical (noninvasive and microinvasive) and restorative or minimally-invasive and invasive treatments. The former are more conservative approaches that stops the disease process through arrest or reversal of carious lesions and minimizes the loss of tooth structure.

Noncavitated carious lesions can be described as surfaces that appear macroscopically intact and without clinical evidence of cavitation.[9] They sometimes are referred to as incipient, initial, early, or white-spot lesions (although these lesions can be white or brown).[10] A cavitated lesion is a carious lesion with a surface that is not macroscopically intact and with a distinct discontinuity or break in the surface integrity, usually determined using visual or tactile means.[9,10] Noncavitated lesions have the potential to reverse by means of chemical interventions or arrest by means of chemical or mechanical interventions. Cavitated lesions are less likely to reverse or arrest without these interventions.

The purpose of this clinical practice guideline is to help clinicians decide which types of nonrestorative treatments or interventions could be used to arrest or reverse existing noncavitated and cavitated carious lesions in adults and children. The target audience for this guideline includes general and pediatric dental practitioners and their support teams, public health dentists, dental hygienists, and community oral health coordinators. Policy makers may also benefit from using this guideline.

This guideline and associated systematic review (O. Urquhart, MPH, written communication, August 2018) are products of an expert panel composed of general, public health, and pediatric dentists and cariologists convened by the ADA Council on Scientific Affairs. Methodological support, stakeholder engagement, and drafting of this clinical practice guideline and its associated systematic review were led by the ADA Center for Evidence-Based Dentistry.

ABBREVIATION KEY

ACP: Amorphous calcium phosphate.
ADA: American Dental Association.
APF: Acidulated phosphate fluoride.
CPP: Casein phosphopeptide.
ICDAS: International Caries Detection and Assessment System.
NaF: Sodium fluoride.
NIDCR: National Institute of Dental and Craniofacial Research.
NIH: National Institutes of Health.
RCT: Randomized controlled trial.
SDF: Silver diamine fluoride.

METHODS

We adhered to the Appraisal of Guidelines for Research and Evaluation Reporting Checklist II[11] and Guidelines International Network—McMaster Guideline Development Checklist[12] when developing this guideline and preparing this manuscript. The panelists first met in person to define the scope, purpose, clinical questions, and target audience. Methodologists at the ADA Center for Evidence-Based Dentistry then conducted a systematic review and network meta-analysis of the literature to address the clinical questions (O. Urquhart, MPH, unpublished data, August 2018). At second and third in-person meetings in October 2017 and February 2018 respectively, the panel formulated recommendation statements by using the Grading of Recommendations Assessment, Development and Evaluation evidence to decision framework, facilitated by methodologists at the ADA Center for Evidence-Based Dentistry (O.U., M.P.T., A.C.-L.).[13] This framework involves consideration of a minimum of 4 factors: balance between benefits and harms,

Table 1. Definition of the certainty in the evidence and strength of recommendations.

DEFINITION OF CERTAINTY (QUALITY) IN THE EVIDENCE*	
Category	**Definition**
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Definition of Strong and Conditional Recommendations and Implications for Stakeholders†		
Implications	**Strong Recommendations**	**Conditional Recommendations**
For Patients	Most people in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help people make decisions consistent with their values and preferences.	Most people in this situation would want the suggested course of action, but many would not.
For Clinicians	Most people should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping people making decisions consistent with their values and preferences.
For Policy Makers	The recommendation can be adapted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

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certainty in the evidence, patient values and preferences, and resource use. The panel discussed the evidence until reaching consensus. We took the decision to a vote when agreement was elusive. In Grading of Recommendations Assessment, Development and Evaluation, the strength of the recommendations can either be strong or be weak or conditional, and these have different implications for patients, clinicians, and policy makers (Table 1).[14-16] Additional details about the methodology we used to develop this clinical practice guideline are available in the Appendix (available online at the end of this article).

RECOMMENDATIONS

How to use the recommendations

We wrote the recommendations in this clinical practice guideline to assist clinicians, patients, and stakeholders in making evidence-based treatment decisions. Clinical judgment should be used to identify situations in which application of these recommendations may not be appropriate.

Question 1. To arrest cavitated coronal carious lesions on primary or permanent teeth, should we recommend silver diamine fluoride, silver nitrate, or sealants?

Advanced Cavitated Lesions on Any Coronal Tooth Surface

Summary of findings

Four studies (7 reports) including 2,115 participants informed these recommendations.[17-23] After 30 months of follow-up, the use of 38% silver diamine fluoride (SDF) solution applied biannually resulted in a 1.13 times greater chance of arresting advanced cavitated lesions on primary teeth than the use of 38% SDF annually (moderate certainty) and a 1.29 times greater chance of arresting advanced cavitated lesions on primary teeth than the use of 12% SDF solution biannually (high certainty).[18,21,22] In absolute terms, for a population with primary teeth and a 50% chance of arresting or reversing advanced cavitated carious lesions on any coronal surface, 6 more lesions would be arrested or reversed of 100 lesions treated with 38% SDF solution applied biannually compared with 38% SDF solution applied annually after 30 months of follow-up. In addition, after

30 months of follow-up, the use of 30% SDF solution annually resulted in a 1.45 times greater chance of arresting advanced cavitated lesions on primary teeth than the use of 30% SDF solution once per week for 3 weeks and a 1.41 times greater chance of arresting advanced cavitated lesions on primary teeth than 5% sodium fluoride (NaF) varnish applied once per week for 3 weeks (high certainty for both comparisons).[19,20] On average, after 24 months of follow-up, 38% SDF solution applied once at baseline resulted in significantly more advanced cavitated lesions on primary teeth arrested than results with no treatment (mean difference: 1.20, 95% confidence interval [CI] 0.49 to 1.91); this was not the case when 12% SDF solution was applied once at baseline and compared with no treatment.[17] We found no evidence on the effect of silver nitrate or sealants for cavitated lesions on coronal tooth surfaces. eTables 1 and 2[17-23] (available online at the end of this article) and the Appendix (available online at the end of this article) provide a complete report of the results.

Recommendations

- To arrest advanced cavitated carious lesions on any coronal surface of primary teeth, the expert panel recommends clinicians prioritize the use of 38% SDF solution (biannual application) over 5% NaF varnish (application once per week for 3 weeks). (Moderate-certainty evidence, strong recommendation.)
- To arrest advanced cavitated carious lesions on any coronal surface of permanent teeth, the expert panel suggests clinicians prioritize the use of 38% SDF solution (biannual application) over 5% NaF varnish (application once per week for 3 weeks). (Low-certainty evidence, conditional recommendation.)

Remarks

- Although investigators in all included studies assessed the effectiveness of SDF in children with primary teeth, the expert panel did not expect SDF to have a substantially different effect when applied on coronal surfaces of permanent teeth. For this reason, the panel provided a strong recommendation for the use of 38% SDF solution in primary teeth and a conditional recommendation for its use on coronal surfaces of permanent teeth given that there is no direct evidence available informing the effectiveness of any concentration of SDF in permanent teeth (serious issues of indirectness).
- Although SDF has been used in other countries for decades, it was just introduced into the United States in 2014, when the US Food and Drug Administration approved the use of SDF to treat hypersensitivity in adults. At the time of publication, 38% SDF solution is the only concentration available in the United States.[24]
- SDF could be used for a broad range of situations, including, but not limited to, when local or general anesthesia is not preferred, when a patient is not able to cooperate with treatment, or when it is necessary to offer a less costly or less invasive alternative.
- Data suggest that SDF may be more effective on anterior teeth than on posterior teeth. Hypotheses to explain this include, but are not limited to, anterior teeth being easier to keep clean and technique-related challenges for posterior teeth (for example, it is easier to maintain a dry field in the anterior teeth).
- One study informed the effect of SDF on International Caries Detection and Assessment System (ICDAS) 3 and 4 lesions, which involved using visual evaluation (with no radiographic assessment) to measure the progression of these lesions to ICDAS 5 and 6.[19] Although the investigators reported results for approximal, occlusal, and facial or lingual surfaces combined, the panel remains uncertain about the effect of SDF on ICDAS 3 and 4 lesions on each of these surfaces separately. We suggest investigators in future studies use a combination of diagnostic strategies (for example, radiographic assessment and visual evaluation) for this type of lesion.
- Hardness of tooth surfaces on probing is an indication that a lesion is arrested. In contrast, the color of the lesion (that is, black) is not an acceptable method to judge arrest of a lesion.
- An adverse effect associated with SDF is black staining of the lesion, which may not be acceptable to some patients, parents, or caregivers.[25]
- In keeping with the concept of informed consent, clinicians should offer or explain all nonsurgical and restorative treatment options and their potential adverse effects (such as blackened tooth surfaces treated with SDF) to all patients.

Question 2. To arrest or reverse noncavitated coronal carious lesions on primary or permanent teeth, should we recommend NaF, stannous fluoride, acidulated phosphate fluoride (APF), difluorsilane, ammonium fluoride, polyols, chlorhexidine, calcium phosphate, amorphous calcium phosphate (ACP), casein phosphopeptide (CPP)–ACP, nano-hydroxyapatite, tricalcium phosphate, or prebiotics with or without 1.5% arginine, probiotics, SDF, silver nitrate, lasers, resin infiltration, sealants, sodium bicarbonate, calcium hydroxide, or carbamide peroxide?

Noncavitated Lesions on Occlusal Surfaces

Summary of findings

Eight studies including 726 participants informed these recommendations.[26-33] Noncavitated occlusal lesions treated with sealants plus 5% NaF varnish,[28,32] sealants alone,[29-31] 5% NaF varnish alone,[28,31-33] 1.23% APF gel,[26] resin infiltration plus 5% NaF varnish,[28] or 0.2% NaF mouthrinse plus supervised toothbrushing[31] had a 2 to 3 times greater chance of being arrested or reversed than results with no treatment (moderate certainty for all comparisons). The combination of sealants plus 5% NaF varnish[28,32] was the most effective at arresting or reversing noncavitated occlusal lesions. eTable 3 (available online at the end of this article) and the Appendix (available online at the end of this article) provide a complete report of the results.

Recommendations

- To arrest or reverse noncavitated carious lesions on occlusal surfaces of primary teeth, the expert panel recommends clinicians prioritize the use of sealants plus 5% NaF varnish (application every 3-6 months) or sealants alone over 5% NaF varnish alone (application every 3-6 months), 1.23% APF gel (application every 3-6 months), resin infiltration plus 5% NaF varnish (application every 3-6 months), or 0.2% NaF mouthrinse (once per week). (Moderate-certainty evidence, strong recommendation.)
- To arrest or reverse noncavitated carious lesions on occlusal surfaces of permanent teeth, the expert panel recommends clinicians prioritize the use of sealants plus 5% NaF varnish (application every 3-6 months) or sealants alone over 5% NaF varnish alone (application every 3-6 months), 1.23% APF gel (application every 3-6 months), or 0.2% NaF mouthrinse (once per week). (Moderate-certainty evidence, strong recommendation.)

Remarks

- The order of treatments included in this recommendation is a ranking of priority that the panel defined when accounting for their effectiveness, feasibility, patient values and preferences, and resource use.
- The panel prioritized the use of sealants plus 5% NaF varnish or sealants alone over the use of all other treatments for occlusal noncavitated lesions on both primary and permanent teeth. Although the studies in which the investigators examined the combination of sealants plus 5% NaF were conducted in primary teeth, the panel had no reason to believe these treatments would have a substantially different effect when applied to permanent teeth.
- Investigators in the studies informing the recommendations for sealants included a mixture of resin-based, glass ionomer cement, and resin-modified glass ionomer sealants and reported a range in sealant retention from 41% through 89%. Maintaining a dry field and using proper technique are essential for sealant effectiveness and retention. If maintaining a dry field is not possible, a hydrophilic sealant material such as glass ionomer cement may be preferred over resin-based material.[34] In settings in which the quality of sealant application cannot be guaranteed, the panel suggests that clinicians consider other treatments included in the recommendations. Notably, enamel removal is unnecessary before sealant application.
- The study[31] in which the investigators provided data about 0.2% NaF mouthrinse also included supervised toothbrushing as a co-intervention.
- Although data from 1 study[28] support the use of resin infiltration plus 5% NaF varnish on occlusal surfaces of primary teeth, resin infiltration has been developed and studied primarily for treating approximal surfaces. The panel advises clinicians to consider the relatively high costs associated with this intervention compared with the cost of sealants.
- To mitigate the risk of experiencing accidental ingestion of high doses of fluoride, 0.2% NaF mouthrinses are not appropriate for uncooperative children who cannot control swallowing. In addition, in-office gels (for example, 1.23% APF gel) require suction to minimize swallowing, especially when used in children.

Noncavitated Lesions on Approximal Surfaces

Summary of findings

Thirteen studies (14 reports) including 2,516 participants informed these recommendations.[35-48] Noncavitated approximal carious lesions treated with the combination of resin infiltration plus 5% NaF varnish[42] had a 5 times greater chance of being arrested or reversed than results with no treatment (very low certainty). When either resin infiltration[45,47,48] or sealants[43-46] were used without another agent, there was a 2 times greater chance of arrest or reversal than results with no treatment (low certainty for both comparisons). Finally, when only 5% NaF varnish[42,43] was used, there was a 2 times greater chance of arrest or reversal; however, these results were not statistically significant (very low certainty). eTable 4 (available online at the end of this article) and the Appendix (available online at the end of this article) provide a complete report of the results.

Recommendation

- To arrest or reverse noncavitated carious lesions on approximal surfaces of primary and permanent teeth, the expert panel suggests clinicians use 5% NaF varnish (application every 3-6 months), resin infiltration alone, resin infiltration plus 5% NaF varnish (application every 3-6 months), or sealants alone. (Low- to very-low-certainty evidence, conditional recommendation.)

Remarks

- The order of treatments included in this recommendation is a ranking of priority that the panel defined when accounting for their effectiveness, feasibility, patient values and preferences, and resource use.
- After detecting an approximal lesion (and when it is not possible or feasible to separate the teeth for direct clinical observation), the clinician must rely on radiographic depth to diagnose the lesion as noncavitated or cavitated. Study investigators included lesions with radiolucencies ranging from the enamel to lesions in the outer one-third of the dentin. The panel emphasizes that approximal lesions that appear limited to the enamel and outer one-third of the dentin on radiographs are most likely noncavitated, and the clinician should prioritize the use of non-restorative interventions.[49]
- Investigators in the studies informing the use of resin infiltration alone conducted the studies in permanent teeth,[45,47] whereas the study investigators examining the use of resin infiltration plus 5% NaF varnish conducted the study in primary teeth.[42] Investigators in 1 study[35] examined the effectiveness of resin infiltration in mixed dentition, and the results suggested that it was significantly more effective in arresting or reversing approximal noncavitated lesions than was the control, described by the investigators as "mock treatment." The panel suggested using these treatments in both primary and permanent teeth because they did not expect them to have a substantially different effect in the 2 types of dentition. Resin infiltration is technique sensitive and may not be appropriate for uncooperative children.
- The evidence supporting the recommendation for sealants on approximal surfaces came from studies in which the investigators evaluated resin-based and glass ionomer cement sealants.[41,43-46] In no included studies did the investigators report on sealant retention for approximal surfaces. In addition, the use of sealants on approximal surfaces requires temporary tooth separation (a few days) and is technique sensitive. The remarks associated with the use of sealants on occlusal surfaces also apply to the use of sealants on approximal surfaces.

Noncavitated Lesions on Facial or Lingual Surfaces

Summary of findings

Five studies including 584 participants informed this recommendation.[26,33,50-52] Noncavitated facial or lingual carious lesions treated with 5% NaF varnish[33] had a 2 times greater chance of being arrested or reversed than results with no treatment (low certainty), whereas those treated with 1.23% APF gel[26] also had a 2 times greater chance of being arrested or reversed than results with oral health education (moderate certainty). When investigators compared 10% CPP-ACP[52] with placebo cream, the results suggested that it may increase the chance of arresting or reversing lesions; however, these results were neither statistically nor clinically significant (low certainty). eTables 5

and 6 (available online at the end of this article) and the Appendix (available online at the end of this article) provide a complete report of the results.

Recommendation

- To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of primary and permanent teeth, the expert panel suggests clinicians use 1.23% APF gel (application every 3-6 months) or 5% NaF varnish (application every 3-6 months). (Moderate- to low-certainty evidence, conditional recommendation.)

Remarks

- The order of treatments included in this recommendation is a ranking of priority that the panel defined when accounting for their effectiveness, feasibility, patient values and preferences, and resource use.
- In-office gels (for example, 1.23% APF gel) require suction to minimize swallowing, especially when used in uncooperative children.

Noncavitated Lesions on Any Coronal Tooth Surface

Summary of findings

Seven studies including 2,365 participants informed this recommendation.[26,33,53-57] Among studies in which the investigators reported data for all coronal surfaces combined, noncavitated carious lesions treated with 5% NaF varnish (low certainty)[33] and 1.23% APF gel (moderate certainty)[26] had a 2 times greater chance of being arrested or reversed than results with no treatment. Although 10% CPP-ACP[57] may increase the chance of arrest or reversal by 3%, these results were neither statistically nor clinically significant (low certainty). eTable 7 (available online at the end of this article) and the Appendix (available online at the end of this article) provide a complete report of the results.

Recommendation

- To arrest or reverse noncavitated carious lesions on coronal surfaces of primary and permanent teeth, the expert panel suggests clinicians do not use 10% CPP-ACP if other fluoride interventions, sealants, or resin infiltration is accessible. (Low-certainty evidence, conditional recommendation.)

Remark

- The panel emphasizes that 10% CPP-ACP should not be used as a substitute for fluoride products.

We found no evidence on the effect of stannous fluoride, difluorsilane, ammonium fluoride, calcium phosphate, ACP, nano-hydroxyapatite, tricalcium phosphate, or prebiotics with or without 1.5% arginine, SDF, silver nitrate, lasers, sodium bicarbonate, calcium hydroxide, or carbamide peroxide for noncavitated lesions on any coronal tooth surface.

Question 3. To arrest cavitated root carious lesions or arrest or reverse noncavitated root carious lesions on permanent teeth, should we recommend NaF, stannous fluoride, APF, difluorsilane, ammonium fluoride, polyols, chlorhexidine, calcium phosphate, ACP, CPP-ACP, nano-hydroxyapatite, tricalcium phosphate, or prebiotics with or without 1.5% arginine, probiotics, SDF, silver nitrate, lasers, resin infiltration, sealants, sodium bicarbonate, calcium hydroxide, or carbamide peroxide?

Noncavitated and Cavitated Lesions on Root Surfaces

Summary of findings

Eight studies including 584 participants informed these recommendations.[58-65] Noncavitated and cavitated root carious lesions treated with 5,000 parts per million fluoride (1.1% NaF) toothpaste or gel[60-62,64] had a 3 times greater chance of arrest or reversal than results with no treatment (low certainty). The use of 1% chlorhexidine plus thymol varnish,[59] 38% SDF solution applied annually,[63] 38% SDF plus potassium iodide[63] applied annually, or 5% NaF varnish[65] also had a 2 to 3 times greater chance of arrest or reversal; however, these results were not statistically significant (very low certainty). We found no evidence on the effect of stannous fluoride, APF, ammonium fluoride, polyols, calcium phosphate, ACP, CPP-ACP, nano-hydroxyapatite, tricalcium phosphate, or prebiotics with or without 1.5% arginine, probiotics, silver nitrate, lasers, resin infiltration, sealants,

Table 2. Summary of clinical recommendations for the nonrestorative treatment of caries.

CLINICAL QUESTION	PRIMARY DENTITION RECOMMENDATIONS	PERMANENT DENTITION RECOMMENDATIONS
To arrest cavitated coronal carious lesions on primary or permanent teeth, should we recommend SDF,* silver nitrate, or sealants?	To arrest advanced cavitated carious lesions on any coronal surface of primary teeth, the expert panel recommends clinicians† prioritize the use of 38% SDF solution (biannual application)‡ over 5% NaF§ varnish (application once per week for 3 weeks) (certainty: moderate; strength: strong).	To arrest advanced cavitated carious lesions on any coronal surface of permanent teeth, the expert panel suggests clinicians prioritize the use of 38% SDF solution (biannual application)‡ over 5% NaF varnish (application once per week for 3 weeks) (certainty: low; strength: conditional).
To arrest or reverse noncavitated coronal carious lesions on primary or permanent teeth, should we recommend NaF, stannous fluoride, APF,¶ difluorsilane, ammonium fluoride, polyols, chlorhexidine, calcium phosphate, ACP,# CPP-ACP, nano-hydroxyapatite, tricalcium phosphate, or prebiotics with or without 1.5% arginine, probiotics, SDF, silver nitrate, lasers, resin infiltration, sealants, sodium bicarbonate, calcium hydroxide, or carbamide peroxide?**	To arrest or reverse noncavitated carious lesions on occlusal surfaces of primary teeth, the expert panel recommends clinicians prioritize the use of sealants plus 5% NaF varnish (application every 3-6 months) or sealants alone over 5% NaF varnish alone (application every 3-6 months), 1.23% APF gel (application every 3-6 months), resin infiltration plus 5% NaF varnish (application every 3-6 months), or 0.2% NaF mouthrinse (once per week) (certainty: moderate; strength: strong).††	To arrest or reverse noncavitated carious lesions on occlusal surfaces of permanent teeth, the expert panel recommends clinicians prioritize the use of sealants plus 5% NaF varnish (application every 3-6 months) or sealants alone over 5% NaF varnish (application every 3-6 months), 1.23% APF gel (application every 3-6 months), or 0.2% NaF mouthrinse (once per week) (certainty: moderate; strength: strong).††
	To arrest or reverse noncavitated carious lesions on approximal surfaces of primary teeth, the expert panel suggests clinicians use 5% NaF varnish (application every 3-6 months), resin infiltration alone, resin infiltration plus 5% NaF varnish (application every 3-6 months), or sealants alone (certainty: low to very low; strength: conditional).††	To arrest or reverse noncavitated carious lesions on approximal surfaces of permanent teeth, the expert panel suggests clinicians use 5% NaF varnish (application every 3-6 months), resin infiltration alone, resin infiltration plus 5% NaF varnish (application every 3-6 months), or sealants alone (certainty: low to very low; strength: conditional).††
	To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of primary teeth, the expert panel suggests clinicians use 1.23% APF gel (application every 3-6 months) or 5% NaF varnish (application every 3-6 months) (certainty: moderate to low; strength: conditional).††	To arrest or reverse noncavitated carious lesions on facial or lingual surfaces of permanent teeth, the expert panel suggests clinicians use 1.23% APF gel (application every 3-6 months) or 5% NaF varnish (application every 3-6 months) (certainty: moderate to low; strength: conditional).††
	To arrest or reverse noncavitated carious lesions on coronal surfaces of primary teeth, the expert panel suggests clinicians do not use 10% CPP-ACP paste if other fluoride interventions, sealants, or resin infiltration is accessible (certainty: low; strength: conditional).	To arrest or reverse noncavitated carious lesions on coronal surfaces of permanent teeth, the expert panel suggests clinicians do not use 10% CPP-ACP paste if other fluoride interventions, sealants, or resin infiltration is accessible (certainty: low; strength: conditional).
To arrest cavitated root carious lesions or arrest or reverse noncavitated root carious lesions on permanent teeth, should we recommend NaF, stannous fluoride, APF, difluorsilane, ammonium fluoride, polyols, chlorhexidine, calcium phosphate, ACP, CPP-ACP, nano-hydroxyapatite, tricalcium phosphate, or prebiotics with or without 1.5% arginine, probiotics, SDF or silver nitrate, lasers, resin infiltration, sealants, sodium bicarbonate, calcium hydroxide, or carbamide peroxide?	Not applicable	To arrest or reverse noncavitated and cavitated carious lesions on root surfaces of permanent teeth, the expert panel suggests clinicians prioritize the use of 5,000 parts per million fluoride (1.1% NaF) toothpaste or gel (at least once per day) over 5% NaF varnish (application every 3-6 months), 38% SDF plus potassium iodide solution (annual application), 38% SDF solution (annual application), or 1% chlorhexidine plus 1% thymol varnish (application every 3-6 months) (certainty: low; strength: conditional).††

* SDF: Silver diamine fluoride. † *Clinicians* refers to the target audience for this guideline, but only those authorized or trained to perform the specified interventions should do so. ‡ In keeping with the concept of informed consent, clinicians should offer or explain all nonsurgical and restorative treatment options and their potential adverse effects (such as blackened tooth surfaces treated with SDF) to all patients. § NaF: Sodium fluoride. ¶ APF: Acidulated phosphate fluoride. # ACP: Amorphous calcium phosphate. ** CPP: Casein phosphopeptide. †† The order of treatments included in this recommendation represents a ranking of priority defined by the panel when accounting for treatment effectiveness, feasibility, patients' values and preferences, and resource utilization. Considerations such as a particular patient's values and preferences, special needs, or insurance status should inform clinical decision making.

sodium bicarbonate, calcium hydroxide, or carbamide peroxide for cavitated or noncavitated lesions on root surfaces. eTable 8[58-65] (available online at the end of this article) and the Appendix (available online at the end of this article) provide a complete report of the results.

Recommendation

- To arrest or reverse noncavitated and cavitated carious lesions on root surfaces of permanent teeth, the expert panel suggests clinicians prioritize the use of 5,000 ppm fluoride (1.1% NaF) toothpaste or gel (at least once per day) over 5% NaF varnish (application every 3-6 months), 38% SDF plus potassium iodide solution (annual application), 38% SDF solution (annual

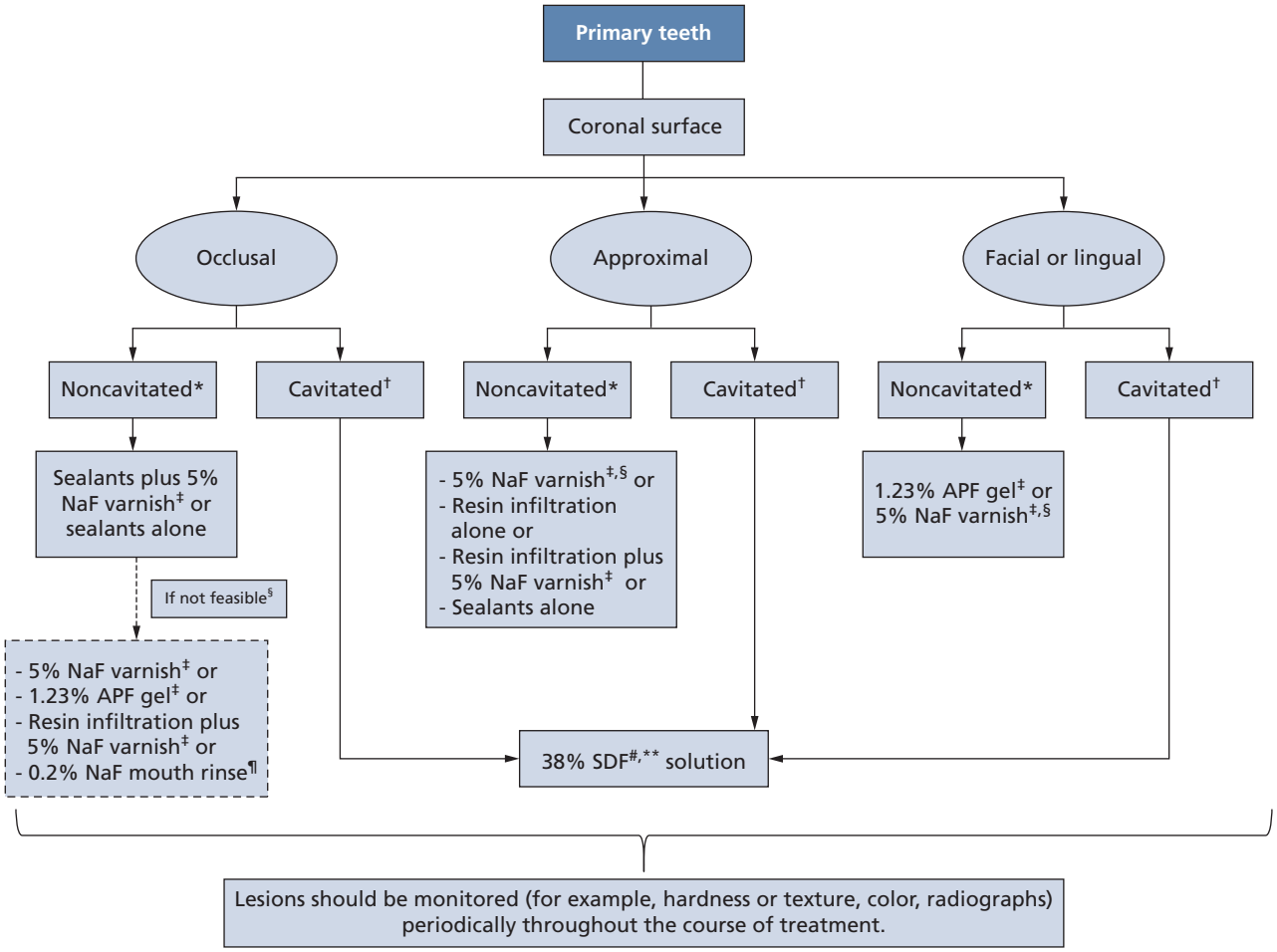

Figure 1. Clinical pathway for the nonrestorative treatment of noncavitated and cavitated carious lesions on primary teeth. APF: Acidulated phosphate fluoride. NaF: Sodium fluoride. SDF: Silver diamine fluoride. * Defined as ICDAS 1-2. † Defined as ICDAS 5-6. ‡ Application every 3 through 6 months. § The order of treatments included in this recommendation represents a ranking of priority defined by the panel when accounting for treatment effectiveness, feasibility, patients' values and preferences, and resource utilization. Considerations such as a particular patient's values and preferences, special needs, or insurance status should inform clinical decision making. ¶ At-home use once per week. # Biannual application. ** In keeping with the concept of informed consent, all nonsurgical and restorative treatment options and their potential side effects (such as blackened tooth surfaces treated with SDF) should be offered and explained to all patients.

application), or 1% chlorhexidine plus 1% thymol varnish (application every 3-6 months). (Low-certainty evidence, conditional recommendation.)

Remarks

- The order of treatments included in this recommendation is a ranking of priority that the panel defined by accounting for their effectiveness, feasibility, patient values and preferences, and resource use.
- Given that noncavitated and cavitated root lesions are difficult to distinguish in practice, the panel did not provide separate recommendations for these 2 types of lesions.
- Investigators conducted all studies in adult or older adult patients (permanent teeth), who are predominantly affected by root caries.
- The use of 5,000 ppm fluoride (1.1% NaF) toothpaste or gel requires patient adherence, which includes filling prescriptions and daily use at home. Because adherence is integral to its success, this intervention may not be feasible for populations in nursing homes and those with special needs. Furthermore, this treatment may not be covered universally by insurance. At the time of publication, some brand-name toothpastes cost 23 cents per toothbrushing, and generic versions cost 17 cents per toothbrushing.[66] If cost is a barrier, other interventions suggested for treating root caries may be more appropriate. Finally, if 38% SDF solution is chosen over 5,000 ppm fluoride (1.1% NaF) toothpaste or gel, the remarks associated with the use of SDF for cavitated lesions on any coronal surface also apply to the use of SDF on root surfaces.

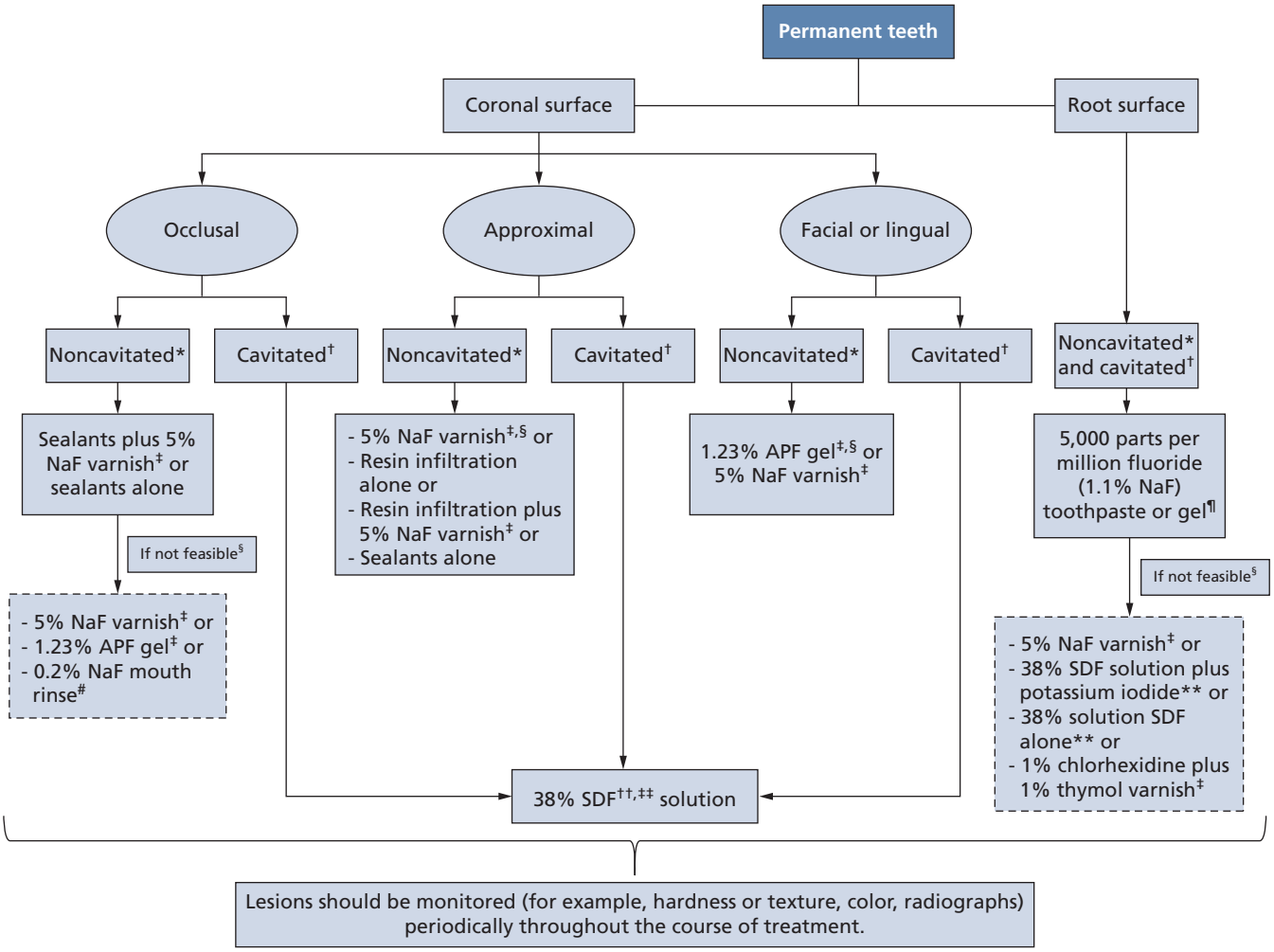

Figure 2. Clinical pathway for the nonrestorative treatment of noncavitated and cavitated carious lesions on permanent teeth. APF: Acidulated phosphate fluoride. NaF: Sodium fluoride. SDF: Silver diamine fluoride. * Defined as ICDAS 1-2. † Defined as ICDAS 5-6. ‡ Application every 3 to 6 months. § The order of treatments included in this recommendation represents a ranking of priority defined by the panel when accounting for treatment effectiveness, feasibility, patients' values and preferences, and resource utilization. Considerations such as a particular patient's values and preferences, special needs, or insurance status should inform clinical decision making. # At-home use once per week. †† Biannual application. ¶ At-home use at least once per day. **Annual application. ‡‡ In keeping with the concept of informed consent, all nonsurgical and restorative treatment options and their potential side effects (such as blackened tooth surfaces treated with SDF) should be offered and explained to all patients.

Table 2 provides information about all recommendations, certainty in the evidence, and strength of recommendations. Figures 1 and 2 illustrate the recommendation statements as an algorithm. A For the Patient page accompanies this guideline and will help clinicians communicate these recommendations to their patients.[67]

DISCUSSION

Implications for practice

This clinical practice guideline is the first in a series on caries management and includes evaluation of only nonrestorative treatments for existing lesions. Other articles in this series will provide guidance on caries prevention, caries detection and diagnosis, and restorative treatments. Many of the interventions included in this guideline's recommendations also are used regularly for caries prevention or as part of restorative treatment and will be reviewed again in those articles. Furthermore, the recommendations included in this article will be contextualized fully once all articles in the series are published and recommendations are collated.

Clinicians can use a variety of treatments to arrest or reverse carious lesions. We approached decision making by considering the type of lesion (noncavitated or cavitated), dentition (primary or permanent), and tooth surface (for example, occlusal). The certainty in the evidence informing our

recommendations ranged from very low to high because of issues of risk of bias, imprecision, indirectness, and inconsistency.[16]

The expert panel emphasizes the importance of actively monitoring noncavitated and cavitated lesions during the course of nonrestorative treatment to ensure the success of the management plan. Clinicians should observe signs of hardness on gentle probing or radiographic evidence of arrest or reversal over time and, if they do not see these signs, should implement additional or alternative treatment options. The panel suggests applying all treatments according to the dosage and technique provided within manufacturers' instructions.

Finally, although we did not include diet counseling as an intervention in this guideline, the panel emphasizes that nonrestorative treatments should be accompanied by a diet low in sugar.[68] The panel will consider dietary modifications as an intervention for the next article on caries prevention.

Implications for research

We urge researchers to conduct high-quality randomized controlled trials (RCTs) on nonrestorative treatments included in this guideline, especially for interventions for which there are a lack of RCTs. We also emphasize the importance of improving the reporting quality of primary studies.

Although high-quality RCTs in which the investigators evaluate the effect of SDF on advanced cavitated coronal lesions and noncavitated and cavitated root lesions were available, we were not able to identify published RCTs providing data about the effect of SDF on noncavitated lesions on approximal surfaces. The panel was eager to explore this indication for SDF because of the very low certainty in the evidence informing the use of other interventions on approximal surfaces. We identified the protocol of an ongoing RCT that may include data about this indication.[69] At the time of publication, we were not able to summarize these data or provide a recommendation for the use of SDF on noncavitated lesions on approximal surfaces.

Finally, we would have benefited from having a minimum set of patient-important outcomes for optimal decision making. This set should be developed and defined with the purpose of achieving standardization in the way outcomes are measured, reported, and summarized in RCTs and systematic reviews.

CONCLUSIONS

To arrest or reverse noncavitated carious lesions in both primary and permanent teeth, the expert panel suggests clinicians prioritize the use of sealants plus 5% NaF varnish on occlusal surfaces, 5% NaF varnish on approximal surfaces, and 1.23% APF gel or 5% NaF varnish alone on facial or lingual surfaces. The expert panel also suggests clinicians prioritize the use of 5,000 ppm fluoride (1.1% NaF) toothpaste or gel to arrest or reverse noncavitated and cavitated lesions on root surfaces of permanent teeth. To arrest advanced cavitated carious lesions on coronal surfaces of primary teeth, the expert panel recommends clinicians prioritize the use of 38% SDF solution biannually. The expert panel extrapolated these results to suggest that clinicians could use 38% SDF solution biannually to arrest advanced cavitated lesions on coronal surfaces of permanent teeth as well. The biannual application of 38% solution SDF for advanced cavitated lesions may be relevant if access to care is limited, for uncooperative patients, or for patients when general anesthetic is not considered safe. ■

SUPPLEMENTAL DATA

Supplemental data related to this article can be found at: https://doi.org/10.1016/j.adaj.2018.07.002.

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APPENDIX

METHODS

Panel configuration and conflicts of interest

The American Dental Association (ADA) Council on Scientific Affairs convened and approved an expert panel. Panel nominees filled out financial and intellectual conflicts of interest forms, and the methodologists subsequently reviewed them. We excluded nominees with major conflicts from the panel. We made these forms available to the panel at the beginning of all in-person meetings (December 2016, October 2017, and February 2018) and updated them periodically. We asked panel members who were highly conflicted to refrain from participating in the discussions when we were formulating recommendations pertaining to their conflict.

Outcomes

The panel defined outcomes important for decision making. These included arrest or reversal of noncavitated and cavitated carious lesions, nausea, fluorosis, vomiting, allergic reactions, staining, tooth sensitivity, soft-tissue trauma, progression of symptoms, pulpal health, lack of retention (for sealants), premature loss or extraction, and secondary caries.

Retrieving evidence

The recommendations contained in this guideline are informed by the results of a systematic review (O. Urquhart, MPH, unpublished data, June 2018). A health sciences librarian (L.B.) searched MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Embase to identify relevant articles for the review. Two of us (O.U., M.P.T.) screened all identified references in duplicate at the title and abstract levels and then during a second stage at a full-text level. Four of us (M.P.T., O.U., L.P., an author of the related systematic review) then extracted data from the included studies and appropriately synthesized the data by using a network meta-analysis. A full report of methods and results from this guideline can be found in our accompanying systematic review (O. Urquhart, MPH, unpublished data, June 2018).

Relative and absolute treatment effects

We calculated relative risks and 95% CIs for dichotomous data and mean differences and 95% CIs for continuous data. The numbers presented in the text are the rounded versions of the numbers presented in the tables. In some cases, we could not pool data in the network meta-analysis. We still included these data, considered unpooled, and we reported relative risks and mean differences at a study level or as the study authors described. We displayed all data from the network meta-analysis by using a modified version of the summary-of-findings tables for the network meta-analysis (J.J. Yepes-Nuñez, MD, MSc, written communication, March 2018). We also calculated absolute treatment effects by using 3 illustrative baseline probabilities for arrest or reversal of carious lesions (20%, 50%, and 70%). For example, someone in the 70% category has a 70% baseline probability for arrest or reversal of their carious lesions without any intervention. The panel chose these numbers arbitrarily to represent different risk profiles that clinicians may see in practice.

Certainty in the evidence

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for the network meta-analysis to assess the certainty in the evidence (high, moderate, low, or very low) at an outcome level for each of the comparisons.[e1] We assessed the domains of risk of bias, inconsistency, imprecision, publication bias, and indirectness for all direct comparisons according to guidance from the GRADE working group.[16] We further considered intransitivity when assessing the certainty of indirect estimates. Finally, when assessing the certainty in the evidence of the network estimates, we considered local incoherence between the direct and indirect estimates. When we could not include studies in the network meta-analysis, we assessed the certainty in the evidence at a study level.

Stakeholder and public feedback

Throughout the guideline development process, we engaged both internal ADA stakeholders and external stakeholder organizations. Internal stakeholders were the Council on Advocacy for Access and Prevention, Council on Dental Benefit Programs, and Council on Dental Practice. External stakeholders were the Academy of Dental Materials, Academy of General Dentistry, Academy of Operative Dentistry, American Academy of Pediatric Dentistry, American Association of Endodontists, American Association of Public Health Dentistry, American Dental Hygienists' Association, Association of State and Territorial Dental Directors, National Institute of Dental and Craniofacial Research and Oral Health America.

We contacted stakeholders twice throughout the process; first to provide feedback regarding the scope, purpose, target audience, and clinical questions for the guideline and a second time to review the recommendation statements. In addition, we posted the recommendation statements on the ADA Center for Evidence-Based Dentistry's Web site (ebd.ada.org) to offer the general public an opportunity to provide feedback. We considered all feedback and included it in the manuscript whenever appropriate.

Updating process

The ADA Center for Evidence-Based Dentistry updates its guidelines every 5 years or whenever newly published evidence could result in a change in the direction or strength of recommendations. We use digital platforms such as MAGICapp and RevMan to store all of our data, thereby facilitating an efficient updating process. Updates and chairside resources for clinicians are available at the ADA Center for Evidence-Based Dentistry Web site.

RESULTS

Noncavitated lesions on occlusal surfaces

After 8 to 12 months of follow-up, for a population with a 50% chance of arresting or reversing noncavitated carious lesions on occlusal surfaces, 19 more to 118 more carious lesions would be arrested or reversed of 100 lesions treated with sealants plus 5% sodium fluoride (NaF) varnish, sealants alone, 5% NaF varnish alone, 1.23% acidulated phosphate fluoride gel, 5% NaF varnish, resin infiltration and 5% NaF varnish, or 0.2% NaF mouthrinse plus supervised toothbrushing compared with no treatment.

Noncavitated lesions on approximal surfaces

After 12 through 30 months of follow-up, for a population with a 50% chance of arresting or reversing noncavitated carious lesions on approximal surfaces, 56 more to 178 more carious lesions would be arrested or reversed of 100 lesions treated with a combination of resin infiltration and 5% NaF varnish, resin infiltration alone, or sealants alone compared with no treatment.

Noncavitated lesions on facial or lingual surfaces

After 12 through 30 months of follow-up, for a population with a 50% chance of arresting or reversing noncavitated carious lesions on facial or lingual surfaces, 12 more to 74 more carious lesions would be arrested or reversed of 100 lesions treated with 5% NaF varnish, 1.23% acidulated phosphate fluoride gel, or 10% casein phosphopeptide—amorphous calcium phosphate paste compared with no treatment, oral health education, and a placebo cream, respectively.

Noncavitated lesions on any coronal tooth surfaces

After 12 through 30 months of follow-up, for a population with a 50% chance of arresting or reversing noncavitated carious lesions on any coronal tooth surface, 2 more to 63 more carious lesions would be arrested or reversed of 100 lesions treated with 5% NaF varnish, 1.23% acidulated phosphate fluoride gel, or 10% casein phosphopeptide—amorphous calcium phosphate paste compared with no treatment.

Noncavitated and cavitated lesions on root surfaces

After 3 through 12 months of follow-up, for a population with a 50% chance of arresting or reversing noncavitated and cavitated carious lesions on root surfaces, 34 more to 98 more carious

lesions would be arrested or reversed of 100 lesions treated with 5,000 parts per million fluoride (1.1% NaF) toothpaste or gel, a combination of 1% chlorhexidine and thymol varnish, 38% silver diamine fluoride solution, a combination of 38% silver diamine fluoride solution and potassium iodide, or 5% NaF varnish compared with no treatment.

e1. Brignardello-Petersen R, Bonner A, Alexander PE, et al. Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. *J Clin Epidemiol.* 2018;93:36-44.

eTable 1. Summary of findings: nonrestorative treatments for the arrest of advanced cavitated lesions on any coronal tooth surface.

TOTAL NO. OF UNPOOLED STUDIES: 4 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§]	NO. OF PEOPLE AT FOLLOW-UP/ NO. OF LESIONS AT LONGEST FOLLOW-UP	SURFACE	STUDY ARM: DOSE, DURATION, OR FREQUENCY	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE[¶]
					Without Intervention (%)[#]	With Intervention	Difference	
Duangthip and Colleagues[20] and Duangthip and Colleagues[19]	309/1,877	Any surface (occlusal, approximal, facial or lingual)	30% SDF[**] solution annually versus 30% SDF solution once per week for 3 weeks		70 per 100	102 per 100	32 per 100 more	High
							(From 15 more to 52 more)	
				1.45	50 per 100	73 per 100	23 per 100 more	
				(1.21 to 1.73)			(From 11 more to 37 more)	
					20 per 100	29 per 100	9 per 100 more	
							(From 4 more to 15 more)	
			30% SDF solution annually versus 5% NaF[††] varnish once per week for 3 weeks		70 per 100	99 per 100	29 per 100 more	High
				1.41			(From 14 more to 46 more)	
					50 per 100	71 per 100	21 per 100 more	
				(1.20 to 1.66)			(From 10 more to 33 more)	
					20 per 100	28 per 100	8 per 100 more	
							(From 4 more to 13 more)	
			30% SDF solution once per week for 3 weeks versus 5% NaF varnish once per week for 3 weeks		70 per 100	68 per 100	2 per 100 fewer	Moderate (imprecision[‡‡])
							(From 14 fewer to 13 more)	

* Sources: Duangthip and colleagues[20] and Duangthip and colleagues[19] (30-month follow-up, primary dentition): black staining was reported as an adverse event. † Sources: Fung and colleagues,[21] Duangthip and colleagues[18] and Fung and colleagues[22] (30-month follow-up, primary dentition): lesions treated with 38% SDF had a statistically significantly increased chance of becoming black than those receiving 12% SDF. Lesions treated semiannually also had a higher chance of becoming black than those treated annually. There was no significant difference in tooth pain, gingiva pain, gingiva swelling, or gingiva bleaching among the 4 groups; these adverse events affected a small proportion of children in each group (1%-7%). ‡ Source: Yee and colleagues[17] (24-month follow-up, primary dentition): The authors reported results as mean differences (MD): −38% SDF and breakfast tea versus no treatment: MD, 1.20; 95% confidence interval [CI], 0.49 to 1.91; 12% SDF versus no treatment: MD, 0.50; 95% CI, −0.21 to 1.21; 38% SDF versus no treatment: MD, 1.10; 95% CI, 0.39 to 1.81; 38% SDF versus 12% SDF: MD, 0.60; 95% CI, −0.23 to 1.43; 38% SDF versus 38% SDF and tea: MD, −0.10; 95% CI, −0.93 to 0.73; 12% SDF versus 38% SDF and tea: MD, −0.70; 95% CI, −1.53 to 0.13. The authors also reported results for 6 and 12 months. § Source: Llodra and colleagues[23] (36 months, primary dentition): after 36 months of follow-up, on average, the 38% SDF group had 0.3 surfaces with arrested caries, whereas the control group had 0.1 ($P < .05$). The SDF group had a higher percentage of black stains (97%) than did the control group, in which only 48% of the inactive lesions were black ($P < .001$). Compared with the control participants, the children treated with SDF had a higher proportion of black stains in inactive lesions ($P < .001$). ¶ When these data were used to inform recommendation 6, the certainty in the evidence was downgraded because of serious issues of indirectness. There is no direct evidence available informing the effectiveness of any concentration of SDF in permanent teeth. # The percentages (20%, 50%, 70%) indicate illustrative baseline probabilities for the arrest or reversal of carious lesions. ** SDF: Silver diamine fluoride. †† NaF: Sodium fluoride. ‡‡ Serious issues of imprecision; 95% CI suggests a moderate harm and moderate benefit. §§ Serious issues of imprecision; 95% CI suggests a small benefit and a moderate benefit.

eTable 1. Continued

TOTAL NO. OF UNPOOLED STUDIES: 4 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§]	NO. OF PEOPLE AT FOLLOW-UP/ NO. OF LESIONS AT LONGEST FOLLOW-UP	SURFACE	STUDY ARM: DOSE, DURATION, OR FREQUENCY	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE[¶]
					Without Intervention (%)[#]	With Intervention	Difference	
				0.97	50 per 100	49 per 100	2 per 100 fewer	
				(0.80 to 1.18)			(From 10 fewer to 9 more)	
					20 per 100	19 per 100	−1 per 100 fewer	
							(From 4 fewer to 4 more)	
Fung and Colleagues,[21] Duangthip and Colleagues,[18] and Fung and Colleagues[22]	799/3,790	Any surface (mesial, occlusal, approximal, distal, facial or lingual)	12% SDF solution annually versus 12% SDF biannually		70 per 100	66 per 100	4 per 100 fewer	High
							(From 9 fewer to 1 more)	
				0.94	50 per 100	47 per 100	3 per 100 fewer	
				(0.87 to 1.02)			(From 7 fewer to 1 more)	
					20 per 100	19 per 100	1 per 100 fewer	
							(From 3 fewer to 0 fewer)	
			38% SDF solution annually versus 12% SDF solution annually		70 per 100	85 per 100	15 per 100 more	High
							(From 9 more to 21 more)	
				1.21	50 per 100	61 per 100	11 per 100 more	
				(1.13 to 1.3)			(From 7 more to 15 more)	
					20 per 100	24 per 100	4 per 100 more	
							(From 3 more to 6 more)	
			38% SDF solution biannually versus 12% SDF solution biannually		70 per 100	90 per 100	20 per 100 more	High
							(From 15 more to 27 more)	
				1.29	50 per 100	65 per 100	15 per 100 more	

eTable 1. Continued

TOTAL NO. OF UNPOOLED STUDIES: 4 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§]	NO. OF PEOPLE AT FOLLOW-UP/ NO. OF LESIONS AT LONGEST FOLLOW-UP	SURFACE	STUDY ARM: DOSE, DURATION, OR FREQUENCY	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE[¶]
					Without Intervention (%)[#]	With Intervention	Difference	
				(1.21 to 1.38)			(From 11 more to 19 more)	
					20 per 100	26 per 100	6 per 100 more	
							(From 4 more to 8 more)	
			38% SDF solution biannually versus 38% SDF solution annually		70 per 100	79 per 100	9 per 100 more	Moderate (imprecision[§§])
							(From 5 more to 14 more)	
				1.13	50 per 100	57 per 100	7 per 100 more	
				(1.07 to 1.2)			(From 4 more to 10 more)	
					20 per 100	23 per 100	3 per 100 more	
							(From 1 more to 4 more)	

eTable 2. Summary of findings: additional follow-up times for nonrestorative treatments for the arrest of advanced cavitated lesions on any coronal tooth surface.

TOTAL NO. OF UNPOOLED STUDIES: 4*,†,‡,§ (7 REPORTS)	STUDY ARM (DOSE, DURATION, OR FREQUENCY)	RELATIVE RISK (95% CONFIDENCE INTERVAL) AND CERTAINTY IN THE EVIDENCE			
Duangthip and Colleagues[20] and Duangthip and Colleagues[19]	30% SDF¶ solution (annually) 30% SDF (once per week for 3 weeks, not reapplied annually) 5% NaF varnish (once per week for 3 weeks, not reapplied annually)	30% SDF solution annually versus 30% SDF once per week for 3 weeks 30 months: 1.45 (1.21 to 1.73); certainty: high 18 months: 1.13 (0.95 to 1.34); certainty: moderate (serious issues of imprecision**) 12 months: 0.72 (0.56 to 0.91); certainty: moderate (serious issues of imprecision**)	30% SDF solution annually versus 5% NaF# varnish once per week for 3 weeks 30 months: 1.41 (1.20 to 1.66); certainty: high 18 months: 1.47 (1.22 to 1.76); certainty: high 12 months: 1.48 (1.11 to 1.97); certainty: high	30% SDF solution once per week for 3 weeks versus 5% NaF varnish once per week for 3 weeks 30 months: 0.97 (0.80 to 1.18); certainty: moderate (serious issues of imprecision**) 18 months: 1.30 (1.07 to 1.57); certainty: high 12 months: 2.08 (1.59 to 2.71); certainty: high	Not applicable
Fung and Colleagues,[21] Duangthip and Colleagues[18] and Fung and Colleagues[22]	12% SDF solution (annually) 12% SDF solution (biannually) 38% SDF solution (annually) 38% SDF solution (biannually)	12% SDF solution annually versus 12% SDF solution biannually 30 months: 0.94 (0.87 to 1.02); certainty: high 24 months: 0.91 (0.84 to 0.98); certainty: moderate (serious issues of imprecision**) 18 months: 0.91 (0.83 to 0.99); certainty: moderate (serious issues of imprecision**) 12 months: 0.85 (0.77 to 0.93); certainty: moderate (serious issues of imprecision**)	38% SDF solution biannually versus 38% solution SDF annually 30 months: 1.13 (1.07 to 1.20); certainty: moderate (serious issues of imprecision**) 24 months: 1.20 (1.13 to 1.27); certainty: high 18 months: 1.15 (1.09 to 1.23); certainty: moderate (serious issues of imprecision**) 12 months: 1.21 (1.12 to 1.30); certainty: high	38% SDF solution biannually versus 12% SDF solution biannually 30 months: 1.29 (1.21 to 1.38); certainty: high 24 months: 1.29 (1.21 to 1.38); certainty: high 18 months: 1.34 (1.25 to 1.43); certainty: high 12 months: 1.30 (1.21 to 1.41); certainty: high	38% SDF solution annually versus 12% SDF solution annually 30 months: 1.21 (1.13 to 1.30); certainty: high 24 months: 1.19 (1.10 to 1.28); certainty: high 18 months: 1.27 (1.18 to 1.38); certainty: high 12 months: 1.27 (1.16 to 1.40); certainty: high

* Sources: Duangthip and colleagues[20] and Duangthip and colleagues[19] (primary dentition): black staining was reported as an adverse event. † Sources: Fung and colleagues[21] and Duangthip and colleagues[18] and Fung and colleagues[22] (primary dentition): lesions treated with 38% SDF had a statistically significantly increased chance of becoming black compared with those receiving 12% SDF. Lesions treated semiannually also had a higher chance of becoming black than did those treated annually. There was no significant difference in tooth pain, gingiva pain, gingiva swelling, or gingiva bleaching among the 4 groups; these adverse events affected a small proportion of children in each group (1%-7%). ‡ Source: Yee and colleagues[17] (24-month follow-up, primary dentition): the authors reported results as mean differences (MD): −38% SDF and tea versus no treatment: MD, 1.20, 95% confidence interval [CI], 0.49 to 1.91; 12% SDF versus no treatment: MD, 0.50, 95% CI, −0.21 to 1.21; 38% SDF versus no treatment: MD, 1.10, 95% CI, 0.39 to 1.81; 38% SDF versus 12% SDF: MD, 0.60, 95% CI, −0.23 to 1.43; 38% SDF versus 38% SDF and tea: MD, −0.10; 95% CI, −0.93 to 0.73; 12% SDF versus 38% SDF and tea: MD, −0.70; 95% CI, −1.53 to 0.13. The authors also reported results for 6 and 12 months. § Source: Llodra and colleagues[23] (36 months, primary dentition): after 36 months of follow-up, on average, the 38% SDF group had 0.3 surfaces with arrested caries, whereas the control group had 0.1 ($P < .05$). The SDF group had a higher percentage of black stains (97%) than did the control group, in which only 48% of the inactive lesions were black ($P < .001$). Compared with the control participants, the children treated with SDF had a higher proportion of black stains in inactive lesions ($P < .001$). ¶ SDF: Silver diamine fluoride. # NaF: Sodium fluoride. ** Serious issues of imprecision.

eTable 3. Summary of findings: nonrestorative treatments for the arrest or reversal of noncavitated lesions on occlusal surfaces.

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 7*,†,‡,§,¶,#,** TOTAL NO. OF PARTICIPANTS IN NETWORK: 694†† TOTAL NO. OF UNPOOLED STUDIES: 1 RANDOMIZED CONTROLLED TRIAL‡‡	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)§§	INTERPRETATION OF FINDINGS
		Without Intervention (%)¶¶	With Intervention	Difference			
0.2% NaF## Mouthrinse plus Supervised Toothbrushing*		70 per 100	137 per 100	67 per 100 more	Moderate (risk of bias***)	0.35 (6/7)	Superior
(Indirect Evidence)				(From 38 more to 102 more)			
	1.95	50 per 100	98 per 100	48 per 100 more			
	(1.54 to 2.46)			(From 27 more to 73 more)			
		20 per 100	39 per 100	19 per 100 more			
				(From 11 more to 29 more)			
1.23% Acidulated Phosphate Fluoride Gel† (Direct Evidence)		70 per 100	149 per 100	79 per 100 more	Moderate (risk of bias†††)	0.53 (3/7)	Superior
				(From 55 more to 108 more)			
	2.13	50 per 100	107 per 100	57 per 100 more			
	(1.79 to 2.54)			(From 40 more to 77 more)			
		20 per 100	43 per 100	23 per 100 more			
				(From 16 more to 31 more)			

* Source: Florio and colleagues[31] (12-month follow-up, permanent dentition): the use of a resin-modified glass ionomer sealant resulted in a 65.5% (19/29) retention rate at 12-month follow-up. † Source: Agrawal and Pushpanjali[26] (12-month follow-up, mixed dentition). ‡ Source: Autio-Gold and Courts[33] (9-month follow-up, primary dentition). § Source: Bakhshandeh and Ekstrand[27] (8- to 34-month follow-up; mean, 22 months; primary dentition): 5% NaF varnish and resin-based sealant. ¶ Source: Honkala and colleagues[32] (12-month follow-up, primary dentition): of the 345 resin-sealed occlusal surfaces, 73.0% (252) were retained fully after 1-year follow-up, whereas 15.1% (52) experienced partial retention. # Source: da Silveira and colleagues[30] (12-month follow-up, permanent dentition): throughout the 12-month study, 40.74% (11/27) of teeth in the glass ionomer sealant group had total retention of the sealant, 40.74% (11/27) had 1 sealant replacement, and 18.52% (5/27) had 2 sealant replacements. ** Source: Borges and colleagues[29] (12-month follow-up, mixed dentition): in the resin-sealant group, 88.5% (23/26) of teeth had full retention, 7.7% (2/26) had partial retention, and 3.85% (1/26) had total loss of sealant at a 12-month follow-up. †† Source: Florio and colleagues[31] did not report loss to follow-up at a person level. They reported the total number of participants randomly assigned to each group at baseline; Borges and colleagues[29] and da Silveira and colleagues[30] did not report loss to follow-up at a person level or the total number of participants randomly assigned to each group at baseline. The number reported is the total number of participants at baseline. The guideline authors used data from occlusal surfaces only from Agrawal and Pushpanjali[26] and Autio-Gold and Courts[33] Although the study authors reported the number of lesions on occlusal surfaces, they did not report the number of participants who had lesions on occlusal surfaces. The number reported is the total number of participants at follow-up; investigators in other studies included in the network reported the total number of participants at follow-up. ‡‡ Source: Altenburger and colleagues[27] (3-week follow-up, permanent dentition): the use of 10% casein phosphopeptide–amorphous calcium phosphate daily for 3 weeks resulted in a 400% increase in caries arrestment (relative risk, 5.00; 95% confidence interval, 0.25 to 98.97) compared with 1,450 parts per million toothpaste daily at 3 weeks of follow-up. §§ The lower the value, the higher the position in the ranking. ¶¶ The percentages (20%, 50%, 70%) indicate illustrative baseline probabilities for the arrest or reversal of carious lesions. ## NaF: Sodium fluoride. *** Serious issues of risk of bias exist because of unclear randomization technique and no information or inadequate allocation concealment. Also, it is unclear whether the outcome assessor, personnel, or patients were blinded and whether outcome data were complete. ††† Serious issues of risk of bias exist because of unclear methods related to allocation concealment, and blinding of participants and personnel. ‡‡‡ Serious issues of risk of bias exist because of unclear methods related to random sequence generation, allocation concealment, and blinding of personnel and participants. §§§ Serious issues of risk of bias exist because of unclear methods related to blinding of personnel or participants, allocation concealment, blinding of outcome assessors, and random sequence generation. ¶¶¶ Serious issues of risk of bias exist because of inadequate allocation concealment and incomplete outcome data. Also, methods related to random assignment or blinding of participants and personnel are unclear. ### The studies informing the no-treatment group consist of no treatment and oral health education.[26,29,30,32,33]

eTable 3. Continued

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 7[*,†,‡,§,¶,#,**] TOTAL NO. OF PARTICIPANTS IN NETWORK: 694[††] TOTAL NO. OF UNPOOLED STUDIES: 1 RANDOMIZED CONTROLLED TRIAL[‡‡]	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)[§§]	INTERPRETATION OF FINDINGS
		Without Intervention (%)[¶¶]	With Intervention	Difference			
5% NaF Varnish[*,‡,§,¶] (Direct and Indirect Evidence)		70 per 100	138 per 100	68 per 100 more	Moderate (risk of bias[‡‡‡])	0.39 (5/7)	Superior
				(From 44 more to 98 more)			
	1.97	50 per 100	99 per 100	49 per 100 more			
	(1.63 to 2.40)			(From 32 more to 70 more)			
		20 per 100	39 per 100	19 per 100 more			
				(From 13 more to 28 more)			
Resin Infiltration plus 5% NaF Varnish[§] (Indirect Evidence)		70 per 100	224 per 100	154 per 100 more	Moderate (risk of bias[§§§])	0.89 (2/7)	Superior
				(From 87 more to 249 more)			
	3.20	50 per 100	160 per 100	110 per 100 more			
	(2.24 to 4.56)			(From 62 more to 178 more)			
		20 per 100	64 per 100	44 per 100 more			
				(From 25 more to 71 more)			
Sealant plus 5% NaF Varnish[§,¶] (Indirect Evidence)		70 per 100	235 per 100	165 per 100 more	Moderate (risk of bias[§§§])	0.94 (1/7)	Superior
				(From 99 more to 255 more)			
	3.35	50 per 100	168 per 100	118 per 100 more			
	(2.42 to 4.64)			(From 71 more to 182 more)			
		20 per 100	67 per 100	47 per 100 more			
				(From 28 more to 73 more)			

eTable 3. Continued

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 7[*,†,‡,§,¶,#,**] TOTAL NO. OF PARTICIPANTS IN NETWORK: 694[††] TOTAL NO. OF UNPOOLED STUDIES: 1 RANDOMIZED CONTROLLED TRIAL[‡‡]	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)[§§]	INTERPRETATION OF FINDINGS
		Without Intervention (%)[¶¶]	With Intervention	Difference			
Sealant[*,#,] (Direct and Indirect Evidence)**		70 per 100	139 per 100	69 per 100 more	Moderate (risk of bias[¶¶¶])	0.40 (4/7)	Superior
				(From 43 more to 101 more)			
	1.98	50 per 100	99 per 100	49 per 100 more			
	(1.62 to 2.44)			(From 31 more to 72 more)			
		20 per 100	40 per 100	20 per 100 more			
				(From 12 more to 29 more)			
No Treatment[†, ‡,¶, #,,###]**					Reference comparator	0.00 (7/7)	Reference comparator
	Reference comparator	Not estimable	Not estimable	Reference comparator			

eTable 4. Summary of findings: nonrestorative treatments for the arrest or reversal noncavitated lesions on approximal surfaces.

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 6 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§,¶,#] TOTAL NO. OF PARTICIPANTS IN NETWORK: 232 TOTAL NO. OF UNPOOLED STUDIES: 7 RANDOMIZED CONTROLLED TRIALS[**,††,‡‡,§§,¶¶,##,***]	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)[†††]	INTERPRETATION OF FINDINGS
		Without Intervention (%)[‡‡‡]	With Intervention	Difference			
5% NaF[§§§] Varnish[*,†] (Indirect Evidence)		70 per 100	160 per 100	90 per 100 more (From 18 fewer to 427 more)	Very low (risk of bias[¶¶¶] and imprecision[###])	0.51 (3/5)	May be superior
	2.29 (0.74 to 7.10)	50 per 100	114 per 100	65 per 100 more (From 13 fewer to 305 more)			
		20 per 100	46 per 100	26 per 100 more (From 5 fewer to 122 more)			
Resin Infiltration[‡,§] (Direct and Indirect Evidence)		70 per 100	148 per 100	78 per 100 more (From 6 more to 219 more)	Low (risk of bias[****] and imprecision[††††])	0.49 (4/5)	May be superior

* Source: Ekstrand and colleagues[42] (12-month follow-up, primary dentition). † Source: Gomez and colleagues[43] (24-month follow-up, mixed dentition). ‡ Source: Martignon and colleagues[45] (12-month follow-up, permanent dentition). § Sources: Meyer-Lueckel and colleagues[47] and Paris and colleagues[48] (36-month follow-up, permanent dentition). Additional follow-ups: 18 months: resin infiltration versus no treatment: relative risk [RR], 1.47; 95% confidence interval [CI], 1.08 to 2.00. ¶ Source: Martignon and colleagues[46] (30-month follow-up, primary dentition): 73.6% of participants experienced light pain during elastic band placement and 65.8% experienced light pain during the sealing process. # Source: Martignon and colleagues[44] (18-month follow-up, permanent dentition). ** Source: Meyer-Lueckel and colleagues[35] (18-month follow-up, mixed dentition): additional fluoride varnish was applied at the discretion of each dentist during the 6-month recall. Therefore, the guideline authors removed this study from the network because they could not account for background fluoride varnish. However, in the resin infiltration group, 94.6% (176/186) of participants experienced no progression compared with 68.8% (128/186) participants in the mock treatment group (RR, 1.38; 95% CI, 1.24 to 1.52). †† Source: Moberg Sköld and colleagues[36] (36-month follow-up, permanent dentition): in patients receiving 0.2% NaF mouthrinse 12 times per year, 59% of caries that could have progressed were prevented compared with findings in patients receiving 6 mouthrinses per year (PF = 30%), 27 mouthrinses per year (PF = 47%), and 20 mouthrinses per year (preventive fraction = 41%). ‡‡ Source: Moberg Sköld and colleagues[37] (36-month follow-up, permanent dentition): the use of 5% NaF varnish twice per year at 6-month intervals resulted in a 17% increase in the chance of experiencing caries arrestment (RR, 1.17; 95% CI, 1.07 to 1.27), the use of 5% NaF varnish 3 times per year all in 1 week, resulted in a 13% increase in the chance of experiencing caries arrestment (RR, 1.13; 95% CI, 1.03 to 1.24), and the use of 5% NaF varnish 8 times per year with 1-month intervals resulted in a 15% increase in the chance of experiencing caries arrestment (RR, 1.15; 95% CI, 1.06 to 1.26) compared with results with no additional fluoride varnish. All the groups in this study received 5% NaF varnish regularly as part of a school program. §§ Source: Modéer and colleagues[38] (36-month follow-up, permanent dentition): the use of 5% NaF varnish (every third month for 3 years) and 0.2% NaF mouthrinse (every 14 days) resulted in a 4% decrease in caries arrestment (RR, 0.96; 95% CI, 0.51 to 1.80) compared with results with 0.2% NaF mouthrinse (every 14 days) at 3 years of follow-up. ¶¶ Source: Petersson and colleagues[39] (36-month follow-up, mixed dentition): patients receiving 5% NaF varnish 3 times per week once per year for 3 years reported 116 surfaces arrested and reversed compared with 78 surfaces arrested and reversed in those receiving 5% NaF varnish every 6 months for 3 years (no total number of surfaces per group reported). ## Source: Peyron and colleagues[40] (12- and 24-month follow-ups, primary dentition): after 1 year of follow-up, of 41 people in the 5% NaF varnish arm, 48.8% (n = 20) of the enrolled patients with 1 or more superficial enamel carious lesions experienced no progression of carious lesions compared with 17.2% (n = 5) of the 29 people with who did not receive 5% NaF varnish. After 2 years of follow-up, of 42 people with 1 or more superficial enamel carious lesions receiving 5% NaF varnish, 33.3% (n = 14) did not experience progression of carious lesions compared with 8.8% (n = 3) of the 34 who did not receive 5% NaF varnish. *** Source: Trairatvorakul and colleagues[41] (12-month follow-up, permanent dentition): The use of sealants and 1.23% acidulated phosphate fluoride gel (at baseline and 6-month recall) resulted in a 1,950% increase in caries arrestment (RR, 20.05; 95% CI, 5.31 to 79.21) compared with 1.23% acidulated phosphate fluoride gel (at baseline and 6-month recall) after 1 year of follow-up. ††† The lower the value, the higher the position in the ranking. ‡‡‡ The percentages (20%, 50%, 70%) indicate illustrative baseline probabilities for the arrest or reversal of carious lesions. §§§ NaF: Sodium fluoride. ¶¶¶ Serious issues of risk of bias exist because of no information regarding allocation concealment or blinding of participants or personnel and incomplete outcome data. ### Serious issues of imprecision; 95% CI suggests large harm and large benefit. **** Serious issues of risk of bias exist because of no information about blinding of participants or personnel and unclear allocation concealment. †††† Serious issues of imprecision; 95% CI suggests a small benefit or a large benefit. ‡‡‡‡ Serious issues of risk of bias due to unclear allocation concealment, incomplete outcome assessment, and no information about blinding of participants and clinicians; in other cases, clinicians were not blinded at all. §§§§ Serious issues of imprecision; 95% CI suggests no benefit or a very large benefit. ¶¶¶¶ Serious inconsistency (I^2 = 87%; P = .0004). #### Studies informing the no-treatment group consist of placebo sealing and flossing instructions, flossing and 1,000 to 1,500 parts per million dentifrice, and mock treatment using water.[44-46,48]

eTable 4. Continued

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 6 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§,¶,#] TOTAL NO. OF PARTICIPANTS IN NETWORK: 232 TOTAL NO. OF UNPOOLED STUDIES: 7 RANDOMIZED CONTROLLED TRIALS[**,††,‡‡,§§,¶¶,##,***]	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)[†††]	INTERPRETATION OF FINDINGS
		Without Intervention (%)[‡‡‡]	With Intervention	Difference			
	2.11	50 per 100	106 per 100	56 per 100 more			
	(1.08 to 4.13)			(From 4 more to 157 more)			
		20 per 100	42 per 100	22 per 100 more			
				(From 2 more to 63 more)			
Resin Infiltration plus 5% NaF Varnish[*] (Indirect Evidence)		70 per 100	321 per 100	251.3 per 100 more	Very low (risk of bias[‡‡‡‡] and imprecision[§§§§])	0.89 (1/5)	May be superior
				(From 0 fewer to 1,392 more)			
	4.59	50 per 100	230 per 100	180 per 100 more			
	(1.00 to 20.88)			(From 0 fewer to 994 more)			
		20 per 100	92 per 100	72 per 100 more			
				(From 0 fewer to 398 more)			
Sealant[†,‡,¶,#] (Direct and Indirect Evidence)		70 per 100	169 per 100	99 per 100 more	Low (risk of bias[¶¶¶] and inconsistency[¶¶¶¶])	0.59 (2/5)	May be superior
				(From 18 more to 251 more)			
	2.41	50 per 100	121 per 100	71 per 100 more			
	(1.26 to 4.58)			(From 13 more to 179 more)			
		20 per 100	48 per 100	28 per 100 more			
				(From 5 more to 72 more)			
No Treatment[‡,§,¶,#,####]							
	Reference comparator	Not estimable	Not estimable	Reference comparator	Reference comparator	0.03 (5/5)	Reference comparator

eTable 5. Summary of findings: nonrestorative treatments for noncavitated lesions on facial or lingual surfaces.

TOTAL NO. OF UNPOOLED STUDIES: 5 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§,¶]	NO. OF PEOPLE AT FOLLOW-UP/ NO. OF LESIONS AT LONGEST FOLLOW-UP	STUDY ARM (DOSE, DURATION, OR FREQUENCY)	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE
				Without Intervention (%)[#]	With Intervention	Difference	
Agrawal and Pushpanjali[26]	257[‡‡]/374	1.23% acidulated phosphate fluoride gel (2 applications) and oral health education		70 per 100	173 per 100	103 per 100 more	Moderate (risk of bias[¶¶])
						(From 67 more to 149 more)	
			2.47	50 per 100	124 per 100	74 per 100 more	
			(1.95 to 3.13)			(From 48 more to 107 more)	
				20 per 100	49 per 100	29 per 100 more	
						(From 19 more to 43 more)	
		Oral health education					Reference comparator
			Reference comparator	Not estimable	Not estimable	Reference comparator	
Autio-Gold and Courts[33]	124[‡‡]/150	5% NaF varnish (2 applications)		70 per 100	161 per 100	91 per 100 more	Low (risk of bias[§§])
						(From 41 more to 164 more)	
			2.30	50 per 100	115 per 100	65 per 100 more	
			(1.58 to 3.34)			(From 29 more to 117 more)	
				20 per 100	46 per 100	26 per 100 more	
						(From 12 more to 47 more)	
		No treatment					Reference comparator
			Reference comparator	Not estimable	Not estimable	Reference comparator	

* Source: Agrawal and Pushpanjali[26] (12-month follow-up, mixed dentition): data for 12 and 18 months are presented in the Appendix (available online at the end of this article). † Source: Autio-Gold and Courts[33] (9-month follow-up, primary dentition). ‡ Source: Bailey and colleagues[52] (12-week follow-up, mixed dentition): data for 4- and 8-week follow-up are presented in the Appendix (available online at the end of this article). One or more adverse events were reported for 86% of participants (n = 39) but no information on the nature of them. There was also 1 or more reported gastrointestinal symptoms in the casein phosphopeptide–amorphous calcium phosphate cream arm. § Source: Turska-Szybka and colleagues[51] (12-month follow-up, primary dentition): the guideline authors could not calculate a relative risk or mean difference. Of the 41 children treated with resin infiltration and 5% NaF fluoride varnish, 75.6% (n = 31) showed no progression or continued activity of the treated spots at any examination. Of the 40 children treated with 5% NaF fluoride varnish, 32.5% (n = 13) of white-spot lesions showed no progression or continued activity (total number of lesions not reported). ¶ Source: Bonow and colleagues[50] (8-week follow-up, mixed dentition): the guideline authors could not calculate a relative risk or mean difference. Patients receiving 1.23% acidulated phosphate fluoride gel had a 65% increased probability for arresting or reversing in the facial or lingual surfaces compared with those in the placebo arm after 8 weeks of follow-up (adjusted relative risk, 1.65; 95% confidence interval, 0.69 to 3.96). # The percentages (20%, 50%, 70%) indicate illustrative baseline probabilities for the arrest or reversal of carious lesions. ** NaF: Sodium fluoride. †† Serious issues of risk of bias exist because of unclear allocation concealment and blinding of personnel or participants. ‡‡ The authors did not report the number of participants who had lesions only on facial or lingual surfaces. This is the number of people at follow-up. §§ Very serious issues of risk of bias exist because of unclear random sequence generation; blinding of participants, personnel, and outcome assessor; and allocation concealment. ¶¶ Serious issues of risk of bias exist because of unclear blinding of outcome assessor and serious imprecision.

eTable 5. Continued

TOTAL NO. OF UNPOOLED STUDIES: 5 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§,¶]	NO. OF PEOPLE AT FOLLOW-UP/ NO. OF LESIONS AT LONGEST FOLLOW-UP	STUDY ARM (DOSE, DURATION, OR FREQUENCY)	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE
				Without Intervention (%)[#]	With Intervention	Difference	
Bailey and Colleagues[52]	45/408	10% casein phosphopeptide–amorphous calcium phosphate cream (2 grams morning and evening) and 900 parts per million NaF[**] mouthrinse (supervised at each visit) and 1,000 ppm NaF dentifrice		70 per 100	86 per 100	16 per 100 more	Low (risk of bias[††])
						(From 4 more to 29 more)	
			1.23	50 per 100	62 per 100	12 per 100 more	
			(1.06 to 1.42)			(From 3 more to 21 more)	
				20 per 100	25 per 100	5 per 100 more	
						(From 1 more to 8 more)	
		Placebo cream (2 g morning and evening) and 900 ppm NaF mouthrinse (supervised at each visit) and 1,000 ppm NaF dentifrice					Reference comparator
			Reference comparator	Not estimable	Not estimable	Reference comparator	

eTable 6. Summary of findings: additional follow-up times for nonrestorative treatments for noncavitated lesions on facial or lingual surfaces.

TOTAL NO. OF UNPOOLED STUDIES: 5*,†,‡	PRIMARY, PERMANENT, OR MIXED TEETH	STUDY ARM	RELATIVE RISK (95% CONFIDENCE INTERVAL) AND CERTAINTY IN THE EVIDENCE
Agrawal and Pushpanjali[26]	Mixed	1.23% acidulated phosphate fluoride gel and oral health education (2 doses, baseline and 6 months) Oral health education	1.23% acidulated phosphate fluoride gel and oral health education versus oral health education 12 months: 2.47 (1.95 to 3.13); certainty: moderate (serious issues of risk of bias because of unclear allocation concealment and blinding of personnel or participants)
Autio-Gold and Courts[33]	Primary	5% NaF varnish (baseline and 4 months later, 2 total applications) No intervention	5% NaF varnish versus no intervention 9 months: 2.30 (1.58 to 3.34); certainty: low (very serious issues of risk of bias because of unclear random sequence generation; blinding of participants, personnel, and outcome assessor; and allocation concealment)
Bailey and Colleagues[52]	Mixed	10% casein phosphopeptide–amorphous calcium phosphate cream and 900 parts per million NaF mouthrinse and 1,000 ppm NaF dentifrice (2 grams morning and night for 12 weeks and mouthrinse supervised at each visit) Placebo cream and 900 ppm NaF mouthrinse and 1,000 ppm NaF dentifrice	10% casein phosphopeptide–amorphous calcium phosphate cream and 900 ppm mouthrinse versus 900 ppm mouthrinse 4 weeks: 1.28 (0.97 to 1.68); certainty: low (serious risk of bias because of unclear blinding of outcome assessor and serious imprecision) 8 weeks: 1.12 (0.93 to 1.36); certainty: low (serious risk of bias because of unclear blinding of outcome assessor and serious imprecision) 12 weeks: 1.23 (1.06 to 1.42); certainty: low (serious risk of bias because of unclear blinding of outcome assessor and serious imprecision)

* Source: Agrawal and Pushpanjali.[26] † Source: Autio-Gold and Courts.[33] ‡ Source: Bailey and colleagues.[52]

eTable 7. Summary of findings: nonrestorative treatments for the arrest or reversal of noncavitated lesions on any coronal tooth surface.

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 3 RANDOMIZED CONTROLLED TRIALS*,†,‡ TOTAL NO. OF PARTICIPANTS IN NETWORK: 628 TOTAL NO. OF STUDIES REPORTED NARRATIVELY (UNPOOLED): 4 RANDOMIZED CONTROLLED TRIALS§,¶,#,**	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)††	INTERPRETATION OF FINDINGS
		Without Intervention (%)‡‡	With Intervention	Difference			
10% Casein Phosphopeptide–Amorphous Calcium Phosphate Paste* (Direct Evidence)		70 per 100	72 per 100	2 per 100 more	Low (risk of bias and imprecision§§)	0.22 (3/4)	May be superior
				(From 7 fewer to 13 more)			
	1.03	50 per 100	52 per 100	2 per 100 more			
	(0.90 to 1.18)			(From 5 fewer to 9 more)			
		20 per 100	21 per 100	1 per 100 fewer			
				(From 2 fewer to 4 more)			
1.23% Acidulated Phosphate Fluoride Gel† (Direct Evidence)		70 per 100	158 per 100	88 per 100 more	Moderate (risk of bias¶¶)	0.89 (1/4)	Superior
				(From 70 more to 107 more)			
	2.25	50 per 100	113 per 100	63 per 100 more			
	(2.00 to 2.53)			(From 50 more to 77 more)			
		20 per 100	45 per 100	25 per 100 more			
				(From 20 more to 31 more)			

* Source: Sitthisettapong and colleagues[57] (12-month follow-up, primary dentition): additional follow-up: 6 months: 10% casein phosphopeptide–amorphous calcium phosphate versus no treatment: relative risk, 1.00 (95% confidence interval, 0.90 to 1.13). † Source: Agrawal and Pushpanjali[26] (12-month follow-up, mixed dentition). ‡ Source: Autio-Gold and Courts[33] (9-month follow-up, primary dentition). § Source: Duarte and colleagues[53] (dentition not reported): 85.4% of noncavitated lesions were arrested in the 0.05% sodium fluoride (NaF) mouthrinse group compared with 85.6% of arrested lesions in the 0.05% NaF mouthrinse and 0.12% chlorhexidine group after 28 days. ¶ Source: Heidmann and colleagues[55] (permanent dentition): in the 0.2% NaF mouth rinse group, 62.5% (n = 270) experienced no progression of noncavitated lesions compared with 68.5% (n = 292) in the placebo mouthrinse group. # Source: Hedayati-Hajikand and colleagues[54] (primary dentition): of 54 people in the probiotic tablet group, 11% (n = 5) of the enrolled patients experienced caries arrest compared with 7% (n = 4) of the 56 participants in the group that received placebo tablets after 1 year. ** Source: Honkala and colleagues[56] (mixed dentition): there was no distinction between cavitated and noncavitated lesions in the study. In the erythritol group, 30.5% (401/1,313) of surfaces showed a decrease in International Caries Detection and Assessment System score compared with 29.8% (456/1,531) in the group receiving sorbitol and 28.3% (449/1,584) in the group receiving xylitol after 3 years of follow-up. †† The lower the value, the higher the position in the ranking. ‡‡ The percentages (20%, 50%, 70%) indicate illustrative baseline probabilities for the arrest or reversal of carious lesions. §§ Serious issues of risk of bias exist because of incomplete outcome data. ¶¶ Serious issues of risk of bias exist because of unclear methods related to allocation concealment and blinding of participants and personnel. ## Very serious issues of risk of bias exist because of unclear methods related to random sequence generation, allocation concealment, and blinding of personnel and participants. *** The studies informing the no-treatment group consist of no treatment, oral health education, placebo paste with 1,000 parts per million fluoride toothpaste, and oral hygiene instructions.[26,33,57]

eTable 7. Continued

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 3 RANDOMIZED CONTROLLED TRIALS[*,†,‡] TOTAL NO. OF PARTICIPANTS IN NETWORK: 628 TOTAL NO. OF STUDIES REPORTED NARRATIVELY (UNPOOLED): 4 RANDOMIZED CONTROLLED TRIALS[§,¶,#,**]	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY IN THE EVIDENCE	P-SCORE (RANKING)[††]	INTERPRETATION OF FINDINGS
		Without Intervention (%)[‡‡]	With Intervention	Difference			
5% Sodium Fluoride Varnish[‡] (Direct Evidence)		70 per 100	151 per 100	81 per 100 more	Moderate (risk of bias[##])	0.78 (2/4)	Superior
				(From 56 more to 110 more)			
	2.15	50 per 100	108 per 100	58 per 100 more			
	(1.80 to 2.57)			(From 40 more to 79 more)			
		20 per 100	43 per 100	23 per 100 more			
				(From 16 more to 31 more)			
No Treatment[*,†,‡,*]**					Reference comparator	0.11 (4/4)	Reference comparator
	Reference comparator	Not estimable	Not estimable	Reference comparator			

eTable 8. Summary of findings: nonrestorative treatments for the arrest or reversal of noncavitated and cavitated lesions on root surfaces.

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 7 RANDOMIZED CONTROLLED TRIALS*,†,‡,§,¶,#,** TOTAL NO. OF PARTICIPANTS IN NETWORK: 834†† TOTAL NO. OF UNPOOLED STUDIES: 1 RANDOMIZED CONTROLLED TRIAL‡‡	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY OF THE EVIDENCE	P-SCORE (RANKING)§§	INTERPRETATION OF FINDINGS
		Without Intervention (%)¶¶	With Intervention	Difference			
1% Chlorhexidine plus 1% Thymol Varnish* (Direct Evidence)		70 per 100	117 per 100	47 per 100 more	Very low (risk of bias## and imprecision***)	0.44 (5/6)	May be superior
	1.67	50 per 100	84 per 100	(From 39 fewer to 372 more)			
	(0.44 to 6.31)			34 per 100 more			
		20 per 100	33 per 100	(From 28 fewer to 266 more)			
				13 per 100 more			
38% SDF† Solution **(Direct Evidence)**		70 per 100	134 per 100	(From 11 fewer to 106 more)	Very low (risk of bias††† and imprecision***)	0.49 (4/6)	May be superior
				64 per 100 more			
	1.99	50 per 100	96 per 100	(From 34 fewer to 411 more)			
	(0.52 to 6.87)			46 per 100 more			
		20 per 100	38 per 100	(From 24 fewer to 294 more)			

* Source: Baca and colleagues[59] (12-month follow-up): participants reported a bitter taste when the placebo varnish was used. † Source: Li and colleagues[63] (12-month follow-up): additional follow-ups: 24 months: 38% silver diamine fluoride (SDF) with potassium iodine versus no treatment: relative risk (RR), 2.87 (95% confidence interval [SDF], 1.44 to 5.74); 38% SDF with potassium iodide versus no treatment: RR, 2.99 (95% CI,1.50 to 5.95); 30 months: 38% SDF versus no treatment: RR, 2.00 (95% CI,1.22 to 3.28); 38% SDF with potassium iodide versus no treatment: RR, 2.06 (95% CI, 1.26 to 3.36). ‡ Source: Schaeken and colleagues[65] (12-month follow-up). § Source: Lynch and colleagues[64] (3-month follow-up). ¶ Source: Ekstrand and colleagues[62] (8-month follow-up). # Source: Baysan and colleagues[60] (6-month follow-up): additional follow-ups: 3 months: cavitated, 5,000 ppm versus no treatment: RR, 4.78 (95% CI, 0.60 to 38.20); noncavitated, 5,000 ppm versus no treatment: RR, 3.39 (95% CI, 1.94 to 5.92). ** Source: Ekstrand and colleagues[61] (8-month follow-up). †† We used the total number of participants at 12-month follow-up from Li and colleagues[63]; Schaeken and colleagues[65] did not report loss to follow-up. The number reported is the total number of participants randomly assigned to each group at baseline. In Ekstrand and colleagues,[61] we did not use data from the 1,450 ppm fluoride toothpaste and 5% sodium fluoride (NaF) varnish arm in the network because of the frequency of the 5% NaF varnish not being reported, which accounted for 76 of the 215 participants at baseline. The number reported is the total number of participants in the 5,000 ppm NaF toothpaste arm and control arm at follow-up. Investigators in other studies included in the network reported the total number of participants at follow-up. ‡‡ Source: Brailsford and colleagues[58]: The use of 1% difluorsilane varnish with 1% chlorhexidine and 1% thymol varnish 5 times in 10 months resulted in a 40% increase in caries arrestment (RR, 1.40; 95% CI, 0.97 to 2.00) compared with 1% difluorsilane applied at the same frequency at 1-year follow-up. §§ The lower the value, the higher the position in the ranking. ¶¶ The percentages (20%, 50%, 70%) indicate illustrative baseline probabilities for the arrest of reversal of carious lesions. ## Serious issues of risk of bias exist because of incomplete outcome data and because blinding of the outcomes assessor was unclear. *** Serious issues of imprecision; 95% CI suggests a large harm and a large benefit. ††† Serious issues of bias exist because of incomplete outcome data and unclear methods related to blinding of personnel. ‡‡‡ Serious issues of risk of bias exist because of unclear methods for all risk of bias domains. It is unclear whether patients were blinded and how many were lost to follow-up. §§§ Serious issues of risk of bias exist because of unclear and inadequate methods of random sequence generation and allocation concealment method. In addition, there is no information about blinding of the outcomes assessor, and outcome data are incomplete. Serious issues of inconsistency (I^2 = 88%; $P < .00001$). ¶¶¶ Studies informing the no-treatment group consist of 1,100 ppm dentifrice, soda water with 1,450 ppm dentifrice, 1,450 ppm dentifrice, placebo varnish, and nonfluoride dentifrice.[59,61,63-65]

eTable 8. Continued

TOTAL NO. OF STUDIES IN NETWORK (POOLED): 7 RANDOMIZED CONTROLLED TRIALS[*,†,‡,§,¶,#,**] TOTAL NO. OF PARTICIPANTS IN NETWORK: 834[††] TOTAL NO. OF UNPOOLED STUDIES: 1 RANDOMIZED CONTROLLED TRIAL[‡‡]	RELATIVE RISK (95% CONFIDENCE INTERVAL)	ANTICIPATED ABSOLUTE EFFECT (95% CONFIDENCE INTERVAL)			CERTAINTY OF THE EVIDENCE	P-SCORE (RANKING)[§§]	INTERPRETATION OF FINDINGS
		Without Intervention (%)[¶¶]	With Intervention	Difference			
				18 per 100 more			
38% SDF plus Potassium Iodide[†] Solution **(Direct Evidence)**		70 per 100	165 per 100	(From 10 fewer to 117 more)	Very low (risk of bias[†††] and imprecision[***])	0.61 (3/6)	May be superior
				95 per 100 more			
	2.36	50 per 100	118 per 100	(From 24 fewer to 519 more)			
	(0.66 to 8.42)			68 per 100 more			
		20 per 100	47 per 100	(From 17 fewer to 371 more)			
				27 per 100 more			
5% NaF Varnish[‡] **(Direct Evidence)**		70 per 100	207 per 100	(From 6.8 fewer to 148.4 more)	Very low (risk of bias[‡‡‡] and imprecision[***])	0.64 (2/6)	May be superior
				137 per 100 more			
	2.96	50 per 100	148 per 100	(From 51 fewer to 2,188 more)			
	(0.27 to 32.26)			98 per 100 more			
		20 per 100	59 per 100	(From 37 fewer to 1,563 more)			
				39 per 100 more			
5,000 Parts Per Million Fluoride (1.1% NaF) Toothpaste or Gel[§,¶,#,**] **(Direct Evidence)**		70 per 100	183 per 100	(From 15 fewer to 625 more)	Low (risk of bias and inconsistency[§§§])	0.69 (1/6)	May be superior
				113 per 100 more			
	2.62	50 per 100	131 per 100	(From 34 more to 254 more)			
	(1.49 to 4.63)			81 per 100 more			
		20 per 100	52 per 100	(From 25 more to 182 more)			
				32 per 100 more			
No Treatment[*,†,‡,§,¶,#,**,¶¶¶]				(From 10 more to 73 more)			
	Reference comparator	Not estimable	Not estimable	Reference comparator	Reference comparator	.1335 (6/6)	Reference comparator