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Screening, Referral, Behavioral Counseling, and Preventive Interventions for Oral Health in Children and Adolescents Ages 5 to 17 Years: A Systematic Review for the U.S. Preventive Services Task Force

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Structured Abstract

Background: Dental caries is common in children and adolescents 5 to 17 years of age. The U.S. Preventive Services Task Force (USPSTF) recommends that primary care clinicians prescribe oral fluoride supplementation in areas with fluoride deficient water and apply fluoride varnish to the primary teeth in children younger than 5 years, but has not addressed oral health screening and prevention in children and adolescents 5 to 17 years of age.

Purpose: To systematically update the evidence on primary care screening and prevention of dental caries in children and adolescents 5 to 17 years of age.

Data Sources: We searched the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews, and MEDLINE to October 3, 2022, and manually reviewed reference lists; with surveillance through July 21, 2023.

Study Selection: Studies on diagnostic accuracy of primary care screening instruments and oral examination; randomized controlled trials **(**RCTs) and non-randomized trials of screening and preventive interventions; cohort studies on risk of fluorosis with fluoride preventive interventions; and cohort studies of oral health screening in primary care.

Data Extraction: One investigator abstracted data and a second investigator checked data abstraction for accuracy. Two investigators independently assessed study quality using methods developed by the USPSTF.

Data Synthesis (Results): Twenty-three studies (reported in 27 publications; 19 RCTs, 3 non-randomized trials, and 1 observational study; total 15,026 participants) and three systematic reviews (with 54 trials; total 20,684 participants) were included in this update. No study compared screening versus no screening. For identification of untreated caries in children 5 to 12 years of age, one study (n=219) found visual screening by a registered nurse associated with sensitivity of 0.92 (95% confidence interval [CI] 0.84 to 0.97) and specificity of 0.993 (95% CI 0.96 to 0.998), and a 17-item questionnaire (n=305) associated with sensitivity of 0.69 (95% CI 0.60 to 0.77) and specificity of 0.88 (95% CI 0.83 to 0.93). No study trial evaluated the effectiveness of primary care oral health behavioral counseling versus no counseling or primary care referral to a dental health provider versus no referral. Fluoride supplements compared with placebo or no intervention were associated with decreased change from baseline to followup in the number of decayed, missing, or filled teeth (DMFT) or decayed, or filled teeth (DFT) increment at 1.5 to 3 years (six trials, N=1,395; mean difference -0.73, 95% CI -1.30 to -0.19) in low socioeconomic, nonfluoridated water, or high caries burden settings; though the only trial in which fluoride supplements were administered at home (rather than in supervised school settings) reported low adherence with no benefit (n=438, mean difference 0.13, 95% CI -0.38 to 0.64). Good-quality systematic reviews found fluoride gels associated with decreased caries in permanent teeth at outcomes closest to 3 years (DMFT/DFT prevented fraction 0.18, 95% CI, 0.09 to 0.27, based on four placebo-controlled trials [N=1,525]), fluoride varnish associated with decreased caries burden at 1 to 4.5 years (decayed, missing, or filled surfaces [DMFS] or decayed or filled surfaces [DFS] prevented fraction 0.43, 95% CI 0.30 to 0.57, based on 14 trials [N=3,419] and DMFT or DFT prevented fraction 0.44, 95% CI 0.11 to 0.76, based on five trials

[N=3,902], and resin-based sealants in children 5 to 10 years of age associated with decreased risk of carious first molars at 24 months (seven trials, N=1,322, odds ratio [OR] 0.12, 95% CI 0.08 to 0.19), 36 months (seven trials, N=1,410, OR 0.17, 95% CI 0.11 to 0.27) and 48 to 54 months (four trials, N=440, OR 0.21, 95% CI 0.16 to 0.28). One trial found silver diamine fluoride associated with fewer new active caries surfaces in deciduous dentition (mean 0.3 vs. 1.4, $p<0.001$) and first permanent molars (mean 0.4 vs. 1.1, $p<0.001$) and decreased likelihood of ≥1 new decayed or filled teeth (relative risk [RR] 0.52, 95% CI 0.40 to 0.70). One fair-quality trial (n=496) found no difference between xylitol versus no xylitol in DMFS increment and another fair-quality trial (n=432) found xylitol associated with decreased caries increment versus no xylitol but no difference versus placebo. Reporting of harms was very limited, although serious harms were not reported.

Limitations: Oral health preventive interventions were administered by dental professionals or in supervised school settings, with uncertain applicability to primary care administration; only English-language articles were included; sparse or no evidence on screening, referral, and some preventive interventions; most studies had methodological limitations; and few studies published after the year 2000.

Conclusions: Supervised administration of fluoride supplements in schools and administration of fluoride gels, varnish, and sealants in dental or school settings improved caries outcomes. Research is needed on the effectiveness of these oral health preventive interventions when administered at home or in primary care settings, and to determine the accuracy of primary care screening, and the benefits and harms of screening, as well as the effectiveness of primary care counseling, dental referral, and other oral health preventive interventions.

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Chapter 1. Introduction and Background

Purpose

Screening, referral, behavioral counseling, and preventive interventions for oral health in children age 5 years through 17 years is a new topic for the U.S. Preventive Services Task Force (USPSTF). However, the USPSTF previously addressed the related topics of counseling to prevent dental and periodontal disease (1996),[1] screening and prevention of dental caries in children younger than 5 years of age (2021),[2] and oral cancer screening (2013)[3]; a concurrent topic addresses screening, referral, behavioral counseling, and preventive interventions for oral health in adults.[4]

In 1996, the USPSTF issued several recommendations on counseling to prevent dental and periodontal disease (note: the grading system used for the 1996 recommendations differed from current USPSTF definitions and are defined below).[1] The USPSTF recommended, for children in communities with water fluoride concentrations below recommended levels, clinicians prescribe supplemental oral fluoride at doses based on age and the water fluoride concentration ("A" recommendation ["good evidence to support the recommendation that the condition be specifically considered in a periodic health examination"]). The USPSTF also recommended counseling patients (ages not specified) to visit a dental care provider on a regular basis, floss daily, brush their teeth daily with a fluoride-containing toothpaste, and appropriately use fluoride for caries prevention and chemotherapeutic mouth rinses for plaque prevention ("B" recommendation ["fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination"]). However, the USPSTF found that effectiveness of clinician counseling to change any of these behaviors had not been adequately evaluated ("C" recommendation ["insufficient evidence to recommend for or against the inclusion of the condition in a periodic health examination"]). Additionally, the USPSTF suggested that clinicians examine the oral cavity of patients (ages not specified) and be alert for obvious signs of oral disease (ungraded statement) ("C" [insufficient] recommendation in 1996; most recently, in 2013, the USPSTF issued an I [insufficient] statement on oral cancer screening).[3]

In 2004, the USPSTF issued recommendations on screening and prevention of dental caries in preschool age (<5 years) children who do not have access to school-based interventions and may lack access to oral health care except through a primary care provider;[5] this topic remains active and was last updated in 2021.[2] In 2006, the USPSTF inactivated the topic of counseling to prevent dental and periodontal disease in primary care populations (including school-age children 5 to 17 years of age), based on the lack of new evidence on the role of the primary care clinician in counseling for dental services to inform updated recommendations. In 2016, the USPSTF received a nomination on the topic of risks and benefits of dental x-rays for screening; oral health was selected as a topic for further refinement. Through the USPSTF topic refinement process, the scope was broadened to address screening, referral, behavioral counseling, and preventive interventions for various oral health conditions in children 5 to 17 years of age. Given current interest in primary care and oral health,[6-8] evidence of gaps in provision of oral health services in school-age children,[9] and potential new evidence to inform recommendations, the USPSTF commissioned a systematic review to address oral health in children 5 to 17 years of

age. For this topic, screening was defined as risk assessment or oral cavity examination; dental x-rays were excluded during topic refinement because of limited relevance to primary care. The new oral health topic focuses on dental caries, the most common oral health condition in children, and was scoped to not overlap with currently active related topics (dental caries in children from birth to age 5 years[10] and oral cancer screening[11]) and does not address school-based[12] or community-based[13] interventions for oral health. A concurrent systematic review was commissioned on screening and preventive services for oral health in adults.[4] This review will be used by the USPSTF to inform the development of new recommendations on screening and prevention in primary care settings for oral health in children 5 to 17 years of age.

Condition Background

Condition Definition

In 2000, the U.S. Surgeon General published the first report on Oral Health in America.[14] An Oral Health in America followup report from the National Institutes was published in 2021.[9] The 2000 report emphasized that, "oral health means much more than healthy teeth. It means being free of chronic oral-facial pain conditions, oral and pharyngeal (throat) cancers, oral soft tissue lesions, birth defects such as cleft lip and palate, and scores of other diseases and disorders that affect the oral, dental, and craniofacial tissues, collectively known as the craniofacial complex." Further, the report stated "the mouth is the center of vital tissues and functions that are critical to total health and well-being across the lifespan."[14] In children, dental caries is the most prevalent oral health condition[9] and is the focus of this review. Oral health conditions that are associated with symptoms (e.g., orofacial pain) or do not require screening (e.g., craniofacial anomalies) and treatment of existing oral health conditions or management of oral health conditions that may occur due to other treatments or medications are outside the scope of the USPSTF.

Prevalence and Burden of Disease/Illness

Dental caries can lead to pain, disability, and decreased wellbeing.[15-18] In addition, infections and tooth loss may result in problems with eating, speaking, smiling, and learning and negatively impact quality of life and social interactions.[19] Caries is common in children; based on NHANES 2011 to 2016 data,[20] the overall prevalence of dental caries in primary teeth in children ages 6 to 8 years was 52 percent; for permanent teeth, the prevalence of dental caries was 17 percent among children 6 to 11 years of age (when permanent teeth start to erupt) and 57 percent among those 12 to 19 years of age. According to the Global Burden of Disease Study, untreated dental caries is the most common health condition worldwide.[21] Among school-aged children, the prevalence of untreated dental caries increases with older age. In 2011 to 2014, the proportion of children with untreated dental caries in permanent teeth was 3.3 percent among those aged 6 to 8 years, 8.2 percent among those aged 9 to 11 years, and 26 percent among those aged 12 to 19 years.[9] Among those 12 to 19 years of age, the mean number of decayed, missing or filled surfaces (DMFS) of permanent teeth was approximately 4.2.

Etiology and Natural History

Dental caries is a multifactorial disease process that occurs when various strains of bacteria colonize the tooth surface and metabolize dietary carbohydrates (especially refined sugars) to produce lactic and other acids, resulting in demineralization of teeth.[22,23] Dental caries first manifests as white spot lesions, which are small areas of demineralization under the enamel surface. At this stage, the caries lesion is usually reversible, if appropriate preventive action is taken (e.g., change in dietary behaviors and/or application of fluoride varnish). If oral conditions do not improve, demineralization progresses and eventually results in irreversible cavities, with a loss of the normal tooth shape and contour. Continued progression of the caries process can lead to pulpitis and tooth loss, and can be associated with complications such as facial cellulitis and systemic infections.[23,24] Dental caries that occurs in permanent teeth is more consequential than that which occurs in deciduous (primary) teeth; on average, eruption of permanent teeth occurs by age 12 except for the second molar (11 to 13 years) and the third molar (17 to 21 years).[25] Data on the prevalence of periodontal disease in children and adolescents are limited. Based on a national survey in 1986 to 1987, gingivitis was observed in approximately 60 percent of children 14 to 17 years of age.[26] A study of 12 year old schoolchildren in Puerto Rico found that gingivitis was present in 80.4 percent of those examined.[27]

Risk Factors

Risk factors for dental caries in children and adolescents include inappropriate dietary practices, poor oral hygiene, not using fluoridated toothpaste, poor caregiver oral health behaviors (inappropriate dietary practices or poor oral hygiene such as lack of tooth brushing), and medications or substances that cause xerostomia; risk factors that may also impact oral health in adolescents include tobacco use, excessive alcohol use, methamphetamine use, and cannabis use.[28,29] As discussed earlier, among children and adolescents 5 to 17 years of age, older age is also associated with increased risk of dental caries.[9,30,31]

Rationale for Screening/Screening Strategies

As noted, oral health issues in children are common, are often untreated, and can lead to tooth loss or irreversible damage and other adverse health outcomes. Children may be asymptomatic and children or caregivers may be unaware of their condition in the early stages of the dental caries process. In addition, children may have inadequate access to dental services due to insurance status or other socioeconomic factors, or not utilize dental services for other reasons.[32,33] Estimates of the proportion of children greater than 5 years and adolescents that receive dental services vary. Based on the 2019 and 2020 National Health Information Survey, the percent of children who had a dental examination or cleaning in the past 12 months was 91 percent among children aged 5 to 11 years and 88 percent among children aged 12 to 17 years overall.[34] However, an analysis of data from the Household Component of the Medical Expenditure Panel Survey found that 49 to 72 percent of children 6 to 11 years of age and 42 to 69 percent of children 12 to 18 years of age had a dental visit in the last year.[35] In both analyses, the proportion that received dental care was lower for children from lower income households. For children who lack access to dental services, interventions and treatments that could prevent

and treat early dental caries could potentially be provided in primary care settings. Therefore, identifying and providing services to prevent oral health issues early in primary care settings could help prevent adverse health outcomes.[36-38]

Screening for oral health conditions and provision of interventions for oral health in primary care also provide an opportunity to potentially reduce disparities in detection and treatment of oral health conditions among socioeconomic and racial/ethnic groups (see subsequent sections on Disparities and Contextual Question 2).

Interventions/Treatment

Screening for oral health conditions includes risk assessment, visual/tactile examination, and imaging (dental x-rays)[39] to identify children with untreated dental caries or periodontal disease, or those at high risk for developing these conditions. Interventions to prevent development of caries focus on reducing the burden of bacteria, reducing the intake of refined sugars, and increasing the resistance of teeth to caries development.[22,40] Counseling interventions include those that address oral hygiene (e.g., brushing twice daily with fluoride toothpaste, flossing daily, or rinses [fluoride or antimicrobial]), diet, tobacco use, and alcohol use, as well as counseling to visit a dentist. Preventive interventions include oral or topical (e.g., varnish) fluoride, dental sealants, xylitol, and referral to a dentist.

Use of fluorides primarily focuses on promoting remineralization of the enamel. Fluoride exposure can be topical (fluoride dentifrices, rinses, gels, foams, varnishes) or systemic (dietary fluoride supplements).[22,40] Fluoridated water has topical as well as systemic effects. The main effect, however, is now believed to be topical. Fluoride is incorporated into the biofilm (dental plaque), saliva and tooth enamel and increases tooth resistance to acid decay, acts as a reservoir for remineralization of caries lesions, and inhibits cariogenic bacteria.[22,24] A potential harm of taking in too much systemic fluoride over a long period of time when the teeth are forming under the gums is dental fluorosis, a visible change in enamel opacity due to altered mineralization. The severity of enamel fluorosis depends on the dose, duration and timing of fluoride intake, and is most strongly associated with cumulative intake during enamel development; children are most susceptible between 15 to 30 months of age.[41,42] Mild fluorosis manifests as small opaque white streaks or specks in the tooth enamel.[43] Severe fluorosis results in discoloration and can result in pitted or rough enamel.[24] In 1999 to 2004, the prevalence of severe enamel fluorosis in the United States was estimated at less than 1 percent.[43,44]

Topical fluoride is typically applied as a varnish with a small brush or as a gel or foam (more commonly used in older, school-aged children).[45] Fluoride varnish application does not require specialized dental devices or equipment and can be applied quickly by both dental professionals and non-dental health professionals in a variety of settings; topical gels and foams typically require special suction to remove excess material. Systemic exposure to fluoride is lower following application of fluoride varnish compared to a gel or foam because smaller amounts are swallowed.[22,45-47] Fluoride varnish results in prolonged contact time between the fluoride and the tooth surface, which maintains a higher level of the calcium fluoride in the biofilm; later the released fluoride promotes remineralization. Fluoride varnish is typically available in the United States as 5 percent sodium fluoride (2.26% F). Fluoride varnish is cleared for marketing by the

U.S. Food and Drug Administration (FDA) as a cavity liner and tooth desensitizer; its use for prevention of caries is off-label.[48] Fluoride gel is typically available as sodium fluoride and acidulated phosphate fluoride.

Silver diamine fluoride (SDF) is a topical solution that is noninvasive, relatively inexpensive, and easy to apply.[49,50] Its mechanism of action is related to the antibacterial properties of silver, in addition to the effects of fluoride. The most common concentration is 38 percent, though it has been evaluated in formulations as low as 10 percent. SDF was cleared for marketing by the FDA in 2014 as a desensitizing agent in adults, similar to fluoride varnish 20 years earlier.[51] SDF has long been used outside the United States to arrest progression of existing caries lesions and avoid the need for restorative treatment. SDF works by the combined effects of silver and fluoride on promoting remineralization, as a short-term germicide, and inhibiting enzymes involved in collagen degradation, all of which result in an arrest of the carious process[49,52]; SDF is also being evaluated for preventing future caries.[53] A potential disadvantage of SDF is cosmetic concerns due to the permanent dark discoloration of active carious lesions by the silver component; however, SDF will not discolor healthy enamel, and carious lesions themselves may be discolored. Based on its potential as a caries treatment, SDF has been granted "breakthrough therapy" designation by the FDA, providing the opportunity for expedited approval for this indication, and a number of clinical trials of SDF for treating or preventing caries are in progress.

Xylitol is a naturally-occurring sugar that cannot be metabolized by the oral microflora and thus has the potential to reduce levels of caries-forming mutans streptococci in the plaque and saliva.[54] Xylitol can be administered topically (e.g., wipes) or via gum, lozenges, or snack foods. FDA allows foods (including chewing gums) that contain xylitol to make the following statement: "Xylitol may reduce the risk of tooth decay.[55]" Other topical antimicrobials such as chlorhexidine varnish or gel and povidone-iodine rinses are not commonly used in the United States. Neither chlorhexidine nor povidone iodine has been approved by FDA for caries reduction or prevention.[56]

Dental sealants are thin coatings applied to the chewing and selected other surfaces of the premolars and molars that form a protective barrier and can prevent cavities (tooth decay) over a prolonged period of time. A variety of sealant materials are available, though the main materials are resins/composites and glass ionomers. Following application, sealants can be activated (cured) using light or chemicals resulting in polymerization of the sealant material and hardening on the tooth surface (some sealants are autopolymerized [not requiring light or chemicals]). Resin-based sealants are classified into four generations, based on the method of polymerizations. First generation sealants utilized ultraviolet light for polymerization and are no longer used; second generation sealants are auto-polymerizing or chemically cured; third generation sealants are activated using visible light; and fourth generation sealants contain fluoride-releasing particles.[57] Glass ionomer sealants contain fluoride and can be classified as low or high viscosity; high viscosity sealants may have better retention on the tooth. Dental sealants are typically applied by dental health professionals in their office or in community settings such as schools.[58] Other interventions typically performed by dental health professionals to prevent dental caries or periodontal disease or to treat disease identified on screening which are considered beyond the scope of primary care practice include teeth cleaning, plaque removal,

and treatments for caries (fillings, crowns, root canals, tooth extractions) and periodontal disease (surgery and grafts).

Potential barriers to provision of oral health services in primary care settings are unfamiliarity with interventions, need for additional training or equipment (e.g., fluoride varnish, dental sealants, or silver diamine fluoride), and non-reimbursement; there are additional barriers to dental referrals from primary care.[59] However, some data in non-adult populations suggest that increased provision of an oral health intervention (fluoride varnish) in young children (less than 5 years of age) primary care settings is feasible.[60,61] For some oral health preventive interventions, state laws or regulations restrict administration to certain dental professionals (e.g., dental sealants can be placed by dentists, dental hygienists, and dental assistants [in certain states]), though such regulations do not apply to medical professionals.

Current Clinical Practice/Recommendations of Other Groups

The 2000 U.S. Surgeon General's report, *Oral Health in America,*[14] and a 2021 followup report from the National Institutes of Health,[9] highlight the importance of integrating oral health into primary care medical settings, primarily focusing on counseling, coordination, and referral. Reports from the Institute of Medicine in 2011 (*Advancing Oral Health in America*,[62] and *Improving Access to Oral Health Care for Vulnerable and Underserved Populations*[63]) and from the Health Resources and Services Administration in 2014 (*Integration of Oral Health and Primary Care Practice*[64]), also emphasized the importance of integrating oral health services in primary care medicine. A U.S. study aimed at improving provision of dental fluoride varnish application in a primary care pediatric practice found that, after implementing a 2 hour training, automatic reminders in electronic health records and automatic fluoride orders for the recommended age groups, fluoride application increased from 14 to 55 percent without impacting patient office flow.[60]

The American Dental Association (ADA) and American Academy of Pediatric Dentistry (AAPD) have issued a number of guidelines on oral health (e.g., sealants, caries, fluoride, prevention of periodontitis) aimed at dental professionals.[65,66] The American Academy of Family Physicians (AAFP) recommends that primary care physicians prescribe oral fluoride supplementation starting at age 6 months for children whose water supply is deficient in fluoride, and provide dietary fluoride supplements for children ages 6 months through 16 years in areas where drinking water levels are suboptimal.[67] The American Academy of Pediatrics (AAP) recommends that pediatricians apply fluoride varnish applied every 3 to 6 months starting at tooth emergence and provide dietary fluoride supplements if the drinking water supply is not fluoridated.[68] Guidelines from AAFP, ADA, AAPD, AAP, and the Community Services Task Force are summarized in **Table 1**. Other groups, such as Smiles for Life and Qualis Health, have also developed educational resources and recommendations on provision of oral health services in primary medical care settings.[68,69] In general, the guidelines recommend counseling and use of topical fluoride, dietary fluoride supplementation in settings with inadequate water fluoridation, and dental sealants as preventive measures in children and adolescents. In some guidelines, the upper age ranges for the recommended interventions are unspecified or unclear.

Disparities

Oral health disparities in children and adolescents have been described with regard to race/ethnicity (Black, Hispanic, American Indian, and Alaska Native persons are disproportionately impacted), socioeconomic status,[70] insurance status, health literacy, immigration status, and educational level.[20,71] Populations with increased prevalence of caries include people with disabilities, individuals living in rural and urban underserved areas, persons without insurance, persons who are publicly insured, and persons experiencing homelessness.[63] In 2011 to 2016, the prevalence of untreated dental caries among children 6 to 11 years of age was approximately 8.1 percent in persons living at <100% of the federal poverty threshold and 3.5 percent among those at ≥200% of the federal poverty threshold[20]; among those 12 to 19 years of age, corresponding rates were 23 percent and 11 percent. Stratified by race/ethnicity, the prevalence of untreated dental caries was approximately 7.5 percent among Mexican American children 6 to 11 years of age, 7 percent among non-Hispanic Black children, and 4.3 percent among non-Hispanic White children; among those 12 to 19 years of age corresponding rates were 21 percent, 20 percent, and 16 percent. (Additional details on oral health disparities are discussed in Contextual Question 2.)

Chapter 2. Methods

Key Questions and Analytic Framework

Using the methods developed by the USPSTF,[72] the USPSTF and the Agency for Healthcare Research and Quality (AHRQ) determined the scope and key questions for this review. Investigators created an analytic framework with the key questions and the patient populations, interventions, and outcomes reviewed for both screening (**Figure 1**) and prevention (**Figure 2**).

Screening Key Questions

1. How effective is screening for oral health performed by a primary care clinician in preventing negative oral health outcomes?
2. How accurate is screening for oral health performed by a primary care clinician in identifying children and adolescents who:
   a. Have oral health issues?
   b. Are at increased risk of future oral health issues?
3. What are the harms of screening for oral health performed by a primary care clinician?

Prevention Key Questions

1. How accurate is screening for oral health performed by a primary care clinician in identifying children and adolescents who are at increased risk of future oral health issues?*
2. How effective is oral health behavioral counseling provided by a primary care clinician in preventing oral health issues?
3. How effective is referral by a primary care clinician to a dental health care provider in preventing oral health issues?
4. How effective are preventive interventions in preventing oral health issues?
5. What are the harms of specific interventions (behavioral counseling, referral, and preventive interventions) to prevent oral health issues?

*This is the same as Key Question 2b from the previous Analytic Framework.

Contextual Questions

Three Contextual Question were also requested by the USPSTF to help inform the report. Contextual Questions are not reviewed using systematic review methodology.

1. a. What is the association between presence or severity of dental caries of deciduous or permanent teeth and pain, quality of life, function, and tooth loss?
   b. What is the association between presence or burden of dental caries of deciduous teeth and subsequent presence or severity of dental caries of permanent teeth?

2. What factors (e.g., race/ethnicity, age, socioeconomic status, cultural factors, educational attainment, or health literacy) are associated with oral health care disparities in children and adolescents?
3. What is the effectiveness of primary care interventions to reduce oral health care disparities in children and adolescents?

Search Strategies

We searched the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews, and Ovid MEDLINE from database inception through October 3, 2022 for relevant studies and systematic reviews. Search strategies are available in **Appendix A1**. We also reviewed reference lists of relevant articles. Ongoing surveillance was conducted to identify major studies published since October 3, 2022 that could affect the conclusions or understanding of the evidence and the related USPSTF recommendation. The last surveillance was conducted on July 21, 2023 and identified no studies affecting review conclusions.

Study Selection

At least two reviewers independently evaluated each study to determine inclusion eligibility. We selected studies on the basis of inclusion and exclusion criteria developed for each key question (**Appendix A2**). Disagreements were resolved by consensus. The selection of literature is summarized in the literature flow diagram (**Appendix A3**). **Appendix A4** lists included studies, and **Appendix A5** lists excluded studies with reasons for exclusion.

This review addresses screening, risk assessment, and preventive interventions for oral health in children 5 to 17 years of age. Separate Analytic Frameworks address *screening* for oral health conditions and *prevention* of oral health conditions, to more clearly distinguish treatment of children with existing dental caries identified by screening (screening Analytic Framework) from treatment of those without dental caries to prevent the development of future caries (prevention Analytic Framework).

For both Analytic Frameworks, the population was asymptomatic children and adolescents 5 to 17 years of age, including pregnant persons. Groups of interest were defined by age (<13 vs. ≥13 years, based on the average age at which all permanent teeth have erupted, with the exception of the third molars), sex, gender, socioeconomic status, race/ethnicity, educational attainment, and health literacy. Studies that selected children and adolescents based on presence of caries were ineligible; however, given the very high prevalence of caries in U.S. children and adolescents, we did not exclude studies of patients based on high baseline mean caries prevalence, if they were not required to have caries to be enrolled. Screening interventions were oral examination or clinical assessment by a primary care provider, or risk assessment by a primary care provider for dental caries using a standardized risk assessment instrument. Preventive interventions were behavioral counseling on oral health, preventive medications (topical fluoride [varnish, foam, or gel], silver diamine fluoride, dental sealants, or xylitol), or referral of persons deemed at high risk for oral disease by a primary care provider to a dental professional. Comparisons were against placebo or no screening/treatment/referral. Dental x-rays were not addressed because

they are not typically obtained in primary care settings or ordered by primary care clinicians. The most commonly reported outcomes were presence of and severity of caries (likelihood of developing caries [dichotomous outcome] or caries burden [continuous outcome, often measured based on the number of decayed, missing, or filled teeth [DMFT index] or surfaces [DMFS index]), morbidity, quality of life, functional status, and harms of screening and treatment. The preventive interventions selected for review were assessed as potentially primary care feasible (defined as not requiring extensive training to administer); studies of such interventions were considered potentially primary care applicable even if the intervention was administered in a dental care or school setting or by a dental health professional. Randomized trials were included for screening and preventive interventions; we also included cohort studies of screening and large cohort studies for dental fluorosis and studies on diagnostic accuracy of oral examination/clinical assessment and risk assessment instruments. In accordance with USPSTF procedures,[72] poor-quality studies were excluded unless higher quality evidence was unavailable or very limited.

Data Abstraction and Quality Rating

For studies meeting inclusion criteria, we created data abstraction forms to summarize characteristics of study populations, interventions (including the specific drug, formulation or material used; dose; frequency; duration; and professional background or training of persons administering the intervention), comparators, outcomes study designs, settings (including clinical setting, geographic status, and fluoridation status, if available), and methods. One investigator conducted data abstraction, which was reviewed for completeness and accuracy by another team member.

Predefined criteria were used to assess the quality of individual controlled trials, systematic reviews, and observational studies by using criteria developed by the USPSTF; studies were rated as "good," "fair," or "poor" per USPSTF criteria, depending on the seriousness of the methodological shortcomings (**Appendix A6**).[72] For each study, quality assessment was performed by two team members. Disagreements were resolved by consensus.

Data Synthesis

Meta-analyses of oral health preventive interventions from high quality systematic review (fluoride gels, fluoride varnish, and dental sealants) were utilized when available and supplemented by subsequently published trials. For fluoride supplements and xylitol, for which there was no high quality systematic review, random effects meta-analysis using the profile likelihood model was performed to summarize effects on caries burden. The primary measure of caries burden was the DMFT index, evaluated as a continuous outcome; if data on the DMFT index were not available, the DMFS index was utilized instead. Because the number of missing teeth is low in this age group and missing teeth may not be due to caries, data for decayed or filled teeth (DFT) or surfaces (DFS) is similar to DMFT or DMFTS and was used if DMFT or DMFS was not reported. Meta-analyses focused on caries burden in permanent teeth based on higher consequence than caries burden in deciduous teeth. Analysis was based on mean difference in change from baseline caries index to followup (caries increment) when available;

otherwise, the mean difference in follow-up values was used. Adjusted differences were utilized when reported. Data for dentin caries (e.g., graded D_3 or greater) were used if available; otherwise data for any (enamel or dentin) caries were used. Arms for comparable interventions within the same study were combined in the primary analysis, so each study was represented once in a meta-analysis, to address correlation among the multiple interventions within the same study and avoid overweighting. For cluster randomized trials, treatment differences that accounted for the intracluster correlation were utilized, if reported. Otherwise, clustering was addressed by calculating the effective sample size using the assumed intracluster correlation before combining with individually randomized trials, resulting in smaller "effective" sample sizes for cluster randomized trials in the meta-analyses than the number of patients actually evaluated. In the primary analysis, an intracluster correlation of 0.02 was assumed, based on the values reported in two trials of fluoride varnish for young children.[73,74] Additionally, a sensitivity analysis was conducted by utilizing an intracluster correlation of 0.045 reported in another trial of fluoride varnish for young children[75]; results of this sensitivity analysis were similar to the primary analysis and are not described further.

Prespecified study-level subgroup analyses were conducted on the following factors, when data were sufficient: control type (placebo or no treatment); setting (school or home); duration of follow-up (<3 years or >3 years); geographic region (Europe/Canada vs. other); and baseline caries burden (high vs. low). Although stratification of trials based on age greater or less than 13 years was planned, there were very few trials of adolescents older than 13 years; therefore, trials were stratified by age greater or less than 10 years. For xylitol, there were only two fair-quality trials; therefore, poor-quality trials were also included in the meta-analysis, with an analysis stratified according to quality. Information on water fluoridation level and provision of oral health education was too limited to conduct subgroup analyses on these factors.

For all meta-analyses, statistical heterogeneity among studies was assessed using the Cochran Q-test and I^2 statistic.[76] All meta-analyses were conducted using Stata/SE 16.1 (StataCorp, College Station, TX). All significance testing was 2-tailed; *P* values of 0.05 or less were considered statistically significant for treatment effects or effect modification; and 0.10 or less, for test of heterogeneity among studies.[77] Assessment for potential small study effects using funnel plots and the Egger test was planned when there were at least 10 studies in a meta-analysis; however, the meta-analyses had fewer than 10 studies,[78] so these were not performed.

For all Key Questions, the overall quality of evidence was determined using the approach described in the USPSTF Procedure Manual.[72] Evidence was rated "good", "fair", or "poor" based on study quality, consistency of results between studies, precision of estimates, study limitations, risk of reporting bias, and applicability.[72]

USPSTF and AHRQ Involvement

The authors worked with USPSTF members at key points throughout the review process to develop and refine the analytic framework and key questions and to resolve issues around scope for the final evidence synthesis.

AHRQ staff provided oversight for the project, coordinated the systematic review, reviewed the draft report, and assisted in an external review of the draft evidence synthesis.

Expert Review and Public Comment

We obtained input to inform the draft work plan from Key Informants to identify important subpopulations and inform the development of the scope and Key Questions. In addition, the draft Research Plan was posted on the USPSTF website for public comment from March 18, 2021, to April 14, 2021. In response, the USPSTF revised the inclusion criteria to clarify that screening is performed by a primary care provider and that preventive interventions are administered by a primary care provider or are feasible to be administered by a primary care provider. The USPSTF made no other changes.

The draft report was reviewed by content experts and Federal collaborative partners (**Appendix A7**), and minor clarifications were made to the report. It was also posted for public comment from May 23, 2023 to June 20, 2023; no public comments were received.

Chapter 3. Results

A total of 8,677 references from electronic database searches and manual searches of recently published studies were reviewed and 531 full-text papers were evaluated for inclusion. Across all key questions, 3 systematic reviews[79-81] (total 20,684 participants; of 54 trials [53 publications])[82-134] and 23 additional studies (in 27 publications)[135-161]; total 15,026 participants) were included (**Appendix A3**). One study accessed diagnostic accuracy of screening[135]; the systematic reviews[79-81] and other 22 studies (19 RCTs[136-154] and three non-randomized trials[155-157]) addressed preventive interventions. Included studies and quality ratings are described in **Appendix B**.

Screening Key Questions

Key Question 1. How Effective Is Screening for Oral Health Performed by a Primary Care Clinician in Preventing Negative Oral Health Outcomes?

No study evaluated the effectiveness of screening versus no screening on oral health outcomes.

Key Question 2a. How Accurate Is Screening for Oral Health Performed by a Primary Care Clinician in Identifying Children and Adolescents Who Have Oral Health Issues?

Summary

- For identification of untreated caries in children 5 to 12 years of age, one study found visual screening by a registered nurse (n=219) associated with sensitivity of 0.92 (95% confidence interval [CI] 0.84 to 0.97) and specificity of 0.993 (95% CI 0.96 to 0.9998) and a 17-item questionnaire (n=305) associated with sensitivity of 0.69 (95% CI 0.60 to 0.77) and specificity of 0.88 (95% CI 0.83 to 0.93).
- No study evaluated the diagnostic accuracy of screening for identifying children and adolescents at increased risk for future oral health issues.

Evidence

Evidence on the diagnostic accuracy of primary care screening in children and adolescents 5 to 17 years of age was very limited. One study assessed the diagnostic accuracy of screening by a registered nurse for untreated dental caries in children 5 to 12 years of age with high caries burden in a rural setting using a visual screening algorithm or a 17-item questionnaire completed by children's parents or guardians (**Appendix B Table 1**).[135] The reference standard was a full (visual and tactile) examination by a dentist. Nurses received 5 hours of training in addition to written material on the screening procedure and diagnostic criteria. The visual screening

algorithm was based on an assessment of the 4 quadrants of the mouth for decayed or restored teeth and associated with a sensitivity of 0.92 (95% CI 0.84 to 0.97) and specificity of 0.993 (95% CI 0.96 to 0.9998) for untreated caries (n=219, prevalence 35.2%) and sensitivity of 0.95 (95% CI 0.91 to 0.98) and specificity of 0.986 (95% CI 0.95 to 0.998) for treated or untreated carious lesions (n=323, prevalence 55.7%). The questionnaire included 17 items on conditions in the child's mouth, demographic characteristics, and socioeconomic status and was associated with a sensitivity of 0.69 (95% CI 0.60 to 0.77) and specificity of 0.88 (95% CI 0.83 to 0.93) for untreated caries (n=305, prevalence 40.9%). The study was rated fair-quality; methodological limitations include unclear blinding of the reference standard to screening results and unclear use of pre-defined thresholds for the screening questionnaire; in addition, diagnostic accuracy estimates were based on smaller numbers of participants than enrolled, for unclear reasons, and the study did not provide detailed questionnaire items (**Appendix B Table 2**).

Key Question 2b. How Accurate Is Screening for Oral Health Performed by a Primary Care Clinician in Identifying Children and Adolescents Who Are at Increased Risk for Future Oral Health Issues?

No study evaluated the diagnostic accuracy of primary care screening for identifying children and adolescents 5 to 17 years of age at risk for future oral health issues.

Key Question 3. What Are the Harms of Screening for Oral Health Performed by a Primary Care Clinician?

No study evaluated harms of primary care screening versus no screening.

Prevention Key Questions

Key Question 1. How Accurate Is Screening Performed by a Primary Care Clinician in Identifying Children and Adolescents Who Are at Increased Risk of Future Oral Health Issues?

As described above (prevention Key Question 2b), no study evaluated the accuracy of primary care screening for identifying children at increased risk of future oral health issues.

Key Question 2. How Effective Is Oral Health Behavioral Counseling Provided by a Primary Care Clinician in Preventing Oral Health Issues?

No study examined the effect of oral health behavioral counseling provided by a primary care clinician on oral health outcomes. While numerous systematic reviews examined oral health counseling or education, the interventions were either provided by dental professionals,[162] were school-based,[163,164] were combined with other interventions (such as supervised tooth brushing), were not feasible for a primary care setting (included tests or procedures not utilized in primary care), or reported intermediate outcomes (such as effects on beliefs about oral health and behaviors).

Key Question 3. How Effective Is Referral by Aa Primary Care Clinician to a Dental Health Care Provider in Preventing Oral Health Issues?

No study evaluated the effect of referral versus no referral to a dental care provider on oral health outcomes.

Key Question 4. How Effective Are Preventive Interventions in Preventing Oral Health Issues?

Summary

Supplements

- Fluoride supplements were associated with decreased caries increment in permanent teeth at 1.5 to 3 years based on the DMFT or DFT (six trials, effective N=1,395; mean difference -0.73, 95% CI -1.30 to -0.19) in low socioeconomic, nonfluoridated water, or high caries burden settings, though statistical heterogeneity was substantial (I^2=80%) and the only trial in which fluoride supplements were self-administered at home (rather than supervised school administration) reported low adherence and no benefit (n=438, mean difference 0.13, 95% CI -0.38 to 0.64).
- One other trial found fluoride supplements associated with decreased caries increment in permanent teeth at 6 years based on the DMFS (n=438, mean difference -2.07, 95% CI -3.16 to -0.97).

Fluoride Gel

- A systematic review (26 trials) found application of topical fluoride gels associated with decreased caries burden in permanent teeth at outcomes closest to 3 years (DMFT/DFT prevented fraction based on all trials 0.32, 95% CI 0.19 to 0.46; I^2=91% [10 trials, N=3,198]; based on four placebo-controlled trials [N=1,525], prevented fraction 0.18, 95% CI, 0.09 to 0.27; I^2=6%). One subsequent trial reported results consistent with the systematic review.

Fluoride Varnish

- A systematic review found fluoride varnish administered by dental professionals associated with decreased caries burden at 1 to 4.5 years based on the DMFS or DFS (14 trials, N=3,419, prevented fraction 0.43, 95% CI 0.30 to 0.57; I^2=75.2%) or DMFT or DFT (five trials, N=3,902, prevented fraction 0.44, 95% CI 0.11 to 0.76, I^2=86%), and reduced risk of developing one or more caries that was not statistically significant (five trials, N=3,253; RR 0.75, 95% CI 0.53 to 1.05; I^2=89.2%). One subsequent trial (n=5,397) reported results consistent with the systematic review.

Sealants

- A systematic review found resin-based sealants administered by dental professionals in children 5 to 10 years of age associated with decreased risk of carious first molars at 24 months (seven trials, N=1,322, odds ratio [OR] 0.12, 95% CI 0.08 to 0.19), 36 months (7 trials, N=1,410 children , OR 0.17, 95% CI 0.11 to 0.27, I^2=90%) and 48 to 54 months (4 trials, N=440 children, OR 0.21, 95% CI 0.16 to 0.28, I^2=45%). At 24 months, the absolute risk difference ranged from 11 percent to 59 percent. Evidence at longer-term (5 to 9 years) followup was limited but also indicated decreased risk (ORs ranged from 0.31 to 0.45), based on one trial at each time point.
- A systematic review (two trials) and one subsequent trial found inconsistent effects of glass ionomer sealants versus no sealants on caries outcomes.

Silver Diamine Fluoride

- One trial (n=452) found SDF administered by dental professionals associated with fewer new surfaces with active caries in the deciduous dentition (mean 0.3 vs. 1.4, p<0.001) and first permanent molars (mean 0.4 vs. 1.1, p<0.001), and decreased likelihood of ≥1 new decayed or filled teeth (26.1% vs. 49.7%, relative risk [RR] 0.52, 95% CI 0.40 to 0.70) in a low fluoridation, high baseline caries burden setting.

Xylitol

- One fair-quality trial (n=496) in a low caries burden setting found no difference between xylitol versus no xylitol at 4 years in D_3MFS increment (mean 2.75 for xylitol for 1 year vs. 3.02 for 2 years vs. 2.74 for no xylitol, p>0.05) or likelihood of D_3MFS >0. Another fair-quality trial (n=432) in a high baseline caries burden setting found no difference between xylitol versus placebo in DMFS increment at 3 years (mean 8.1 vs. 8.3, p>0.05), but decreased DMFS increment versus no xylitol (mean increment 8.1 vs. 12.4, p<0.05). Xylitol was administered under supervision at school in both trials.
- Eight other trials (effective N=1,646) found xylitol associated with reduced DMFS increment versus no xylitol (mean difference -2.38, 95% CI -3.66 to -1.15), but had serious methodological limitations and were rated poor-quality.

Evidence

Supplements

Seven trials (reported in eight publications) evaluated dietary fluoride supplements versus placebo or no fluoride supplement in children 5 years of age or older (**Appendix B Table 3**).[136-

[142,158] The number of participants in the trials ranged from 116 to 1,034 (total N=3,382). Three trials were conducted in the United States, three trials in the United Kingdom, and one trial in Taiwan. All trials recruited children from schools and were published prior to 1990 except for one,[140] which was published in 2013. Four trials were conducted in communities without water fluoridation.[136,138,139] The other three trials did not report water fluoridation status; of these, two trials[137,142] were conducted in low socioeconomic status settings and the third[140] focused on children with disabilities. The mean age of participants was 10 years in one trial and 12.5 years in one trial; in the other trials, the mean age was less than 10 years (range 5.3 to 9.2 years). At baseline, caries prevalence ranged from DMFT or DFT of 1.19 to 4.62, DMFS of 1.07 to 8.58, or dmfs of 3.32 to 3.66 in studies that provided this information. In one trial,[136] 100 percent of participants were White; otherwise, race or ethnicity was not reported. In three trials, the proportion of participants who were women ranged from 35 percent to 59 percent; gender and sex were otherwise unreported. Fluoride supplements were administered daily as acidulated phosphate fluoride or sodium fluoride tablets. In one trial of older (mean age 12.5 years) children,[137] fluoride supplements were taken at home; in all other trials fluoride supplements were administered at school under supervision. The duration of followup ranged from 1.5 to 6 years.

All trials had unclear randomization and allocation concealment methods and were rated fair-quality (**Appendix B Table 4**). Other methodological limitations included open-label design (trials of fluoride versus no fluoride) and high attrition. Two trials were cluster randomized but had no adjustment for clustering.[140,141]

Fluoride supplements were associated with a decreased caries increment compared with placebo or supplement in permanent teeth at 1.5 to 3 years, based on the DMFT or DFT (6 trials, effective N=1,395; mean difference -0.73, 95% CI -1.30 to -0.19; **Figure 3**); however, statistical heterogeneity was substantial (I^2=80%).[136-142,158] Results were similar when one trial[140] that focused on children with disabilities was excluded (five trials, effective N=1,270; mean difference -0.75, 95% CI -1.47 to -0.09, I^2=84%). This trial was also published much more recently (2013) than the other trials (published in or before 1988), but reported an estimate for reduction in DMFT increment (one trial, n=125, mean difference -0.63, 95% CI -1.27 to 0.01) that was very similar to the older trials. In a stratified analysis (**Table 2**), fluoride supplements were not associated with reduced DMFT/DFT increment in one trial[137] in which fluoride was administered at home (n=178, mean difference 0.13, 95% CI -0.38 to 0.64), whereas all trials in which fluoride supplement were administered at school reported reduced DMFT/DFT increment (five trials, effective N=1,217; range in mean differences -0.38 to -1.64, pooled mean difference -0.88, 95% CI -1.43 to -0.40; I^2=74%; p for interaction by administration setting=0.15; **Figure 4**). The trial in which fluoride supplements were administered at home also enrolled the oldest children (mean age 12.5 years, compared with 5.3 to 10 years in the other trials) and reported low adherence, with 15 percent of children randomized to fluoride supplements obtaining scheduled refills during the study. The reduction in DMFT/DFT increment was larger in trials that used a placebo control (four trials, effective N=855; mean difference -0.97, 95% CI -1.69 to -0.32, I^2=79%)[136,138-140,142,158] than those that used a no fluoride supplement control (two trials, effective N=540, mean difference -0.32, 95% CI -1.20 to 0.67, I^2=85%; p for interaction=0.24; **Figure 5**),[137,141] and in trials with longer (≥3 years) duration of followup (three trials, effective N=826; mean difference -1.15, 95% CI -1.97 to -0.48, I^2=81%)[136,141,142] versus shorter (<3 years)

followup (3 trials, effective N=574; mean difference -0.26, 95% CI -0.77 to 0.20, I^2=48%; p for interaction=0.09; **Figure 6**).[137,138,140] However, there was no statistically significant interaction for any of these factors, though stratified analyses were limited by small numbers of trials. There was no difference in estimates when trials were stratified according to mean age 10 years or older (two trials, N=540; mean difference -0.68, 95% CI -2.87 to 1.38, I^2=92%)[136,137] or less than 10 years (four trials, effective N=855, mean difference -0.77, 95% CI -1.30 to -0.26, I^2=73%; p for interaction=0.85).[138,140-142]

One trial reported caries burden based on the number of affected tooth surfaces and was not pooled with the others, which reported caries burden based on number of affected teeth. It found fluoride supplements associated with reduced DMFS increment (n=438, mean difference -2.07, 95% CI -3.16 to -0.97).[139]

Fluoride Gel

One systematic review[79] and one subsequent trial[143] (not included in the systematic review) evaluated fluoride gels versus placebo or no gel in children 5 years of age or older.

The systematic review (searches conducted through November 2014) was rated good-quality (**Appendix B Table 5**) and included 26 randomized or quasi-randomized trials[82-106] (in 25 publications; one publication was considered two studies[98]) of fluoride gels versus placebo or no treatment in children 5 years of age or older. Two other trials in the review evaluated children under 5 years of age and are not discussed further.[165,166] Across the trials, sample sizes ranged from 41 to 732 (total N=8,619; **Appendix B Table 6**). Fluoride gel was administered as acidulated phosphate fluoride (APF; 12,300 parts per million F) in 20 trials; other formulations were sodium fluoride (NaF, 12,500 parts per million F), amine fluoride (AmF, 12,500 parts per million [ppm] F) or stannous fluoride (SnF_2, 2,425 ppm F). Gels were applied using a tray (19 trials), brush (6 trials), or floss (1 trial). Fluoride gels were compared against placebo in 16 trials and against no gel in 10 trials. In 15 trials, fluoride gels were applied by a dental professional (frequency 1 to 4 times per year); in 11 trials, gels were self-applied (mostly 5 times per year) with supervision by a dental hygienist or other (non-dental professional) adult. In seven trials, gels were applied at a dental clinic (including school dental clinics); nineteen trials reported administration of the gel at school. Ages at enrollment ranged from 5 to 15 years. Twelve trials focused primarily on children less than 10 years of age and 12 trials focused on children 10 years of age or older; one trial included children with an average age of 10.5 years,[105] and one trial included children exclusively 13 years of age or older.[90] In the trials with self-applied fluoride gels, mean ages ranged from 7 to 13 years. In 24 trials that provided baseline information on caries burden in permanent teeth, mean DMFS or ranged from 0 to 12.2, with 11 trials reporting DMFS of 3 or less. Twelve trials were conducted in the United States, six trials in Europe, four in Brazil, and one each in Canada, Israel, China and Venezuela. Two trials[105,106] exclusively recruited participants from clinics; all other trials recruited participants from schools. Five trials were published from 1990 to 2005 (three in or after 2000); the other trials were published between 1967 and 1988. Two trials reported adequate exposure of children to fluoride through drinking water at 1.0 ppm fluoride[89] or an undefined level,[103] nine trials reported exposure to fluoride toothpaste, and two trials reported that children received fluoride tablets. One trial reported that all children received oral health education;[106] otherwise provision of oral health

education was not described. Among trials that described socioeconomic status, one trial in the United States[87] and one trial in Israel[101] evaluated a low socioeconomic status population, two trials reported low socioeconomic status in 20 to 30 percent of participants,[96,106] and one trial was conducted in a high socioeconomic status population.[98]

Of the trials in the systematic review, one[96] was cluster randomized (by school class) and the others were individually randomized. One trial was assessed as having unclear risk of reporting bias, but was otherwise assessed as being at low risk of bias.[105] In the other trials, common methodological limitations included use of a quasi-randomized design (seven trials),[82,83,90,92-94,99] unclear randomization or allocation concealment methods (19 trials), open-label (including trials that utilized a no treatment control) design (10 trials), and high attrition (14 trials).

One additional trial (n=986) not included in the systematic review evaluated 1% sodium fluoride and hydrofluoric acid (NaF-HF) gel versus placebo administered by dental hygienists via trays in school settings in children 6 to 7 years of age at baseline in a nonfluoridated setting in North Korea (drinking water fluoride concentration <0.1 ppm F) (**Appendix B Table 7**).[143] All children received oral health education. The trial was rated good-quality (**Appendix B Table 8**).

The systematic review found fluoride gels associated with decreased risk of caries burden in permanent teeth at outcomes reported closest to 3 years, based on the DFT or DMFT (10 trials, N=3,198, prevented fraction 0.32, 95% CI 0.19 to 0.46 [prevented fraction is the difference in increment between the control and intervention groups, divided by the control group increment]). There was marked statistical heterogeneity (I^2=91%), which could be explained by control type. The prevented fraction was lower in four trials that used a placebo control (N=1,525, prevented fraction 0.18, 95% CI, 0.09 to 0.27) with very low statistical heterogeneity (I^2=6%). In six trials (N=1,673) that utilized a no treatment control, the prevented fraction was 0.43 (95% CI 0.29 to 0.57, I^2=90%). Findings were similar in analyses for caries burden on affected permanent tooth surfaces at outcomes closest to 3 years, based on the DFS or DMFS (overall: 25 trials, N=8,479, prevented fraction 0.28, 95% CI 0.19 to 0.36, I^2=82%; placebo control: 15 trials, N=5,671, prevented fraction 0.21, 95% CI 0.15 to 0.28, I^2=38%; no treatment control: 10 trials, N=2,808, prevented fraction 0.38, 95% CI 0.24 to 0.52, I^2=86%). The prevented fraction of 0.28 corresponded to a difference in DMF/DMFS increment of 0.27 (95% CI 0.18 to 0.37). The systematic review did not perform an analysis stratified by age; we conducted a supplemental analysis of data reported in the systematic review that found pooled estimates were similar when placebo-controlled trials were stratified according to mean age 10 years of age and older (six trials, N=2,039; DMFS or DFS prevented fraction 0.19, 95% CI 0.07 to 0.30, I^2=53%) or younger than 10 years of age (nine trials, N=3,632; DMFS or DFS prevented fraction 0.23, 95% CI 0.13 to 0.33, I^2=31%; **Figure 7**). One trial of children 13 years or older (n=280) reported a prevented DMFS fraction at 3 years of 0.12 (95% CI -0.32 to 0.56); fluoride gel was associated with decreased likelihood of developing one or more new carious lesions (RR 0.82, 95% CI 0.68 to 0.99).[90]

The systematic review found no subgroup differences in effects of fluoride gels on DFS/DMFS prevented fraction (the most commonly reported outcome) according to baseline levels of caries (p for interaction=0.27); exposure to fluoridated water (p for interaction=0.68), fluoride toothpaste (p for interaction=0.23), or any background fluoride (p for interaction=0.16); whether

gels were professionally or self-applied (p for interaction=0.31); method of administration (tray, paint/brush or floss; p for interaction=0.71); frequency of gel applications (greater or less than twice yearly; p for interaction=0.42); fluoride gel concentration (greater or less than 10,000 ppm F); duration of followup (years; p=0.65); receipt of prior prophylaxis (p for interaction=0.75); and dropout rate (p for interaction=0.82).

A sensitivity analysis in which trials at high risk of bias due to allocation concealment were excluded provided results similar to the overall pooled estimate for prevented DMS/DMFS fraction; however, the prevented DMS/DMFS fraction was lower than the overall pooled estimate (and similar to the estimate for placebo-controlled trials) in a sensitivity analysis in which trials at high or unclear risk for blinding of outcome assessment were excluded (prevented fraction 0.22, 95% CI 0.16 to 0.29; I^2=75%).

A subsequent randomized trial (n=986) reported results consistent with the systematic review (**Appendix B Table 7**).[143] The trial found a newly developed subacidic fluoride gel (1% NaF-HF) associated with decreased caries burden in the first permanent molar (D_1MFT) or second permanent molar (D_2MFT) in children 6 to 7 years of age when administered as a single application, two applications 7 days apart, or two applications 6 months apart. At 1 year, the prevented fraction was 0.34 to 0.64 for D_1MFT and 0.56 to 0.88 for D_2MFT (p<0.001 for all fluoride gel groups versus placebo for both outcomes). The caries increment in the third molars (D_3MFT) was very small (0.08 in the placebo group, compared with 0.56 for D_1MFT and 0.50 for D_2MFT), with no difference between fluoride gel versus placebo (p=0.20).

Fluoride Varnish

A systematic review[80] and one subsequent trial[144] (not included in the systematic review) evaluated fluoride varnish versus placebo or no varnish in children 5 years of age or older. The systematic review (searches conducted through May 2013) was rated good-quality (**Appendix B Table 9**) and included 22 trials of fluoride varnish versus placebo or no varnish; however, eight trials evaluated children under 5 years of age and are outside the scope this report. Across the remaining 14 trials, sample sizes ranged from 95 to 2,604 (total N=6,965, **Appendix B Table 10**). Children were 5 to 12 years of age at baseline in nine trials, and 12 to 15 years of age in four trials[108,114,117,118]; one study[107] included children from 7 to 14 years of age. Children were recruited from schools in nine trials[107-110,112,115-117,119]; recruitment settings were not described in five trials.[111,113,114,118,120] The duration of followup ranged from 1 to 4.5 years. Four trials were conducted in Sweden,[113,114,117,118] two trials each in Brazil,[107,119] India,[111,120] and the United Kingdom.,[112,116] and one trial each in Canada,[110] China,[115] Germany,[108] and Spain.[109] Mean DMFS ranged from 0.37 to 2.44 (five trials) and mean DMFT ranged from 0.3 to 1.93 (five trials) among children 12 and under. In children over 12 years, two trials reported mean DMFS of 6.15 and 29.2. Two trials focused on children in low socioeconomic status settings[107,112] and the other trials included children from various socioeconomic status settings or did not report socioeconomic status. Information on race/ethnicity was not reported. Four trials were published prior to 1990,[110,113,114,118] three between 1990 and 1997,[108,109,120] and seven[107,111,112,115-117,119] between 2005 and 2012.

Fluoride varnish was most commonly administered as 5 percent sodium fluoride varnish (22,600 parts per million) every six months. One trial applied varnish as either 22,600 or 56,300 ppm fluoride two or four times per year,[108] one trial applied either 7,000 or 22,600 ppm fluoride every six months, one trial applied 22,600 ppm fluoride three times in one week,[111] and one trial administered 22,600 ppm fluoride two, three, or eight times[117] per year. In all trials, fluoride varnish was applied by dentists, dental nurses, or dental hygienists in school or at local clinics. Fluoride varnish was compared against placebo in four trials[108,110,115,120] and against no treatment in ten trials. One trial[108] reported that children had no background fluoride exposure; seven trials reported exposure to fluoridated drinking water ranging from 0.24 ppm to 0.9 ppm, with 3 trials at least 0.07 ppm, and nine reported fluoride exposure through toothpaste, or a community fluoride rinsing program. Four trials[107,111,115,119] provided oral health education to all children in the experimental and control groups; otherwise, information on oral health education was not reported. Four trials blinded fluoride providers and participants to treatment[107,108,110,120] and the others were open-label or did not provide information on blinding. Three trials were cluster-randomized at the school level,[109,112,116] four were adequately randomized at the individual participant level,[111,112,115,116,118,120] and eight trials did not adequately randomize participants or randomization methods were unclear.[107,108,110,113,114,117,119] Other methodological limitations in the trials noted by the systematic review included unclear or inadequate allocation concealment methods (79% of trials) and important between-group baseline differences (21% of trials).

One additional cluster-randomized trial[144] (n=5,397) published after the systematic review compared 5 percent fluoride varnish every six months to no treatment in 6 and 7 year old children in rural China (**Appendix B Table 11**). Community water contained less than 0.2 mg/L fluoride. Fluoride was applied by dentists in a school setting. All children and their parents in both treatment and control groups received oral health education annually, and children received toothbrushes and fluoride toothpaste. The proportion of children with caries in primary teeth was high (86%); the caries burden in permanent teeth at baseline was low (mean DFS 0.035), due to the young age of children in the trial. The trial used an open-label design and was rated fair-quality (**Appendix B Table 12**).

Among children 5 years of age or older, the systematic review found fluoride varnish associated with reduced caries burden in permanent teeth at one to 4.5 years, based on the number of affected surfaces (14 trials, N=3,419, prevented DMFS/DFS fraction 0.43, 95% CI 0.30 to 0.57), though statistical heterogeneity was present (I^2=75.2%). Based on the range of caries increments observed in the control groups, the pooled prevented fraction would correspond to an absolute reduction in DMFS or DFS increment of 0.07 to 3.32. There was no interaction between baseline caries severity (p for interaction=0.18); background exposure to fluoridated water (p for interaction=0.22), fluoride toothpaste (p for interaction=0.41), or any fluoride source (p for interaction 0.66); fluoride varnish concentration 5% or greater (p for interaction=0.28); followup duration (p for interaction=0.42); prior varnish exposure (p for interaction=0.18); application more than 2 times per year (p for interaction=0.59); time since permanent teeth eruption (less or greater than 2 years; p for interaction=0.82); control type (placebo or no varnish; p for interaction=0.76); or use of individual versus cluster randomization (p for interaction=0.13) and effects of fluoride varnish on caries increment. Fluoride varnish was also associated with reduced caries burden in permanent teeth at 1 to 3 years, based on the number of affected teeth (five trials, N=3,902, DMFT or DFT prevented fraction 0.44, 95% CI 0.11 to 0.76, I^2=86%), and with

a non-statistically significant reduced risk of developing one or more caries (five trials, N=3,253; RR 0.75, 95% CI 0.53 to 1.05; I^2=89.2%).

The systematic review also included three trials of children 6 to 8 years of age that reported the association between use of fluoride varnish and caries burden in primary teeth. Two trials found fluoride varnish associated with reduced caries burden in primary teeth (prevented dmfs or dfs fraction 0.2, 95% CI 0.02 to 0.38[110] and 2.12, 95% CI 0.23 to 4.01[111]), and one trial found no association (prevented dmfs fraction –0.02, 95% CI –0.39 to 0.35[112]). The latter trial[112] also found no association between use of fluoride varnish and likelihood of developing one or more carious lesions in primary teeth (n=282; RR 1.06, 95% CI 0.84 to 1.33).

One cluster-randomized trial[144] published subsequent to the systematic review compared 5 percent fluoride varnish every six months to no treatment in 6 and 7 year old children not exposed to fluoridated water in rural China (n=5,397). Results were consistent with the systematic review in finding fluoride varnish associated with reduced caries burden of permanent teeth at three years (DFS in first molar 0.41 vs. 0.64 at 24 months, p<0.001 and 0.67 vs. 1.03 at 36 months, p<0.001).

Sealants

A systematic review[81] and two subsequent trials[145,146] (not included in the systematic review) evaluated sealants versus no sealants in children 5 years of age or older. One additional study[159] not in the review reported longer duration followup for a trial included in the systematic review. The systematic review (searches conducted through August 2016) was rated good-quality (**Appendix B Table 13**) and included 16 trials of a sealant versus no sealant[81] (**Appendix B Table 14**). Fifteen trials (N=4,195 participants) evaluated a resin-based sealant, and three trials (N=905 participants) evaluated a glass ionomer sealant (two trials evaluated both a resin-based and glass ionomer sealant). For resin-based sealants, the systematic review included 10 trials of an autopolymerized sealant, one trial of a light-polymerized resin sealant without fluoride, and four trials of a light-polymerized resin sealant with fluoride (first-generation resin based sealants were excluded). For glass ionomer sealants, the systematic review included one trial each of an autopolymerized low viscosity sealant, a light-cured low-viscosity sealant, and a resin-modified sealant. In all trials, children were recruited from schools. Children were 6 to 10 years of age at baseline in all trials except for one,[133] in which baseline age was 12 to 13 years. In six studies that provided information on baseline caries prevalence, mean dft or dmft ranged from 2.24 to 5.38 in five trials of children 5 to 10 years of age[115,119,122,127,128] and one trial[133] reported a mean DMFT of 1.81 in children 12 to 13 years of age. Four trials were conducted in the United States or Canada, three trials in China, four trials in Europe, and one trial each in Brazil, Colombia, New Zealand, and Thailand. Two trials focused on children in low socioeconomic status settings;[128,133] the other trials did not focus on low socioeconomic status settings or did not report socioeconomic status. Five trials were published between 2011 and 2014, one trial was published in 2005, and 10 trials were published between 1976 and 1995.

In all trials, sealants were applied to occlusal surfaces of permanent premolar or molar teeth by dentists or other dental professionals, except for one trial[133] in which sealants were administered by dentists or schoolteachers with 3 days of training. Sealants were applied to sound surfaces or

on enamel lesions (e.g., ICDAS II scale 0 to 3). Settings for sealant administration were school dental clinics, office-based dental clinics, or mobile dental settings (e.g., vans). One trial[119] was conducted in a setting with tap water fluoridation level of 0.7 ppm F, three trials reported that they were conducted in settings with fluoridated tap water but did not report the level,[121,123,132] one trial reported mixed fluoridation status (five schools in fluoridated towns and five in non-fluoridated towns),[126] and the other trials reported community fluoridation levels <0.7 ppm or did not provide information regarding fluoridation levels. Two trials reported that all children received oral health education[128,134]; information on oral health education was otherwise not reported. The trials were unable to effectively blind outcome assessors because sealant materials are visible; other methodological limitations in the trials noted by the systematic review included unclear or inadequate randomization (33% of trials) and unclear allocation concealment methods (37% of trials). Attrition was unclear or high in one of seven trials at 12 months followup, one of nine trials at 24 months, two of seven trials at 36 months, and three of five trials at 48 to 54 months. One trial with 60 months of followup reported low attrition and the only trials that reported outcomes at 72 and 84 months had high attrition.

Two additional trials were not included in the systematic review (**Appendix B Tables 15 and 16**).[145,146] One trial (n=187) evaluated an autopolymerized glass ionomer sealant versus no sealant administered by a dentist to children 6 to 8 years of age in a low-income, fluoridated water (to 0.7 mg/L) setting in Brazil.[145] The trial was rated fair-quality; in addition to open-label design, it also had unclear allocation concealment methods. Another trial conducted in a pediatric dentistry clinic in Turkey (n=50 children, 200 molars) utilized a randomized, split mouth technique comparing two types of resin fissure sealants versus a glass-ionomer cement sealant versus no sealant to children between 7 and 12 years of age with a baseline mean DMFT of 0.08.[146] The trial was rated fair-quality. One additional publication[159] reported 3-year followup of a trial of a light-polymerized resin-based sealant with fluoride, for which 1-year data were included in the systematic review.

Among children 5 to 10 years of age, the systematic review found resin-based sealants associated with decreased risk of carious first molars at 24 months (seven trials, N=1,322, OR 0.12, 95% CI 0.08 to 0.19, I^2=72%). Although statistical heterogeneity was present, estimates favored sealants in all trials; ORs ranged from 0.06 to 0.32 in the trials. The proportion of patients that developed carious first lesions in the no sealant arms of the trials ranged from 16 percent to 70 percent in the trials; based on the pooled estimate, the absolute risk difference ranged from 11 percent to 51 percent. There was no interaction between study design (parallel-group versus split-mouth) and effects on likelihood of caries. Findings were similar at 36 months (seven trials, N=1,410, OR 0.17, 95% CI 0.11 to 0.27, I^2=90%) and at 48 to 54 months (four trials, N=440, OR 0.21, 95% CI 0.16 to 0.28, I^2=45%). The subsequent study[159] reporting longer duration (3-year) followup for a trial included in the systematic review reported results consistent with the review's 3-year pooled estimate (adjusted hazard ratio [HR] 0.33, 95% CI 0.24 to 0.46). An additional, subsequent study also found consistent results with fewer caries in those who received the resin-based sealant (3.0% to 9.4%) than those without sealants (25.7%) after 18 months (RR 0.24, 95% CI 0.08 to 0.72).[146]

Evidence on risk of caries at longer-term followup was limited, with one trial finding a resin-based sealant associated with decreased risk of caries at 5 years (n=165, OR 0.31, 95% CI 0.23

to 0.43),[130] 7 years (n=67, OR 0.45, 95% 0.34 to 0.59),[123] and 9 years (n=120, OR 0.35, 95% CI 0.22 to 0.55).[122] One trial found resin-based sealants associated with reduction in caries burden at 24 months based on the DFS increment (n=671, mean difference -0.65, 95% CI -0.83 to -0.47).[133]

Evidence on effectiveness of resin-based sealants among children >10 years of age was limited to one trial that found resin-based sealants compared with no treatment associated with decreased change from baseline in DMFS index among children 12 to 13 years of age at baseline (n=671, mean difference -0.24, 95% CI -0.36 to -0.12).[133] There was insufficient evidence to determine how effects of sealants varied according to sex, race/ethnicity, socioeconomic status and other social determinants, because studies did not report analyses stratified according to these factors. There was also insufficient evidence to determine how community water fluoridation levels or use of oral health education impacted effectiveness of sealants, because most trials did not report these factors.

Evidence on the effectiveness of glass ionomer sealants versus placebo was limited and somewhat inconsistent. At 24 months, the systematic review included one trial that found a glass ionomer sealant associated with decreased likelihood of carious first molars (n=372, OR 0.46, 95% CI 0.23 to 0.91)[127]; however, another trial in the systematic review found a very small, non-statistically significant difference in DFS increment (n=404, mean difference -0.18, 95% CI -0.39 to 0.03).[133] In the latter trial, effects of glass ionomer sealants were very similar when administered by a dentist or by a schoolteacher with 3 hours of training. One subsequent trial also found no difference between a glass ionomer sealant versus no sealant in risk of carious first molars at 3 years (n=187, HR 0.90, 95% CI 0.55 to 1.49).[145] However, another subsequent trial found fewer caries associated with glass ionomer cement sealants versus no sealants (3.0% versus 25.7%) after 18 months (RR 0.12, 95% CI 0.02 to 0.88).[146]

Silver Diamine Fluoride

One trial (n=452) evaluated SDF solution for prevention of caries in children older than 5 years of age (**Appendix B Table 17**).[147] The trial enrolled 6 year old schoolchildren (mean age 6.3 years) in a low community fluoridation setting (0.09 ppm F) with high baseline caries burden (mean dmfs 3.6) in Cuba. Children were randomized to 38 percent SDF solution applied to primary canines and occlusal surfaces of molars and first permanent molars every 6 months for 36 months versus no SDF. The trial did not report how persons administering SDF were trained; all children received oral health education (tooth brushing instruction and dietary recommendations) and received mouth rinses every 2 weeks with 0.2 percent sodium fluoride. The trial was rated fair-quality; methodological limitations included unclear randomization and allocation concealment methods and unclear blinding of persons administering SDF (**Appendix B Table 18**).

At 36 months, SDF was associated with fewer new surfaces with active caries in the deciduous dentition (mean 0.3 vs. 1.4, $p<0.001$), fewer surfaces with active caries (decayed or filled surfaces) in first permanent molars (mean 0.4 vs. 1.1, $p<0.001$), and decreased likelihood of experiencing at least 1 new decayed or filled tooth (26.1% vs. 49.7%, RR 0.52, 95% CI 0.40 to 0.70).

Xylitol

Ten trials evaluated xylitol versus no xylitol in children five years of age or older (**Appendix B Table 19**).[148-157,160,161] Sample sizes ranged from 145 to 976 (total N=4,267).Two trials were conducted in Finland and one each in Lithuania, Estonia, Hungary, Kuwait, French Polynesia, Canada, Belize, and the United States. At baseline, mean age was under 10 years in four trials[150,151,154,156] and 10 years of age or older in five trials.[148,149,152,153,155,157] No trial reported mean age of participants of 13 years or older; one trial included participants up to 27 years, with 12 percent between 19 and 27 years of age (mean age not reported).[155] Two trials evaluated children with low baseline caries burden (based on mean DMFS 2.10 or 82.7% with $D_3MFS=0$).[148,152] One trial[154] recruited children from an institutional children's home and one trial[155] recruited children from a school for those with physical disabilities; all other trials recruited children through local schools. Xylitol was administered as a candy, gum, lozenge, or lollipop in concentrations that ranged from 49 percent to 64.7 percent xylitol; xylitol was typically administered three to five times per day[148-150,155] and total daily xylitol dose ranged from 4.3 to 20 grams.[151,154,156] One trial compared xylitol candy versus placebo (non-xylitol) candy[151] and one trial compared xylitol versus no xylitol or a placebo gum[153]; in all other trials the control was no xylitol (without placebo). Xylitol was distributed and administered under supervision at school or in the child's institution by teachers or school nurses in all trials; in three trials parents also administered xylitol when children were at home.[149,153,156] One trial was conducted in a community with fluoridated drinking water (concentration <1.5 mg/mL),[152] three trials[149,153,157] were conducted in nonfluoridated settings (<0.02 ppm fluoride [F] concentrations), and fluoridated water status was not reported in six trials. Six trials[149-152,154,156] provided fluoride rinses, toothpastes, or varnishes to all participants and three trials[150,151,156] included children participating in caries prevention programs of oral health instruction and other oral health preventive interventions (e.g., varnish and/or sealants). One U.S. trial reported that 96 percent of participants were Black children and 94 percent of participants had access to a federal reduced cost/free school lunch program[151]; information regarding race/ethnicity and socioeconomic status was otherwise not described. Five trials were published between 1985 and 1995, and five trials were published between 2000 and 2015.

One trial individually allocated children to interventions[155]; in all other trials, children were allocated to interventions in clusters based on school, classroom, institution, or geographic setting. All trials had methodological limitations (**Appendix B Table 20**). Three trials[155-157] were non-randomized and all other trials had unclear randomization methods. Only two trials reported adequate allocation concealment.[152,153] Among the cluster trials, the number of clusters ranged from three to 21; none of the cluster trials except for one[151] reported analyses adjusted for clustering. Only two trials utilized a placebo (non-xylitol gum or candy) control[151,153]; all other trials used a no xylitol control and were open-label. Other methodological limitations were baseline between-group differences and high attrition. Two trials were rated fair-quality[152,153] and the others were rated poor-quality. Due to the lack of higher-quality trials, poor-quality trials were included, though results are described separately for the fair-quality trials.

The two fair-quality trials found no benefit of xylitol or reported results that varied depending on control type.[152,153] One cluster trial[152] enrolled 10-year old children (n=496) in Finland in an area

with natural fluoridation and low baseline caries burden (82.7% of children had D_3MFS=0; D_3MFS indicates caries lesions that extend into the dentin). It found no difference between xylitol lozenges versus no xylitol in caries burden (based on clinical or radiological findings) at 4 years based on the D_3MFS increment (mean 2.75 for xylitol for 1 year vs. 3.02 for 2 years vs. 2.74 for no xylitol, p>0.05) or likelihood of D_3MFS >0 (versus placebo, adjusted OR 1.12, 95% CO 0.44 to 2.86 for xylitol 1 year and OR 1.01, 95% CI 0.40 to 2.56 for xylitol 2 years), though estimates were imprecise. Another cluster trial (n=432)[153] evaluated children (mean age 11.6 years) with high baseline caries burden (mean DMFS 13.2 to 15.3) in a non-fluoridated setting in Lithuania. Results differed depending on the control intervention evaluated. The trial found no difference between xylitol gum five times daily versus placebo (non-xylitol) gum in caries burden in permanent teeth based on the DMFS [all stages] at 3 years (mean increment 8.1 vs. 8.3, p>0.05). However, xylitol gum was associated with decreased DMFS increment versus no xylitol (mean 8.1 vs. 12.4, p<0.05). Xylitol and placebo gum were also associated with similar likelihood of experiencing a DMFS increment ≥14 (versus reference of sorbitol/carbamide gum, adjusted OR 0.2, 95% CI 0.1 to 0.5 for xylitol gum and 0.3 (95% CI 0.27 to 0.7 for placebo gum).

When all trials (fair-quality or poor-quality) were pooled, xylitol was associated with decreased caries burden in permanent teeth versus no xylitol or placebo at 2 to 4 years, based on the DMFS increment (10 trials, effective [after adjustment for clustering] N=1,955; mean difference -2.38, 95% CI -3.66 to -1.15, I^2=94%; **Figure 8**).[148-157] Two poor-quality trials also evaluated the association between xylitol versus no xylitol and caries burden based on the DMFT increment and reported similar findings, though the difference was not statistically significant (two trials, effective N=387, mean difference -1.52, 95% CI -3.36 to 0.26, I^2=92%; **Figure 8**).[154,155,160,161] In an analysis stratified by control type, there was no difference in DMFS increment between xylitol versus placebo (two trials, effective N=328, mean difference 0.23, 95% CI -0.90 to 1.21, I^2=0%[151,153]), but xylitol was associated with reduced DMFS increment versus no xylitol (nine trials, effective N=1,661, mean difference -2.84, 95% CI -4.15 to -1.63, I^2=92%)[148-150,152-157]; however, there was no statistically significant interaction with control type (p for interaction=0.08). When trials were stratified by quality, xylitol was associated with reduced DMFS increment in the poor-quality trials (eight trials, effective N=1,646, mean difference -2.38, 95% CI -3.66 to -1.15, I^2=94%; **Figure 9**).[148-151,154-157] There was no difference between xylitol versus no xylitol or placebo in the fair-quality trials (two trials, effective N=344, mean difference -0.04, 95% -2.56 to 1.12, I^2=51%),[152,153] though the pooled estimate is difficult to interpret due to inconsistency in the two trials and differences in settings (low[152] versus high[153] caries burden) and control types evaluated (no xylitol in one trial[152] and no xylitol or placebo in one trial[153]) with no statistically significant interaction between trial quality and effects of xylitol on DMFS increment (p for interaction=0.22). Limiting the analysis of fair-quality trials to no xylitol controls did not resolve the inconsistency (mean DMFS increment difference 0.15, 95% CI -0.73 to 1.02[152] versus -4.30, 95% CI -7.87 to -0.73).[153] Xylitol was associated with reduced DMFS increment versus no xylitol or placebo in analyses stratified by age (<10 versus ≥10 years), setting (school versus institutional home), geographic region (Europe, North America, or other), duration of followup (<3 vs. ≥3 years), and baseline caries burden (low [based on 83% of children with D_3MFS=0 or mean DMFS=2.01 at baseline[148,152]] versus not low) (**Table 3**). However, stratified analyses were limited by small numbers of trials, with serious methodological limitations.

Key Question 5. What Are the Harms of Specific Interventions (Behavioral Counseling, Referral, and Preventive Interventions) to Prevent Oral Health Issues?

Summary

Supplements

- One trial reported no adverse events; harms were otherwise not reported.

Fluoride Gel

- Evidence on adverse events was very limited, with two trials finding no association between use of fluoride gels and acute toxicity (nausea, gagging, vomiting; N=490, absolute risk difference 0.01, 95% CI -0.01 to 0.02, I^2=0%).

Fluoride Varnish

- Evidence on harms was very limited; five trials reported no adverse events and one trial reported 12 of 1,473 children reported adverse events (the most commonly nausea). All adverse events were described as self-limiting, although four children were withdrawn due to mild adverse events.

Sealants

- Reporting of harms was limited, with three trials of resin-based sealants reporting no harms.

Silver Diamine Fluoride

- In one trial, SDF was associated with increased likelihood of inactive caries and black stain in deciduous teeth (97% vs. 48%, p<0.001) and in first permanent molars (86% vs. 67%, p<0.001).

Xylitol

- Evidence on harms of xylitol was very limited; one trial reported one withdrawal from xylitol due to diarrhea.

Evidence

Supplements

Evidence on harms of fluoride supplements was very limited. One trial (n=349), which enrolled children with disabilities, reported no adverse events.[140] Harms were otherwise not reported.

Fluoride Gel

Data on adverse events associated with fluoride gels was very limited. None of 26 trials included in the systematic review[79] reported on staining of tooth surfaces. Two trials included in the systematic review reported on acute toxicity (nausea, gagging, or vomiting), with one trial reporting no events and a pooled analysis finding no difference between gel versus placebo or no treatment (N=490, absolute risk difference 0.01, 95% CI -0.01 to 0.02, I^2=0%[91,99]). The systematic review found no difference between fluoride gel versus placebo in risk of study withdrawal (19 trials, N=8,695, RR 1.03, 95% CI 0.89 to 1.19); the trials did not report risk of withdrawal specifically for adverse events.

One subsequent trial (n=986) of fluoride gels versus placebo reported no harms except for a slightly sour taste soon after gel application in most children (data not provided).[143]

Fluoride Varnish

Five of 16 trials included in a good-quality systematic review of varnish[80] reported adverse events. Four trials[107,115,117,119] (N=1,704) reported no adverse events, and one trial (n=2,967[116]) reported 12 of 1,473 children assigned to varnish reported adverse events (the most common adverse event was nausea, occurring in seven children). All adverse events were described as self-limited, although four children were withdrawn due to mild adverse events. Adverse events were not described in the no varnish group. One subsequent trial of varnish (n=5,397) reported no adverse events.[144]

Sealants

Only three[115,122,128] of the 16 trials of sealants versus no sealants included in the systematic review reported harms. All (N=775) evaluated a resin-based sealant and reported no adverse events. The trial of a glass ionomer sealant published subsequent to the systematic review did not report harms.[145]

Silver Diamine Fluoride

One trial (n=452) found SDF associated with increased likelihood of black stained inactive caries in deciduous teeth (97% vs. 48%, $p<0.001$) and in first permanent molars (86% vs. 67%, $p<0.001$).[147]

Xylitol

Evidence on harms of xylitol was very limited. One trial (n=296) reported one withdrawal from xylitol due to diarrhea.[152] Nine other trials of xylitol did not report harms.[148-151,153-157]

Contextual Questions

Contextual Question 1a. What Is the Association Between Presence or Severity of Dental Caries of Deciduous or Permanent Teeth and Pain, Quality of Life, Function, and Tooth Loss?

No study evaluated the longitudinal association between improvements in measures of dental caries in children 5 to 18 years of age and health outcomes such as pain, quality of life, function, or tooth loss. However, observational studies indicate a negative cross-sectional association between presence of caries or higher caries burden and worse quality of life and school performance. Evidence also indicates an association between presence or severity of dental caries and dental pain.

A systematic review[167] of 23 cross-sectional studies (N=12,604) of adolescents 11 to 18 years of age found previous caries experience, DMFT index, and presence of caries in primary teeth associated with a lower level of oral health-related quality of life (measured using the Child Oral Impact on Daily Performances instrument [Child-OIDP]), based on qualitative synthesis. The most frequently affected dimensions on the Child-OIDP were eating, teeth brushing, and emotional status. Another systematic review included 11 observational studies of children 3 to 12 years of age (N=6,293).[168] The systematic review found presence of dental caries (six studies, OR 1.66, 95% CI 1.43 to 1.88, I^2=83.5%) or periodontal disease (three studies, OR 1.66, 95% CI 1.12 to 1.18, I^2=0%) each associated with increased likelihood of having poor oral health-related quality of life.

Regarding dental pain, a systematic review found presence of dental caries associated with increased likelihood of tooth pain among children and adolescents (OR 3.49, 95% CI 2.70 to 4.51), based on 19 studies.[169] The prevalence of tooth pain was 48.1 percent among children with dental caries lesion, compared with 27.3 percent among those without caries.

Dental caries was also associated with negative impacts on school performance and attendance. One systematic review found having one or more decayed teeth was associated with increased likelihood of poor school performance (five studies, N=3,205; OR 1.44, 95% CI 1.24 to 1.64) and poor school attendance (five studies, N=4,416; OR 1.57, 95% CI 1.08 to 2.05).[170] Another systematic review reported similar findings, with poor oral health (based on high caries burden, presence of untreated caries, or presence of other unmet dental needs) associated with increased likelihood of poor academic performance (five studies; OR 1.52, 95% CI 1.20 to 1.83) and absenteeism (four studies; OR 1.43; 95% confidence interval, 1.24 to 1.63).[171] Results should be interpreted with caution given potential confounding related to socioeconomic status or other factors associated with both dental caries and lower school performance or attendance.

Contextual Question 1b. What Is the Association Between Presence or Burden of Dental Caries of Deciduous Teeth and Subsequent Presence or Severity of Dental Caries of Permanent Teeth?

One systematic review of prospective longitudinal cohorts or randomized controlled trials found that baseline caries prevalence was the best single predictor of future caries in schoolchildren and adolescents; though diagnostic accuracy was limited (nine studies, N=8,234, sensitivity 0.54 to 0.59, specificity 0.72 to 0.73, RR 1.03 to 4.9, and OR 3.0 to 13).[172] The review did not specifically evaluate the association between dental caries in primary teeth and subsequent dental caries in permanent teeth, but noted that the first few years after tooth eruption was the period of highest risk for caries incidence in permanent teeth.

Long-term longitudinal studies on the association between dental caries in primary teeth and caries in permanent teeth or other long-term outcomes are very limited. A longitudinal study of two New Zealand birth cohorts (n=922 and 931) that followed participants from 5 to 40 or 45 years of age each found high dental caries experience as children associated with decreased likelihood of "excellent" self-rated health as adults (incidence rate ratios 0.76, 95% CI 0.50 to 1.14 and 0.69, 95% CI 0.47 to 1.00).[173] A small (n=25), prospective, longitudinal (15-year) German cohort study found that children 3 to 5 years of age who underwent dental treatment under general anesthesia for severe caries had markedly higher caries burden 15 years later when compared against children 3 to 5 years of age with no caries (mean difference in DMFS 14.8; p=0.001).[174]

Contextual Question 2. What Factors (e.g., Race/Ethnicity, Age, Socioeconomic Status, Cultural Factors, Educational Attainment, or Health Literacy) Are Associated With Oral Health Care Disparities in Children and Adolescents?

Based on NHANES 2011 to 2016 data (**Table 4**),[20] the overall prevalence of dental caries in primary teeth in children ages 6 to 8 years was 52 percent; for permanent teeth, the prevalence of dental caries was 17 percent among children 6 to 11 years of age (when permanent teeth start to erupt) and 57 percent among those 12 to 19 years of age. A number of factors have been associated with oral health care disparities in U.S. children and adolescents, likely related to decreased access to dental care and presence of other negative social determinants of health. The prevalence of dental caries was generally higher in non-Hispanic Black and Mexican American children and adolescents compared with non-Hispanic White children and adolescents. For children 6 to 8 years of age, the prevalence of caries in primary teeth was 54 percent for non-Hispanic Black youth and 73 percent for Mexican American youth, compared with 44 percent for non-Hispanic White youth, with a prevalence of untreated caries of 22.4, 20.0, and 13.2 percent, respectively. For those 12 to 19 years of age, the prevalence of caries in permanent teeth was 57, 66, and 54 percent, respectively, with a prevalence of untreated caries of 20.4, 20.8, and 15.6 percent, respectively. Data from the National Survey of Children's Health also indicated disparities by race/ethnicity.[175] In 2018 to 2019, among children 6 to 11 years of age, the

proportion with dental caries in the last year was 9.3 percent for non-Hispanic White youth and ranged from 11.1 to 12.2 percent for Hispanic youth and non-Hispanic Black, Asian, or other youth. The proportion that received fluoride treatment was 55 percent for non-Hispanic White youth and ranged from 37.8 to 44.3 percent for Hispanic youth and non-Hispanic Black or Asian youth.

There was also an association between socioeconomic status and prevalence of dental caries and untreated caries (**Table 4**). Among children 6 to 8 years of age, the prevalence of dental caries in primary teeth was 64.4 percent among those at <100 percent of the Federal poverty level (FDL), 60.1 percent among those at 100 to 199 percent of FDL, and 40.4 percent among those at ≥200 percent of FDL; the prevalence of untreated caries was 22.3, 20.9, and 11.1 percent, respectively. Among those 12 to 19 years of age, the prevalence of dental caries in permanent teeth was 64.9 percent among those at <100 percent FPL, 65.3 percent among those 100 to 199 percent FPL, and 48.7 percent among those at ≥200 percent FPL; the prevalence of untreated caries was 22.7, 20.9, and 11.1 percent, respectively.

Data also indicate some disparities in receipt of preventive treatments by race/ethnicity and socioeconomic status. Among those 12 to 19 years of age, the proportion with dental sealants on permanent teeth was 37 percent for non-Hispanic Black youth, compared with 45 percent for Mexican American youth and 53 percent for non-Hispanic youth. The proportion with dental sealants on permanent teeth was 43 percent for those at less than 100 percent of the FPL, 48 percent for those at 100 to 200 percent of the FPL, and 51 percent for those at 200 percent or greater of the FPL.

High oral health burdens have been reported in American Indian and Alaska Native Children. According to the 2016-2017 Indian Health Service Oral Health Survey, among children 6 to 9 years of age, 87 percent had dental caries (all teeth), 47 percent had untreated caries, and 44 percent had received dental sealants.[176] In the 2019 to 2020 Indian Health Service Oral Health Survey, 74 percent of American Indian and Alaska Native adolescents 13 to 15 years of age had caries experience and 45 percent had untreated caries.[177]

Evidence on the association between social determinants of health other than socioeconomic status and disparities in oral health in children has tended to focus on children less than 5 years of age, rather than those 5 to 19 years of age. A study of 283 Boston-area children 6 to 10 years of age found that children of immigrant caregivers had higher baseline caries burden than children of U.S.-born caregivers (mean number of carious surfaces 11.5 versus 9.4, adjusted for race/ethnicity, age, gender, and caregiver smoking status).[178] Children of immigrant caregivers who preferred to speak non-English languages had higher caries burden than children of immigrant caregivers who preferred to speak English. Other factors that have been associated with caries in children and adolescents include lower level of parental education and living in rural areas.[179,180]

Contextual Question 3. What Is the Effectiveness of Primary Care Interventions to Reduce Oral Health Care Disparities in Children and Adolescents?

No study evaluated the effectiveness of primary care interventions to reduce oral health disparities in children and adolescents.

Chapter 4. Discussion

Summary of Review Findings

Table 5 summarizes the evidence reviewed for this report. Dental caries is common in U.S. children and adolescents 5 to 17 years of age and is often untreated, potentially resulting in adverse oral and other health outcomes. Disparities in oral health, related in part to social determinants, including inadequate access to dental services, suggest a potential role for primary care providers in oral health screening and prevention in this age group. This report updates and expands upon a 1996 USPSTF recommendation on oral health counseling by focusing on oral health screening and prevention in children and adolescents 5 to 17 years of age. It complements other USPSTF reviews on oral health topics, including a concurrent review on oral health screening and prevention in adults[4] and prior USPSTF reviews on dental caries screening and prevention in children less than 5 years of age [10] and on screening for oral cancer.[11]

Evidence on screening was very limited. No study compared outcomes of primary care screening versus no screening in this age group. One study[135] found oral health visual screening by a nurse following 5 hours of training associated with high sensitivity and specificity for untreated caries and a 17-item parent- or guardian-reported questionnaire associated with moderate sensitivity and high specificity for untreated caries, but requires validation. No study evaluated the diagnostic accuracy of primary care screening for identifying children at risk of future oral health issues.

Several oral health preventive interventions improved caries outcomes when administered in school or dental settings. However, evidence demonstrating effectiveness with home or primary care administration was lacking. Fluoride supplements were associated with a small decrease in the DMFT/DFT increment (mean difference <1 affected tooth) in low socioeconomic, non-fluoridated water, or high caries burden settings. However, fluoride supplements were administered in school under supervision in all trials except for one that evaluated home self-administration in older (mean 12.5 years) children that reported low adherence with no benefit.[137] Fluoride gels, fluoride varnish, and sealants were each associated with improved caries outcomes when administered in schools or in dental clinics. Gels were administered by dental professionals or were self-administered with supervision by a dental or non-dental professional and varnish, and sealants were administered by dental professionals. The prevented caries fraction (defined as the difference in caries increment between intervention and control, divided by control increment) was larger for varnish (0.44[80]) than for gels (0.32 based on all trials and 0.18 based on placebo-controlled trials[79]). Resin-based sealants, which are placed on the occlusive surfaces of permanent molars, strongly reduced the likelihood of developing carious first molars (ORs ranged from 0.12 to 0.21).[81] Few trials evaluated glass ionomer sealants and results were inconsistent.[81] One trial found SDF for prevention associated with decreased active caries surfaces in deciduous dentition (mean difference 1.1) and first permanent molars (mean difference 0.7), and decreased likelihood of 1 or more new caries (RR 0.52, 95% CI 0.40 to 0.70);[147] SDF has primarily been utilized to arrest existing caries.[52] Evidence on xylitol was difficult to interpret. Although most trials found xylitol improved caries outcomes, six of eight trials were rated poor-quality due to serious methodological limitations (including

open-label design, non-randomized design, unclear randomization and allocation concealment, and high attrition). Two fair-quality trials of xylitol either found no benefit of xylitol (versus no xylitol[152]) or reported results that varied depending on the control type (large benefit versus no xylitol but no benefit versus xylitol[153]).

Assessment and reporting of harms of preventive interventions was sparse, although serious harms were not reported. Trials that did report harms typically stated that there were no adverse events, but did not describe methods used to assess harms. No study evaluated the association between exposure to fluoride via oral health preventive interventions in children older than 5 years of age and adolescents and risk of fluorosis. Studies on risks of fluoride exposure have primarily focused on exposure during early childhood, at earlier stages of enamel and neurocognitive development. A challenge in evaluating harms associated with exposure to fluoride is separating outcomes related to fluoride in preventive interventions from other (e.g., environmental, food) sources.

No study compared primary care counseling versus no counseling or primary care referral to a dental professional versus no referral.

Limitations

There were important limitations in the evidence available to address the benefits and harms of primary care oral health screening and prevention in children and adolescents 5 to 17 years of age. As noted above, there was almost no evidence to assess benefits and harms of oral health screening in this age group. For prevention, there were no studies of primary care counseling versus no counseling or primary care referral to a dental professional versus no referral. Trials of oral health primary care intervention focused on caries outcomes, with no trials reporting effects on quality of life or function (including school performance), or other health outcomes. Trials of oral health primary care interventions had serious methodological limitations, and reporting of harms was very poor. Importantly, several factors may reduce applicability of the available evidence to U.S. primary care practice. First, the preventive interventions were administered by dental professionals or in supervised school settings in almost all trials. One trial of fluoride supplements administered at home (rather than at school under supervision) reported low adherence and no benefit[137]; the effectiveness and feasibility of other oral health preventive interventions administered in primary care settings or without supervision in school is unknown. Second, with the exception of fluoride varnish, few trials of oral health preventive interventions have been published since 2000, which could reduce applicability to current practice, due to differences in oral health behaviors and epidemiology of caries over time. Third, reporting of factors that could affect the effectiveness of oral health preventive interventions such as water fluoridation status, oral health behaviors, and provision of oral health education was suboptimal and inconsistent, making it difficult to understand the context under which trials were conducted.

There were also potential limitations in the review methods. First, we excluded non-English language primary articles, which could result in language bias. However, we did not identify non-English language articles that appeared likely to impact conclusions, and we included systematic reviews that did not have an English language restriction. Second, we did not search for studies published only as abstracts. Third, we were unable to assess for publication bias with

graphical or statistical methods for small sample effects, due to small numbers of studies with serious methodological limitations.[78] Fourth, we utilized previously published systematic reviews, rather than relying exclusively on primary studies. However, the systematic reviews were only utilized if they were assessed as good-quality and the reviews were supplemented with subsequently published primary studies.[181] Fifth, we did not evaluate the effectiveness of tooth brushing or flossing, as these are performed outside the primary care setting and are routinely recommended. Rather, the review addressed the effectiveness of counseling on oral health, including tooth brushing, flossing and diet. Sixth, meta-analyses conducted on fluoride supplements and xylitol had substantial statistical heterogeneity and the analysis for xylitol included trials with serious methodological limitations. To address statistical heterogeneity, we utilized a random effects model and conducted stratified analyses on study-level factors potentially associated with heterogeneity, including study setting, duration of followup, age category, control type, and baseline caries burden. For xylitol, we focused on the findings of the fair-quality trials and described how they differed from the poor-quality trials. Seventh, we focused on trials comparing oral health preventive interventions versus placebo or no treatment. Head-to-head trials could also be informative, particularly if they compare interventions administered in primary care settings. However, a recent systematic review found insufficient evidence to determine the comparative effectiveness of varnish and sealants administered by dental professionals[182] and another systematic review found insufficient evidence to determine the comparative effectiveness of resin-based versus glass ionomer sealants.[81]

Emerging Issues/Next Steps

SDF was cleared for U.S. marketing by the FDA in 2014 as a desensitizing agent in adults.[51] Although it has been used to arrest existing caries, this use is off-label. Similarly, use of SDF for prevention of caries is also off-label. Two U.S. trials in elementary children older than 5 years of age with SDF for prevention are ongoing; both are designed as head-to-head trials of SDF versus sealants or varnish without a placebo or no treatment control group.[53,183] A potential disadvantage of SDF is permanent dark discoloration of active caries lesions by the silver component, which may affect acceptability. However, active caries lesions themselves may be discolored, and may result in other cosmetic consequences.

There are also barriers to administration of oral health preventive interventions such as varnish, sealants, or SDF in primary care settings, including the need for additional training and equipment. Even if such interventions are effective in dental settings, the effectiveness, feasibility, acceptability and uptake (by clinicians and patients) for school-age children and adolescents in primary care settings is unknown. There is some evidence of increased uptake in 2018 compared to 2008 of primary care administration of fluoride varnish in younger (<5 years) children,[184] suggesting feasibility in primary care settings with older children and adolescents. Applying SDF is considered similar technically to applying varnish[50] and limited evidence indicates that applying SDF in primary care settings is feasible.[185] Application of sealants is more technically challenging than application of varnish and evidence on implementation by non-dental professionals in primary care settings is lacking. Prior to implementation, it would be important for payers and other stakeholders to clarify reimbursement of primary care clinicians for provision of oral health preventive interventions.

Relevance for Priority Populations

Disparities among children and adolescents 5 to 17 years of age in oral health have been described with regard to age, race/ethnicity, socioeconomic status, insurance status, health literacy, immigration status, educational level, pregnancy status, and living in rural and urban underserved areas.[20,63,71] Understanding the independent contribution of these factors to disparities is complicated by marked intersectionality. Limited evidence from subgroup analyses indicated no statistically significant differences in effects of fluoride supplements or fluoride gels based on age (greater or less than 10 years of age) or in effects of fluoride varnish based on time since permanent teeth eruption (greater or less than 2 years),[80] a proxy for age. Few trials enrolled adolescents (13 to 17 years of age) and there was insufficient evidence to determine how effectiveness of oral health preventive interventions differed in adolescents versus children 5 to 12 years of age. No trial evaluated how effects of oral health preventive interventions varied according to race/ethnicity, socioeconomic status, educational level, insurance status, and other social determinants. Although some trials of oral health preventive interventions were conducted in low socioeconomic status or other under-resourced settings, details regarding socioeconomic status were reported by few trials. A key rationale for primary care oral health screening and prevention is the potential to reduce disparities in oral health outcomes related to access to care or other factors; however, no trial evaluated effects of screening or provision of preventive services in primary care settings.

Future Research

Research is needed on benefits and harms of primary care screening versus no screening, primary care counseling versus no counseling, and primary care referral to a dental professional versus no referral. Research is needed to determine whether benefits of fluoride gels, fluoride varnish, and sealants observed in dental and school settings are attainable and feasible in current primary care practice. Studies showing effectiveness of SDF for prevention in dental or school settings would support subsequent research of SDF for prevention in primary care settings. Importantly, trials of gels, varnish, sealants, and SDF should describe the training and equipment utilized when they are administered in primary care settings and studies on primary care referral should describe approaches to facilitate coordination between primary care and dentistry, in order to facilitate potential future implementation efforts. Well-conducted trials are needed to clarify effectiveness of fluoride supplements and xylitol, particularly when administered outside of supervised school settings. Trials should report water fluoridation levels, oral health behaviors (e.g., tooth brushing, use of fluoridated toothpaste), provision of oral health education, and baseline oral health status, so that the context in which effective interventions are delivered is better understood. Studies should enroll representative populations, including those disproportionately impacted by poor oral health, and focus on higher prevalence settings (e.g., low socioeconomic status, high oral health burdens, and rural and urban underserved settings). Research is needed on the accuracy of questionnaires that can be used for screening in primary care settings to identify children more likely to have or develop dental caries or periodontal disease. In addition to outcomes related to oral health such as caries burden, trials should assess and report outcomes related to quality of life, social and school performance, function, and other health outcomes, as well as harms.

Conclusions

Supervised administration of fluoride supplements in schools and administration of fluoride gels, varnish, and sealants in dental or school settings improved caries outcomes. Research is needed on the effectiveness of these oral health preventive interventions when administered at home or in primary care settings, and to determine the accuracy of primary care screening, and the benefits and harms of screening, as well as the effectiveness of primary care counseling, dental referral, and other oral health preventive interventions.

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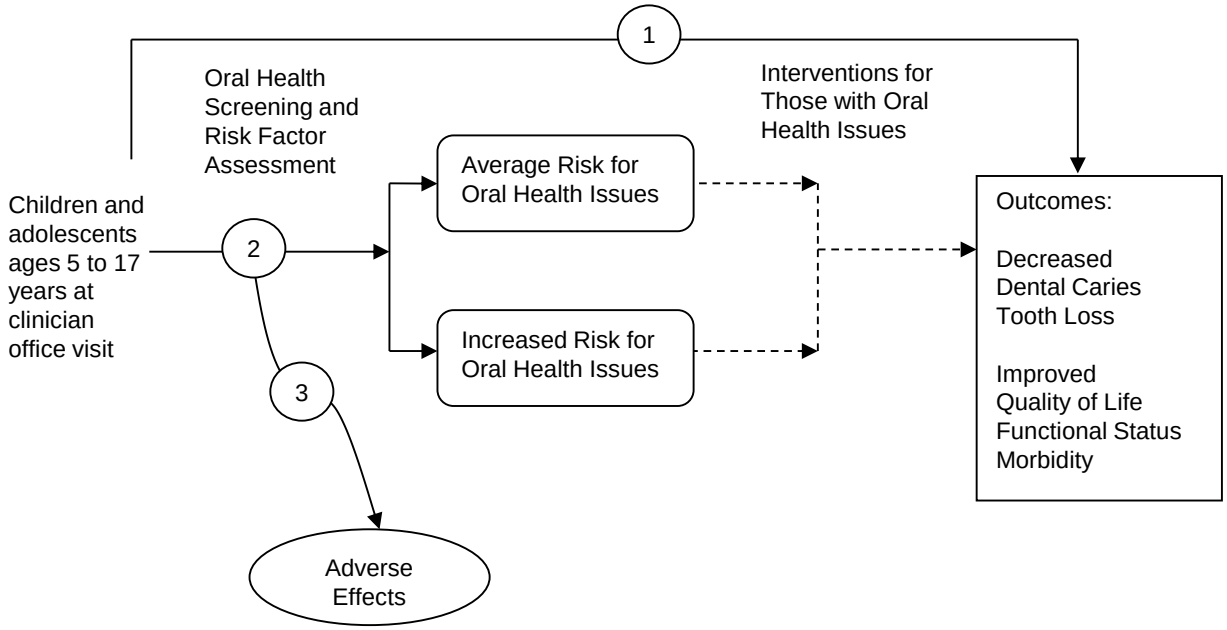
Figure 1. Analytic Framework and Key Questions - Screening for Oral Health in Children and Adolescents Ages 5 to 17 Years

Analytic Framework

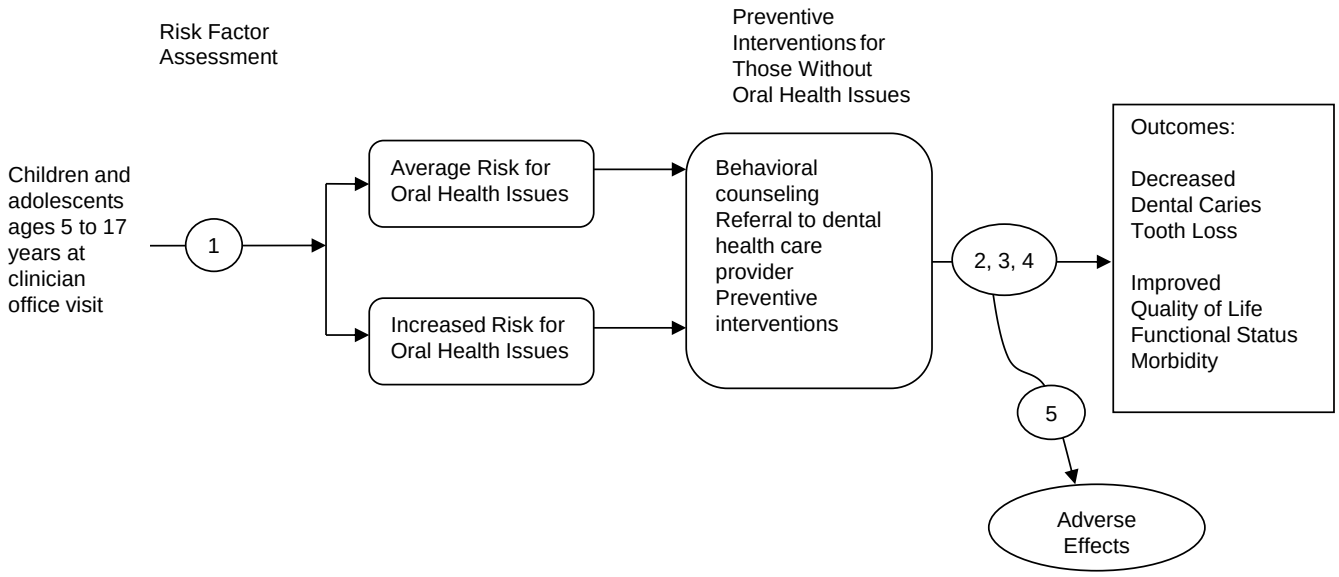


Key Questions

1. How effective is screening for oral health performed by a primary care clinician in preventing negative oral health outcomes?
2. How accurate is screening for oral health performed by a primary care clinician in identifying children and adolescents who:
   a. Have oral health issues?
   b. Are at increased risk of future oral health issues?
3. What are the harms of screening for oral health performed by a primary care clinician?

Figure 2. Analytic Framework and Key Questions - Interventions to Prevent Oral Health Issues in Children and Adolescents Ages 5 to 17 Years

Analytic Framework

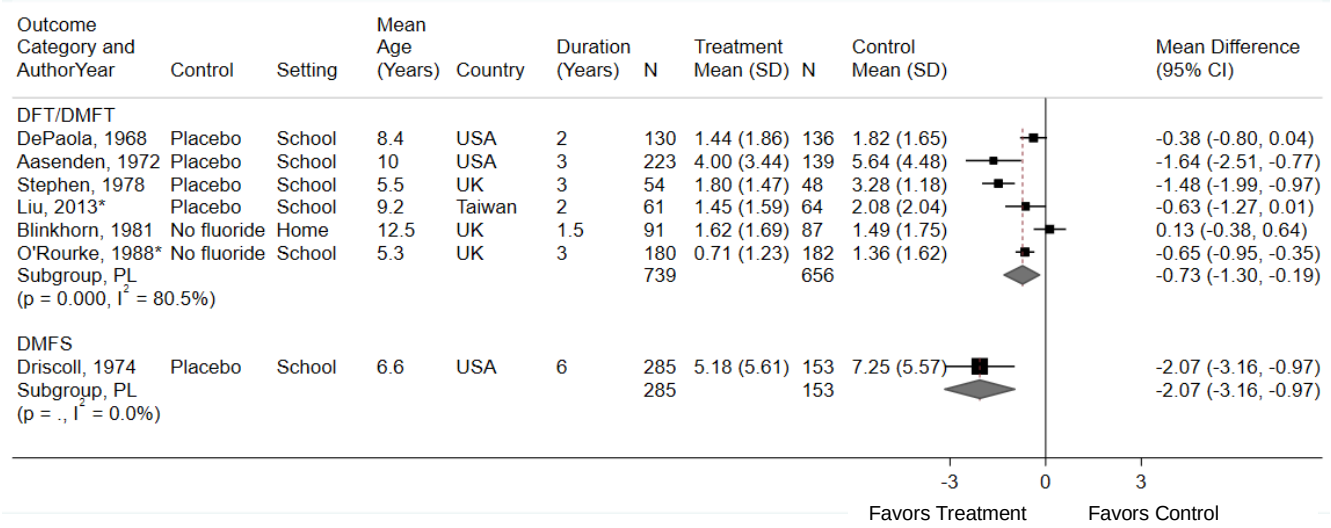


Key Questions

1. How accurate is screening for oral health performed by a primary care clinician in identifying children and adolescents who are at increased risk of future oral health issues?*
2. How effective is oral health behavioral counseling provided by a primary care clinician in preventing oral health issues?
3. How effective is referral by a primary care clinician to a dental health care provider in preventing oral health issues?
4. How effective are preventive interventions in preventing oral health issues?
5. What are the harms of specific interventions (behavioral counseling, referral, and preventive interventions) to prevent oral health issues?

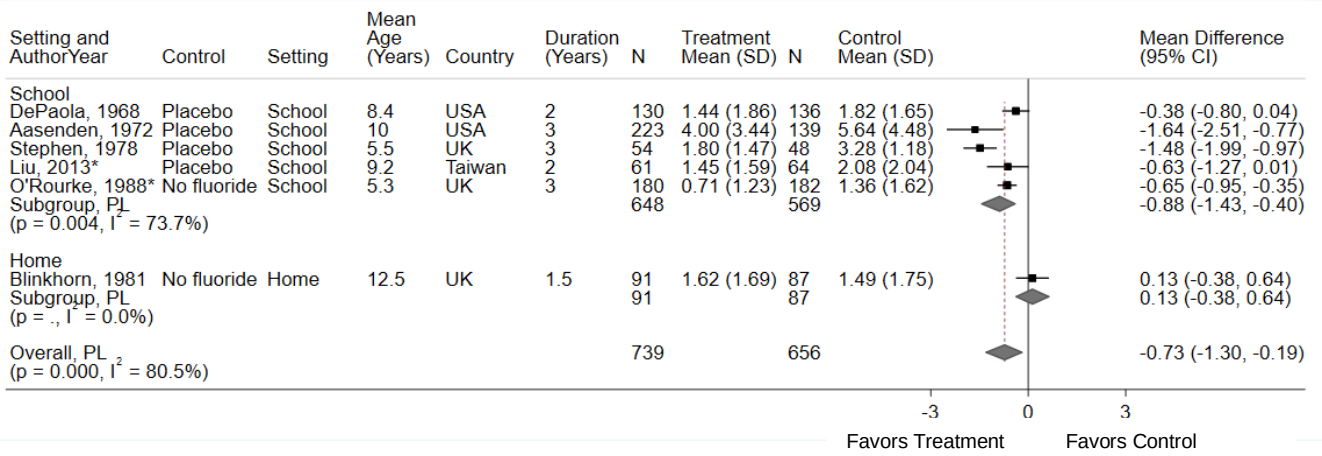
*This is the same as Key Question 2b from the previous Analytic Framework.

Figure 3. Fluoride Supplement vs. No Supplement or Placebo, Caries Increment in Permanent Teeth at 1.5 to 3 Years



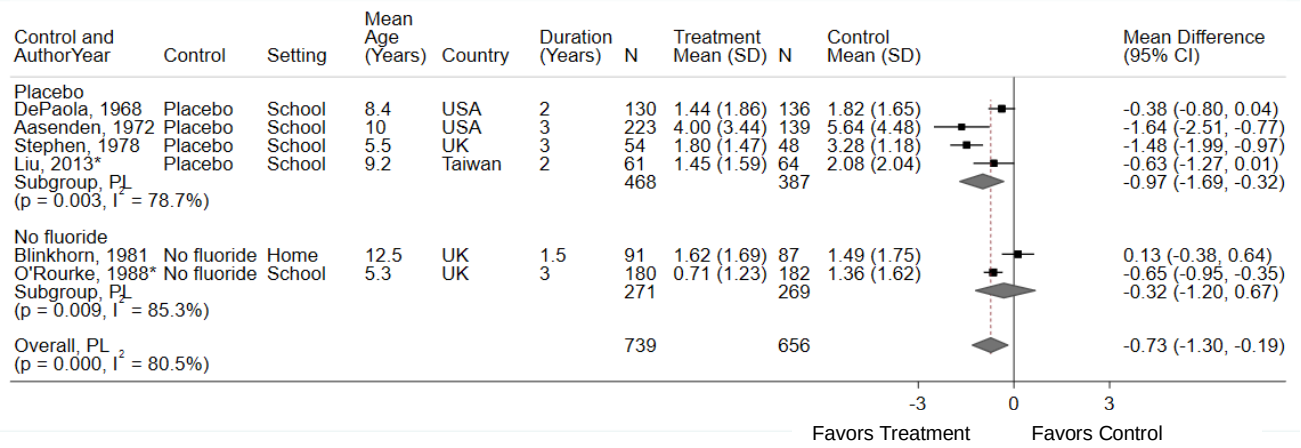
Abbreviations: CI = confidence interval; DFT = Decayed and Filled Teeth; DMFS = Decayed, Missing, and Filled Surfaces; DMFT = Decayed, Missing, and Filled Teeth; PL = profile likelihood; SD = standard deviation; UK = United Kingdom; USA = United States of America.

Figure 4. Fluoride Supplement vs. No Supplement or Placebo, DMFT/DFT Increment, Stratified by Administration Setting



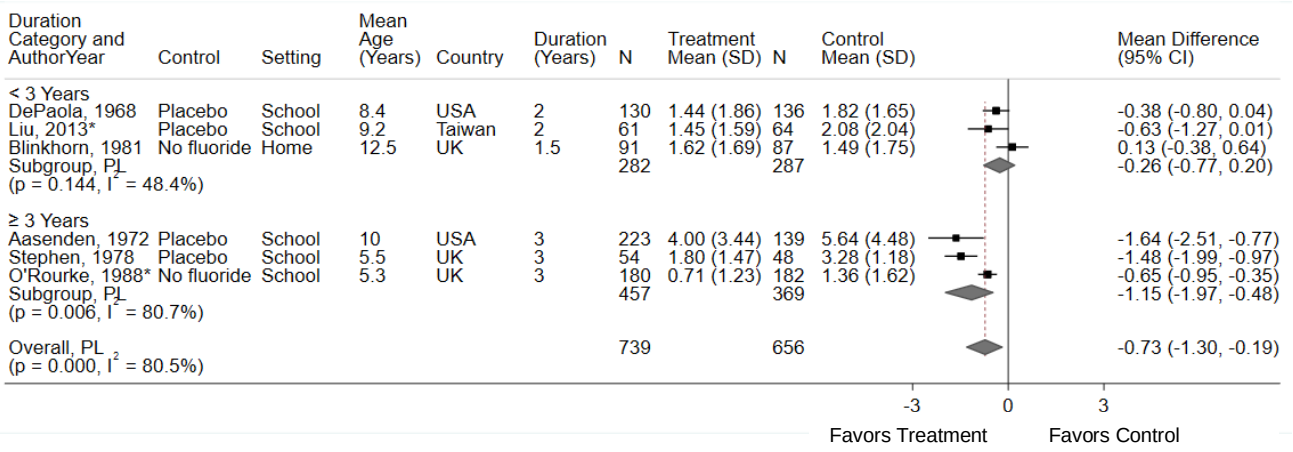
Abbreviations: CI = confidence interval; DFT = Decayed and Filled Teeth; DMFT = Decayed, Missing, and Filled Teeth; PL = profile likelihood; SD = standard deviation; UK = United Kingdom; USA = United States of America.

Figure 5. Fluoride Supplement vs. No Supplement or Placebo, DMFT/DFT Increment, Stratified by Control Type



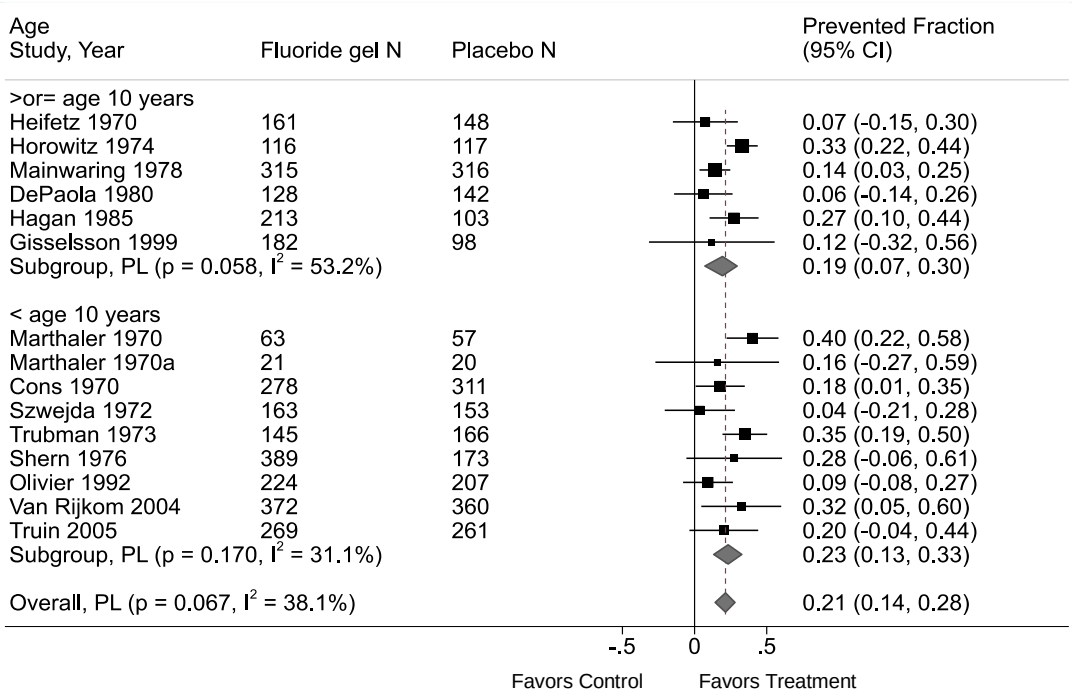
Abbreviations: CI = confidence interval; DFT = Decayed and Filled Teeth; DMFT = Decayed, Missing, and Filled Teeth; PL = profile likelihood; SD = standard deviation; UK = United Kingdom; USA = United States of America.

Figure 6. Fluoride Supplement vs. No Supplement or Placebo, DMFT/DFT Increment, Stratified by Duration of Followup



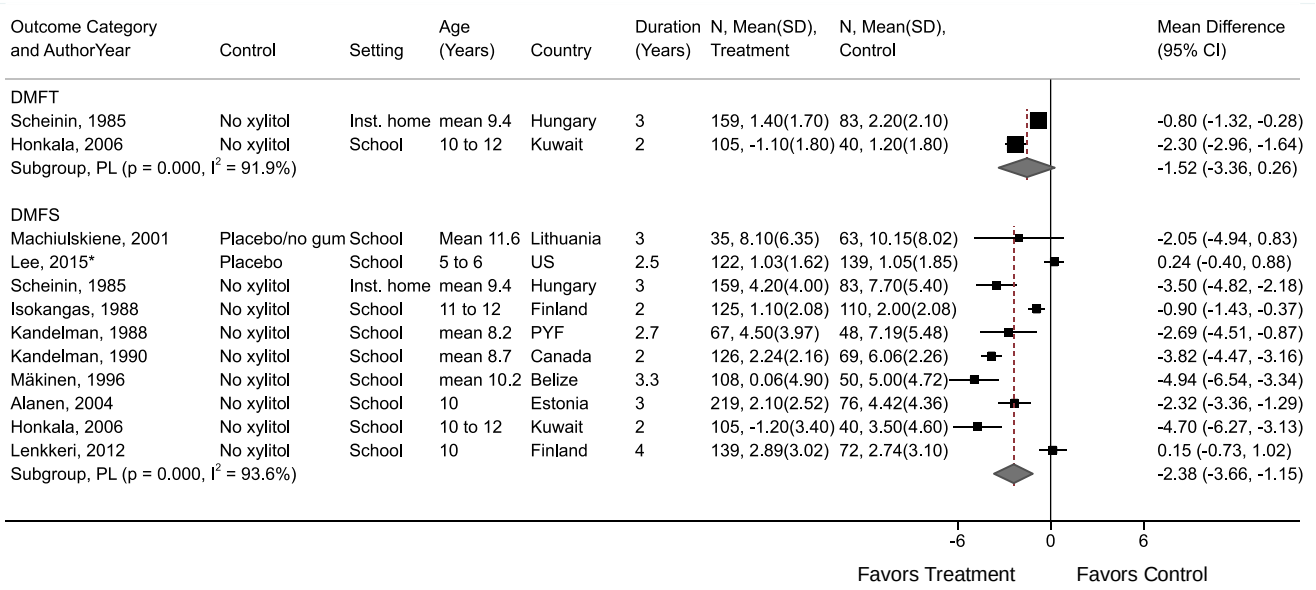
Abbreviations: CI = confidence interval; DFT = Decayed and Filled Teeth; DMFT = Decayed, Missing, and Filled Teeth; PL = profile likelihood; SD = standard deviation; UK = United Kingdom; USA = United States of America.

Figure 7. Fluoride Gel vs. Placebo, DMFS/DFS Prevented Fraction, Stratified by Age ≥10 Years vs. <10 Years



Abbreviations: CI = confidence interval; DFS = Decayed and Filled Surfaces; DMFS = Decayed, Missing, and Filled Surfaces; PL = profile likelihood

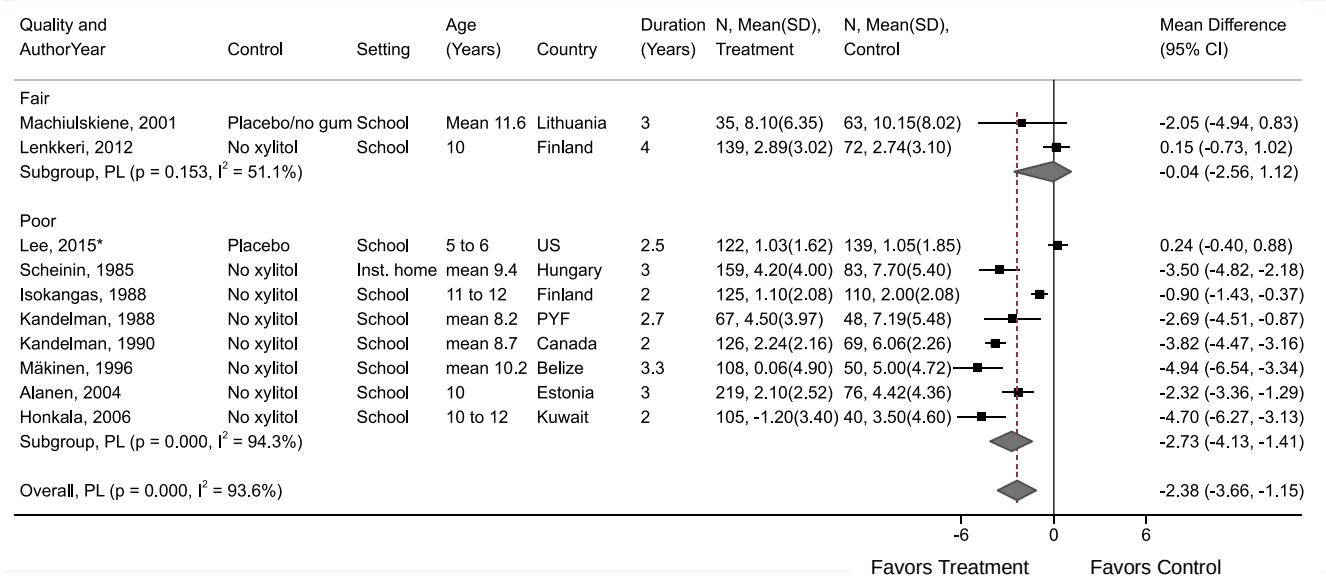
Figure 8. Xylitol vs. No Xylitol or Placebo, DMFS Increment at 2 to 4 Years



*Original sample size, trial reported an estimate that adjusted for clustering; the estimate also adjusted for gender, baseline caries burden, surface-years at risk, and study cohort.

Abbreviations: CI = confidence interval; DMFS = Decayed, Missing, and Filled Surfaces; DMFT = Decayed, Missing, and Filled Teeth; PL= profile likelihood; PYF = French Polynesia; SD = standard deviation.

Figure 9. Xylitol vs. No Xylitol or Placebo, DMFS Increment at 2 to 4 years, Stratified by Trial Quality



*Original sample size; trial reported an estimate that adjusted for clustering.

Abbreviations: CI = confidence interval; DMFS = Decayed, Missing, and Filled Surfaces; PL= profile likelihood; PYF = French Polynesia; SD = standard deviation.

Table 1. Recommendations of Other Groups

Organization	Recommendation
American Dental Association (ADA), 2013-2020[65]	Recommends 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. Recommends against the use of 10% casein phosphopeptide–amorphous calcium phosphate. Found that sealants are effective in preventing and arresting pit-and-fissure occlusal carious lesions of primary and permanent molars in children and adolescents compared with the nonuse of sealants or use of fluoride varnishes. Concluded that sealants could minimize the progression of noncavitated occlusal carious lesions (also referred to as initial lesions) that receive a sealant. Recommends the following for people at risk of developing dental caries: 2.26% fluoride varnish or 1.23% fluoride (acidulated phosphate fluoride) gel, or a prescription-strength, home-use 0.5% fluoride gel or paste or 0.09% fluoride mouth rinse for patients 6 years or older. Only 2.26% fluoride varnish is recommended for children younger than 6 years.
American Academy of Pediatric Dentistry (AAPD), 2016[66]	Advocates that oral health care must be included in the design and provision of individual, community-based, and national health care programs to achieve comprehensive health care. Supports professional prophylaxis to instruct the caregiver and child or adolescent in proper oral hygiene techniques; remove dental plaque, extrinsic stain, and calculus deposits from the teeth; facilitate the examination of hard and soft tissues; and introduce dental procedures to the young child and apprehensive patient. Encourages the application of professional fluoride treatments for all individuals at risk for dental caries. Supports the delegation of fluoride application to auxiliary dental personnel or other trained allied health professionals by prescription or order of a dentist after a comprehensive oral examination or by a physician after a dental screening has been performed. Encourages dental providers to talk to parents and caregivers about the benefits of fluoride and to proactively address fluoride hesitance through chairside and community education. Supports the use of silver diamine fluoride as part of an ongoing caries management plan with the aim of optimizing individualized patient care consistent with the goals of a dental home. Supports delegation of application of silver diamine fluoride to auxiliary dental personnel or other trained health professionals according to a state's dental practice act by prescription or order of a dentist after a comprehensive oral examination. Supports the use of xylitol and other sugar alcohols as non-cariogenic sugar substitutes, recognizing that presently there is a lack of consistent evidence showing significant reductions in MS and dental caries in children. Recognizes that the large dose and high frequency of xylitol used in clinical trials may be unrealistic in clinical practice.
American Academy of Family Physicians (AAFP), 2018[67]	Recommends primary care physicians prescribe oral fluoride supplementation starting at age 6 months for children whose water supply is deficient in fluoride, as well as provide dietary fluoride supplement for children ages 6 months through 16 years in areas where drinking water levels are suboptimal. Recommends physician education in oral condition screening and management, as well as the consequences of poor oral hygiene on overall health, and encourages collaboration of family physicians with dental health practitioners to provide comprehensive medical care.
American Academy of Pediatrics (AAP), 2020[68]	Recommends that pediatricians perform oral health risk assessments on all children at every routine well-child visit beginning at 6 months of age; administration of fluoride varnish at least one every 6 months for all children and every 3 months for children at high risk for caries, starting when the first tooth erupts and until establishment of a dental home; and provision of dietary fluoride supplements if drinking water supply is not fluoridated.

Table 1. Recommendations of Other Groups

Organization	Recommendation
Community Preventive Services Task Force (CPSTF), 2013[186]	Recommends community water fluoridation to reduce tooth decay (strong evidence). Recommends school-based programs to deliver dental sealants and prevent dental caries (tooth decay) among children (strong evidence). Found insufficient evidence to determine the effectiveness of community-based initiatives to promote use of dental sealants. Although strong evidence exists for the efficacy of sealants and their delivery through school-based programs for preventing caries (tooth decay), few studies examined uptake of sealants following community-based promotion initiatives and their results were inconsistent.

Abbreviations: AAFP = American Academy of Family Physicians; AAP = American Academy of Pediatrics; AAPD = American Academy of Pediatric Dentistry; ADA = American Dental Association; CPSTF = Community Preventive Services Task Force.

Table 2. Fluoride Supplements vs. Placebo or No Supplement, DMFT or DFT Increment

Analysis	Number of trials (effective N)*	Mean difference in DMFT or DFT increment (95% CI)	I^2	p for interaction
All trials	6 (1,395)	-0.73 (-1.30 to -0.19)	80%	--
Control type				0.24
• Placebo	4 (855)	-0.97 (-1.69 to -0.32)	79%	--
• No fluoride	2 (540)	-0.32 (-1.20 to 0.67)	85%	--
Administration setting				0.15
• School	5 (1,217)	-0.88 (-1.43 to -0.40)	74%	--
• Home	1 (178)	0.13 (-0.38 to 0.64)	--	--
Age category				0.85
• Mean <10 years	4 (855)	-0.77 (-1.30 to -0.26)	73%	--
• Mean ≥10 years	2 (540)	-0.68 (-2.87 to 1.38)	92%	--
Duration of follow-up				0.09
• <3 years	3 (569)	-0.26 (-0.77 to 0.20)	48%	--
• ≥3 years	3 (826)	-1.15 (-1.97 to -0.48)	81%	--

*After adjustment for clustering (assuming intracluster correlation=0.02).
Abbreviations: CI = confidence interval; DFT = Decayed, Filled Teeth; DMFT = Decayed, Missing, and Filled Teeth.

Table 3. Xylitol vs. Placebo or No Xylitol, DMFS Increment

Analysis	Number of trials (effective N)[#]	Mean difference in DMFS increment (95% CI)	I^2	p for interaction
All trials	10 (1,955)	-2.38 (-3.66 to -1.15)	94%	--
Control type				0.36
• Placebo	2 (328)	0.23 (-0.90 to 1.21)	0%	--
• No xylitol	9 (1,661)	-2.84 (-4.15 to -1.63)	92%	--
Setting				0.57
• School	9 (1,713)	-2.26 (-3.66 to -0.91)	94%	--
• Institutional home	1 (242)	-3.50 (-4.82 to -2.18)	--	--
Age category				0.99
• Mean <10 years	4 (813)	-2.39 (-4.57 to -0.28)	96%	--
• Mean ≥10 years	6 (1,142)	-2.37 (-4.24 to -0.60)	91%	--
Geographic region				0.93
• Europe	5 (1,081)	-1.60 (-3.11 to -0.22)	85%	--
• North America	2 (578)	-1.79 (-6.69 to 3.11)	99%	--
• Other[*]	3 (418)	-4.23 (-5.70 to -2.58)	48%	--
Duration of follow-up				0.88
• <3 years	5 (951)	-2.29 (-3.66 to -1.15)	96%	--
• ≥3 years	5 (1004)	-2.48 (-4.44 to -0.59)	90%	--
Quality				0.22
• Fair	2 (309)	-0.04 (-2.56 to 1.12)	51%	--
• Poor	8 (1,646)	-2.38 (-3.66 to -1.15)	94%	--
Baseline caries burden				0.29
• Low[^]	2 (506)	-1.06 (-4.06 to 1.90)	92%	--
• Not low	8 (925)	-2.74 (-4.19 to -1.34)	94%	--

[*]Kuwait, Belize, and French Polynesia.
[^]D3MFS=0 in 83% of children or mean DMFS=2.01 at baseline.
[#]After adjustment for clustering (assuming intracluster correlation=0.02).
Abbreviations: CI = confidence interval; DMFS = Decayed, Missing, and Filled Surfaces.

Table 4. NHANES Oral Health Data, Years 2011–2016

Outcome	Results
Dental Caries	Prevalence of dental caries in primary teeth in children ages 6-8 years: 52.1% By gender: male vs female: 55.4% vs 48.1% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 43.9% vs 53.8%* vs 72.8%* By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 64.4%* vs 60.1%* vs 40.4% Prevalence of dental caries in permanent teeth (DMFT>or=1) in children ages 6-11 years: 17.4% By age: 6-8 vs 9-11: 9.6% vs 24.7%* By gender: male vs female: 15.6% vs 19.0%* By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 13.4% vs 21.6%* vs 24.5%* By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 24.6%* vs 19.3%* vs 12.0% Prevalence of dental caries in permanent teeth (DMFT>or=1) in adolescents ages 12-19 years: 56.8% By age: 12-15 vs 16-19: 47.6% vs 65.9%* By gender: male vs female: 55.9% vs 57.7% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 54.3% vs 57.1% vs 68.9%* By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 64.9%* vs 65.3%* vs 48.7%
Untreated Tooth Decay	Prevalence of untreated tooth decay in primary teeth (dft>or=1) in children ages 6-8 years: 16.4% By gender: male vs female: 17.4% vs 15.2% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 13.2% vs 22.4%* vs 20.0%* By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 22.3%* vs 20.9%* vs 11.1% Prevalence of untreated tooth decay in permanent teeth (DT>or=1) in children ages 6-11 years: 5.2% By age: 6-8 vs 9-11: 2.7% vs 7.6%* By gender: male vs female: 4.9% vs 5.5% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 4.3% vs 7.1%* vs 7.5%* By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 8.1% vs 5.6% vs 3.5% Prevalence of untreated tooth decay in permanent teeth (DT>or=1) in adolescents ages 12-19 years: 16.6% By age: 12-15 vs 16-19: 12.7% vs 20.4%* By gender: male vs female: 17.7% vs 15.4% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 15.6% vs 0.4%* vs 20.8%* By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 22.7%* vs 20.9%* vs 11.1%
Dental Sealants	Prevalence of dental sealants on permanent teeth in children ages 6-11 years: 41.7% By age: 6-8 vs 9-11: 32.1% vs 50.7% By gender: male vs female: 40.4% vs 42.9% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 43.6% vs 31.7%* vs 44.4% By poverty status (federal poverty level): <100% FPL vs 100-199% FPL vs >or=200% FPL: 37.8%* vs 40.0% vs 44.9% Prevalence of dental sealants on permanent teeth in adolescents ages 12-19 years: 48.1% By age: 12-15 vs 16-19: 51.7% vs 44.5%* By gender: male vs female: 46.8% vs 49.1% By race and ethnicity: Non-Hispanic White vs Non-Hispanic Black vs Mexican American: 53.2% vs 37.2%* vs 45.0%* By poverty status: <100% FPL vs 100-199% FPL vs >or=200% FPL: 42.7%* vs 48.4% 51.1%

Source: CDC Oral Health Surveillance Report 2019[20]

Table 4. NHANES Oral Health Data, Years 2011–2016

Abbreviations: dft = decayed, filled (primary) teeth; DMFT = Decayed, Missing, and Filled Teeth; DT = decayed teeth; FPL = Federal poverty level; NHANES = National Health Nutrition and Examination Survey.
* $p<0.05$ based on t-test for differences between two periods or two groups within each characteristic.

Table 5. Summary of Evidence - Oral Health in Children and Adolescents Ages 5 to 17 Years

Analytic Framework	Key question	Number of studies (k) participants (n) Study design	Summary of findings by outcome	Consistency/ precision Reporting bias	Overall quality	Body of evidence limitations	Strength of evidence	Applicability
Screening	KQ 1 Screening effectiveness	No studies	--	--	--	--	--	--
	KQ 2 Screening accuracy a. In persons who have oral health issues b. In persons who are at increased risk for future oral health issues	a. k=1 cross-sectional study n=305 b. No studies	Visual screen by registered nurse: sensitivity 0.92 (95% CI 0.84 to 0.97) and specificity 0.993 (95% CI 0.96 to 0.9998) for untreated caries 17-item questionnaire: sensitivity 0.69 (95% CI 0.60 to 0.77) and specificity 0.88 (95% CI 0.83 to 0.93) for untreated caries	Unable to assess consistency (1 study) Reasonably precise Reporting bias: Not detected	Fair	Single study with methodological limitations; results unvalidated	Low	Nurses received 5 hours of training; questionnaire based on report by children's parents or guardians; study conducted in rural setting with high prevalence of untreated caries (35%)
	KQ 3 Screening harms	No studies	--	--	--	--	--	--
Prevention	KQ 1 Screening accuracy* (identification of persons at risk for future caries)	No studies	--	--	--	--	--	--
	KQ 2 Behavioral counseling	No studies	--	--	--	--	--	--
	KQ 3 Referral	No studies	--	--	--	--	--	--

Table 5. Summary of Evidence - Oral Health in Children and Adolescents Ages 5 to 17 Years

Analytic Framework	Key question	Number of studies (k) participants (n) Study design	Summary of findings by outcome	Consistency/ precision Reporting bias	Overall quality	Body of evidence limitations	Strength of evidence	Applicability
Prevention	KQ 4 Preventive interventions *Supplements*	k=7 trials N=3,382	Fluoride supplements were associated with decreased DMFT/DFT increment at 1.5 to 3 years (mean difference -0.73, 95% CI -1.30 to -0.19; 6 trials) when administered in schools under supervision; however, the only trial in which fluoride supplements were administered at home reported low adherence and no benefit (mean difference 0.13, 95% CI -0.38 to 0.64).	Serious inconsistency No imprecision Reporting bias: Not suspected	Fair	All trials had methodological limitations; substantial statistical heterogeneity	Low	Supplements administered in school under supervision in all trials except 1; all trials published prior to 1990 except for 1; no trial of adolescents an all trials but 1 focused on children <10 years of age; trials conducted in high caries burden, low socioeconomic status, or low fluoridation settings; six trials conducted in the U.S. or U.K. and 1 trial conducted in Taiwan
	KQ 4 Preventive interventions *Fluoride gel*	k=1 SR (26 trials) and 1 subsequent RCT N=8,619 (SR) + 986 (subsequent RCT)	A SR found fluoride gels associated DMFT/DFT prevented fraction at outcomes closest to 3 years of 0.32 (95% CI 0.19 to 0.46; I^2=91% [10 trials, N=3,198]; based on 4 placebo-controlled trials [N=1,525], the prevented fraction was 0.18, 95% CI, 0.09 to 0.27; I^2=6%). One subsequent trial reported consistent results.	Consistent (based on placebo-controlled trials) No imprecision Reporting bias: Not suspected	Fair	Most trials had methodological limitations; statistical heterogeneity when all (placebo- and non-placebo-controlled) trials pooled; few placebo-controlled trials	Moderate	18 trials conducted in the United States, Europe, or Canada; only 1 trial focused on adolescents; gels were applied by dental professional or under supervision and applied in dental clinics or schools; limited reporting of water fluoridation levels and socioeconomic status; most trials conducted in high caries burden settings; 22 trials published prior to 1990

Table 5. Summary of Evidence - Oral Health in Children and Adolescents Ages 5 to 17 Years

Analytic Framework	Key question	Number of studies (k) participants (n) Study design	Summary of findings by outcome	Consistency/ precision Reporting bias	Overall quality	Body of evidence limitations	Strength of evidence	Applicability
Prevention	KQ 4 Preventive interventions *Fluoride varnish*	k=1 SR (14 trials) and 1 subsequent RCT N=6,965 (SR) + 5,397 (subsequent RCT)	A SR found fluoride varnish associated with DMFS/DFS prevented fraction of 0.43 (95% CI 0.30 to 0.57; 14 trials), DMFT/DFT prevented fraction of 0.44 (95% CI 0.11 to 0.76; 5 trials); and reduced risk of developing ≥1 caries (RR 0.75, 95% CI 0.53 to 1.05; I^2=89.2%; 5 trials). One subsequent trial reported results consistent with the SR.	Some inconsistency present No imprecision Reporting bias: Not suspected	Fair	Most trials had methodological limitations; statistical heterogeneity present	Moderate	9 trials conducted in Europe (no trials conducted in the United states); no trial focused on adolescents; varnish applied by dental professionals at school or in dental clinics; limited reporting of water fluoridation levels and socioeconomic status; 7 trials published prior to 1998
	KQ 4 Preventive interventions *Sealants*	Resin-based sealant: k=1 SR (15 RCTs) N=4,195 (15 RCTs) and 1 supplemental RCT, n=50 Glass ionomer sealant: k=1 SR (3 RCTs) and 2 subsequent RCTs N=905 (SR) + 237 (RCTs)	Resin-based sealants: A SR found resin-based sealants associated with decreased risk of carious first molars at 24 months (7 trials, OR 0.12, 95% CI 0.08 to 0.19), 36 months (7 trials, OR 0.17, 95% CI 0.11 to 0.27, I^2=90%) and 48 to 54 months (4 trials, OR 0.21, 95% CI 0.16 to 0.28, I^2=45%). Glass ionomer sealants: A SR (2 trials) and 1 subsequent trial found inconsistent effects of glass ionomer sealants versus no sealants on caries outcomes.	Resin-based sealants: No inconsistency No imprecision Glass ionomer sealants: Serious inconsistency Serious imprecision Reporting bias (all sealants): Not suspected	Fair	Open-label design; few trials of glass ionomer sealants	Moderate	9 trials conducted in the U.S., Europe, Canada, or New Zealand; limited information on socioeconomic status and fluoridation levels; higher caries burden settings; variability in sealants evaluated; 10 trials published prior to 1996; sealants applied by dental professionals

Table 5. Summary of Evidence - Oral Health in Children and Adolescents Ages 5 to 17 Years

Analytic Framework	Key question	Number of studies (k) participants (n) Study design	Summary of findings by outcome	Consistency/ precision Reporting bias	Overall quality	Body of evidence limitations	Strength of evidence	Applicability
Prevention	KQ 4 Preventive interventions *SDF*	k=1 RCT n=452	SDF associated with fewer new surfaces with active caries in deciduous dentition (mean 0.3 vs. 1.4, p<0.001) and first permanent molars (mean 0.4 vs. 1.1, p<0.001), and decreased likelihood of ≥1 new decayed or filled teeth (26.1% vs. 49.7%, RR 0.52, 95% CI 0.40 to 0.70)	Unable to assess consistency (1 trial) No imprecision Reporting bias: Not suspected	Fair	One trial with methodological limitations	Low	Trial conducted in Cuba in high caries burden setting in children 6 years of age; training of person administering SDF not reported; children received oral health education and performed fluoride mouth rinses
	KQ 4 Preventive interventions *Xylitol*	k=10 trials N=4,267	1 fair-quality trial found no difference between xylitol versus no xylitol in caries outcomes at 4 years, and one fair-quality trial found no difference between xylitol versus placebo in DMFS increment at 3 years, but decreased DMFS increment versus no xylitol 8 other trials found xylitol associated with reduced DMFS increment versus no xylitol (mean difference -2.38, 95% CI -3.66 to -1.15), but had serious methodological limitations and were rated poor-quality	Some inconsistency No imprecision Reporting bias: Not suspected	Fair (based on fair-quality trials)	Only 2 fair-quality trials; potential differences in outcomes based on control type	Low	6 trials conducted in Europe (no trials in the United States); no trial focused on adolescents; xylitol administered under supervision at school in all trials except 1; four trials published in or prior to 1991; fluoride exposure varied information on SES not provided

Table 5. Summary of Evidence - Oral Health in Children and Adolescents Ages 5 to 17 Years

Analytic Framework	Key question	Number of studies (k) participants (n) Study design	Summary of findings by outcome	Consistency/ precision Reporting bias	Overall quality	Body of evidence limitations	Strength of evidence	Applicability
Prevention	KQ 5 Harms of preventive interventions	Supplements: k=1 trial N=349 Gel: k=2 trials N=490 Varnish: k=6 trials N=8,574 Sealants: k=3 trials N=775 SDF: k=1 trial N=452 Xylitol: k=1 trial N=296	Supplements: 1 trial reported no AEs Gels: No difference between gel versus placebo or no treatment in acute toxicity (nausea, gagging, or vomiting): absolute risk difference 0.01 (95% CI -0.01 to 0.02) Varnish: 5 trials reported no AEs and 1 trial reported 0.04% of children allocated to varnish reported a self-limited AE (most commonly, nausea), with 4 withdrawals due to mild AEs Sealants: 3 trials of resin-based sealants reported no AEs SDF: SDF associated with increased likelihood of inactive caries and black stain in deciduous teeth (97% vs. 48%, p<0.001) and first permanent molars (86% vs. 67%, p<0.001) Xylitol: 1 trial reported one withdrawal from xylitol due to diarrhea	Consistency uncertain, due to sparse data Serious imprecision Potential reporting bias, as few trials reported harms	Poor	Few trials reported harms or harms reporting was suboptimal	Low	Evidence on harms was very sparse, limiting assessments of applicability

Table 5. Summary of Evidence - Oral Health in Children and Adolescents Ages 5 to 17 Years

*This is the same as KQ 2b from the screening framework.
Abbreviations: AE = adverse events; CI = confidence interval; DFS = Decayed and Filled Surfaces; DMFS = Decayed, Missing, and Filled Surfaces; DFT = Decayed and Filled Teeth; DMFT = Decayed, Missing, and Filled Teeth; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; SDF = silver diamine fluoride; SES = socioeconomic status; SR = systematic review; U.K. = United Kingdom; U.S. = United States.

Overall

Database: EBM Reviews - Cochrane Database of Systematic Reviews

1 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti.
2 limit 1 to full systematic reviews
3 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti.
4 2 and 3

Screening

Database: Ovid MEDLINE(R) ALL (Systematic Reviews)

1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab,kf.
6 or/1-5
7 Mass Screening/
8 screen*.ti,ab,kf.
9 Risk Assessment/
10 Risk Factors/
11 risk.ti,ab,kf.
12 or/7-11
13 6 and 12
14 limit 13 to (meta analysis or "systematic review")
15 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,kf,sh.
16 14 and 15
17 limit 16 to english language
18 14 not 15
19 limit 18 to english language
20 from 19 keep 1-1844

Database: EBM Reviews - Cochrane Central Register of Controlled Trials

1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab.
6 or/1-5
7 Mass Screening/
8 screen*.ti,ab.
9 Risk Assessment/
10 Risk Factors/

11 risk.ti,ab.
12 or/7-11
13 6 and 12
14 conference abstract.pt.
15 "journal: conference abstract".pt.
16 "journal: conference review".pt.
17 "http://.www.who.int/trialsearch*".so.
18 "https://clinicaltrials.gov*".so.
19 14 or 15 or 16 or 17 or 18
20 13 not 19
21 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,sh.
22 20 and 21

Database: Ovid MEDLINE(R) ALL

1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab,kf.
6 or/1-5
7 Mass Screening/
8 screen*.ti,ab,kf.
9 Risk Assessment/
10 Risk Factors/
11 risk.ti,ab,kf.
12 or/7-11
13 Primary Health Care/
14 ("primary care" or "general practic*" or "family medicine" or "family practic*").ti,ab,kf.
15 13 or 14
16 6 and 12 and 15
17 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,kf,sh.
18 16 and 17

Database: Ovid MEDLINE(R) ALL

1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab,kf.
6 or/1-5
7 Mass Screening/
8 screen*.ti,ab,kf.
9 Risk Assessment/
10 Risk Factors/

11 risk.ti,ab,kf.
12 or/7-11
13 6 and 12
14 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,kf,sh.
15 13 and 14
16 exp "Sensitivity and Specificity"/
17 (diagnos* adj2 accura*).ti,ab,kf.
18 16 or 17
19 15 and 18
20 limit 15 to randomized controlled trial
21 (random* or control* or trial or cohort).ti,ab.
22 15 and 21
23 19 or 20 or 22

Interventions

Database: Ovid MEDLINE(R) ALL (Systematic Reviews)

1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab,kf.
6 or/1-5
7 Counseling/
8 health education/ or health education, dental/ or health promotion/ or patient education as topic/
9 exp Cariostatic Agents/
10 "Pit and Fissure Sealants"/
11 exp Dentifrices/
12 Xylitol/
13 "Referral and Consultation"/
14 (counsel* or education or fluoride or "silver diamine" or sealant* or xylitol or referral).ti,ab,kf.
15 or/7-14
16 6 and 15
17 limit 16 to (meta analysis or "systematic review")
18 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,kf,sh.
19 17 and 18
20 17 not 19
21 limit 20 to english language
22 limit 19 to english language

Database: EBM Reviews - Cochrane Central Register of Controlled Trials

1 Oral Health/
2 Mouth Diseases/

3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab.
6 or/1-5
7 Counseling/
8 health education/ or health education, dental/ or health promotion/ or patient education as topic/
9 exp Cariostatic Agents/
10 "Pit and Fissure Sealants"/
11 exp Dentifrices/
12 Xylitol/
13 "Referral and Consultation"/
14 (counsel* or education or fluoride or "silver diamine" or sealant* or xylitol or referral).ti,ab.
15 or/7-14
16 6 and 15
17 limit 16 to english language
18 conference abstract.pt.
19 "journal: conference abstract".pt.
20 "journal: conference review".pt.
21 "http://.www.who.int/trialsearch*".so.
22 "https://clinicaltrials.gov*".so.
23 18 or 19 or 20 or 21 or 22
24 17 not 23
25 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,sh.
26 24 and 25

Database: Ovid MEDLINE(R) ALL
1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab,kf.
6 or/1-5
7 Counseling/
8 health education/ or health education, dental/ or health promotion/ or patient education as topic/
9 exp Cariostatic Agents/
10 "Pit and Fissure Sealants"/
11 exp Dentifrices/
12 Xylitol/
13 "Referral and Consultation"/
14 (counsel* or education or fluoride or "silver diamine" or sealant* or xylitol or referral).ti,ab,kf.

15 or/7-14
16 Primary Health Care/
17 ("primary care" or "general practic*" or "family medicine" or "family practic*").ti,ab,kf.
18 16 or 17
19 6 and 15 and 18
20 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,kf,sh.
21 19 and 20
22 limit 21 to english language

Database: Ovid MEDLINE(R) ALL

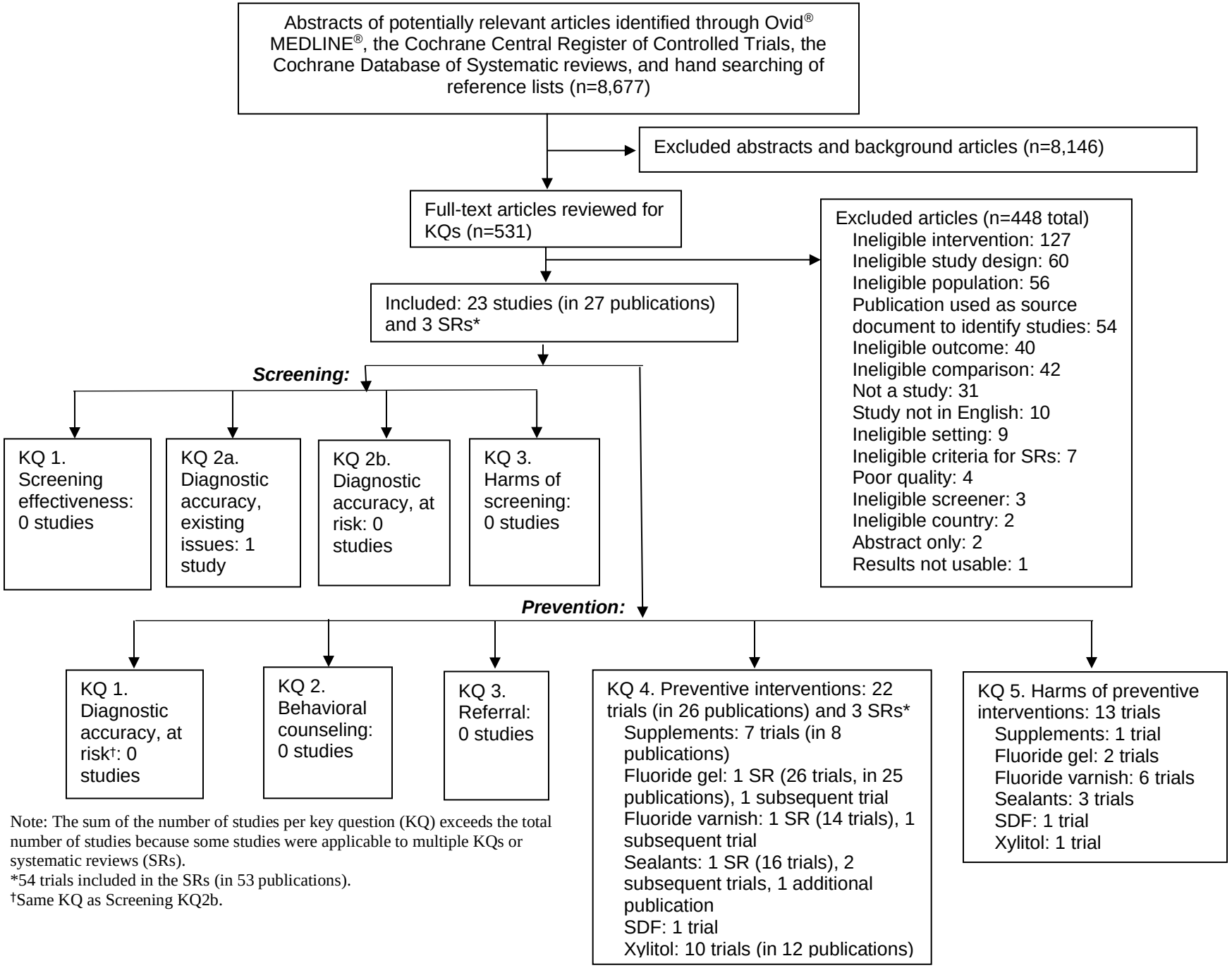
1 Oral Health/
2 Mouth Diseases/
3 exp Periodontal Diseases/
4 exp Tooth Diseases/
5 ("oral health" or "oral disease*" or "dental caries" or "tooth decay" or "periodontal disease" or periodontitis or gingivitis or "gum disease").ti,ab,kf.
6 or/1-5
7 Counseling/
8 health education/ or health education, dental/ or health promotion/ or patient education as topic/
9 exp Cariostatic Agents/
10 "Pit and Fissure Sealants"/
11 exp Dentifrices/
12 Xylitol/
13 "Referral and Consultation"/
14 (counsel* or education or fluoride or "silver diamine" or sealant* or xylitol or referral).ti,ab,kf.
15 or/7-14
16 6 and 15
17 (child* or pediatric* or youth or teen* or adolescen* or "school age*").ti,ab,kf,sh.
18 16 and 17
19 limit 18 to randomized controlled trial
20 (random* or control* or trial or cohort).ti,ab,kf.
21 18 and 20
22 19 or 21

Appendix A2. Inclusion and Exclusion Criteria

Category	Included	Excluded
Populations	Asymptomatic children starting at age 5 years through adolescents age 17 years Populations of interest include groups defined by: age (those with deciduous teeth vs. permanent dentition), sex, socioeconomic status, race/ethnicity, educational attainment, and health literacy	Children younger than age 5 years (this population is addressed in a separate USPSTF recommendation) Adults age 18 and older (this population is addressed in a separate USPSTF recommendation)
Interventions	Screening: • Oral examination/clinical assessment by a primary care provider • Risk assessment by a primary care provider for dental caries based on history, examination, standardized risk-assessment instrument, or some combination thereof Preventive interventions: • Behavioral counseling/education by a primary care provider • Preventive medications (topical fluoride [varnish, foam, or gel], oral fluoride supplementation, silver diamine fluoride, dental sealants, and xylitol-containing products) that are feasible to be administered by a primary care provider • Referral of persons deemed at high risk for oral diseases by a primary care provider to a dental care health provider	Treatment for existing oral health issues
Comparisons	No intervention or placebo	Active treatment
Outcomes	Dental caries (incidence and severity) Tooth loss Morbidity Quality of life Functional status Harms of screening and treatment (e.g., dental fluorosis, tooth staining, bone effects, and neurological effects)	Cost effectiveness
Setting	Primary care or applicable to U.S. primary care practice (e.g., screening or preventive interventions do not require specialized dental training or equipment and are feasible for implementation in primary care); includes tele-dentistry approaches based in primary care settings	Dental clinics providing interventions not available in primary care settings
Study Design	Screening: Trials and cohort studies Preventive interventions: Trials; large cohort studies for selected harms (e.g., dental fluorosis) Risk assessment: Studies of diagnostic accuracy or risk prediction	Case-control studies or uncontrolled studies
Study Quality	Good or fair quality	Poor quality

Abbreviations: U.S. = United States; USPSTF = U.S. Preventive Services Task Force.

Appendix A3. Literature Flow Diagram



Note: The sum of the number of studies per key question (KQ) exceeds the total number of studies because some studies were applicable to multiple KQs or systematic reviews (SRs).
*54 trials included in the SRs (in 53 publications).
†Same KQ as Screening KQ2b.

Appendix A4. List of Included Studies

1. Aasenden R, DePaola PF, Brudevold F. Effects of daily rinsing and ingestion of fluoride solutions upon dental caries and enamel fluoride. Arch Oral Biol. 1972 Dec;17(12):1705-14. doi: 10.1016/0003-9969(72)90233-6. PMID: 4405216.

2. Ahovuo-Saloranta A, Forss H, Walsh T, et al. Pit and fissure sealants for preventing dental decay in permanent teeth. Cochrane Database Syst Rev. 2017 07 31;7:CD001830. doi: 10.1002/14651858.CD001830.pub5. PMID: 28759120.

Trials Included in Ahouvo-Saloranta 2017 Systematic Review:

Bojanini J, Garces H, McCune RJ, et al. Effectiveness of pit and fissure sealants in the prevention of caries. J Prev Dent. 1976 Nov-Dec;3(6):31-4. PMID: 1069846.

Bravo M, Montero J, Bravo JJ, et al. Sealant and fluoride varnish in caries: a randomized trial. J Dent Res. 2005;84(12):1138-43. doi: 10.1177/154405910508401209. PMID: 16304443.

Brooks JD, Mertz-Fairhurst EJ, Della-Giustina VE, et al. A comparative study of two pit and fissure sealants: two-year results in Augusta, Ga. J Am Dent Assoc. 1979 May;98(5):722-5. doi: 10.14219/jada.archive.1979.0149. PMID: 374449.

Charbeneau GT, Dennison JB. Clinical success and potential failure after single application of a pit and fissure sealant: a four-year report. J Am Dent Assoc. 1979 Apr;98(4):559-64. doi: 10.14219/jada.archive.1979.0112. PMID: 372286.

Erdogan B, Alaçam T. Evaluation of a chemically polymerized pit and fissure sealant: results after 4.5 years. J Paediatr Dent. 1987;3:11-3.

Hunter PB. A study of pit and fissure sealing in the School Dental Service. N Z Dent J. 1988 Jan;84(375):10-2. PMID: 3133616.

Liu BY, Lo EC, Chu CH, et al. Randomized trial on fluorides and sealants for fissure caries prevention. J Dent Res. 2012;91(8):753-8. doi: 10.1177/0022034512452278. PMID: 22736448.

Liu Y, Rong W, Zhao X, et al. [Caries prevention effect of resin based sealants and glass ionomor sealants]. Chung Hua Kou Chiang Hsueh Tsa Chih. 2014 Apr;49(4):199-203. PMID: 24969592.

Muller-Bolla M, Lupi-Pegurier L, Bardakjian H, et al. Effectiveness of school-based dental sealant programs among children from low-income backgrounds in France: a pragmatic randomized clinical trial. Community Dent Oral Epidemiol. 2013;41(3):232-41. doi: 10.1111/cdoe.12011. PMID: 23072366.

Reisbick MH, Thanos CE, Berson RB, et al. Benefit from sealants in a moderately fluoridated community. CDA J. 1982 Jan;10(1):53-6. PMID: 6213312.

Richardson AS, Waldman R, Gibson GB, et al. The effectiveness of a chemically polymerized sealant in preventing occlusal caries: two year results. Dent J. 1978 Jun;44(6):269-72. PMID: 277401.

Rock WP, Gordon PH, Bradnock G. The effect of operator variability and patient age on the retention of fissure sealant resin. Br Dent J. 1978 Aug 1;145(3):72-5. doi: 10.1038/sj.bdj.4804121. PMID: 278624.

Sheykholeslam Z, Houpt M. Clinical effectiveness of an autopolymerized fissure sealant after 2 years. Community Dent Oral Epidemiol. 1978;6(4):181-4. doi: 10.1111/j.1600-0528.1978.tb01146.x. PMID: 278700.

Songpaisan Y, Bratthall D, Phantumvanit P, et al. Effects of glass ionomer cement, resin-based pit and fissure sealant and HF applications on occlusal caries in a developing country field trial. Community Dent Oral Epidemiol. 1995;23(1):25-9. doi: 10.1111/j.1600-0528.1995.tb00193.x. PMID: 7774173.

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7. Driscoll WS, Heifetz SB, Korts DC. Effect of acidulated phosphate-fluoride chewable tablets on dental caries in schoolchildren: results after 30 months. J Am Dent Assoc. 1974 Jul;89(1):115-20. doi: 10.14219/jada.archive.1974.0338. PMID: 4151915.

8. Driscoll WS, Heifetz SB, Korts DC. Effect of chewable fluoride tablets on dental caries in schoolchildren: results after six years of use. J Am Dent Assoc. 1978;97(5):820-4. PMID: 102674.

9. Hesse D, Guglielmi CAB, Raggio DP, et al. Atraumatic Restorative Treatment-Sealed versus Nonsealed First Permanent Molars: a 3-Year Split-Mouth Clinical Trial. Caries Res. 2021; 55(1):12-20. doi: 10.1159/000506466. PMID: 33326970.

10. Honkala E, Honkala S, Shyama M, et al. Field trial on caries prevention with xylitol candies among disabled school students. Caries Res. 2006;40(6):508-13. doi: 10.1159/000095650. PMID: 17063022.

11. Isokangas P, Alanen P, Tiekso J, et al. Xylitol chewing gum in caries prevention: a field study in children. J Am Dent Assoc. 1988 Aug;117(2):315-20. doi: 10.1016/s0002-8177(88)72017-6. PMID: 3166474.

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16. Liu HY, Hung HC, Hsiao SY, et al. Impact of 24-month fluoride tablet program on children with disabilities in a non-fluoridated country. Res Dev Disabil. 2013;34(9):2598-605. PMID: 23747945.

17. Llodra JC, Rodriguez A, Ferrer B, et al. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. J Dent Res. 2005;84(8):721-4. doi: 10.1177/154405910508400807. PMID: 16040729.

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20. Marinho CCV, Worthington HV, Walsh T, et al. Fluoride gels for preventing dental caries in children and adolescents. Cochrane Database Syst Rev. 2015(2)doi: 10.1002/14651858.CD002280.pub2. PMID: 26075879.

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Abadia S. Prevenção da cárie dentária através da aplicaçãotópica de gel de flúor fosfato ácido, utilizando-se isolamentorelativo e absoluto. Baurú (SP): Universidade de São Paulo. 1978.

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Trials Included in Marinho 2013 Systematic Review:

Arruda AO, Senthamarai Kannan R, Inglehart MR, et al. Effect of 5% fluoride varnish application on caries among school children in rural Brazil: a randomized controlled trial. Community Dent Oral Epidemiol. 2012;40(3):267-76. PMID: 22150341.

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Hardman MC, Davies GM, Duxbury JT, et al. A cluster randomised controlled trial to evaluate the effectiveness of fluoride varnish as a public health measure to reduce caries in children. Caries Res. 2007;41(5):371-6. doi: 10.1159/000104795. PMID: 17713337.

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Tagliaferro EP, Pardi V, Ambrosano GM, et al. Occlusal caries prevention in high and low risk schoolchildren. A clinical trial. Am J Dent. 2011;24(2):109-14. PMID: 21698991.

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23. O'Rourke CA, Attrill M, Holloway PJ. Cost appraisal of a fluoride tablet programme to Manchester primary schoolchildren. Community Dent Oral Epidemiol. 1988 Dec;16(6):341-4. doi: 10.1111/j.1600-0528.1988.tb00578.x. PMID: 3144446.

24. Rim KH, Jong MC, Hwang CJ, et al. Preventive effect of subacidic 1% NaF-HF gel on dental caries in 6- to 7-year-old schoolchildren: a randomized controlled trial. Quintessence Int 0(0):318-26. doi: 10.3290/j.qi.b912653. PMID: 33491385.

25. Scheinin A, Banoczy J. Xylitol and caries: the collaborative WHO oral disease preventive programme in Hungary. Int Dent J. 1985 Mar;35(1):50-7. PMID: 3858229.

26. Scheinin A, Bánóczy J, Szöke J, et al. Collaborative WHO xylitol field studies in Hungary. I. Three-year caries activity in institutionalized children. Acta Odontol Scand. 1985 Dec;43(6):327-47. doi: 10.3109/00016358509046517. PMID: 3879082.

27. Scheinin A, Pienihakkinen K, Tiekso J, et al. Collaborative WHO xylitol field studies in Hungary. VII. Two-year caries incidence in 976 institutionalized children. Acta Odontol Scand. 1985 Dec;43(6):381-7. doi: 10.3109/00016358509046523. PMID: 3879087.

28. Stephen KW, Campbell D. Caries reduction and cost benefit after 3 years of sucking fluoride tablets daily at school. A double-blind trial. Br Dent J. 1978;144(7):202-6. PMID: 416842.

29. Uzel I, Gurlek C, Kuter B, Ertugrul F, Eden E. Caries-Preventive Effect and Retention of Glass-Ionomer and Resin-Based Sealants: A Randomized Clinical Comparative Evaluation. Biomed Res Int. 2022 Jun 20;2022:7205692. doi: 10.1155/2022/7205692. PMID: 35769675.

30. Wang Z, Rong W, Xu T. Effect of Fluoride Varnish in Caries Prevention on Permanent First Molars: a 36-Month Cluster Randomized Controlled Trial. Pediatr Dent. 2021;43(2):82-7. PMID: 33892830.

Appendix A5. List of Excluded Studies

1. Adair PM, Burnside G, Pine CM. Analysis of health behaviour change interventions for preventing dental caries delivered in primary schools. Caries Research. 2013;47 Suppl 1(Suppl 1):2-12. doi: 10.1159/000351829. PMID: 24107603. **Exclusion reason:** Ineligible intervention
2. Adair SM. Evidence-based use of fluoride in contemporary pediatric dental practice. Pediatric dentistry. 2006 Mar-Apr;28(2):133-42; discussion 92-8. PMID: 16708788. **Exclusion reason:** Not a study
3. Agrawal N, Pushpanjali K. Feasibility of including APF gel application in a school oral health promotion program as a caries-preventive agent: a community intervention trial. J Oral Sci. 2011;53(2):185-91. doi: 10.2334/josnusd.53.185. PMID: 21712623. **Exclusion reason:** Ineligible population
4. Ahovuo-Saloranta A, Forss H, Walsh T, et al. Sealants for preventing dental decay in the permanent teeth. Cochrane Database of Systematic Reviews. 2013 Mar 28(3):CD001830. doi: 10.1002/14651858.CD001830.pub4. PMID: 23543512. **Exclusion reason:** Used as source document
5. Ahovuo-Saloranta A, Hiiri A, Nordblad A, et al. Pit and fissure sealants for preventing dental decay in the permanent teeth of children and adolescents. Cochrane Database of Systematic Reviews. 2008 Oct 08(4):CD001830. doi: 10.1002/14651858.CD001830.pub3. PMID: 18843625. **Exclusion reason:** Used as source document
6. Ahovuo-Saloranta A, Hiiri A, Nordblad A, et al. Pit and fissure sealants for preventing dental decay in the permanent teeth of children and adolescents. Cochrane Database of Systematic Reviews. 2004(3):CD001830. doi: 10.1002/14651858.CD001830.pub2. PMID: 15266455. **Exclusion reason:** Used as source document
7. Al Dehailan L, Martinez-Mier EA. Prevention Program Including Fluoride Varnish and 1450-ppm Fluoride Toothpaste Targeting Young Children in Clinical Setting in UK did not Stop Sental Caries From Developing but Slowed Lesion Progression. J Evid Based Dent Pract. 2019;19(2):207-9. doi: 10.1016/j.jebdp.2019.05.013. PMID: 31326059. **Exclusion reason:** Ineligible population
8. Al-Janabi WH, Al-Sultani HFF. The effect of maternal level of mother education on the prevalence of dental caries in school aged children. Indian J Public Health Res Dev. 2019;10(6):1264-8. doi: 10.5958/0976-5506.2019.01468.2. PMID: CN-01979814. **Exclusion reason:** Ineligible intervention
9. AlHumaid J, Salloot Z, Al-Ansari A, et al. Contribution of preventive methods in controlling caries among Saudi primary schoolchildren: a population-based cross-sectional study. Acta Odontol Scand. 2018 Aug;76(6):422-6. doi: 10.1080/00016357.2018.1425899. PMID: 29320886. **Exclusion reason:** Ineligible intervention
10. Allmark C, Green HP, Linney AD, et al. A community study of fluoride tablets for school children in portsmouth. results after six years. Br Dent J. 1982 Dec 21;153(12):426-30. doi: 10.1038/sj.bdj.4804967. PMID: 6961931. **Exclusion reason:** Poor quality
11. Almabadi ES, Bauman A, Akhter R, et al. The Effect of a Personalized Oral Health Education Program on Periodontal Health in an At-Risk Population: a Randomized Controlled Trial. Int J Environ Res Public Health. 2021;18(2):846. doi: 10.3390/ijerph18020846. PMID: 33478179. **Exclusion reason:** Ineligible intervention
12. Alrashdi M, Cervantes Mendez MJ, Farokhi MR. A Randomized Clinical Trial Preventive Outreach Targeting Dental Caries and Oral-Health-Related Quality of Life for Refugee Children. Int J Environ Res Public Health. 2021;18(4):1686. doi: 10.3390/ijerph18041686. PMID: 33578661. **Exclusion reason:** Ineligible intervention

13. Alvesalo L, Brummer R, Le Bell Y. On the use of fissure sealants in caries prevention. A clinical study. Acta Odontol Scand. 1977;35(3):155-9. doi: 10.3109/00016357709056004. PMID: 331847. **Exclusion reason:** Ineligible intervention

14. Andruskeviciene V, Milciuviene S, Bendoraitiene E, et al. Oral health status and effectiveness of caries prevention programme in kindergartens in Kaunas city (Lithuania). Oral health prev. 2008;6(4):343-8. doi: 10.3290/j.ohpd.a14181. PMID: 19178101. **Exclusion reason:** Ineligible population

15. Anonymous. Evidence-based Clinical Practice Guideline for the Use of Pit-and-Fissure Sealants. Pediatric dentistry. 2016 Oct 15;38(5):120-36. doi: 10.1016/j.adaj.2016.06.001. PMID: 28206888. **Exclusion reason:** Used as source document

16. Anonymous. Use of Pit-and-Fissure Sealants. Pediatric dentistry. 2017 Sep 15;39(6):156-72. PMID: 29179354. **Exclusion reason:** Used as source document

17. Anonymous. Systematic review and meta-analysis of randomised controlled trials on the effectiveness of school-based dental screening versus no screening on improving oral health in children. Br Dent J. 2017 May 12;222(9):675. doi: 10.1038/sj.bdj.2017.403. PMID: 28496244. **Exclusion reason:** Not a study

18. Anonymous. Use of Pit-and-Fissure Sealants. Pediatric dentistry. 2018 Oct 15;40(6):162-78. PMID: 32074886. **Exclusion reason:** Used as source document

19. Anopa Y, Conway DI. Exploring the cost-effectiveness of child dental caries prevention programmes. Are we comparing apples and oranges? Evid Based Dent. 2020 03;21(1):5-7. doi: 10.1038/s41432-020-0085-7. PMID: 32221482. **Exclusion reason:** Ineligible outcome

20. Antunes LA, Andrade MR, Leao AT, et al. Systematic review: change in the quality of life of children and adolescents younger than 14 years old after oral health interventions: a systematic review. Pediatric dentistry. 2013 Jan-Feb;35(1):37-42. PMID: 23635896. **Exclusion reason:** Ineligible intervention

21. Aps JKM, Lim LZ, Tong HJ, et al. Diagnostic efficacy of and indications for intraoral radiographs in pediatric dentistry: a systematic review. European Archives of Paediatric Dentistry: Official Journal of the European Academy of Paediatric Dentistry. 2020 Aug;21(4):429-62. doi: 10.1007/s40368-020-00532-y. PMID: 32390073. **Exclusion reason:** Ineligible intervention

22. Armfield JM, Spencer AJ. Community effectiveness of fissure sealants and the effect of fluoridated water consumption. Community Dent Health. 2007 Mar;24(1):4-11. PMID: 17405464. **Exclusion reason:** Ineligible study design

23. Arora A, Khattri S, Ismail NM, et al. School dental screening programmes for oral health. Cochrane Database of Systematic Reviews. 2019 Aug 8;8(8):Cd012595. doi: 10.1002/14651858.CD012595.pub3. PMID: 31425627. **Exclusion reason:** Ineligible setting

24. Arora A, Khattri S, Ismail NM, et al. School dental screening programmes for oral health. Cochrane Database of Systematic Reviews. 2017 12 21;12(12):CD012595. doi: 10.1002/14651858.CD012595.pub2. PMID: 29267989. **Exclusion reason:** Ineligible study design

25. Arora S, Kumar JV, Moss ME. Does water fluoridation affect the prevalence of enamel fluorosis differently among racial and ethnic groups? J Public Health Dent. 2018 03;78(2):95-9. doi: 10.1111/jphd.12258. PMID: 29171664. **Exclusion reason:** Ineligible intervention

26. Arrow P. Cost minimisation analysis of two occlusal caries preventive programmes. Community Dent Health. 2000 Jun;17(2):85-91. PMID: 11349992. **Exclusion reason:** Ineligible outcome

27. Azarpazhooh A, Main PA. Fluoride varnish in the prevention of dental caries in children and adolescents: a systematic review. J Can Dent Assoc. 2008 Feb;74(1):73-9. PMID: 18298889. **Exclusion reason:** Used as source document

28. Azarpazhooh A, Main PA. Pit and fissure sealants in the prevention of dental caries in children and adolescents: a systematic review. J Can Dent Assoc. 2008 Mar;74(2):171-7. PMID: 18353204. **Exclusion reason:** Used as source document

29. Azarpazhooh A, Main PA. Fluoride varnish in the prevention of dental caries in children and adolescents: a systematic review. Hawaii Dent J. 2009 Jan-Feb;40(1):6-7, 10-3; quiz 7. PMID: 19449609. **Exclusion reason:** Used as source document

30. Azevedo MS, Goettems ML, Torriani DD, et al. Factors associated with dental fluorosis in school children in southern Brazil: a cross-sectional study. Pesqui Odontol Bras. 2014;28doi: 10.1590/1807-3107bor-2014.vol28.0014. PMID: 24878674. **Exclusion reason:** Ineligible study design

31. Babaei A, Pakdaman A, Hessari H. Effect of an Oral Health Promotion Program Including Supervised Toothbrushing on 6 to 7-Year-Old School Children: A Randomized Controlled Trial. Front Dent. 2020 Aug;17(19):1-9. doi: 10.18502/fid.v17i19.4313. PMID: 33615295. **Exclusion reason:** Ineligible study design

32. Bader JD, Rozier G, Harris R, et al. Dental Caries Prevention: The Physician's Role in Child Oral Health Systematic Evidence Review [Internet]. Agency for Healthcare Research and Quality (US). 2004 04;04:04. PMID: 20722125. **Exclusion reason:** Not a study

33. Bader JD, Rozier RG, Lohr KN, et al. Physicians' roles in preventing dental caries in preschool children: a summary of the evidence for the U.S. Preventive Services Task Force. Am J Prev Med. 2004 May;26(4):315-25. doi: 10.1016/j.amepre.2003.12.001. PMID: 15110059. **Exclusion reason:** Ineligible population

34. Bader JD, Shugars DA, Vollmer WM, et al. Design of the xylitol for adult caries trial (X-ACT). BMC oral health. 2010;10(22)doi: 10.1186/1472-6831-10-22. PMID: 20920261. **Exclusion reason:** Not usable

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Appendix A6. Criteria for Assessing Internal Validity of Individual Studies

Design	Criteria	Definition of good	Definition of fair	Definition of poor
Systematic reviews	• Comprehensiveness of sources considered/search strategy used • Standard appraisal of included studies • Validity of conclusions • Recency and relevance (especially important for systematic reviews)	Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions	Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies	Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies
RCTS and cohort studies	• Initial assembly of comparable groups: ○ For RCTs: Adequate randomization, including first concealment and whether potential confounders were distributed equally among groups ○ For cohort studies: Consideration of potential confounders, with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts • Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination) • Important differential loss to follow up or overall high loss to follow up • Measurements: equal, reliable, and valid (includes masking of outcome assessment) • Clear definition of interventions • All important outcomes considered • Analysis: adjustment for potential confounders for cohort studies or intention-to treat analysis for RCTs	Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow up ≥80%); reliable and valid measurement instruments are used and applied equally to all groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, intention-to-treat analysis is used for RCTs.	Studies are graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially, but some question remains whether some (although not major) differences occurred with follow up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is used for RCTs.	Studies are graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Intention-to-treat analysis is lacking for RCTs.

Appendix A6. Criteria for Assessing Internal Validity of Individual Studies

Design	Criteria	Definition of good	Definition of fair	Definition of poor
Diagnostic Accuracy Studies	• Screening test relevant, available for primary care, and adequately described • Credible reference standard, performed regardless of test results • Reference standard interpreted independently of screening test • Indeterminate results handled in a reasonable manner • Spectrum of patients included in study • Sample size • Reliable screening test	Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; assesses reliability of test; has few or handles indeterminate results in a reasonable manner; includes large number (>100) of broad-spectrum patients with and without disease	Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; has moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients	Has a fatal flaw, such as: Uses inappropriate reference standard; improperly administers screening test; biased ascertainment of reference standard; has very small sample size or very narrow selected spectrum of patients

Source: U.S. Preventive Services Task Force. Procedure Manual. Accessed at https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual/procedure-manual-appendix-vi-criteria-assessing-internal-validity-individual-studies

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Federal Partners

- The Centers for Disease Control and Prevention (1 reviewer)
- The National Institute of Child Health and Human Development (3 reviewers)
- The National Institute of Dental and Craniofacial Research (3 reviewers)

Appendix B Table 1. Data Abstraction of Diagnostic Accuracy Study

Author, year	Screening test	Reference standard	Country Setting	Screener	Population	Sample size	Proportion with condition	Definition of a positive screening exam	Proportion unexaminable by screening test	Analysis of screening failures
Beltran, 1997[136]	Visual screening	Pediatric dentist exam	United States Rural school	Registered nurse with written material on procedures and diagnostic criteria, 5 hours of training	Children 5 to 12 years	219-323	Caries with restorations present: 39.1% Untreated caries: 35.2% Treated or untreated caries: 55.7% Fluorosis: 40.3% Injuries: 12.1% Sealants: 6.8% Non-urgent treatment needed: 18.4% Urgent treatment needed: 10.7% Any treatment needed: 27.2%	Identification of caries, fluorosis, injuries, sealants, need for treatment	Appears to be none	Not applicable
Beltran, 1997[136] Same study as above, 2 different measures	Question-naire sent home to parents	Pediatric dentist exam	United States Rural school	Registered nurse	Children 5 to 12 years	305-611	No caries vs. restorations present: 40.7% No caries vs. untreated decay: 40.9% Injuries: 11.5% Sealants: 7.1%	NR	Excluded: 10% Excluded: 34% Excluded: 3% Excluded: 33%	NR

Appendix B Table 1. Data Abstraction of Diagnostic Accuracy Study

Author, year	Proportion who underwent reference standard and included in analysis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	AUC	Quality rating
Beltran, 1997[136]	Appears to be all	Caries with restorations present: 96.7 Untreated caries: 92.2 Treated or untreated caries: 95.0 Fluorosis: 72.3 Injuries: 79.5 Sealants: 59.1 Non-urgent treatment needed: 66.0 Urgent treatment needed: 100.0 Any treatment needed: 79.6	Caries with restorations present: 99.3 Untreated caries: 99.3 Treated or untreated caries: 98.6 Fluorosis: 96.4 Injuries: 97.5 Sealants: 99.7 Non-urgent treatment needed: 99.2 Urgent treatment needed: 100.0 Any treatment needed: 99.2	Caries with restorations present: 98.9 Untreated caries: 98.6 Treated or untreated caries: 98.8 Fluorosis: 93.1 Injuries: 81.6 Sealants: 92.9 Non-urgent treatment needed: 94.6 Urgent treatment needed: 100.0 Any treatment needed: 97.2	Caries with restorations present: 97.9 Untreated caries: 95.9 Treated or untreated caries: 94.0 Fluorosis: 83.8 Injuries: 97.2 Sealants: 97.1 Non-urgent treatment needed: 92.8 Urgent treatment needed: 100.0 Any treatment needed: 92.8	NR	Fair
Beltran, 1997[136] Same study as above, 2 different measures	Appears to be all	No caries vs. restorations present: 93.3 No caries vs. untreated decay: 68.8 Injuries: 20.0 Sealants: 56.7	No caries vs. restorations present: 89.1 No caries vs. untreated decay: 88.3 Injuries: 87.3 Sealants: 89.3	No caries vs. restorations present: 84.5 No caries vs. untreated decay: 80.4 Injuries: 16.9 Sealants: 28.2	No caries vs. restorations present: 95.1 No caries vs. untreated decay: 80.3 Injuries: 89.4 Sealants: 93.4	NR	Fair

Abbreviations: AUC=area under the curve; CI = confidence interval; NR=not reported.

Appendix B Table 2. Quality Assessment of Diagnostic Accuracy Study

Author, year	Repre-sentative spectrum	Random or con-secutive sample	Screening test adequately described	Screening cutoffs pre-defined	Credible reference standard	Reference standard applied to all screened patients	Same reference standard applied to all patients	Reference standard and screening examin-ation inter-preted independ-ently	Reference standard assessed by blinded assessor	Screening test assessed by blinded assessor	High rate of uninter-pretable results, non-compli-ance with screening test, or attrition	Analysis includes patients with uninter-pretable results or non-compli-ance	Quality rating
Beltran, 1997[136]	Yes	Yes	Visual exam yes/ Question-naire no	Unclear (Question-naire)	Yes	Unclear	Yes	Unclear	Unclear	Yes	Unclear (sample sizes for diagnostic accuracy estimates lower than number enrolled for unclear reasons)	Not applicable Not applicable	Fair

Appendix B Table 3. Data Abstraction of Fluoride Supplement Trials

Author, year	Study design	Intervention A	Intervention B	Intervention C	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information	Eligibility criteria
Aasenden, 1972[137]	RCT	Daily rinsing and ingestion of 5 ml APF (0.02% F, 0.1 M phosphate, pH 4.0) for 3 years	Daily rinsing and ingestion of 5 ml neutral NaF (0.02% F) and no phosphate for 3 years	Placebo	Instructed to keep in the mouth for 1 minute then swallow	Teacher dispensed the rinses	Age, mean 10 years old (from those analyzed) % female: 47% (from those analyzed) Race/ethnicity: 100% White	DF teeth: 4.26 vs 4.61 vs 4.30 DF surfaces: 7.32 vs 8.58 vs 7.99 (from those analyzed) Non-fluoridated water 0.1 ppm No previous exposure to F supplements or fluoridated water, but the majority had a history of some kind of topical F exposure	Children ages 8-11 years from middle-class suburban community
Blinkhorn, 1981[138]	"Field study", RCT	1 mg dissolving fluoride (2.2 mg NaF)	No fluoride	NA	Also included oral health education, including dietary advice and oral hygiene instruction	NR	Age, mean: 12.5 years old % female: 59% Race/ethnicity: NR	DMFT, mean (SD): 4.62 (3.25) vs 4.28 (3.24)	Children ages 11-13 years accepting routine dental care in a socially deprived area
DePaola, 1968[139]	RCT	APF chewable tablet, daily (sodium fluoride 2.2 mg, sodium biphosphate 70 mg, hexamic acid 25 mg)	Placebo (sodium biphosphate 70 mg, hexamic acid 25 mg)	NA	NR	Dental assistant distributed the tablets	Age, mean: 8.4 years % female: NR Race/ethnicity: NR	DF, mean: 4.41 vs 4.09 No. of surfaces available for carious attack, mean: 54.11 vs 55.25 No history of fluoride supplements Non-fluoridated water supply: 0.07 ppm fluoride	School children in grades 1-3
Driscoll, 1974[140]	RCT	APF chewable tablet once a day	APF chewable tablet twice a day (2nd tablet 3 hours later)	Placebo	Instructed to chew, rinse with, and swallow tablet	Teacher and nonprofessional person who performed monthly visits for project assistance	Age, mean: 6.62 years % female: NR Race/ethnicity: NR	DMF surfaces, mean (SE): 1.40 (0.12) vs 1.07 (0.10) vs 1.35 (0.14); group that received 2 tablets/day had lower DMF surfaces at baseline Negligible amounts of fluoride in water sources (<0.3 ppm fluoride)	School children in grades 1-2

Appendix B Table 3. Data Abstraction of Fluoride Supplement Trials

Author, year	Study design	Intervention A	Intervention B	Intervention C	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information	Eligibility criteria
Driscoll, 1978[159] (longer term follow up to Driscoll, 1974)	Same as Driscoll, 1974	Same as Driscoll, 1974	Same as Driscoll, 1974	Same as Driscoll, 1974	Interventions were continued for 6 years	Same as Driscoll, 1974	Same as Driscoll, 1974	Same as Driscoll, 1974	Same as Driscoll, 1974
Liu, 2013[141]	Cluster RCT	Fluoride tablet, 1.0 mg NaF daily for 24 months; placed in mouth by teachers	Placebo	NA	NR	Teacher	Age, mean: 9.4 vs 9.0 years % female: 35% vs 41% Race/ethnicity: NR	DMFT index, mean (SD): 1.19 (1.64) vs 1.08 (1.96), p=0.64 DMFS index, mean (SD): 2.12 (3.55) vs 1.89 (4.09), p=0.66 Frequency of tooth brushing per day:<3 times: 87% vs 60%, p<0.0001>or =3 times, after meals: 9% vs 36%, p<0.0001	Children with disabilities aged 6-12 years
O'Rourke, 1988[142]	Cluster RCT, schools matched on socio-economic status, then randomized	Fluoride tablet, 1 mg daily	No fluoride	NA	NR	NR	Age, mean: 5.3 years old % female: NR Race/ethnicity: NR	Caries prevalence in primary dentitions: 3.66 vs 3.32 Prior to water fluoridation	School children ages 4-5 years old
Stephen, 1978[143]	Cluster RCT, schools matched on age, parental SES, and deciduous caries experience, then randomized	Fluoride tablet, 1 mg daily	Placebo	NA	Instructed to suck on the tablet, let it dissolve slowly	Teacher	Age, mean: 5.5 years old (+or - 1 month) % female: NR Race/ethnicity: NR	No. of erupted first permanent molars at baseline: 70 vs 31	School children ages 5.5 to 5.7 years old from social classes IV and V (lower SES)

Appendix B Table 3. Data Abstraction of Fluoride Supplement Trials

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of follow up	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Aasenden, 1972[137]	545 (numbers NR by arm)	362 (109 vs 114 vs 139)	33.6% overall Appears placebo group had a higher retention than the intervention groups	United States, Massa-chusetts 2 grammar schools	3 years	Mean percentage reductions in DFS: 30% (=or-12%) vs 27% (+or- 16%); no significant differences between the intervention arms; mean incremental tooth and surface scores consistently smaller than those of the control groups, which became statistically significant after year 2: New DF teeth, mean (SE), all 3 years: 3.83 (0.31) vs 4.17 (0.34) vs 5.64 (0.38), p<0.01 New DF surfaces, mean (SE), all 3 years: 8.66 (0.78) vs 8.98 (0.78) vs 12.29 (0.89), p<0.01 Caries reduction in the teeth initially erupted in intervention arms vs placebo: 25%: Teeth present initially, mean (SE): 6.48 (0.59) vs 6.42 (0.61) vs 8.64 (0.66), p<0.05 Teeth erupted during study, mean (SE): 2.18 (0.33) vs 2.56 (0.32) vs 3.65 (0.39), p<0.01	NR	Fair	Davies, Rose-Hoyt Pharma-ceutical Division, The Kendall Company and by a USPHS Grant
Blinkhorn, 1981[138]	242 (NR by group)	178 (91 vs 87)	27% vs 26%	United Kingdom Community health centers; children recruited from 9 high schools	18 months	DMFT, mean SD at 18 months: 1.62 (1.69) vs 1.49 (1.75); difference mean (SE) 0.12 (0.26); difference percentage -8%; p=ns Referred for periodontal treatment: Baseline: 52.75% (48/91) vs 48.28% (42/87) 18 month follow up: 48.35% (44/91) vs 40.23% (35/87) Net difference: 4.40% (4/91) vs 8.05% (7/87)	NR	Fair	NR
DePaola, 1968[139]	327 (162 vs 165)	266 (130 vs 136)	19.8% vs 17.6%	United States, MassachusettsSchool	2 years	DF, mean, at 24 months: 4.45 vs 3.90 No. of surfaces available for carious attack, mean: 55.71 vs 55.29No. of teeth erupting between 1st and 3rd examinations, mean: 4.76 vs 4.77 No. of surfaces erupting between 1st and 3rd examinations, mean: 23.80 vs 23.85 Observed DF increment: teeth: 1.44 (1.86) vs 1.82 (1.65); ; difference in observed and net increments: 23%; p=0.05 Observed DF increment: surfaces: 3.60 (3.63 vs 4.48 (3.06); difference in observed and net increments: 20%; p=0.05 Caries increments in surfaces that erupted during the study, at 24 months: No. of surfaces, mean: 23.80 vs 23.85 DFS increment, mean: 0.85 (0.72) vs 0.610 (1.22), percentage difference 63; p=0.01	NR	Fair	NR

Appendix B Table 3. Data Abstraction of Fluoride Supplement Trials

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of follow up	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Driscoll, 1974[140]	1,034 (345 vs 345 vs 344) No. for those with at least 1 erupted permanent tooth at baseline: 981 (325 vs 324 vs 332)	611 (202 vs 197 vs 212)	41% vs 43% vs 38%	United States, North Carolina 9 elementary schools	30 months	30 months DMF surfaces, mean (SE): 1.55 (0.16) vs 1.00 (0.11) vs 1.48 (0.18) Incremental DMF surface scores, mean (SE): Teeth present at baseline (n=611): 2.16 (0.19) vs 1.68 (0.16) vs 2.31 (0.19); group A difference from placebo 6.2%; group B difference from placebo 27.2% Teeth erupting during the study (n=640): 0.21 vs 0.24 vs 0.33; group A difference from placebo 36.5%; group B difference from placebo 27.3% Analysis of variance of mean DMF surface increments for teeth present at baseline (to correct for imbalance at baseline): By study group: F value 3.23; p=0.04 By blocks (baseline DMFS and dental age): F value 4.42; p<0.005	NR	Fair	NR
Driscoll, 1978[159] (longer term follow up to Driscoll, 1974)	Same as Driscoll, 1974	438 (150 vs 135 vs 153)	57% vs 61% vs 56%	Same as Driscoll, 1974	6 years	6 years Incremental DMF surface scores, mean (SE): Early erupting teeth: 4.13 (0.36) vs 4.07 (0.38) vs 5.30 (0.35); group A difference from placebo 22.1%; group B difference from placebo 23.2% Late erupting teeth: 1.09 (0.18) vs 1.08 (0.19) vs 1.95 (0.17); group A difference from placebo 44.1%; group B difference from placebo 44.6% All teeth combined: 5.22 (0.46) vs 5.14 (0.48) vs 7.25 (0.45); group A difference from placebo 28.0%; group B difference from placebo 29.1% Analysis of variance of mean DMF surface increments (to correct for imbalance at baseline): Early erupting teeth By study group: F value 3.80; p=0.02 By blocks: F value 3.96; p<0.01 Late erupting teeth By study group: F value 8.13; p<0.01 By blocks: F value 15.63; p<0.01All teeth combined By study group: F value 6.92; p<0.01By blocks: F value 8.16; p<0.01	NR	Same as Driscoll, 1974	Same as Driscoll, 1974

Appendix B Table 3. Data Abstraction of Fluoride Supplement Trials

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of follow up	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Liu, 2013[141]	349 (163 vs 186) 6 schools (3 vs 3)	217 (103 vs 114) 6 schools (3 vs 3)	37% vs 39%	Taiwan 6 schools, special schools for children with disabilities	24 months	DMFT index, mean (SD): 2.64 (2.38) vs 3.16 (3.04), p=0.17 DMFS index, mean (SD): 4.27 (5.17) vs 5.30 (6.74), p=0.21DMFT, mean (SD) difference: 1.45 (1.59) vs 2.08 (2.04, p=0.0113; -30.42% of improvement/reduction in DMFT index DMFS, mean (SD) difference: 2.16 (2.60) vs 3.41 (3.93), p=0.0056; -36.84% of improvement/reduction in DMFS index Stepwise multiple regression analysis on dental caries protection factors: intervention vs control group, estimate (SE): DMFT: -0.70 (0.17), 95% CI -1.04 to -0.36; p<0.0001 DMFS: -0.80 (0.25), 95% CI -1.30 to -0.30, p=0.0019	"No side effects or adverse events were reported by the parents/ caregivers or school teachers during the study period"	Fair	Bureau of Health Promotion, Department of Health
O'Rourke, 1988[142]	769 children (no. in each arm NR)	529 (263 vs 266)	31% overall 6 children withdrawn during the course of the study	United Kingdom 22 schools	3 years	dmft, mean (SD), year 3: 1.23 (1.69) vs 1.50 (1.73); percentage difference and caries reduction: 0.27 dmft and 18%, p=ns DMFT, mean (SD), year 3: 0.71 (1.23) vs 1.36 (1.52); percentage difference and caries reduction: 0.65 DMFT and 48%, "statistically significant"	NR	Fair	Manchester Health Authority
Stephen, 1978[143]	116 (61 vs 55)	102 (54 vs 48)	11.5% vs 12.7%	United Kingdom 24 schools initially, over 3 years children were distributed across 38 schools	3 years	DMF, mean (SE), year 3: 1.80 (0.2) vs 3.28 (0.17); % reduction 45.5%, p<0.001 DMFS, mean (SE), year 3: 3.02 (0.51) vs 5.96 (0.54); % reduction 49.3%, p<0.02 DMF, mean (SE), year 3, + grade 1 sticky fissure lesions for first permanent molars which were unerupted at baseline: 1.12 (0.18) vs 2.81 (0.17); % reduction 60.1%, p<0.001 DMFS, mean (SE), year 3, + grade 1 sticky fissure lesions for first permanent molars which were unerupted at baseline: 1.45 (0.32) vs 4.91 (0.45); % reduction 70.5%, p<0.001 DMF, mean (SE), year 3, - grade 1 sticky fissure lesions for first permanent molars which were unerupted at baseline: 0.52 (0.14) vs 2.47 (0.19); % reduction 79.0%, p<0.001 DMFS, mean (SE), year 3, - grade 1 sticky fissure lesions for first permanent molars which were unerupted at baseline: 0.81 (0.28) vs 4.34 (0.47); % reduction 81.3%, p<0.001	NR	Fair	Zyma Ltd provided test and placebo preparations

Appendix B Table 3. Data Abstraction of Fluoride Supplement Trials

Abbreviations: APF = acidulated phosphate fluoride; DF = decayed and filled; DFS = decayed and filled surfaces; DMF = decayed, missing, filled; DMFS = decayed, missing, or filled tooth surfaces; DMFT = Decayed, Missing and Filled Teeth; NA = not applicable; NaF = sodium fluoride; NR = not reported; ns = not significant; RCT = randomized controlled trial; SD = standard deviation; SE = standard error; SES = socioeconomic status; USPHS = United States Public Health Service.

Appendix B Table 4. Quality Assessment of Fluoride Supplement Trials

Author, year	Random-ization adequate?	Allocat-ion conceal-ment adequate?	Groups similar at baseline?	Out-come assess-ors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis	Patients with missing data analyzed?	Accept-able levels of overall attrition (<20%) and between-group differ-ences (<10%) in attrition?	Post-random-ization exclus-ions	Avoid-ance of selective outcomes reporting	Adjusted for cluster correlat-ion?	Quality rating
Aasenden, 1972[137]	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	No	No Assume yes, but numbers in initial arms NR	Unclear	Yes	NA	Fair
Blinkhorn, 1981[138]	Unclear	Unclear	Yes	Yes	Not possible	No	Yes	Unclear	No Yes	Unclear	Yes	NA	Fair
DePaola, 1968[139]	Unclear	Unclear	Yes	Yes	Not possible	Yes	Yes	No	Yes Yes	Unclear	Yes	NA	Fair
Driscoll, 1974[140] and Driscoll, 1978[159]	Unclear	Unclear	No, group that received 2 tablets/ day had lower DMF surfaces at baseline	Yes	Yes	Partial (blinded to fluoride once daily vs. placebo; children allocated to twice daily fluoride were not blinded to additional dose)	Yes	No	No Yes	Unclear	Yes	NA	Fair

Appendix B Table 4. Quality Assessment of Fluoride Supplement Trials

Author, year	Random-ization adequate?	Allocat-ion conceal-ment adequate?	Groups similar at baseline?	Out-come assess-ors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis	Patients with missing data analyzed?	Accept-able levels of overall attrition (<20%) and between-group differ-ences (<10%) in attrition?	Post-random-ization exclus-ions	Avoid-ance of selective outcomes reporting	Adjusted for cluster correlat-ion?	Quality rating
Liu, 2013[141]	Unclear	Unclear	No, more children in the control group brushed their teeth >3 times a day, p<0.001	Unclear	Unclear	Yes	Yes	No	No Yes	Unclear	Yes	Unclear	Fair
O'Rourke, 1988[142]	Unclear	Unclear	Yes	Yes	Unclear	No	Yes	No	No Yes	Unclear	Yes	No	Fair
Stephen, 1978[143]	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	No	Yes Yes	Unclear	Yes	NA	Fair

Abbreviations: DMF = decayed, missing, filled; NA = not applicable; NR = not reported.

Appendix B Table 5. Quality Assessment of Fluoride Gel Systematic Review

Author, year	"A priori" design provided?	Duplicate study selection and data abstract-ion?	Compre-hensive literature search performed?	Searched for more than published studies?	List of included and excluded studies provided?	Character-istics of the included studies provided?	Scientific quality of included studies assessed and docu-mented?	Study conclusions supported by the evidence?	Methods used to combine the findings of studies appro-priate?	Likelihood of publication bias assessed?	Conflict of interest stated for systematic review or individual studies?	Quality rating
Marinho, 2015[80]	Yes	Yes	Yes	Yes	Yes	Yes	Yes Yes	Yes	Yes	Yes	Yes Yes	Good

Appendix B Table 6. Data Abstraction of Fluoride Gel Systematic Review

Author, year	Literature databases	Date of last search	Inclusion criteria	No. of studies and study designs	Total N	Intervention A	Intervention B	Baseline age	Baseline, % female
Marinho, 2015[80]	Cochrane Oral Health Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via OVID, EMBASE via OVID, CINAHL via EBSCO, LILACS and BBO via the BIREME Virtual Health Library, ProQuest Dissertations and Theses, Web of Science Conference Proceedings, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform on 5 November 2014 Also searched reference lists of articles and contacted selected authors and manufacturers	Update of 2002 review No search date restriction through Nov 2014 (Studies published between 1967 and 2005)	Randomized or quasi-randomized controlled trials where blind outcome assessment was stated or indicated, comparing topically applied fluoride gel with placebo or no treatment in children up to 16 years The frequency of application had to be at least once a year, and study duration at least one year The main outcome was caries increment measured by the change in decayed, missing and filled tooth surfaces in both permanent and primary teeth (D(M)FS and d(e/m)fs)	Permanent tooth surfaces: k=26 (25 in meta-analysis)	Permanent tooth surfaces: N=8,619 (range 41 to 732) (N=8,479 contributed to meta-analysis)	Fluoride gel was administered as: Acidulated phosphate fluoride in 20 trials (APF, 12,300 parts per million F); other formulations were sodium fluoride (NaF, 12,500 parts per million F), amine fluoride (AmF, 12,500 ppm F) or stannous fluoride (SnF2, 2,425 ppmF) Gels were applied using a tray (19 trials), brush (6 trials), or floss (1 trials)	Placebo or no treatment	Range: 5 to 15 years; 12 years old at start: 15 trials	Similar numbers of males and females (where these data were reported), with the exception of 1 study which included male participants only

Appendix B Table 6. Data Abstraction of Fluoride Gel Systematic Review

Author, year	Baseline race/ ethnicity	Baseline oral health information	Outcomes	Adverse events	Quality rating
Marinho, 2015[80]	NR	Mean DMFS or ranged from 0 to 12.2, with 11 trials reporting DMFS of 3 or less	Outcome = prevented fraction, the difference in mean caries increments between the treatment and control groups expressed as a percentage of the mean increment in the control group D(M)FS: Permanent tooth surfaces, nearest to 3 years: D(M)FS pooled prevented fraction estimate (25 trials, N=8,479): 28% (95% CI 19% to 36%); I^2=82% Subgroup and meta-regression analyses: The pooled estimated treatment effect was 17% greater (95% CI 3% to 31%); I^2=73% in trials with no treatment rather than placebo control groups: D(M)FS prevention fraction, no treatment control group (10 trials, N=2,808): 0.38% (95% CI 0.24 to 0.52%); I^2=86% D(M)FS prevention fraction, placebo-control trials (15 trials, N=5,671): 0.21% (95% CI 0.15 to 0.28%), I^2=38% No other significant associations: Univariate meta-regression suggested no significant association between estimates of D(M)FS PFs and baseline levels of caries, background exposure to other fluoride sources, background exposure to fluoridated water, background exposure to fluoride toothpaste, gel application mode (operator/self-applied), gel application self-applied method (tray or paint/brush or floss), frequency of gel application and fluoride concentration Further univariate meta-regression analyses on other characteristics not specified a priori showed no significant association between estimates of D(M)FS PFs and length of follow up (duration of study in years), prior prophylaxis, or dropout rate D(M)FT: D(M)FT pooled prevented fraction estimate (all 10 trials): 32% (95% CI 19 to 46%); I2=91% D(M)FT prevention fraction, no treatment control group (6 trials): 43% (95% CI 29 to 57%); I^2=90% D(M)FT prevention fraction, placebo-control trials (4 trials): 18% (95% CI 9 to 27%); I^2=6%	Signs and symptoms of acute toxicity during the application of the gel (2 trials, n=490): risk difference 0.01, 95% CI -0.01 to 0.02; p=0.36; I^2=0%	Good

Abbreviations: AmF = amine fluoride; APF = acidulated phosphate fluoride; BBO = Brazilian Bibliography of Dentistry; CI = confidence interval; CINAHL = Cumulative Index to Nursing and Allied Health Literature; defs = decayed, extraction needed, filled surfaces; D(M)FS/T = decayed, (missing) and filled permanent surfaces or teeth; d(e/m)fs = decayed (extracted/missing) and filled surfaces; LILACS = Latin American and Caribbean Health Sciences Literature; NaF = sodium fluoride; PF = prevented fraction; SnF2 = stannous fluoride; WHO = World Health Organization.

Appendix B Table 7. Data Abstraction of Additional Fluoride Gel Trial

Author, year	Study design	Intervention A	Intervention B	Intervention C	Intervention D	Other notes about intervention	Interventionist	Baseline study character-istics	Baseline oral health information	Eligibility criteria
Rim, 2021[144]	RCT	1 application of 1% subacidic NaF-HF gel	2 applications of 1% subacidic NaF-HF gel at a 7-day interval	2 applications of 1% subacidic NaF-HF gel at a 6-month interval	Placebo control	All groups also received a school dental prevention program, comprised of education on tooth brushing methods and anti-caries effects of fluoride, and fluoride gel administration Gel applied via tray	Trained dental hygienists	Age, mean (SD): 6.5 (0.5) in all groups % female: 50% vs 50% vs 49% vs 52% Race/ ethnicity: NR	D_1MFT, mean (SD): 0.69 (0.84) vs 0.61 (0.83) vs 0.62 (0.85) vs 0.63 (0.87) D_2MFT, mean (SD): 0.20 (0.51) vs 0.25 (0.57) vs 0.24 (0.59) vs 0.21 (0.53) D_3MFT, mean (SD): 0.06 (0.26) vs 0.08 (0.30) vs 0.04 (0.20) vs 0.08 (0.28) Tooth brushing frequency: Less than once per day: 43% vs 48% vs 47% vs 49% Once a day: 54% vs 51% vs 51% 49% More than once per day: 3.7% 1.1% vs 2.2% 1.9% Fluoride concentration in drinking water is less than 0.1 ppm (2015 to 2016 in Pyongyang city)	6 to 7 year old grade 1 school children School children using fluoride toothpaste or fluoride additives on a regular basis and those with fissure sealants were excluded

Appendix B Table 7. Data Abstraction of Additional Fluoride Gel Trial

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Rim, 2021[144]	1,077 random-ized (269 vs 269 vs 269 vs 270)	986 (240 vs 248 vs 252 vs 246)	10.8% (29/269) vs 7.8% (21/269) vs 6.3% (17/269) vs 8.9% (24/270)	Korea 8 elementary schools	1 year	A vs B vs C vs D D_1MFT increment (initial caries), mean (SD): 0.37 (0.70) vs 0.18 (0.62) vs 0.21 (0.65) vs 0.56 (0.80), p<0.001 D_2MFT increment (enamel caries), mean (SD): 0.22 (0.52) vs 0.06 (0.26) vs 0.18 (0.51) vs 0.50 (0.72), p<0.001 D_3MFT increment (dentin caries), mean (SD): 0.03 (0.18) vs 0.05 (0.21) vs 0.07 (0.32) vs 0.08 (0.26), p=0.197 Prevented fractions (difference in mean caries increments between the treatment and control groups expressed as a percentage of the mean increment in the control group): D_1MFT increment, mean: 34% lower vs 68% lower vs 64% lower; all three test groups were significantly lower than the control (p<0.001). Group 1 showed a statistically significant difference from group 2 and group 3 (p=0.001), but no significant difference was observed between group 2 and group 3 D_2MFT increment, mean: 56% lower vs 88% lower vs 64% lower; all three test groups were significantly lower than the control (p< 0.001). Group 2 was significantly different from group 1 and group 3 (p<0.01), whereas no significant difference was found between group 1 and group 3 (p=0.212) D_3MFT increment, mean: no significant difference was found across the groups (p=0.197)	"During the trial, no side effects were reported except for complaints of a slightly sour taste soon after application in most of the subjects"	Good	Department of Education and Public Health Office, Pyongchon District People's Committee, Pyongyang, DPR of Korea, and Pyongyang University of Medical Sciences

Abbreviations: DMFT = Decayed, Missing and Filled Teeth; NaF-HF = sodium fluoride and hydrofluoric acid; NR = not reported; ppm = parts per million; RCT = randomized controlled trial; SD = standard deviation.

Appendix B Table 8. Quality Assessment of Additional Fluoride Gel Trial

Author, year	Random-ization adequate?	Allocation conceal-ment adequate?	Groups similar at baseline?	Outcome assessors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis	Patients with missing data analyzed?	Acceptable levels of overall attrition (<20%) and between-group differences (<10%) in attrition?	Post-random-ization exclus-ions	Avoid-ance of selective outcomes reporting	Adjusted for cluster correl-ation?	Quality rating
Rim, 2021[144]	Yes (block)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes Yes	No	Yes	NA	Good

Abbreviations: NA = not applicable.

Appendix B Table 9. Quality Assessment of Fluoride Varnish Systematic Review

Author, year	"A priori" design provided?	Duplicate study selection and data abstract-ion?	Compre-hensive literature search performed?	Searched for more than published studies?	List of included and excluded studies provided?	Charact-eristics of the included studies provided?	Scientific quality of included studies assessed and documented?	Study conclusions supported by the evidence?	Methods used to combine the findings of studies appro-priate?	Likelihood of publication bias assessed?	Conflict of interest stated for systematic review or individual studies?	Quality rating
Marinho, 2013[81]	Yes	Yes Yes	Yes	Yes	Yes Yes	Yes	Yes Yes	Yes	Yes	Yes	Yes No	Good

Appendix B Table 10. Data Abstraction of Fluoride Varnish Systematic Review

Author, year	Literature databases	Date of last search	No. of studies and study designs	Total N	Intervention A	Intervention B	Baseline study character-istics	Baseline oral health information	Outcomes	Adverse events	Quality rating
Marinho, 2013[81]	Cochrane Oral Health Group's Trial Register, Cochrane Central Register of Controlled Trials, MEDLINE Ovid, CINAHL EBSCO, LILACS, BBO, Embase Ovid, ProQuest Dissertations and Theses, Web of Science Conference Proceedings, clinicaltrials.gov.	Database inception to May 2013	13 RCTs in permanent teeth and 1 RCT in deciduous teeth SR included 22 RCTs; we report the results for permanent teeth (children over age 5)	6,965	Fluoride varnish 22,600 ppm fluoride (11 RCTs), 7000 or 22,600 (1 RCT), 56000 ppm fluoride (1 RCT) Varnish applied in schools, dental offices, or not reported Frequency: every 6 months (8 RCTs), 3 times per year (1 RCT), 4 times per year (1 RCT), 3 times in one week (1 RCT), 2 to 4 times per year (1 RCT), and 3 to 8 times per year (1 RCT)	No treatment (10 RCTs) Placebo (3 RCTs)	Range: 5 to 14 % female: NR Race/ ethnicity: NR	Background fluoride exposure: Drinking water (7 RCTs) Toothpaste (5 RCTs) Fluoride rinsing program (3 RCTs)	Permanent Teeth: DMFS increment (prevented fraction) nearest to 3 years (13 trials): 0.43, 95% CI 0.30 to 0.57; I^2=75% DMFT prevented fraction (5 trials): 0.44, 95% CI 0.11 to 0.76; I^2=86% Proportion developing one or more new caries in permanent dentition (5 trials): RR 0.75, 95% CI 0.53 to 1.05; I^2=89% Primary Teeth: d(e/m)fs increment (prevented fraction) nearest to 3 years (3 trials in children ≥5 years): IV 0.20, 95% CI 0.02 to 0.38; IV -0.02, 95% CI -0.39 to 0.35; IV 2.12, 95% CI 0.23 to 4.01 Proportion developing one or more new caries (1 trial): RR 1.05, 95% CI 0.84 to 1.33	NR	Good

Abbreviations: BBO = Brazilian Bibliography of Dentistry; CI = confidence interval; CINAHL = Cumulative Index to Nursing and Allied Health Literature; d(e/m)fs = decayed (extracted/missing) and filled surfaces; DMFS = decayed, missing, or filled tooth surfaces; DMFT = Decayed, Missing and Filled Teeth; LILACS = Latin American and Caribbean Health Sciences Literature; NR = not reported; ppm = parts per million; RCT = randomized controlled trial; RR = relative risk.

Appendix B Table 11. Data Abstraction of Additional Fluoride Varnish Trial

Author, year	Study design	Intervention A	Intervention B	Other notes about intervention	Interventionist	Baseline age	Baseline, % female	Baseline race/ ethnicity	Baseline oral health information	Eligibility criteria
Wang, 2021[145]	RCT-cluster randomized	5% (22,600 ppm) sodium fluoride varnish at 6 month intervals	No treatment	All children and parents were provided with annual oral health education Oral hygiene instructions were given every 6 months by providing toothbrush and fluoride toothpaste	Dentists and assistants	Mean 6.83 (0.42 SD) years	46%	NR	Primary dentition, prevalence: 86.5% Permanent first molars, mean (SD): 0.035 (0.34)	6 to 7 years of age Excluded: gingivitis, ulcers, hypoplastic defects, fluorosis, pit and fissure sealed PFMs

Appendix B Table 11. Data Abstraction of Additional Fluoride Varnish Trial

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/harms	Quality rating	Sponsor
Wang, 2021[145]	5,397	5,005 (2,385 vs. 2,620) at 24-months; 4,596 (2,235 vs. 2,361) at 36-months	10.2% vs. 4.4% at 24-months 15.9% vs. 13.8% at 36-months	China 107 first grade classrooms in three low-fluoridated cities in rural China Public health measures and dental care were not commonly applied in these cities	36 months	A vs. B DFS permanent first molar at 24 months, mean (SD): 0.41 (1.22) vs. 0.64 (1.64), p<0.001 DFS permanent first molar at 36 months, mean (SD): 0.67 (1.64) vs. 1.03 (2.07), p<0.001	No adverse effects reported; one child complained of taste of varnish without nausea or vomiting	Fair	NR

Abbreviations: DFS = decayed and filled surfaces; NR = not reported; PFM = porcelain fused to metal; ppm = parts per million; RCT = randomized controlled trial; SD = standard deviation.

Appendix B Table 12. Quality Assessment of Additional Fluoride Varnish Trial

Author, year	Random-ization adequate?	Allocation conceal-ment adequate?	Groups similar at baseline?	Outcome assessors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis?	Patients with missing data analyzed?	Acceptable levels of overall attrition (<20%) and between-group differences (<10%) in attrition?	Post-random-ization exclus-ions?	Avoidance of selective outcomes reporting?	Adjusted for cluster correlat-ion?	Quality rating
Wang, 2021[145]	Yes (cluster-randomized)	No	Yes	Yes	No	No	Unclear	No	Yes Yes	No	Yes	No	Fair

Appendix B Table 13. Quality Assessment of Sealants Systematic Review

Author, year	"A priori" design provided?	Duplicate study selection and data abstract-ion?	Compre-hensive literature search performed?	Searched for more than published studies?	List of included and excluded studies provided?	Charact-eristics of the included studies provided?	Scientific quality of included studies assessed and docu-mented?	Study conclus-ions supported by the evidence?	Methods used to combine the findings of studies appro-priate?	Likelihood of publication bias assessed?	Conflict of interest stated for systematic review or individual studies?	Quality rating
Ahovuo-Saloranta, 2017[82]	Yes	Yes	Yes	Yes	Yes	Yes	Yes Yes	Yes	Yes	Planned to conduct if there were more than 10 studies in an analysis	Yes Yes	Good

Appendix B Table 14. Data Abstraction of Sealants Systematic Review

Author, year	Literature databases	Date of last search	Inclusion criteria	No. of studies and study designs	Total N	Intervention A	Intervention B	Intervention C	Baseline age
Ahovuo-Saloranta, 2017[82]	Cochrane Oral Health's Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE Ovid, Embase Ovid, ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform	Update of review published in 2004, 2008, and 2013 Searches from inception to August 2016	RCTs comparing sealants with no sealant for preventing caries of occlusal surfaces of premolar or molar teeth in children and adolescents aged up to 20 years Required at least 1 year follow up Excluded first generation resin-based sealants	Resin-based sealant versus no sealant: 15 trials Glass ionomer sealant versus no sealant: 3 trials	Resin-based sealant versus no sealant: N=3,620 participants in 14 studies plus 575 tooth pairs in 1 study Glass ionomer sealant versus no sealant: N=905 participants	Resin-based sealant Autopolymerised resin sealant (bis-GMA): 10 studies Light-cured resin sealant: 1 study Light-polymerized resin sealant with fluoride: 4 studies	Glass ionomer sealant Autopolymerised low-viscosity glass ionomer sealant: 1 study Light-cured low-viscosity glass ionomer sealant: 1 study Resin-modified glass ionomer cement: 1 study	No sealant	Range 5 to 16 years "Demographic characteristics (such as sex, age, and socio-economic level) were described and assessed to be balanced across groups in all studies"

Appendix B Table 14. Data Abstraction of Sealants Systematic Review

Author, year	Baseline % female	Baseline race/ ethnicity	Baseline oral health information	Outcomes	Adverse events	Quality rating
Ahovuo-Saloranta, 2017[82]	"Demographic characteristics (such as sex, age, and socio-economic level) were described and assessed to be balanced across groups in all studies"	NR	"Trials rarely reported background exposure to fluoride of trial participants or baseline caries prevalence" Caries prevalence reported in 6 studies: DMFT, mean: 0 to 1.81 dmft, mean: 0 to 5.38 3 studies excluded caries free children Fluoridated water: Yes in 3 studies No in 7 studies Yes and no in 1 study NR in 5 studies Oral health motivation and education reported in 3 studies	Resin-based sealant versus no sealant (A vs C): Dentine caries in permanent molars, 24 months (7 trials, N=1,548): Assuming that 16% of the control tooth surfaces were decayed during 24 months of follow-up (160 carious teeth per 1000), then applying a resin-based sealant would reduce the proportion of carious surfaces to 5.2% (95% CI 3.13% to 7.37%); relative effect OR 0.12, 95% CI 0.08 to 0.19 Assuming that 40% of control tooth surfaces were decayed (400 carious teeth per 1000), then applying a resin-based sealant would reduce the proportion of carious surfaces to 6.3% (95% CI 3.84% to 9.63%); relative effect OR 0.12 (95% CI 0.08 to 0.19) Assuming 70% of control tooth surfaces were decayed, there would be 19% decayed surfaces in the sealant group (95% CI 12.3% to 27.2%); relative effect OR 0.12 (95% CI 0.08 to 0.19) Caries yes/no: 12 months (7 studies): OR 0.17, 95% CI 0.10 to 0.30; I^2=81% 24 months (7 studies): OR 0.12, 95% CI 0.08 to 0.19; I^2=73% 36 months (7 studies): OR 0.17, 95% CI 0.11 to 0.27; I^2=90% 48 to 54 months (4 studies): OR 0.21, 95% CI 0.16 to 0.28; I^2=45% Glass ionomer sealant versus no sealant (B vs C): Dentine caries in permanent molars (3 studies) at 24 months: 2 studies (N=426) favored glass ionomers compared to no sealant, and 1 study (n=404) did not find a difference between the groups evaluated Caries yes/no at 24 months (1 study): 0.46, 95% CI 0.23 to 0.91 DFS increment at 24 months (1 study): mean difference -0.18, 95% CI -0.39 to 0.03	Resin-based sealant versus no sealant: 2 trials assessed AEs and none were reported Glass ionomer sealant versus no sealant: not assessed in studies	Good Individual studies: Authors rated all studies as high ROB because outcome assessors cannot be blinded; other domains >70% low ROB

Abbreviations: AE = adverse events; CI = confidence interval; DFS = decayed and filled surfaces; DMFT = Decayed, Missing and Filled Teeth; GMA = glycidyl methacrylate; NR = not reported; OR = odds ratio; RCT = randomized controlled trial; ROB = risk of bias.

Appendix B Table 15. Data Abstraction of Additional Sealants Trial and Longer-term Followup of Previous Trial

Author, year	Study design	Intervention(s)	Control	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information	Eligibility criteria
Muller-Bolla, 2016[160] *Longer term (3 year) follow up to a study included in the SR (Muller-Bolla, 2013 reported 1 year results)*	RCT (split mouth)	Resin-based sealant	No sealant	School-based program	Dental professional and student	Age, mean 6.4 years (SD 0.4) % female: 48% Baseline race/ ethnicity: NR	d_{3-6}ft, mean (SD): 2.8 (3.3) D_{3-6}MFT (first permanent molar), mean (SD): 0.2 (0.5) Water fluoridation NR, but stated "..they regularly used fluoride toothpaste"	French children recruited from low-income backgrounds attending elementary school The 36–46 and/or 16–26 tooth pairs were included in each child if sufficiently erupted for sealing Tooth pairs were excluded when a dental sealant or dentinal carious (ICDAS 3-6) lesion was present on one of the teeth
Hesse, 2021[146]	RCT (split mouth)	Atraumatic restorative treatment (ART)-sealant (prevention)	No sealant	School-based program; all children received tooth brushing instructions including suggestion of fluoride toothpaste and dietary advice every 6 months for a period of 3 years by a mouth hygienist	Trained dental students	Age, mean 7 years (SD 0.7) % female: 49% Baseline race/ ethnicity: NR	DMFT/dmft, mean (SD): 4.08 (3.09) Water fluoridation 0.7 mg/L	School-children aged 6-8 years from a low-income populations with limited access to health care presenting the 4 first permanent molars without clinically detectable dentine caries lesions
Uzel, 2022[147]	RCT (split mouth)	A. Resin-based sealant, type 1 B. Resin-based sealant, type 2 C. Glass ionomer sealant	No sealant	All children also received oral health education during their regular visits	Dentists (assumed)	Age, mean: 8.18 years % female: 56% Baseline race/ethnicity: NR	DMFT, mean (SD): 0.08 (0.27) dft, mean (SD): 2.88 (2.71) dfs, mean (SD): 4.14 (4.21)	Children aged 7-12 years attending a university pediatric dentistry clinic who were healthy, without any systemic diseases, whose maxillary and mandibular first permanent molars have completely erupted with sound and intact fissures, with deep fissures with 0 and 1 scores (ICDAS)

Appendix B Table 15. Data Abstraction of Additional Sealants Trial and Longer-term Followup of Previous Trial

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Muller-Bolla, 2016[160] *Longer term (3 year) follow up to a study included in the SR (Muller-Bolla, 2013 reported 1 year results)*	276 children (457 tooth pairs)	228 children (378 tooth pairs) Split-mouth design	Children: 17.4% (228/276) Tooth pairs: 17.3% (378/457)	France 16 elementary schools	3 years	Survival analysis, 3 years: Carious lesions in first permanent molars, overall: adjusted HR 0.33, 95% CI 0.24 to 0.46 --Carious lesions (ICDAS 3-6) at baseline: adjusted HR 0.32; 95% CI: 0.23 to 0.46 --No carious lesions (ICDAS 0-2) at baseline: adjusted HR 0.42; 95% CI 0.16 to 1.12	NR	Fair	Dentsply, the city of Nice, and the Conseil General des Alpes Maritimes
Hesse, 2021[146]	187 children	187 children and 748 molars (374 teeth vs 374 teeth) Split-mouth design 4 molars included for each child	Children: 18% Teeth: 18 teeth in each arm	Brazil 26 public schools	3 years	Cumulative survival rates of dentine cavity-free first permanent molars: 90% vs.90.8%, p=0.70 Cox regression with shared frailty analysis of cavitated dentine first permanent molars and associated factors: By comparison arm: HR 0.90, 95% CI 0.55 to 1.49 By baseline caries: HR 1.19, 95% CI 1.09 to 1.33 For every 1-unit increase in the baseline DMFT/dmft, there is a 19% greater chance of caries lesion development for both ART-sealed and non-sealed molars	NR	Fair	Conselho Nacional de Desenvolvimento Científico e Tecnológico and two authors received a research productivity scholarship from CNPq
Uzel, 2022[147]	50 children (200 molars)	50 children (200 molars) Split-mouth design 4 molars included for each child	Children: 24%	Turkey University pediatric dentistry clinic	18 months	Resin-based sealants vs. no sealant: 3.0%-9.4% vs. 25.7%, RR 0.24, 95% CI 0.08 to 0.72 Glass ionomer cement sealant vs. no sealant: 3.0% vs. 25.7%, RR 0.12, 95% CI 0.02 to 0.88	NR	Fair	NR

Abbreviations: ART = atraumatic restorative treatment; CI = confidence interval; CNPq = National Council for Scientific and Technological Development; d3-6ft = decayed (ICDAS 3-6) and filled teeth; D3-6MFT = decayed (ICDAS 3-6), missing and filled teeth; DMFT = Decayed, Missing and Filled Teeth; HR = hazard ratio; ICDAS = International Caries Detection and Assessment System; NR = not reported; RCT = randomized controlled trial; SD = standard deviation; SR = systematic review.

Appendix B Table 16. Quality Assessment of Additional Sealants Trial and Longer-term Followup of Previous Trial

Author, year	Random-ization adequate?	Allocation conceal-ment adequate?	Groups similar at baseline?	Outcome assessors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis?	Patients with missing data analyzed?	Acceptable levels of overall attrition (<20%) and between-group differences (<10%) in attrition?	Post-random-ization exclus-ions	Avoidance of selective outcomes reporting	Adjusted for cluster correlate-ion?	Quality rating
Muller-Bolla, 2016[160]	Yes	Unclear	Yes	Not possible	Not possible	Not possible	Yes	No	Yes Yes (split mouth design)	No	Yes	NA	Fair
Hesse, 2021[146]	Yes	Yes	Yes	Not possible	Not possible	Not possible	NR	Yes	Yes Yes (split mouth design)	No	Yes	NA	Fair
Uzell, 2022[147]	Yes	Yes	Yes	Yes	Not possible	Yes	No	No	Moderate (24%) Yes (split mouth design)	NR	Yes	NA	Fair

Appendix B Table 17. Data Abstraction of Silver Diamine Fluoride Trial

Author, year	Study design	Intervention A	Intervention B	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information	Eligibility criteria
Llodra, 2005[148]	RCT	38% SDF solution applied to primary canines and molars and first permanent molars every 6 months for 36 months	Placebo	All schools in the city run a program for 6 to 15-year-old school children, which includes tooth brushing instruction, dietary recommendations, and mouth rinses every 2 weeks with 0.2% sodium fluoride	NR; examinations were carried out at the school by a study examiner	Age, mean 6.3 (0.5 SD) years % female: 49% Race/ ethnicity: NR	dmfs, mean (SE) Whole sample: 3.6 (0.2) vs. 3.5 (0.3) Schoolchildren followed for 36 months: 3.7 (0.3) vs. 3.4 (0.3) No. surfaces with active caries (SE) Whole sample: 3.0 (0.2) vs. 2.9 (0.3) Schoolchildren followed for 36 months: 3.3 (0.3) vs. 2.9 (0.2) Decayed or filled surfaces in first permanent molars (DFS-1M) (SE): 0.3 (0.0) vs. 0.4 (0.1)	School children 6 years of age

Appendix B Table 17. Data Abstraction of Silver Diamine Fluoride Trial

Author, year	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Llodra, 2005[148]	452	373 (180 vs. 193)	A vs. B: 20% (45/225) vs. 15% (34/227)	Cuba Cuban school-children recruited at a government-funded dental health center located in an area with low community water fluoridation levels (0.9 ppm F)	36 months	A vs. B at 36 months Mean number of new surfaces with active caries in deciduous dentition (mean, SE): 0.3 (0.1) vs. 1.4 (0.2), p<0.001 Surfaces with inactive caries in deciduous dentition (mean, SE): 2.8 (0.3) vs. 1.8 (0.3), p<0.05 New surfaces with active caries (decayed or filled surfaces) in first permanent molars (DFS-1M) (mean, SE): 0.4 (0.1) vs. 1.1 (0.1), p<0.001 New decayed surfaces in first permanent molars (DS-1M) (mean, SE): 0.1 (0.0) vs. 0.2 (0.1), p=0.09 New filled surfaces in first permanent molars (FS-1M) (mean, SE): 0.3 (0.0) vs. 0.9 (0.1), p<0.001 Surfaces with inactive caries in first permanent molars: 0.3 (0.1) vs. 0.1 (0.0), p<0.05 DFT increment ≥1: 26.1% (47/180) vs. 49.7% (96/193), RR 0.52 (95% CI 0.40 to 0.70)	Surfaces with inactive caries and black stain in deciduous teeth: 97% vs. 48%, p<0.001 Surfaces with inactive caries and black stain in first permanent molars: 86% vs. 67%, p<0.001	Fair	Government (Balearic Islands)

Abbreviations: CI = confidence interval; dmfs = decayed, missing, or filled tooth surfaces; DFS-1M = active decayed surfaces in first permanent molars; DFT = decayed, restored tooth index; DS-1M = new decayed surfaces in first permanent molars; FS-1M = filled surfaces in first permanent molars; NA = not applicable; NR = not reported; ppm = parts per million; RCT = randomized controlled trial; RR = relative risk; SD = standard deviation; SDF = silver diamine fluoride; SE = standard error.

Appendix B Table 18. Quality Assessment of Silver Diamine Fluoride Trial

Author, year	Random-ization adequate?	Allocation conceal-ment adequate?	Groups similar at baseline?	Outcome assessors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis?	Patients with missing data analyzed?	Acceptable levels of overall attrition (<20%) and between-group differences (<10%) in attrition?	Post-random-ization exclus-ions?	Avoidance of selective outcomes reporting?	Adjusted for cluster correlat-ion?	Quality rating
Llodra, 2005[148]	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Yes	No	Yes Yes	No	Yes	NA	Fair

Abbreviations: NA=not applicable.

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Study design	Intervention A	Intervention B	Intervention C	Intervention D	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information
Alanen, 2000[149]	Cluster trial (12 schools)	Xylitol-malitol candy with 49% xylitol, 2-3 pieces 3 times daily (8 pieces total) on school days Group A1: received intervention for 2 years Group A2: received intervention for 3 years	Xylitol-polydextrose candy with 49% xylitol, 2-3 pieces 3 times daily (8 pieces total) on school days Group B1: received intervention for 2 years Group B2: received intervention for 3 years	Xylitol gum with 49% xylitol 3 times per day on school days, for 3 years	No xylitol	NA	Teacher	Age, mean: 10 years % female: 54% at final examination Race/ ethnicity: NR	DMFS=2.01 Water fluoridation: NR
Honkala, 2006[156]	Trial (individually allocated from two schools)	49% xylitol candies, three times per school day	No xylitol	NA	NA	NA	School nurse	Age: 10 to 12 years: 42/176 (24%) 13 to 15 years: 64/176 (36%) 16 to 18 years: 49/176 (28%) 19 to 27 years: 21/176 (12%) % female: NR Race/ ethnicity: NR	A vs. B DMFT, mean (SD): 4.3 (4.6) vs. 4.4 (4.0), p=0.68 DMFS, mean (SD): 7.3 (11.4) vs. 7.1 (8.3), p=0.53 Water fluoridation: NR
Isokangas, 1988[150]	Cluster trial (number of clusters unclear)	64.7% xylitol chewing gum, three times daily at school and home	No xylitol	NA	NA	All children participated in organized dental health programs, including fluoride tablets, fluoride dentifrice, and weekly fluoride rinses at school	Dental nurse at school and parents at home	Age: 11-12 years % female: 49% at 2 year followup Race/ ethnicity: NR	Boys: no difference in cariesGirls: fewer caries in group A than group BWater fluoridation: <0.1 ppm F

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Study design	Intervention A	Intervention B	Intervention C	Intervention D	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information
Kandelman, 1988[157]	Cluster trial (3 islands)	Xylitol products (various gums and candies), totaling 20g xylitol daily at school or home	Xylitol products (various gums and candies), totaling 20g xylitol daily at school or home	No xylitol	NA	All children were supplied with fluoride dentifrice and received regular instruction on oral hygiene.	Teacher	Age, mean: 8.2 years % female: NR Race/ ethnicity: NR	DMFS: mean 1.50 to 17.33 in group A, 2.58 to 8.22 in group B, and 2.31 to 14.00 in group C (stratified by age, with increasing prevalence by age) Water fluoridation: NR
Kandelman, 1990[151]	Cluster trial (13 schools)	65% xylitol chewing gum three times daily on school days	15% xylitol/50% sorbitol chewing gum three times daily on school days	No xylitol	NA	All children participated in oral health program including oral health education and fluoride rinsing.	Teacher	Age, mean: 8.7 years % female: 49% Race/ ethnicity: NR	DMFS, mean (SD): 6.33 (4.31) vs. 6.27 (4.06) vs. 5.67 (4.26)Fluoride mouth rinse (mean months of exposure): 16.9 vs. 18.0 vs. 19.0 Water fluoridation: NR
Lee, 2015[152]	Cluster trial (5 schools)	Gummy bears containing 2.6 grams xylitol, three times daily on school days	Placebo gummy bears	NA	NA	All children received oral health education, toothbrush, fluoridated toothpaste, fluoride varnish, and dental sealants on first permanent molars	Outreach workers	Age: 5 to 6 years % female: 53% Race/ ethnicity: African American: 77%	Caries burden, dmfs/DMFS: 0: 112/260 (43%) vs. 138/265 (52%) 1-5:68/260 (26%) vs. 66/265 (25%) ≥6: 80/260 (31%) vs. 61/265 (23%) Water fluoridation: NR

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Study design	Intervention A	Intervention B	Intervention C	Intervention D	Other notes about intervention	Interventionist	Baseline study characteristics	Baseline oral health information
Lenkkeri, 2012[153]	Cluster trial (21 schools)	49% Xylitol/47.46% maltitol lozenges three times daily on school days for 1 year (average 190 days per year)	49% Xylitol/47.46% maltitol lozenges three times daily on school days for 2 years (average 190 days per year)	Control	Two group evaluating erythritol are not included in this review	All children participated in routine caries prevention programs, including fluoride toothpaste	Teacher	Age, mean: 10 years % female: 53% Race/ ethnicity: NR	D_3MFS=0: 410/496 (82.7%) Water fluoridation status: Naturally fluoridated (concentration <1.5 mg/mL)
Machiulskiene, 2001[154]	Cluster RCT (5 schools)	Xylitol gum five times per day	Control gum five times per day	No gum	Two groups evaluating sorbitol gum are not included in this review	NA	Teacher at school and parent at home	Age, mean: 11.6 years % female: 51% Race/ ethnicity: NR	DMFS, mean (SD):A: 13.2 (8.9)B: 15.3 (8.0)C: 14.3 (8.0) Water fluoridation status: <0.2 ppm F
Makinen, 1995[158]	Cluster RCT (19 schools)	65% xylitol pellet gum five times per day	65% xylitol pellet gum three times per day	No gum	NA	No oral health education, most children in Belize use toothbrushes and fluoride toothpaste	Teacher at school, parents at home	Age, mean years: 10 vs. 9.9 vs. 10.2 % female: 48.6% vs. 35.8% vs. 54.5 Race/ ethnicity: NR	DMFS, mean (SD): 5.7 (5.2) vs. 4.0 (5.1) vs. 4.8 (5.4) Water fluoridation: no water fluoridation
Scheinin 1985,[155] Scheinin 1985,[162] Scheinin 1985,[161]	Cluster trial (11 clusters)	Xylitol: 20g/day in various candies and gums + 10% xylitol containing sodium mono-fluoro-phosphate dentifrice	No fluoride or xylitol: fluoride-free dentifrice	NA	NA	NA	NR	Age: 6 to 12 years % female: 41% Race/ ethnicity: NR	DMFS, mean (SD): 4.6 (5.0) vs. 4.3 (4.2) vs. 4.8 (4.6) Water fluoridation: NR

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Eligibility criteria	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Alanen, 2000[149]	10 year old children in 4th grade in participating schools	N=740 A1: 125 A2: 89 B1: 105 B2: 93 C: 148 D: 180	N=567 A1: 96 A2: 73 B1: 71 B2: 66 C: 115 D: 146	Overall: 23% A1: 23% A2: 18% B1: 32% B2: 29% C: 22% D: 19%	Estonia Schools	3 years	A1 vs. A2 vs. B1 vs. B2 vs. C vs. D DMFS increment at 3 years, mean (SD): 2.50 (2.34) vs. 1.72 (2.04) vs. 1.68 (2.63) vs. 2.77 (3.05) vs. 1.87 (2.55) vs. 4.42 (4.36); p<0.000001 for D vs. all other groups	NR	Poor	Leaf Company (xylitol products) Finnish Dental Association
Honkala, 2006[156]	Persons 10 to 27 years of age in participating schools for physically disabled individuals with high caries experience (88% of participants were 10 to 18 years of age)	216	N=145 A: 105 B: 40	33%	Kuwait Schools	2 years	A vs. B Change from baseline, mean (SD) DMFT: -1.1 (1.8) vs. 1.2 (1.8), p<0.001 DMFS: -1.2 (3.4) vs. 3.5 (4.6), p<0.001 Age and baseline caries experience were controlled as covariates	NR	Poor	Leaf Company Kuwait University Grant
Isokangas, 1988[150]	11 to 12 year old children in fifth and sixth grades in participating schools	366	N=324 A: 172 B: 152	11%	Finland School	3 years	A vs. B D_{1-2}MFS increment: 1.3 vs. 2.3 at 2 years, p<0.01; p<0.01 for all types of surfaces (mean values not reported) D_2MFS increment: 1.1 vs. 2.0 at 2 years, p<0.001	NR	Poor	Leaf Company
Kandelman, 1988[157]	6 to 12 years old children attending participating schools	746	468 A: 164 B: 109 C: 195	37%	French Polynesia School	32 months	A vs. B vs. C D_{1-4}MFS increment, mean (SD): 4.58 (4.27) vs. 4.37 (3.48) vs. 7.19 (5.48); p<0.001 for A or B vs. C Baseline caries data was treated as a covariate	NR	Poor	Xyrofin Ltd.; and Adams Brands, Inc. supplied some test products

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Eligibility criteria	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Kandelman, 1990[151]	Children 8 to 9 years (third grade) in participating schools	574	274 A: 87 B: 90 C: 97	52%	Canada School	24 months	A vs. B vs. C DMFS increment (mean, 95% CI): 1.40 (95% CI 1.0 to 1.7) vs. 1.56 (95% CI 1.1 to 1.8) vs. 3.40 (95% CI 3.0 to 3.7) at 1 year; 2.09 (95% CI 1.5 to 2.4) vs. 2.39 (95% CI 1.7 to 2.6) vs. 6.06 (95% CI 5.6 to 6.5) Age, gender, baseline DMFS, baseline plaque, observer, and surfaces at risk were treated as covariates	NR	Poor	Warner Lambert Ltd supplied gum
Lee, 2015[152]	Children 5 to 6 years in participating schools	562	A: 122 B: 139	53.5%	Ohio, U.S. School	30 months	A vs. B New dmfs at 30 months, mean (SD): 5.7 (7.6) vs. 4.7 (6.7), p=0.45 New DMFS at 30 months, mean (SD): 1.03 (1.62) vs. 1.05 (1.85), p=0.55	Gastrointestinal discomfort: 17 (group NR)	Poor	Health and Human Services grant
Lenkkeri, 2012[153]	Children in grade 4 at participating schools	344	296 A: 96 B: 99 C: 101	14.30%	Finland School	4 years	A vs. B vs. C D_3MFS (clinical and radiographical) increment at 4 years, mean (SD): 2.75 (2.7) vs. 3.02 (3.3) vs. 2.74 (3.1) D_3MFS (clinical) increment at 4 years, mean (SD): 1.64 (2.1) vs. 1.64 (2.4) vs. 1.52 (2.3) D_3MFS >0 (clinical and radiographical) at 4 years: 81% (78/96) vs. 80% (79/99) vs. 77% (78/101); adjusted OR 1.12 (95% CI 0.44 to 2.86) for A vs. C and 1.01 (95% CI 0.40 to 2.56) for B vs. C D_3MFS >0 (clinical) at 4 years: 58% (56/96) vs. 53% (53/99) vs. 57% (58/101)	1 study with-drawal due to diarrhea	Fair	CSM leaf provided xylitol lozenge

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Eligibility criteria	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Machiulskiene, 2001[154]	Children 9 to 14 years of age in participating schools	366	3-year analysis: Clinical: 276 A: 99 B: 97 C: 80 Radio-graphic: 231 A: 99 B: 95 C:37	Clinical: 28% Radio-graphic: 39%	Lithuania School	3 years	A vs. B vs. C DMFS (all stages) increment, mean (95% CI, adjusted mean): 5.5 (4.1 to 6.8; 5.9) vs. 5.4 (4.1 to 6.8; 5.3) vs. 6.7 (5.5 to 7.9; 6.5) at 2 years (p>0.05 for A vs. B or C); 8.1 (6.8 to 9.3; 8.4) vs. 8.3 (6.7 to 9.9; 8.1) vs. 12.4 (10.7 to 14.2; 12.1) at 3 years (p<0.05 for A vs. C; p>0.05 for A vs. B) DMFS (cavitated stages) increment, adjusted mean: 2.9 (2.1 to 3.6; 2.8) vs. 3.1 (2.3 to 3.8; 2.9) vs. 4.0 (3.2 to 4.9; 4.0) at 2 years (p>0.05 for A vs. B or C); 3.4 (2.7 to 4.2; 3.3) vs. 4.3 (3.3 to 5.2; 4.0) vs. 5.3 (4.2 to 6.4; 5.2) at 3 years (p<0.05 for A vs. C, p>0.05 for A vs. B) DMFS (x-ray) increment, adjusted mean: 3.2 (2.6 to 3.8; 3.1) vs. 2.7 (2.0 to 3.4; 2.9) vs. 3.5 (2.3 to 4.6; 3.5) at 3 years (p>0.05 for A vs. B or C) DMFS increment ≥14 (reference sorbitol/ carbamide gum): adjusted OR 0.2 (95% CI 0.1 to 0.5) for xylitol gum, 0.3 (95% CI 0.2 to 0.7) for control gum, 0.9 (95% CI 0.5 to 1.8) for no gum	NR	Fair	Dandy A/S, Vejle, Denmark, Aarhus University Research Foundation, Nordic Council of Ministers

Appendix B Table 19. Data Abstraction of Xylitol Trials

Author, year	Eligibility criteria	No. enrolled	No. analyzed	Attrition	Country Setting	Duration of followup	Outcomes	Adverse events/ harms	Quality rating	Sponsor
Makinen, 1995[158]	Children in grade 4 at participating schools	NR	379 A: 125 B: 133 C: 121	NR (unable to calculate)	Belize School	40 months	A vs. B vs. C Change in DMFS at 40 months, mean (SD): -0.8 (0.5) vs. 0.9 (0.5) vs. 4.9 (0.5) A vs. C: p=0.0001 B vs. C: p=0.0001 Adjusted for gender, age, number of sound surfaces at baseline	NR	Poor	Leaf Group
Scheinin 1985,[155] Scheinin 1985,[162] Scheinin 1985,[161]	6 to 12 years old children (primarily orphans) living in participating institutions	1,219	976 at 2 years A: 399 B: 356 C: 221 689 at 3 years A: 278 B: 266 C: 145	20%	Hungary Institutional home	2 years	A vs. B D_{1-4}MFS increment, mean (SD): 3.8 (3.7) vs. 6.0 (4.7) at 2 years; 4.2 (4.0) vs. 7.7 (5.4) at 3 years D_{2-4}MFS increment, mean (SD): 1.8 (2.4) vs. 2.5 (2.7) at 2 years; 2.3 (2.8) vs. 3.5 (3.3) at 3 years D_{3-4}MFS increment at 2 years, mean (SD): 1.8 (2.1) vs. 1.9 (2.3) D_{2-4}MFT increment, mean (SD): 1.2 (1.4) vs. 1.6 (1.6) at 2 years; 1.4 (1.7) vs. 2.2 (2.1) at 3 years D_{3-4}MFT increment, mean (SD): 1.6 (1.6) vs. 1.6 (1.9) at 3 years	NR	Poor	NR

Abbreviations: CI = confidence interval; CSM = D1-2MFS = decayed (ICDAS 1-2), missing and filled surfaces; D2MFS = decayed (ICDAS 2), missing and filled surfaces; D3MFS = decayed (ICDAS 3), missing and filled surfaces; DMFS = decayed, missing, or filled tooth surfaces; D2-4MFT = decayed (ICDAS 2-4), missing and filled teeth; DMFT = Decayed, Missing and Filled Teeth; NA = not applicable; NR = not reported; OR = odds ratio; ppm = parts per million; RCT = randomized controlled trial; SD = standard deviation.

Appendix B Table 20. Quality Assessment of Xylitol Trials

Author, year	Random-ization adequate?	Allocation concea-lment adequate?	Groups similar at baseline?	Outcome assessors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis?	Patients with missing data analyzed?	Acceptable levels of overall attrition (<20%) and between-group differences (<10%) in attrition?	Post-random-ization exclus-ions	Avoid-ance of selective outcomes reporting	Adjusted for cluster correlat-ion?	Quality rating
Alanen, 2000[149]	Unclear	Unclear	Unclear	Unclear	No	No	Yes	No	No No	No	Yes	No	Poor
Honkala, 2006[156]	No	No	Yes	No	No	No	Yes	No	No Yes	No	Yes	NA	Poor
Isokangas, 1988[150]	Unclear	Unclear	No	Yes	No	No	Yes	No	Yes Yes	No	Yes	No	Poor
Kandel-man, 1988[157]	No	No	No	No	No	No	Yes	No	No Yes	No	Yes	No	Poor
Kandel-man, 1990[151]	Unclear	Unclear	Yes	No	No	No	Yes	No	No Yes	No	Yes	No	Poor
Lee, 2015[152]	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No	No Yes	No	Yes	No	Poor
Lenkkeri, 2012[153]	Unclear	Yes	Yes	Yes	Yes	No	Yes	No	Yes Yes	No	Yes	Yes for dichot-omous outcomes No for contin-uous outcomes	Fair
Machiul-skiene, 2001[154]	Unclear	Yes	No	Unclear	Unclear	Yes (xylitol gum vs. non-xylitol gum)	Yes	No	No Yes	No	Yes	No	Fair
Makinen, 1995[158]	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	No	Unclear No	Unclear	Yes	No	Poor

Appendix B Table 20. Quality Assessment of Xylitol Trials

Author, year	Random-ization adequate?	Allocation concea-lment adequate?	Groups similar at baseline?	Outcome assessors masked?	Care provider masked?	Patient masked?	Intention-to-treat analysis?	Patients with missing data analyzed?	Acceptable levels of overall attrition (<20%) and between-group differences (<10%) in attrition?	Post-random-ization exclus-ions	Avoid-ance of selective outcomes reporting	Adjusted for cluster correlat-ion?	Quality rating
Scheinin, 1985[155] Scheinin, 1985[162] Scheinin, 1985[161]	Unclear	Unclear	No	Unclear	No	No	Yes	No	No Yes	No	Yes	No	Poor

Abbreviations: NA=not applicable.