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Prevention of Dental Caries in Children Younger Than 5 Years Old: Systematic Review to Update the U.S. Preventive Services Task Force Recommendation

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Suggested Citation

Structured Abstract

**Background:** A 2004 U.S. Preventive Services Task Force (USPSTF) review recommended that primary care clinicians prescribe oral fluoride supplementation to preschool children over the age of 6 months whose primary water source is deficient in fluoride but found insufficient evidence to recommend for or against risk assessment of preschool children by primary care clinicians for the prevention of dental caries.

**Purpose:** To systematically update the 2004 USPSTF review on prevention of dental caries in children younger than age 5 years by medical primary care clinicians.

**Methods:** We searched the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the 1st quarter of 2013) and Ovid MEDLINE® (1999 through March 8, 2013) and manually reviewed reference lists.

**Results:** No randomized trial or observational study compared clinical outcomes between children younger than age 5 years screened and not screened by primary care clinicians for dental caries. One good-quality cohort study found primary care pediatrician examination following 2 hours of training associated with a sensitivity of 0.76 for identifying a child with one or more cavities and 0.63 for identifying children age <36 months in need of a dental referral compared with a pediatric dentist evaluation. No study evaluated the accuracy of risk-assessment tools applied by primary care clinicians to identify children younger than age 5 years at increased risk for future dental caries. We identified no new trials on the effects of oral fluoride supplementation in children younger than 5 years on dental caries outcomes. Three randomized trials published since the prior USPSTF review were consistent with three previous trials in finding fluoride varnish more effective than no fluoride varnish in reducing caries incidence in higher risk children younger than age 5 years (percent reduction in caries increment, 18 to 59%), although in all trials fluoride varnish was applied by dental personnel. Three trials reported no clear effects of xylitol versus no xylitol on caries incidence in children younger than 5 years. Five new observational studies in an updated systematic review were consistent with previous findings of an association between early childhood exposure to systemic fluoride and enamel fluorosis. Other than diarrhea, reported in two trials of xylitol, harms were poorly reported in trials of caries prevention interventions. Evidence on the effectiveness of educational or counseling interventions and the effectiveness of primary care referral to a dentist remains sparse or unavailable.

**Limitations:** Only English-language articles were included. Due to limited evidence from randomized trials, we included nonrandomized trials. Studies conducted in resource-poor settings may be of limited applicability to screening in the United States.

**Conclusions:** Evidence previously reviewed by the USPSTF found oral fluoride supplementation effective at reducing caries incidence in children younger than age 5 years but associated with risk of enamel fluorosis. New evidence supports the effectiveness of professionally applied fluoride varnish at preventing caries in higher risk children younger than age 5 years. Research is needed to understand the accuracy of primary care oral health.
examination and caries risk assessment, primary care referral to dental care, and effective parental and caregiver/guardian educational and counseling interventions.
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Chapter 1. Introduction

Purpose and Previous U.S. Preventive Services Task Force Recommendation

This report was commissioned by the U.S. Preventive Services Task Force (USPSTF) in order to update its 2004 recommendation on prevention of dental caries by medical primary care clinicians in children younger than age 5 years.1

In 2004, the USPSTF recommended that primary care clinicians prescribe dietary fluoride supplementation to children over the age of 6 months whose primary water source is deficient in fluoride (B recommendation).1 This recommendation was based on fair evidence that in young children with low fluoride exposure, prescription of dietary fluoride supplements by primary care clinicians is associated with reduced risk of dental caries that outweighs potential harms of enamel fluorosis, which in the United States is primarily manifested as mild cosmetic discoloration of teeth.2

In 2004, the USPSTF also concluded that the evidence was insufficient to recommend for or against routine risk assessment of children younger than age 5 years by primary care clinicians for the prevention of dental disease (I recommendation). The USPSTF found no validated risk-assessment tools or algorithms for assessing dental disease risk by primary care clinicians and little evidence on the accuracy of primary care clinicians in assessing dental disease risk or in performing oral examinations.3 In addition, the USPSTF found little evidence on the effectiveness of counseling parents or referring high-risk children to dental care providers in reducing risk of caries and related dental disease. Therefore, the USPSTF concluded that there was insufficient evidence to determine the balance between benefits and harms of routine risk assessment to prevent dental disease in children younger than age 5 years.

Condition Definitions

Dental caries, or tooth decay, is an infectious process involving breakdown of the tooth enamel. Caries form through a complex interaction between cariogenic acid-producing bacteria in combination with fermentable carbohydrates and other dietary, genetic, behavioral, social, and cultural factors.3-5

Children are susceptible to caries as soon as the first teeth appear, which usually occurs around age 6 months. Early childhood caries is defined as the presence of one or more decayed (noncavitated or cavitated), missing (due to caries), or filled tooth surfaces (dmf) in preschool-age children.6 The abbreviation dmfs refers to decayed, missing, or filled primary tooth surfaces, and dmft refers to decayed, missing, or filled primary teeth (one tooth may have more than one affected surface).
Prevalence and Burden of Disease

Dental caries is the most common chronic disease of children in the United States and is increasing in prevalence among young children. The National Health and Nutrition Examination Survey (NHANES) found that the prevalence of caries in primary teeth in 2- to 5-year-olds increased from approximately 24 to 28 percent between the periods 1988 to 1994 and 1999 to 2004. Approximately three-quarters of children with caries had not received treatment for the condition.

Dental caries disproportionately affects minority and economically disadvantaged children. NHANES found that 54 percent of children age 2 to 11 years in families below the Federal poverty threshold experienced primary tooth dental caries, compared with one-third of children in families with incomes above 200 percent of the poverty threshold. Mexican-American children were more likely to experience dental caries in primary teeth (55%) than were black children (43%) or white children (39%), and were more likely to have untreated dental caries (33, 28, and 20%, respectively). In addition to higher prevalence, the severity of dental caries is also greater in economically disadvantaged and minority children.

Early childhood caries is associated with pain and loss of teeth, as well as impaired growth, decreased weight gain, and negative effects on quality of life. Repairs or extractions of carious teeth can be traumatic experiences for young children and occasionally result in serious complications. Early childhood caries is also associated with failure to thrive; can affect appearance, self-esteem, speech, and school performance; and is associated with future caries in both the primary and permanent dentitions. Premature loss of primary molars due to early childhood caries can result in loss of arch space, leading to crowding of the permanent teeth, affecting aesthetics and potentially requiring orthodontic correction. In 2000, the U.S. Surgeon General estimated that over 50 million school hours are lost each year nationally due to dental-related concerns. More recent data indicate that more than 4 million school hours are lost each year due to dental care in the State of North Carolina, with over 700,000 of these hours lost due to dental pain or infection.

Etiology and Natural History

Dental caries is a disease that occurs when bacteria, predominantly Streptococcus mutans, colonize the tooth surface and metabolize dietary carbohydrates (especially refined sugars) to produce lactic and other acids, resulting in demineralization of teeth. In children age 12 to 30 months, caries typically initially affects the maxillary primary incisors and first primary molars, reflecting the pattern of eruption. 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 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 leads to pulpitis and tooth loss, and can be associated with complications such as facial cellulitis and systemic infections.
Risk Factors and Indicators

Risk factors for dental caries in young children include high levels of cariogenic bacterial colonization, frequent exposure to dietary sugar and refined carbohydrates, inappropriate bottle feeding, low saliva flow rates, developmental defects of tooth enamel, low socioeconomic status, previous caries, maternal caries, high maternal levels of cariogenic bacteria, and poor maternal oral hygiene.13,15 Other risk factors include lack of access to dental care, low community water fluoride levels, inadequate tooth brushing or inadequate use of fluoride-containing toothpastes, and lack of parental knowledge regarding oral health.8

Rationale for Screening and Screening Strategies

Screening for dental caries and risk for caries in young children prior to school entry could identify caries at an earlier and reversible stage, and lead to interventions to treat existing caries, prevent progression of caries, and reduce incidence of future lesions. Screening strategies typically include oral health risk assessment and visual examination to identify high-risk children, including those who already have caries. Primary care clinicians can play an important role in screening for dental caries because many young children routinely see a primary care provider starting shortly after birth but do not see a dentist until they are older.16 Approximately three-quarters of children under age 6 years did not have at least one visit to a dentist in the previous year, although the proportion with a visit increased from 21 percent in 1996 to 25 percent in 2004.17 Access to dental care is limited by many factors, including shortages in dentists treating young children, particularly children who are not insured or who are publicly insured.18 Once children enter school, there are additional opportunities for screening and treatment.19

Interventions and Treatment

In young children at risk for dental caries, interventions focus on reducing the burden of bacteria, reducing the intake of refined sugars, and increasing the resistance of teeth to caries development.3,15 Strategies to reduce the burden of bacteria include the use of fluoride, parental counseling to improve oral hygiene, xylitol, and topical antimicrobials such as chlorhexidine or povidone-iodine. Educational and behavioral interventions can reduce intake of refined sugars through changes in diet and feeding practices. Children with caries or at risk of caries can also be referred for needed dental care.

Fluoride increases the resistance of teeth to caries development. Fluoride exposure can be topical (fluoride dentifrices, rinses, gels, foams, varnishes) or systemic (dietary fluoride supplements).3,15 Effects of fluoridated water are both topical and systemic. After exposure, fluoride is incorporated into 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.3,14 A potential harm of excessive systemic fluoride exposure is enamel fluorosis, a visible change in enamel opacity due to altered mineralization. The severity of change depends on the dose, duration and timing of fluoride intake, and is most strongly
associated with cumulative intake during enamel development. Mild fluorosis manifests as small opaque white streaks or specks in the tooth enamel.\textsuperscript{2} Severe fluorosis results in discoloration and pitted or rough enamel.\textsuperscript{14} The prevalence of severe enamel fluorosis in the United States was estimated at less than 1 percent in the period 1999 to 2004.\textsuperscript{2}

Topical fluoride is typically applied as a varnish in young children. Unlike fluoride gels, which are commonly used in older school-aged children, fluoride varnish does not require specialized dental devices or equipment and can be applied quickly without the risk of the child swallowing large amounts, which can cause transient gastric irritation.\textsuperscript{3} Compared with other topical fluoride application methods (such as acidulated phosphate fluoride or sodium fluoride gel), systemic exposure to fluoride is low following application of fluoride varnish.\textsuperscript{20,21} The varnish results in prolonged contact time between the fluoride and the tooth surface, enhancing incorporation into the tooth surface layers and more prolonged release. Fluoride varnish is typically available in the United States as 5-percent sodium fluoride (2.26\% fluoride).

Xylitol is a naturally occurring sugar with properties that reduce levels of caries-forming mutans streptococci in the plaque and saliva.\textsuperscript{22} In young children, xylitol can be administered as a syrup or topically via wipes. In older children, xylitol can also be administered in gum, lozenges, or snack foods. Other topical antimicrobials such as chlorhexidine varnish and povidone-iodine rinses are not in common use in young children in the United States or are not available, as in the case of chlorhexidine varnish.

**Current Clinical Practice**

Since the publication of the Surgeon General’s Report on Oral Health in 2000,\textsuperscript{8} many organizations have emphasized the importance of preventive oral health care for young children, particularly in the primary care setting. The American Academy of Pediatrics (AAP) has developed an oral health risk-assessment tool for use in primary care settings starting at the 6-month visit, along with suggested interventions for children at risk.\textsuperscript{23} The American Academy of Pediatric Dentistry (AAPD) developed the Caries-risk Assessment Tool (CAT), designed for use by dental and nondental personnel.\textsuperscript{24} Although the vast majority of pediatricians agree with recommendations on oral health screening, only about half report examining the teeth of more than half of their patients age 0 to 3 years, and few (4 percent) report regularly applying fluoride varnish.\textsuperscript{18}

**Recommendations of Other Groups**

In 2003, the AAP issued a policy statement that encouraged practitioners to incorporate oral-health–related services into their practice by engaging in oral health assessments, anticipatory guidance, and preventive services, including making referrals to dentists. More specifically, an oral health assessment was recommended for all children by age 6 months and a first dental visit by age 1 year.\textsuperscript{25} These recommendations were reaffirmed in 2009 and were also endorsed by the Bright Futures program.\textsuperscript{26,27} In a second policy statement, the AAP supported the use of dietary fluoride supplementation and the application of fluoride varnish for children at risk for dental
The American Dental Association (ADA) recommends the application of fluoride varnish every 6 months in preschool children at moderate risk of dental caries and every 3 to 6 months in those at high risk. The American Academy of Family Physicians, the ADA, and others recommend that clinicians consider the use of dietary fluoride supplementation in children age 6 months to 16 years who lack access to adequately fluoridated drinking water. Recommended doses of dietary fluoride supplementation range from 0.25 to 1.0 mg per day, depending on age, the level of community or household water fluoridation, and ingestion of other dietary fluoride sources. Dietary fluoride supplementation is not recommended when water fluoridation levels are greater than 0.6 parts per million fluoride (ppm F) or when caries risk is low.

The U.S. Centers for Disease Control and Prevention recommend that clinicians counsel parents about appropriate use of fluoride toothpaste, especially in children under age 2 years; prescribe dietary fluoride supplements in children at high risk of dental caries whose drinking water lacks adequate fluoride, and limit the use of products with high fluoride concentration, such as varnish and gel, to high-risk individuals. It recommends that clinicians account for overall ingestion of fluoride through diet, drinking water, and other sources and consider the risk of dental fluorosis before prescribing supplements or applying products with high fluoride concentration.

The AAPD recommends use of xylitol in age-appropriate formulations for moderate- and high-risk children. The ADA recommends xylitol in children age 5 years or older, recommends against use of chlorhexidine varnish, and found insufficient evidence to determine effectiveness of povidone-iodine.
Chapter 2. Methods

Key Questions and Analytic Framework

Using methods developed by the USPSTF,\textsuperscript{34,35} representatives from 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 population, interventions, and outcomes reviewed (Figure 1). The target population was asymptomatic children younger than age 5 years, including children with existing dental caries who need additional preventive or restorative interventions for untreated disease. Community interventions for prevention of dental caries and school-based interventions for older children are addressed elsewhere by the U.S. Community Services Task Force.\textsuperscript{36}

We also addressed a “contextual question” requested by the USPSTF to help inform the report. Contextual questions address background areas deemed important by the USPSTF for informing its recommendations. Contextual questions are not reviewed using systematic review methodology, but rather summarize the evidence from key informative studies.

Key Questions

1. How effective is oral screening (including risk assessment) by the primary care clinician in preventing dental caries in children younger than 5 years of age?
2. How accurate is screening by the primary care clinician in identifying children younger than 5 years of age who:
   a. Have cavitated or noncavitated caries lesions?
   b. Are at increased risk for future dental caries?
3. What are the harms of oral health screening by the primary care clinician?
4. How effective is parental or caregiver oral health education by the primary care clinician in preventing dental caries in children younger than 5 years of age?
5. How effective is referral by a primary care clinician to a dentist in preventing dental caries in children younger than 5 years of age?
6. How effective is preventive treatment (dietary fluoride supplementation, topical fluoride application, or xylitol) in preventing dental caries in children younger than 5 years of age?
7. What are the harms of specific oral health interventions for prevention of dental caries in children younger than 5 years of age (parental or caregiver oral health education, referral to a dentist, and preventive treatments)?

Contextual Question

What percentage of children younger than 5 years of age in the United States have access to dental care, and what factors are associated with access to dental care in this population? (Access to dental care is defined as the ability of a child to receive dental care services, based on availability of dental care providers and/or ability to pay for those services.)
Key Question 1 focuses on direct evidence on the effectiveness of oral screening (defined to include oral examination as well as risk assessment for future caries) by medical primary care clinicians in preventing future dental caries and associated complications compared with not screening. Such direct evidence on the effectiveness of screening interventions may be limited. Therefore, the remainder of the analytic framework (Key Questions 2 through 7) evaluates the chain of indirect evidence needed to link screening with improvement in important health outcomes. Links in the chain of indirect evidence include the accuracy of screening by primary care clinicians in identifying children with dental caries or at increased risk of developing caries, the effectiveness of primary care interventions for reducing the incidence of dental caries and associated complications, and harms (including dental fluorosis) associated with screening and preventive treatments. It is implicit in the indirect chain of evidence that, to understand benefits and harms of screening, it is necessary but not sufficient to show that children at risk for dental caries can be identified; it is also necessary to show that there are effective treatments for those identified.

**Search Strategies**

We searched Ovid MEDLINE® (January 1999 to March 8, 2013) and the Cochrane Library Database (through the first quarter of 2013) for relevant articles. Search strategies are shown in Appendix A1. We also reviewed reference lists of relevant articles.

**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). Articles were selected for full review if they were about dental caries in preschool children, were relevant to a Key Question, and met the predefined inclusion criteria. We restricted inclusion to English-language articles and excluded studies published only as abstracts. Studies of nonhuman subjects were also excluded, and studies had to report original data.

For all Key Questions, we included studies of children younger than age 5 years, including those with dental caries at baseline. We focused on studies of screening or diagnostic accuracy performed in primary care settings. For preventive treatments (Key Question 6), we also included studies of treatments feasible in primary care (treatments not requiring extensive dental-specific training) that were performed in non–primary care settings, but noted whether the treatment was administered by people with dental training. Interventions were parental or caregiver education, referral to a dentist by a primary care clinician, and preventive treatments, including dietary fluoride supplementation, topical fluoride application, xylitol, and antimicrobial rinses and varnishes. Outcomes were decreased incidence of dental caries and associated complications, and harms, including dental fluorosis. We included randomized, controlled trials, nonrandomized, controlled clinical trials, and cohort studies for all Key Questions. We also included an updated systematic review of observational studies on risk of
enamel fluorosis that was originally included in the 2004 USPSTF review. Appendix A3 shows the results of our literature search and selection process, and Appendix A4 lists excluded studies with reasons for exclusion.

**Data Abstraction and Quality Rating**

One investigator abstracted details about each article’s study design, patient population, setting, screening method, treatment regimen, analysis, followup, and results. A second investigator reviewed data abstraction for accuracy. Two investigators independently applied criteria developed by the USPSTF to rate the quality of each study as good, fair, or poor (Appendix A5). Discrepancies were resolved through a consensus process.

**Data Synthesis**

We assessed the aggregate internal validity (quality) of the body of evidence for each Key Question (good, fair, poor) using methods developed by the USPSTF based on the number, quality, and size of studies; consistency of results among studies; and directness of evidence. Meta-analysis was not attempted due to methodological shortcomings in the studies and differences across studies in design, interventions, populations, and other factors.

**External Review**

The draft report was reviewed by content experts, USPSTF members, AHRQ Project Officers, and collaborative partners, and revised prior to finalization (Appendix A6).

**Response to Comments Received During the Public Comment Period**

This evidence report was posted for public comment from May 21 to June 20, 2013. The systematic review team reviewed and considered comments relevant to the report and referred comments relevant to the recommendation statement to the USPSTF. No comments pointed out missing studies that met inclusion criteria or errors in the evidence reviewed. Therefore, the public comment process resulted in no changes to the findings or the conclusion of the evidence report.
Chapter 3. Results

Key Question 1. How Effective Is Oral Screening (Including Risk Assessment) by the Primary Care Clinician in Preventing Dental Caries in Children Younger Than Age 5 Years?

No randomized trial or observational study compared clinical outcomes between children younger than 5 years of age screened and not screened by primary care clinicians.

Key Question 2a. How Accurate Is Screening by the Primary Care Clinician in Identifying Children Younger Than Age 5 Years Who Have Cavitated or Noncavitated Caries Lesions?

Summary

One good-quality study found primary care pediatrician examination of children younger than age 36 months following 2 hours of oral health education associated with a sensitivity of 0.76 for identifying a child with one or more cavities and 0.63 for identifying children in need of a dental referral compared with a pediatric dentist evaluation. Specificity was 0.95 for identifying children with cavities and 0.98 for identifying children who needed a dental referral. A study included in the 2004 USPSTF review found pediatrician examination following 4 hours of oral health education associated with a sensitivity of 1.0 and specificity of 0.87 for identifying nursing caries (defined as caries involving one or more of the maxillary central or lateral incisors or the primary molars, but excluding the mandibular incisors) in children age 18 to 36 months.

Evidence

The 2004 USPSTF review included one fair-quality study that found a pediatrician oral health exam of children age 18 to 36 months following 4 hours of training associated with a sensitivity of 1.0 and specificity of 0.87 for identifying nursing caries compared with a pediatric dentist exam. A second study included in the prior USPSTF review found a non–dental nurse exam associated with high sensitivity and specificity, but it enrolled children age 5 to 12 years and is therefore of limited applicability to younger children.

One good-quality study not included in the prior USPSTF review evaluated the accuracy of caries screening of children younger than age 36 months (n=258) by primary care pediatricians following 2 hours of oral health education (Appendices B1 and B2). The study enrolled Medicaid-eligible children (9.7 percent with a cavity at baseline; mean, 0.3 cavities/child) attending a private pediatric group practice in North Carolina. Compared with a pediatric dentist evaluation, it found a sensitivity of 0.76 (19/25) and specificity of 0.95 (222/233) for identifying...
a child with one or more cavities, a sensitivity of 0.49 (39/80) and specificity of 0.99 (3,210/3,235) for identifying a tooth with a cavity, and a sensitivity of 0.63 (17/27) and specificity of 0.98 (225/231) for identifying children in need of a dental referral. The need for referral was determined by the presence of a cavity, soft tissue pathology, or evidence of tooth or mouth trauma.

No study evaluated the accuracy of primary care screening for noncavitated caries (e.g., white spot) lesions.

**Key Question 2b. How Accurate Is Screening by the Primary Care Clinician in Identifying Children Younger Than Age 5 Years Who Are at Increased Risk for Future Dental Caries?**

The prior USPSTF review found no study on the accuracy of assessment by primary care clinicians in identifying children at risk for future dental caries.³ Although risk-assessment tools for use in primary care settings are available from the AAP, the AAPD, and the ADA, we found no study on the accuracy of risk assessment by primary care clinicians using these or other instruments.

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

No randomized trial or observational study compared harms between children age 5 years or younger screened and not screened by primary care clinicians.

**Key Question 4. How Effective Is Parental or Caregiver Oral Health Education by the Primary Care Clinician in Preventing Dental Caries in Children Younger Than Age 5 Years?**

**Summary**

No trial specifically evaluated an educational or counseling intervention by a primary care clinician to prevent dental caries. One fair-quality and one poor-quality nonrandomized trial found multifactorial interventions that included an educational component associated with decreased caries outcomes in underserved children younger than age 5 years.⁴³-⁴⁵

**Evidence**

The 2004 USPSTF review found no studies on the effectiveness of oral health educational or counseling interventions administered by a primary care clinician.³ We identified no trials published since the 2004 review that specifically evaluated an educational or counseling
intervention, although two nonrandomized, controlled clinical trials (reported in three publications) evaluated oral health educational interventions as a part of multicomponent interventions (Appendices B3 and B4).43-45 One study was rated fair quality45 and the other poor quality.43,44 In addition to using a nonrandomized design, other methodological shortcomings in the poor-quality study were high attrition and failure to adjust for confounders.

The fair-quality trial found a multicomponent intervention including additional pediatrician training, provision of an educational brochure, and electronic medical record reminders associated with decreased incidence of cavities versus usual care after 1 year: 18 versus 32 percent; adjusted hazard ratio (HR), 0.23; 95-percent confidence interval (CI), 0.09 to 0.62.45 Children were age 6 months to 5 years at enrollment and recruited from an urban underserved setting. Results were adjusted for age, race/ethnicity, socioeconomic status, and dietary and oral health risk. The trial used a cluster design, with one intervention and one demographically similar control clinic. Baseline caries prevalence was about 6 percent.

The poor-quality trial also found a multicomponent intervention (including provision of educational materials, counseling on oral hygiene, and provision of toothbrush and toothpaste) associated with a lower prevalence of caries compared with usual care (54 vs. 64%; p=0.03), dental extraction (3 vs. 12%; p<0.0001), and mean dmft score (2.2 vs. 3.7; p<0.001).33,44 The intervention was administered to children between age 8 months and 32 months recruited from primary care clinics in an urban deprived setting, and outcomes were assessed at age 5 years. The intervention was administered by health visitors (registered nurses with further training in child health, health promotion, prevention, and education) at healthy-child visits.

Key Question 5. How Effective Is Referral by a Primary Care Clinician to a Dentist in Preventing Dental Caries in Children Younger Than Age 5 Years?

Summary

No study directly evaluated the effects of referral by a primary care clinician to a dentist on caries incidence. A fair-quality retrospective cohort study (n=14,389) found that having a first dental preventive visit after age 18 months in children with existing dental disease was associated with increased risk of subsequent dental procedures compared with having a first visit before age 18 months, but the study was not designed to determine referral source.46

Evidence

The 2004 USPSTF report identified no studies on the effects of referral by a primary care clinician to a dentist on dental caries outcomes.3 We identified no study published since the 2004 USPSTF report that specifically evaluated effects of primary care referral on dental caries outcomes. However, one study may provide indirect evidence on the effects of earlier referral for untreated dental disease. It was a fair-quality retrospective cohort study that found that, among Medicaid children with existing dental disease (n=14,389), having a first dental visit after age 18
months was associated with increased risk of subsequent dental procedures between age 43 and 72 months compared with having an earlier first visit (before age 18 months) after adjusting for sex, race, number of well-child visits, and other factors (Appendixes B5 and B6); the incidence density ratio ranged from 1.1 to 1.4, depending on time of first dental visit. There was no difference in risk of subsequent dental procedures among children without existing dental disease at baseline. The study does not directly address the Key Question because it was not designed to determine whether a primary care referral was the source of the initial preventive visit.

**Key Question 6. How Effective Is Preventive Treatment (Dietary Fluoride Supplementation, Topical Fluoride Application, or Xylitol) in Preventing Dental Caries in Children Younger Than Age 5 Years?**

**Summary**

We identified no trials published since the 2004 USPSTF review on effects of dietary fluoride supplementation on dental caries incidence in children younger than age 5 years. One randomized trial and four other trials included in the 2004 USPSTF review found dietary fluoride supplementation in settings with water fluoridation levels below 0.6 ppm F associated with decreased caries incidence versus no fluoridation: percent reduction in caries increment ranged from 48 to 72 percent for primary teeth and from 51 to 81 percent for tooth surfaces.

We identified three randomized trials published since the 2004 USPSTF review that found fluoride varnish more effective than no fluoride varnish in reducing caries incidence: percent reduction in caries increment, 18 to 59 percent. Results were consistent with those of three randomized trials included in the prior USPSTF review: percent reduction in caries increment, 37 to 63 percent. Most trials were conducted in low socioeconomic status settings with low community water fluoridation levels, but benefits were also observed in studies conducted in adequately fluoridated settings.

Three trials reported no clear effects of xylitol versus no xylitol on caries outcomes in children younger than age 5 years, and one trial found no difference between xylitol and tooth brushing, but the trials varied with respect to dosing and formulation of xylitol. The most promising results were from a single small trial of xylitol wipes. Evidence from single trials of chlorhexidine varnish or povidone-iodine solution in children younger than age 5 years was too limited to determine effectiveness.

**Evidence**

**Dietary Fluoride Supplementation**

We identified no trials published since the 2004 USPSTF review on effects of dietary fluoride supplementation on dental caries outcomes in children younger than age 5 years. The 2004 USPSTF review included six trials of dietary fluoride supplements. Sample sizes ranged
from 140 to 815 children. Only one of the trials was clearly randomized. None of the nonrandomized trials adjusted for potential confounders. Other methodological limitations were inadequate blinding and high or unreported attrition. The trials were also clinically heterogeneous and varied with respect to age at enrollment (ranging from 2–3 weeks to 18–39 months), duration of followup (range, 2 to 6 years), dose of fluoride (range, 0.25 to 1.0 mg, varying in part based on child’s age), and setting, including one Chinese trial that recruited 2-year-old children from kindergarten.

The single randomized trial (n=140; fluoridation <0.1 ppm F) found use of 0.25 mg fluoride drops or chews associated with decreased incidence of caries versus no fluoride supplementation in Taiwanese children 2 years of age at enrollment. Percentage reduction in incidence ranged from 52 to 72 percent for dmft and from 51 to 81 percent for dmfs, depending on whether fluoride was given as tablets or drops. Across all six trials, percentage reductions in incidence with fluoride supplementation ranged from 32 to 72 percent for dmft and 38 to 81 percent for dmfs versus placebo (vitamin drops) or no supplementation. Five trials were conducted in settings with water fluoridation levels below current thresholds for supplementation (<0.6 ppm F). Excluding the trial conducted in a setting above this fluoridation threshold, incidence reductions were from 48 to 72 percent for dmft and 51 to 81 percent for dmfs. Two trials with extended followup also found dietary fluoride supplementation in early childhood associated with decreased incidence of caries at 7 to 10 years of age: reductions ranged from 33 to 80 percent.

Topical Fluoride

The 2004 USPSTF review included six trials on the effectiveness of professionally applied fluoride varnish in preventing dental caries in primary teeth. Two trials were randomized and one used alternate allocation. The other three were not randomized, with sample sizes ranging from 142 to 225. All of the trials enrolled children between age 3 and 5 years and followed patients for 2 years or 9 months. Community water fluoridation status met recommended thresholds in one trial and was not reported in the other two. Fluoride varnish was applied as 2.26 percent fluoride (Duraphat®) for two applications separated by 4 or 6 months, or as four applications over 2 years. No trial used a placebo or control treatment, and only one clearly reported blinded outcomes assessment. The percent reduction in incident caries lesions ranged from 37 to 63 percent (p<0.01 in all trials), with an absolute reduction in the mean number of cavities per child of 0.67 to 1.24 per year.

We identified seven trials published since the 2004 USPSTF review on professionally applied topical fluoride in children younger than age 5 years. We rated three trials good quality, three fair quality, and one poor quality (Appendix B4). Six trials were randomized; the poor-quality trial used alternate allocation. Shortcomings in the fair-quality trials included high loss to followup, failure to describe adequate blinding, and failure to describe adequate allocation concealment.

Three trials (two good quality and one fair quality) evaluated fluoride varnish (2.26% fluoride) applied every 6 months versus no fluoride varnish. Sample sizes ranged from 280 to 1,146 children. Two trials conducted in rural aboriginal populations in Canada (no fluoridation) and...
Australia (<0.6 ppm F for >90% of children) had baseline dmfs scores of 3.8 and 11\textsuperscript{48} and used a cluster design. The third trial enrolled underserved, primarily Hispanic and Chinese, children in an urban U.S. setting with adequate fluoridation (1 ppm F) who were caries free at baseline.\textsuperscript{49} As in the trials included in the 2004 USPSTF review, fluoride varnish was applied by dental personnel in all studies.

All three trials found use of fluoride varnish associated with decreased incidence of caries after 2 years, although the difference was not statistically significant in the Canadian study.\textsuperscript{47} Percent reductions in dmfs increment were 18 and 24 percent in the studies of rural aboriginal populations\textsuperscript{47,48} and 59 percent in the U.S. trial.\textsuperscript{49} Absolute mean reductions in the number of affected surfaces ranged from 1.0 to 2.4. Fluoride varnish was also associated with decreased risk of having any cavity. The poor-quality trial, which evaluated 2.26 percent fluoride varnish applied every 3 months in Chinese children (with or without removal of carious tissue), reported findings consistent with those of the fair-quality trials.\textsuperscript{69}

Two trials evaluated effectiveness of other methods for administering topical fluoride\textsuperscript{69,70} Both were conducted in China. One good-quality trial found 1.23-percent acidulated phosphate fluoride foam applied every 6 months more effective (p=0.03) than placebo (mean percent reduction in dmfs increment, 24\%; absolute mean reduction in affected surfaces, 1.2).\textsuperscript{70} A poor-quality trial found 38-percent silver diamine fluoride solution every 12 months somewhat more effective than 2.26-percent fluoride varnish every 3 months.\textsuperscript{69}

Two trials found multiple fluoride varnish applications within a 2-week period associated with no clear differences versus a standard application schedule of every 6 months,\textsuperscript{71,72} and one trial found no clear difference between a once versus twice yearly schedule.\textsuperscript{49}

### Xylitol

Xylitol was not an included intervention in the 2004 USPSTF review. We identified four fair-quality\textsuperscript{50-52,73} and two poor-quality trials\textsuperscript{53,74} of xylitol in children age 6 months to 5 years (Table 2 and Appendixes B4 and B7). Two trials enrolled children from settings in which water was not fluoridated\textsuperscript{73} or inadequately fluoridated,\textsuperscript{53} and the other four did not report water fluoridation status. Five trials were randomized\textsuperscript{50-52,73,74} and one used a nonrandomized design.\textsuperscript{53}

Three trials compared xylitol with no xylitol.\textsuperscript{50,52,53} They varied with respect to dosing and formulation of xylitol. A fair-quality randomized trial (n=115) found xylitol tablets (0.48 g) associated with reduced dmfs increment after 2 years, but the difference was not statistically significant (mean percent reduction, 52\%; absolute mean reduction in affected surfaces, 0.42).\textsuperscript{52} The trial enrolled 2-year-old Swedish children, with the intervention consisting of a xylitol tablet at bedtime for 6 months, followed by two tablets daily. One small (n=37) fair-quality randomized trial found xylitol wipes used three times per day for 1 year markedly more effective than placebo wipes in reducing caries among children age 6 months to 35 months (reduction in dmfs increment, 91\%; p<0.05).\textsuperscript{50} A poor-quality nonrandomized trial found no effect of xylitol chewing gum (1.33 g) four times daily on incidence of caries in 4-year-old children in Japan.\textsuperscript{53}

Two studies compared xylitol with topical fluoride.\textsuperscript{51,74} A cluster randomized trial found no
difference between 65-percent xylitol gum three times per day versus tooth brushing with fluoride, but it was conducted in a supervised daycare setting and enrolled children up to age 6 years, potentially limiting its applicability to younger children. A poor-quality trial found xylitol chewable tablets (1.2 g three times daily) more effective than fluoride varnish once every 6 months.54

One fair-quality randomized trial found xylitol syrup 8 g per day in two or three divided doses more effective than one 2.67 g dose daily in reducing incidence of caries outcomes.73

**Other Interventions**

One fair-quality cluster randomized trial (n=290) of children age 4 to 5 years in rural China found 40-percent chlorhexidine acetate varnish associated with decreased caries outcomes versus placebo varnish, with a 37-percent reduction in dmfs incidence in the molar teeth and mean absolute dmfs-molar reduction of 0.6 (Table 3 and Appendixes B4 and B7).54

A fair-quality randomized trial (n=83) of high-risk children age 16 months in Puerto Rico found 0.2 ml of 10-percent povidone-iodine solution applied every 2 months associated with decreased incidence of white spot lesions on maxillary teeth after 1 year (8 vs. 32%; relative risk [RR], 0.24; 95% CI, 0.1 to 0.8).55

**Key Question 7. What Are the Harms of Specific Oral Health Interventions for Prevention of Dental Caries in Children Younger Than Age 5 Years (Parental or Caregiver Oral Health Education, Referral to a Dentist, and Preventive Treatments)?**

**Summary**

Five new studies in an updated systematic review were consistent with previous studies in finding an association between early childhood ingestion of systemic fluoride and enamel fluorosis of the permanent dentition. Studies were observational and had methodological shortcomings, including use of retrospective recall to determine exposures. Other than diarrhea, reported in two trials of xylitol, harms were poorly reported in trials of caries prevention interventions, and no trials reported incidence or prevalence of fluorosis with fluoride varnish.

**Evidence**

No trial reported risk of dental fluorosis associated with early childhood ingestion of dietary fluoride supplements. The 2004 USPSTF review included a systematic review of 14 observational studies on risk of fluorosis, based on literature searches conducted through September 1997. Ten of the studies relied on retrospective parental recall of early childhood fluoride ingestion to determine subsequent risk of fluorosis in the permanent dentition. In the other four, early childhood supplemental fluoride use had been recorded at the time of exposure. The dosages of fluoride supplementation in the studies generally exceeded current...
recommendations. Prevalence of fluorosis ranged from 10 to 49 percent in the studies that relied on retrospective parental recall, and from 15 (on central incisors only) to 67 percent in the studies that recorded supplement use during early childhood. The odds ratios (ORs) for dental fluorosis associated with regular early childhood use ranged from 1.3 to 10.7 in the studies that relied on retrospective recall, and RRs ranged from 4.2 to 15.6 in the studies that recorded supplement use at the time of exposure.

The systematic review included in the 2004 USPSTF review has subsequently been updated with searches conducted through June 2006 (Appendices B8 and B9). The update included five additional observational studies on the association between early childhood intake of fluoride supplements and risk of fluorosis. Determinations of early childhood exposures were all based on retrospective parental recall, with fluorosis assessed at age 8 to 14 years. Results of the new studies were consistent with those from the original systematic review, with intake of fluoride supplements prior to 7 years of age (primarily before 3 years of age) associated with increased risk of fluorosis. Risk estimates ranged from an OR of 10.8 (95% CI, 1.9 to 62) with intake during the first 2 years of life to a slight increase in risk (OR, 1.1 to 1.7, depending on comparison). One study reported a dose-dependent association, with an OR of 1.8 (95% CI, 1.4 to 2.4) for each year of supplementation. We identified no studies published since the updated systematic review on the association between early childhood intake of dietary fluoride supplements and risk of enamel fluorosis.

No study reported the risk of fluorosis associated with use of fluoride varnish. However, the degree of systemic exposure following application of fluoride varnish is believed to be low.

Two trials reported diarrhea in 11 percent of children allocated to xylitol chewing gum or syrup. Other trials of xylitol did not report rates of diarrhea.

**Contextual Question. What Percentage of Children Younger Than Age 5 Years in the United States Have Access to Dental Care, and What Factors Are Associated With Access to Dental Care in This Population?**

Based on a national telephone survey (n=89,071) of parents performed in 2003 to 2004, 23 percent of children age 1 to 5 years lacked dental insurance coverage in the previous year, 51 percent did not receive dental care, and 3.5 percent had a perceived unmet dental need. Children who lacked dental insurance were also less likely to receive preventive care and more likely to have a perceived unmet need for care. In multivariate analyses, factors associated with lack of dental insurance coverage among all children age 1 to 17 years were being a foreign-born Hispanic, having a non-English primary language spoken at home, having three or more children in the family, lower socioeconomic status, rural residence, living in the South, and lower household education level. An analysis based on 2004 Medical Expenditure Panel Survey (MEPS) data also found that a primary care provider’s recommendation for dental care was associated with a threefold increased likelihood (OR, 2.9; 95% CI, 2.2 to 3.9) of having a subsequent dental visit. In 2009, based on MEPS data, the proportion of children age 1 to 5...
years with a dental visit in the prior year was 31 percent (95% CI, 28 to 34%).  

Several studies have shown that expanding access to dental coverage for low-income families through the State Children’s Health Insurance Program (SCHIP) and Medicaid programs was associated with an increase in preventive dental visits in eligible children. Higher Medicaid payment levels were associated with higher rates of receipt of care.
Chapter 4. Discussion

Summary of Review Findings

Dental caries is highly prevalent in children younger than age 5 years. A high proportion of children in this age group do not receive recommended dental care, suggesting a potential role for primary care providers in dental caries prevention. However, as in the 2004 USPSTF review, we found no direct evidence on the effects of screening for dental caries by primary care clinicians in children younger than age 5 years versus no screening on caries incidence and related outcomes. Other evidence reviewed for this update is summarized in Table 4.

Newer evidence identified for this update was consistent with findings from the 2004 USPSTF review in showing that fluoride varnish in children younger than age 5 years is effective at reducing caries incidence. Because trials were primarily conducted in higher risk children (based on community water fluoride levels or socioeconomic status), the applicability of these findings to children not at increased risk may be limited, particularly for studies conducted in countries and settings in which sources of fluoride and health behaviors differ markedly from the United States. In all trials the varnish was applied by dental personnel, although fluoride varnish is believed to be easily applied with minimal training.

We identified no new trials on the effectiveness of dietary fluoride supplementation in children younger than age 5 years. Although the 2004 USPSTF review found dietary fluoride supplementation to be effective at reducing caries incidence in children younger than age 5 years primarily in settings with water fluoridation levels less than 0.6 ppm F, conclusions were mostly based on nonrandomized trials. Newer observational studies were consistent with the 2004 USPSTF review in finding an association between early childhood intake of dietary fluoride supplementation and risk of enamel fluorosis. Risk of enamel fluorosis appears to be impacted by total intake of fluoride (from supplements, drinking water, other dietary sources, and dentifrices), as well as age at intake, with intake before age 2 to 3 years appearing to confer the highest risk. Although the prevalence of enamel fluorosis has increased in the United States, severe fluorosis is uncommon, with a prevalence of less than 1 percent.

Trials of xylitol in children younger than age 5 years found no clear effects on caries incidence, although studies differed in the doses and formulations evaluated. The most promising results were from a small trial of xylitol wipes that reported a marked decrease in caries incidence, but they require confirmation. Evidence on the effectiveness of other interventions not in common use in the United States in young children, such as chlorhexidine varnish and povidone-iodine solution, is limited to single trials, precluding reliable conclusions.

Evidence remains limited on the accuracy of primary care clinicians in identifying caries lesions in children younger than age 5 years or in predicting caries incidence. One study not included in the prior USPSTF review found that primary care pediatricians missed 37 percent of children in need of a dental referral and 24 percent of children with a cavity compared with a pediatric dentist exam, although specificity was high. No study evaluated the diagnostic accuracy of caries risk-assessment instruments administered by primary care clinicians, despite the availability of instruments designed for use in primary care settings.

Prevention of Dental Caries in Children
assessed caries risk-assessment instruments in children younger than age 5 years, but the instruments were not administered by primary care providers or in primary care settings. In addition, these instruments often incorporate findings from an oral examination by dental personnel and include tests not commonly obtained in primary care (such as mutans streptococci levels, saliva secretion level, or saliva buffer capacity), potentially limiting applicability of findings to primary care settings.94,95

No trial specifically evaluated the effectiveness of parental or caregiver/guardian education on caries outcomes, although limited evidence from two trials suggests that multifactorial interventions in which education is a component could be effective.43-45 Although some evidence indicates that health care providers’ recommendation for dental care increases the likelihood of subsequent dental visits in young children,81 no trial evaluated the effectiveness of primary care referral to a dentist on caries outcomes. One retrospective cohort study found an association between an early (prior to age 18 months) dental visit and fewer subsequent dental procedures in children with dental disease at baseline.46

**Limitations**

We excluded non–English-language articles, which could result in language bias, although we identified no non–English-language studies that would have met inclusion criteria. We did not search for studies published only as abstracts, and we could not formally assess for publication bias with graphical or statistical methods because of small numbers of studies for each Key Question and differences in the study design, populations, and outcomes assessed. We found few or no randomized trials for a number of Key Questions. Therefore, we included nonrandomized trials, as well as observational studies (for harms), which are more susceptible to bias and confounding than are well-conducted randomized trials.

**Emerging Issues**

The increasing prevalence of dental caries in young children is an important emerging issue.9 The reasons for this trend are not completely understood but could include changes in dietary patterns, access to dental care, demographics, or socioeconomic status.

**Future Research**

Research is needed to identify effective oral health educational and counseling interventions for parents and caregivers and guardians of young children. Research is also needed to validate the accuracy and utility of caries risk-assessment instruments for use in primary care settings and to determine how referral by primary care clinicians of young children for dental care affects caries outcomes. Additional trials would strengthen conclusions regarding the effectiveness of dietary fluoride supplementation in young children, especially in the current U.S. context of exposure to multiple sources of fluoride, and trials are needed to demonstrate that results from trials of fluoride varnish applied by dental personnel can be reproduced in primary care settings.
Conclusions

Dietary fluoride supplementation and fluoride varnish appear to be effective at preventing caries outcomes in higher risk children younger than age 5 years. Dietary fluoride supplementation in early childhood is associated with risk of enamel fluorosis, which is usually mild. More research is needed to understand the accuracy of oral health examination and caries risk assessment by primary care clinicians, primary care referral for dental care, and effective parental or caregiver educational and counseling interventions.
References


Figure 1. Analytic Framework

Oral Screening and Risk Factor Assessment

1. Oral Screening and Risk Factor Assessment
   - Children 0 to 5 years old at clinician office visit

2. Average risk dental caries
   - Oral Screening and Risk Factor Assessment

3. Increased risk dental caries
   - Oral Screening and Risk Factor Assessment

4. a) Parental or caregiver/guardian oral health education
   b) Referral to dentist
   - Interventions

5. Outcome: Decreased Dental Caries and Associated Complications

6. Preventive treatments
   - Interventions

7. Adverse Effects

Adverse Effects
<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Country; Setting; Fluoridation Status</th>
<th>Age at Enrollment</th>
<th>Sample Size</th>
<th>Followup (Years)</th>
<th>Mean Caries Increment</th>
<th>Absolute Reduction in Caries Increment</th>
<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
</table>
| Chu et al., 2002³⁹ Poor | Controlled clinical trial | A: Removal of carious tissue plus 38% silver diamine fluoride solution every 12 months  
B: 38% silver diamine fluoride solution every 12 months  
C: Removal of carious tissue plus 5% sodium fluoride varnish every 3 months  
D: 5% sodium fluoride varnish every 3 months  
E: Placebo (water) | China; Kindergarten; Water fluoridation status: <0.2 ppm | 4 years | 308 | 2.5 | New caries surfaces:  
A: 0.26  
B: 0.47  
C: 0.89  
D: 0.70  
E: 1.58 p for ANOVA <0.001, E vs. others | A: 1.32  
B: 1.11  
C: 0.69  
D: 0.88  
E vs. others | A: 84%  
B: 70%  
C: 44%  
D: 56%  
E vs. others | Arrested caries surfaces:  
A: 2.49  
B: 2.82  
C: 1.45  
D: 1.54  
E: 1.27 p for ANOVA <0.001, E vs. others |
<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
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<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
</table>
| Jiang et al., 2005*    | Cluster RCT (15 clusters) | A: 0.6-0.8 g of 1.23% acidulated phosphate fluoride foam applied every 6 months, max 4 applications  
B: Placebo foam | China; Kindergarten; Water fluoridation status: 0.1-0.3 ppm | 3.5-3.6 years | 318 | 2 | 1.2 | 24% | A vs. B |  
No increase in dmfs: 38% (64/167) vs. 26% (40/151) dmfs  
Increase of 1 to 5: 34% (56/167) vs. 38% (58/151) dmfs  
Increase of 6 to 10: 17% (28/167) vs. 18% (27/151) dmfs  
Increase of >10: 11% (19/167) vs. 17% (26/151) |
Table 1. Summary of Topical Fluoride Preventive Treatments

<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
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</tr>
</thead>
</table>
| Lawrence et al., 2008* | Cluster RCT (20 clusters) | A: 0.3-0.5 ml 5% sodium fluoride varnish applied to full primary dentition every 6 months  
B: No fluoride varnish | Canada; Rural Aboriginal communities; Water fluoridation status: No fluoridation | 2.5 years | 1146 | 2 | dmfs  
A: 11.0 (4.3)*  
B: 13.4 (6.1)*  
p=0.24 (p=0.18)* | 2.4 (1.8)* | 18% (29%)* | A vs. B  
Dental caries in aboriginal cohort: 72% (595/832) vs. 75% (247/328), adjusted OR 0.72 (95% CI 0.42 to 1.25); NNT 26  
Dental caries in those caries free at baseline: 44% (157/354) vs. 58% (73/126); adjusted OR 0.63 (95% CI 0.33 to 1.1); NNT 7.4 |
| Slade et al., 2011* | Cluster RCT (30 clusters) | A: 0.25 ml of 5% sodium fluoride varnish to maxillary anterior teeth/molars, mandibular molars/incisors every 6 months, education/advice to caregiver with toothbrush/paste provided, community oral health promotion program  
B: No interventions | Australia; Rural Aboriginal communities; Water fluoridation status: 81-92% had <0.6 ppm F | 2.8 years | 666 | 2 | dmfs  
A: 7.3  
B: 9.6†  
p<0.05 | 2.3 | 24% | A vs. B |
Table 1. Summary of Topical Fluoride Preventive Treatments

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<th>Absolute Reduction in Caries Increment</th>
<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
</table>
| Weinstein et al., 2001¹ | RCT with 3 treatment groups | A: One application of 5% fluoride varnish at baseline and 6 months  
B: Three applications of 5% fluoride varnish within 2 weeks of baseline  
C: Three applications of 5% fluoride varnish within 2 weeks of baseline and 6 months | United States; Head Start programs; Water fluoridation status: NR | 3-5 years | 111 | 1 | Clinical dmfs:  
A: 4.6  
B: 3.2  
C: 4.7  
p=0.65  
Radiographic mean dmfs:  
A: 0.9  
B: 0.5  
C: 0.1  
p=0.28 | Not calculated | Not calculated |
| Weinstein et al., 2009² | RCT with 2 treatment groups | A: One 5% fluoride varnish treatment and 2 placebo treatments every 6 months  
B: One set of three 5% fluoride varnish treatments over 2 weeks once per year and 3 placebo treatments over 2 weeks 6 months later | United States Recruitment setting: Head Start programs  
Water fluoridation status: NR (Yakima voters approved fluoridation in 1999) | 55-56 months | 515 | 3 | dmfs  
A: 7.4  
B: 9.8  
p=0.001 | 2.4 | 24% | Adjusted rate ratio of new tooth decay in primary surfaces 1.13 (95% CI 0.94 to 1.37) |
### Table 1. Summary of Topical Fluoride Preventive Treatments

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</tr>
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</table>
| Weintraub et al., 2006<sup>2</sup>, <sup>3</sup> Fair | RCT | A: 0.1 mL of 5% sodium fluoride varnish per arch applied twice per year with 4 intended applications  
B: 0.1 mL of 5% sodium fluoride varnish per arch applied once per year with 2 intended applications  
C: No fluoride varnish | United States; Family dental center and public health center serving primarily low-income, underserved Hispanic and Chinese populations; Water fluoridation status: ~1 ppm | 1.8 years | 280 | 2 | $d_{2,fs}$  
A: 0.7  
B: 0.7  
C: 1.7  
p<0.01 for A or B vs. C | 1.0 | 59% (A + B vs. C) | A vs. B vs. C  
Caries lesions at 12 months: 13% (11/83) vs. 15% (13/86) vs. 29% (27/92); RR 0.45 (95% CI 0.24 to 0.85); NNT 7 for A vs. C and 0.52 (95% CI 0.28 to 0.93); NNT 8 for B vs. C  
Caries lesions at 24 months: 4.3% (3/70) vs. 14% (10/69) vs. 24% (15/63); RR 0.18 (95% CI 0.06 to 0.59); NNT 6 for A vs. C and 0.61 (95% CI 0.30 to 1.26); NNT 11 for B vs. C |

<sup>*Children caries free at baseline.</sup>  
<sup>†Adjusted.</sup>  
<sup>‡In the fluoride varnish treatment group some children received a placebo varnish instead of fluoride varnish due to protocol errors.</sup>  
<sup>§Participants caries free at baseline.</sup>

**Abbreviations:** ANOVA = Analysis of Variance; CI = confidence interval; $d_{2,fs}$ = number of decayed or filled surfaces; dmfs = number of decayed, missing and filled surfaces; F = fluoride; g = gram; mL = milliliter; NNT = number needed to treat; NR = not reported; OR = odds ratio; ppm = parts per million; RCT = randomized controlled trial; RR = relative risk.
<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Country; Setting; Fluoridation Status</th>
<th>Age at Enrollment</th>
<th>Sample Size</th>
<th>Followup (Years)</th>
<th>Mean Caries Increment</th>
<th>Absolute Reduction in Caries Increment</th>
<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
</table>
| Alamoudi et al., 2012 | RCT          | A: Xylitol chewable tablets (1.2 g, 84% xylitol) chewed for 5 minutes 3 times daily  
B: Fluoride varnish every 6 months throughout study | Saudi Arabia Recruitment setting: Well baby clinics and dental clinics  
Water fluoridation status: NR | 2 to 5 years | 34 | 1.5 | dmft  
A: 0.8  
B: 4.4  
p=not reported | 3.6 | 82% | A vs. B  
dmft at baseline: 8.4 vs. 10.3 (p=0.19)  
dmft at 18 months: 9.2 vs. 14.7 (p=0.001) |
| Kovari et al., 2003\* | Cluster RCT (11 clusters) | A: 65% Xylitol gum 3 times per day, chewed for 3-5 minutes, for total of 2.5 g/day  
B: Tooth brushing with 0.05% NaF toothpaste after lunch | Finland Recruitment setting: Daycare centers  
Water fluoridation status: NR | 3 to 6 years | 786 | 3-6 | NR | NR | NR | A vs. B  
Caries at 7 years old: 31% (98/316) vs. 35% (149/427), RR 0.88 (95% CI 0.72 to 1.10)  
Caries at 9 years old: 43% (133/310) vs. 51% (221/434), RR 0.84 (95% CI 0.72 to 0.99)  
dmft: 1.1 vs. 1.0 at 7 years, 1.2 vs. 1.6 at 9 years |
<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Country; Setting; Fluoridation Status</th>
<th>Age at Enrollment</th>
<th>Sample Size</th>
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<th>Mean Caries Increment</th>
<th>Absolute Reduction in Caries Increment</th>
<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
</table>
| Milgrom et al., 2009* | RCT          | A: Xylitol 8 g per day syrup, divided into 2 doses (4 g per dose)  
               | Marshall Islands Recruitment setting: Community based  
               | 14 to 16 months  
               | 94          | 1            | Number of decayed teeth  
               | A: 0.6  
               | B: 1.0  
               | C: 1.9  
               | p<0.05 for A or B vs. C  
               | A: 1.3  
               | B: 0.9 vs. C  
               | A vs. B vs. C  
               | Tooth decay: 24.2% (8/33) vs. 40.6% (13/32) vs. 51.7% (15/29), RR 0.47 (95% CI 0.23 to 0.94) for A vs. C and 0.79 (95% CI 0.45 to 1.4) for B vs. C  
               | Incidence rates for decayed primary teeth per year: 0.66 vs. 1.10 vs. 2.20 |
| Oscarson et al., 2006 | RCT          | A: One 0.48 g xylitol tablet at bedtime after brushing for 6 months; then 1 tablet twice daily to age 3 years and 6 months  
               | Sweden Recruitment setting: Public dental clinic  
               | 25 months  
               | 115         | 2            | dmf s  
               | A: 0.38  
               | B: 0.80  
               | p>0.05  
               | 0.42      | 52%         | A vs. B  
               | Dental caries: 18% (10/55) vs. 25% (16/63), OR 0.65 (95% CI 0.27 to 1.59) |
Table 2. Summary of Xylitol Preventive Treatments

<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Country; Setting; Fluoridation Status</th>
<th>Age at Enrollment</th>
<th>Sample Size</th>
<th>Followup (Years)</th>
<th>Mean Caries Increment</th>
<th>Absolute Reduction in Caries Increment</th>
<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
</table>
| Seki et al., 2011<sup>53</sup> Poor | Cluster, nonrandomized controlled clinical trial (3 clusters) | A: Xylitol chewing gum (100% xylitol, 1.33 g); 1 pellet chewed 5 minutes 4 times daily  B: No intervention | Japan Recruitment setting: Preschool  Water fluoridation status: NR (states fluoridation “limited” in Japan) | 66-72% 4 years old | 161 | 1 | dfs A: 3.3  B: 3.4  
  p>0.05 | 0.1 | 3% | A vs. B  Development of caries from baseline to 6 months: 1.7 vs. 1.6 (p>0.05)  Development of caries from 6 months to 1 year: 1.6 vs. 1.8 (p>0.05) |

| Zhan et al., 2012<sup>50</sup> Fair | RCT | A: Xylitol wipes, 2 at a time, 3 times per day (estimated daily dosage 4.2 g) every 3 months  B: Placebo wipes | United States  Recruitment setting: University pediatric clinic  Water fluoridation status: Not reported | 6-35 months | 37 | 1 | dmfs<sup>†</sup> A: 0.05  B: 0.53  
  p=0.01 | 0.48 | 91% | A vs. B  New caries lesions at 1 year:† 5% vs. 40% (p=0.03); NNT 3  ITT analysis of new caries lesions at 1 year: 5% vs. 32%; RR 0.14 (95% CI 0.02 to 1.07); NNT 4 |

*Baseline caries status not defined.  †Numbers based on per protocol analysis.

**Abbreviations:** CI = confidence interval; dfs = decayed and filled surfaces; dmfs = decayed, missing, and filled surfaces; dmft = decayed, missing, and filled teeth; g = grams; ITT = intention-to-treat; NaF = sodium fluoride; NNT = number needed to treat; NR = not reported; OR = odds ratio; RCT = randomized, controlled trial; RR = relative risk.
Table 3. Summary of Other Preventive Treatments

<table>
<thead>
<tr>
<th>Author, Year, Quality</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Country; Setting; Fluoridation Status</th>
<th>Age at Enrollment</th>
<th>Sample Size</th>
<th>Followup (Years)</th>
<th>Mean Caries Increment</th>
<th>Absolute Reduction in Caries Increment</th>
<th>Reduction in Caries Increment</th>
<th>Other Dental Caries Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Du et al., 2006&lt;sup&gt;54&lt;/sup&gt; Fair</td>
<td>Cluster RCT (14 clusters)</td>
<td>A: 40% w/w chlorhexidine acetate varnish every 6 months B: Placebo varnish</td>
<td>China Kindergartens in rural communities; Water fluoridation status: 0.1-0.3 ppm</td>
<td>4-5 years</td>
<td>290</td>
<td>2</td>
<td>dmfs-molar: A: 1.0 B: 1.6 p=0.036</td>
<td>0.6</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>Lopez et al., 2002&lt;sup&gt;55&lt;/sup&gt; Fair</td>
<td>RCT</td>
<td>A: 0.2 ml of 10% povidone-iodine solution every 2 months B: Placebo solution</td>
<td>United States Women, infants, and children clinic in Puerto Rico; Water fluoridation status: NR</td>
<td>16 months</td>
<td>83</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>A vs. B*</td>
</tr>
</tbody>
</table>

*Participants were caries free at baseline.

**Abbreviations:** CI = confidence interval; dmfs = decayed, missing, filled surfaces; mL = milliliter; NR = not reported; ppm = parts per million; RCT = randomized, controlled trial; RR = relative risk; w/w = weight/weight.
<table>
<thead>
<tr>
<th>Main Findings From 2004 USPSTF Review</th>
<th>Number and Type of Studies Identified for Update</th>
<th>Limitations</th>
<th>Consistency</th>
<th>Applicability</th>
<th>Summary of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Question 1. How effective is oral screening (including risk assessment) by the primary care clinician in preventing dental caries in children younger than age 5 years?</td>
<td>No evidence</td>
<td>No studies</td>
<td>No studies</td>
<td>No studies</td>
<td>No randomized trial or observational study compared clinical outcomes between children younger than 5 years of age screened and not screened by primary care clinicians.</td>
</tr>
<tr>
<td>Key Question 2a. How accurate is screening by the primary care clinician in identifying children younger than age 5 years who have cavitated or noncavitated caries lesions?</td>
<td>One study found pediatrician examination following 4 hours of oral health education associated with a sensitivity of 1.0 and specificity of 0.87 for identifying nursing caries in children 18-36 months of age.</td>
<td>1 cohort study</td>
<td>Evidence limited to 1 study</td>
<td>N/A</td>
<td>One study found primary care pediatrician examination following 2 hours of oral health education associated with a sensitivity of 0.76 for identifying a child with 1 or more cavities and 0.63 for identifying children &lt;36 months of age in need of a dental referral, compared with a pediatric dentist evaluation.</td>
</tr>
<tr>
<td>Key Question 2b. How accurate is screening by the primary care clinician in identifying children younger than age 5 years who are at increased risk for future dental caries?</td>
<td>No evidence</td>
<td>No studies</td>
<td>No studies</td>
<td>No studies</td>
<td>No study evaluated the accuracy of risk-assessment tools applied by primary care clinicians to identify children at increased risk for future dental caries.</td>
</tr>
<tr>
<td>Key Question 3. What are the harms of oral health screening by the primary care clinician?</td>
<td>No evidence</td>
<td>No studies</td>
<td>No studies</td>
<td>No studies</td>
<td>No randomized trial or observational study compared harms between children younger than 5 years of age screened and not screened by primary care clinicians.</td>
</tr>
</tbody>
</table>
### Table 4. Summary of Evidence

<table>
<thead>
<tr>
<th>Key Question 4. How effective is parental or caregiver oral health education by the primary care clinician in preventing dental caries in children younger than age 5 years?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No evidence</td>
</tr>
<tr>
<td>1 randomized trial, 1 nonrandomized trial</td>
</tr>
<tr>
<td>Overall quality: Poor</td>
</tr>
<tr>
<td>Limitations: Nonrandomized design, high attrition, failure to adjust for confounders</td>
</tr>
<tr>
<td>Consistency: Moderate inconsistency</td>
</tr>
<tr>
<td>Applicability: Education evaluated as part of a multifactorial intervention</td>
</tr>
<tr>
<td>Summary of Findings: No trial specifically evaluated an educational or counseling intervention to prevent dental caries. Two studies found multifactorial interventions that included an educational component associated with decreased incidence or prevalence of cavities in underserved children younger than 5 years of age.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key Question 5. How effective is referral by a primary care clinician to a dentist in preventing dental caries in children younger than age 5 years?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No evidence</td>
</tr>
<tr>
<td>1 cohort study</td>
</tr>
<tr>
<td>Overall quality: Poor</td>
</tr>
<tr>
<td>Limitations: Study not designed to determine whether a primary care referral was the source of the initial preventive visit</td>
</tr>
<tr>
<td>Consistency: N/A</td>
</tr>
<tr>
<td>Applicability: Medicaid population, higher risk children</td>
</tr>
<tr>
<td>Summary of Findings: No study directly evaluated the effects of referral by a primary care clinician to a dentist on caries incidence. One study found a first dental preventive visit after 18 months of age in children with existing dental disease associated with increased risk of subsequent dental procedures compared with a first visit before 18 months of age, but was not designed to determine referral source.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key Question 6. How effective is preventive treatment with dietary fluoride supplementation in preventing dental caries in children younger than age 5 years?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Six trials of dietary fluoride supplements. One randomized trial and 4 other trials found oral fluoride supplementation in settings with water fluoridation levels below 0.6 ppm F associated with decreased caries incidence vs. no fluoridation (ranges of 48-72% for primary teeth and 51-81% for primary tooth surface).</td>
</tr>
<tr>
<td>No studies</td>
</tr>
<tr>
<td>Overall quality: Fair</td>
</tr>
<tr>
<td>Limitations: Limitations in previously reviewed studies include use of nonrandomized design, not controlling for confounders, inadequate blinding, and high or unreported attrition</td>
</tr>
<tr>
<td>Consistency: N/A</td>
</tr>
<tr>
<td>Applicability: No studies</td>
</tr>
<tr>
<td>Summary of Findings: We identified no new trials on the effects of dietary fluoride supplementation in children younger than 5 years of age on dental caries incidence.</td>
</tr>
</tbody>
</table>
# Table 4. Summary of Evidence

<table>
<thead>
<tr>
<th>Main Findings From 2004 USPSTF Review</th>
<th>Number and Type of Studies Identified for Update</th>
<th>Overall Quality*</th>
<th>Limitations</th>
<th>Consistency</th>
<th>Applicability</th>
<th>Summary of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Question 6. How effective is preventive treatment with topical fluoride application (fluoride varnish) in preventing dental caries in children younger than age 5 years?</td>
<td>Three randomized trials found fluoride varnish more effective than no fluoride varnish in reducing caries incidence (percent reduction 37-63%, with an absolute reduction in the mean number of cavities per child of 0.67-1.24 per year).</td>
<td>6 randomized trials, 1 trial using alternate allocation</td>
<td>High loss to followup, failure to describe adequate blinding, and failure to describe adequate allocation concealment</td>
<td>Consistent</td>
<td>Rural settings with inadequate fluoridation or low socioeconomic status settings</td>
<td>Three randomized trials published since the prior review found fluoride varnish more effective than no fluoride varnish in reducing caries incidence (percent reduction in caries increment 18-59%). Other trials evaluated methods of topical fluoride application not used in the United States or compared different doses or frequencies of topical fluoride.</td>
</tr>
<tr>
<td>Key Question 6. How effective is preventive treatment with xylitol in preventing dental caries in children younger than 5 years of age?</td>
<td>No studies (not included in the prior review).</td>
<td>5 randomized trials; 1 nonrandomized</td>
<td>Variability in xylitol formulation and dosing</td>
<td>Some inconsistency</td>
<td>Children from settings in which water was not fluoridated or fluoridation limited</td>
<td>Three trials reported no clear effects of xylitol vs. no xylitol on caries incidence in children younger than 5 years, with the most promising results from a small (n=37) trial of xylitol wipes. One trial found no difference between xylitol and toothbrushing.</td>
</tr>
<tr>
<td>Key Question 7. What are the harms of specific oral health interventions for prevention of dental caries in children younger than 5 years of age (parental or caregiver oral health education, referral to a dentist, and preventive treatments)?</td>
<td>One systematic review of 14 observational studies found dietary fluoride supplementation in early childhood associated with increased risk of fluorosis; odds ratios ranged from 1.3-15.6 and prevalence ranged from 10-67%.</td>
<td>5 observational studies in an updated systematic review</td>
<td>Use of retrospective parental recall to determine exposures</td>
<td>Consistent</td>
<td>Doses of fluoride generally higher than currently recommended</td>
<td>Five observational studies in an updated systemic review were consistent with previously reported findings in showing an association between early childhood ingestion of systemic fluoride and enamel fluorosis. Other than diarrhea reported in 2 trials of xylitol, harms were poorly reported in trials of caries prevention interventions in children younger than 5 years of age.</td>
</tr>
</tbody>
</table>

*Overall quality* is based on new evidence identified for this update plus previously reviewed evidence.

**Abbreviations:** USPSTF = U.S. Preventive Services Task Force.
Appendix A1. Search Strategies

Database: Ovid MEDLINE® without Revisions <1999 to March 8, 2013>
Search Strategy:

1     exp physicians/
2     exp pediatrics/ or pediatrician$.mp.
3     exp nurse practitioners/
4     exp nurse's aides/
5     exp physician assistants/
6     exp nurse clinicians/
7     nurses/
8     Primary care physician$.mp.
9     General practitioner$.mp.
10    Primary care clinician$.mp.
11    exp ambulatory care facilities/
12    exp primary health care/
13    exp physician's role/
14    exp physician's practice patterns/
15    exp mass screening/
16    exp health behavior/
17    exp health promotion/
18    exp infant welfare/
19    exp health services accessibility/
20    exp child health services/
21    exp "referral and consultation"/
22    1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
     or 19 or 20 or 21
23    limit 22 to (english language and humans)
24    limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial,
     phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta
     analysis or multicenter study or randomized controlled trial or technical report or validation
     studies)
25    exp epidemiologic study characteristics/
26    exp epidemiologic research design/
27    exp questionnaires/
28    (25 or 26 or 27) and 23
29    24 or 28
30    exp dental caries/
31    Dental screening.mp. or exp dental care for children/
32    dental care/ or dental examination.mp. or exp diagnosis, oral/
33    30 or 31 or 32
34    29 and 33
35    limit 34 to (infant <1 to 23 months> or preschool child <2 to 5 years>)
Appendix A1. Search Strategies

Database: Ovid MEDLINE® without Revisions <1999 to March 8, 2013>
Search Strategy:

1 exp physicians/
2 exp pediatrics/ or pediatrician$.mp.
3 exp nurse practitioners/
4 exp nurse's aides/
5 exp physician assistants/
6 exp nurse clinicians/
7 nurses/
8 Primary care physician$.mp.
9 General practitioner$.mp.
10 Primary care clinician$.mp.
11 exp ambulatory care facilities/
12 exp primary health care/
13 exp physician's role/
14 exp physician's practice patterns/
15 exp mass screening/
16 exp health behavior/
17 exp health promotion/
18 exp infant welfare/
19 exp health services accessibility/
20 exp child health services/
21 exp "referral and consultation"
22 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23 limit 22 to (english language and humans)
24 limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or technical report or validation studies)
25 exp epidemiologic study characteristics/
26 exp epidemiologic research design/
27 exp questionnaires/
28 (25 or 26 or 27) and 23
29 24 or 28
30 exp MOTHERS/
31 exp PARENTS/
32 30 or 31
33 exp dental health services/ or dental utilization.mp. or exp dental care/
34 29 and 33
35 limit 34 to (infant <1 to 23 months> or preschool child <2 to 5 years>)
Appendix A1. Search Strategies

Database: Ovid MEDLINE® without Revisions <1999 to March 8, 2013>

Search Strategy:

--------------------------------------------------------------------------------
1     exp physicians/
2     exp pediatrics/ or pediatrician$.mp.
3     exp nurse practitioners/
4     exp nurse's aides/
5     exp physician assistants/
6     exp nurse clinicians/
7     nurses/
8     Primary care physician$.mp.
9     General practitioner$.mp.
10    Primary care clinician$.mp.
11    exp ambulatory care facilities/
12    exp primary health care/
13    exp physician's role/
14    exp physician's practice patterns/
15    exp mass screening/
16    exp health behavior/
17    exp health promotion/
18    exp infant welfare/
19    exp health services accessibility/
20    exp child health services/
21    exp "referral and consultation"/
22    1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23    limit 22 to (english language and humans)
24    limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or technical report or validation studies)
25    exp epidemiologic study characteristics/
26    exp epidemiologic research design/
27    exp questionnaires/
28    (25 or 26 or 27) and 23
29    24 or 28
30    exp mothers/
31    exp parents/
32    30 or 31
33    exp fluorides, topical/
34    exp fluorides/
35    exp cariostatic agents/
36    Supplemental fluoride$.mp.
37    Fluoride tab$.mp.
38    Fluoride drop$.mp.

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39  Fluoride varnish$.mp.
40  33 or 34 or 35 or 36 or 37 or 38 or 39
41  29 and 40
42  limit 41 to (newborn infant <birth to 1 month> or infant <1 to 23 months> or preschool child <2 to 5 years>)

Database: Ovid MEDLINE® without Revisions <1999 to March 8, 2013>
Search Strategy:
--------------------------------------------------------------------------------
1  exp physicians/
2  exp pediatrics/ or pediatrician$.mp.
3  exp nurse practitioners/
4  exp nurse's aides/
5  exp physician assistants/
6  exp nurse clinicians/
7  nurses/
8  Primary care physician$.mp.
9  General practitioner$.mp.
10 Primary care clinician$.mp.
11  exp ambulatory care facilities/
12  exp primary health care/
13  exp physician's role/
14  exp physician's practice patterns/
15  exp mass screening/
16  exp health behavior/
17  exp health promotion/
18  exp infant welfare/
19  exp health services accessibility/
20  exp child health services/
21  exp "referral and consultation"/
22  1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
or 19 or 20 or 21
23  limit 22 to (english language and humans)
24  limit 23 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial,
phase iii or clinical trial, phase iv or controlled clinical trial or evaluation studies or meta
analysis or multicenter study or randomized controlled trial or technical report or validation
studies)
25  exp epidemiologic study characteristics/
26  exp epidemiologic research design/
27  exp questionnaires/
28  (25 or 26 or 27) and 23
29  24 or 28
30  exp MOTHERS/
31  exp PARENTS/
32  30 or 31
33  exp dental care for children/
Appendix A1. Search Strategies

34 exp dental caries/
35 exp oral hygiene/
36 exp oral health/
37 exp health education, dental/
38 exp diet, cariogenic/
39 exp dental care/
40 33 or 34 or 35 or 36 or 37 or 38 or 39
41 29 and 40
42 limit 41 to (infant <1 to 23 months> or preschool child <2 to 5 years>)

Database: Ovid MEDLINE® and Ovid OLDMEDLINE® <1946 to March 8, 2013>
Search Strategy:
--------------------------------------------------------------------------------
1     exp "Pit and Fissure Sealants"
2     exp Dental Caries/
3     exp fluorosis, dental/
4     2 or 3
5     1 and 2
6     limit 5 to "all child (0 to 18 years)"
7     ((tooth or teeth or pit or pits or fissur$) adj5 seal$).mp. [mp=title, abstract, original
title, name of substance word, subject heading word, protocol supplementary concept, rare disease
supplementary concept, unique identifier]
8     2 and 7
9     limit 8 to "all child (0 to 18 years)"
10    ((tooth or teeth or enamel$ or crown or root or dental$ or molar$ or incisor$ or bicuspid$ or
canine$ or premolar$) adj5 (decay$ or cario$ or decay$ or cavit$ or fluorosis$)).mp. [mp=title, abstract, original
title, name of substance word, subject heading word, protocol supplementary concept, rare
disease supplementary concept, unique identifier]
11    1 and 10
12    limit 11 to "all child (0 to 18 years)"
13    6 or 9 or 12
14    (201206$ or 201207$ or 201208$ or 201209$ or 20121$).ed.
15    13 and 14
16    exp Tooth Demineralization/
17    ((tooth or teeth or root$ or crown$ or dental$ or dentis$) adj5 (caries or cario$ or decay$
or cavit$ or fluorosis$)).mp.
18    16 or 17
19    xylitol.mp.
20    18 and 19
21    limit 20 to "all child (0 to 18 years)"

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <February 2013>
Search Strategy:
--------------------------------------------------------------------------------
1     (physician$ or pediatrician$ or general practi$ or primary care or primary health care or
nurse or nurses or (nurs$ adj3 (care or caring or cared or cares)) or screen$ or (health$ adj3

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(behav$ or promot$ or access$)) or referral$ or consult$ or counsel$ or parent$ or mother$ or father$ or guardian$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (62097)
2   ((dental$ or tooth or teeth$) adj7 (caries or decay$ or fluorid$ or xylitol or sealant$ or sealing or cariostat$ or fluorosis) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (968)
3   ((dental or dentist$ or oral) adj7 (screen$ or fluorid$ or checkup$ or (check$ adj up) or exam or exams or examine$ or examination$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (343)
4   ((dental or dentist$ or oral) adj3 (hygien$ or health$ or prophyla$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (384)
5   2 or 3 or 4 (1263)
6   1 and 5 (239)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <1999 to February 2013>
Search Strategy:

1   (physician$ or pediatrician$ or general practi$ or primary care or primary health care or nurse or nurses or (nurs$ adj3 (care or caring or cared or cares)) or screen$ or (health$ adj3 (behav$ or promot$ or access$)) or referral$ or consult$ or counsel$ or parent$ or mother$ or father$ or guardian$).mp. [mp=title, abstract, full text, keywords, caption text] (6578)
2   ((dental$ or tooth or teeth$) adj7 (caries or decay$ or fluorid$ or xylitol or sealant$ or sealing or cariostat$ or fluorosis) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, abstract, full text, keywords, caption text] (43)
3   ((dental or dentist$ or oral) adj7 (screen$ or fluorid$ or checkup$ or (check$ adj up) or exam or exams or examine$ or examination$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, abstract, full text, keywords, caption text] (39)
4   ((dental or dentist$ or oral) adj3 (hygien$ or health$ or prophyla$) adj10 (child$ or pediatric$ or infant$ or infancy or toddler$)).mp. [mp=title, abstract, full text, keywords, caption text] (47)
5   2 or 3 or 4 (78)
6   1 and 5 (75)
## Appendix A2. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
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<th>Include</th>
<th>Exclude</th>
</tr>
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<tr>
<td><strong>Population</strong></td>
<td>All key questions: Asymptomatic children less than 5 years of age</td>
<td>All key questions: Animal studies, adults, children older than preschool age (&gt;5 years), symptomatic</td>
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<tr>
<td><strong>Interventions</strong></td>
<td>Key questions 1-3: Oral screening and risk factor assessment performed by primary care clinicians</td>
<td>Key questions 1-3: Community or school-based interventions</td>
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<td></td>
<td>Key questions 4 and 5: Parent/caregiver oral health education and/or referral to dentist</td>
<td>Key questions 4 and 5: Interventions not performed in primary care settings</td>
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<td></td>
<td>Key questions 6 and 7: Preventive treatments: including oral fluoride supplementation, topical fluoride application, or xylitol</td>
<td>Key questions 6 and 7: Treatments not available for preschool children or not available in the United States</td>
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<tr>
<td><strong>Outcomes</strong></td>
<td>All key questions: Reduced dental caries and associated outcomes</td>
<td>All key questions: Cost-effectiveness</td>
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<tr>
<td></td>
<td>Key questions 2 and 3: Diagnostic accuracy and measures of risk prediction</td>
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<tr>
<td></td>
<td>Key question 7: Dental fluorosis, emotional stress, acute toxicity, and other associated complications</td>
<td></td>
</tr>
<tr>
<td><strong>Study types and designs</strong></td>
<td>Key questions 1, 4, 5, and 6: Randomized controlled trials, non-randomized controlled clinical trials, and cohort studies</td>
<td>Key questions 1, 2, 4, 5, and 6: Case-control studies, uncontrolled intervention studies</td>
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<tr>
<td></td>
<td>Key question 2: Studies of diagnostic accuracy or risk prediction</td>
<td>All key questions: Opinion, editorials, or case reports</td>
</tr>
<tr>
<td></td>
<td>Key questions 3 and 7: Randomized controlled trials, cohort studies, case-control studies, and systematic reviews</td>
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</table>
Appendix A3. Literature Flow Diagram

Abstracts of potentially relevant articles identified through MEDLINE, Cochrane*, and other sources† (N = 1,215)

Excluded abstracts and background articles (n = 676)

Full text articles reviewed for relevance to Key questions (n = 539)

Articles excluded (n = 519)
- Excluded because it doesn’t address a key question or meet inclusion criteria, but pulled to provide background information = 111
- Wrong population = 115
- Wrong intervention = 50
- Wrong publication type = 71
- Conducted prior to 2000 (except xylitol) = 3
- Foreign language = 21
- Wrong outcome = 77
- Wrong setting = 14
- Not applicable to United States population = 4
- In prior report = 53

Final included studies‡: 20

Key Question 1: 0
Key Question 2: 1
Key Question 3: 0
Key Question 4: 2
Key Question 5: 1
Key Question 6: 15
Key Question 7: 3

*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Identified from reference lists, hand searching, suggested by experts, etc.
‡Studies that provided data and contributed to the body of evidence were considered “included.”
§Studies may have provided data for more than one key question.
Appendix A4. Excluded Studies List

Key to exclusion codes

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<th>Code</th>
<th>Reason</th>
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<td>Excluded because it doesn’t address a key question or meet inclusion criteria, but pulled to provide background information</td>
</tr>
<tr>
<td>3</td>
<td>Wrong population</td>
</tr>
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<td>Wrong intervention</td>
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<td>5</td>
<td>Wrong publication type</td>
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<td>6</td>
<td>Conducted prior to 2000 (except xylitol)</td>
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<tr>
<td>7</td>
<td>Foreign language, otherwise included</td>
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<td>8</td>
<td>Wrong outcome</td>
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<td>Wrong setting</td>
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<td>10</td>
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<td>11</td>
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List of excluded studies

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Exclusion code: 3

Appendix A4. Excluded Studies List

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Exclusion code: 8

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Exclusion code: 8

Exclusion code: 8

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Exclusion code: 3

Exclusion code: 2

Exclusion code: 2

Exclusion code: 2
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

Exclusion code: 2

Exclusion code: 2

Exclusion code: 2

Exclusion code: 2

Ammari AB, Bloch-Zupan A, Ashley PF. Systematic review of studies comparing the anti-caries efficacy of children's toothpaste containing 600 ppm of fluoride or less with high fluoride toothpastes of 1,000 ppm or above. Caries Res. 2003;37(2):85-92, [PMID: 12652045]
Exclusion code: 3

Exclusion code: 2

Exclusion code: 4

Exclusion code: 8

Anttonen V, Larmas M, Raitio M. Children were guaranteed regular check ups in dental study. BMJ. 1999;319(7222):1432, [PMID: 10574873]
Exclusion code: 5

Exclusion code: 4

Exclusion code: 5
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Prevention of Dental Caries in Children  55  Pacific Northwest Evidence-based Practice Center
Appendix A4. Excluded Studies List

Exclusion code: 2

Exclusion code: 3

Exclusion code: 8

Exclusion code: 5

Exclusion code: 5

Exclusion code: 5

Caufield PW, Griffen AL. *DENTAL CARIES: An Infectious and Transmissible Disease.* 2000. 0031-3955
Exclusion code: 2

Exclusion code: 11

Exclusion code: 2

Exclusion code: 2

Exclusion code: 4

Exclusion code: 3

Exclusion code: 11
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

Exclusion code: 10

Exclusion code: 2

Exclusion code: 4

Exclusion code: 4

Exclusion code: 5

Exclusion code: 5

Exclusion code: 5

Exclusion code: 3

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Exclusion code: 2

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Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

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Exclusion code: 2

Exclusion code: 3

Exclusion code: 3

Exclusion code: 2

Exclusion code: 8

Exclusion code: 2

Exclusion code: 2

Exclusion code: 11

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Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

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Exclusion code: 5

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Appendix A4. Excluded Studies List

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Exclusion code: 8

Exclusion code: 2

Exclusion code: 2

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Exclusion code: 7


Appendix A4. Excluded Studies List

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Exclusion code: 3

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Exclusion code: 8
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

Exclusion code: 11

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Exclusion code: 11

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Exclusion code: 5

Exclusion code: 5

Exclusion code: 2

Exclusion code: 2

Exclusion code: 8

Exclusion code: 9

Exclusion code: 5
Appendix A4. Excluded Studies List

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Exclusion code: 3

Exclusion code: 3

Exclusion code: 2

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Exclusion code: 3

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Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

Exclusion code: 11

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Exclusion code: 2

Exclusion code: 4

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Exclusion code: 11

Exclusion code: 2

Exclusion code: 11
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

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Appendix A4. Excluded Studies List

Exclusion code: 3

Exclusion code: 5

Exclusion code: 5

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Exclusion code: 11

Exclusion code: 11

Exclusion code: 11

Exclusion code: 2

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Exclusion code: 3

Exclusion code: 3

Marinho CV, Higgins PJ, Sheiham A, Logan S. One topical fluoride (toothpastes, or mouthrinses, or gels, or varnishes) versus another for preventing dental caries in children and adolescents [Systematic Review]. Cochrane Database Syst Rev. 2009(1), [PMID: 14583954]
Exclusion code: 3
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Exclusion code: 11

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Exclusion code: 3

Exclusion code: 4

Exclusion code: 3

Exclusion code: 3

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Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

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Exclusion code: 11

Riordan PJ. Dental fluorosis decline after changes to supplement and toothpaste regimens. Community Dentistry and Oral Epidemiology. 2002;30(3):233-240, [PMID: 12000347]
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Appendix A4. Excluded Studies List

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Appendix A4. Excluded Studies List

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Exclusion code: 3

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Appendix A4. Excluded Studies List

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Exclusion code: 8

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Exclusion code: 5

Exclusion code: 3

Exclusion code: 8

Exclusion code: 3
Appendix A4. Excluded Studies List


Spittle B. *Fluoride poisoning: Is fluoride from your drinking water and other sources making you sick?* International Society for Fluoride Research (New Zealand); 2012. Exclusion code: 5


Stijacic T, Schroth RJ, Lawrence HP. Are Manitoba dentists aware of the recommendation for a first visit to the dentist by age 1 year? *Journal of the Canadian Dental Association.* 2008;74(10):903a-903h, [PMID: 19126358] Exclusion code: 8

Strippel H. Effectiveness of structured comprehensive paediatric oral health education for parents of children less than two years of age in Germany. *Community Dent Health.* 2010;27(2):74-80, [PMID: 20648883] Exclusion code: 8


Svenson D, Bridges D. Xylitol: the sugar that prevents tooth decay. *Dent Hyg (Chic).* 1977;51(9):401, [PMID: 348510] Exclusion code: 2
Appendix A4. Excluded Studies List


Tavener JA, Davies GM, Davies RM, Ellwood RP. The prevalence and severity of fluorosis in children who received toothpaste containing either 440 or 1,450 ppm F from the age of 12 months in deprived and less deprived communities. *Caries Res.* 2006;40(1):66-72, [PMID: 16352884] Exclusion code: 4


Appendix A4. Excluded Studies List

Exclusion code: 3

Exclusion code: 8

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Exclusion code: 5

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Exclusion code: 3

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Exclusion code: 2

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Exclusion code: 4
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List

Exclusion code: 7

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Exclusion code: 8

Exclusion code: 8

Exclusion code: 11

Exclusion code: 8

Exclusion code: 2

Exclusion code: 5

Exclusion code: 5

Exclusion code: 4
Appendix A4. Excluded Studies List


Appendix A4. Excluded Studies List


Appendix A5. U.S. Preventive Services Task Force Quality Rating Criteria for Randomized, Controlled Trials and Observational Studies

Randomized, controlled trials (RCTs)

Criteria:

- Initial assembly of comparable groups: RCTs—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; 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
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention-to-treat analysis for RCTs; for cluster RCTs, correction for correlation coefficient

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (followup at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

Fair: Studies will be graded “fair” if any or all of the following problems occur, without the important limitations noted in the “poor” category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in 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.

Poor: Studies will be graded “poor” if any of the following major limitations 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 at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.
Appendix A5. U.S. Preventive Services Task Force Quality Rating Criteria for Randomized, Controlled Trials and Observational Studies

Diagnostic accuracy studies

Criteria:

- Screening test relevant, available for primary care, adequately described
- Study uses a credible reference standard, performed regardless of test results
- Reference standard interpreted independently of screening test
- Handles indeterminate results in a reasonable manner
- Spectrum of patients included in study
- Sample size
- Administration of reliable screening test
- Random or consecutive selection of patients
- Screening cutoff pre-determined
- All patients undergo the reference standard

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease; study attempts to enroll a random or consecutive sample of patients who meet inclusion criteria screening cutoffs pre-stated.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a “medium” spectrum of patients (i.e. applicable to most screening settings).

Poor: Has important limitation such as: uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size of very narrow selected spectrum of patients.

Sources: Harris et al, 200134 and USPSTF Procedure Manual35
Appendix A6. List of Reviewers

Expert reviewers

Kevin J. Donly, D.D.S., M.S., Professor and Chair, Department of Developmental Dentistry, University of Texas Health Science Center at San Antonio

William Frese, M.D., M.P.H., Assistant Professor, University of Illinois at Chicago

David M. Krol, M.D., M.P.H., Senior Program Officer, Robert Wood Johnson Foundation

Steven M. Levy, D.D.S., M.P.H., Wright-Bush-Shreves Endowed Professor of Research, Department of Preventive and Community Dentistry, College of Dentistry, University of Iowa

Charlotte W. Lewis, M.D., M.P.H., Associate Professor of Pediatrics, University of Washington School of Medicine

Amr M. Moursi, D.D.S., Ph.D., Chair, Department of Pediatric Dentistry, New York University, College of Dentistry

Francisco Ramos-Gomez, D.D.S., M.S., M.P.H., Professor, Section of Pediatric Dentistry, University of California Los Angeles, School of Dentistry

Federal reviewers

Joseph Chin, M.D., M.S., Medical Officer, Centers for Medicare & Medicaid Services

Barbara Gooch, D.M.D., M.P.H., Associate Director for Science, Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention

Susan Griffin, Ph.D., Health Economist, Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention

## Appendix B1. Diagnostic Accuracy Studies for the Prevention of Dental Caries

<table>
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<tr>
<th>Author, Year, Title</th>
<th>Screening Test</th>
<th>Reference Standard</th>
<th>Country Setting Screener</th>
<th>Population</th>
<th>Sample Size</th>
<th>Proportion With Condition</th>
<th>Positive Screening Exam Definition</th>
<th>Proportion Un-examinable by Screening Test</th>
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</thead>
<tbody>
<tr>
<td>Beltran et al., 1997&lt;sup&gt;11&lt;/sup&gt; Validity of two methods for assessing oral health status of populations</td>
<td>Nurse exam (no previous dental experience; received written material on procedures and diagnostic criteria for conditions to be evaluated)</td>
<td>Pediatric dentist exam</td>
<td>U.S. rural school nurse</td>
<td>Children 5-12 years old attending school</td>
<td>n=258 children</td>
<td>Cavitated lesions: 9.7% (mean 0.3/child)</td>
<td>ID of untreated decay ID of need for treatment (urgent or nonurgent)</td>
<td>Appears to be none</td>
</tr>
<tr>
<td>Pierce et al., 2002&lt;sup&gt;10&lt;/sup&gt; Accuracy of pediatric primary care providers’ screening and referral for early childhood caries</td>
<td>Primary care pediatrician exam following 2 hours of training</td>
<td>Pediatric dentist exam</td>
<td>U.S. pediatric group practice primary care pediatrician</td>
<td>Children &lt;36 months of age with erupted teeth participating in the &quot;Into the Mouths of Babes&quot; program. Excluded if received fluoride varnish and oral screening within 3 months or were very ill</td>
<td>n=258 children</td>
<td>Cavitated lesions: 9.7% (mean 0.3/child)</td>
<td>ID of a cavitated lesion ID of need for referral</td>
<td>Appears to be none</td>
</tr>
<tr>
<td>Serwint et al., 1993&lt;sup&gt;10&lt;/sup&gt; Child-rearing practices and nursing caries</td>
<td>Pediatrician exam (not primary care provider) following 4 hours of training</td>
<td>Pediatric dentist exam</td>
<td>U.S. general pediatric clinic pediatrician</td>
<td>Children 18-36 months of age, mother primary caretaker Excluded for developmental delay or facial abnormalities</td>
<td>n=110 children</td>
<td>Nursing caries (caries involving one or more teeth including the maxillary central or lateral incisors or the primary molars but sparing the mandibular incisors): 20% (22/110)</td>
<td>ID of nursing caries</td>
<td>NR</td>
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### Appendix B1. Diagnostic Accuracy Studies for the Prevention of Dental Caries, Continued

<table>
<thead>
<tr>
<th>Author, Year, Title</th>
<th>Analysis of Screening Failures</th>
<th>Proportion Who Underwent Reference Standard and Included in Analysis</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beltran et al., 1997 &lt;sup&gt;41&lt;/sup&gt;&lt;br&gt;Validity of two methods for assessing oral health status of populations</td>
<td>NA</td>
<td>Appears to be all &lt;br&gt;Untreated decay: 0.92 (71/77) &lt;br&gt;Any treatment needed: 0.80 (70/88)</td>
<td>Untreated decay: 0.99 (141/142) &lt;br&gt;Any treatment needed: 0.99 (233/235)</td>
<td>Untreated decay: 0.99 (71/72) &lt;br&gt;Any treatment needed: 0.97 (70/72)</td>
<td>Untreated decay: 0.96 (141/147) &lt;br&gt;Any treatment needed: 0.93 (233/251)</td>
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<tr>
<td>Pierce et al., 2002 &lt;sup&gt;39&lt;/sup&gt;&lt;br&gt;Accuracy of pediatric primary care providers' screening and referral for early childhood caries</td>
<td>NA</td>
<td>Appears to be all &lt;br&gt;Patient-level analysis: 0.76 (19/25) &lt;br&gt;Tooth-level analysis: 0.49 (39/80) &lt;br&gt;Need for referral: 0.63 (17/27)</td>
<td>Patient-level analysis: 0.95 (222/233) &lt;br&gt;Tooth-level analysis: 0.99 (3210/3235)</td>
<td>Need for referral: 0.98 (225/231)</td>
<td>Need for referral: 0.74 (17/23)</td>
<td>Good</td>
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<tr>
<td>Serwint et al., 1993 &lt;sup&gt;40&lt;/sup&gt;&lt;br&gt;Child-rearing practices and nursing caries</td>
<td>NR</td>
<td>55% (61/110)</td>
<td>1.0 (n/N not calculable)</td>
<td>0.87 (n/N not calculable)</td>
<td>Not calculable</td>
<td>Not calculable</td>
<td>Fair</td>
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</tbody>
</table>

**Abbreviations:** ID = identification; NA = not applicable; NR = not reported; U.S. = United States.
## Appendix B2. Quality Ratings for Diagnostic Accuracy Studies

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<tr>
<th>Author, Year, Title</th>
<th>Representative Spectrum</th>
<th>Random or Consecutive Sample</th>
<th>Screening Test Adequately Described</th>
<th>Screening Cutoffs Predefined</th>
<th>Credible Reference Standard</th>
<th>Reference Standard Applied to All Screened Patients</th>
<th>Same Reference Standard Applied to All Patients</th>
<th>Reference Standard and Screening Examination Interpreted Independently</th>
<th>High Rate of Uninterpretable Results or Noncompliance With Screening Test</th>
<th>Analysis Includes Patients With Uninterpretable Results or Noncompliance</th>
<th>Quality Rating</th>
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<tr>
<td>Beltran et al., 1997&lt;sup&gt;41&lt;/sup&gt; Validity of two methods for assessing oral health status of populations</td>
<td>Yes</td>
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<td>Yes</td>
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<tr>
<td>Pierce et al., 2002&lt;sup&gt;38&lt;/sup&gt; Accuracy of pediatric primary care providers' screening and referral for early childhood caries</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<td>Good</td>
</tr>
<tr>
<td>Serwint et al., 1993&lt;sup&gt;43&lt;/sup&gt; Child-rearing practices and nursing caries</td>
<td>Yes</td>
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<td>Yes</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<td>No</td>
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<td>Fair</td>
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## Appendix B3. Trials of Educational Interventions for the Prevention of Dental Caries

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<tr>
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<th>Study Design</th>
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<th>Number Approached, Eligible, Analyzed</th>
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</thead>
<tbody>
<tr>
<td>Davies et al., 2007&lt;sup&gt;44&lt;/sup&gt; Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area</td>
<td>Cluster, nonrandomized controlled clinical trial (2 clusters)</td>
<td>A: Series of interventions from age 8-32 months by health visitor including provision of educational materials, counseling on oral hygiene, and provision of toothbrush and toothpaste</td>
<td>Age at time of initial followup evaluation (mean, years): 4 vs. 4</td>
<td>Children 8 months of age attending a primary care clinic</td>
<td>Number approached: 1545 (839 vs. 706)</td>
<td>UK Primary care clinics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B: No intervention</td>
<td>Female: 48% vs. 49%</td>
<td></td>
<td>Number eligible: 1545 (839 vs. 706)</td>
<td></td>
</tr>
<tr>
<td>Davies et al., 2005&lt;sup&gt;43&lt;/sup&gt; A staged intervention dental health promotion programme to reduce early childhood caries</td>
<td></td>
<td></td>
<td>Non-white: 51% vs. 37%</td>
<td></td>
<td>Number enrolled: 1545 (839 vs. 706)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Proportion of adults unemployed: 24% vs. 22%</td>
<td></td>
<td>Number analyzed: 1545 (839 vs. 706)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Jarman index (under-privileged area score): 39 vs. 40</td>
<td></td>
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<tr>
<td>Kressin et al., 2009&lt;sup&gt;49&lt;/sup&gt; Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention</td>
<td>Cluster, nonrandomized, controlled clinical trial (2 clusters)</td>
<td>A: Multi-component intervention including training of pediatricians in patient-centered counseling, providing parents/caregivers with educational brochure, and editing the electronic medical record to prompt counseling</td>
<td>Age &lt;1 year: 1% vs. 3%</td>
<td>Parents/caregivers of children 6 months-5 years of age attending well-child visits</td>
<td>Number approached: NR</td>
<td>U.S.</td>
</tr>
<tr>
<td></td>
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<td>B: Usual care</td>
<td>Age 1 to &lt;2 year: 55% vs. 55%</td>
<td>Excluded for congenital oral anomalies, ectodermal dysplasias, or other disease other than caries</td>
<td>Number eligible: NR</td>
<td></td>
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<td></td>
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<td></td>
<td>Age 2 to &lt;3 year: 25% vs. 26%</td>
<td></td>
<td>Number enrolled: 1087 (635 vs. 452)</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>Caregiver employed: 57% vs. 69% (p&lt;0.0001)</td>
<td></td>
<td>Number analyzed: 1045</td>
<td></td>
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<td></td>
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<td></td>
<td>White: 17% vs. 45% (p&lt;0.0001 for differences in race)</td>
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<td></td>
<td>Black: 76% vs. 35%</td>
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<td></td>
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<td>Asian: 6% vs. 19%</td>
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<td></td>
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<td>Hispanic: 13% vs. 15%</td>
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<td></td>
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<td></td>
<td>Diet summary score (0-6 scale): 3.2 vs. 3.5 (p&lt;0.0001)</td>
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<td></td>
<td>Hygiene summary score (0 to 6 scale, higher= better): 4.9 vs. 4.5 (p&lt;0.0001)</td>
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<td></td>
<td>Tooth-monitoring summary score (0-3 scale): 0.7 vs. 0.9 (p=0.02)</td>
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<td></td>
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<td></td>
<td>Baseline caries: 5.8% vs. 6.4% (p=0.66)</td>
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</table>
### Appendix B3. Trials of Educational Interventions for the Prevention of Dental Caries, Continued

<table>
<thead>
<tr>
<th>Author, Year, Title</th>
<th>Sponsor</th>
<th>Followup Duration</th>
<th>Confounders Adjusted for in Analysis</th>
<th>Outcomes</th>
<th>Adverse Events/Harms</th>
<th>Attrition</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davies et al., 2007&lt;sup&gt;44&lt;/sup&gt; Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area</td>
<td>National Health Service Research and Development Programme for Primary Dental Care</td>
<td>Evaluated at ages 3-4 years and age 5 years</td>
<td>None</td>
<td>A vs. B at 3-4 year old followup; all children and restricted to children who attended developmental check and MMR vaccination (n=1207, 649 vs. 558)</td>
<td>Caries experience: 34% vs. 40%, p=0.01; 29% vs. 39%, p=0.001</td>
<td>Not reported</td>
<td>Poor</td>
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<td></td>
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<td>Nursing caries: 21% vs. 23%, p=0.49; 17% vs. 24%, p=0.003 dmft (mean): 1.5 vs. 1.7, p=0.09; 1.2 vs. 1.7, p=0.001</td>
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<td>dmfs (mean): 3.3 vs. 3.7, p=0.35; 2.6 vs. 3.8, p=0.008 A vs. B at 5 year old followup; restricted to children who attended developmental check and MMR vaccination (n=539, 253 vs. 286)</td>
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<td></td>
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<td>Caries experience: 54% vs. 64%, p=0.03</td>
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<td></td>
<td>Nursing caries: 20% vs. 32%, p=0.002</td>
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<td>Extraction: 3% vs. 12%, p&lt;0.001</td>
<td>dmft (mean): 2.2 vs. 3.7, p&lt;0.001</td>
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<tr>
<td>Davies et al., 2005&lt;sup&gt;43&lt;/sup&gt; A staged intervention dental health promotion programme to reduce early childhood caries</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Kressin et al., 2009&lt;sup&gt;45&lt;/sup&gt; Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention</td>
<td>NIH/NIDCR and VA</td>
<td>1 year</td>
<td>Length of enrollment, sex, race, treatment before 42 months, continuously enrolled in Medicaid number of well-child visits</td>
<td>A vs. B</td>
<td>Caries (irreversible cavitated lesions): 18% vs. 32%, adjusted HR 0.23 (95% CI 0.09 to 0.62)</td>
<td>NR</td>
<td>42/1087 enrolled were not analyzed</td>
</tr>
</tbody>
</table>

**Abbreviations:** AHRQ = Agency for Healthcare Research and Quality; CI = confidence interval; dmfs = decayed missing filled surfaces; dmft = decayed missing filled teeth; HR = hazard ratio; MMR = measles, mumps, and rubella; NIDCR = National Institute of Dental and Craniofacial Research; NIH = National Institutes of Health; NR = not reported; UK = United Kingdom; U.S. = United States; VA = Veterans Affairs.
## Appendix B4. Quality Ratings of Randomized, Controlled Trials

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<tbody>
<tr>
<td>Alamoudi et al., 2012* Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Chu et al., 2002** Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin carries in Chinese pre-school children</td>
<td>No</td>
<td>No</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Unclear</td>
<td>Yes</td>
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<tr>
<td>Davies et al., 2007** Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area Davies et al., 2005* A staged intervention dental health promotion programme to reduce early childhood caries</td>
<td>Not randomized</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
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<tr>
<td>Du et al., 2006* A two-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Jiang et al., 2005* The effect of a bi-annual professional application of APF foam on dental caries increment in primary teeth: 24-month clinical trial</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</table>
## Appendix B4. Quality Ratings of Randomized, Controlled Trials

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<tbody>
<tr>
<td>Kovari et al., 2003&lt;sup&gt;1&lt;/sup&gt; Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland</td>
<td>NR</td>
<td>NR</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Kressin et al., 2009&lt;sup&gt;2&lt;/sup&gt; Pediatric clinicians can help reduce rates of early childhood caries: Effects of a practice based intervention</td>
<td>Not randomized</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lawrence et al., 2008&lt;sup&gt;3&lt;/sup&gt; A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Milgrom et al., 2009&lt;sup&gt;4&lt;/sup&gt; Xylitol pediatric topical oral syrup to prevent dental caries</td>
<td>Yes</td>
<td>Unclear</td>
<td>No (age)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Oscarson et al., 2006&lt;sup&gt;5&lt;/sup&gt; Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children</td>
<td>NR</td>
<td>NR</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Seki et al., 2011&lt;sup&gt;6&lt;/sup&gt; Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomized trial</td>
<td>No</td>
<td>No</td>
<td>Unclear (dfs index)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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</table>
## Appendix B4. Quality Ratings of Randomized, Controlled Trials

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<tr>
<td>Slade et al., 2011&lt;sup&gt;11&lt;/sup&gt; Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes; some difference in fluoridation status</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Weinstein et al., 2001&lt;sup&gt;11&lt;/sup&gt; Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
</tr>
<tr>
<td>Weinstein et al., 2009&lt;sup&gt;12&lt;/sup&gt; Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition</td>
<td>Yes</td>
<td>Unclear</td>
<td>No; mean dmfs were not balanced</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
</tr>
<tr>
<td>Weintraub et al., 2006&lt;sup&gt;13&lt;/sup&gt; Fluoride varnish efficacy in preventing early childhood caries</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes; stated no imbalances apparent</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Zhan et al., 2012&lt;sup&gt;14&lt;/sup&gt; Effects of xylitol wipes on carcinogenic bacteria and caries in young children</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Author, Year, Title</td>
<td>Loss to Followup: Differential/High</td>
<td>Intention-To-Treat (ITT) Analysis</td>
<td>Post-Randomization Exclusions</td>
<td>Outcomes Pre-Specified</td>
<td>Funding Source</td>
<td>External Validity</td>
<td>Quality Rating</td>
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<tr>
<td>Alamoudi et al., 2012&lt;sup&gt;a&lt;/sup&gt; Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs</td>
<td>Yes (very high)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>The Deanship of Scientific Research, King Abdulaziz University, Jeddah, Saudi Arabia (Project No. 429/011-9)</td>
<td>Fair</td>
<td>Poor</td>
<td></td>
</tr>
<tr>
<td>Chu et al., 2002&lt;sup&gt;b&lt;/sup&gt; Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin carries in Chinese pre-school children</td>
<td>No/No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>A research grant from The University of Hong Kong (CRCG)</td>
<td>Limited: Chinese fluoridated water, 73% used fluoridated toothpaste</td>
<td>Poor</td>
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</tr>
<tr>
<td>Davies et al., 2007&lt;sup&gt;c&lt;/sup&gt; Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>National Health Service Research and Development Programme for Primary Dental Care</td>
<td>Fair</td>
<td>Poor</td>
<td></td>
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<tr>
<td>Davies et al., 2005&lt;sup&gt;d&lt;/sup&gt; A staged intervention dental health promotion programme to reduce early childhood caries</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Du et al., 2006&lt;sup&gt;e&lt;/sup&gt; A two-year randomized clinical trial of chlorhexidine varnish on dental carries in Chinese preschool children</td>
<td>No/Unclear</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>The National Key Technologies R &amp; D Program of the tenth Five-Year Plan, the Ministry of Science and Technology, and the National Committee for Oral Health, China</td>
<td>Limited: Chinese children in China, no organized oral health care programs, but access to fluoridated water</td>
<td>Fair</td>
<td></td>
</tr>
<tr>
<td>Jiang et al., 2005&lt;sup&gt;f&lt;/sup&gt; The effect of a bi-annual professional application of APF foam on dental carries increment in primary teeth: 24-month clinical trial</td>
<td>No/No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>National Key Technologies R &amp; D Program of the Tenth-five Year Plan, the Ministry of Science and Technology, China (2004BA720A24)</td>
<td>Limited: Chinese children, fluoridated water, no organized health care programs, limited use of fluoride toothpaste</td>
<td>Good</td>
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<tr>
<td>Author, Year, Title</td>
<td>Loss to Followup: Differential/High</td>
<td>Intention-To-Treat (ITT) Analysis</td>
<td>Post-Randomization Exclusions</td>
<td>Outcomes Pre-Specified</td>
<td>Funding Source</td>
<td>External Validity</td>
<td>Quality Rating</td>
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<tr>
<td>Kovari et al., 2003&lt;sup&gt;13&lt;/sup&gt; Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>NR</td>
<td>Limited</td>
<td>Fair</td>
<td></td>
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<tr>
<td>Kressin et al., 2009&lt;sup&gt;15&lt;/sup&gt; Pediatric clinicians can help reduce rates of early childhood caries: Effects of a practice based intervention</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>NIDCR, NIH, and VA</td>
<td>Fair</td>
<td>Fair</td>
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<tr>
<td>Lawrence et al., 2008&lt;sup&gt;17&lt;/sup&gt; A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children</td>
<td>No/No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>The Institute of Aboriginal Peoples’ Health of the Canadian Institutes of Health Research (Grant MOP-64215) and the Toronto Hospital for Sick Children Foundation (Grant XG 03-067)</td>
<td>Limited: Aboriginal communities in rural Canada</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>Milgrom et al., 2009&lt;sup&gt;13&lt;/sup&gt; Xylitol pediatric topical oral syrup to prevent dental caries</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>The Maternal and Child Health Bureau (HRSA) and NIDCR</td>
<td>Fair</td>
<td>Fair</td>
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<tr>
<td>Oscarson et al., 2006&lt;sup&gt;19&lt;/sup&gt; Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Grants from Count of Vasterbotten, the Patient Revenue Fund for Dental Prophylaxis and the Swedish Dental Society</td>
<td>Fair</td>
<td>Fair</td>
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<tr>
<td>Seki et al., 2011&lt;sup&gt;30&lt;/sup&gt; Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-randomized trial</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>The Uemura Fund, Nihon University School of Dentistry</td>
<td>Fair</td>
<td>Poor</td>
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<tr>
<td>Slade et al., 2011&lt;sup&gt;48&lt;/sup&gt; Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial</td>
<td>No/No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Project grant 320858 from the Australian National Health and Medical Research Council</td>
<td>Limited: Aboriginal communities in rural Australia</td>
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### Appendix B4. Quality Ratings of Randomized, Controlled Trials, Continued

<table>
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<tr>
<th>Author, Year, Title</th>
<th>Loss to Followup: Differential/High</th>
<th>Intention-To-Treat (ITT) Analysis</th>
<th>Post-Randomization Exclusions</th>
<th>Outcomes Pre-Specified</th>
<th>Funding Source</th>
<th>External Validity</th>
<th>Quality Rating</th>
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<tbody>
<tr>
<td>Weinstein et al., 2001&lt;sup&gt;1&lt;/sup&gt; Equivalence between massive versus standard fluoride varnish treatments in high caries children aged 3-5 years</td>
<td>Yes/Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Grant R03 DE012138 from NIDCR, NIH</td>
<td>Head Start program</td>
<td>Fair</td>
</tr>
<tr>
<td>Weinstein et al., 2009&lt;sup&gt;2&lt;/sup&gt; Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition</td>
<td>No/No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Grants R01DE14403 and U54DE14254 from NIDCR, NIH</td>
<td>Head Start program</td>
<td>Fair</td>
</tr>
<tr>
<td>Weintraub et al., 2006&lt;sup&gt;3&lt;/sup&gt; Fluoride varnish efficacy in preventing early childhood caries</td>
<td>Yes/No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>USPHS research grants P60DE13058 and U54DE142501 from NIDCR and NCMHD, NIH; and by UCSF’s Department of Preventive and Restorative Dental Sciences</td>
<td>Limited; &quot;Under-serviced&quot; community in U.S.; all non-white</td>
<td>Fair</td>
</tr>
<tr>
<td>Zhan et al., 2012&lt;sup&gt;4&lt;/sup&gt; Effects of xylitol wipes on carcinogenic bacteria and caries in young children</td>
<td>No/Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>California Society of Pediatric Dentistry Foundation (a Graduate Scientific Research Award from AAPD) and NIH/NIDCR grant U54 DEQ19285</td>
<td>Single center</td>
<td>Fair</td>
</tr>
</tbody>
</table>

**Abbreviations:** AAPD = American Academy of Pediatric Dentistry; dfs = decayed filled surfaces; dmfs = decayed missing filled surfaces; HRSA = Health Resources and Services Administration; NCMHD = National Center on Minority Health and Health Disparities; NIDCR = National Institute of Dental and Craniofacial Research; NIH = National Institutes of Health; NR = not reported; UCSF = University of California San Francisco; U.S. = United States; USPHS = U.S. Public Health Service; VA = U.S. Department of Veterans Affairs.
### Appendix B5. Cohort Study of Dental Referral From a Primary Care Clinician for the Prevention of Dental Caries

<table>
<thead>
<tr>
<th>Author, Year, Title</th>
<th>Interventions</th>
<th>Population Characteristics</th>
<th>Eligibility Criteria</th>
<th>Number Approached, Eligible, Enrolled, Analyzed</th>
<th>Country</th>
<th>Sponsor</th>
<th>Followup Duration</th>
<th>Adjusted Confounders in Analysis</th>
<th>Outcomes</th>
<th>Adverse Events/Harms</th>
<th>Attrition</th>
<th>Quality Rating</th>
</tr>
</thead>
</table>
| Beil et al., 2012    | A: First preventive dental visit by age 18 months  
B: First preventive dental visit after age 18 months  
C: No preventive dental visits before age 18 months | Primary or secondary dental preventive visit before age 18 months vs. between age 18-42 months  
Female: 46% vs. 48-51%  
Non-white race: 67% vs. 66-67%  
Number of well-child visits: 1.8 vs. 1.4-1.7  
Percent of population in county under 18 months of age enrolled in Medicaid: 30% vs. 31-33%  
Dentists per capita in county: 5.1 vs. 4.5-4.9 | Children enrolled in North Carolina Medicaid prior to first birthday, enrolled for at least 12 months, with a paid claim for dental care  
Excluded if received dental services in medical office as part of the Into the Mouths of Babes fluoride varnish program | Approached: 165,383  
Eligible: 19,888  
Enrolled: 19,888  
Analyzed: 19,888 | U.S. | AHRQ and NIDCR | Through age 72 months | Age, race/ethnicity, caregiver employment, caregiver education, language spoken at home, diet score, hygiene score, tooth monitoring score | First preventive visit at age 18-24, 25-30, 31-36, or 37-42 months vs. <18 months (reference)  
Tertiary preventive visit: Incidence density ratio: 0.98 (0.87-1.1), 1.1 (0.94-1.2), 1.1 (0.96-1.2), and 1.4 (0.95-1.2)  
Tertiary preventive visit: Incidence density ratio: 1.2 (1.0-1.4), 1.2 (1.1-1.4), 1.1 (0.99-1.3), and 1.4 (1.2-1.6) | None | Fair |

**Abbreviations:** AHRQ = Agency for Healthcare Research and Quality; NIDCR = National Institute of Dental and Craniofacial Research; NR = not reported; U.S. = United States.
<table>
<thead>
<tr>
<th>Author, Year, Title</th>
<th>Did Study Attempt to Enroll a Random Sample or Consecutive Patients Meeting Inclusion Criteria (Inception Cohort)?</th>
<th>Were Groups Comparable at Baseline?</th>
<th>Did Study Use Accurate Methods for Ascertaining Exposures, Potential Confounders, and Outcomes?</th>
<th>Were Outcome Assessors and/or Data Analysts Blinded to Treatment?</th>
<th>Did the Article Report Attrition?</th>
<th>Did Study Perform Appropriate Statistical Analyses on Potential Confounders?</th>
<th>Is There Important Differential Loss to Followup or Overall High Loss to Followup?</th>
<th>Were Outcomes Pre-Specified and Defined, and Ascertained Using Accurate Methods?</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beil et al., 2012* Effect of early preventive dental visits on subsequent dental treatment and expenditures</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Fair</td>
</tr>
</tbody>
</table>
## Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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<tbody>
<tr>
<td>Chu et al., 2002&lt;sup&gt;86&lt;/sup&gt; Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children</td>
<td>Controlled clinical trial</td>
<td>A: Removal of carious tissue plus 38% silver diamine fluoride solution every 12 months B: 38% silver diamine fluoride solution every 12 months C: Removal of carious tissue plus 5% sodium fluoride every 3 months D: 5% sodium fluoride varnish every 3 months E: Placebo (water)</td>
<td>Age, mean: 4 years Female: 44% Race: NR dmfs score: 3.92 Used fluoridated toothpaste: 73% Children from 8 kindergartens with caries in upper primary anterior teeth</td>
<td>Number approached: NR Number eligible: NR Number enrolled: 375 (76 vs. 77 vs. 76 vs. 73 vs. 73) Number analyzed: 308 (61 vs. 62 vs. 62 vs. 61 vs. 62)</td>
<td>China recruitment setting: Kindergarten Water fluoridation status: &lt;0.2 ppm</td>
<td>University of Hong Kong</td>
<td>2.5 years</td>
<td>A vs. B vs. C vs. D vs. E</td>
<td>New caries surfaces: 0.26 vs. 0.47 vs. 0.89 vs. 0.70 vs. 1.58, p for ANOVA &lt;0.001 (E vs. others) Arrested caries surfaces: 2.49 vs. 2.82 vs. 1.45 vs. 1.54 vs. 1.27; p for ANOVA &lt;0.001 (E vs. others) Absolute reduction in caries increment: 1.32 vs. 1.11 vs. 0.69 vs. 0.88 vs. E as comparator (vs. others) Reduction in caries increment: 84% vs. 70% vs. 44% vs. 56% vs. E as comparator (vs. others)</td>
<td>No adverse events detected</td>
<td>Overall 18%; 20% vs. 18% vs. 16% vs. 15%</td>
<td>Poor</td>
</tr>
</tbody>
</table>
## Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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</tr>
</thead>
<tbody>
<tr>
<td>Jiang et al., 2005&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Cluster RCT (15 clusters)</td>
<td>A: 0.6-0.8 g of 1.23% acidulated phosphate fluoride foam applied every 6 months, max 4 applications</td>
<td>Children from 4 kindergartens</td>
<td>Number approached: NR</td>
<td>China recruitment setting: Kindergarten Water fluoridation status: 0.1-0.3 ppm</td>
<td>National Key Technologies R&amp;D Program of the Tenth-five Year Plan, Ministry of Science and Technology, China</td>
<td>2 years</td>
<td>A vs. B</td>
<td>No increase in dmfs: 38% (64/167) vs. 26% (40/151)</td>
<td>No adverse events detected</td>
<td>A vs. B: 20% (42/209) vs. 17% (32/183)</td>
<td>Good</td>
</tr>
<tr>
<td>Lawrence et al., 2008&lt;sup&gt;52&lt;/sup&gt;</td>
<td>Cluster RCT (20 clusters)</td>
<td>A: 0.3-0.5 ml 5% sodium fluoride varnish applied to full primary dentition every 6 months</td>
<td>Children ages 6 months-5 years, with at least 1 primary tooth, residing in First Nations community in study region, with signed consent from primary caregiver</td>
<td>Number approached: 1,793</td>
<td>Canada recruitment setting: Rural Aboriginal communities Water fluoridation status: No fluoridation</td>
<td>Institute of Aboriginal Peoples’ Health/Canadian Institutes of Health Research; Toronto Hospital for Sick Children Foundation</td>
<td>2 years</td>
<td>A vs. B</td>
<td>Dental caries in aboriginal cohort: 72% (595/832) vs. 75% (247/328), adjusted OR 0.72 (95% CI 0.42 to 1.25); NNT 26</td>
<td>One child allergic to lanolin experienced an adverse event</td>
<td>One child allergic to lanolin experienced an adverse event</td>
<td>Good</td>
</tr>
</tbody>
</table>
## Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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<tbody>
<tr>
<td></td>
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<td>Caries experience: 73% vs. 69% (p=0.50)</td>
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<td>no teeth, stainless steel crowns only, ulcerative gingivitis, stomatitis or allergy to colophony component</td>
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<td></td>
<td>Net dmfs increment in aboriginal cohort, mean: 11 vs. 13.4; adjusted difference, mean (SE) 2.4 (2.0), p=0.24; prevented fraction 18%</td>
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<td>Net dmfs increment in those caries free at baseline, mean (SE): 4.3 (0.5) vs. 6.1 (0.8); adjusted difference, mean (SE): 1.8 (1.3); p=0.18; prevented fraction 29%</td>
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<td></td>
<td>Absolute reduction in caries increment: 2.4 (1.8)</td>
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<td></td>
<td>Reduction in caries increment: 18% (29%)</td>
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</tr>
</tbody>
</table>
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<th>Sponsor</th>
<th>Followup Duration</th>
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<th>Adverse Events/Harms</th>
<th>Attrition</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slade et al., 2011[^1^] Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial</td>
<td>Cluster RCT (30 clusters)</td>
<td>A: 0.25 ml of 5% sodium fluoride varnish to maxillary anterior teeth/ molars, mandibular molars/incisors every 6 months, education/ advice to caregiver with toothbrush/ paste provided, community oral health promotion program</td>
<td>Aboriginal identity, permanent residency in community, 18-48 months old, no history of asthma, signed informed consent of caregivers</td>
<td>Number approached: 685</td>
<td>Australia recruitment setting: Rural Aboriginal communities Water fluoridation status: See population characteristics</td>
<td>Australian National Health and Medical Research Council</td>
<td></td>
<td>2 years</td>
<td>A vs. B</td>
<td>Net dmfs increment per child, (mean)</td>
<td>Adjusted for cluster effects: 6.9 vs. 9.9, difference 3.0 (95% CI 1.2 to 4.9), prevented fraction 31%</td>
<td>Adjusted for cluster effects plus fluoride concentration in water: 6.2 vs. 9.7, difference 3.5 (95% CI 1.9 to 5.1), prevented fraction 36%</td>
</tr>
</tbody>
</table>
### Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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</tr>
</thead>
</table>
| Weinstein et al., 2001 | RCT with 3 treatment groups | A: One application of 5% fluoride varnish at baseline and 6 months  
B: Three applications of 5% fluoride varnish within 2 weeks of baseline  
C: Three applications of 5% fluoride varnish within 2 weeks of baseline and 6 months | Age: NR  
Female: 46%  
Race: 90% Hispanic, 10% Caucasian or Native American  
Clinical dmfs, mean: 11 vs. 13 vs. 10  
Radiographic dmfs, mean: 3.5 vs. 3.1 vs. 3.4  
Mean dmft for entire population: 6.0 | Children ages 3-5 years, with ≥1 carious lesion in primary molars and no fluoride treatment in the previous 6 months | Number approached: NR  
Number eligible: 156  
Number enrolled: 156 (51 vs. 52 vs. 53)  
Number analyzed: 111 (32 vs. 36 vs. 43) | U.S. recruitment setting: Head Start programs  
Water fluoridation status: NR (Yakima voters approved fluoridation in 1999) | NIDCR, NIH grants | 1 year | A vs. B vs. C  
Radiographic dmfs increment, mean: 0.9 vs. 0.5 vs. 0.1, p=0.28  
Clinical dmfs increment, mean: 4.6 vs. 3.2 vs. 4.7, p=0.65  
Absolute reduction in caries increment: Not calculated  
Reduction in caries increment: Not calculated | Study states no loss to followup from adverse events | A vs. B vs. C: 33% (17/51) vs. 27% (14/52) vs. 13% (7/53)  
Note: Study states 119 subjects examined at 1-year visit, but analysis shows 111 | Fair |
## Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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<tbody>
<tr>
<td>Weinstein et al., 2009&lt;sup&gt;2&lt;/sup&gt; Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition</td>
<td>RCT with 2 treatment groups</td>
<td>A: One 5% fluoride varnish treatment and 2 placebo treatments every 6 months</td>
<td>Hispanic children ages 36-71 months, living in study county, with at least one sound primary tooth surface present</td>
<td>A vs. B</td>
<td>Number approached: 787</td>
<td>U.S. recruitment setting: Head Start programs</td>
<td>NIDCR, NIH grants</td>
<td>3 years</td>
<td>A vs. B</td>
<td>New tooth decay in primary surfaces (number of surfaces per child): 7.4 vs. 9.8, p=0.001; adjusted rate ratio 1.13 (95% CI 0.94 to 1.37)</td>
<td>A vs. B: 27% (84/306) vs. 29% (86/294); 38% (230/600) not followed entire 3 years</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
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<td>B: One set of three 5% fluoride varnish treatments over 2 weeks once per year and 3 placebo treatments over 2 weeks 6 months later</td>
<td></td>
<td></td>
<td>Number eligible: 600</td>
<td>Water fluoridation status: NR (Yakima voters approved fluoridation in 1999)</td>
<td></td>
<td></td>
<td></td>
<td>Absolute reduction in caries increment: 2.4</td>
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<tr>
<td></td>
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<td></td>
<td>Children were excluded if they were developmentally unable to participate in the study</td>
<td>Number enrolled: 600 (306 vs. 294)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduction in caries increment: 24%</td>
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</tr>
</thead>
<tbody>
<tr>
<td>Weintraub et al., 2006&lt;sup&gt;49&lt;/sup&gt;</td>
<td>RCT</td>
<td>A: 0.1 mL of 5% sodium fluoride varnish per arch applied twice per year with 4 intended applications&lt;br&gt;B: 0.1 mL of 5% sodium fluoride varnish per arch applied once per year with 2 intended applications&lt;br&gt;C: No fluoride varnish</td>
<td>Age, mean: 1.8 years&lt;br&gt;Female: 53%&lt;br&gt;Race: 47% Hispanic, 46% Asian, 7% other race/ethnicity&lt;br&gt;All caries free at baseline, see eligibility criteria</td>
<td>Children ages 6-44 months with 4 erupted maxillary incisors, all primary teeth caries-free without demineralized, white spots, born in San Francisco or fluoridated community in the San Francisco Bay Area, planning to reside in San Francisco for at least 2 years, parent providing informed consent&lt;br&gt;Excluded children with medical problems or medications affecting oral health (e.g., cleft lip or palate)</td>
<td>Number approached: NR&lt;br&gt;Number eligible: NR&lt;br&gt;Number enrolled: 376&lt;br&gt;Number analyzed: 280 (87 vs. 93 vs. 100)</td>
<td>U.S. recruitment setting: Family dental center and public health center serving primarily low-income, underserved Hispanic and Chinese populations&lt;br&gt;Water fluoridation status: ~1 ppm</td>
<td>NIDCR; National Center for Minority Health and Health Disparities; UCSF Department of Preventive and Restorative Dental Sciences</td>
<td>2 years</td>
<td>Caries lesions at 12 months: 11/83 vs. 13/86 vs. 27/92; RR 0.45 (95% CI 0.24 to 0.83) NNT 7 for A vs. C and 0.52 (95% CI 0.28 to 0.93) NNT 8 for B vs. C&lt;br&gt;Caries lesions at 24 months: 3/70 vs. 10/69 vs. 15/63; RR 0.18 (95% CI 0.06 to 0.59) NNT 6 for A vs. C and 0.61 (95% CI 0.30 to 1.26) NNT 11 for B vs. C&lt;br&gt;dmfs, mean: 0.7 vs. 0.7 vs. 1.7; p&lt;0.01 for A vs. C and B vs. C&lt;br&gt;dmfs + precavitated lesions, mean: 1.4 vs. 1.3 vs. 2.7; p&lt;0.01 for A vs. C and B vs. C&lt;br&gt;Absolute reduction in caries increment: 1.0&lt;br&gt;Reduction in caries increment: 59% (A + B vs. C)</td>
<td>No adverse events detected</td>
<td>A vs. B vs. C: 31% (39/126) vs. 25% (31/124) vs. 21% (26/126)</td>
<td>Fair</td>
</tr>
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<tr>
<td>Alamoudi et al., 2012&lt;sup&gt;24&lt;/sup&gt; <em>Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs</em></td>
<td>RCT</td>
<td>A: Xylitol chewable tablets (1.2 g, 84% xylitol) chewed for 5 minutes 3 times daily B: Fluoride varnish, every 6 months throughout study</td>
<td>Age: 2-5 years Female: NR Race: NR (conducted in Saudi Arabia) High mutans streptococci (≥10⁵ CFU): 100% vs. 100% Baseline dmft score: 8.37 vs. 10.27 (p=0.191) Excluded children with systemic disorders such as diabetes, hyperglycemia or sleeping disorders; irregular medications; removable dental prosthesis, or prone to TMJ complaints; and children attending clinics without mothers, or reared by a nanny</td>
<td>Mothers and children with high count of salivary MS (≥10⁵), presence of one or more decayed or filled primary teeth in mothers</td>
<td>Number approached: 62 Number eligible: 60 Number enrolled: 60 (30 vs. 30) Number analyzed: 34 (21 vs. 13)</td>
<td>Saudi Arabia recruitment setting: Well baby clinics and dental clinics Water fluoridation status: NR</td>
<td>Deanship of Scientific Research, King Abdulaziz University, Jeddah, Saudi Arabia</td>
<td>18 months</td>
<td>A vs. B dmft score at 6 months (mean): 8.95 vs. 13.00, p=0.024 dmft score at 12 months (mean): 9.64 vs. 13.12, p=0.041 dmft score at 18 months (mean): 9.19 vs. 14.69, p=0.001 dmft, mean: 0.8 vs. 4.4; p=NR Absolute reduction in caries increment: 3.6 Reduction in caries increment: 82%</td>
<td>NR</td>
<td>Poor</td>
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<tr>
<td>Kovari et al., 2003&lt;sup&gt;31&lt;/sup&gt; Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland</td>
<td>Cluster RCT (11 clusters)</td>
<td>A: 65% Xylitol gum 3 times per day, chewed for 3-5 minutes, for total of 2.5 g/day B: Toothbrushing with Aquafresh with 0.05% NaF after lunch</td>
<td>Age: 3-6 years Female: 46.9% (184/392) vs. 46.7% (247/529) Non-white: NR Risk level: NR</td>
<td>Children in the town of Savolinna, Finland, ages 3-6 years attending daycare centers</td>
<td>Number approached: NR Number eligible: NR Number enrolled: 921 Number analyzed: 786 (392 vs. 529)</td>
<td>Finland recruitment setting: Daycare centers Water fluoridation status: NR</td>
<td>NR</td>
<td>3-6 years (up to age 9 years)</td>
<td>Caries-free at 7 years old: 69% (218/316) vs. 65% (278/427), RR 1.06 (95% CI 0.96 to 1.17) Caries-free at 9 years old: 57% (177/310) vs. 49% (213/434), RR 1.16 (95% CI 1.02 to 1.33) Decayed/missing/filled teeth: 1.1 vs. 1.0 at 7 years, 1.2 vs. 1.6 at 9 years dmft, mean: NR Absolute reduction in caries increment: NR Reduction in caries increment: NR</td>
<td>NR</td>
<td>A vs. B 16.3% (64/392) vs. 13.4% (71/529) at age 9 years followup</td>
<td>Fair</td>
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<tr>
<td>Author, Year, Title</td>
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<tr>
<td>Milgrom et al., 2009</td>
<td>RCT</td>
<td>A: Xylitol 8 g/day syrup, divided into 2 doses (4 g per dose)</td>
<td>Age: 15.9 vs. 13.7 vs. 15.6 months</td>
<td>Children ages 9-15 months</td>
<td>Number approached: 110</td>
<td>Marshall Islands</td>
<td>HRSA's Maternal and Child Health Bureau and NIDCR</td>
<td>1 year</td>
<td>A vs. B vs. C</td>
<td>Tooth decay: 24.2% (8/33) vs. 40.6% (13/32) vs. 51.7% (15/29), RR 0.47 (95% CI 0.23 to 0.94) for A vs. C and 0.79 (95% CI 0.45 to 0.1.4) for B vs. C</td>
<td>Fair</td>
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<td>B: Xylitol 8 g/day syrup, divided into 3 doses (2.67 g per dose)</td>
<td>Female: 58% vs. 56% vs. 48%</td>
<td>Excluded for history of esophageal or digestive disease, congenital craniofacial malformations or history of adenoidectomy, or lower than 10th percentile of U.S. standard weight and height</td>
<td>Number eligible: 108</td>
<td>Recruitment setting: Community-based</td>
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<td>Mean decayed teeth: 0.6 vs. 1.0 vs. 1.9; p=0.05 for A or B vs. C; incidence rate ratio 0.30 (95% CI 0.13 to 0.66) for A vs. C and 0.50 (95% CI 0.26 to 0.96) for B vs. C</td>
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<td>C: Xylitol 2.67 g dose syrup, 1 dose per day</td>
<td>Non-white: NR</td>
<td>Water fluoridation status: Drinking water not fluoridated (supplemental and topical fluoride not available)</td>
<td>Number enrolled: 100</td>
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<td>Decayed primary teeth per year: 0.66 vs. 1.10 vs. 2.20</td>
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<td>Risk level: NR</td>
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<td>Number analyzed: 94 (33 vs. 32 vs. 29)</td>
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<td>Absolute reduction in caries increment: 1.3 vs. 0.9 vs. C as comparator (vs. others)</td>
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<td>Reduction in caries increment: 68% vs. 47% vs. C as comparator (vs. others)</td>
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</tbody>
</table>
### Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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<tr>
<td>Oscarson et al., 2006 &amp; 2008</td>
<td>RCT</td>
<td>A: One 0.48 g xylitol tablet at bedtime after brushing for 6 months; then 1 tablet twice daily to age 3 years and 6 months</td>
<td>Healthy children age 2 years Excluded children with severe disabilities or uncooperative for oral exam</td>
<td>Number approached: NR Number eligible: NR Number enrolled: 132 (66 vs. 66) Number analyzed: 115 (55 vs. 63)</td>
<td>Sweden recruitment setting: Public dental clinic Water fluoridation status: NR</td>
<td>County of Vasterbotten, The Patent Revenue Fund for Dental Prophylaxis and Swedish Dental Society</td>
<td>2 years</td>
<td>A vs. B</td>
<td>Dental caries: 18% (10/55) vs. 25% (16/63), OR 0.65 (95% CI 0.27 to 1.59)</td>
<td>16.7% (11/66) vs. 4.5% (3/66)</td>
<td>Fair</td>
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## Appendix B7. Trials of Treatments for the Prevention of Dental Caries

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<tr>
<td>Seki et al., 2011*</td>
<td>Cluster, non-randomized controlled clinical trial (3 clusters)</td>
<td>A: Xylitol chewing gum (100% xylitol); 1 pellet chewed 5 minutes 4 times daily</td>
<td>Baseline data only reported by group for children who completed followup Age 4 years old: 66% vs. 72% Female: 46% vs. 48% Race: NR (conducted in Japan) dfs index (mean): 2.5 vs. 4.2 (p=0.07) Individual plaque mutans streptococci score: 0.5 vs. 0.7 Salivary mutans streptococci score &gt;0: 25% vs. 42%</td>
<td>Attending preschool in one region in Tokyo</td>
<td>Number approached: NR Number eligible:432 Number enrolled: 248 (142 vs. 106) Number analyzed: 161(76 vs. 85)</td>
<td>Japan recruitment setting: Preschool Water fluoridation status: Not reported (states fluoridation &quot;limited&quot; in Japan)</td>
<td>Uemura Fund, Nihon University School of Dentistry from the Ministry of Education, Science, Sports, Culture and Technology, Japan</td>
<td>1 year A vs. B Development of caries from baseline to 6 months: 1.7 vs. 1.6 (p&gt;0.05) Development of caries from 6 months to 1 year: 1.6 vs. 1.8 (p&gt;0.05) Mean development of caries: 3.3 vs. 3.4; p&gt;0.05 Absolute reduction in caries increment: 0.1 Reduction in caries increment: 3%</td>
<td>Diarrhea in 11% (6/76) in xylitol group</td>
<td>A vs. B 46% (66/142) vs. 20% (21/106) Poor</td>
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<tr>
<td>Zhan et al., 2012*</td>
<td>RCT</td>
<td>A: Xylitol wipes, 2 at a time, 3 times per day (estimated daily dosage 4.2 g) every 3 months B: Placebo wipes</td>
<td>Age: 6-35 months vs. 6-35 months Female: 36% vs. 40% Mothers with healthy children aged 6-35 months; mothers were primary care givers (&gt;8 hours daily) and with</td>
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<td>A vs. B Mean new decayed surfaces: 0.05 vs. 0.53 (p=0.01) New caries lesions at 1 year: 5% vs. 40%</td>
<td>None</td>
<td>A vs. B 9% (2/22) vs. 23% (5/22) Fair</td>
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<tr>
<td>Du et al., 2006&lt;sup&gt;46&lt;/sup&gt; A two-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children</td>
<td>Cluster RCT (14 clusters)</td>
<td>A: 40% w/w chlorhexidine acetate varnish every 6 months; B: Placebo varnish</td>
<td>Age: NR Female: NR Race: NR (study conducted in China) dmfs-molar, mean: 2.8 vs. 2.6, p=0.39</td>
<td>All children ages 4-5 years, attending 1 of 4 kindergartens in study district</td>
<td>Number approached: NR Number eligible: NR Number enrolled: 334 Number analyzed: 290 (155 vs. 135)</td>
<td>China recruitment setting: Kindergartens in rural communities Water fluoridation status: NR</td>
<td>Award from AAPD, and NIH NIDCR grant U54-DEO19285</td>
<td>2 years</td>
<td>A vs. B dmfs-molar increment, mean: 1.0 vs. 1.6, mean difference 0.6, 37% reduction in caries molar increment, p = 0.036</td>
<td>Absolute reduction in caries increment: 0.6 Reduction in caries increment: 37%</td>
<td>13% (44/334) overall</td>
<td>Fair</td>
</tr>
<tr>
<td>Lopez et al., 2002&lt;sup&gt;55&lt;/sup&gt; Topical antimicrobial therapy in the prevention of early childhood caries: a followup</td>
<td>RCT</td>
<td>A: 0.2 ml of 10% povidone iodine solution applied every 2 months; B: Placebo solution</td>
<td>Age, mean (range): 16 (12-19) months Female: 48% Non-white: 20%</td>
<td>Infants attending 1 clinic with unremarkable medical history, 4 maxillary primary incisors with no visible defects and</td>
<td>Number approached: NR Number eligible: NR Number</td>
<td>U.S. recruitment setting: Women, infants, and children clinic in Puerto Rico</td>
<td>National Institute of Health Grants; University of Puerto Rico</td>
<td>1 year</td>
<td>A vs. B White spot lesions on maxillary primary incisors at 1 year: 8% (3/39) vs. 32% (14/44); RR 0.24 (95% CI 0.1 to 0.8)</td>
<td>No adverse events detected</td>
<td>Fair</td>
<td></td>
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</tbody>
</table>

**Other Interventions**

- **Du et al., 2006<sup>46</sup>**
  - **A:** 40% w/w chlorhexidine acetate varnish every 6 months
  - **B:** Placebo varnish
  - **Study Type:** Cluster RCT (14 clusters)
  - **Population:** All children ages 4-5 years, attending 1 of 4 kindergartens in study district
  - **Eligibility:** All children ages 4-5 years, attending 1 of 4 kindergartens in study district
  - **Number:** Number approached: NR Number eligible: NR Number enrolled: 334 Number analyzed: 290 (155 vs. 135)
  - **Country:** China
  - **Sponsor:** Award from AAPD, and NIH NIDCR grant U54-DEO19285
  - **Followup Duration:** 2 years
  - **Outcomes:** A vs. B dmfs-molar increment, mean: 1.0 vs. 1.6, mean difference 0.6, 37% reduction in caries molar increment, p = 0.036
  - **Attrition:** 13% (44/334) overall
  - **Quality Rating:** Fair

- **Lopez et al., 2002<sup>55</sup>**
  - **A:** 0.2 ml of 10% povidone iodine solution applied every 2 months
  - **B:** Placebo solution
  - **Study Type:** RCT
  - **Population:** Infants attending 1 clinic with unremarkable medical history, 4 maxillary primary incisors with no visible defects and
  - **Eligibility:** Infants attending 1 clinic with unremarkable medical history, 4 maxillary primary incisors with no visible defects and
  - **Number:** Number approached: NR Number eligible: NR Number
  - **Country:** U.S.
  - **Sponsor:** National Institute of Health Grants; University of Puerto Rico
  - **Followup Duration:** 1 year
  - **Outcomes:** A vs. B White spot lesions on maxillary primary incisors at 1 year: 8% (3/39) vs. 32% (14/44); RR 0.24 (95% CI 0.1 to 0.8)
  - **Attrition:** No adverse events detected
  - **Quality Rating:** Fair
**Appendix B7. Trials of Treatments for the Prevention of Dental Caries**

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<tbody>
<tr>
<td>report</td>
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<td>NR</td>
<td>All children high risk (used bottle at bedtime containing cariogenic liquid, 2 consecutive positive <em>streptococcus mutans</em> cultures)</td>
<td>were caries free, who used a bottle at naptime/bedtime containing cariogenic liquid, and had 2 consecutive positive <em>streptococcus mutans</em> cultures from pooled maxillary incisor plaque</td>
<td>enrolled: 83 (39 vs. 44)</td>
<td>Water fluoridation status: NR</td>
<td>Mean white spot lesions: NR</td>
<td>Absolute reduction in caries increment: NR</td>
<td>Reduction in caries increment: NR</td>
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</table>

**Abbreviations:** AAPD = American Academy of Pediatric Dentistry; ANOVA = Analysis of Variance; CI = confidence interval; CFU = colony forming unit; dmfs = decayed, missing, filled surfaces; dmft = decayed, missing, filled teeth; g = gram; HRSA = Health Resources and Services Administration; ITT = intention to treat; mL = milliliter; MS = mutans streptococcus; NaF = sodium fluoride; NIDCR = National Institute of Dental and Craniofacial Research; NIH = National Institutes of Health; NNT = number needed to treat; NR = not reported; OR = odds ratio; ppm = parts per million; RCT = randomized controlled trial; RR = relative risk; SE = standard error; TMJ = temporomandibular joint disorder; UCSF = University of California San Francisco; U.S. = United States.
### Appendix B8. Systematic Review of Fluorosis Due to Fluoride Supplements

<table>
<thead>
<tr>
<th>Author, Year, Title</th>
<th>Databases Searched, Date of Last Search</th>
<th>Number and Type of Studies</th>
<th>Methods For Rating Methodological Quality of Primary Studies</th>
<th>Methods for Synthesizing Results of Primary Studies</th>
<th>Number of Patients (Treatment and Control)</th>
<th>Adverse Events</th>
<th>Quality Rating</th>
</tr>
</thead>
</table>
| Ismail and Hasson, 2008<sup>3a</sup> Fluoride supplements, dental caries, and fluorosis: A systematic review | MEDLINE: 1966-June 2006  
Cochrane: up to 2nd quarter 2006  
EMBASE: 1974-2006 | 5 observational studies | Cochrane Handbook of Systematic Reviews | Qualitative analyses only, due to high heterogeneity of subjects, outcomes, and duration of followup | Not reported | 5 observational studies reported fluorosis outcomes associated with early childhood use of fluoride supplementation  
All studies found an association between fluoride G2 supplementation in early childhood and risk of fluorosis  
One study (n=383) found OR increased by 84% per year of use of fluoride supplements (95% CI 1.4 to 2.5)  
One study (n=188) OR 10.8 in children started on fluoride supplements within the first 2 years of life (95% CI 1.9 to 61.6)  
Largest study (n=3978) found slightly increased risk that ranged from OR 1.1 to 1.7 | Good |

**Abbreviations:** CI = confidence interval; OR = odds ratio.
### Appendix B9. Quality Rating of Systematic Review

| Author, Year, Title                                                                 | Ismail and Hasson, 2008<sup>30</sup>  
|                                                                                     | *Fluoride supplements, dental caries, and fluorosis: a systematic review* |
| Study Design Pre-Determined?                                                        | Yes                                                                 |
| Dual Review of Studies and Data Abstraction?                                        | Not reported                                                        |
| Comprehensive Literature Search?                                                    | Yes                                                                 |
| Publication Status Used as Inclusion Criteria?                                      | No                                                                  |
| List of Included and Excluded Studies Provided?                                     | No                                                                  |
| Characteristics of Included Studies Provided?                                       | Yes                                                                 |
| Included Studies Quality Assessed?                                                 | Yes                                                                 |
| Quality of Included Studies Considered in Formulating Conclusions?                 | No                                                                  |
| Appropriate Methods Used to Combine Studies?                                       | Yes                                                                 |
| Publication Bias Assessed?                                                         | No                                                                  |
| Conflict of Interest Stated?                                                       | Yes                                                                 |
| Quality Rating                                                                      | Good                                                                |