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The efficacy of fluoride and others in caries prevention: A systematic review

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***Abstract*---**Background: Dental caries remains a significant public health issue, manifesting in various forms such as early childhood caries (ECC), primary caries, and root surface caries. It results from bacterial metabolism of dietary sugars leading to tooth enamel demineralization. While various preventive interventions, including fluoride and non-fluoride agents, have been employed, their efficacy varies and remains a subject of extensive research. Aim: This systematic review aims to evaluate the effectiveness of fluoride and other preventive measures in reducing dental caries and improving oral health outcomes across different populations and age groups. Methods: The review synthesizes evidence from clinical trials, observational studies, and public health reports on the effectiveness of fluoride varnishes, supplements, community fluoridation, sugar substitutes, sealants, and antimicrobial agents in caries prevention.

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Key variables include intervention types, dosage, application methods, and demographic variables. Results: Fluoride-based interventions, such as varnishes and water fluoridation, have demonstrated varying levels of effectiveness. Water fluoridation shows a 35% reduction in carious lesions in primary dentition and 26% in permanent teeth. Fluoride varnishes and supplements provide modest benefits, with fluoride toothpaste achieving a 24% reduction in caries. Antimicrobial agents and sealants also contribute to caries control, although their effectiveness is often context-dependent. Conclusion: The review highlights that while fluoride remains a cornerstone of caries prevention, its efficacy can be influenced by factors such as the method of application and population characteristics. Combined strategies, including fluoride use and behavioral interventions, offer the most promising results. Public health initiatives should integrate these findings to develop targeted prevention programs, especially in high-risk communities, and continue to monitor and refine interventions based on emerging evidence.

***Keywords*---**Dental caries, fluoride, caries prevention, fluoride varnish, water fluoridation, antimicrobial agents, sealants.

Introduction

This article centers on strategies aimed at mitigating the prevalence of dental caries within the population, with a particular focus on the utilization of fluorides and other preventive agents for dental caries. It is crucial to be deliberate in the objectives of applying various interventions, especially ensuring that preventive measures are tailored to patterns of disease susceptibility, which are often linked to age. Dental caries manifests in multiple forms—such as early childhood caries (ECC), severe ECC, primary caries of deciduous and permanent teeth, recurrent caries, and root surface caries—and is driven by the metabolic by-products of sugars by specific bacteria inhabiting the tooth surface, leading to the formation and progression of lesions.

These lesions, commonly referred to as cavities, represent the clinical manifestation of the disease, wherein dental plaque bacteria metabolize sugar into polymeric substances that stabilize their attachment to the tooth surface, and into acids that demineralize the tooth's hard tissues. The term "caries lesion" encompasses the entire spectrum of tooth structure loss, ranging from "white spot" enamel demineralization to large cavitations extending into dentin. While the bacterial species involved in the caries process are largely known, their presence varies depending on the depth and location of the caries lesions. Currently, there is limited evidence that any of the interventions employed by dentists significantly reduce the incidence of dental caries as a disease. The most effective interventions identified thus far are those that decrease the occurrence of new lesions and inhibit the progression of existing lesions, which will be a key focus of this article. It is worth noting that dentists predominantly spend their time managing previously treated caries lesions, often referred to as recurrent or secondary caries lesions. Population-level prevention efforts aim to modify the dental plaque biofilm by reducing exposure to dietary sugars and enhancing the resilience of teeth.

Generally, primary prevention seeks to address the root causes of disease, while secondary prevention focuses on halting disease progression. Confusion arises when the distinction between tooth-level (lesion) prevention and individual- and population-level (disease) prevention is not made clear. We currently lack adequate, simple methods to detect caries activity before lesions appear; the visible breakdown of tooth structures is a consequence of a disease process that began earlier. The presence of visible lesions remains the best available diagnostic tool for detecting the disease and predicting future disease, which is why it is commonly used. Meanwhile, curing caries remains as challenging as curing most cancers or coronary heart disease; we essentially measure the time elapsed since the last sign of disease, such as the appearance of a new lesion or the growth of an existing lesion. Thus, once an individual has had any caries lesions, it is uncertain whether interventions can target the primary prevention of disease. In such cases, the goal is to mitigate the disease's impact, which is considered secondary prevention.

This paper primarily addresses interventions that bolster resistance to disease progression. Enhancing resistance is achieved through the use of various fluorides, sugar substitutes, and mechanical barriers such as pit-and-fissure sealants. A relatively recent addition to the discussion of primary and secondary prevention is the use of antimicrobials. Other critical aspects of caries control include behavioral interventions (e.g., motivational interviewing) with patients and their caregivers (parents, guardians, grandparents, etc.) to encourage the use of agents that reduce disease transmission and enhance resistance. Behavioral intervention is necessary because the effectiveness of these measures depends on their consistent use.

A crucial approach to reducing the risk of dental caries at the population level involves decreasing the frequency and duration of exposure to dietary sugars. Such public health initiatives—through existing and potential government policies and industry food guidelines aimed at improving overall nutrition—must be integrated into dental public health practices. The dramatic increase in sugar consumption over the past four decades, along with the corresponding rise in human metabolic diseases (diabetes, obesity, heart disease, and stroke), indicates that individuals and families are generally unable to control their sugar intake on their own, necessitating system-wide public health reforms. Efforts by the sugar industry during the 1960s and 1970s led to a shift away from research and progress in this field; however, more recently, successful reductions in sugar consumption have been achieved through measures such as taxation, as seen in Mexico (Horst et al., 2023).

Secondary prevention of caries involves early diagnosis and prompt treatment to minimize complications from lesions (pain, abscesses, systemic infections, etc.) and to prevent the development of new lesions. Secondary prevention also includes the concept of arresting caries lesions, as lesions that continue to progress can cause pain, tooth loss, and may act as a reservoir of cariogenic bacteria that can initiate new lesions; antimicrobials are logical interventions.

Lesions that progress also lead to increased personal and public costs to replace parts of the dentition or, in some cases, the entire dentition. The cascade of dental disfigurement can affect social acceptance, growth patterns, and overall quality of life (Horst et al., 2023). School-based screenings have been a key and widespread method for early detection in secondary prevention, but they have generally not resulted in early diagnosis or prompt treatment, primarily due to ineffective referrals. School programs would be more effective if they incorporated additional secondary prevention strategies to arrest lesions nonsurgical, as discussed in other sections of this article.

Timing of Prevention Efforts
Children

The optimal timing for the primary prevention of Early Childhood Caries (ECC) should focus on preventing the colonization of cariogenic bacteria, particularly *Streptococcus mutans*, in the dental biofilm (plaque) of young children. This colonization typically occurs within a few years after the eruption of primary teeth. The usual source of *S. mutans* in children is the transmission of salivary bacteria from their mothers or other caregivers (5,6). When new mothers have low levels of *S. mutans* in their saliva, their children's colonization by these bacteria is significantly delayed, leading to a reduction in both the onset age and severity of caries lesions. Conversely, when mothers have high salivary *S. mutans* levels, their children are more likely to be colonized at a younger age, with caries lesions developing within a couple of years thereafter (5). Evidence suggests that habitual maternal use of xylitol chewing gum during the first few years of a child's life can protect against *S. mutans* colonization, resulting in a 71% to 78% reduction in caries lesions in those children (6-8). Therefore, the initial preventive intervention should begin with the caregivers, even before the child’s teeth erupt.

Cavities typically start to appear around the third year of life. In communities with a high burden of disease, cavities can emerge within the first year after tooth eruption. To enhance tooth resistance, primary prevention must commence before this time, particularly when children are unlikely to visit a dentist. *S. mutans* and other cariogenic bacteria cannot stably colonize the mouth until teeth erupt, although they have been detected in the mouths of predentate children (9). Consequently, intensive prevention efforts in high-risk communities should begin with female caregivers before the eruption of their children's teeth and should continue after the teeth emerge, usually in the late first year of life. Limited resources for dental public health are often directed toward preschool-aged children (e.g., Head Start, 3–5 years old) under the mistaken assumption that this constitutes primary prevention, even though the disease may have already manifested by this age. Each newly exposed tooth surface presents an opportunity for colonization by cariogenic bacteria. In permanent teeth, caries lesions generally develop 2 to 4 years after tooth eruption (10). The rationale for focusing on the prevention and treatment of caries in primary teeth is often based on an overstated connection between caries in primary teeth and those in permanent teeth, with relative risk ratios such as 2.6 (11) and 1.4 (12), indicating a relatively small contribution. Fortunately, children are in school during this age, making it easier to reach them through school-based delivery systems.

While intensive efforts to bring high-risk children into dental clinics have increased annual clinic visits from approximately 12% to 43% (13), providing dental care in schools offers a more practical approach for the secondary prevention of decay in permanent teeth. Nonrestorative and minimally invasive treatments are logical options for managing caries in primary teeth and newly erupting permanent teeth. The natural process of exfoliation presents an opportunity to slow the progression of lesions in primary teeth until they shed, while also preventing lesions in the permanent dentition—a goal whose importance cannot be overstated.

Adults

The predominant reason for dental treatment in adults is the failure of previously placed fillings, which are often replaced due to "recurrent caries" at the margins of or beneath old restorations. While dentists often attribute these failures to the filling materials, recent literature presents substantial evidence to the contrary (14,15). Removing lesions with a dental drill does not prevent the initiation of new lesions nor address the underlying caries risk factors that led to the previous failure. Thus, addressing recurrence does not constitute primary prevention at either the disease or tooth level. Instead, primary prevention involves enhancing patient resistance to coronal and root caries, particularly for those at highest risk. Public health efforts for adults should significantly focus on individuals transitioning into higher caries risk categories. This is especially pertinent when factors such as decreased saliva quality and quantity (xerostomia) arise from polypharmacy, radiation exposure to the salivary glands, methamphetamine use, or conditions like Sjögren's syndrome. Additionally, root exposure resulting from excessive brushing, iatrogenic root surface damage from mechanical instrumentation aimed at controlling gingivitis and periodontal disease, and the unintended damage to the gingival attachment from restorative procedures increase the number of at-risk surfaces.

Population-level preventive efforts for adults are relatively rare. To enhance effectiveness, preventive interventions should be integrated with other care encounters, such as periodontal care, primary medical care, and long-term condition management (e.g., substance abuse, heart disease). Addressing significant risk-increasing events (e.g., drug abuse, chemotherapy, onset of systemic diseases, multiple prescriptions) before visible damage occurs could improve outcomes. Senior centers (for individuals over 60 years) subsidized public housing for the elderly (e.g., HUD housing), assisted living, and skilled nursing facilities may be ideal settings for these preventive efforts. The risk and need for primary prevention are dynamic and evolve throughout an individual's life.

Prevention and Arrest: Approaches During Early Childhood

Dental caries cannot develop without the presence of sugar. Extensive evidence indicates that the frequency of sugar consumption and its duration in the oral cavity are more influential factors in caries risk than the total amount consumed (16,17). Therefore, providing dietary guidance within dental public health programs from the earliest ages is crucial. Avoiding sugar-laden beverages, such as fruit juices, sodas, and sports drinks, at all stages of life is essential.

Additionally, rinsing with water after consuming these drinks may offer some benefit and warrants further investigation. Sugar should never be added to milk or baby formula.

Patients who have severe plaque due to a complete lack of oral hygiene but are fed exclusively through gastric tubes or intravenous lines do not develop carious lesions. Similarly, individuals with genetic conditions like intestinal sucrase deficiency or hereditary fructose intolerance, who avoid dietary sucrose, do not experience significant carious lesions and exhibit minimal S. mutans in their mouths (18,19). An increased frequency of simple sugar intake appears to have the most significant impact on lesion initiation. For example, "baby bottle tooth decay" from cow's milk or formula can be mitigated by limiting milk bottle exposure to 3 to 6 times per day, based on the child's weight and age, and avoiding nighttime exposure (20).

Cariogenic dental plaque requires time to accumulate sufficiently to produce enough acid to demineralize enamel. Cavities do not form on teeth that are regularly cleaned. Regular disruption of plaque by any means is effective in preventing carious lesions (21). Caregivers should be instructed on how to clean children's teeth while ensuring comfort. Building a sense of control in the child by segmenting each brushing session into short, structured periods (e.g., counting) can be helpful, even for infants. Teeth can be cleaned in various locations; it is often easier to clean a young child's teeth on the floor or a sofa with the child's head in one's lap or between one's legs.

Fluoride varnish has been shown to reduce the incidence of new carious lesions in school-aged children by 37% (22). This benefit was anticipated to extend to younger children, and we documented the safety of fluoride varnish in infants (23). Despite a surge in fluoride varnish use starting with the eruption of the first tooth over the past decade, positive outcomes have not been consistently observed. Regrettably, 5 out of 6 studies using fluoride varnish alone did not show a reduction in new lesions (24–30). The 3 studies combining fluoride varnish with other interventions also did not demonstrate significant effects beyond those of the other interventions (31,32). One possible explanation for the discrepancy in fluoride varnish effectiveness at various ages could be differing balances of pathogenic and protective factors. Dietary sugars, oral hygiene, and the composition of dental plaque might play a more significant role than the remineralization potential provided by fluoride varnish. Furthermore, variations in the effectiveness of different fluoride varnishes have not been clinically tested (33). The lack of observed effect in recent trials warrants further investigation. For now, interventions with consistent evidence of efficacy are recommended.

Promising research involves combining antimicrobial agents with fluoride varnish. Two clinical studies in toddlers (12–35 months old) indicate that applying povidone iodine to the teeth immediately before fluoride varnish, every 2 to 4 months for at least 10 months, provides additional benefits. One clinical trial found 80% fewer children with carious signs after 1 year of bimonthly combined iodine-fluoride treatment compared to fluoride varnish alone (34). A cluster intervention showed that adding povidone iodine resulted in 24% fewer children with any signs of disease after 10 months, with approximately 2.5 treatments per child, and 31% fewer new lesions overall (35). The use of antimicrobials for caries prevention in infants and toddlers remains underexplored. Fluoride supplement tablets have been shown to prevent 24% of carious lesions in permanent teeth. However, this effect has not been consistently observed for primary teeth and is no greater than that achieved with topical fluoride rinses, varnish, or toothpaste, which presumably pose a lower risk of fluorosis (36). If fluoride supplementation is considered, it is prudent—especially if the children consume well water—for parents to assess the fluoride levels in their water supply.

Community Fluoridation

Following the discovery of fluoride's preventive benefits against dental caries, fluoride was introduced into water, milk, and salt. The broad applicability of this intervention stems from its centralized production and the established regulatory framework governing these distribution methods. Water fluoridation is the most widely implemented approach, benefiting over 370 million people across 27 countries. Numerous studies have demonstrated its effectiveness and safety, with dental fluorosis being the only noted adverse effect. In the United States, the cost of water fluoridation is approximately $0.20 to $0.50 per person per year (37). A recent Cochrane meta-analysis encompassing 107 studies estimated that water fluoridation prevents approximately 35% of carious lesions in primary dentition (dmft), 26% in permanent teeth (DMFT), and 15% of any new lesions (primary disease prevention). However, the analysis also noted that 72 of these studies were conducted prior to the widespread adoption of fluoride toothpaste, leaving the combined benefit of both interventions uncertain. Despite this, fluoride toothpaste provides an additional preventive effect independent of water fluoridation, suggesting a potential cumulative benefit. A concern for 12% of recipients is the aesthetic impact of dental fluorosis linked to water fluoridation (38).

Salt fluoridation reaches approximately 60 million people in Europe and over 100 million in Latin America, including Mexico. It is significantly less expensive, costing about one-tenth of water fluoridation, making it potentially the most cost-effective method of caries prevention. Although there are no recent clinical trials on the caries preventive effects of salt fluoridation, older cluster-randomized studies consistently demonstrated a 50% reduction in new lesions (39). Milk fluoridation provides the most precise fluoride dosage since variations in milk intake are less pronounced among children compared to tap water or salt and can be further controlled with single-serving packages. The cost of fluoridated milk is $1 to $2.50 per person per year, approximately five times that of water fluoridation. Consequently, only about 1 million children receive fluoridated milk (40). Despite several demonstration projects, a recent Cochrane review identified only one placebo-controlled clinical trial of milk fluoridation, which observed a 31% reduction in carious lesions in primary dentition; however, the control group’s lesion increment in permanent dentition was too minimal to draw definitive conclusions (41).

While these fluoridation strategies primarily target children, their impact can extend across all age groups. In countries with high consumption of processed foods, such as the United States, Mexico, and Canada, where there is also a high prevalence of dental caries, physicians often recommend reducing salt intake due to its association with hypertension and cardiovascular disease. Gestational hypertension presents similar concerns. Therefore, despite the compelling cost-effectiveness of salt fluoridation, its use among older adults or pregnant women should be approached cautiously and warrants further investigation. As milk consumption decreases during later childhood, community water fluoridation remains the preferred large-scale intervention for caries prevention throughout adulthood.

The Importance of Fluoride Toothpaste

The widespread adoption of fluoride toothpaste has had a significant impact on oral health. In the United States, an average of three tubes of fluoride toothpaste are sold per person annually. Clinical trials show that fluoride toothpaste prevents about 24% of carious lesions compared to non-fluoride toothpaste, with this effect remaining significant even when combined with fluoride in drinking water. A meta-analysis of fluoride concentrations reveals a dose-response relationship, with the highest concentrations (2400 to 2800 ppm) achieving up to 37% prevention of lesions. Over-the-counter (OTC) fluoride toothpastes (1000 to 1500 ppm) have been shown to prevent new lesions in 12% of patients (42). Despite increased fluoride concentrations in recent years, no placebo-controlled trials have been conducted in the past 30 years, though earlier trials indicated a 25% reduction in carious lesions with calcium phosphate toothpaste compared to no toothpaste. Brushing with non-fluoridated toothpaste or no toothpaste does not prevent new lesions, though brushing itself helps prevent gingivitis.

For children under six years old, toothpaste with 850–1150 ppm fluoride is recommended, while higher fluoride concentrations (5000 ppm) are suggested for older children and adults. The efficacy of fluoride toothpaste for primary prevention of tooth decay is well-documented, showing a 20% to 30% reduction in dental caries in populations using fluoridated toothpaste. Supervised tooth brushing in schools and the "spit, don’t rinse" advice from organizations like the Oral Health Foundation further support this practice. Additionally, providing free toothpaste and advice through home visits effectively reduces caries and the need for dental extractions in lower socioeconomic groups (43). While toothpaste use has not been a successful public health measure for preventing early childhood caries (ECC), its benefits are notable, with a retrospective study in Australia showing extensive protection against tooth decay despite a small increase in fluorosis risk. Most fluorosis cases are clinically insignificant, and delaying the introduction of fluoride toothpaste until after the first birthday can further reduce fluorosis risk (44, 45).

Parents need guidance on choosing fluoride toothpaste and proper brushing techniques. Confusion over labeling and advertising often leads to misconceptions about the appropriate amount of toothpaste and the brushing process. Many parents mistakenly think children can brush their own teeth at a very young age, when they typically need assistance until around age seven. Educating parents about proper brushing techniques and the benefits of fluoride toothpaste is crucial for effective caries prevention.

Fluoride Rinses, Foams, Varnishes, and High Fluoride Toothpastes

Fluoride can effectively prevent caries lesions using various delivery systems, including rinses, foams, varnishes, and gels. Fluoride varnishes are popular due to their quick application and effectiveness, requiring only a brief application twice a year to maximize caries prevention. Although foams may be preferred for their texture, varnishes are still highly effective. Professional application of fluoride primarily promotes enamel remineralization, achieving up to 37% prevention of lesions. Despite the wide range of fluoride delivery methods, the adoption rate for these treatments remains low, with only about half of dental offices using fluoride varnish (Kevin Thomas of Elevate Oral Care, personal communication, 2016). Fluoride rinses can reduce carious lesions by 27% and may be particularly useful for teenagers or others who find rinsing simpler than brushing. While studies show equivalent outcomes for rinses, gels, varnishes, and toothpastes, the most cost-effective approach is typically using standard fluoride toothpaste until permanent teeth are fully formed, followed by higher fluoride toothpaste and semiannual varnish applications (42, 47). Stannous fluoride in toothpaste, though effective, has not been extensively studied in recent modern trials, and concerns about tooth staining and taste persist. Further evaluation of stannous fluoride's effectiveness is needed.

Silver Diamine Fluoride

Silver diamine fluoride (SDF) is a topical treatment for caries lesions and high-risk surfaces, such as molar fissures or roots. With a fluoride concentration of approximately 5%, along with 25% silver ions and 8% ammonia, SDF works by penetrating enamel and dentin, killing bacteria, and reinforcing demineralized structures. FDA-approved in 2014 and widely adopted since 2015, SDF has demonstrated rapid uptake among dentists. Clinical trials have shown that SDF can arrest carious lesions and prevent new lesions, with a success rate of up to 90% after two years of treatment. Although SDF stains treated lesions black, indicating effectiveness, this side effect is generally accepted as a trade-off for avoiding more invasive treatments. SDF application is simple and cost-effective, making it suitable for use by a range of dental and medical professionals, including those in remote or underserved areas (48-60).

Sealants for Primary Prevention

Dental sealants form mechanical barriers that protect occlusal surfaces from dental plaque and food particles, addressing the limitations of water fluoridation, particularly on pits and fissures. While sealants are still used in public health, evidence suggests that topical fluorides are often more cost-effective. Resin sealants require skilled application and have not shown significant differences in preventive effects compared to fluoride varnish. Despite the cost, sealants are a standard care practice for preventing lesions on treated surfaces. Glass ionomer cements, which release fluoride and do not require a dry field for application, offer a promising alternative, showing equivalence to resin sealants in caries prevention. Their ease of application and additional fluoride release make them a viable option, particularly in challenging clinical settings. Public health programs should focus on the effective use of sealants and topical fluorides, considering cost-effectiveness and clinical outcomes. Monitoring sealant retention alone may not fully capture their effectiveness in preventing caries lesions, necessitating a shift toward evaluating actual caries prevention (61-73).

Conclusion

This systematic review provides a comprehensive evaluation of the effectiveness of fluoride and other preventive measures in controlling dental caries. Despite the wide array of interventions available, fluoride remains the most extensively studied and widely implemented preventive agent. The review demonstrates that fluoride-based methods—such as varnishes, supplements, and community water fluoridation—are effective in reducing the incidence of carious lesions, albeit with varying degrees of success. Water fluoridation is particularly notable for its broad impact, with evidence suggesting a 35% reduction in carious lesions in primary dentition and a 26% reduction in permanent teeth. Fluoride varnishes and supplements show modest efficacy, with fluoride toothpaste consistently proving beneficial in preventing caries. However, the review also underscores the limitations of current interventions. The effectiveness of fluoride varnish alone has been inconsistent, and the impact of fluoride supplements is less pronounced for primary teeth. Newer interventions, such as antimicrobial agents and sealants, offer additional preventive benefits but are often influenced by specific application contexts and population characteristics. The review highlights the need for a multi-faceted approach to caries prevention. Combining fluoride-based treatments with behavioral interventions and public health strategies, such as reducing dietary sugar intake and promoting consistent oral hygiene practices, appears to be the most effective method for reducing caries prevalence. Public health initiatives should focus on integrating these interventions into community programs, especially in high-risk populations, to optimize caries prevention efforts. Future research should continue to explore the efficacy of combined interventions and investigate the potential benefits of emerging technologies in caries prevention. By leveraging a comprehensive approach and continually adapting strategies based on emerging evidence, significant strides can be made in mitigating the impact of dental caries on public health.

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