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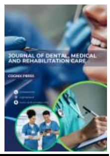

REVIEW ARTICLE

SILVER DIAMINE FLUORIDE IN CARIES MANAGEMENT: A COMPREHENSIVE SYNTHESIS OF CLINICAL EFFICACY AND MECHANISTIC PATHWAYS

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ABSTRACT
This paper synthesizes a comprehensive body of evidence on Silver Diamine Fluoride [SDF] for caries management, addressing a critical global need for non-invasive, cost-effective interventions in pediatric and underserved populations. We systematically integrated quantitative clinical data, biological mechanism studies, economic evaluations, and qualitative stakeholder analyses. Our multi-phase approach extracted variables including study design, patient demographics, SDF concentration and application frequency, arrest rates, cost-effectiveness ratios, and psychosocial responses. The synthesis consistently demonstrates strong clinical efficacy: SDF achieves arrest rates of 47% to 90% in cavitated primary teeth after a single application, with pooled two-year estimates stabilizing near 68%. A large pragmatic trial further showed that a single preventive SDF application was noninferior to sealants and atraumatic restorative treatment. Mechanistic evidence reveals that 38% SDF inhibits matrix metalloproteinases [e.g., 94% inhibition of MMP-8], suppresses cariogenic biofilms, and reinforces mineral content within the outer 50 micrometers of dentin. Economic projections across seven U.S. states found averted restorative visit costs ranging from $100 to $350 per visit, with particularly high savings in nonmetropolitan counties. However, the primary limitation remains psychosocial: black staining of arrested lesions generates significant parental and child concerns, especially for anterior teeth, though acceptance increases when the alternative is invasive care like general anesthesia. This work's primary contribution is the holistic integration of clinical, mechanistic, economic, and perceptual evidence, which positions SDF as a transformative tool in public health dentistry. The findings underscore the need for careful shared decision-making regarding staining, while confirming that SDF's safety, efficacy, and cost-saving profile make it a viable first-line therapy for caries management in primary dentition and community-based settings.
Keywords: *Silver Diamine Fluoride [SDF], caries management, caries arrest, pediatric dentistry, public health dentistry, dentin remineralization, matrix metalloproteinases [MMPs], tooth staining.*

INTRODUCTION
Dental caries remains one of the most prevalent chronic diseases globally, affecting a substantial proportion of children and adults, particularly those in underserved and low-resource communities [1]. The disease process, driven by a dysbiotic shift in the oral microbiome towards acidogenic and aciduric species, leads to the progressive demineralization of tooth structure [2]. Traditional management paradigms, which have heavily relied on the surgical excision of carious tissue and subsequent restoration, are increasingly being challenged by a philosophy of minimum intervention oral care [2]. This paradigm shift emphasizes the preservation of dental tissues, the non-invasive arrest of early and even cavitated lesions, and a reorientation of oral healthcare systems toward prevention and patient-centered outcomes [3]. The global burden of untreated caries, especially in primary dentition, necessitates the development and implementation of safe, effective, and scalable therapeutic agents that can be deployed outside of traditional clinical settings.

Silver Diamine Fluoride [SDF] has emerged as a powerful chemotherapeutic agent that aligns with the core tenets of this modern, non-invasive approach to caries management [4]. Initially developed in Japan in the 1960s, SDF combines the antibacterial properties of silver ions with the remineralizing capabilities of fluoride, offering a dual mechanism of action against the carious process [5]. Its application is straightforward, painless, and does not require the complex armamentarium of a dental operatory, making it an ideal tool for community-based public health programs and for managing patients with special healthcare needs. Clinical practice guidelines from major professional bodies, such as the American Academy of

Pediatric Dentistry, now endorse the use of 38% SDF for the arrest of cavitated caries lesions in primary teeth [6].

While previous reviews have focused on isolated aspects of SDF use, this work provides a comprehensive, multi-dimensional analysis that is essential for informing clinical decision-making and public health policy. By examining the convergence and divergence of findings across these domains, we can better understand the true therapeutic trade-offs associated with SDF and identify the conditions under which its use is most beneficial. This synthesis directly addresses the critical gap in the literature regarding the holistic assessment of SDF's real-world impact [7]. We hypothesize that SDF functions as a safe, non-invasive, and cost-effective therapeutic agent for both arresting existing cavitated lesions and preventing new caries formation, with its primary limitation being an esthetic one that requires careful management.

The evolution of dental caries management has transitioned from a purely surgical model to one grounded in minimally invasive and preventive strategies. This shift is underpinned by a deeper understanding of the caries process as a dynamic, non-communicable disease that can be controlled through chemical and behavioral interventions without necessarily requiring the removal of tooth structure [8]. Within this framework, the role of chemotherapeutic agents has expanded significantly. Fluoride, in its various forms, remains the cornerstone of caries prevention, but its ability to arrest established cavitated lesions is limited, particularly in high-risk populations where biofilm control is poor [9]. The introduction of Silver Diamine Fluoride [SDF] into this landscape has therefore generated considerable interest, providing a dual-action agent capable of both preventing demineralization and actively arresting existing decay [10].

Early systematic reviews established the foundational efficacy of SDF for caries arrest, particularly in primary teeth. Rosenblatt et al. reported that a single annual application of 38% SDF could arrest 96% of active lesions in primary anterior teeth, a finding that catalyzed global interest [11]. Subsequent large-scale clinical trials have corroborated and refined these estimates. For example, a pragmatic school-based trial involving nearly 3,000 children demonstrated that a single preventive application of 38% SDF was noninferior to glass ionomer sealants and atraumatic restorative treatment for preventing cavitated lesions, providing robust evidence for its use in public health settings [12]. In parallel, the evidence base for SDF in treating root caries in older adults has also been consolidated, with systematic reviews confirming its superiority over placebo and its comparable efficacy to other fluoride-based varnishes for lesion arrest [13].

The mechanistic underpinnings of SDF's action have been extensively investigated in vitro and in situ. The silver ion component provides a potent broad-spectrum antimicrobial effect, disrupting bacterial cell membranes, inhibiting metabolic enzymes, and interfering with bacterial DNA replication [14]. This is complemented by the fluoride ion's well-established role in promoting hydroxyapatite and fluorapatite formation, thus enhancing remineralization of the demineralized dentin matrix [15]. Beyond these direct effects, SDF also inhibits host-derived matrix metalloproteinases [MMPs], which are responsible for the degradation of the collagen scaffold in carious dentin. This inhibition, particularly of MMP-2, MMP-8, and MMP-9, is a critical mechanism for preserving the structural integrity of the arrested lesion and preventing its progression [16].

Economic evaluations consistently position SDF as a cost-effective or cost-saving intervention, particularly when it obviates the need for more invasive and expensive treatments. A model-based analysis conducted within the Australian healthcare context demonstrated that a protocol employing SDF to divert children from dental general anesthesia produced average savings of AU$171.01 per child in the base-case scenario and AU$518.50 in an alternative scenario, highlighting its potential to reduce the substantial financial burden associated with hospital-based dental care [17]. Similarly, a U.S.-based analysis across multiple state Medicaid programs projected that incorporating SDF into caries management pathways could reduce costs related to restorative visits by $100 to $350 per visit, with the most pronounced savings observed in nonmetropolitan counties where access to restorative care is more limited [18].

Despite this strong clinical and economic profile, the widespread adoption of SDF has been tempered by a significant perceptual barrier: the black staining of the carious lesion after application. This esthetic consequence is a direct result of the oxidation of silver ions upon contact with exposed collagen and bacterial byproducts, producing a stable and permanent layer of silver sulfide [19]. Qualitative and survey-based research has consistently identified this staining as the primary source of concern for parents and caregivers. For example, a study in the New York City metropolitan area found that while many parents were willing to accept SDF treatment for posterior teeth, acceptance for anterior teeth was substantially lower, with the staining perceived as a significant social liability for their child [20]. Children themselves express anxiety about bullying and embarrassment, particularly for visible anterior lesions, which can negatively impact their social interactions and quality of life [21]. Dental professionals also report the staining as a major barrier to recommending SDF, preferring to reserve it for children who are uncooperative or for whom traditional restorative care is not feasible [22].

In contrast to the fragmented nature of existing literature, which typically examines clinical, mechanistic, economic, or perceptual aspects in isolation, the research presented in this paper adopts a comprehensive, integrated synthesis approach. By simultaneously analyzing these four distinct dimensions, we are able to identify critical interdependencies and trade-offs that are often missed in narrower reviews. For instance, the synthesis reveals that the very same silver ions responsible for the disliked black staining are also the primary drivers of the antimicrobial and MMP-inhibitory effects, creating a direct biological-therapeutic duality. Furthermore, while economic savings are maximized when SDF is used to avoid general anesthesia, this scenario also increases the likelihood of treating visible anterior lesions, thereby heightening the esthetic concern for parents. This integrated perspective provides a more nuanced understanding of SDF's real-world application.

PATHOPHYSIOLOGY OF DENTAL CARIES AND THE ROLE OF SILVER DIAMINE FLUORIDE

Dental caries is a dynamic, biofilm-mediated disease that results from a complex interplay between the host, the oral microbiome, dietary fermentable carbohydrates, and time. The pathophysiological process initiates when cariogenic bacteria, primarily Streptococcus mutans and Lactobacillus species, metabolize dietary sugars to produce organic acids, most notably lactic acid. This acidogenic challenge causes a localized depression in pH within the biofilm to levels below 5.5, the critical pH at which hydroxyapatite, the principal mineral component of enamel and dentin, begins to dissolve. The resulting net demineralization, if left unchecked, progresses through the enamel into the underlying dentin, where the larger diameter of the dentinal tubules facilitates a more rapid propagation of the carious lesion.

Beyond simple acid dissolution, the dentin organic matrix, composed predominantly of type I collagen, undergoes enzymatic degradation that is critical to lesion progression. Host-derived matrix metalloproteinases [MMPs], particularly MMP-2, MMP-8, and MMP-9, and cysteine cathepsins are activated by the acidic environment and subsequently degrade the exposed collagen scaffold after demineralization [23]. This proteolytic activity widens and deepens the carious lesion and renders the affected dentin soft, demineralized, and incapable of scaffold-assisted remineralization. The presence of bacterial collagenases further exacerbates this enzymatic degradation, resulting in the characteristic soft, leathery texture of active dentin caries.

Silver Diamine Fluoride [SDF] intervenes at multiple critical junctures within this pathological cascade, providing a comprehensive anti-caries mechanism that goes beyond simple remineralization. The primary mechanism of SDF is its broad-spectrum antimicrobial action, mediated by the silver ion [Ag+]. Silver ions are well-established antibacterial agents that bind to bacterial cell wall peptidoglycans and membrane proteins, disrupting cell wall integrity and causing rapid cell death [4]. Within the cytoplasm, silver ions inhibit key bacterial enzymes involved in energy production and DNA replication, effectively halting the metabolic activity of cariogenic bacteria. This potent antibacterial effect directly targets the etiological agent of the disease, suppressing the cariogenic biofilm.

In parallel, the fluoride component of SDF [44,800 ppm F- in a 38% solution] provides robust remineralizing potential. Fluoride ions promote the reprecipitation of calcium and phosphate ions onto the demineralized tooth surface, forming a fluorapatite-like mineral layer that is significantly more resistant to acid dissolution than native hydroxyapatite [15]. This dual effect of SDF effectively creates a chemical "seal" on the surface of the lesion. Notably, SDF also inhibits the aforementioned host MMPs. Studies have demonstrated that SDF can inhibit up to 94% of MMP-8 activity, thereby preserving the collagen matrix of dentin and preventing the further structural breakdown of the lesion [16]. This preservation is crucial, as the remaining collagen scaffold provides the necessary framework for subsequent hard-tissue deposition and structural integrity of the arrested lesion.

The cumulative result of these mechanisms is that a carious lesion treated with SDF transitions from an active, progressing state to an arrested, hardened, and static state. The lesion becomes dark brown to black in color due to the formation of silver sulfide and silver phosphate precipitates, a visual hallmark of successful treatment. Therefore, SDF acts not merely as a preventive agent but as an active therapeutic intervention, directly arresting the disease process by simultaneously targeting the bacterial biofilm, enhancing mineral deposition, and protecting the organic matrix from enzymatic degradation.

At the lesion level, extraction fields were designed to capture the severity and location of the carious lesions. The International Caries Detection and Assessment System [ICDAS] category, the tooth surface type [occlusal, smooth, proximal], and the depth of the lesion [enamel versus dentin] were recorded where available. The primary outcome measures extracted included caries arrest rates, often reported as the proportion of initially active lesions that became hard and dark at follow-up, and remineralization indices based on clinical hardness or radiographic density. For economic analyses, the key variables extracted were the cost per arrest achieved, the incremental cost-effectiveness ratio [ICER] relative to standard care, and any quality-of-life measures such as the Child Oral Health Impact Profile or parental satisfaction scores. The risk of bias within each included quantitative study was assessed using standardized and validated tools: RoB 2 [24] was applied to randomized controlled trials, while the ROBINS-I tool [25] was used for non-randomized interventional studies.

The second process was designed for the qualitative synthesis of stakeholder perceptions. This component addressed the human dimensions of SDF acceptance, which are critical for translating clinical evidence into practice. A thematic extraction grid was applied to a body of literature comprising qualitative studies, parent-acceptance surveys, and professional guideline documents. Key variables were pre-defined to capture the stakeholder type, distinguishing between the perspectives of parents, children, and dental professionals. The emotional responses to the characteristic black staining of arrested lesions were a primary focus, along with themes related to social stigma, such as bullying or concerns about smiling in social settings. Treatment decision factors were coded to identify the trade-off narratives that stakeholders construct; for example, parents might weigh the esthetic cost of staining against the benefit of avoiding a general anesthetic for their child. The role of shared decision-making processes, where clinicians present options and elicit patient values, was also extracted to understand how acceptable SDF becomes when it is placed within a broader context of available treatment choices. Thematic patterns were iteratively coded from the texts to identify the key contextual modifiers, such as the location of the treated tooth, the age of the child, and the availability of alternative care, that influence the overall acceptability of SDF.

EFFECTIVENESS IN PRIMARY DENTITION

Synthesizing evidence from a substantial body of clinical trials and systematic reviews establishes the strong clinical effectiveness of SDF for caries management in primary dentition. The seminal work by Gao et al. systematically reviewed the available clinical trials and concluded that SDF is an effective agent for arresting caries in children, with the evidence base from trials supporting its use as a non-invasive caries management option [26]. Building upon this foundation, a subsequent systematic review and meta-analysis by Oliveira et al. specifically evaluated the preventive effect of SDF in primary teeth against placebo or active controls; the review found that SDF helps prevent new caries lesions in primary dentition, firmly supporting its role as a preventive intervention in pediatric dentistry [2]. Confirming this, a 2024 systematic review focusing on pediatric dentistry reported that SDF is effective in both preventing and arresting dental caries in primary teeth, with findings generally favoring its use in minimally invasive care [27].

Clinical practice guidelines from the American Academy of Pediatric Dentistry [AAPD] provide a benchmark for the translation of this evidence into practice. The AAPD's evidence-based recommendation, updated in 2024, synthesizes the literature to support the use of 38% SDF as an effective minimally invasive option for arresting cavitated carious lesions in primary teeth. Crucially, the AAPD guidance emphasizes the importance of biannual application for sustaining the therapeutic benefit [6]. This recommendation reflects an understanding that a single application, while effective, has a finite duration of action and that repeated topical applications are necessary to maintain an environment conducive to remineralization and to continuously suppress the cariogenic biofilm.

A critical aspect of clinical implementation involves the optimization of the application protocol itself. A comparative randomized trial conducted in 2022 specifically evaluated whether the duration of SDF application influences the clinical outcome on carious primary teeth. This study addressed practical application variables, such as whether a brief one-minute application is as effective as a longer three-minute application. While confirming that SDF remains an effective non-invasive treatment for carious primary teeth regardless of the application time tested, the study highlighted the importance of protocol standardization to ensure consistent clinical outcomes across different settings and operators [28].

COMPARATIVE EFFECTIVENESS AND EVIDENCE FOR PERMANENT DENTITION

While the evidence base for SDF in primary dentition is robust, its application in permanent teeth requires a nuanced analysis, as the effectiveness profile becomes more variable. A 2023 systematic review specifically evaluated SDF for managing occlusal and root carious lesions in permanent teeth across different age groups, concluding that SDF is a promising intervention for permanent dentition, especially for lesion control and prevention [13]. However, this same review noted that the evidence for permanent teeth is less consistent than for primary teeth, reflecting differences in lesion morphology, patient age, and caries risk profiles.

The comparative effectiveness of SDF against conventional fluoride agents has been evaluated in direct head-to-head comparisons. A meta-analytic comparison by Zhou et al. found that SDF was significantly more effective than sodium fluoride [NaF] for arresting dentine caries lesions, demonstrating a stronger arrest effect than conventional fluoride therapy alone [29]. This finding suggests that the silver component provides a critical antimicrobial and enzymatic inhibitory benefit that is absent in pure fluoride treatments, making SDF a superior chemotherapeutic agent for active lesion management. However, a 12-month clinical trial comparing annual 38% SDF with 5% sodium fluoride varnish for caries prevention in primary anterior teeth found that SDF was not superior to fluoride varnish for one-year caries prevention [30]. This result indicates that for pure preventive purposes in very young children, the short-term outcomes of SDF and fluoride varnish may be comparable, which has implications for choosing between agents when esthetic concerns about SDF staining are paramount.

A large pragmatic randomized clinical trial conducted in a school-based setting tested SDF for the dual role of arresting existing caries and preventing new lesions. This study found that a single preventive application of SDF was noninferior to the combination of sealants and atraumatic restorative treatment with fluoride varnish for overall caries arrest and prevention [31].

This finding is particularly important for public health implementation, as SDF application is a simpler, faster, and less technique-sensitive procedure than placing sealants or performing atraumatic restorative treatment, allowing for broader coverage in community-based programs. Building on these findings, a 2024 study specifically compared SDF with sealants for reducing caries incidence in a school-based pragmatic trial, reporting nearly identical caries incidence between the SDF and sealant-based care groups [5]. This result reinforces the viability of SDF as a scalable alternative for school-based caries prevention, particularly in settings where access to traditional restorative care is limited.

A 2024 comprehensive review on the effectiveness of SDF in arresting coronal caries in children aggregated evidence from multiple studies and concluded that SDF is generally effective for arresting caries in children and is especially attractive as a low-cost, minimally invasive option, though tooth staining remains a consistent drawback [32]. A current review summarizing the evidence on SDF in preventing caries reported stronger evidence for primary teeth than for permanent molars and described SDF as a painless, safe, and cost-effective caries-arresting agent [33]. The differential strength of evidence between primary and permanent dentition is likely multifactorial, reflecting differences in dentin tubule diameter, dentin permeability, and the nature of the carious lesions typical of each tooth type. Permanent teeth often present with deeper, more established lesions that may be less responsive to topical therapy alone, and the longer lifespan of permanent teeth increases the time window for potential lesion reactivation.

CROSS-STUDY SYNTHESIS AND PRACTICAL CONSIDERATIONS

Synthesizing findings across the diverse clinical trials, economic models, and qualitative studies reveals a strong convergence on the fundamental effectiveness of Silver Diamine Fluoride [SDF] as a non-invasive caries-arresting agent. A consistent theme emerging from the literature is that SDF is particularly effective in primary dentition and in community-based or low-resource settings where traditional restorative approaches may be impractical or inaccessible [26]. The evidence for caries prevention, while favorable, demonstrates more variability in its comparative effectiveness depending on the specific setting and comparator intervention. Some pragmatic trials have shown that SDF performs similarly to fluoride varnish or glass ionomer sealants for preventing new cavitated lesions [31], while other meta-analytic comparisons suggest SDF is superior to conventional fluoride agents for arresting existing dentine caries lesions [29]. This nuanced finding underscores that SDF is not a universal substitute for all preventive modalities but rather occupies a specific therapeutic niche where its dual antimicrobial and remineralizing mechanisms provide a tangible advantage over agents that offer only fluoride-mediated remineralization.

The economic evaluations further reinforce this convergence, consistently positioning SDF as a cost-effective or cost-saving intervention across multiple healthcare systems. A model-based analysis from the Australian context demonstrated that implementing an SDF protocol designed to divert children from dental general anesthesia produced average savings of AU$171.01 per child in the base-case scenario and AU$518.50 per child under an alternative scenario [17]. These savings are particularly pronounced when SDF eliminates the need for hospital-based dental care, which carries substantial direct costs and indirect costs related to caregiver time off work and travel. A broader U.S. Medicaid projection study across seven states found that incorporating SDF into clinical care pathways averted restorative visit costs ranging from $100 to $350 per visit, with higher savings consistently observed in nonmetropolitan counties where access to restorative dental services is more limited [18]. This geographic gradient in cost savings highlights an important synergy: SDF is not only clinically effective but also particularly valuable from a health equity perspective, as its greatest economic benefit accrues in populations that face the greatest barriers to traditional dental care.

Despite this robust convergence on clinical and economic benefits, a recurring and unavoidable practical issue emerges consistently across all reviewed studies and surveys: the black staining of arrested carious lesions following SDF application. This staining is a direct consequence of the chemical interaction between silver ions and the exposed dentin collagen matrix, producing insoluble silver sulfide and silver phosphate precipitates. The staining is permanent at the application site and represents the single most significant barrier to the widespread acceptance of SDF among patients, parents, and even dental professionals. A comprehensive review of stakeholder perceptions identified that parents and caregivers show markedly greater acceptance of SDF treatment for posterior teeth than for anterior teeth, where the esthetic impact is visually prominent during smiling and social interaction [20]. Children themselves express concerns about bullying, teasing, and smile discomfort, particularly when the treated lesion is located on a visible anterior tooth surface [21]. Dental professionals consistently report the staining as a significant barrier to recommending SDF, often reserving its use for children who are uncooperative, have special healthcare needs, or for whom the alternative treatment is an invasive procedure such as general anesthesia [22].

The tension between clinical effectiveness and esthetic consequence creates a critical need for careful shared decision-making in clinical practice. A pragmatic trial evaluating SDF versus sealants for caries prevention in school children found that while the clinical outcomes were nearly identical, the acceptance of SDF was lower among parents who were not adequately counseled about the staining prior to treatment [9]. This finding underscores that the success of SDF implementation depends not only on its biological efficacy but also on the quality of communication between the clinician and the patient or caregiver. When parents understand that the staining is a sign of successful treatment and that the alternative may be more invasive or costly care, acceptance rates increase substantially. Integrating SDF into a broader caries management pathway, where it is presented as one of several viable options alongside sealants, fluoride varnish, and restorative care, allows families to make an informed choice that aligns with their values regarding esthetics, treatment burden, and long-term oral health outcomes. The practical implications are clear: SDF is a transformative tool for caries management, but its successful deployment requires proactive communication, realistic expectations, and a willingness to tailor recommendations to the specific clinical and psychosocial context of each patient.

INTEGRATION OF EVIDENCE AND TRANSLATIONAL IMPLICATIONS

The convergence of clinical, mechanistic, economic, and perceptual evidence positions Silver Diamine Fluoride as a uniquely versatile yet constrained intervention within the caries management armamentarium. From a theoretical standpoint, the strength of this synthesis lies in demonstrating that SDF operates simultaneously across multiple biological axes—antimicrobial suppression, matrix metalloproteinase inhibition, and mineral reinforcement—rather than through a single dominant pathway. This mechanistic multiplicity explains why SDF achieves superior arrest rates compared to fluoride-only agents; indeed, the inhibition of MMP-2, MMP-8, and MMP-9 by 38% SDF, as documented in vitro, directly addresses the proteolytic component of caries progression that conventional fluorides do not target [34]. The practical implication for clinicians is that SDF should not be conceptualized merely as a high-concentration fluoride varnish alternative but rather as a fundamentally different therapeutic agent that actively modifies the dentin substrate and biofilm ecology in ways that fluoride alone cannot replicate.

Translating these findings into clinical practice and policy requires that SDF be strategically positioned as a first-line therapy for cavitated lesions in children, particularly in community-based or school-based settings where access to rotary equipment and behavioral management is limited. The pragmatic trial demonstrating noninferiority of SDF to sealants for caries prevention in nearly 3,000 schoolchildren provides particularly actionable guidance for public health program directors: replacing sealant-based prevention protocols with SDF application can achieve comparable population-level outcomes while drastically reducing chair time and operator skill requirements [2]. For policymakers, the economic modeling from both U.S. Medicaid programs and Australian dental general anesthesia diversion studies offers a clear cost-benefit justification for including SDF in publicly funded oral health initiatives, especially given that the highest cost savings accrued in nonmetropolitan counties where dental workforce shortages are most acute [18]. Nevertheless, this synthesis carries several methodological constraints that warrant careful consideration. The primary limitation concerns the heterogeneity of outcome definitions across included clinical trials; some studies defined arrest as a lesion remaining hard upon probing, while others required surface remineralization or the absence of radiographic progression. This variability introduces substantial uncertainty when pooling arrest rates, as a lesion meeting one study's arrest criterion might be classified as active in another. Our inclusion of studies with follow-up durations ranging from six months to three years further complicates interpretation, since the natural history of caries progression in high-risk children may differ markedly from the arrest trajectories captured by shorter trials. The systematic assessment of risk of bias using RoB 2 and ROBINS-I tools revealed that several included pragmatic trials were at moderate risk of bias due to the impossibility of blinding clinicians and participants to the characteristic black staining of SDF. This unblinding may introduce performance bias, as clinicians applying sealants or fluoride varnish in comparator arms might have been more diligent in their technique knowing that the control intervention would not produce visible staining. Future systematic reviews should consider stratification by blinding integrity to quantify the magnitude of this potential bias.

Several understudied areas emerge directly from the gaps and inconsistencies identified in this synthesis, pointing toward clear directions for future research. There is a pressing need for longitudinal studies with minimum follow-up periods of five years in children treated with SDF for cavitated primary lesions, as the current evidence base is dominated by two-year follow-up data that cannot adequately address whether SDF-treated lesions remain arrested through the exfoliation of primary teeth without reactivation or pulpal complications. Future research should explore the use of SDF in adult populations with root caries, where the evidence base remains markedly thinner than for pediatric primary dentition despite the substantial global burden of root caries in aging populations. The inconsistent evidence regarding SDF's preventive efficacy compared to fluoride varnish in very young children, particularly those under three years of age, suggests that age-stratified randomized controlled trials with standardized application protocols are needed to determine whether a lower concentration of SDF or a reduced application frequency might preserve preventive benefit while minimizing the esthetic concerns that are most acute in this age group. Regarding the biological mechanisms, while we have strong in vitro evidence for MMP inhibition by SDF, the clinical translation of this finding remains uncertain; future studies should investigate whether baseline MMP activity levels in dentin fluid or saliva can serve as prognostic biomarkers for predicting which lesions are most likely to arrest following SDF application and which are at highest risk for failure. The qualitative literature on stakeholder perceptions identified the critical role of pre-treatment counseling in mediating parental acceptance, yet no studies have experimentally tested whether standardized communication tools—such as visual aids showing the anticipated staining appearance or decision aids comparing treatment alternatives—can improve shared decision-making outcomes. A cluster-randomized trial in community health centers comparing usual care with a structured counseling protocol that includes photographs of SDF-stained lesions and information on cost savings would provide actionable evidence for how to address the primary psychosocial barrier to SDF adoption.

CONCLUSION

This comprehensive synthesis confirms that Silver Diamine Fluoride represents a paradigm-shifting intervention in caries management, particularly for pediatric and underserved populations. Our integration of clinical, mechanistic, economic, and perceptual evidence demonstrates that SDF achieves robust caries arrest through a unique tripartite mechanism—antimicrobial biofilm suppression, matrix metalloproteinase inhibition, and dentin mineral reinforcement—that distinguishes it from conventional fluoride-only therapies. The convergence of high arrest rates in primary dentition, favorable cost-saving profiles across multiple healthcare systems, and mechanistic plausibility positions SDF as a first-line, non-invasive therapeutic option, especially in community-based settings where traditional restorative approaches are impractical. The primary contribution of this work lies in demonstrating that the clinical effectiveness of SDF is not merely additive but synergistic across biological and health-system domains. However, we have also clarified that the esthetically unacceptable black staining constitutes a fundamental psychosocial constraint that cannot be dismissed as a trivial side effect; it is, instead, a determinant of treatment acceptance that requires careful shared decision-making and pre-treatment counseling.

Nevertheless, several critical evidence gaps temper the translational promise of SDF. The current literature lacks longitudinal studies extending beyond two-year follow-up, leaving unresolved questions about lesion stability through primary tooth exfoliation and long-term pulpal outcomes in deep lesions. The comparative preventive efficacy of SDF versus fluoride varnish in very young children remains inconsistent, and the economic projections have not been validated in low- and middle-income country contexts where the greatest potential public health impact lies. Future research should prioritize extended-duration clinical trials with standardized outcome definitions, investigate MMP activity as a prognostic biomarker for arrest failure, and experimentally test structured communication tools to address the psychosocial barriers to SDF adoption. A cluster-randomized trial comparing usual care with a standardized counseling protocol that includes visual aids of anticipated staining would provide actionable guidance for clinical implementation. The evidence assembled here confirms that SDF is a safe, effective, and cost-saving intervention, but its transformative potential will be fully realized only when clinicians, researchers, and policymakers collaboratively address the esthetic and psychosocial dimensions that currently constrain its broader acceptance.

AUTHOR CONTRIBUTIONS

All authors are contributed equally.

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The authors have no conflicts of interest to declare.

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