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Effectiveness of silver diamine fluoride in caries prevention and arrest: a systematic literature review

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Abstract

This study aimed to evaluate the scientific evidence regarding the effectiveness of silver diamine fluoride (SDF) in preventing and arresting caries in the primary dentition and permanent first molars. A systematic review (SR) was performed by 2 independent reviewers using 3 electronic databases (PubMed, ScienceDirect, and Scopus). The database search employed the following key words: “*topical fluorides*” AND “*children*” AND “*clinical trials*”; “*topical fluorides*” OR “*silver diamine fluoride*” AND “*randomized controlled trial*”; “*silver diamine fluoride*” AND “*children*” OR “*primary dentition*” AND “*tooth decay*”; “*silver diamine fluoride*” OR “*sodium fluoride varnish*” AND “*early childhood caries*”; and “*silver diamine fluoride*” AND “*children*”. Inclusion criteria were articles published in English, from 2005 to January 2016, on clinical studies using SDF as a treatment intervention to evaluate caries arrest in children with primary dentition and/or permanent first molars. Database searches provided 821 eligible publications, of which 33 met the inclusion criteria. After the abstracts were prescreened, 25 articles were dismissed based on exclusion criteria. The remaining 8 full-text articles were assessed for eligibility. Of these, 7 publications were included in the SR. These included 1 study assessing the effectiveness of SDF at different concentrations; 3 studies comparing SDF with other interventions; 2 investigations comparing SDF at different application frequencies and with other interventions; and 1 study comparing semiannual SDF applications versus a control group. The literature indicates that SDF is a preventive treatment for dental caries in community settings. At concentrations of 30% and 38%, SDF shows potential as an alternative treatment for caries arrest in the primary dentition and permanent first molars. To establish guidelines, more studies are needed to fully assess the effectiveness of SDF and to determine the appropriate application frequency.

Dental caries is the most frequent childhood chronic disease worldwide.^{1–3} Early childhood caries (ECC), the presence of 1 or more decayed, missing, or filled tooth surfaces (dmfs) in any primary tooth in a preschool-aged child, has been recognized by the American Dental Association as an important public health issue.⁴

In recent years, a reduction in overall caries indicators has been reported; however, an increase in ECC has been documented.^{5–7} If ECC remains untreated, oral health–related quality of life, body weight, growth, school attendance, and school performance can be affected.^{8,9} In addition, children with ECC treated under general anesthesia have a higher predisposition to develop dental caries in the permanent dentition.¹⁰ Because a severe ECC experience is an important predictor for adult caries, strategies to prevent and control ECC are important to improve general and oral health.^{11–13}

Feeding habits and a variety of biological, environmental, and socioeconomic factors are involved in the development of ECC.^{14,15} One important socioeconomic factor is the lack of child dental insurance. Access to dental insurance has been found to correlate with age and is inversely related to family income and the educational level of the mother.¹⁶ ECC is therefore exacerbated in children residing in underprivileged areas, where carious lesions remain untreated due to limited financial resources and facilities.^{17,18}

Dental caries can be prevented or arrested.¹⁹ Moreover, preventive measures for ECC are more cost effective than emergency room visits or restorative treatments when the illness has been established.^{20,21} A variety of evidence-based approaches for caries prevention have been reported; however, these strategies demand significant financial investment and depend on the availability of oral health workforces and facilities.¹⁸ Effective ECC preventive measures include the use of fluoride varnish—such as 5% sodium fluoride (NaF)—and the use of fluoridated toothpaste.^{22–25} In the management of cavitated ECC, atraumatic restorative treatment (ART) has been recommended. ART is painless, is low cost, and can be applied outside the clinical setting or when conventional treatment is not available. A disadvantage of this treatment is its high rate of failure.²⁶

Interest in the use of silver diamine fluoride (SDF) has been growing. SDF has been used as an alternative treatment for caries prevention and arrest.²⁷ In 2014, SDF was approved by the US Food and Drug Administration as a treatment for dentinal sensitivity.²⁸ SDF had been used off-label for caries arrest; however, it was recently approved (code D1354) as an interim caries-arresting medicament.²⁹

In vitro studies have demonstrated that SDF increases the pH of biofilm, reduces dentin demineralization, and has antimicrobial action against cariogenic bacteria.³⁰ However, treated teeth sometimes develop black stains as a result of silver phosphate precipitation.³¹ Ex vivo and in vivo studies on cavitated extracted teeth from children receiving semiannual applications of SDF have shown effectiveness in arresting lesions as well as higher fluoride uptake compared to fluoride varnish and acidulated phosphate fluoride gel.^{32,33}

Clinical studies have demonstrated the effectiveness of SDF in childhood caries prevention and arrest. Semiannual applications of SDF at 38% concentration have been recommended.³⁴ SDF has been suggested for difficult-to-treat lesions and patients with high

caries risk, including those with medical or behavioral complications, those who require multiple treatment visits, or those without access to dental care.³⁵

The purpose of this systematic literature review was to evaluate the scientific evidence regarding the effectiveness of SDF in preventing and arresting dental caries in the primary dentition and permanent first molars.

Materials and methods

A systematic literature database search was performed by 2 independent reviewers using PubMed, ScienceDirect, and Scopus. The search included the following sets of key words:

- “Topical fluorides” AND “children” AND “clinical trials”
- “Topical fluorides” OR “silver diamine fluoride” AND “randomized controlled trial”
- “Silver diamine fluoride” AND “children” OR “primary dentition” AND “tooth decay”
- “Silver diamine fluoride” OR “sodium fluoride varnish” AND “early childhood caries”
- “Silver diamine fluoride” AND “children”

The following filters were applied to these terms: clinical trial, published in the last 10 years (or since 2005), English, and journal (or dental journal).

The search was conducted from August 2015 to January 2016. Inclusion criteria were a randomized controlled trial (RCT) using SDF as 1 of the interventions, a population of children with primary dentition and/or permanent first molars, and manuscripts published in English from 2005 to January 2016. Exclusion criteria included other study designs, manuscripts in different languages or published outside the target timeframe, RCTs not using SDF as 1 of the interventions, and/or adults or children with complete permanent dentitions. The research question addressed was: In children who have caries in primary teeth and/or permanent first molars, is the use of silver diamine fluoride more effective than other strategies in the prevention and/or arrest of carious lesions?

A database was developed to compare and assess each reviewer search. Three eligibility phases were employed: titles, abstracts, and full-text screening. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement guidelines were followed.³⁶ The data extraction form included the study design, SDF concentration and frequency, other treatment interventions used, SDF application techniques, and SDF adverse events. The outcomes reported were mean number of surfaces with new, active, and inactive caries at baseline and follow-up; mean numbers of arrested surfaces; the percentage of caries arrested; and caries increment. The risk of bias was assessed using a simplified analysis adapted from recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions*.³⁷

Results

A total of 1136 manuscripts were initially identified in database searches: 395 articles from PubMed, 255 articles from ScienceDirect, and 486 articles from Scopus (Chart). After duplicate records were eliminated, 821 articles remained. Of these, 33 met the inclusion criteria. After the abstracts were prescreened, 25 articles were dismissed based on the exclusion criteria, and the reviewers agreed to include 8 publications in the full-text article assessment phase. After review of the full text, the reviewers decided, by consensus, to exclude 1 of the reports due to inconsistencies in the description of the study design and results. Finally, a total of 7 studies were included in the systematic review.

One study compared semiannual SDF applications versus a control group, 3 studies compared SDF with other treatment interventions, and 1 study assessed the effectiveness of SDF at different concentrations.^{38–42} The remaining 2 studies compared SDF at different application frequencies and with other treatment interventions.^{43,44}

The RCTs had various durations (12–36 months) and were conducted in different countries. Two of the 7 studies were conducted in Brazil.^{39,41} The sample size was calculated according to the number of children or the number of carious surfaces. The caries diagnostic criteria used in these studies varied: decayed, missing, or filled teeth (dmft) or dmfs indices; International Caries Detection and Assessment System (ICDAS); visual criteria; or World Health Organization (WHO) criteria. The 7 selected studies could be categorized into 2 groups: children with primary dentition (4 studies) or children with primary dentition and at least 1 permanent first molar (3 studies).^{38–44} Studies in both groups evaluated the prevention and/or arrest of caries and compared SDF with other preventive measures: glass ionomer cement (GIC), cross-toothbrushing technique (CTT), interim restorative treatment, and fluoride varnish.

The articles included in this review were mainly conducted in school settings (kindergarten and primary schools). Only 1 of the studies was conducted in a dental school.³⁹ Therefore, the context of these studies was basically outside the clinical setting (Table 1).

The SDF concentrations and sources in the selected studies are detailed in Table 2. A summary of the results of each study is presented in Table 3. The majority of the studies agreed that both 30% and 38% solutions were more effective for caries arrest than other interventions. In 4 studies, the effectiveness of 38% SDF in caries prevention and/or arrest was determined.^{38,40,42,43} One of the clinical trials reported that a 38% SDF solution was significantly more effective for caries prevention in primary teeth (80% fewer new caries lesions; $P < 0.05$) and first molars (65% fewer new caries lesions; $P < 0.001$) compared to a control group.³⁸ Also, children who received SDF treatment exhibited significantly more surfaces with inactive caries. Another study found that the caries arrest rate was significantly higher (53%) when 38% SDF was applied semiannually than when 38% SDF (37%) or GIC (28.6) was applied annually ($P < 0.001$).⁴³ Another investigation showed that 38% SDF, with or without tea, was significantly more efficient in caries arrest in the primary dentition, both at 6 months and at 12 months, than 12% SDF and a control group ($P < 0.001$).⁴⁰ Only 1

study reported that SDF was less effective than ART sealants; however, the trial design and follow-up showed deviations from the original protocol.⁴²

Two studies compared the effectiveness of SDF with temporary restorations in the arrest of caries.^{41,42} One of the studies found that 30% SDF was 1.73 times more effective to arrest caries (relative risk, 66.9%) than an interim restorative technique (relative risk, 38.6%) after 6 and 12 months ($P < 0.05$).⁴¹ The other study reported caries increments in toothbrushing and nontoothbrushing children treated with ART sealants or SDF as well as control groups. The hazard ratio (HR) was significantly lower in both sealant groups—with toothbrushing (HR, 0.12; confidence interval [CI], 0.02–0.61; $P < 0.01$) and without toothbrushing (HR, 0.33; CI, 0.20–0.54; $P < 0.001$)—than in the groups treated with SDF or the control groups.⁴²

One of the selected studies compared the effectiveness of 30% SDF versus fluoride varnish in caries arrest rates.⁴⁴ One group received SDF at baseline and again after 1 year; another group received 3 SDF applications at weekly intervals; and the third group received 3 applications of 5% NaF fluoride varnish at weekly intervals. After 1 year, the group receiving 3 SDF applications exhibited significantly higher caries arrest rates than did the other 2 treatments ($P < 0.001$). However, after 18 months the caries arrest rate of those receiving annual SDF application was significantly higher (40%) than that of those receiving intensive SDF or NaF varnish applications (35% and 27%, respectively).⁴⁴

Another study compared the effectiveness of SDF with GIC and CTT.³⁹ After 3 and 6 months, applications of 10% SDF showed a significantly greater capacity for arresting caries than both GIC and CTT. Additionally, a general reduction in active lesions was noted in all study groups ($P < 0.05$).³⁹

Reports of adverse events in the present systematic review (SR) were uncommon. The presence of black discoloration in the arrested lesions was disclosed in 2 studies.^{38,44} One of these studies also reported the development of reversible, small, white lesions in the oral mucosa.³⁸

As stated previously, the evaluation of the risk of bias for the studies included in this review was based on the recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions*.³⁷ Due to incomplete data or information omission, biases were difficult to identify clearly. Corresponding authors were not contacted; therefore, a general analysis was conducted. Inclusion and exclusion criteria were not defined in all studies. The randomization and allocation processes were not clearly stated in most of these studies. One of the manuscripts stated that “the authors were unable to perform a double- or single-blind study because it was impossible to mask the examiner for the materials.”⁴¹ In another study, caries arrest was not recorded if the lesion was not totally arrested.⁴⁴ Overall, the determination of the arrested caries was not consistent. Results reporting based on the aims and outcomes was not clearly stated. With regard to the study design, the type of study (such as split-mouth design) and any changes due to lack of compliance (as reported in 1 study) are relevant issues to be considered. The most relevant biases found were selection

(concealment of allocation sequence) and detection (failure to blind participants and personnel).

Discussion

A solution of 38% SDF has been reported as an effective treatment for caries arrest.⁴⁵ SDF is usually recommended for children with a high risk of developing caries, often those living in poor conditions or developing countries.^{34,46} As reported previously, SDF was recently accepted in the United States as a temporary treatment to promote caries arrest; therefore, it is necessary to evaluate the current evidence about this product.²⁹ Such information could improve the delivery of oral healthcare services for dental caries, especially in children.

Previous systematic reviews have reported that silver compounds are useful in caries management to prevent and arrest lesions in the primary and permanent dentition.^{27,31,47} SDF is an alternative treatment for controlling dental caries when other approaches are not available. It is a minimally invasive, low-cost, and simple method that can reduce fear and anxiety in young children. In addition, it could be applied in community settings.^{48,49}

The selected studies in this SR used a variety of SDF concentrations, application frequencies, follow-up intervals, and outcomes. Different SDF concentrations (10%, 12%, 30%, and 38%) are available. SDF review articles have recommended the use of a 38% concentration intervention for prevention and arrest of dental caries in children.^{34,35,45,46,50} In the present SR, the use of SDF at concentrations of 30% and 38% was more effective for arresting caries. However, the determination of an optimal SDF application frequency was hindered due to differences in study design among the selected studies.

The main adverse events associated with SDF applications are pulpal irritation, dental staining, and oral soft tissue irritation.⁴⁷ SDF has been reported as innocuous to the dental pulp.^{31,46} Several studies have highlighted the black dental stains that appear after SDF application as one of its disadvantages.^{31,35} An in vitro study demonstrated that tooth discoloration could be reduced by the incorporation of potassium iodide to SDF during application.⁵¹ On the other hand, minor oral mucosal irritation, a reversible, rare event, is not commonly reported by investigators. Few side effects were reported in the studies reviewed for the present SR. In the selected studies that used 30% and 38% SDF, adverse events such as black stains and oral lesions were reported.^{38,44} This finding suggests that lower SDF concentrations might reduce the onset of adverse events; however, these levels are less effective in arresting caries.

This SR has some limitations. For example, the review analyzed only manuscripts written in English; however, results of additional SDF clinical trials conducted in countries where SDF is available have been published in other languages. This filter could have introduced bias into the analysis. Moreover, an analysis of bias was not conducted, because the authors were unable to contact the primary authors of the studies and clarify issues related to the risks assessed or adverse events and side effects (publication bias). Trial reporting of the assessed studies could suggest additional biases such as selection (concealment of allocation sequence), detection (failure to blind participants and personnel), and other biases. In

addition, differences between examiner criteria or stringency of the examiner limited a comparative analysis of caries arrest detection.

Trial reporting is heterogenous; therefore, the use of a standardized protocol for reporting SDF clinical trials is necessary. The Consolidated Standards of Reporting Trials (CONSORT) Statement may be useful to prevent deficiencies during result dissemination.⁵² In addition, a qualitative SR to determine other important factors, such as parents' perception and children's acceptance of treatment, should be part of the comprehensive assessment of the potential public health impact of SDF.⁵³

None of the studies in this review compared the effectiveness of 30% versus 38% concentrations of SDF in caries arrest; such studies are necessary to help in determining an ideal (effective and safe) SDF concentration. More studies using standardized protocols for study designs, detection criteria, outcomes, and statistical designs are needed to enable a full assessment of the effectiveness of SDF in caries prevention and control, determine the appropriate application frequency, and establish treatment guidelines.

Conclusion

A systematic review of 7 studies indicated that SDF, at concentrations of 30% and 38%, is more effective than other preventive management strategies for arresting dentinal caries in the primary dentition. Additionally, 30% and 38% concentrations of SDF show potential as a caries preventive treatment in primary teeth and permanent first molars. Standardized SDF protocols must be developed to allow meaningful study comparisons and establish treatment guidelines.

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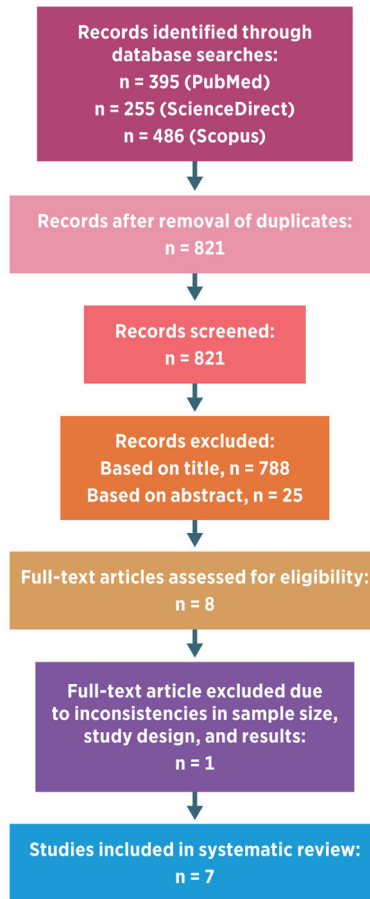


Chart.
Selection of studies for the systematic review.

Table 1

Designs of the studies included in the systematic review.

<p>Llodra et al (2005),³⁸ Cuba</p> <hr/> <p><i>Design:</i> 36 mo; RCT; blind <i>Site:</i> 1 primary school <i>Visits:</i> 7 (every 6 months) <i>Sample:</i> N = 452 (95% CI, 80% power) <i>Randomization:</i> individual random basis <i>Inclusion criteria:</i> age 6 y <i>Diagnostic criteria:</i> DMFS; caries activity; changes in dentin hardness and color <i>TX group:</i> 38% SDF application every 6 mo <i>Control:</i> no SDF; demographic characteristics not defined <i>SDF application technique:</i> in primary teeth, no removal of carious tissue; in permanent teeth, removal of carious tissue <i>SDF adverse events:</i> black stains; white lesions in oral mucosa in 3 participants (It is not clear whether these 3 children also developed black stains.)</p> <hr/> <p>Braga et al (2009),³⁹ Brazil</p> <hr/> <p><i>Design:</i> 30 mo; pilot RCT; blind <i>Site:</i> Dental School of the University of São Paulo <i>Visits:</i> baseline and 3, 6, 12, 18, and 30 mo <i>Sample:</i> N = 66 first molars (22 children) <i>Randomization:</i> assignment randomly selected and distributed in groups <i>Inclusion criteria:</i> age 5–7 y with first molar with occlusal active initial caries without cavitation <i>Diagnostic criteria:</i> modified Carvalho index (visual); radiographs at 6, 12, and 30 mo <i>TX groups:</i> cross-toothbrushing technique; 10% SDF; glass ionomer cement <i>SDF application technique:</i> applied in active caries lesions <i>SDF adverse events:</i> black stains</p> <hr/> <p>Yee et al (2009),⁴⁰ Nepal</p> <hr/> <p><i>Design:</i> 24 mo; RCT; blind <i>Sites:</i> kindergarten and primary schools <i>Visits:</i> baseline and follow-up (6, 12, and 24 mo) <i>Sample:</i> N = 976 (80% power, $\alpha = 0.05$) <i>Randomization:</i> computer-generated list During randomization, sociodemographic characteristics were distributed homogenously between groups. <i>Inclusion criteria:</i> age 3–9 y <i>Diagnostic criteria:</i> DMFT and caries activity (changes in dentin hardness) <i>TX groups:</i> 38% SDF without tea (SDF applied for 2 min); 38% SDF with tea (SDF applied for 2 min); 12% SDF without tea (SDF applied for 2 min) <i>Control:</i> no treatment <i>SDF application technique:</i> no caries removal <i>SDF adverse events:</i> none reported</p> <hr/>
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Dos Santos et al (2012),⁴¹ Brazil

Design: 12 mo; RCT

Sites: municipal schools

Visits: baseline, 6 mo, and 12 mo

Sample: N = 91 (90% CI, $\alpha = 0.05$)

Randomization: by school

Inclusion criteria: age 5–6 y with primary teeth with active caries lesion with score of ICDAS 5

Diagnostic criteria: ICDAS (code 5); Miller criteria; active caries lesions in the SDF group; failure of the sealant in the interim restorative treatment group (consistency of the dentin, resistance to probing)

TX groups: 30% SDF; interim restorative treatment

SDF application technique: in primary teeth, no removal of carious tissue

SDF adverse events: none reported

Monse et al (2012),⁴² Philippines

Design: 18 mo; RCT; blind

Sites: 8 public elementary schools

Visits: nonspecified

Sample: N = 1016 (80% power, $\alpha = 0.05$)

Randomization: class list

Inclusion criteria: age 6–8 y with at least 1 erupted permanent first molar with a sound occlusal surface

Diagnostic criteria: WHO procedure tools and caries scores

TX groups: 38% SDF plus tannic acid (1 application); ART glass ionomer cement sealants plus high-viscosity material

Control: no TX

Due to noncompliance with the brushing program (3 schools), children were divided into nonbrushers and brushers during analysis.

SDF application technique: sound occlusal surfaces (or surfaces with enamel caries) of all erupted permanent first molars

SDF adverse events: none reported

Zhi et al (2012),⁴³ China

Design: 24 mo; RCT; blind

Sites: 6 kindergartens

Visits: 6-mo intervals

Sample: N = 212 (80% power, $\alpha = 0.05$)

Randomization: computer-generated list

Inclusion criteria: age 3–4 y with active dentin caries not involving the pulp

Diagnostic criteria: visual and tactile inspection

TX groups: 38% SDF every 12 mo; 38% SDF every 6 mo; glass ionomer cement every 12 mo

SDF application technique: removal of carious tissue by hand instruments

SDF adverse events: none reported

Duangthip et al (2016),⁴⁴ Hong Kong

Design: 18 mo; RCT; blind

Sites: 16 kindergartens

Visits: baseline and 6, 12, and 18 mo

Sample: N = 304 (1670 lesions) (80% power, $\alpha = 0.05$)

Randomization: stratified randomization

Inclusion criteria: age 3–4 y with at least 1 tooth with untreated active dentin caries not involving pulp

Diagnostic criteria: diagnosis of dentin caries by visual and tactile detection (ICDAS codes 5–6); visible plaque index

TX groups: 30% SDF at baseline every 12 mo; 30% SDF (3 applications at weekly intervals from baseline); 5% sodium fluoride varnish (3 applications at weekly intervals from baseline)

SDF application technique: no removal of carious tissue

SDF adverse events: black stains

Abbreviations: ART, atraumatic restorative treatment; CI, confidence interval; DMFT, decayed, missing, and filled teeth; ICDAS, International Caries Detection and Assessment System; RCT, randomized controlled trial; SDF, silver diamine fluoride; TX, treatment; WHO, World Health Organization.

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Table 2

Concentrations and source of silver diamine fluoride in the studies included in the systematic review.

Concentration	Product	Manufacturer	Country	Studies
38%	Fluoroplat	NAF Laboratorios	Argentina	Llodra et al ³⁸
10%	Cariostatic	Inodon Laboratório	Brazil	Braga et al ³⁹
12%	SDF	PROBEM Laboratório de Produtos Farmacêuticos Odontológicos	Brazil	Yee et al ⁴⁰
30%	Cariestop	Biodinâmica	Brazil	Dos Santos et al ⁴¹ ; Duangthip et al ⁴⁴
38%	Saforide	Bee Brand Medical/Toyo Seiyaku Kasei	Japan	Yee et al ⁴⁰ ; Monse et al ⁴² ; Zhi et al ⁴³

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Table 3

Results of the studies included in the systematic review.

Study (year)	Objective	Statistical analysis	Results
Llodra et al (2005) ³⁸	Assess the effectiveness of 6-month application of 38% SDF in preventing and arresting caries in primary and permanent teeth and compare with results in a control group	Student <i>t</i> test Multiple linear regression	N = 452 Drop-out: n = 79 SDF was more effective for caries reduction in primary teeth (80%) and first molars (65%) than a control group.
Braga et al (2009) ³⁹	Compare the effectiveness of SDF in arresting occlusal caries in erupting permanent first molars with the effectiveness of other noninvasive approaches (CTT and GIC)	Kruskal-Wallis test Friedman test	N = 66 first molars (22 children) Drop-out: n = 8 (molars) After 3 and 6 months, 10% SDF showed a significantly higher capacity than CTT and GIC for arresting caries. A general reduction in active lesions was noted in all groups (<i>P</i> < 0.05).
Yee et al (2009) ⁴⁰	Compare the effectiveness of a single application of 38% or 12% SDF, with or without the use of a reducing agent (tea), in arresting caries	ANOVA Student <i>t</i> test	N = 976 Drop-out: n = 342 The number of arrested carious surfaces was significantly higher in 38% SDF and 38% SDF plus tea groups at 6 and 12 months (<i>P</i> < 0.001) and 24 months (<i>P</i> < 0.01) than it was in 12% SDF and control groups.
Dos Santos et al (2012) ⁴¹	Compare the caries-arresting properties of 30% SDF with those of IRT using GIC	Descriptive statistics Chi-square test Fisher exact test	N = 91 (345 teeth) Drop-out: n = 23 teeth After 12 months, SDF was 1.73 (95% CI, 1.38–2.18) times more effective in arresting caries (RR, 66.9%) than IRT (RR, 38.6%) (<i>P</i> < 0.05).
Monse et al (2012) ⁴²	Compare the effectiveness of 1 application of 38% SDF with that of ART sealants and no treatment in the prevention of dentinal caries (D3 lesions)	Chi-square test Cox proportional hazard model	N = 1016 children Drop-out: n = 312 children The caries increment was lower in toothbrushing children than in nontoothbrushing children. HR was statistically significant for the nontreated children (HR, 0.43; CI, 0.21–0.87; <i>P</i> < 0.02) and the sealant-treated children (HR, 0.15; CI, 0.03–0.072; <i>P</i> < 0.02).
Zhi et al (2012) ⁴³	Compare the effectiveness of annual and semiannual topical application of SDF solution with that of annual application of GIC in arresting active dentin caries in primary teeth	Chi-square test ANOVA Multilevel nonlinear logistic regression model	N = 212 (719 lesions) Drop-out: n = 31 The group receiving 6-month applications of SDF showed higher caries arrest rates (OR, 2.98; CI, 1.35–6.69; <i>P</i> = 0.007) than groups receiving annual applications of SDF or GIC.
Duangthip et al (2016) ⁴⁴	Compare the effectiveness of 3 topical fluoride application protocols (weekly SDF [3×], annual SDF, and NaF [3×]) in arresting dentin caries in the primary dentition	Chi-square test ANOVA Survival analysis (Bayesian approach)	N = 304 (1670 lesions) Drop-out: n = 29 At 6 and 12 months, groups receiving intensive application of SDF had higher caries arrest rates than other treatment groups (annual SDF and weekly NaF varnish applications). At 18 months, the group receiving an annual SDF application presented a higher caries arrest rate (40%) than the groups receiving intensive SDF and NaF treatments (<i>P</i> < 0.001).

Abbreviations: ANOVA, analysis of variance; ART, atraumatic restorative treatment; CI, confidence interval; CTT, cross-toothbrushing technique; GIC, glass ionomer cement; HR, hazard ratio; IRT, interim restorative technique; NaF, sodium fluoride; OR, odds ratio; RR, relative risk; SDF, silver diamine fluoride.