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EFFECTIVENESS OF TOPICAL SILVER DIAMINE FLUORIDE FOR MANAGEMENT OF DENTAL CARIES IN CHILDREN AND EARLY ADOLESCENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Aim of the study This review aims to assess the effectiveness of topical SDF compared to no treatment or other alternative treatments for management of dental caries in children and early adolescents. **Materials and methods** Several databases were searched to include randomized controlled trials that compared SDF with placebo or no treatment and other interventions. Records published until January 2025 without language restriction were included. Quality assessment was performed using the Cochrane risk of bias tools. For meta-analysis effect-sizes were calculated for continuous and categorical outcomes. **Results** Findings from 37 randomized controlled trials that met inclusion criteria revealed potential benefit of SDF application compared to no treatment or placebo in caries arrest and prevention of new caries in primary dentition with follow-up intervals ranging from 3-36 months. In addition, pooled analysis of studies suggested that SDF was more effective than other conservative treatments in arresting caries while for prevention of caries SDF benefit was comparable to other fluoride agent application or less beneficial in primary dentition. **Conclusions** These results provide further evidence for clinical application of SDF in treatment of carious lesions in primary dentition. Further research and rigorous designed clinical trials are warranted to confirm these findings and explore the potential of topical SDF alone or combined with other agents for caries management in pediatric population.

Key words: Caries arrest; Dental caries; Prevention; Primary dentition; Silver diamine Fluoride

INTRODUCTION

Despite water fluoridation in many countries [1, 2] and the widespread use of fluoridated dental products,[3] resulting considerable reduction in caries incidence, dental caries remains a highly prevalent public health concern in children and adolescents worldwide [4, 5]. The global estimate of early childhood caries prevalence was reported to range from 34% to 72% with the highest rate reported for Middle East and found to be significantly associated with socioeconomical conditions [5]. Similarly, in school-aged children and early adolescents (5-14 years), incident cases of dental care have increased over 15% during the last two decades [4]. Children with dental caries can experience tooth pain [6], poor academic achievement and school absenteeism [7] as well as reduced quality of life [8]. These trends highlight the need to focus attention on prevention and intervention efforts to effectively manage dental caries in pediatric population.

Several fluoride agents have shown to be efficacious in management of dental caries especially in younger children. In the last five years, research and clinical interest in application of silver diamine fluoride (SDF) as an alternative conservative treatment option for dental caries arrest and prevention has increased exponentially [9]. The so-called “silver-fluoride bullet” due to the antibacterial effect of silver nitrate combined with the remineralization ability of sodium fluoride has been heralded as an effective caries-preventive intervention [10].

First developed in Japan more than six decades ago, apart from caries management in primary teeth, SDF has been found to be effective in a broad range of clinical applications in dentistry including reducing dentine hypersensitivity [11], prevention of secondary caries [12, 13] and root caries lesions in permanent teeth [14]. The main drawback with the use of SDF is the black staining of arrested carious lesion due to silver particles, however the esthetic appearance does not influence satisfaction of parents and deemed acceptable

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[15], since parents prefer to delay or avoid the possibility of invasive treatment or general anaesthesia [16]. In light of the ease of use, cost-effectiveness, management of caries in uncooperative younger children and less chairside than other treatment options, a number of systematic reviews [12, 17-19] and meta-analyses [20-26] have been recently published on the effectiveness of SDF in arresting or preventing dental caries. However, none of the recent meta-analyses were focused on evaluating SDF application compared to other treatments in young children and early adolescents for management of caries. These meta-analyses were not on SDF comparison but a range of professionally applied fluoride treatments.[22] and included all age groups [20, 21] reported caries arrest only [20, 23, 24, 26] or prevention as outcome only [25].

Since the demographic at highest risk of dental caries is young children and adolescents [4, 5], the overarching aim of this systematic literature review and meta-analysis was therefore to evaluate evidence for effectiveness of topical SDF compared to other conservative treatments for management of dental caries and prevention during early childhood early adolescents.

MATHERIALS AND METHODS

Search strategy

Databases searches were conducted in PubMed, Embase, SCOPUS and Web of Science from inception to 30th January 2025 inclusive without any language restrictions. In addition, manual searches of citations and references of potential eligible studies were searched for relevant studies. The search strategy was based on combining key words with controlled vocabulary (MeSH terms) using the concepts related to children AND Silver Diamine Fluoride AND Dental caries (Table 1 and Table 2).

Selection criteria

Following uploading and deduplication of retrieved records from databases in Endnote reference manager (Endnote X9.3.3 version), potentially eligible studies were initially screened by title and abstract then by full-text screening. Studies were considered eligible if they were peer-reviewed randomized clinical trial (RCT) with at least 3 months of follow-up, reported on healthy children up to 14 years of age, involved treatment with topical SDF compared to other alternatives or placebo, and reported on caries arrest or prevention as an outcome. Studies that were non-randomized trials, included children with special needs, participants 15 years or older, reported on SDF combined with other materials or as part of restoration, did not include a comparator and were on other outcomes than management of caries were excluded. When more than one eligible study included same sample, the study with longer follow-up was included for data synthesis. Full details of eligibility criteria can be found in Table 3.

Data collection

Studies that met the inclusion criteria were further considered for data extraction and risk of bias assessment. Data extraction from eligible studies included authors, publication year, country of study, population characteristics including sample size at baseline, intervention and comparator details, type of dentition and severity of lesion, outcome of interest, duration of follow-up and finding related to outcomes of interest.

Assessment of risk of bias

Potential risk of bias of eligible studies were assessed using the revised Cochrane Risk of Bias tool for randomized trials (RoB.2) [27]. This tool is designed to assess randomization, deviations from intended interventions, missing outcome data, measurement of outcome, selection of reported results and overall bias [27]. The items are ranked as low risk of bias, high risk of bias and some concern if the risk of bias is unclear. Robvis visualization tool was used to construct a risk of bias assessment plot [28].

Data synthesis and statistical methods for meta-analysis

Data were computed using fixed-effect model meta-analysis and categorized according to numeric (continuous) and non-numeric (categorical) types. The software Review manager Revman 5.4.1 was used to perform the meta-analysis and generate an overall pooled prevalence estimate, Forest-plot and funnel plot. The categorical data was expressed as Odds Ratio (OR) with 95% confidence interval. The continuous data was expressed as mean difference (MD) with 95% confidence interval (CI). Chi-square test was used for validity of results. The inconsistency statistic (I2) was used for comparison of data. The inconsistency level

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more than 80% shows that a considerable inconsistency in results of studies and suggesting that studies not measure the same concepts. A p-value less than 5% was considered as statistical significance. Pooled analysis was considered if two or more studies compared the effect of SDF versus alternative or no treatment for outcomes of interest (caries arrest and prevention of caries). For each study, data reported at the longest follow-up time point was used. Potential publication bias (reporting bias) was investigated in any meta-analysis that included more than 10 studies by assessing for asymmetry in a funnel plot [29].

RESULTS

Study selection

The initial search strategy identified 5674 records from databases and manual searches. After deduplication and initial screening of 2225 records, the full-text of 72 publications that met eligibility criteria were reviewed and 39 records were deemed eligible. Since two of the randomized controlled trials with different follow-up duration were published as four records, we therefore only included two of the records with the longest follow-ups for a total of 37 randomized controlled trials in the final analysis. Most of excluded studies did not report on relevant outcomes, SDF intervention or randomized design with adequate follow-up period. Also records that did not include a comparison to SDF and just compared different SDF application protocols were excluded (Fig. 1).

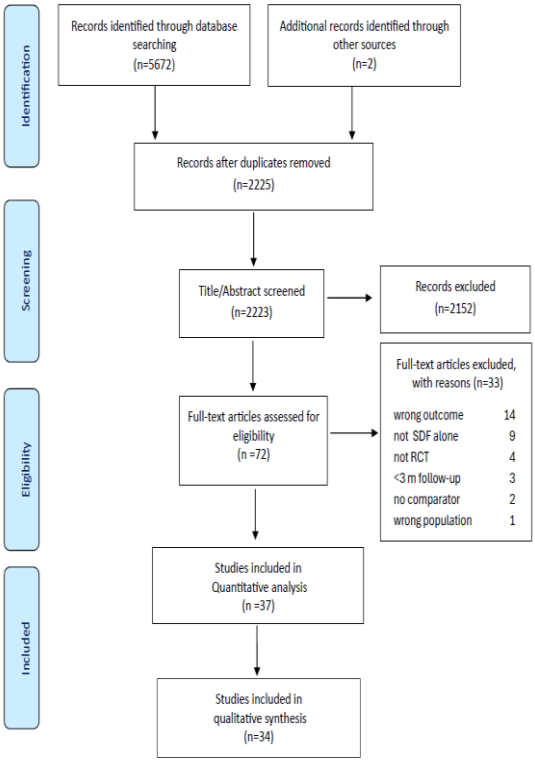

Figure 1. Flow chart of study process

Study characteristics

The summary of the main characteristics of included studies is presented in Table 4. All the eligible studies in the review were RCTs with 31 trials double-arm and 6 trials multi-arm studies. Most of the studies were conducted in Egypt (n= 7) followed by India (n= 6), Brazil (n=5), Hong Kong (n=4), Syria (n=3), Thailand (n=3), China (n= 2) and USA (n=2) with one study conducted in each of the following countries: Cambodia, Cuba, Nepal, Nigeria, and Saudi Arabia. All studies included children younger than 12 years and twelve studies had a follow-up of more than 12 months (ranged from 3 months to 36 months). Nearly half of studies applied SDF biannually (n=18), a third as a single application (n=11) with four studies applied SDF annually, two studies quarterly, and two studies applied SDF two to four weeks apart.

More than half of the studies compared topical SDF to other fluoride varnish applications (n=19) of which majority were compared to 5% sodium fluoride varnish (n=11, 58%) followed by nano silver fluoride (n=6, 32%). Ten studies compared SDF to no treatment or placebo, eight trials compared SDF to minimally invasive restorative treatments (one was invasive restoration), while four studies compared SDF to sealants or infiltrates, and five studies with multiple arms compared SDF to either other techniques or SDF combined with other treatments. More than three-quarters of studies used 38% SDF (n=30) and the rest applied 30% SDF (n=5) or 10% SDF (n=2). Outcome assessment was variable with lesion severity assessed based on different criteria where majority of studies (n=24) used the international caries detection and assessment system (ICADS) criteria and five studies did not report lesion severity. The effectiveness of SDF in arresting dental caries was examined in 23 studies, prevention efficacy in eight studies while six studies reported on both caries arrest and preventive effectiveness as outcomes. Four studies reported on permanent teeth with the rest

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on primary teeth.

Quality assessment

The overall risk of bias assessment was performed for 36 studies since the study by Mattos- et al (2015) had insufficient information in all domains to allow risk of bias assessment. More than half of studies (n=26) had at least one domain with some concern or high risk of bias (Fig. 2). In total, 12 studies were judged as low risk, 8 with some concern and 16 studies judged to be of high concern (Fig. 2). In particular, these methodological issues due to insufficient information regarding deviation from trial protocol, unclear selective reporting, attrition and inadequate information about outcome assessment affected quality rating of the included studies (Fig. 3).

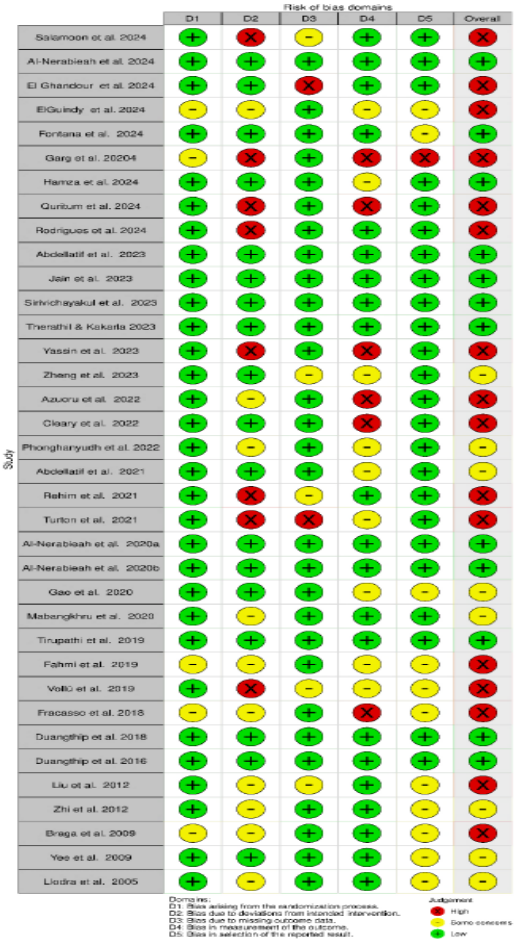

Figure 2. Risk of bias summary

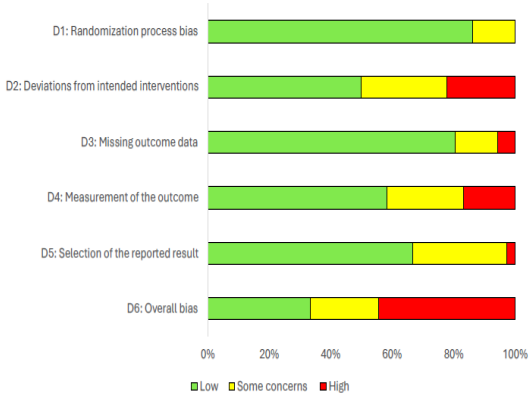

Figure 3. Risk of bias graph

Outcome of the included studies

Nearly half of the included studies found topical SDF application was effective compared to no treatment or other alternative treatment options (n= 18), while 43% of studies found comparable efficacy (n=16), two studies found other options more effective than SDF and one study reported SDF combined with fluoride varnish more effective than SDF alone. In terms of caries arrest majority of studies favoured SDF (n=13/29) while most studies that reported prevention as an outcome showed comparatively similar effectiveness (n=10/29) between SDF and other interventions (or placebo) when applied as a single or biannual application. However, the number of applications or concentration of SDF did not appear to correlate with the number of studies that reported caries arrest or preventive effect of SDF compared to other treatments, but pooled analysis was not done due to high heterogeneity among studies to confirm this. Of the four studies that reported on caries arrest and or preventive effect on permanent molars, SDF application was more effective than other treatments for caries management in three studies while effectiveness was comparable to the control in one study.

Meta-analysis

Data from 34 studies were quantitatively analysed since one study did not have sufficient outcome data to be included [30], one study reported application of SDF compared to laser treatment [31], and one study compared SDF to combination of SDF and fluoride varnish [32]. In addition, pooled analysis was not possible on two studies that had multiple arms comparing SDF to SDF combined with other materials [33, 34]. Majority of the studies were highly

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heterogenous. Studies that could not be pooled for a meta-analysis due to differences in SDF concentrations, frequency of applications, and duration of treatment are described narratively.

Comparison of SDF to placebo or no treatment

A total of ten studies provided data on caries arrest [33, 35-38] and caries prevention [36, 39-42] in primary teeth with two studies on caries arrest [36, 43] and one on caries prevention [36] in permanent teeth for this comparison. Pooled data from studies reporting continuous outcomes (Fig. 4A), showed effectiveness in favour of SDF compared to placebo/no treatment but not statistically significant difference for caries arrest outcome (MD: 0.10, 95%CI: -0.06 to 0.27, p=0.22) [33, 35, 36]. However, compared to placebo SDF application was significantly effective at caries prevention (MD: -0.57, 95%CI: -0.74 to -0.40, p<0.00001) (Fig. 4B) [36, 39].

Meta-analysis for categorical data on caries arrest (Fig. 4C) showed significant effect in favour of SDF compared to placebo or no treatment (OR: 3.49, 95%CI: 2.63 to 4.62, p<0.00001) [37, 38, 43]. Similarly, there was significant benefit in favour of SDF for caries prevention (Fig. 4D) (OR: 2.22, 95%CI: 1.23 to 3.99, p=0.008). Separate data for permanent teeth was only available from one study which showed statistically significant benefit in favour of SDF compared to no treatment for both caries arrest (OR: 0.20, 95%CI: 0.01 to 0.39, p=0.04) and caries prevention (OR: -0.73, 95%CI: -1.01 to -0.46, p<0.00001) [36].

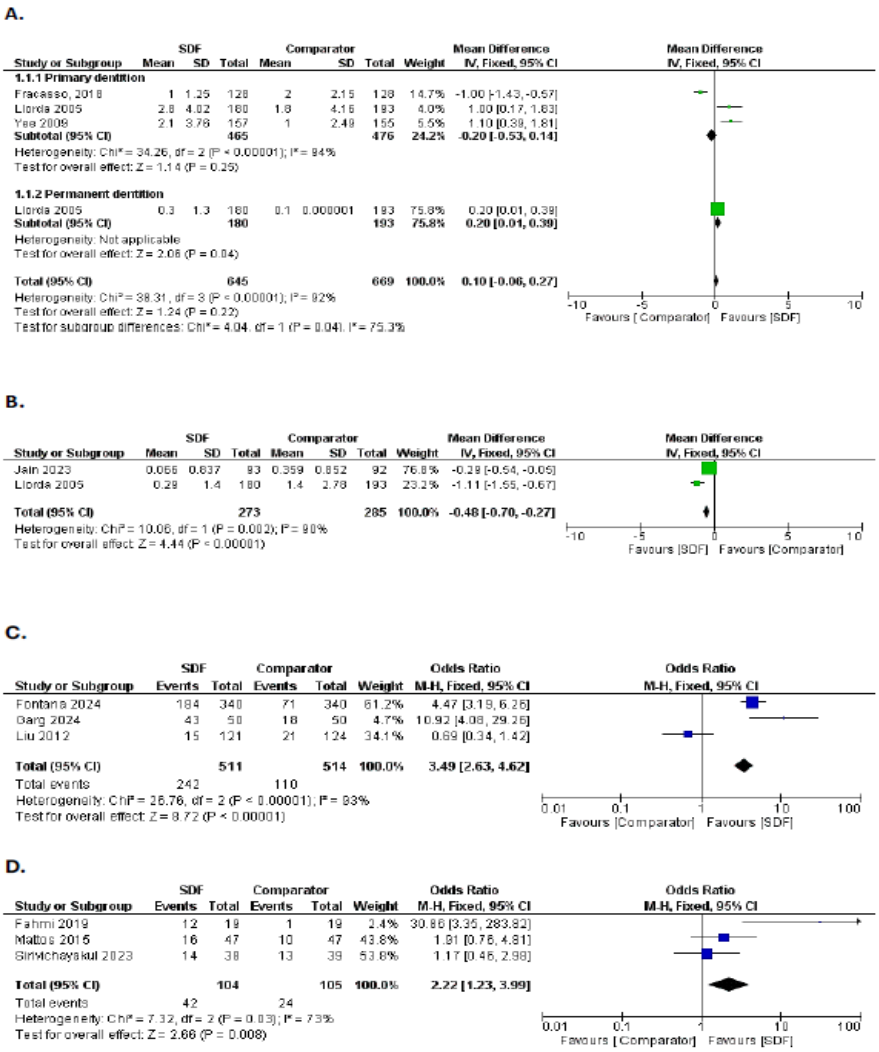

Figure 4. Forest plot for pooled analysis of SDF versus placebo/no treatment. A) continuous data on caries arrest, B) continuous data for caries prevention, C) categorical data on caries arrest, D) categorical data on caries prevention. CI is the confidence interval; df is the degrees of freedom.

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Comparison of SDF to other topical fluoride agents and sealants

In total, data was provided by 23 studies on caries arrest [34, 44-55] and caries prevention [39, 41-44, 49, 53, 56-58] in primary teeth with one study on caries arrest [44] and two studies on caries prevention [43, 44] in permanent teeth for this comparison. Pooled data from 13 studies reporting categorical outcomes for arrested caries (Fig. 5A) showed that SDF compared to other topical fluoride agents was significantly beneficial in arresting caries at the longest follow-up (OR: 1.39, 95%CI: 1.28 to 1.52, p<0.00001). However, the funnel plot was asymmetrical since five studies were outside the 95% CI suggesting the presence of publication bias (Fig. 6). In contrast, pooled analysis of eight studies (Fig. 5B) was statistically significant in favour of other fluoride agents compared to SDF in preventing caries (OR:1.37, 95%CI:15 to 1.64, p=0.0005). Continuous data from two studies showed similar effectiveness between SDF and other varnishes (Fig. 5C) for prevention of caries [49, 58]. Of note these two studies did not report the severity of lesions.

Although data was available from three studies on the use of sealants/resin infiltrate compared to SDF, however pooled analysis was not possible due to differences in concentration of SDF used. In all of these three studies, application of SDF compared to sealant/infiltrate was found to be more effective in arresting caries [35] (OR:7.15, 95%CI: 0.81 to 63.30, p=0.08) and prevention of caries [41, 43] (OR:1.99, 95%CI:0.95 to 4.7, p=0.07) but not significant. A further study which did not provide sufficient outcome data for analysis found that while the rate of arrested caries in permanent first molars was significantly higher in children treated with 10% SDF than those treated with sealant after six months, however after 30 months all groups were comparatively effective at arresting carious lesions [30].

Comparison of SDF to conservative restorative treatment

Eight studies provided data on caries arrest [59-66] and one on caries prevention [61] in primary teeth for this comparison. The pooled analysis of categorical data (Fig. 5D) showed that SDF was significantly more effective at arresting caries than restorative treatment in primary teeth (OR: 1.46, 95%CI: 1.05 to 2.03, p=0.02) [59-61, 63-66]. Continuous data for one study showed comparative effectiveness between SDF and restorative treatment for caries arrest (MD: 0.22, 95%CI: -0.40 to 0.84, p=0.49) [62]. Analysis of one study showed that restorative treatment was non-significantly more effective at preventing caries than SDF application (OR: 9.14, 95%CI: 0.49 to 172.21, p=0.14) [61].

Comparison of SDF to combination of SDF with other materials

Three studies with multiple arms compared SDF to SDF combined with other materials [33, 34] or other non-invasive techniques [30] for caries arrest or caries prevention outcomes. In one study, topical application of 38% SDF alone or with tannic acid was effective while 12%SDF was not effective at arresting varies lesions in primary teeth [33]. In a four-armed parallel-design RCT that compared SDF to SDF plus potassium iodide (KI) or aqueous silver fluoride (AgF) plus KI, both SDF and AgF showed comparative benefits at arresting caries compared to the KI combination [34]. When combined with fluoride varnish (5% NaF) significantly greater caries arrest effect was reported compared to application of SDF alone on moderate lesions [32]. A study that compared SDF to sealant and cross tooth-brushing technique found that while arrested caries in permanent first molars was significantly higher at six-months with SDF application, however after 30 months all groups were comparatively effective [30]. A further study that compared application of SDF to iodide laser irradiation found that while both therapies were effective, SDF had a non-significant higher inhibitory effect on caries prevention in primary molars [31].

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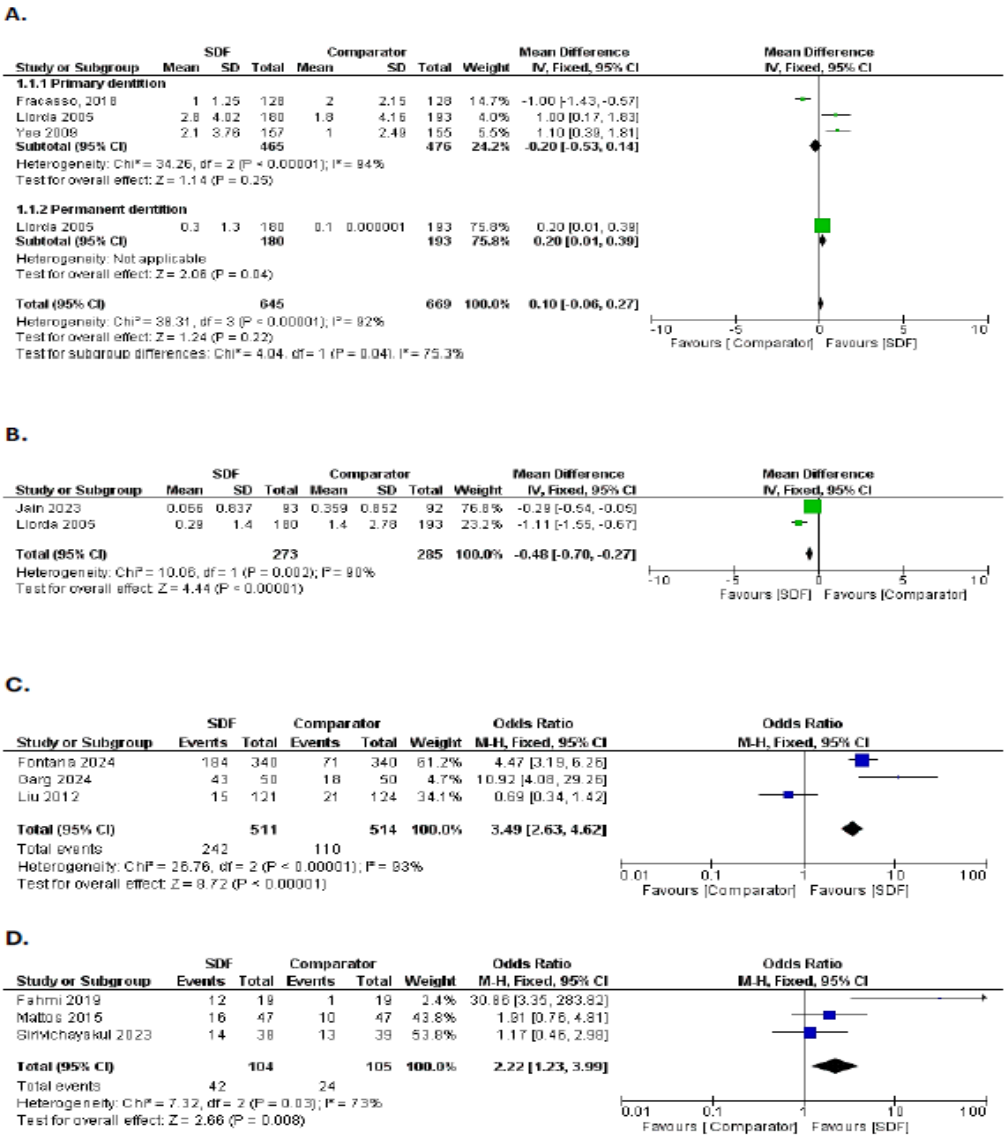

Figure 5. Forest plot for pooled Analysis of SDF versus other topical fluoride varnishes and restoration. A) categorical on caries arrest, B) categorical data for caries prevention, C) continuous data on caries prevention. D) Forest plots for restorative treatment categorical data on caries arrest. CI is the confidence interval; df is the degrees of freedom.

DISCUSSIONS

This study is the largest pooled analysis of SDF compared to other alternative conservative treatments for management of caries in children and early adolescents to date. The focus of this systematic review and meta-analysis was primarily on the efficacy of SDF in arresting and preventing dental caries compared to no treatment or alternative conservative treatments in children and early adolescents. Overall, the meta-analysis findings are in agreement with previous analyses that indicate for primary dentition SDF may offer benefit in management of dental caries in particular preventing caries compared to no treatment in children and early adolescents [20, 21, 26, 67]. In addition, quantitative analysis showed that for primary dentition SDF is significantly effective or comparative to other conservative treatment in arresting caries. However, SDF offered little, or no benefit compared to other fluoride varnishes for preventing dental caries in primary dentition. The differences were mainly due to high heterogeneity across the included studies and wide confidence intervals of some of the studies. Although SDF is not commonly applied in

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permanent dentition, however few studies reported its benefit to arrest and prevent caries in newly erupted first permanent molars [30, 36, 43, 44]. Due to differences in SDF concentrations and comparators. a meta-analysis was not possible to analyse the effectiveness of SDF in permanent molars for caries management and more research in this area is needed.

The available evidence indicates that compared to placebo (or no treatment) SDF was more effective at arresting caries and preventing progression of existing caries consistently across both continuous and categorical data sets. The pooled analysis of comparison with other fluoride agent applications demonstrated that SDF was significantly more effective in arresting caries, whereas for prevention of new caries SDF benefit was comparable to other fluoride agent application or less beneficial in primary dentition. This discrepancy is likely due to the use of differences in detection criteria and statistical analysis of outcomes for caries prevention, highlighting the need for standardized analysis and definition of caries incidence or prevention in research. While compared to conservative restorations, pooled analysis showed that SDF was significantly effective or comparative to restorative treatment in arresting caries, a small study that reported caries prevention outcome found that restorative treatment was more effective than SDF in prevention of secondary caries [61]. This study did not use atraumatic restorative treatment unlike other studies but conventional restorative treatment with local anaesthetic and was included in this review due to limited number of studies on prevention of secondary caries, highlighting an area of research that needs further evaluation to explore use of SDF for preventing progression and development of caries. In addition, a few studies reported benefits of SDF compared to sealants or resin infiltrates although our analysis revealed benefit of SDF compared to sealant (or resin infiltrate) for both caries arrest and primary prevention, this effect was not statistically significant and clinical relevance warrants further investigation.

Apart from SDF comparison with placebo and other alternative interventions, few studies also reported SDF comparison to other techniques, materials, or SDF combined with other anticaries agents. Although evidence was limited and statistical pooling was not possible owing to high heterogeneity, nevertheless the two studies on comparison to other techniques showed that SDF application was comparable to cross-brushing technique for arresting caries in erupting first permanent molars after 30-month follow-up period [30] while more beneficial than laser irradiation in preventing caries lesions in primary molars at 12-month follow-up [31]. Furthermore, application of SDF alone or combined with reducing agent (tannic acid) was found to be more effective than no treatment while 12%SDF was not effective at arresting varies lesions in primary teeth [33]. In another randomized trial compared to application of SDF alone, combination of SDF with fluoride varnish was found to be more effective at caries arrest in primary teeth [32]. However, SDF alone was more effective at arresting caries than SDF-KI combination [34]. These studies highlight the need to explore SDF combination with other non-invasive interventions to evaluate efficiency and effectiveness at caries management.

Previous meta-analyses findings are largely in agreement with our results. A recent Cochrane review concluded that SDF offers benefit in caries arrest compared to placebo/no treatment in primary dentition with limited evidence on effectiveness of SDF in preventing progression of existing caries [21]. Consistent with our findings, other meta-analyses have found SDF was more effective than other active treatments or placebo for arresting caries in primary teeth after 12-months of follow-up [26] and significantly reduced the development of new dentin caries lesions compared to placebo (or no treatment) or other fluoride varnish applications [25]. In addition, SDF has been shown to be more effective at arresting cavitated lesions in primary molars at higher concentration and when applied biannually at 12-months or greater follow-up [24]. However, an overall pooled analysis of studies on the efficacy of SDF for caries arrest on the individual, tooth, and surface levels did not show statistically significant difference between SDF and control or other alternative interventions [20], highlighting the differences in selection of studies, eligibility criteria and methodological design of reviews. Collectively, our meta-analysis and previous evidence support clinical benefit of SDF as a minimally invasive intervention for management of caries in children and early adolescents.

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Strengths and Limitations

This systematic review and meta-analysis had several strengths including searches of several databases and the quality of evidence was based on pooling a large number of relevant studies that despite high variability in methodology showed SDF was more effective than placebo/no treatment or conservative interventions in caries management. Furthermore, while the Cochrane review and other meta-analysis studies based their conclusions for SDF comparison to control or other alternative interventions on pooled analysis limited to one or two studies, most of our meta-analysis included three or more studies with up to 13 studies for caries arrest outcome when comparing SDF to other fluoride varnishes. In addition, recent years has seen an exponential growth in research published on effectiveness of SDF with a third of our included studies published in the last two years alone. Nevertheless, more research is needed to confirm and strengthen our findings to draw more definitive conclusions on the preventative benefit of SDF in caries prevention.

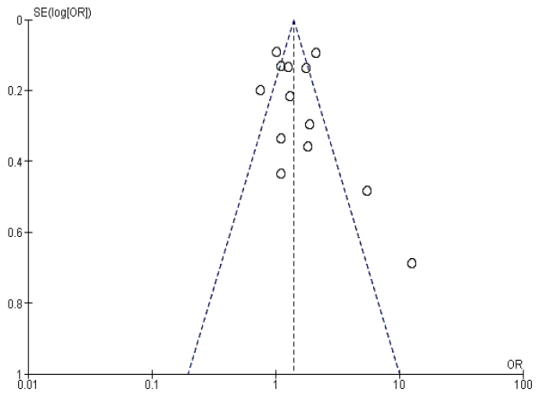

Figure 6. funnel plot for evaluating the presence of publication bias

The findings of this review should be interpreted in consideration of a number of limitations. Majority of studies did not provide information on local level of water fluoridation or socioeconomic demographics of participants such as limited access to dental care which are important variables to consider and future trials should take these factors into account. Only a third of the eligible studies were considered to have low risk of bias as most had methodological deficiencies which affected quality rating of the included studies. The studies were highly heterogeneous and varied greatly in design, SDF application protocol, outcome measures (e.g., variations in scales for cavitated lesions), analysis of outcomes and follow-up periods. Specifically, the variability in the statistical analysis of outcomes was quite high which meant that few studies could be pooled together for comparison and therefore statistical analysis underpowered to detect statistical significance for some of the meta-analyses. Although this reduction in primary or secondary caries prevention benefit of SDF may be clinically relevant, the high heterogeneity ($I^2 > 80\%$) and wide confidence intervals of some of the studies may limit the reliability of these findings. More rigorous designed studies and high-quality evidence are needed on the benefits of SDF applications for prevention of caries lesions in both primary and permanent dentition.

We did not analyse different approaches to SDF application and compare effectiveness of various concentrations of SDF in caries arrest as a recent Cochrane review comprehensively analysed these comparisons to identify effective and safe concentration of clinical SDF application [21]. Nevertheless, more research is warranted to develop evidence-based application protocols to determine effective and safe concentration of SDF application.

Although it was outside the scope of this review to assess preference, acceptability, and satisfaction using SDF treatment among professionals or parents, several studies have demonstrated acceptability by parents [44, 68-70] but the drawback of black staining of arrested carious lesions was a barrier to wide use of SDF by oral health professionals [71, 72]. Despite this conclusion future controlled clinical trials should explore professional use of SDF and parents together with patients self-reported outcomes.

CONCLUSIONS

1. SDF was more effective than other conservative treatments in arresting caries The second conclusion.
2. SDF was comparable or less beneficial to other fluoride agents for caries prevention.
3. SDF was more effective in caries arrest and prevention than no treatment or placebo.

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Table 1. Key search terms based on the Population, Exposure and Outcome Framework.

Framework	Key terms
Target populations	Children OR child OR early adolescent OR "preschool child" OR "Child, Preschool"[Mesh]
Exposure	"silver diamine fluoride" OR "silver diamine" OR "silver fluoride" OR "diamine silver" OR "Silver Nitrate" OR AgF OR Ag-nano OR "Silver Compounds/administration and dosage"[Mesh]
Outcomes	"demineral*" OR "remineral*" OR caries OR decay OR "dental decay" OR cavit* OR lesion OR "carious lesion" OR "caries arrest" OR "Dental Caries"[Mesh] OR "Dental caries/prevention and control"[Mesh]

Table 2. Search strategy for PubMed*

No.	Search term combinations
#1	Children OR child OR early adolescent OR Pediatric OR paediatric OR "preschool child" OR "Child, Preschool"[Mesh]
#2	"silver diamine fluoride" OR "silver diamine" OR "silver fluoride" OR "diamine silver" OR "Silver Nitrate" OR AgF OR Ag-nano OR "Silver Compounds/administration and dosage"[Mesh]
#3	"demineral*" OR "remineral*" OR caries OR decay OR "dental decay" OR cavit* OR lesion OR "carious lesion" OR "caries arrest" OR "Dental Caries"[Mesh] OR "Dental caries/prevention and control"[Mesh]
#4	Review OR "Systematic review" OR "Meta-analysis"
#5	#1 AND #2 AND #3 NOT #4
#6	#1 AND #2 NOT #4
#7	#2 AND #3 NOT #4
#8	#7 AND filters Infant: birth-23 months, Preschool Child: 2-5 years, Child: 6-12 years, Adolescent: 13-18 years
Total**	#5 AND #6 AND #8

*The search was adapted for other databases.

Table 3. Eligibility criteria.

Study Framework	Inclusion criteria	Exclusion criteria
Study Population	Healthy children and early adolescents aged 0-14 years	In vitro or Animal studies Middle-late adolescents (15-18 years) and adults (>18 years) Medically compromised children
Exposure	Topical Silver diamine fluoride (SDF) of any concentration	SDF combined with other materials or as part of restoration Other preventative methods

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Comparator	No intervention, placebo, other fluoride agents, any cariostatic agent, sealant, dental restorative materials	No control No comparator Different approaches to SDF application
Outcomes	Primary or secondary caries prevention arrest carious lesions	Other outcomes
Study Design	Randomized controlled trials	Quasi-experimental, observational, retrospective, case-control studies Cross- sectional, cohort, case- series, case reports, reviews conference proceedings, Commentaries or letters to editor, Theses
Others	At least 3 months of follow-up No language or date restrictions	Less than 3 months follow- up
Filters to apply	None	
Databases to search (4 in total)	PubMed, Embase, SCOPUS, Web of Science	

Table 4. Characteristics of included studies

Study Country	Population characteristics*	Intervention	Comparator	Teeth/ Lesion severity	Outcome assessment [Follow-up]	Findings
Salamoon et al. 2024 **Egypt**	Total 62 <6 years	38% SDF Biannual application	Sodium Fluoride Varnish (5% NAF) 3-monthly application	Anterior & posterior primary teeth ICDAS 3,4,or 5	ICDAS II criteria Visual assessment of lesions [3,6,9,12m]	Application of biannual SDF was significantly more effective at arresting caries and reducing new caries development than NAF application after 6 & 12 months.
Al-Nerabieah et al. 2024 **Syria**	Total 100 6-9 years 58% M	38% SDF Quarterly application	CPP-ACP Fluoride Varnish	Permanent First Molars MIH	ICDAS II criteria EAPD criteria Reveal fluorescence dental loupes [3,6,9,12m]	Treatment with SDF showed a significantly lower incidence of caries & higher rate of arrested caries that CPPACPFV treatment
El Ghandour et al. 2024 **Egypt**	Total 100 2-5 years	38% SDF Single application repeated in 2-4 weeks	ART (GIC) Caries excavated	Anterior & posterior primary teeth ICDAS 5 or 6	ICDAS II criteria Visual assessment of lesions [3,6,9, 12m]	Application of biannual SDF was significantly more effective at arresting caries than ART treatment after 12 months
El Guindy et al. 2024 **Egypt**	Total 22 6-8 years	38% SDF Single application	Diode laser (980 nm wavelength)	Primary second molars ICDAS 0-2	ICDAS II criteria Visual assessment of lesions [3,6,12m]	While SDF and Diode laser irradiation were both effective, SDF had a non-significant higher inhibitory effect on caries progression in primary molars
Fontana et al. 2024 **USA**	Total 599 1-6 years 47% M	38% SDF Biannual application	Placebo	Primary teeth Severe early childhood caries (S-ECC) ICDAS 5 or 6	ICDAS II criteria Visual assessment of lesions [8 m follow-up]	SDF treatment significantly improved arrest of active cavitated lesions in young children With S-ECC
Garg et al. 2024 **India**	Total 100 3-6 years 52% M	38% SDF Biannual application	Placebo	Primary teeth Severity not reported	clinical exams digital radiographs [6,12m]	SDF arrested caries significantly at higher rate (87% of lesions) than Placebo (35%) after 12 months
Hamza et al. 2024 **Egypt**	Total 135 3–5-years 46% M	38% SDF Biannual application	ART (GIC) Caries excavated or ultraconservative treatment (UCT)	Primary Molar (occlusal) ICDAS 5 or 6	ICDAS II criteria Visual assessment of lesions [3,6,12m]	Caries arrest rate of UCT was significantly lower than SDF and ART. SDF requires less chair time and children are less anxious than during ART.
Quritum et al. 2024 **Egypt**	Total 360 ≤ 4 years	38% SDF Biannual application	Nano Silver Fluoride (NSF) Single application	Primary teeth ICDAS ≥ 3	ICDAS II criteria Visual assessment of lesions [6,12m]	At 12 months, NSF group showed significantly higher arrest rate than SDF group at lesion level (71% vs 56%, p <0.001)
Rodrigues et al. 2024 **Brazil**	Total 118 2-5 years 65% M	38% SDF Biannual application	ART (GIC) Caries excavated	Primary Molars (occlusal) 69% First Molar 49% Second Molar ICDAS 5 or 6	ICDAS II criteria Visual assessment Radiographs [6,12m]	Caries arrest was similar between the SDF and ART group but SDF required less treatment time
Abdellatif et al. 2023	Total 220 ≤ 4 years	38% SDF Biannual application	38% SDF + 5% NaF Biannual	Primary teeth ICDAS ≥ 3	ICDAS II criteria Visual assessment [6 m]	SDF + NaF had significantly greater caries arrest effect than SDF alone on moderate lesions

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Egypt	50% M		application (5% NaF varnish alone: 3 month application)			
Jain et al. 2023 **India**	Total 285 3–6 years	38% SDF Single application	Placebo or 5% NaF varnish	Non-cavitated Primary teeth ICDAS 0	ICDAS II criteria Visual assessment using LED magnifying loupes [6,12m]	Compared to placebo (46%) and 5% NAF (52%), SDF was most effective in preventing dental caries (72%) & most cost-saving fluoride therapy after 12 months
Sirivichayakul et al. 2023 **Thailand**	Total 190 4–6 years In: 50% M NaF: 45% M C: 52% M	38% SDF Biannual application	Placebo or 5% NaF varnish Biannual application	Primary teeth: 27% Canine 48% First molar 25% Second molars ICDAS 1-3	Visual assessment Bitewing radiographs [6,12,18m]	No statistically significant differences in prevention of approximal caries development between 38%SDF, 5%NaF or placebo after 18 months
Therathil & Kakarla 2023 **India**	Total 58 4-6 years 45% M	38% SDF Single application	25% silver nitrate (SN) + 5% NaF varnish	Primary First Molars active carious lesions in enamel or extending to dentine without pulp involvement	ICDAS II criteria Visual inspection [3m,6m]	Comparable effectiveness of SDF and 25%SN+5%NaF in arresting caries in primary molars.
Yassin et al. 2023 **India**	Total 165 ≤ 4 years In: 46% M NaF: 47% M	38% SDF Single application	5% NaF varnish Single application + Motivational interviewing	Primary teeth ICDAS ≥ 3	ICDAS II criteria [6 m]	Arrested caries rate for advanced lesion was significantly higher in the SDF (60%) than the NaF+MI (50%) group (p=0.01)
Zheng et al. 2023 **Hong Kong**	Total 688 3-4 years	38% SDF Single application	5% NaF varnish Single application	Primary 6 upper anterior teeth Severity not reported	WHO criteria dmft index [12m]	No difference in the caries preventive effect between SDF and FV on upper anterior teeth
Azuoru et al. 2022 **Nigeria**	Total 240 4- 10 years In 53% M C 50% M	38% SDF Single application	Restorative treatment (GIC) Caries excavated	57% Primary second Molars ICDAS 5 or 6	ICDAS II criteria Visual assessment of lesions [2 wk, 1m, 3m]	More children experienced caries arrest with 38% SDF at 2 weeks, 1 month and 3 months than restorative treatment (p< 0.001).
Cleary et al. 2022 **USA**	Total 98 2-10 years In 47% M C 62% M	38% SDF biannual application	Restorative treatment Caries excavated	63.3% Primary molars 21.4% Primary canines 15.3% Primary incisors ICDAS 5 or 6	ICDAS score Visual inspection Radiograph [12m]	While 38% SDF was effective at arresting 74% lesions, however restorative treatment showed significantly fewer failures than biannual application of 38% SDF
Phonghanyudh et al. 2022 **Thailand**	Total 290 1–3 years In 41% M NaF 44% M	38% SDF biannual application	5% NaF varnish biannual application	Active dentine caries 66% Non-cavitated enamel caries 34% Cavitated enamel caries ICDAS 2 or 3	ICADAS II criteria Visual assessment [6m, 12m,18m]	SDF and NAF showed comparable effectiveness in arresting enamel caries in primary teeth
Abdellatif et al. 2021 **Saudi Arabia**	Total 79 3-8 years In 43% M C 39% M	38% SDF 2 application Baseline 6months	ART (GIC) Caries excavated	34% Primary anteriors 66% Primary molars ICDAS 4, 5 or 6	ICDAS II criteria Tactile examination [12m]	No difference was found between SDF and ART in arresting caries in primary teeth
Rehim et al. 2021 **Egypt**	Total 62 1-6 years In: 65% M NaF: 45% M	38% SDF biannual application	5% NaF varnish Quarterly application	Carious anterior Primary teeth Early Childhood Caries (ECC)	Visual assessment [3,6,9,12m]	Biannual application of 38% SDF was significantly more effective than 5% NaF varnish in preventing new caries after 123 months..
Turton et al. 2021 **Cambodia**	Total 421 3-11 years 53% M	38% SDF biannual application	Aqueous silver fluoride solution (AgF) or AgF+ KI or SDF+KI	Primary teeth: 55% Molar lesion 45% Incisor lesion ICDAS ≥ 3	ICDAS II criteria Visual assessment [6m, 12m]	both AgF and SDF can effectively arrest carious lesions on primary teeth. When combined with Ki better aesthetics is achieved but lower arrest rate

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Al-Nerabieah et al. 2020a **Syria**	Total 63 3–5 years 46% M	38% SDF biannual application	Nano-Silver Fluoride with green tea extract (NSF-GTE)	Anterior & Posterior Primary teeth ICDAS 5	ICDAS II criteria visual & tactile inspection [3 wk, 3m, 6m]	Caries arrest was higher in SDF than NSF-GTE but not statistically significant after 6 months.
Al-Nerabieah et al. 2020b **Syria**	Total 119 3–5 years 42% M	38% SDF Single application	5% NaF varnish Single application	Primary teeth: 40% Anterior lesions 60% Posterior lesions 40% Single surface 60% Multiple surface	Nyvad criteria visual and tactile inspection [3 wk, 6m]	Both SDF and NSF were effective in arresting carious dentine lesions in primary teeth after 6 months
Gao et al. 2020 **Hong Kong**	Total 1070 3-4 years 55% M	38% SDF biannual application	25 % AgNO3 solution + 5 % NaF varnish biannual application	Primary teeth Lesion severity Not reported	dmfs scores clinical examination [6,12,18,24,30 m]	Both treatment were effective at arresting caries at 30 month follow-up.
Mabangkhru et al. 2020 **Thailand**	Total 302 1-3 years In: 60% M C: 54% M	38% SDF biannual application	5% NaF varnish Biannual application	Primary teeth severity of caries experience dmft=1–4 and dmft>4	dmfs scores visual-tactile examination [6m,12m]	Biannual application of SDF showed higher caries-arrest effectiveness (twice more) than 5% NaF varnish at 12 month follo0w-up.
Tirupathi et al. 2019 **India**	Total 50 6- 10 years SDF: 39% M NSSF: 33% M	38% SDF Single application	5% NSSF varnish	Primary molar teeth Mount & Hume caries classification (mild, moderate, enlarged)	visual and tactile examination [1,3,6,12m]	Both SDF and NSSF were comparable in effectively preventing progression of dentinal caries in primary molars after 12 months.
Fahmi et al. 2019 **India**	Total 40 5-7 years	38% SDF single application	Placebo	Primary teeth Active caries lesions with exposed dentine (level 3)	Not reported [1m,6m]	SDF was significantly more effective than placebo in arresting caries
Vollú et al. 2019 **Brazil**	Total 68 2-5 years 61% M	30% SDF biannual application	ART (GIC) Caries excavated	Primary molar teeth (occlusal) ICDAS 5 or 6	ICDAS II criteria Visual-tactile examination [3m, 6m,12m]	Both SDF and ART were effective at arresting dentine caries in primary teeth at 12 months with SDF requiring less chair time
Fracasso et al. 2018 **Brazil**	Total 32 3-5 years 59% M	10% SDF Quarterly application	RM-GIC or Resin sealant or No treatment	Primary second molars Early childhood caries	Greene & Vermillion Index visual and tactile examination [3,6,12,24,36m]	Although SDF groups showed highest caries rate no statistical difference. All fluoride treatments were effective and comparable in preventing & arresting caries after 36 months.
Duangthip et al. 2018 **Hong Kong**	Total 371 3–4 years 60% M	30% SDF Annual applications (3 times: 0m,12m, 24m) Or 30% SDF Weekly application (3 times: 0,1,2 wk)	5% NaF varnish Weekly application (3 times: 0,1,2 wk)	48-52% Primary Molars ICDAS 3-6	ICDAS II criteria Visual-tactile examination [6,12,18,24,30m]	While the three fluoride treatments were comparable in effective arrest of moderate caries lesion, annual application of SDF was more effective than three-weekly application of SDF or NAF varnish in in arresting dentine caries lesions after 30 months of follow-up
Duangthip et al. 2016 **Hong Kong**	Total 304 3–4 years 60% M	30% SDF Annual Or 30% SDF Weekly	5% NaF varnish Weekly application (3 times: 0,1,2 wk)	64-66% Primary upper anterior teeth ICDAS 3-6	ICDAS II criteria Visual-tactile examination	Annual or three weekly applications of SDF was more effective than three weekly applications of NaF varnish in arresting dentine caries in primary teeth after 18 months

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		application (3 times: 0,1,2 wk)			[6,12,18m]	
Mattos-Silveira et al. 2015 **Brazil**	Total 141 3-10 years 48% M	30% SDF Single application	Resin infiltration (Icon) or Placebo (flossing)	Primary molars (approximal surface) ICDAS 5 or 6	ICDAS II criteria visuo-tactile examinations Bitewing Radiograph [6,12,24m]	SDF and infiltration were comparable in controlling caries progression in approximal surfaces. ††
Liu et al. 2012 **China (Southern)**	Total 501 Mean age 9 years 50% M	38% SDF annual application	Placebo or Resin sealant or 5% NAF (biannual)	First permanent molars ICDAS codes 4-6	ICDAS II criteria visuo-tactile examinations [24m]	All 3 preventive methods were effective and comparable in preventing pit & fissure caries in permanent molars after 24 months
Zhi et al. 2012 **China (Southern)**	Total 212 3-4 years 54% M	38% SDF annual application or 38% SDF biannual application	ART (Fuji VII) biannual application	51-56% Primary upper anteriors Active dentine caries not involving the pulp	ICDAS II criteria visuo-tactile examinations [6,12,18,24m]	Effectiveness of annual application of SDF was comparable to GIC sealant in arresting active dentine caries in primary teeth. Increasing frequency of SDF applicant can increase the caries arrest rate.
Braga et al. 2009 **Brazil**	Total 22 5-7 years	10% SDF 2 application 1 week apart	sealants (GIC) cross tooth-brushing technique (CTT)	First Permanent Molars active initial caries without cavitation on occlusal surfaces	visual inspection modified Carvalho index (visual) Radiographs [3, 6, 12, 18,30m]	All groups showed a general reduction in active lesions ($P < 0.05$) Arrested caries was significantly higher in the 10% SDF than CTT and GIC groups after 3 and 6 months
Yee et al. 2009 **Nepal**	Total 976 3-9 years 56% M	38% SDF Single application	Placebo 38% SDF + tannic acid 12% SDF	Primary teeth Severity not reported	visual inspection [6,12,24m]	Only single application of 38% SDF alone or with tannic acid was effective in arresting caries in primary teeth, and 12% SDF was not effective
Llodra et al. 2005 **Cuba**	Total 452 6-15 years 51% M	38% SDF Biannual application	Placebo	Primary teeth & Permanent first molars Severity not reported (presence of a cavity)	visual inspection [6,12,24, 36m]	Biannual application of a 38% SDF solution was effective at arresting caries in deciduous teeth & first permanent molars

† Sample size at randomization

†† There was no caries outcome data reported in Mattos-Silveira et al. 2015. Relevant Findings were extracted from a conference Abstract by Mattos-Silveira et al. 2017

Abbreviations. ART: Atraumatic restorative treatment; C Comparator; CPP-ACPFV: casein phosphopeptide-amorphous calcium phosphate fluoride varnish; EAPD: European Association of Paediatric De Fluoride varnish; GIC: Glass Ionomer; Cement; In: Intervention; ICDAS: international caries detection and assessment system; KI: Potassium Iodide; MIH: Molar incisor hypomineralization; NSSF: 5% N incorporated Sodium Fluoride; RM-GIC: resin modified glass ionomer cement; SDF: Silver Diamine Fluoride

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