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Review Article

Effectiveness of Professional Fluoride Applications in Preventing Dental Caries in Resource-Limited Settings

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ABSTRACT

This review systematically examined the safety and effectiveness of professionally applied fluoride treatments in preventing and halting dental caries among children in low- and middle-income countries (LMICs). We included randomized controlled trials from LMICs comparing professional fluoride applications with placebo, no treatment, health education alone, or standard care, with a minimum follow-up of one year. The review considered topical fluoride agents, including silver diamine fluoride (SDF), sodium, nano silver fluoride (NSF) and fluoride (NaF), acidulated phosphate fluoride. Searches were conducted in five databases (PubMed, Scopus, Embase, Web of Science, and Cochrane Library) in May 2022. A random-effects meta-analysis was performed where applicable. A total of 33 studies, comprising 16,375 children aged 1.5–14 years, were included in the qualitative synthesis. Quantitative meta-analysis included 17 studies with 4,067 participants. Adverse events were reported in 14 studies, none of which were serious. SDF and NSF significantly arrested caries in primary teeth ($p < 0.05$) relative to placebo or no intervention. Fluoride varnishes and gels effectively reduced new caries formation in primary teeth ($p < 0.05$) but did not significantly affect permanent teeth ($p > 0.05$). Overall, the certainty of evidence was low. Professionally applied fluorides appear effective and safe for caries prevention and arrest in children in LMICs, providing evidence to guide clinical recommendations. Nevertheless, the limited number of high-quality trials underlines the need for further rigorous research to confirm these outcomes.

Keywords: Developing countries, Dental caries, Fluorides, LMICs, Systematic review, Professionally applied fluorides

Introduction

Tooth decay is among the most widespread chronic conditions not caused by infection and continues to be a significant global health concern. Reports from the World Health Organization indicate that 60%–90% of schoolchildren and a majority of adults are affected, often resulting in the eventual loss of permanent teeth later in life [1]. Although preventable, this disease may begin with mild tooth sensitivity but can progress to major health issues. Common consequences include pain, difficulty in chewing, cosmetic and self-image concerns, sleep problems, malnutrition, impaired speech, as well as missed days at school or work—each of which diminishes quality of life [2, 3].

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The occurrence of dental caries shows sharp contrasts between high-income nations (HICs) and those classified as low- and middle-income (LMICs) [4]. Causes appear at various layers—ranging from individual choices to family context, culture, environment, and economic background [5]. In LMICs, individual vulnerabilities include eating patterns, oral hygiene behaviors, infant feeding methods, low birth weight, and genetic defects of teeth. At the household level, risk is influenced by the mother's education, awareness of oral health, family attitudes toward hygiene, day-to-day oral practices, and overall income [6]. On a broader scale, traditions, community norms, environmental factors, and national policies such as taxes on sugar or fluoridated public water supplies can either protect against or contribute to the problem [6].

In wealthier countries, the rate of tooth decay has gradually declined in recent decades [1, 7]. This improvement is largely linked to the regular use of fluoride, better living conditions, lifestyle changes, and greater personal responsibility for oral health [1, 7]. On the other hand, research by Peterson *et al*. on the "global burden of oral diseases" documented rising levels of caries in many developing regions, explained mainly by growing sugar intake combined with limited fluoride exposure [7]. Because of weak healthcare systems, low public awareness about dental health, and the absence of comprehensive national strategies, most LMICs have been unable to apply preventive programs based on scientific evidence, restricting the population-wide benefits of fluoride [1].

In many low- and middle-income nations, introducing community water fluoridation has not been realistic because of limited expertise, high operational costs, and the absence of centralized water networks [8]. In contrast, in wealthier countries, fluoride toothpaste has become the most common tool for preventing tooth decay [1]. Yet, in less affluent areas, unequal access remains a challenge since many households cannot afford this basic preventive product [8, 9]. Another measure used mainly for groups at higher risk of cavities is the professional use of topical fluorides [8, 10]. These can be delivered in different preparations—such as gels, foams, varnishes, silver diamine fluoride (SDF), and nano silver fluoride (NSF) [11]—all containing elevated fluoride concentrations [12, 13]. Among these, fluoride varnish (FV) and SDF are especially valued because they are simple to apply and can be safely used on very young children, even by non-dental providers with adequate training [8].

Spending on health is widely acknowledged as an essential driver of both social development and economic progress [14]. When preventive and minimally invasive dental care begins in childhood, it can greatly reduce the financial burden of treatment in later years [15]. For countries with limited resources, the establishment of evidence-informed policies and oral health initiatives centered on prevention is critical, since treatment costs are high and pose a major strain on national health budgets [16]. Although research consistently supports the safety and benefit of professional fluoride applications, most of this evidence originates from high-income settings [17]. Therefore, evaluating the impact of these interventions in LMICs is particularly important [18]. To address this gap, a systematic review of available studies from these regions was carried out. The main purpose of this review was to assess how effective and safe professionally applied fluorides are in preventing and controlling dental caries in LMIC populations.

Materials and Methods

Registration and reporting of the review

This systematic review was conducted in accordance with the PRISMA reporting standards. The protocol has been officially registered with PROSPERO under ID CRD42022337075.

Eligibility criteria for study selection

Study design

We included only randomized controlled trials (RCTs) with human subjects that had a minimum follow-up of one year. Studies performed in laboratory settings, in situ models, or on animals were not eligible. These inclusion and exclusion parameters were defined following the PICO model.

Participants (P)

Eligible studies involved participants of any age living in LMICs, including assessments of both primary and permanent dentition. Research focusing on special populations—such as individuals receiving orthodontic treatment, patients with cancer, or those experiencing xerostomia—was excluded.

Interventions (I)

The review considered interventions using professionally applied fluoride agents, including sodium fluoride (NaF), acidulated phosphate fluoride (APF), silver diamine fluoride (SDF), and nano silver fluoride (NSF). Interventions involving fluoride mouthwashes or combined preventive methods were excluded.

Control groups (C)
Studies were included if control groups received placebo, no treatment, oral health education only, or standard care.

Outcome measures (O)
Three primary outcomes were evaluated:
1. Arrest of caries progression, measured as the proportion of teeth with arrested lesions.
2. Incidence of new caries, assessed using DMFT/DMFS or dmft/dmfs (deft/def) indices.
3. Side effects or adverse events, either self-reported or clinically diagnosed.

Note: Noncavitated white spot lesions were excluded from the outcome assessment.

Search strategy
An electronic search was carried out by the lead researcher in collaboration with a librarian across five major databases: PubMed, Embase, Scopus, Web of Science, and the Cochrane Library, covering publications from January 2000 to May 2022. Only articles written in English were considered. Since titles and abstracts rarely specified countries or their income classification, the initial search did not filter for LMICs. During the screening phase, a checklist of LMICs published by the Cochrane Library [19] was used to determine eligibility.

Data management
Study screening
Following the removal of duplicate records, references were imported into Covidence for screening. Two reviewers independently examined titles and abstracts, applying the predefined inclusion and exclusion criteria. Discrepancies were resolved through discussion, and studies meeting criteria proceeded to full-text review.

Data extraction
Two reviewers independently extracted relevant information using a pre-designed form in Covidence, including:
- Study characteristics: title, lead author, objectives, study location and setting, initial sample size, dropout rate, final analyzed sample, duration of the study, follow-up period, baseline comparability, method of randomization, blinding, sequence generation, and allocation concealment.
- Participant information: age group (children or adults) and dentition type.
- Intervention details: fluoride type used, application frequency, and duration.
- Control information: type of control group intervention (e.g., placebo, no treatment, oral health education, or standard care).
- Outcomes: dentition type (primary, permanent, or both), tooth type evaluated (all teeth or molars), percentage of arrested caries, number of lesions arrested at tooth and surface levels, mean DMFT/DMFS or dmft/dmfs (deft/def) scores, any reported adverse events, and methods for evaluating side effects.

Note: Noncavitated white spot lesions were excluded from outcome assessment.

Risk of bias evaluation
The methodological quality of the included trials was appraised using the Cochrane RoB 2 tool [20]. For individually randomized studies, five key areas were examined: randomization procedures, deviations from planned interventions, completeness of outcome data, outcome measurement, and selective reporting. For cluster-randomized trials, a sixth domain—timing of participant recruitment or identification—was also assessed. Each domain contains a set of guiding questions, which inform the assignment of a risk rating as either low, some concerns, or high. The overall bias judgment for a study was determined based on the ratings across its domains: a study rated as low risk in all domains was classified as having low overall risk; if at least one domain raised some concerns but none were high, the study was considered to have some concerns overall; and if any domain was rated as high risk, the study's overall bias was categorized as high [21].
Assessment of reporting quality

To evaluate reporting completeness, the CONSORT 25-item checklist was applied [22]. Each checklist item was scored 1 if adequately reported and 0 if not. Items deemed irrelevant for a particular trial—such as 7b (interim analyses/stopping rules) and 14b (reasons for trial termination)—were designated as "not applicable" (NA). When calculating adherence, the denominator excluded all NA items, while the numerator comprised all items adequately reported, resulting in the study's percentage compliance with CONSORT guidelines [23].

Evaluation of evidence confidence

The overall reliability of the evidence was assessed using the GRADE methodology (Grades of Recommendation, Assessment, Development, and Evaluation). This system classifies evidence into four levels of certainty: high, moderate, low, and very low. Evidence derived from randomized trials begins at a high certainty rating. However, the confidence level may be lowered if the studies exhibit bias, inconsistent findings, indirect evidence, imprecise results, or potential publication bias. Each factor typically reduces certainty by one level, with the possibility of a maximum three-level downgrade when multiple issues are present [21, 24].

Data handling and analysis

Studies were initially organized by their main outcomes. Relevant information was then extracted, collated, and displayed in **Tables 1 and 2**, including all essential details. The effectiveness of professionally applied fluoride interventions was first evaluated qualitatively at the level of individual studies. For quantitative assessment, STATA version 17 was used to calculate pooled effect sizes along with 95% confidence intervals. In trials with more than one intervention group compared against a single control, intervention arms were merged into a single comparison whenever feasible. If merging was not possible, the most appropriate intervention group was selected according to inclusion criteria, excluding the others [21]. Effect sizes from fluoride varnishes, gels, and foams were combined to produce an overall estimate, which was visualized using forest plots.

Table 1. Summarizes the studies according to the proportion of caries arrest observed.

Lead Author(s) and Year	**Location**	**Context**	**Applied Treatment (IG)**	**Treatment Schedule**	**Comparison Arm (CG)**	**Duration of Study (years)**	**Age at Study Start (years)/Mean Age (SD)**	**Initial Dental Condition**	**Final Outcome Measured**	**Outcomes (IG-intervention group, CG-control group) percentage, mean (standard deviation or standard error)**
Treatments Targeting Primary Teeth										
dos Santos Jr *et al*., 2014	Brazil	Community-based	NSF	Single use	Purified water	1	6.31 (0.60)	Deep caries lesions	Percentage of teeth with halted caries	IG: 66.7%, CG: 34.7%, p < 0.05
Nagireddy *et al*., 2019	India	Academic setting	NSF	One-time application	Saline rinse	1	6.00 (0.60)	Deep caries lesions	Tooth-specific caries cessation rate	IG: 65.2%, CG: 28.8%, p < 0.05
Llodra *et al*., 2005	Cuba	Educational facility	38% SDF	Every six months	No intervention	3	6	Unclear (ongoing caries)	Average count of surfaces with stabilized caries (standard error)	IG: 2.80 (0.30), CG: 1.80 (0.30), p < 0.05

Chu *et al.*, 2002	China	Early childhood center	38% SDF	Once per year	Plain water	2.5	4.00 (0.80)	Deep caries lesions	Mean number of surfaces with controlled caries	IG: 2.82 (0.30), CG: 1.27 (0.19), p < 0.05
Yee *et al.*, 2009	Nepal	School premises	38% SDF	Single administrat ion	Untreated control	2	5.20 (1.20)	Unclear (teeth with decay)	Average number of surfaces with arrested decay	IG: 2.10 (0.30), CG: 1.00 (0.20), p < 0.05
Treatments Targeting Permanent First Molar Teeth										
Florio *et al.*, 2001	Brazil	School environment	2.26% Na FV	Biannually	Oral hygiene education	1	6	Early enamel caries	Percentage of teeth with stabilized caries	IG: 83.3%, CG: 72.7%, p > 0.05
Llodra *et al.*, 2005	Cuba	Academic institution	38% SDF	Twice yearly	No treatment	3	6	Unclear (ongoing caries)	Mean count of surfaces with non-progressing caries (standard error)	IG: 0.30 (0.10), CG: 0.10 (0.00), p < 0.05

Abbreviations: FV = fluoride varnish; Na = sodium; NSF = nano silver fluoride; SDF = silver diamine fluoride.

Table 2. Overview of studies evaluating the occurrence of new dental caries.

Principal Investigator(s) and Publication Year	**Country**	**Study Venue**	**Administered Therapy (IG)**	**Dosing Regimen**	**Reference Cohort (CG)**	**Study Period (years)**	**Starting Age (years)/Average Age (SD)**	**Outcome Measured at Conclusion**	**Results (IG-intervention group, CG-control group) percentage, mean (SD, SE, or 95% CI)**
Therapies for Primary Teeth									
Andruskevicie ne *et al.*, 2008	Lithuania	Educationa l institution	APF gel	Every four months	Untreated group	2	3	Increase in dmfs index	IG: 0.55 (0.04), CG: 1.41 (0.08), p < 0.05
H Jiang *et al.*, 2005	China	Academic facility	APF foam	Semi-annually	Inactive placebo	2	3–4	Growth in dmfs index	IG: 3.80 (0.90), CG: 5.00 (1.00), p < 0.05
Memarpour *et al.*, 2016	Iran	Clinical setting	Na FV with dental health guidance	Twice per year	1. Inactive varnish 2. Dental health guidance	1	1–2	Percentage decrease in caries susceptibility	IG: 31.80% vs. CG1, p < 0.05; IG: −3.56% vs. CG2, p > 0.05
Memarpour *et al.*, 2015	Iran	Healthcare facility	Na FV plus oral care education	Every four months	Non-active varnish	1	1–3	Rise in dmft index	IG: 0.31 (0.90), CG: 2.00 (2.00), p < 0.05

Agarwal *et al.*, 2022	India	Community environment	FV	At baseline, 6, and 12 months	Plain water	3	3.29 (0.28)	Change in dmft index	IG: 4.14 (7.03), CG: 5.00 (6.50), p < 0.05
Latifi-Xhemajli *et al.*, 2019	Kosovo	School campus	FV	Quarterly	No therapy	2	6–30 months	dmfs index value	IG: 5.20 (10.5), CG: 10.10 (12.90), p < 0.05
Patil *et al.*, 2017	India	Unspecified location	Na FV	Thrice within one week	No intervention	1	6–7	dmfs index value	IG: 0.59 (0.05), CG: 0.50 (0.07), p > 0.05
Gugwad *et al.*, 2011	India	Unspecified location	Na FV	Three applications in one week	No therapy	1	6–7	defs index value	IG: 4.60 (4.90), CG: 6.50 (7.30), p < 0.05
Munoz-Millan *et al.*, 2018	Chile	School grounds	FV	Every six months	Inactive varnish	2	2–3	Proportion of children developing new caries	IG: 45%, CG: 55.6%, p > 0.05
Oliveira *et al.*, 2014	Brazil	Medical center	Na FV	Biannual application	Non-active varnish	2	2.40 (0.90)	dmfs index value	IG: 2.00 (4.00), CG: 2.80 (4.20), p > 0.05
Turska-Szybka *et al.*, 2021	Poland	Daycare centers	1. Ammonium FV 2. Na FV	Every three months	Oral care education	1	49 months	Growth in dmfs index	IG1: 1.56 (2.85), IG2: 0.83 (5.73), CG: 3.75 (3.90), p < 0.05
Agouropoulos *et al.*, 2014	Greece	Early education setting	Difluorosilane FV	Semi-annually	Inactive varnish	2	3.30 (0.80)	Increase in dmfs index	IG: 2.90 (5.30), CG: 3.00 (5.20), p < 0.05
Therapies for Primary Molar Teeth									
Fracasso *et al.*, 2018	Brazil	Hospital facility	SDF	Quarterly	No therapy	3	3–5	Percentage of teeth without caries	IG: 80%, CG: 87%, p > 0.05
Therapies for Permanent Teeth									
Ersin *et al.*, 2008	Turkey	Academic setting	NaF gel	Twice yearly	Health awareness program	2	11–13	Average DS score	IG: 0.88 (1.47), CG: 1.05 (2.01), p > 0.05
Agrawal & Pushpanjali, 2011	India	Community locale	APF gel	Every six months	No therapy	1	9–16	DMFS index value	IG: 4.32 (1.43), CG: 4.63 (1.48), p > 0.05
Arruda *et al.*, 2012	Brazil	School facility	Na FV	Biannual dosing	Placebo	1	6–14	Rise in DFS index	IG: 4.61 (3.54–5.67), CG: 7.72 (6.26–9.18), p < 0.05
Souza *et al.*, 2021	Brazil	Educational campus	1. Titanium Tetra FV 2. Na FV	Weekly for 4 weeks, then at 6 and 12 months	Non-active varnish	1.5	6–7	Proportion of caries-affected surfaces (mean and SD)	IG1: 1.83 (2.30), IG2: 2.30 (3.50), CG: 6.93 (9.40), p < 0.05
Rodakowska *et al.*, 2012	Poland	School grounds	NaF V	Every six months	1. Elmex Gel brushing biweekly (16 times) 2. Elmex Gel brushing 6 times yearly	1	7	DMF index increase	IG: 0.25 (0.68), CG1: 0.40 (0.92), CG2: 0.48 (0.89), p > 0.05

Therapies for Permanent First Molar Teeth									
Kukleva & Kondeva, 2001	Bulgaria	Educational setting	F gel	Every three months	No intervention	3	7	Percentage reduction in caries	IG: 61.93%
Rim *et al.*, 2021	Korea	School environment	1% sub-acidic NaF-HF gel	1. One dose 2. Two doses, 7-day gap 3. Two doses, 6-month gap	Placebo	1	6–7	D2MFT increase (enamel caries)	IG1: 0.37 (0.70), IG2: 0.18 (0.62), IG3: 0.21 (0.65), CG: 0.56 (0.80), $p < 0.05$ D3MFT increase (dentinal caries): IG1: 0.03 (0.18), IG2: 0.05 (0.21), IG3: 0.07 (0.32), CG: 0.08 (0.26), $p > 0.05$
Han Jiang *et al.*, 2005	China	Academic facility	1. APF foam 2. APF Gel	Semi-annually	No therapy	2	6.50 (0.40)	Average caries progression	All surfaces: IG1: 0.39 (0.65), IG2: 0.38 (0.69), CG: 0.50 (0.87), $p > 0.05$ Smooth surfaces: IG1: 0.16 (0.39), IG2: 0.17 (0.38), CG: 0.27 (0.45), $p < 0.05$
Monse *et al.*, 2012	Philippines	School setting	SDF	Single application	No intervention	1.5	6–8	Hazard ratio	Group 1 (school brushing with fluoride toothpaste): 1.16 (0.51–2.63), $p > 0.05$ Group 2 (no school brushing with fluoride toothpaste): 0.71 (0.45–1.11), $p > 0.05$
Liu *et al.*, 2012	China	Educational institution	1. SDF 2. Na FV	1. Single dose 2. Biannually	Water	2	9.1	Percentage of pit & fissure sites with new caries	IG1: 2.2%, CG2: 2.4%, CG: 4.6%, $p < 0.05$
Abreu-Placeres *et al.*, 2019	Dominican Republic	School dental clinic	FV	1. Quarterly 2. Semi-annually	Control	1	6–7	Average number of new caries surfaces	AOR for IG1 vs. CG: 1.46 (1.18–1.81), $p < 0.05$ AOR for IG2 vs. CG: 1.06 (0.84–1.34), $p > 0.05$
Wang *et al.*, 2021	China	School campus	Na FV	Every six months	No therapy	3	6–7	Average DFS score	IG: 0.67 (1.64), CG: 1.03 (2.07), $p < 0.05$
Pereira *et al.*, 2011	Brazil	Educational setting	Na FV	Biannually	Oral care education	2	6–8	Mean DMF on occlusal surfaces	High risk: IG: 0.29 (0.68), CG: 0.39 (0.72), $p < 0.05$ Low risk: IG: 0.09 (0.29), CG: 0.12 (0.40), $p > 0.05$
Therapies for Premolar Teeth									
Kalnina & Care, 2016	Latvia	University environment	NaF varnish	Every six months	No intervention	1	10	Percentage of surfaces with new caries	IG: 0%, CG: 3.5%, $p > 0.05$

Abbreviations: APF = acidulated phosphate fluoride; dmft/dmfs or DMFT/DMFS = decayed, missing, and filled teeth or surfaces; Na = sodium; FV = fluoride varnish; SDF = silver diamine fluoride.

The initial search across the five databases yielded 6483 articles, specifically: PubMed (1655), Embase (1570), Cochrane Library (1928), Web of Science (500), and Scopus (830). After removing duplicates via EndNote and the SR Accelerator tool, 2822 unique studies remained. Screening the titles and abstracts led to 206 full-text articles being reviewed, from which 33 studies met the inclusion criteria for the systematic review. Of these, only 17 were eligible for meta-analysis, due to variations in evaluated outcomes, dentition types, and measurement approaches.

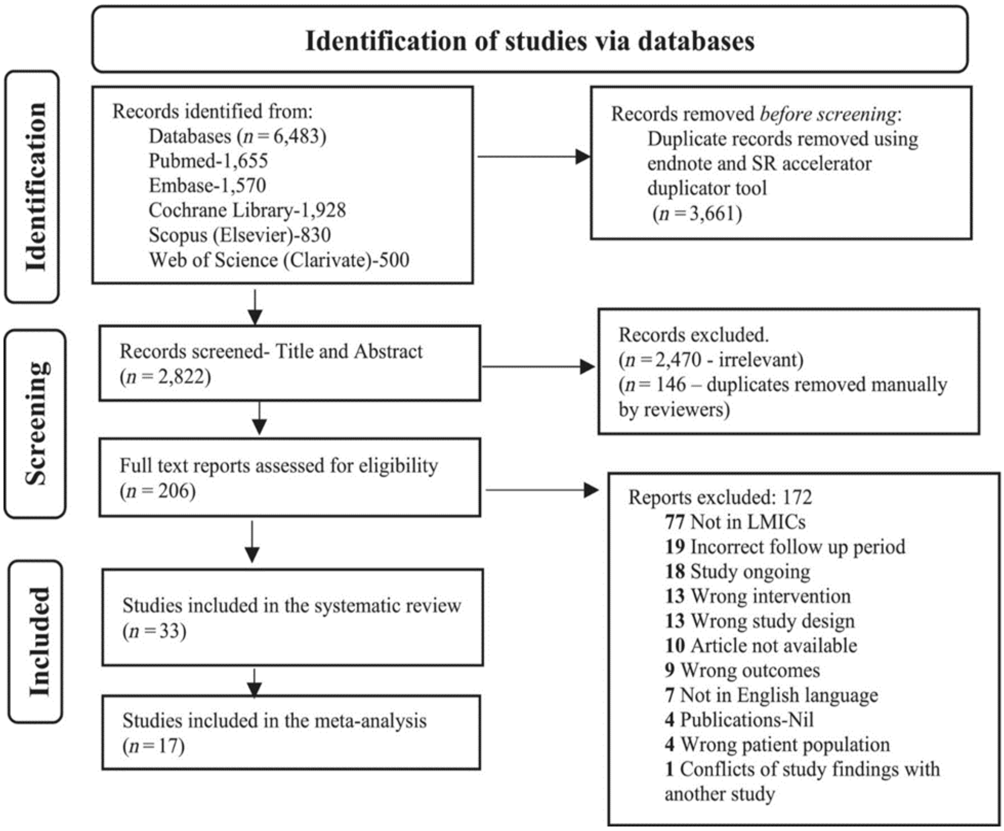

Figure 1. The PRISMA diagram depicting the selection process.

The 33 included studies were grouped according to the primary outcomes: 14 studies examined the safety of professionally applied fluorides, 6 assessed caries arrest, and 27 investigated the development of new caries. This grouping for the systematic review and meta-analysis is illustrated in **Figure 2**.

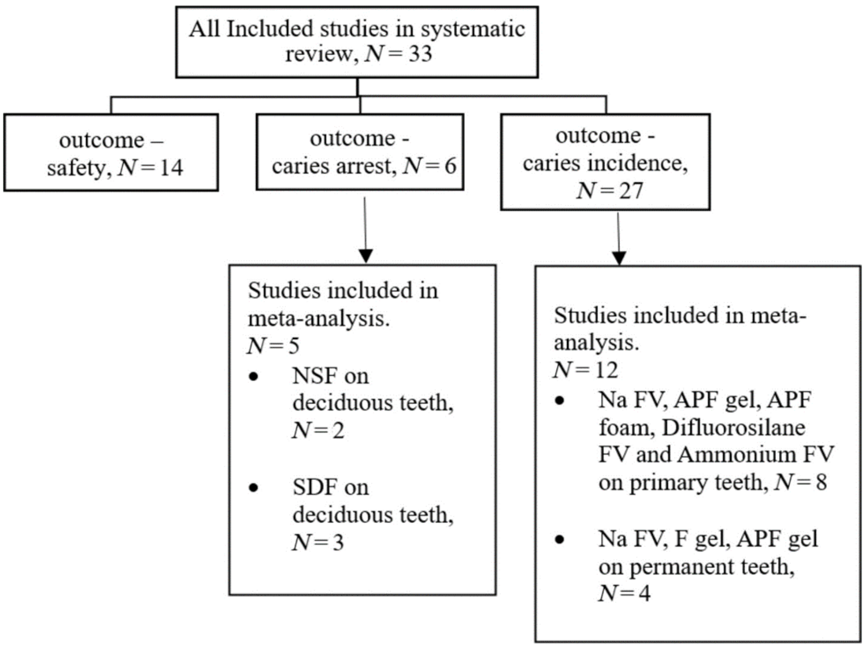

Figure 2. Categorization of included studies in systematic review and meta-analysis.
abbreviations: APF = acidulated phosphate fluoride; Na FV = sodium fluoride varnish; NSF = nano silver fluoride; SDF = silver diamine fluoride.

Across all studies, a total of 16,375 children were randomized, with 4067 participants contributing data to the meta-analysis. The age range of participants was 1.5–14 years. The majority of studies were conducted in school, preschool, or community settings, with a few carried out in hospital environments. Follow-up durations ranged from 12 - 36 months. The fluoride interventions included ammonium FV, Na FV, fluoride gels (NaF and APF), difluorosilane FV, APF foam, NSF, and SDF.

The risk of bias across studies is summarized in **Figure 3**, showing that only six trials were rated as low risk in all domains [25–30]. Reporting quality, measured by adherence to CONSORT guidelines, ranged from 24% to 88% across the 33 studies.

D1	Randomization process	+	Low risk
D2	Deviations from the intended interventions	!	Some concerns
D3	Missing outcome data	-	High risk
D4	Measurement of the outcome		
D5	Selection of the reported result		
Overall	Risk of bias judgement for the study		

Study ID	D1	D2	D3	D4	D5	Overall
dos Santos Jr et al., 2014	+	+	+	+	+	+
Nagireddy et al., 2019	!	+	-	+	+	-
Llodra et al., 2005	!	+	!	+	+	!
Chu et al., 2002	!	+	+	+	+	!
Yee et al., 2009	!	+	+	+	+	!
Florio et al., 2001	!	-	+	!	+	-
Andruskeviciene et al., 2008	!	-	+	!	+	-
H Jiang et al., 2005	!	!	+	+	+	!
Memarpour et al., 2016	+	+	+	!	+	!
Memarpour et al., 2015	!	+	!	+	+	!
Agarwal et al., 2022	+	+	+	+	+	+
Latifi-Xhemajli et al., 2019	!	+	-	+	+	-
Patil et al., 2017	!	+	+	!	+	!
Gugwad et al., 2011	!	-	!	!	+	-
Munoz-Millan et al., 2018	+	+	+	+	+	+
Oliveira et al., 2014	+	+	+	+	+	+
Turska-Szybka et al., 2021	+	+	+	+	+	+
Agouropoulos et al., 2014	+	+	+	+	+	+
Fracasso et al., 2018	!	+	+	-	+	-
Ersin et al., 2008	!	-	+	+	+	-
Agrawal & Pushpanjali, 2011	!	-	-	+	+	-
Arruda et al., 2012	+	-	!	!	+	-
Souza et al., 2021	!	+	+	+	+	!
Rodakowska et al., 2012	!	+	!	!	+	!
Kukleva & Kondeva, 2001	!	!	-	-	!	-
Rim et al., 2021	+	+	!	+	+	!
Han Jiang et al., 2005	!	-	+	!	+	-
Monse et al., 2012	!	+	!	+	+	!
Liu et al., 2012	!	+	-	-	+	-
Abreu-Placeres et al., 2019	!	!	+	!	+	!
Wang et al., 2021	+	+	!	+	+	!
Pereira et al., 2011	!	+	+	!	+	!
Kalnina & Care, 2016	!	+	+	!	+	!

Figure 3. Risk of Bias Evaluation

Safety of professionally applied fluorides

Among the 33 studies included, only 14 specifically monitored adverse events associated with professional fluoride applications. The timing and method of these safety assessments varied, including immediate post-application checks, 30-minute and 1–2-hour evaluations, as well as follow-ups at 1 week, 3 months, 6 months, and 12 months. Some studies provided limited details on how side effects were assessed, whereas others described structured approaches, such as parent questionnaires during follow-up, direct observation immediately after application, and phone interviews with caregivers to identify any adverse events. No serious reactions—such as vomiting, nausea, or allergic responses—were reported. Minor effects, however, were noted in a few cases, including unpleasant taste [31–33], foul odor [26], and tooth discoloration [29, 30].

Effectiveness for caries arrest

The six studies focused on caries arrest included participants from five LMICs: Brazil (2 studies), India, Nepal, China, and Cuba (1 study each). Interventions used were fluoride varnish (FV) in one study [34], silver diamine fluoride (SDF) in three studies [35–37], and nano silver fluoride (NSF) in two studies [13, 27] **(Table 1)**.

Five of these studies examined SDF and NSF for primary teeth with active carious lesions. The three SDF studies reported a significant increase in the mean number of arrested surfaces compared to controls (water or no treatment) ($p < 0.05$) [35–37]. The two NSF studies assessed dentinal carious lesions, with one reporting a 66.7% arrest rate versus water ($p < 0.05$) [27] and the other a 65.2% arrest rate compared with saline ($p < 0.05$) [13].

Two separate meta-analyses were conducted. **Figure 4** displays the percentage of carious surfaces arrested by NSF, while **Figure 5** shows the mean number of arrested surfaces for SDF. Compared with water or saline, NSF increased caries arrest by 34%, although the overall certainty of evidence was low due to limited sample sizes and high risk of bias [21, 24]. SDF-treated teeth had a mean of 1.13 additional arrested surfaces over controls, with the certainty of evidence also rated low due to bias and inconsistencies among the included trials [21, 24].

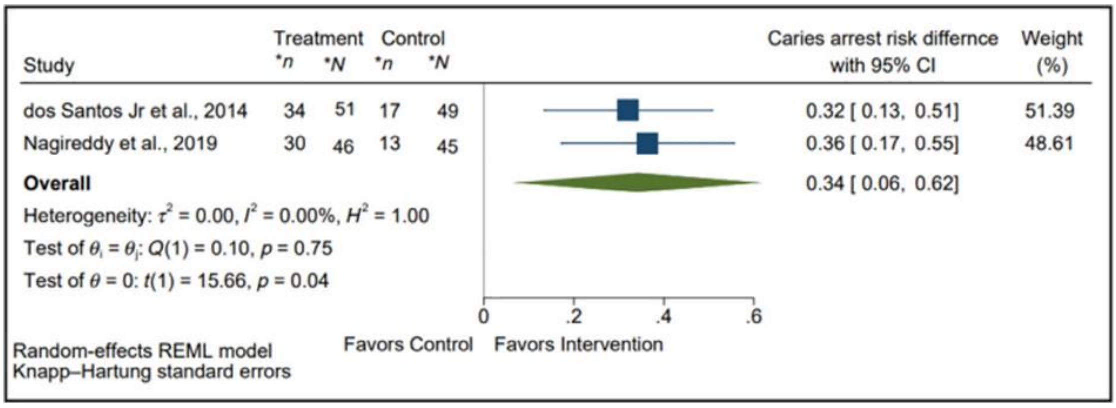

Figure 4. Comparison of caries arrest in primary teeth between groups treated with nano silver fluoride (NSF) and controls receiving water or saline. N represents the total number of teeth, and n is the number of teeth where caries were arrested.

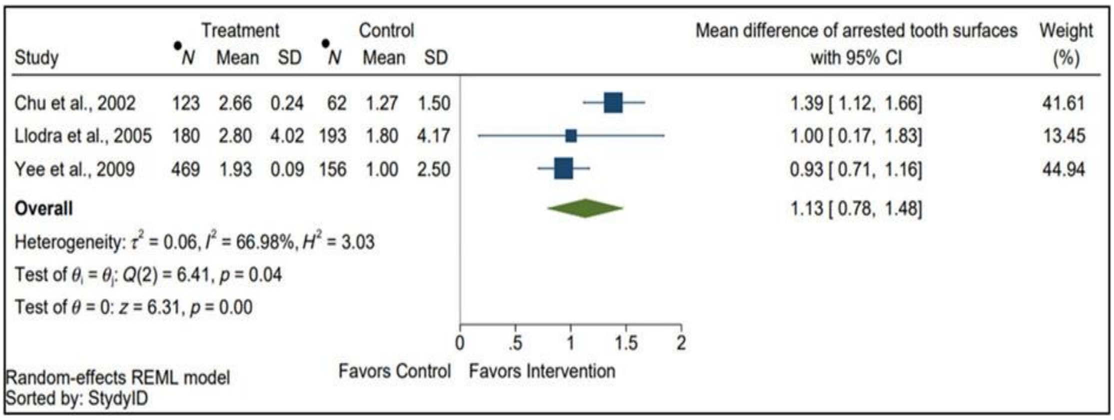

Figure 5. Average number of arrested carious surfaces in primary teeth treated with silver diamine fluoride (SDF) versus control groups (water or no treatment). N indicates the total tooth surfaces.

Two studies examined permanent first molars [34, 36]. Llodra *et al*. observed that children who received SDF had a higher mean of 0.3 arrested surfaces compared with 0.1 in the control group, showing statistical significance ($p < 0.05$). In contrast, Florio *et al*. evaluated fluoride varnish (FV) on enamel caries in permanent first molars and found no meaningful difference compared to controls, which received oral hygiene guidance and home plaque management ($p > 0.05$).

Effectiveness of professionally applied fluorides in preventing new caries

A total of 27 studies investigated the preventive effects of professional fluoride applications on new carious lesions. These trials spanned 15 countries, including Brazil (5), China (4), India (4), Poland (2), Iran (2), and one study each from Korea, Greece, Latvia, the Philippines, Lithuania, Dominican Republic, Bulgaria, Chile, Turkey, and Kosovo (per UN Resolution 1244). **Table 2** summarizes these studies.

Out of these 27 studies, 13 focused on primary teeth, testing agents such as APF foam, APF gel, sodium fluoride varnish (Na FV), ammonium FV, NaF-HF gel, difluorosilane FV, and SDF. Of these, eight studies reported a significant decrease in new caries compared with placebo, no treatment, or oral health education ($p < 0.05$) [25, 29, 38–43]. Meanwhile, four studies observed no significant difference in caries incidence ($p > 0.05$) [26, 28, 30, 44, 45].

A meta-analysis of eight studies **(Figure 6)** showed that professional fluoride applications—including NaF varnish, APF gel/foam, ammonium FV, and difluorosilane FV—were associated with a mean dmfs increment 1.32 lower than in the control groups, indicating a meaningful reduction in caries formation ($p < 0.05$). The evidence certainty, however, was rated low due to concerns about bias and variability among the studies [21, 24].

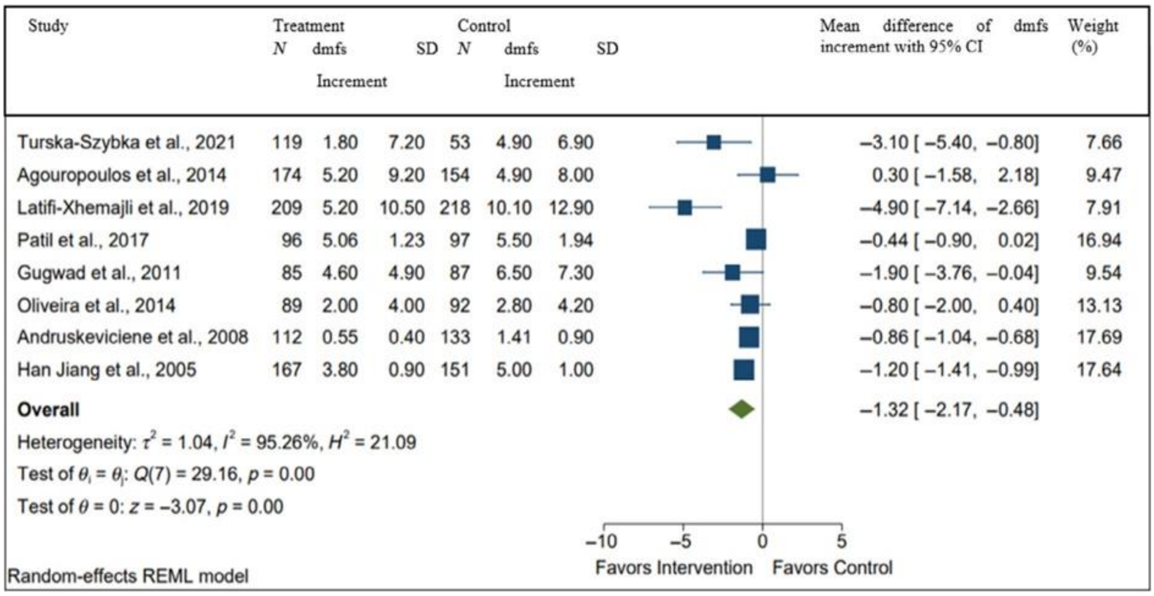

Figure 6. Forest plot representing the occurrence of new caries in primary teeth treated with professional fluoride applications, including APF gel and foam, ammonium fluoride varnish, NaF varnish, and difluorosilane FV.

Key: APF, acidulated phosphate fluoride; FV, fluoride varnish; NaF, sodium fluoride; N, total teeth evaluated; dmfs, decayed, missing, and filled surfaces; SD, standard deviation.

Among the 27 studies reviewed, 13 examined permanent teeth, analyzing how professional fluoride applications affected the formation of new carious lesions. The studies employed several types of fluoride, such as NaF-HF gel, NaF gel, titanium tetra FV, APF foam, APF gel, sodium FV, and SDF. Out of these 13 studies, seven demonstrated a statistically significant reduction in caries compared to placebo or no treatment ($p < 0.05$) [31–33, 46–49], whereas six did not report significant differences ($p > 0.05$) [50, 51]. One notable finding by Kukleva and Kondeva indicated a 62% reduction in caries on permanent first molars over a 36-month follow-up with fluoride varnish [52].

A meta-analysis including four studies **(Figure 7)** revealed that, overall, professionally applied fluorides did not produce a statistically significant decrease in new caries incidence on permanent teeth ($p > 0.05$). The confidence in these results was considered very low, primarily due to risk of bias, inconsistency among studies, and imprecision [21, 24].

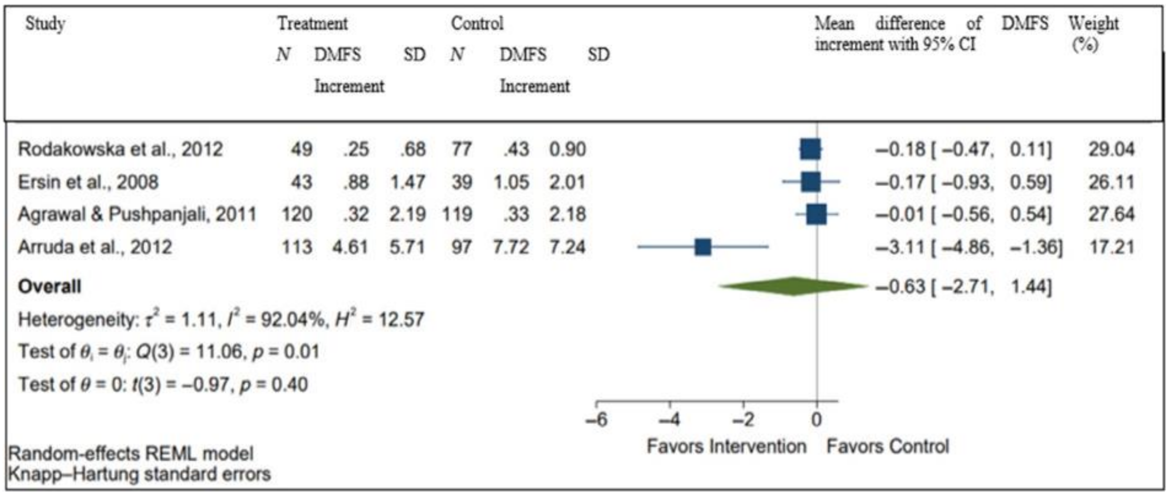

Figure 7. Forest plot showing new caries development in permanent teeth following treatment with professional fluoride applications (NaF gel, APF gel, Na FV).

Key: APF, acidulated phosphate fluoride; FV, fluoride varnish; NaF, sodium fluoride; N, total teeth assessed; SD, standard deviation; DMFS, decayed, missing, and filled surfaces.

Just one study addressed premolars, reporting that NaF varnish did not significantly reduce the occurrence of new carious lesions compared with the control group ($p > 0.05$) [53].

Results and Discussion

This review is the first to systematically examine the safety and effectiveness of professional fluoride applications for preventing and arresting dental caries in populations living in LMICs. Across the included studies, no serious adverse events were reported following fluoride treatments. The limited available data indicate that nano silver fluoride (NSF) and silver diamine fluoride (SDF) can effectively halt caries progression in primary teeth. Furthermore, professional fluoride products, such as NaF varnish, APF gel/foam, ammonium fluoride varnish, and difluorosilane varnish, were found to reduce the occurrence of new carious lesions in primary teeth. However, for permanent teeth, applications like NaF gel, APF gel, and Na FV did not show clear preventive benefits.

Although the review included 33 studies, meta-analysis was feasible only for subsets due to differences in outcomes and measurement methods. Consequently, four separate meta-analyses were conducted on smaller study groups, yielding low-certainty evidence. Despite these limitations, the results provide useful guidance for developing national public health strategies targeting dental caries reduction in LMICs. The adherence to Cochrane review standards enhances the credibility of this evidence, even if it is limited.

Generalization of these findings to all LMICs should be approached with caution. The studies covered 17 countries, which account for roughly 15% of all LMICs, with most research originating from Brazil, China, and India. While classified as LMICs, these countries have higher resources compared with many other LMICs. This highlights the urgent need to conduct well-designed RCTs across a broader range of LMICs to strengthen the global evidence base and support more comprehensive public health recommendations.

The review included only English-language publications, which may have introduced minimal bias, as the number of relevant non-English studies is comparatively low. A comprehensive search of five electronic databases was performed to maximize coverage. Publication bias was not formally assessed due to the small number of studies included in the meta-analyses. As noted by Sedgwick and Marston, at least 5–10 studies are required for reliable funnel plot analysis [54]. Nevertheless, some studies conducted in LMICs may remain unpublished or appear only in local journals due to financial or logistical barriers, suggesting the potential for publication bias.

The evidence gathered in this review aligns with international studies regarding the use of professionally applied fluoride for both preventing and halting dental caries. Across the 14 studies evaluated for safety, no major adverse effects were reported, supporting the conclusion that these treatments are generally safe [55, 56]. Nevertheless, several of these studies lacked detailed explanations of how safety outcomes were monitored, reflecting a gap in reporting standards in primary research. In agreement, Jabin *et al*. [57] highlighted the effectiveness of silver diamine fluoride (SDF) in stopping caries progression in primary teeth. Additionally, findings from a Cochrane review indicated that fluoride varnish prevented 37% of caries in primary teeth and reduced new lesions by 43% in permanent teeth [58]. Contrastingly, De Sousa *et al*. [59] observed that the anticaries effect of fluoride varnish in preschool children remained uncertain.

Even though the certainty of evidence in this review was rated low, global studies consistently demonstrate that topical fluoride applications provide substantial clinical benefits, improving oral health outcomes while potentially reducing costs compared with routine care [60–62]. Given that this review focused specifically on LMIC settings, there is a clear need for further high-quality primary research, particularly studies that incorporate cost-effectiveness analyses across a wider spectrum of LMICs. Such evidence would enhance the robustness of future systematic reviews and provide a stronger foundation for policy development.

Conclusion

This review contributes meaningful insights into the role of professional fluoride interventions in LMICs, supporting the design of evidence-based dental public health programs. However, due to the limited volume and low certainty of current evidence, additional research is required to reinforce these findings and enable more confident conclusions.

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