



Effectiveness of fluoride varnishes on oral health: A systematic review

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Abstract

Background: Professionally topical fluoride such as fluoride varnish was approved for preventing and remineralizing dental caries in primary and permanent dentitions. As such, fluoride varnish occupies a privileged place since it is the only topical fluoride for professional use applicable for children under 6 years of age, due to its simplicity, speed, rapidity and safety of use. The aim of this study was to investigate the efficacy of professional fluoride varnish in preventing and managing dental caries in primary teeth.

Method: A systematic search of publications from 2013 to 2020 was conducted using 3 databases: PubMed, Cochrane Library and Web of Science. The key words used were “fluoride varnish, children, prevention, remineralization and early childhood caries”. Reviews, non-English articles, and irrelevant studies were excluded.

Results: in this article, a total of 08 reports were retained: 4 systematic reviews and 4 trials were included in this review. Three reports investigated the preventive effect on primary teeth using fluoride varnish: 2 comparing fluoride varnish with no treatment and 1 comparing fluoride varnish with standard health program. Two trials investigated the managing effect of dental caries on primary teeth comparing fluoride varnish with standard health program. 1 review reported an arresting effect on dentine caries using silver diamine fluoride.

4 Meta-analysis were performed using 5% Sodium fluoride varnish, to prevent and manage caries, and the preventive fraction ranged from 23% to 70%; highest percentage of 69.9% preventive fraction was observed.

Conclusion: The effectiveness of fluoride varnish for the prevention of dental caries was proved, however it depended on the individual caries risk, the area of living of the child and if it is used in complement with a standard health program. On the other hand, the effectiveness of fluoride varnish for the management of dental caries depended on the localization of dental caries.

Keywords: Caries; Child dentistry; Remineralization; Demineralization; Oral hygiene; Prevention

1. Introduction

The rapidity of installation and the severity of the development of early childhood caries implies the use of all possible and effective preventive measures [1].

Fluoride applications are remarkable weapons against caries [2]; used not only in primary or secondary prevention but also for the remineralization and management of the lesions [3].

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As such, Fluoride Varnish (FV) occupies a privileged place since it is the only topical fluoride for professional use applicable for children under 6 years of age, due to its simplicity, speed, and safety of use [3].

The objective of this systematic review was to assess the effectiveness of fluoride varnishes in preserving dental health in the prevention and management of caries in primary teeth.

2. Material and methods

2.1. Search Strategy and Databases

A methodic search to identify all the relevant studies was conducted on 3 databases: PubMed Cochrane Library and Web of Science.

The search included the following sets of key words:

- “fluoride varnish” AND “children” AND “primary teeth”
- “fluoride varnish” AND “primary teeth” AND “prevention”
- “fluoride varnish” AND “remineralization”
- “fluoride varnish” AND “early childhood caries”

The following filters were applied to these terms: clinical trial, published since 2013, English, and journal (or dental journal)

2.2. Selection Criteria

Articles were included based on the following criteria:

Table 1 Inclusion criteria

Type of study	controlled clinical trials, randomized, or quasi-randomized clinical trials (RCT), Systematic reviews (SR), and meta- analysis (MA)
Type of population	children with primary teeth
Type of intervention	application of topical fluoride varnish (NaF), to primary dentition, in any quantity, concentration or application interval
Comparator	No treatment Placebo treatment oral preventive health program (parental education + tooth brushing) SDF (Silver Diamine Fluoride)
Outcomes	caries reduction, tooth remineralization, Preventive Fraction (PF), dmfs, Progression Index (PI), decay reduction
Languages	English
Studies up to 2013	

2.3. Exclusion Criteria

Articles were excluded if they did not meet the selection criteria. Children with any systematic pathology or long-term medication were excluded from this review. Fluoride varnish interventions provided outside the dental office or dental school were also excluded.

2.4. Data Extraction

One reviewer (Z.FZ.) screened the titles and abstracts of the identified studies from the database independently and in duplicate. Consensus was obtained by discussion and consultation with the calibrated reviewer (F.R.) to resolve any

disagreements during study selection and data extraction. Studies not respecting the precited inclusion criteria were excluded. The reviewer (Z.FZ.) extracted data from the studies using a data extraction form.

The following data was collected in the form of a table: author and year of publication, objective and type of the study, age of participants and controls, intervention modality, clinical outcomes, and conclusion (Appendix)

3. Results

3.1. Study Selection

The initial search identified a total of 372 citations identified from electronic literature from 2013 to 2020 in the 3 databases. Among them, 310 citations were removed.

After screening the title and abstract manually, the investigators reached an agreement that 62 potentially relevant reports trials met the inclusion criteria, with 54 reports excluded because of being classified as irrelevant population, irrelevant intervention, irrelevant comparator, review articles, editorials etc.

The remaining 08 reports were categorized into 2 groups for assessment. Group 1 had 03 reports, which investigated the use of professional fluoride application to prevent dental caries in primary dentition and the group 2 investigated remineralization and management of dental caries in primary dentition (05 reports)

The recapitulation of our strategy of search of articles has been represented in the systematic review flow diagram (Figure 1).

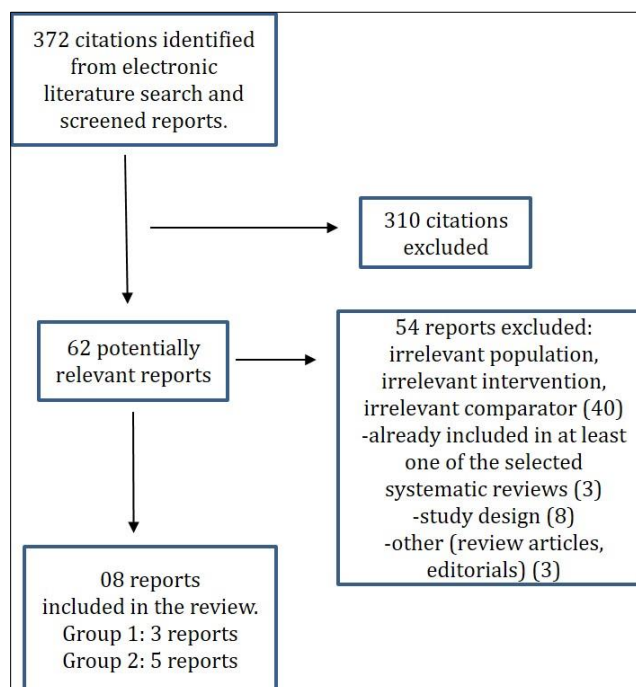


Figure 1 Selection of Included Studies

3.2. Study Characteristics

3.2.1. Study design

In this updated review 08 reports have been included which focused on primary teeth and were published between 2013 and 2020

- 4 Systematic Review (3 SR + MA, 1 SR)
- 4 Randomized Controlled Trials.

Table 2 Summary of trials of professionally applied fluorides alone versus no treatment or placebo treatment in preventing dental caries

First Author, year	Objective	Type of study	Age of the participants	Intervention(s)	Clinical Outcomes	Conclusion
Marinho et al, 2013 [5]	To determine the effectiveness of FV in preventing tooth decay in children and adolescents	a systematic review and meta-analysis 22 randomized and quasi-randomized trials (10 analyzed for primary teeth)	children under 16	FV Vs no treatment Placebo treatment	PF was 37% (P <0.0001)	FV was found to be effective in prevention and inhibiting caries development in primary teeth when compared to no treatment.
Xhemajli et al, 2019 [6]	To test the effectiveness of FV in preventing caries in early childhood in children at high risk of caries	RCT	6 to 30 months	FV applied four times a year, every three months. Vs no treatment (control)	The PF in the two groups was 49% in the test group after two years.	The application of FV four times a year prevented the incidence and reduced the severity of caries in pre-school children.

PF: preventive fraction, RCT: randomized controlled trials, FV: fluoride varnish

Table 3 Summary of trials of professionally applied fluorides alone versus standard preventive oral health program in preventing dental caries

First Author, year	Objective	Type of study	Age of the children	Intervention(s)	Clinical Outcomes	Conclusion
Jiang et al, 2014 [7]	To investigate the effectiveness of hands-on training in parental toothbrushing, with or without semi-annual applications of 5% NaF in preventing ECC	RCT	8 to 23 months	Group 3 : Parental educational materials and toothbrushing training + semiannual application of 5% NaF varnish (Clinpro White Varnish) to all erupted teeth Vs Group 1: One-time oral parental educational talk Vs Group 2: Oral parental educational talk and hands-on toothbrushing training + follow-up with a dentist every 6 months + placebo varnish	At baseline, mean dmft score in Gp 1 to Gp 3 was 15.5, 15.6, and 15.3 At 24-month follow-up, mean new dmft scores in Gp 1 to Gp 3 were 0.3, 0.2, and 0.3, respectively ($p > 0.05$).	In young children with low risk of dental caries and in a water fluoridated area, semi-annual application of 5% sodium FV may not have an additional effect on preventing ECC of dental caries compared to provision of oral health education alone

RCT: randomized controlled trials, FV: fluoride varnish, NaF: Sodium fluoride varnish, ECC: early childhood caries

The two groups have been defined as:

Group 1: prevention of dental caries: 1 SR, 2 RCT (TABLE 2, TABLE 3)

Group 1 had 3 studies, which investigated the use of professional fluoride application to prevent dental caries on primary teeth. Among them, 1 meta-analysis and 1 trial compared the use of FV vs no treatment or placebo treatment with the outcome proving the effectiveness of FV in preventing ECC (Marinho et al. 2013), (Latifi-Xhemajli et al. 2019). 1 trial compared the use of FV vs the standard preventive oral health program wherein effectiveness of FV in preventing dental caries for children at low risk and in water fluoridated areas could not be proved (Jiang et al. 2014).

Table 4 Summary of trials of professionally applied fluorides alone versus no treatment or placebo treatment in managing dental caries

First Author, year	Objective	Type of study	Age of the children	Intervention(s)	Clinical Outcomes	Conclusion
Timms, et al, 2020 [8]	To assess the effectiveness of fluoride varnish in preschool children for reducing the incidence of caries in dentine.	a systematic review and meta-analysis	from 6 months to 5 years	FV Vs no treatment Placebo treatment	PF of 24.15% (95% CI 12.91–35.38) for FV.	There is modest and uncertain evidence for FV reducing the risk of developing dentine caries in pre-school children.
Lenzi et al, 2016 [9]	To assess the effectiveness of the application of VF in remineralization of the initial carious lesions of the enamel	systematic review and meta-analysis	from 3 to 12 years old	Duraphat (2 to 4 months apart), Fluorniz (4 applications 1 week apart), Fluoridin (3 quarterly applications) Vs no treatment	Decay reduction of 2.04% (P = 0.0009) in the VF group.	1 application every 4 months or 4 times a year was found to be effective in remineralization of primary teeth
Gao et al, 2016[10]	Assess the effectiveness of the application of VF or caries arresting effect and remineralization in children	SR 17 RCT: 10 investigating remineralizations (6 using NaF varnish) 7 investigating arresting effect on dentine caries 4 studies included in meta-analysis of NaF	8 to 23 months	Remineralization: 5% NaF varnish Arresting: silver diamine fluoride Vs chlorhexidine vs no treatment Vs cross tooth vs brushing technique Vs glass ionomer	Overall percentage of remineralized enamel caries was 63.6 % (95 % CI: 36.0 % - 91.2 %; p < 0.001 P < 0.001). Proportion of arrested dentine caries was 65.9 % (95 % CI: 41.2 % - 90.7 %; p < 0.001)	Effectiveness of fluoride varnish in remineralization of early childhood caries (ECC) was proved. It was found that NaF could remineralise early enamel caries. Professionally applied 5 % sodium fluoride varnish can remineralise early enamel caries and 38 % silver diamine fluoride is effective in arresting dentine caries.

PF: preventive fraction, RCT: randomized controlled trials, FV: fluoride varnish, NaF: Sodium fluoride varnish, ECC: early childhood caries

Group 2: management of dental caries: 3 SR, 2 RCT (TABLE 4, TABLE 5)

Group 2 comprised 05 studies investigating the management of dental caries (enamel and dentine) on the primary teeth. Two meta-analysis and one SR compared FV to no treatment (Lenzi et al. 2016) (Gao et al. 2016) (Timms et al. 2020), and 2 RCT compared FV to the preventive oral health program (Anderson et al. 2016), (Memarpour et al. 2016).

Table 5 Summary of trials of professionally applied fluorides alone versus standard preventive oral health program in managing dental caries

First Author, year	Objective	Type of study	Age of the children	Intervention(s)	Clinical Outcomes	Conclusion
Anderson et al, 2017 [11]	To assess the impact of biannual treatment with fluoride varnish	Cluster-randomized controlled trial	from 1 to 3 years of age	Test group: The standard preventive intervention + FV every half year (Duraphat®, 22.6 mg of fluoride per ml, Colgate-Palmolive)	Between 12–24 months PI reference group was 23.2% vs Test Group 28.9% p< 0,5	No additive effect of FV intervention on the progression of surface-level dental caries in 1–3-year-old children participating in a prevention program was found. The education of parents in the use fluoride toothpaste as they start brushing the teeth of their children was found to be essential
				Vs reference group: standard preventive oral health program (including oral health information and a toothbrush and a tube of toothpaste (1,000 - 1,450 ppm fluoride)	Between 24–36 months PI reference group was 20.2% vs Test Group 21% p = 0,91	
Memarpour et al, 2016 [12]	To Evaluate the remineralization of primary teeth	Clinical trials (randomized controlled trials June 2012 to June 2013)	from 12 to 36 months	Oral health education + 5%NaF varnish (DuraShield) applied at baseline and 6 months (group 3)	caries risk reduction: group 2 28% (95% CI: -39.05 to -17.45)	4 applications of FV in conjunction with oral hygiene education were found to be effective in reducing the WSL area.
				Vs no preventive intervention (group 1) Vs Oral health education + placebo varnish (group 2)	group 3 31% (95% CI: -41.88 to -21.73). p > 0,05 (95% CI: -8.58 to 1.47).	

RCT: randomized controlled trials, FV: fluoride varnish, NaF: Sodium fluoride varnish, PI: progression index, WSL: white spot lesions

When comparing FV to no treatment, one meta-analysis investigated the enamel carious lesion and found that FV was effective for the remineralization of enamel carious lesions (decay reduction of 2,04%) [7]. One meta-analysis reported the lowest PF in this review (24,15%) and encouraged the use of FV for the management of dentine carious lesion [9] and the last one investigated both (enamel and dentine) [8]. In the last report SDF was used in dentine lesion which concluded that SDF was effective in arresting dentine lesions in primary teeth (proportion of arrested caries was 65,9%) [8].

One trial compared effectiveness of FV in the remineralization of WSL (White Spot Lesion) and found a proportion of caries risk reduction of 31% in the FV+OHE (Oral Hygiene Education) group and concluded that FV in conjunction with oral health education was effective in reducing the WSL area in the oral health program [11]. One trial found that there was no additive effect of FV in the management of dentine caries, and that the education of parents in the use of fluoride toothpaste is essential [10].

The main question addressed by this review was the effectiveness of FV in prevention and management of caries in children.

4. Discussion

Fluoride varnish in primary teeth has been described as the most convenient means of professionally applied topical fluoride agent [12],[13]. Its efficacy is as valid in the field of prevention as in the management of dental caries [14].

In the primary dentition, fewer studies can be found testing FV, and their results indicate differing effectiveness depending on the type of study, whether they were randomized or not, the age of the children and individual caries risk.

4.1. Prevention of dental caries

This systematic review showed that FV was effective for inhibiting and preventing caries development in primary teeth and was the treatment of choice to prevent ECC (Early Childhood Caries) in children.

Two studies [4], [5] in our review determined the effectiveness of FV in preventing tooth decay in primary teeth when compared to no treatment or placebo treatment.

In the Cochrane systematic review conducted by Marinho et al. 2013 the PF was 37%, while Xhemajli et al. 2019 found a higher PF of 49% in primary dentition. A study conducted in 2006 [15], found that this value ranged from 52 to 92%, which supported the use of fluoride varnish to prevent ECC and reduce the caries increment in children [16], [17].

We may explain the difference of these results by the type of the randomization and the age of the children. Marinho et al. 2013 did randomized and quazi-randomised studies on children under age 16 while Latifi-Xhemajli et al. 2019 limited the study on children under 3 years old.

The main finding of our review was when comparing FV to placebo or no treatment indicated, the FV efficacy due to the early use on young age children. It seems the earlier the VF is applied, the better will be its effectiveness in terms of prevention.

Oral health education programs can enhance parents' knowledge and performance in children's oral health [18], [19], [20]. Our review concluded the effectiveness of FV in the prevention of dental caries when it is used in complement with a standard health program depending on the individual caries risk and the area of living of the child. Based on our findings and within limitations, no difference was found between the use of the standard preventive oral health program alone and in combination with FV on primary teeth.

In policy document the use of FV, as part of preventive measures is essential [21], [22], but in young children with low risk of dental caries and in water fluoridated area (0.5 ppm), hands-on training in parental toothbrushing with or without semi-annual application of 5% NAF may not have additional effect on preventing ECC compared to only provision of oral health education to parents.

Jiang et al. 2014 conducted a RCT in area of optimally fluoridated water and investigated the effectiveness of hands-on training in parental toothbrushing, with or without semi-annual applications of 5% NAF in preventing ECC. Children were allocated to one of the three groups: Group 1(control, one-off oral health education talk to parents); Group 2 (oral health education talk and parental toothbrushing training, reinforced every 6 months); Group 3 (semi-annual application of fluoride varnish onto child's teeth in addition to the intervention provided to Group 2). At baseline, mean dmft score in Group 1 to Group 3 was 15.5, 15.6, and 15.3 respectively and then after a 24-month follow-up, the mean new dmft scores in Group 1 to Group 3 were 0.3, 0.2, and 0.3, respectively ($p > 0.05$).

It was concluded in our review that in a water fluoridated area, provision of individual oral health education to parents alone without semi-application of FV may be sufficient for preventing ECC in young children below age 3 with low risk of dental caries [23], but in children with high risk of caries the application of FV was essential to reduce the incidence and the severity of caries in pre-school children [5].

4.2. Management of dental caries

In active incipient carious lesions, fluoride gets accumulated on bacterial plaque and saliva as calcium fluoride because of topical fluoride application, such as varnishes [24]. The acidic environment reacts with the enamel surface by

stimulating available calcium fluoride dissolution to inhibit the demineralization and enhances the remineralization [25]. The presence of active lesions indicates that the reservoir of fluoride formed as a result of the use of fluoride toothpaste or fluoridated water (high frequency and low concentration) has not been enough to positively affect the demineralization–remineralization process [26]. In this sense, the association of fluoride in a low frequency and high concentration through professional topical application is suggested [14].

This systematic review concluded that effectiveness of FV for the management of dental caries depends on the localization of the dental caries (enamel or dentine). FV was an effective product to stop the progression of enamel carious lesions in primary teeth, but there is modest and uncertain evidence that it could reduce the risk of developing dentine caries in pre-school children.

The meta-analysis conducted by Lenzi et al. 2016, showed that FV is an effective approach for arresting the progression of enamel carious lesions in primary teeth. There was a statistically higher decrease in caries prevalence in the fluoride varnish group as compared to the no treatment group, the overall clinical outcome was a decrease of 2.04 (95% CI, -3.25 to -0.84; $P = 0.0009$) in the number of enamel carious lesions in the varnish versus control or no treatment group.

Also, Gao et al. 2016 conducted a meta-analysis to assess effectiveness of the application of VF for caries arresting effect and remineralization in children. Six studies investigated NaF varnish and found it could remineralize early enamel caries. Only one study of NaF reported the dimension change of caries lesion, five studies of NaF reported the percentage of demineralized early enamel caries. In the meta-analysis, the overall percentage of remineralization was 63.6% greater than no treatment (95% confidence interval [CI], 36.0% to 91.2%; $P < 0.001$) concerning enamel lesions. 7 RCT investigated arresting effect on dentine caries and found a proportion of arrested dentine caries 65.9 % (95 % CI: 41.2 % - 90.7 %; $p < 0.001$) when applying a 38% solution SDF (44,800 ppm F).

A meta-analysis conducted by Timms et al. 2020, showed that applying FV alone in preschool children in order to reduce the incidence of dentine caries may not be effective, the main clinical outcome was a PF of 24,15 % for dentine caries which was lower than the studies by Marinho et al. 2013, and Latifi-Xhemajli et al. 2019. (33,7%, 49% respectively) as mentioned earlier in this review.

In conclusion, professionally applied 5 % NAF shows the capability to remineralize early enamel caries in children [27]. On the other hand, SDF solution at 38 % is effective in arresting active dentine caries. Because the number of clinical trials that studied the arresting effect of dental caries is limited, more clinical trials should be performed [8].

Education in oral health, either with or without the use of FV, was an effective method that reduced caries in younger children [11].

Based on the results seen earlier by Jiang et al. 2014, regarding prevention of dental caries in children, daily use of fluoridated toothpaste was a preventive method which showed high quality of evidence. But concerning the management of dental caries, the effectiveness of FV with or without fluoride toothpaste depends on the progression and as well the location of the carious lesions [28].

A study by Memarpour et al. 2016, examined fluoride varnish (DuraShield, three applications quarterly) versus no treatment versus Oral Health Education (OHE) alone for the remineralization of WSL on primary teeth of children aged 12 to 36 months. After 12 months, children in the OHE group had 28% less caries, whereas those in the OHE + FV group had 31% less caries compared to the control group. Results showed a significant reduction in the amount of caries in the OHE and OHE + FV groups compared to the control group. On the other hand, there was no significant difference between the OHE and OHE + FV groups in the numbers of caries.

In agreement with those results, several studies reported that the combination of an oral health education program and the use of FV in public health programs reduced ECC and enhanced enamel caries remineralization [29],[30],[31].

However, some studies found that the application of FV failed to reduce caries in high-risk preschool children [10] and concluded that there was no additive effect of FV intervention in the management of dentine caries, when used in complement with a standard health program. This agreed with a recent study conducted to prevent early childhood caries in Iran which compared the caries development in children whose mothers did not receive any oral health education with the development of dental caries in children where oral health education was given separately or in combination with application of fluoride varnish [11].

Treatment with fluoride varnish biannually had no impact on caries progression on the buccal surfaces of primary incisors or the occlusal surfaces of primary molars [32], [33]. In public health interventions of dental caries, the parental educational including recommendations of toothbrushing with fluoride toothpaste was found to be essential [34].

Concretely, comparing the use of VF alone or in addition to a national prevention program, the results differed, depending on the child's individual caries risk and whether it was a question of prevention or management of dental caries. In terms of prevention, no additive effect of FV, when used in complement with a standard health program was found, on the other hand, four applications of FV in conjunction with oral hygiene education were effective in reducing the WSL area and were effective in term of remineralization of enamel lesions [17].

The RCT of Xhemajli et al. 2019, was conducted to test the effectiveness of FV in preventing ECC in children at high risk of caries. FV was applied four times a year, every three months. Regarding the frequency of FV application, [30] presented higher dmfs values and found that children at high caries risk aged 9-30 months benefitted more from four treatments per year, with a PF of 35%. Children with four or more fluoride varnish treatments had 15.5 dmfs versus children with 0-3 treatments who had a mean dmfs of 23.4 [14]. Nevertheless, the included studies presented different protocols for the treatment of white-spot lesions, using diverse application times and intervals as well as different commercial brands; both 4 applications at weekly intervals or 3 applications with quarterly intervals were effective in reversing active enamel carious lesions in permanent dentition. On the other hand, 2 applications of FV over 4 months on primary teeth led to 81.2% lesion inactivation, whereas only 37.8% were arrested in the control group (no treatment) at 9 months' follow-up.

These results were in agreement with those seen previously by Xhemajli et al. 2019, which leads us to deduce that 4 applications of FV per year are effective for the prevention of ECC and also for the arrest of enamel caries demineralization and the optimization of their remineralization.

5. Conclusion

The main conclusion of this paper was:

For preventing dental caries:

- FV was effective in prevention and inhibiting caries development in primary teeth when compared to no treatment.
- In young children with low risk of caries, and in water fluoridated area, provision of oral health education alone was found to be sufficient.

For management of dental caries:

- In enamel carious lesions, FV alone was an effective product to stop the progression of the lesions in primary teeth, but in dentine lesions, there is modest and uncertain evidence for fluoride varnish alone being able to reduce the risk of developing dentine caries in pre-school children.
- Four applications of FV per year were found to be effective to arrest enamel caries and optimize its remineralization.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors declare that they have no conflicts of interest to disclose.

Statement of ethical approval

All authors gave their final approval and agreed to be accountable for all aspects of the work.

Abbreviations

FV: Fluoride Varnish;
NaF: Sodium fluoride;
SDF: Silver diamine fluoride;
WSL: Whit Spot Lesions;
RCT: Randomized Controlled Trials;
SR: Systematic reviews;
MA: and meta- analysis;
ECC: Early Childhood Caries;
PF: Prevention Fraction;
PI: Progression Index

Author contributions

Author 1: Contributed to conception, design, data acquisition and interpretation, performed all statistical analyses, drafted and critically revised the manuscript.

Author 2: Contributed to conception, design, and critically revised the manuscript.

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