

The Frequency of Fluoride Varnish Application for Prevention of Dental Caries – A Systematic Review and Meta-Analysis

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History

- Submission Date: 21-02-2022;
- Revised Date: 03-03-2022;
- Accepted Date: 09-04-2022.

DOI : 10.5530/ijmedph.2022.2.16

Article Available online

<http://www.ijmedph.org/v12/i2>

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ABSTRACT

Background: Oral health is now increasingly regarded as a crucial component of overall health and well-being. Fluoride varnish (FV) is thought to be safe, well-tolerated by children and simple to administer by health professionals for the prevention of dental caries. Since the year 2000, various reviews on the use of fluoride therapy in the prevention of dental caries have been published, but none on the frequency of fluoride varnish application. Hence aim of this systematic review is to evaluate the frequency of fluoride varnish application for prevention of dental caries in children. **Objectives:** To assess the effectiveness of frequency of fluoride varnish application in prevention of dental caries among preschool children. **Methodology:** **Search Strategy:** We searched the following databases for Randomized controlled trials (RCTs) in PubMed, Cochrane, Wiley, Proquest, Science Direct and Google Scholar which yielded 5657 articles. After screening the titles, 5657 articles were ruled out since they were unrelated to the systematic review's goals. The remaining 75 articles were searched for duplication using Mendeley Software. Out of 75 articles, 12 articles were found to be duplicates. The remaining 63 articles were screened through abstracts and full text screening as next step. Out of 63 articles, 53 were excluded for various reasons like did not meet the inclusion criteria. Finally, 10 articles were qualitatively analyzed after which they were included in the systematic review and 6 in meta-analysis. Various key words included for screening were "Fluoride Varnish", "Dental Caries", "Varnish Effectiveness" and "Frequency". Extraction of the information and assessment of the methodological quality of the included studies using Risk of Bias was done by two authors (DV and RS). Meta-analysis using the random-effects model was conducted for the outcome (dmft score) after application of fluoride varnish. Mean difference (MD) or standardized mean difference (SMD) were used to estimate the effect, with 95% confidence intervals. **Study Eligibility:** All the studies published from January 2005 to April 2020, conducted among children between 0 to 5 years, articles published in English language were included. Studies conducted on animals, a review and a systematic review, participants aged above 5 years were excluded. **Study appraisal and synthesis methods:** Studies were assessed for quality with the help of pre-determined criteria which categorized the studies into high, medium and low quality. Random effect model was used for performing meta-analysis. **Results:** In total, 10 articles were included for qualitative synthesis. Various fluoride varnish and their frequency were assessed in the prevention of dental caries. All the studies had used Sodium fluoride varnish as a material however 3 studies have specifically mentioned the name, Durashield, Durafleur and Cavityshield respectively. Three studies have mentioned that they have applied fluoride varnish thrice in two weeks while rest of them have applied semiannually i.e.; once in every six months. The pooled overall cumulative mean difference of the dmft score after application of fluoride varnish was 2.67. **Conclusion:** Intensive application (Thrice in two weeks) of fluoride varnish gave better results when compared with semiannual application (Twice in a year) of fluoride varnish in preventing dental caries in preschool children. **Key words:** Fluoride varnish, Dental caries, Frequency, Preschool children, Varnish effectiveness, Prevention.

INTRODUCTION

Dental caries is one of the most common pandemic chronic infectious childhood disorders, and it is preventable and manageable on an individual and population basis. According to a 2009 World Health Organization research, dental caries affected about

60%–90% of schoolchildren and the majority of adults in industrialised countries.¹ Caries is still more prevalent in some developing countries, such as India, Brazil, China, Thailand, and the Republic of Niger, despite remarkable advances in evidence-

Cite this article : Deepika V, Sankeshwari RM, Ankola AV, Hampiholi V, Jalihal S, Choudhury AR, *et al.* The Frequency of Fluoride Varnish Application for Prevention of Dental Caries – A Systematic Review and Meta-Analysis. Int J Med Public Health. 2022;12(2):82-7.

based caries research and effective preventive practises. The poorest, under-privileged, certain ethnic minorities, and immigrant populations bear the brunt of the disease's impact.²

Fluoride varnish (FV) is thought to be safe, well-tolerated by youngsters, and simple to administer by health professionals.³ These characteristics, together with its alleged anti-caries advantages, have led to it being generally suggested as the primary professional fluoride therapy for the prevention of dental caries in children under the age of six.⁴

Even though several reviews of the use of fluoride therapies in preventing dental caries have been published since the year 2000, there is no reviews regarding the frequency of fluoride varnish application. In a study by Weintraub *et al.*⁵ children who received intended fluoride treatments had a statistically significantly lower percentage of children with caries incidence (any decaying or filled surfaces at the last follow-up inspection) than children who did not receive fluoride varnishes. The findings of this study back up the use of fluoride varnish to prevent ECC and caries in very young infants. The regular semi-annual administration of FV may not be sufficient in avoiding ECC in children at high risk for caries formation in the primary dentition. An extensive reapplication strategy (three doses in the first two weeks) has been indicated to provide higher protection from caries advancement than a single application.⁶ Semiannual applications of fluoride varnishes were originally recommended ten years ago.⁷ Annual applications (1-4 times a year) of varnish have also been recommended. There is still no solid evidence of superiority of this regime. Hence aim of this systematic review is to evaluate the frequency of fluoride varnish application for prevention of dental caries in children.

METHODOLOGY

Focused Question

The research question was developed according to the Population, Intervention, Comparison, Outcome and Study Design format:

“Which is the most effective frequency of fluoride varnish application for prevention of dental caries among preschool children?”

PICO FORMAT

P(Population): Preschool children who are at risk of dental caries

I(Intervention): Intensive application of fluoride varnish (Thrice in two weeks)

C(Comparison): Other methods of fluoride varnish applications

O(Outcome): Incidence of caries using dmft score

S (Study Designs): Randomized Controlled Trials, Clinical trials.

PROTOCOL AND REGISTRATION

The review has been registered in PROSPERO; The registration number of this review is CRD42020200285 and can be accessed on the website <http://www.crd.york.ac.uk/prospero/index.php>.

SEARCH STRATEGY

The electronic search was performed with the databases PubMed, Proquest, Wiley, Science direct, EBSCO, Cochrane Library, Embase, Scopus, Web of Science and Google Scholar with a platform-specific search strategy consisting of combinations of controlled terms (MeSH) and text words. Additional hand searching of literature was also performed. Studies included were only in English language, which were published between the years of 2005 to 2020. Studies published in other than English languages were excluded from the study. The keywords for search were selected by reviewing the literature. The search strategy terms included “Fluoride Varnish”, “Dental Caries”, “Varnish Effectiveness” and “Frequency” with no additional filters.

ELIGIBILITY CRITERIA

Inclusion and exclusion criteria were fixed and the studies were screened based on the criteria mentioned below: -

INCLUSION CRITERIA

Following are the inclusion criteria for this systematic review:

1. **Study design:** Randomized controlled trials, Case control and cohort studies.
2. **Participants:** Children between age group between 0 to 5 years who are at high risk of dental caries.
3. **Intervention:** Fluoride varnish application.
4. **Comparisons:** Different frequencies of fluoride varnish application.
5. **Outcome:** Assessment of best method for application of fluoride varnish assessed using dmft score.
6. Articles published in English.
7. Year of publication from January 2005 to April 2020
8. All original articles.

EXCLUSION CRITERIA

1. Review articles
2. Articles published in other languages.

STUDY SELECTION AND SCREENING PROCESS

All titles and abstracts retrieved through the search technique were individually examined and included if they matched the inclusion criteria by one review author (DV). The entire texts of all of the studies that were featured were later obtained. The full texts of the articles were obtained, and they were screened by reading the entire article before deciding if they matched the inclusion requirements. The level of concordance between the two reviewers (DV and RS) was 0.92 for titles and abstracts and 0.94 for whole texts, as measured by Cohen's kappa. Whenever there was a question or disagreement about whether a study was eligible for inclusion, the issue was resolved by consulting with a third author (AA). Finally, ten studies were found and included in the systematic review. All of the studies that were excluded were noted, along with the explanation for each study's exclusion. The journal titles, research authors, and institutions where the studies were conducted were not hidden from the writers.

DATA EXTRACTION

A standardized data extraction form was prepared by DV in Microsoft Excel and assessed by two authors (DV and RS). Any disagreement between the authors was resolved by discussion. The following criteria were predetermined for extracting the data: -

- The major interest was to evaluate the frequency of fluoride varnish application and the change in the mean dmft values after follow up.
- Studies that compared fluoride varnish with other modalities of dental caries prevention were also considered.

Data items included for extracting the data were

- **Article detail:** Author name, Country and Year
- **Study Setting:** Whether the study was Randomized controlled trial or clinical trial?
- **Aim:** Study intention in each study
- **Age/ Age Group:** Age or age group considered in the study
- **Sample Size:** Sample size for the particular age or age group

- **Follow up:** For how long was the clinical study followed to assess dental caries status?
- **Type of fluoride varnish used:** Which type of fluoride varnish was applied in the respective study?
- **Frequency:** What was the frequency of fluoride varnish applied?
- **Interpretation:** Interpretation of dmft before and after intervention.
- **Outcome:** How did the outcome was assessed or which index was used to assess the outcome?

ASSESSMENT OF RISK OF QUALITY OR BIAS

The approach advised by the Cochrane Collaboration's tool for Randomized controlled trials was used to assess the risk of bias of the included research. For non-randomized controlled trials, there is the ROBINS – I tool.⁸ The investigations were evaluated both internally and outside. 85 The first stage was to provide a brief summary of all of the research that were included. The following criteria were used to assess the probability of bias in studies:• Random sequence generation

- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcome assessment
- Incomplete outcome data
- Other bias

STATISTICAL ANALYSIS

For statistical analysis, STATASE 16.1 was employed. The primary summary metrics were mean differences and effect size. To show the differences between several intervention groups and publication bias, forest plots and funnel plots were designed. Where p 0.05, the overall estimated effect was classified as significant.

DATA SYNTHESIS

To decide whether to use random effect model of fixed effect model, heterogeneity of the studies was analyzed. Statistical heterogeneity was tested using I2 statistics (0%-40% not important, 30%-60%: Representing moderate heterogeneity, 50%-90%: representing substantial heterogeneity, 75%-100% as considerable heterogeneity) as described by the PRISMA protocol for writing systematic review. If the heterogeneity was above 50% then random effect model was used for conducting meta-analysis. The weight for each study, and estimates prevalence with upper and lower confidence intervals was obtained. Statistical software STATASE was used to do meta-analysis.

RESULTS

Study Selection

In the systematic review for evaluation of frequency of application of fluoride varnish in the prevention of dental caries among 0 to 5 years old children, the process of selection was initiated by stepwise screening of the articles. 1048 records were identified through data search using search strategy in PubMed. 3510 records were identified through data search using search strategy in Google scholar. 476, 17,345,261 records were identified through data search using search strategy in Proquest, Cochrane, Wiley and Science Direct respectively. Total articles number arrived to be 5657. Second step was screening through titles. And after screening through titles 5582 articles were excluded because they were not related to the objectives of the systematic review. 75 articles which remained were screened for duplicates through Mendeley Software. Out of 75 articles, 12 articles were found to be duplicates. The remaining 63 articles were screened through abstracts and full text screening as next

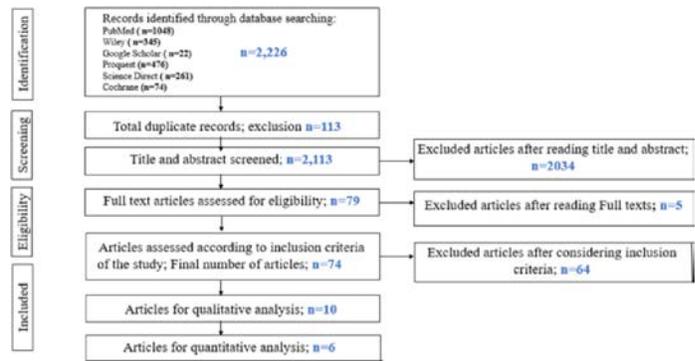


Figure 1: Search Strategy.

step. Out of 63 articles, 53 were excluded for various reasons like did not meet the inclusion criteria. Finally, 10 articles were qualitatively analyzed after which they were included in the systematic review and 6 articles were considered for meta-analysis. (Figure 1).

STUDY CHARACTERISTICS

There are 10 studies^[9-11,6,12-17] included in this systematic review. All the studies included in the systematic review are Randomized controlled trials. Age of the study participants ranged from 0 to 5 years. All the studies had procured informed consent from the parents and guardians prior to the conduct of the study. A total of 6238 children were part of the studies among which 3860 children received fluoride varnish application semi-annually and 2378 children received 3 applications within 2 weeks period. Children received various fluoride varnish like Durashield, Durafluor and Cavity Shield. Fluoride varnish was applied by dental professionals in all the included studies. Overall, there was no attrition observed at end of follow - up period. All the studies had used Sodium fluoride varnish as a material however 3 studies have specifically mentioned the name, Durashield, Durafluor and Cavityshield respectively.

Frequency of Fluoride Application

Frequency of fluoride application was found to be 2 types. In three studies children received an intensive fluoride varnish treatment i.e. application of fluoride varnish thrice in two weeks. Children of other 7 studies have received semiannual application of fluoride varnish.

Effect of Fluoride Varnish Application

The intervention reduced the risk of surface level caries by 25% over two years (RR=0.75; 95 percent CL = 0.71, 0.80). [Divaris et al. 2021].¹⁰ The mean (SD) numbers of newly decaying primary tooth surfaces detected after three years in the fluoride varnish and placebo groups were 9.8 (8.6) and 7.4 (7.7), respectively. Caries rates in the test group were up to 36% higher, indicating that the trial failed to reveal a clear difference in efficacy between fluoride varnish application and placebo. [Weinstein et al., 2009].⁶ Hands-on teaching in parental tooth brushing, with or without rigorous application of 5% sodium fluoride varnish, may have an extra effect on preventing ECC in young infants in a water fluoridated area [Emily et al. 2014].¹² A two-year course of rigorous fluoride varnish prevents primary tooth dentin caries better than a placebo varnish [Olievera et al.]. When compared to routine dental health care, a randomized clinical research failed to show that the semiannual use of sodium fluoride varnish would prevent children from developing dental caries lesions into dentin [Laila et al.].¹⁵

When compared to baseline, the intense fluoride varnish group had a substantial reduction in S. Mutans levels ($p < 0.001$) at the 3-month visit. Post hoc testing revealed a reduction within one week of using the intense fluoride varnish ($p < 0.001$), followed by another drop between one and two weeks ($p < 0.001$). A frequent FV treatment schedule has been proposed as a vehicle for prolonging fluoride contact with the enamel surface, enhancing the synthesis of fluoridated hydroxyapatite, and reducing enamel solubility in an acidic environment, hence improving FV therapy benefits [Slade et al. 2018].¹⁷ Meta - Analysis was performed to assess the frequency of fluoride varnish application and its effect on dental caries. Main interest was to assess the best method of application of fluoride varnish amongst the 2 techniques i.e., intensive application and semi-annual application, which were used in the studies. 6 studies were included for meta-analysis. Dmft scores before and after interventions were used to plot forest plots. The results obtained from the analysis showed high precision values while considering 95% confidence interval. 6 studies were assessed the effect of fluoride varnish application on dental caries. The pooled overall mean of the dmft score after intervention was found to be 2.67 [Figures 2 and 3].

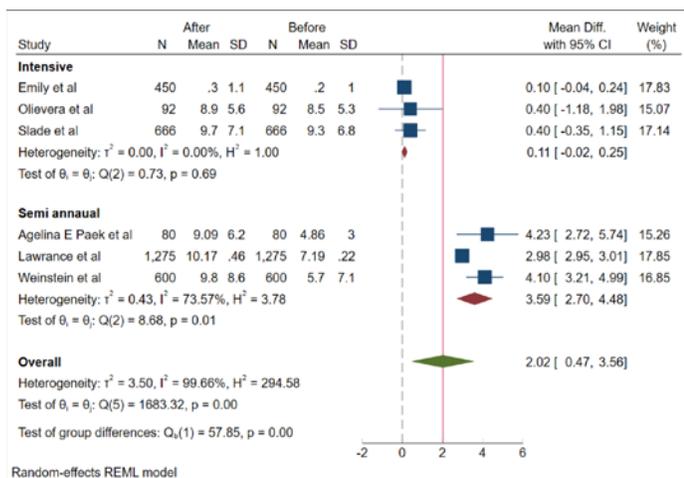


Figure 2: Forest plot showing effect of Fluoride varnish application on dental caries.

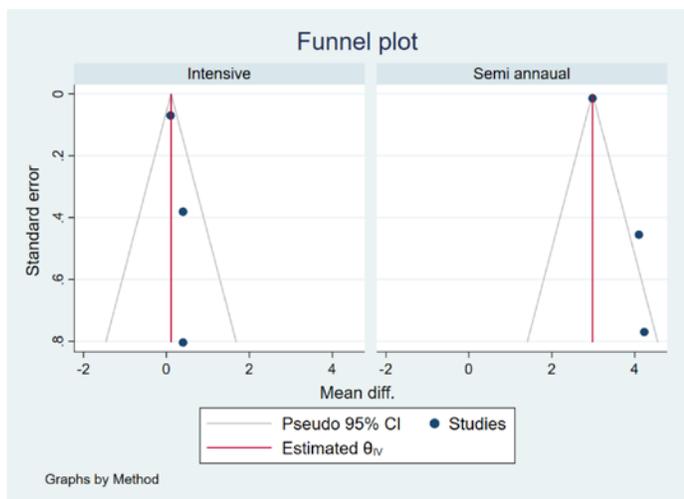


Figure 3: Funnel plot showing publication bias.

Risk of BIAS in Included Study

10 Randomized controlled trials were assessed for risk of bias. All 10 articles included in the study had low risk of bias. 9 studies had low/unclear risk of bias with respect to blinding of the participants. One study reported incomplete outcome of data. 7 studies showed low/unclear risk of bias regarding selection of study participants. 1 study showed high risk of bias in attrition bias. [Figures 4 and 5].

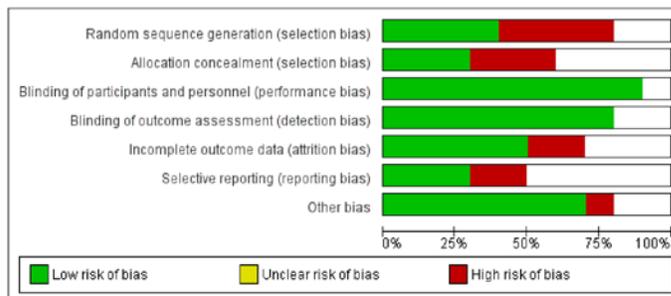


Figure 4: Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

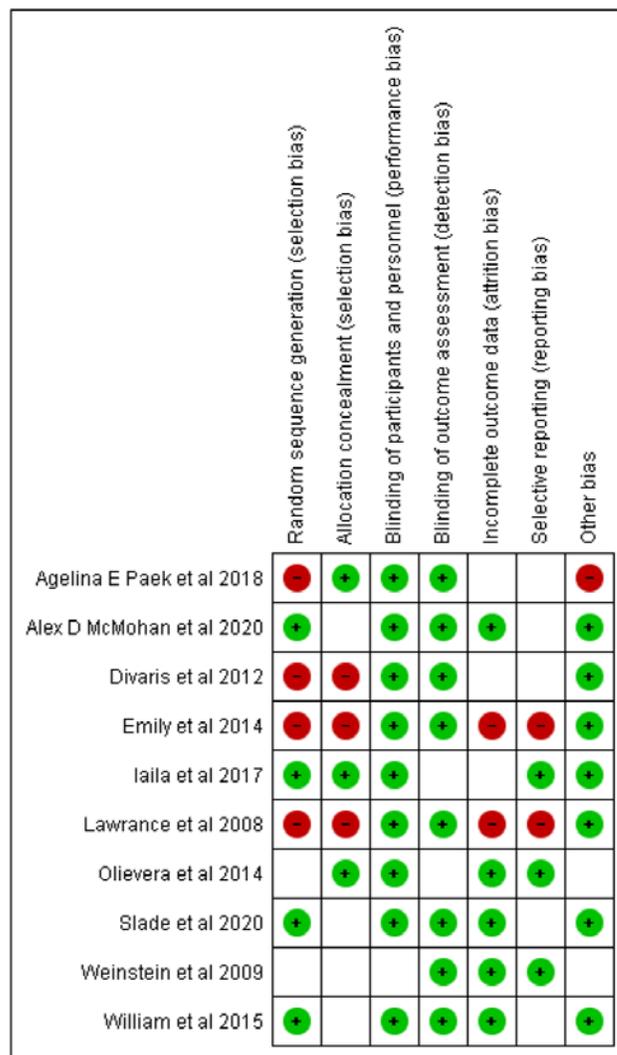


Figure 5: Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

DISCUSSION

Using qualitative syntheses, this systematic review evaluated the efficacy of fluoride varnish in preschoolers. The results demonstrated a statistically significant difference favoring fluoride varnish at the surface level. Overall, the varnish group had a lower caries increase of one surface per child or less. This distinction may be clinically insignificant. There was no discernible difference in tooth structure between children who got Fluoride varnish and those who did not. The DMFs and DMFT data is usually the chosen method for computing dental caries outcome because it is considered simple to read and allows the combining of different caries measuring methods (dmfs, dfs, ds, dmft, dft, dt). The results of our systematic review showed that fluoride varnish is moderately effectively in the reduction of dental caries. In the study conducted by Slade *et al.*¹⁷ a significant reduction ($P < 0.001$) in MS levels was observed in the intensive FV treatment group at the 3-month visit compared with baseline. This result is supported by two *in-vitro* studies [Pettersson *et al.* and Skold *et al.*]^{18,19} using an intensive fluoride varnish regimen showed that multi fluoride application provided a high deposit on the enamel surface. In superficial, microscopic cavities, the regimen was able to nearly stop all the carious processes.

In a separate trial, Divaris *et al.*¹⁰ found that the intervention reduced the 2-year surface-level caries risk by 25% (relative risk, RR = 0.75; 95 percent CL = 0.71, 0.80). The efficacy of FV was highly variable depending on the baseline surface pathology. Lawrance *et al.*²⁰ used cluster analysis to correct for intra-cluster correlation among children in the same community and found that FV therapy resulted in an 18% reduction in the 2-year mean 'net' dmfs increment for Aboriginal children and a 25% reduction for all children. The adjusted odds ratio for caries incidence in the controls was 1.96 times greater than in the FV group (95 percent CI = 1.08–3.56; $P = 0.027$). Olievera *et al.*¹⁴ found that using an aggressive fluoride varnish for two years protects primary tooth dentin caries more efficiently than using a placebo varnish.

A more recent study [Schwendicke *et al.* 2018]²¹ revised the Cochrane evidence to get more recent FV efficacy data and applied it to diverse caries risk situations in 12-year-olds in Germany. The authors concluded that administering FV at the dentist office is unlikely to be cost-effective in low-caries-risk individuals, and that it should be limited to high-caries-risk populations or administered in nonclinical settings. These findings, however, apply to the permanent teeth rather than the primary dentition. Our findings revealed that the efficacy of FV is lower in recent trials than in earlier trials. This could be because older studies have a larger risk of bias, particularly selection bias, which can overstate the benefit of therapies.

Limitation of the systematic review: Large heterogeneity was observed amongst the studies. Also, future studies showed focus more on larger sample size and longer follow-up periods.

CONCLUSION

When comparing the outcomes of intensive fluoride varnish application (three times in two weeks) to semiannual fluoride varnish application (twice a year) in avoiding dental caries in preschool children, intensive application (three times in two weeks) produced better results. FV in the dentist office, on the other hand, is unlikely to be cost-effective in low-caries-risk individuals, implying that it should be limited to high-caries-risk populations.

ACKNOWLEDGEMENT

We would like to thank faculty of Department of Public Health Dentistry, KLE VK Institute of Dental Sciences, Belagavi, India, for their support and guidance.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

FV: Fluoride Varnish; **CRD:** Centre for Reviews and Dissemination; **MeSH:** Medical subject heading; **RCT:** Randomized controlled trial; **DV:** Deepika V; **RS:** Roopali Sankeshwari; **AA:** Anil Ankola; **ROBINS -1:** Risk of bias in Non-randomized studies of Intervention – 1; **STATASE:** Statistics and Data; **PRISMA:** Preferred reporting items for systematic review and meta-analysis; **DC:** Dental Caries; **ECC:** Early Childhood Caries; **F:** Fluoride.

SUMMARY

It is now widely recognized that oral health is an important part of overall health and well-being and we, as dental professionals, can be proud of how far we have come in enhancing the oral health of both adults and children. Fluoride varnish (FV) is thought to be safe, well-tolerated by children and simple to administer by health professionals for the prevention of dental caries. Even though several reviews of the use of fluoride therapies in preventing dental caries have been published since the year 2000, there is no reviews regarding the frequency of fluoride varnish application. Hence aim of this systematic review is to evaluate the frequency of fluoride varnish application for prevention of dental caries in children. To study and evaluate the frequency of fluoride varnish application in prevention of dental caries among 0- to 5-year-old children.

We searched the following databases for Randomized controlled trials (RCTs) in PubMed, Cochrane, Wiley, Proquest, Science Direct and Google Scholar which yielded 5657 articles. Second step was screening through titles. And after screening through titles, 5657 articles were excluded because they were not related to the objectives of the systematic review. 75 articles which remained were screened for duplicates through Mendeley Software. Out of 75 articles, 12 articles were found to be duplicates. The remaining 63 articles were screened through abstracts and full text screening as next step. Out of 63 articles, 53 were excluded for various reasons like did not meet the inclusion criteria. Finally, 10 articles were qualitatively analyzed after which they were included in the systematic review. Various key words included for screening were "Fluoride Varnish", "Dental Caries", "Varnish Effectiveness" and "Frequency". Extraction of the information and assessment of the methodological quality of the included studies using Risk of Bias was done by two authors (DV & RS). Meta-analysis using the random-effects model was conducted for the outcome (dmft score) after application of fluoride varnish. Mean difference (MD) or standardized mean difference (SMD) were used to estimate the effect, with 95% confidence intervals.

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after application of fluoride varnish was 2.67. A significant reduction in MS levels and dmft score was observed in intense fluoride varnish treatment (Thrice in two weeks) group. Application of fluoride varnish every 6 months does not prevent primary tooth dentin caries incidence effectively.

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Cite this article : Deepika V, Sankeshwari RM, Ankola AV, Hampiholi V, Jaliha S, Choudhury AR, et al. The Frequency of Fluoride Varnish Application for Prevention of Dental Caries – A Systematic Review and Meta-Analysis. *Int J Med Public Health.* 2022;12(2):82-7.