

CADTH Reference List

# Fluoride Varnish for the Prevention and Management of Dental Issues

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## Key Messages

- CADTH found 1 systematic review, 10 randomized controlled trials, and 1 non-randomized study about the clinical effectiveness of different formulations of fluoride varnish for the prevention and management of dental issues.
- CADTH found 2 evidence-based guidelines about the use of fluoride varnish for the prevention and management of dental issues.

## Research Questions

1. What is the clinical effectiveness of different formulations of fluoride varnish for the prevention and management of dental issues?
2. What are the evidence-based guidelines regarding the use of fluoride varnish for the prevention and management of dental issues?

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was fluoride varnish. No filters were applied to limit retrieval by study type. Comments, newspaper articles, editorials, and letters were excluded. Where possible, retrieval was limited to the human population. The search was completed on September 6, 2022, and limited to English-language documents published since January 1, 2017. Internet links were provided, where available.

### Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in [Table 1](#). Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of the selected publications. Open access full-text versions of evidence-based guidelines were reviewed when available, and relevant recommendations were summarized.

## Results

One systematic review,<sup>1</sup> 10 randomized controlled trials,<sup>2-11</sup> and 1 non-randomized study<sup>12</sup> were identified about the clinical effectiveness of different formulations of fluoride varnish for

**Table 1: Selection Criteria**

Criteria	Description
Population	People of any age
Intervention	Any formulation of fluoride varnish (e.g., 5% sodium fluoride with sucralose, 5% sodium fluoride with xylitol, 2.5% sodium fluoride with sucralose with hydroxyapatite and xylitol, 1.5% ammonium fluoride)
Comparator	Q1: Alternative formulations of fluoride varnish Q2: Not applicable
Outcomes	Q1: Clinical benefits (e.g., incidence of dental caries, severity of tooth decay, tooth remineralization, fluoride uptake) and harms (e.g., adverse events) Q2: Recommendations regarding best practices (e.g., treatment protocols [e.g., frequency of applications], appropriate patient populations, advice on which formulations should or should not be used)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, evidence-based guidelines

the prevention and management of dental issues. Two evidence-based guidelines<sup>13,14</sup> were identified about the use of fluoride varnish for the prevention and management of dental issues. No relevant health technology assessments were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in [Appendix 1](#).

### Overall Summary of Findings

One systematic review,<sup>1</sup> 10 randomized controlled trials,<sup>2-11</sup> and 1 non-randomized study<sup>12</sup> were identified about the clinical effectiveness of different formulations of fluoride varnish for the prevention and management of dental issues. The formulations studied were 0.9% difluorsilane,<sup>1</sup> chlorhexidine-fluoride,<sup>2</sup> 5% sodium fluoride (NaF) plus tricalcium phosphate (TCP),<sup>3,4,8,12</sup> 5% NaF plus casein phosphopeptide amorphous calcium phosphate (CPP-ACP),<sup>6,8,9,11</sup> titanium tetrafluoride (TiF<sub>4</sub>),<sup>5</sup> 5% NaF plus 10% polyvinylpyrrolidone-iodine (PVP-I),<sup>7</sup> and 1.5% ammonium fluoride.<sup>10</sup> Most studies compared their fluoride varnish of interest to 5% NaF.<sup>1-7,9-12</sup> Poza-Pascual et al. (2021)<sup>8</sup> compared the efficacy of 5% NaF plus CPP-ACP with 5% NaF plus TCP. Radha et al. (2020)<sup>11</sup> compared 5% NaF plus CPP-ACP with both 5% NaF and 5% NaF plus amorphous calcium phosphate. The majority of studies were in children.<sup>1,4-8,10,11</sup> Two studies examined the occurrence of adverse events associated with fluoride varnish.<sup>7,10</sup> No harms were observed with the use of 5% NaF plus PVP-I,<sup>7</sup> 1.5% ammonium fluoride,<sup>10</sup> or 5% NaF.<sup>10</sup> Detailed study characteristics are presented in [Table 2](#).

Seven studies examined the clinical effectiveness of various fluoride varnishes for the prevention of dental caries or white spot lesions (WSL).<sup>1-3,5,7,8,10</sup> A systematic review<sup>1</sup> found that out of 8 professionally applied fluorides, only 2 were shown to be effective at preventing early childhood caries. Of these, 0.9% difluorsilane varnish ranked higher than 5% NaF varnish.<sup>1</sup> Two randomized controlled trials conducted in young children found that TiF<sub>4</sub><sup>5</sup> and 5% NaF plus 10% PVP-I<sup>7</sup> both reduced caries occurrence compared to 5% NaF. Two randomized controlled trials found no difference in preventive effect between the varnishes studied.<sup>3,10</sup>

Six randomized controlled trials<sup>2,4-6,9,11</sup> and 1 non-randomized study<sup>12</sup> compared the effectiveness of 5% NaF to another varnish formulation in the treatment of caries or WSLs.

Chen et al. (2021)<sup>4</sup> showed that, after the administration of 25% silver nitrate, 5% NaF plus TCP had a higher caries arrest rate compared to 5% NaF. The comparative effectiveness of 5% NaF plus CPP-ACP varied across studies. One study<sup>11</sup> showed that 5% NaF plus CPP-ACP reduced the size of WSLs but did not differ in the number of active WSLs when compared to 5% NaF and 5% NaF plus ACP. Another study<sup>9</sup> showed that although 5% NaF plus CPP-ACP was more effective at caries arrest and reversal than 5% NaF at 3 months, both groups were equally effective by 6 and 12 months of treatment. Conversely, Mekky et al. (2021)<sup>6</sup> showed that 5% NaF plus CPP-ACP resulted in a greater decrease in active lesions compared to 5% NaF. Neither chlorhexidine-fluoride<sup>2</sup> or TiF<sub>4</sub><sup>5</sup> were clinically superior at caries arrest and/or reversal compared to 5% NaF.

Three studies compared a fluoride varnish that could be applied to wet teeth (e.g., Nupro White, Clinpro) to a fluoride varnish that required application to dry teeth only.<sup>8,9,12</sup> By the end of the study period, no difference in effectiveness was observed when Nupro White (5% NaF) was compared to MI Varnish (5% NaF plus CPP-ACP) in the treatment of dental caries.<sup>9</sup> A non-randomized controlled study<sup>12</sup> concluded that Clinpro (5% NaF plus TCP) was more effective at remineralizing mild lesions and Duraphat (5% NaF) was more effective at remineralizing moderate lesions.

A position statement on caries prevention in Indigenous children<sup>13</sup> and guidelines from the U.S. Preventive Services Task Force<sup>14</sup> recommend the application of fluoride varnish in children starting at the age of primary tooth eruption by primary care clinicians<sup>13,14</sup> or by trained lay workers.<sup>13</sup> The Canadian Pediatric Society recommends reapplication of fluoride varnish every 3 to 6 months.<sup>13</sup>

**Table 2: Summary of Included Clinical Effectiveness Studies**

Study citation	Study design, population	Intervention and comparator(s)	Relevant outcome(s)	Author's conclusions
<b>Systematic reviews</b>				
Manchanda et al. (2022) <sup>1</sup>	SR with 24 RCTs; NMA with 10 RCTs <b>Population:</b> Children younger than 6 years <b>N = NR</b>	<b>Intervention:</b> Professionally applied topical fluorides (e.g., 0.9% DFS; 5% NaF) <b>Comparator:</b> Professionally applied topical fluorides (e.g., 0.9% DFS; 5% NaF)	ECC prevention	Two professionally applied fluorides (0.9% DFS and 5% NaF varnish) were effective at preventing ECC. Of these, 0.9% DFS was ranked highest.
<b>Randomized controlled trials</b>				
Park et al. (2022) <sup>2</sup>	<b>Study design:</b> Placebo-controlled RCT <b>Population:</b> Elderly adults with 2 or 3 non-cavitated root carious lesions <b>N = 23</b>	Application at 0, 3, 6, and 9 months <b>Intervention:</b> Chlorhexidine-fluoride (Cervitec F) <b>Comparator:</b> 5% NaF (Duraphat)	Fluorescence loss on QLF images Lesion volume Bacterial activity	The greatest reduction in fluorescence, lesion volume, and bacterial activity was observed in Cervitec F. However, no superiority of a specific varnish application was confirmed over the observation period.

Study citation	Study design, population	Intervention and comparator(s)	Relevant outcome(s)	Author's conclusions
Sardana et al. (2022) <sup>3</sup>	<p><b>Study design:</b> RCT</p> <p><b>Population:</b> Patients with multi-bracketed fixed orthodontic appliances</p> <p><b>N = 99</b></p>	<p>Quarterly application</p> <p><b>Intervention:</b> 5% NaF + TCP with standard OHI</p> <p><b>Comparator:</b> 5% NaF with standard OHI</p>	WSL occurrence	NaF varnish and NaF plus TCP varnish both reduced the odds of WSLs. There was no significant difference among the treatment groups in preventing WSLs.
Chen et al. (2021) <sup>4</sup>	<p><b>Study design:</b> Parallel, double-blind RCT</p> <p><b>Population:</b> Children, aged 3 years, with active primary tooth dentine caries</p> <p><b>N = 408</b></p>	<p>Semiannual following application of 25% silver nitrate</p> <p><b>Intervention:</b> 5% NaF + TCP</p> <p><b>Comparator:</b> 5% NaF</p>	Caries arrest rate	After 25% silver nitrate application, a 5% NaF plus functionalized TCP varnish was more effective than a 5% NaF varnish at arresting dentine caries in primary teeth.
De Souza et al. (2021) <sup>5</sup>	<p><b>Study design:</b> Placebo-controlled RCT</p> <p><b>Population:</b> Children, aged 6 to 8 years</p> <p><b>N = 60</b></p>	<p>Application once a week for the first 4 weeks, then at 6 and 12 months</p> <p><b>Intervention:</b> TiF<sub>4</sub></p> <p><b>Comparator:</b> 5% NaF</p>	<p>ICDAS score</p> <p>Fluorescence loss</p> <p>Visual plaque index</p> <p>Degree of acceptability</p> <p>New caries lesions</p>	<p>TiF<sub>4</sub> reduced fluorescence and incidence of new caries, whereas NaF did not show any changes.</p> <p>ICDAS scores, visual plaque index, and satisfaction were similar between treatments.</p>
Mekky et al. (2021) <sup>6</sup>	<p><b>Study design:</b> RCT</p> <p><b>Population:</b> Children aged 3 to 5 years with ≥ 4 active WSLs on their anterior primary teeth</p> <p><b>N = 44</b></p>	<p>Three applications, 2 weeks apart</p> <p><b>Intervention:</b> 5% NaF + CPP-ACP (MI Varnish)</p> <p><b>Comparator:</b> 5% NaF (Duraphat)</p>	<p>Oral hygiene debris index</p> <p>Number of active WSLs</p> <p>DIAGNOdent score</p>	MI Varnish significantly decreased the number of active WSLs and the DIAGNOdent score compared to Duraphat Varnish.
Milgrom et al. (2021) <sup>7</sup>	<p><b>Study design:</b> Parallel, double-blind, active control RCT</p> <p><b>Population:</b> Children aged 49 to 84 months</p> <p><b>N = 284</b></p>	<p>Application every 3 months</p> <p><b>Intervention:</b> 5% NaF + 10% PVP-I</p> <p><b>Comparator:</b> 5% NaF</p>	<p>Surface-level primary molar caries lesion increment</p> <p>Harms</p>	The varnish containing NaF plus PVP-I had a lower caries lesion increment value than NaF varnish alone. No harms were observed with the use of NaF plus PVP-I.
Poza-Pascual et al. (2021) <sup>8</sup>	<p><b>Study design:</b> RCT</p> <p><b>Population:</b> Children, aged 4 to 12 years, at high caries risk</p> <p><b>N = 58</b></p>	<p>Application every 3 months</p> <p><b>Intervention:</b> 5% NaF + CPP-ACP (MI Varnish)</p> <p><b>Comparator:</b> 5% NaF + TCP (Clinpro White)</p>	<p>Plaque and hygiene index</p> <p>Caries incidence</p>	NR

Study citation	Study design, population	Intervention and comparator(s)	Relevant outcome(s)	Author's conclusions
Sleibi et al. (2021) <sup>9</sup>	<b>Study design:</b> RCT <b>Population:</b> Adults, aged 45 to 92 years, with xerostomia and primary root caries <b>N = 80</b>	Application at 0, 3, 6, and 12 months <b>Intervention:</b> 5% NaF + CPP-ACP (MI Varnish) <b>Comparator:</b> 5% NaF (Nupro White)	Severity Index for root caries DIAGNOdent score Plaque index Surface roughness Lesion dimension	Both varnishes had the potential to arrest or reverse root caries. They both showed significant improvement in the caries severity and plaque indices, surface roughness, lesion dimension and DIAGNOdent readings.
Turska-Szybka et al. (2021) <sup>10</sup>	<b>Study design:</b> Parallel RCT <b>Population:</b> Children, aged 36 to 71 months, with ≥ 1 non-cavitated lesion <b>N = 180</b>	Application every 3 months <b>Intervention:</b> 1.5% ammonium fluoride (Fluor Protector S) <b>Comparator:</b> 5% NaF (Duraphat)	Caries incidence Adverse events	Both varnishes reduced the incidence of caries to an equal degree. No adverse effects were observed or reported.
Radha et al. (2020) <sup>11</sup>	<b>Study design:</b> RCT <b>Population:</b> Children with active WSL on primary maxillary anterior teeth <b>N = 60</b>	Application at 0, 2, 4, 12, and 24 weeks <b>Intervention:</b> 5% NaF + CPP-ACP (MI Varnish) <b>Comparator:</b> 5% NaF; 5% NaF + ACP	WSL activity and dimension	MI Varnish showed a statistically significant reduction in WSL dimension compared to the other varnish types. There was no difference between groups with change of active to inactive WSL.
<b>Non-randomized studies</b>				
Biondi et al. (2017) <sup>12</sup>	<b>Study design:</b> Non-randomized controlled <b>Population:</b> NR <b>N = NR</b>	Application at 15 and 30 days <b>Intervention:</b> 5% NaF + TCP (Clinpro) <b>Comparator:</b> 5% NaF (Duraphat)	Mineral density	Clinpro was more effective at remineralization in mild lesions and Duraphat was more effective in moderate lesions.

ACP = amorphous calcium phosphate; CPP-ACP = casein phosphopeptide; DFS = difluorosilane; ECC = early childhood caries; ICDAS = International Caries Detection and Assessment System; NaF = sodium fluoride; NMA = network meta-analysis; NR = not reported; OHI = oral hygiene instructions; PVP-I = polyvinylpyrrolidone-iodine; QLF = quantitative light-induced fluorescence; RCT = randomized controlled trial; SR = systematic review; TCP = tricalcium phosphate; TiF<sub>4</sub> = titanium tetrafluoride; WSL = white spot lesion.

## References

### Health Technology Assessments

No literature identified.

### Systematic Reviews

1. Manchanda S, Sardana D, Liu P, et al. Topical fluoride to prevent early childhood caries: systematic review with network meta-analysis. *J Dent.* 2022 Jan; 116: 103885. [PubMed](#)

### Randomized Controlled Trials

2. Park KJ, Meisner T, Gunther E, et al. Arrest of root caries with an adjuvant chlorhexidine-fluoride varnish over a 12-months observation period: a QLF-analyzed, placebo-controlled, randomized, clinical trial (RCT). *Odontology.* 2022 Jan; 110(1): 193-202. [PubMed](#)
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5. de Souza BM, de Souza Silva MS, Silva Braga A, et al. Acceptability and effect of TIF4 on dental caries: a randomized controlled clinical trial. *Bras Oral Res.* 2021 Dec 6; 35: e121. [PubMed](#)
6. Mekky AI, Dowidar KML, Talaat DM. Casein phosphopeptide amorphous calcium phosphate fluoride varnish in remineralization of early carious lesions in primary dentition: randomized clinical trial. *Pediatr Dent.* 2021 Jan 15; 43(1): 17-23. [PubMed](#)
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8. Poza-Pascual A, Serna-Munoz C, Perez-Silva A, Martinez-Beneyto Y, Cabello I, Ortiz-Ruiz AJ. Effects of fluoride and calcium phosphate-based varnishes in children at high risk of tooth decay: a randomized clinical trial. *Int J Environ Res Public Health.* 2021 Sep 24; 18(19): 10049. [PubMed](#)
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10. Turska-Szybka A, Gozdowski D, Twetman S, Olczak-Kowalczyk D. Clinical effect of two fluoride varnishes in caries-active preschool children: a randomized controlled trial. *Caries Res.* 2021; 55(2): 137-143. [PubMed](#)
11. Radha S, Kayalvizhi G, Adimoulame S, et al. Comparative evaluation of the remineralizing efficacy of fluoride varnish and its combination varnishes on white spot lesions in children with ECC: a randomized clinical trial. *Int J Clin Pediatr Dent.* 2020 Jul-Aug; 13(4): 311-317. [PubMed](#)

### Non-Randomized Studies

12. Biondi AM, Cortese SG, Babino L, Fridman DE. Comparison of mineral density in molar incisor hypomineralization applying fluoride varnishes and casein phosphopeptide-amorphous calcium phosphate. *Acta Odontol Latinoam.* 2017 Dec; 30(3): 118-123. [PubMed](#)

### Guidelines and Recommendations

13. Holve S, Braun P, Irvine JD, Nadeau K, Schroth RJ. Early childhood caries in Indigenous communities. *Paediatr Child Health.* 2021 Jul;26(4):255-258. . Available from: <https://cps.ca/en/documents/position/early-childhood-caries>. Accessed 2022 Sep 8. [PubMed](#)  
See: Clinical Care Recommendations (sixth bullet point)
14. Prevention of dental caries in children younger than 5 years: screening and interventions. *Final recommendation statement.* Rockville (MD): U.S. Preventive Services Task Force; 2021: <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-dental-caries-in-children-younger-than-age-5-years-screening-and-interventions1>. Accessed 2022 Sep 8 .  
See: Recommendation Summary (second row)



## Appendix 1: References of Potential Interest

### Systematic Reviews

#### Alternative Methodology

15. Goff SL, Gahlon G, Geissler KH, Dick AW, Kranz AM. Variation in current guidelines for fluoride varnish application for young children in medical settings in the United States. *Front Public Health*. 2022 Mar 4; 10: 785296. [PubMed](#)

#### Mixed Intervention – Topical Fluoride Therapy

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#### Unclear Comparator

19. Jafarzadeh D, Rezapour R, Abbasi T, et al. The effectiveness of fluoride varnish and fissure sealant in elementary school children: a systematic review and meta-analysis. *Iran J Public Health*. 2022 Feb; 51(2): 266-277. [PubMed](#)
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### Randomized Controlled Trials

#### Alternative Outcome – Surrogate Measure

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25. Patel PM, Hugar SM, Halikerimath S, et al. Comparison of the effect of fluoride varnish, chlorhexidine varnish and Casein Phosphopeptide- Amorphous Calcium Phosphate (CPP-ACP) varnish on salivary streptococcus mutans level: a six month clinical study. *J Clin Diagn Res*. 2017 Aug; 11(8): ZC53-ZC59. [PubMed](#)

#### Alternative Outcomes – Fluoride Concentrations

26. Al Dehailan L, Lippert F, Gonzalez-Cabezas C, Eckert GJ, Martinez-Mier EA. Fluoride concentration in saliva and biofilm fluid following the application of three fluoride varnishes. *J Dent*. 2017 May; 60: 87-93. [PubMed](#)
27. Lockner F, Twetman S, Stecksén-Blicks C. Urinary fluoride excretion after application of fluoride varnish and use of fluoride toothpaste in young children. *Int J Paediatr Dent*. 2017 Nov; 27(6): 463-468. [PubMed](#)
28. Downey D, Dennison J, Eckert GJ, et al. Fluoride levels in unstimulated whole saliva following clinical application of different 5% NaF varnishes. *Caries Res*. 2018; 52(6): 431-438. [PubMed](#)

#### Premolar Extractions

29. Shah M, Paramshivam G, Mehta A, et al. Comparative assessment of conventional and light-curable fluoride varnish in the prevention of enamel demineralization during fixed appliance therapy: a split-mouth randomized controlled trial. *Eur J Orthod*. 2018 Apr 6; 40(2): 132-139. [PubMed](#)

#### Alternative Comparator – Other Varnishes

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## Non-Randomized Studies

### *No Comparator*

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## Guidelines and Recommendations

### *Unclear Methodology*

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## Review Articles

34. Garcia RI, Gregorich SE, Ramos-Gomez F, et al. Absence of fluoride varnish-related adverse events in caries prevention trials in young children, United States. *Prev Chronic Dis.* 2017 Feb 16; 14: E17. [PubMed](#)

## Additional References

### *Extract of Rapid Report*

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