

# Effectiveness, safety, and acceptance of silver diamine fluoride therapy and its implications for dental hygiene practice: Position paper and statement from the Canadian Dental Hygienists Association

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## ABSTRACT

**Background:** This study reviews the literature on the short- and long-term effectiveness, safety, and acceptance of silver diamine fluoride (SDF) therapy for children and adults with carious lesions and/or dentinal hypersensitivity as it applies to dental hygiene practice. **Methods:** Using the scoping review methodology by Levac (2010), the authors retrieved 662 records from 7 electronic databases, 3 clinical trial registries, and Google. Thirty-eight publications met the following inclusion criteria: clinical application of SDF on human subjects; published in English between 2000 and 2017. Results were synthesized under categories defined by the principles of a health technology assessment. **Results:** Data regarding clinical and prospective trials of SDF were available for 3 indications: arresting carious lesions (age range: 3 to 8 years), arresting root carious lesions (age range: 65 to 85 years), and reducing dentinal hypersensitivity (age range: 43 to 44 years). The longest follow-up period was 36 months. Adverse events and parent/caregiver acceptance were reported in most studies. **Discussion:** A broad range of evidence on the effectiveness, safety, and acceptance suggests that SDF could be used within the dental hygiene armamentarium. Current evidence and guidelines support the use of SDF for arresting carious lesions in primary dentition, but there is limited evidence for the use of SDF to arrest root caries or reduce dentinal hypersensitivity. Gaps in research on training requirements, treatment protocols, and long-term effectiveness and safety were also identified. **Conclusion:** Evidence suggests that SDF could be an effective and safe therapy to add to the dental hygiene clinical armamentarium for the management and arrest of coronal caries in primary dentition, with further research required to support its use for other clinical applications.

## RÉSUMÉ

**Contexte :** La présente étude examine la documentation sur l'efficacité et la sécurité à court et à long terme, ainsi que l'acceptation de la thérapie au fluorure d'argent diamine (FAD) chez les enfants et les adultes ayant des lésions carieuses ou de l'hypersensibilité dentinaire, tel qu'elle s'applique à la pratique d'hygiène dentaire. **Méthodologie :** En se servant de la méthodologie de l'examen de la portée par Levac (2010), les auteurs ont repéré 662 dossiers de 7 bases de données électroniques, 3 registres d'essais cliniques et Google. Trente-huit publications ont répondu aux critères d'inclusion suivants : application clinique du FAD sur des sujets humains, publiés en anglais entre 2000 et 2017. Les résultats étaient synthétisés en catégories définies par les principes d'une évaluation des technologies de la santé. **Résultats :** Les données provenant d'essais cliniques et prospectifs du FAD étaient accessibles selon les 3 indicateurs suivants : l'arrêt des lésions carieuses (intervalle d'âge : de 3 à 8 ans), l'arrêt des lésions carieuses radiculaires (intervalle d'âge : de 65 à 85 ans), et la réduction de l'hypersensibilité dentinaire (intervalle d'âge : de 43 à 44 ans). La période de suivi la plus longue était de 36 mois. Des événements indésirables et l'acceptation parentale ou du soignant ont été signalés dans la plupart des études. **Discussion :** Une vaste gamme de preuves sur l'efficacité, la sécurité et l'acceptation suggère que le FAD pourrait être utilisé au sein de l'arsenal thérapeutique de l'hygiène dentaire. Ces données probantes et les lignes directrices courantes appuient l'utilisation du FAD pour arrêter les lésions carieuses dans la dentition primaire, mais les preuves sont limitées lorsqu'il s'agit de l'utilisation du FAD pour arrêter la carie radiculaire ou réduire l'hypersensibilité dentinaire. Les lacunes en matière de recherche sur le plan des exigences de formation, des protocoles thérapeutiques et de l'efficacité et de la sécurité à long terme étaient aussi définies. **Conclusion :** Les données probantes suggèrent que le FAD pourrait être une thérapie efficace et sécuritaire à ajouter à l'arsenal thérapeutique de l'hygiène dentaire clinique pour la gestion et l'arrêt des caries coronaires de la dentition primaire, exigeant de la recherche supplémentaire pour en appuyer l'usage dans d'autres applications cliniques.

**Key words:** adverse effects, caries arrest, coronal caries, dentinal sensitivity, root caries, silver diamine fluoride

**CDHA Research Agenda category:** risk assessment and management; capacity building of the profession

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## CANADIAN DENTAL HYGIENISTS ASSOCIATION POSITION STATEMENT

Silver diamine fluoride (SDF) is a non-invasive, clinically applied treatment that has been used as an interim therapy for managing active coronal and root caries and reducing dentinal hypersensitivity. In 2017, SDF was approved by Health Canada as a natural health product and anticaries agent for children 3 years or older and adults. Research on SDF is of moderate quality but demonstrates comparable effectiveness of SDF to fluoride varnish and dental sealants in preventing and arresting coronal caries in primary dentition. The most common side effect of SDF is black staining of treated teeth.

Dental hygienists are encouraged to provide high-quality, evidence-based, and individualized care for their clients. While permanent restorations remain the gold standard for managing active caries, evidence suggests that SDF would be beneficial in low resource settings, especially in populations with limited access to dental care where comprehensive dental treatment is not available. The Canadian Dental Hygienists Association (CDHA) recommends that SDF be used as an interim therapy for children and monitored until permanent treatment is available. While there are gaps in evidence regarding the effectiveness of SDF in adults and in medically compromised populations, dental hygienists are encouraged to use their discretion and review the benefits and risks of SDF—including effectiveness, safety, and cost—in their process of care. CDHA continues to support education and research initiatives to enhance and inform the use of SDF in dentistry.

## INTRODUCTION

Silver diamine fluoride (SDF) is used around the world primarily for reducing dentinal hypersensitivity and arresting carious lesions.<sup>1,2</sup> It was recently introduced in North America, and in 2017, was approved by Health Canada as a natural health product and anticaries agent for children 3 years or older and adults.<sup>3</sup> The emergence of SDF in North America has provoked interest within the dental community in understanding its use in practice.

SDF is hypothesized to prevent or arrest coronal caries, arrest root caries, and reduce dentinal hypersensitivity. Although ongoing studies are being carried out to understand its exact mechanism of action, evidence has shown that SDF inhibits dentin demineralization, preserves collagen and inhibits its breakdown, and increases dentin hardness.<sup>4</sup> In laboratory studies, silver ions have been shown to degrade bacterial cell walls, disrupt DNA synthesis and replication, and disrupt intracellular metabolic activity.<sup>5</sup> When applied to dentin, silver increases resistance to acid dissolution and enzymatic digestion.<sup>4,5</sup> In addition to the therapeutic effect of silver, free silver ions can turn carious lesions black when exposed to environmental oxygen, which has been recognized as a common side effect of SDF.<sup>1</sup>

The combined action of antimicrobial silver with the remineralization effects of fluoride suggests that SDF would be effective at arresting carious lesions and reducing dentinal hypersensitivity. Earlier claims suggest that SDF has the potential to control pain and infection, is easy and simple to use, affordable, requires minimal personnel time and training, and is non-invasive.<sup>1</sup> Thus, SDF could be a valuable addition to the armamentarium for dental hygiene care. However, no review has systematically evaluated these claims,<sup>5-13</sup> and there remains lack of clarity on the practical aspects of SDF, including safety, cost, and effectiveness, for the management of carious lesions and dentinal hypersensitivity.

Dental hygienists practising in various settings, as well as regulators, professional groups, and the public, require practical information on SDF in order to understand its role in clinical care. A health technology assessment

(HTA) is well suited to address this need as it involves a systematic evaluation of relevant knowledge of the properties and effects of health care therapies within the context of their intended use.<sup>14</sup> The HTA process combines evidence-based medicine, economics, organizational aspects, and social, ethical and legal considerations to produce information that will help guide future decision making in a health care field.<sup>15</sup> Therefore, the purpose of this study is to review the published literature on the short- and long-term effectiveness, safety, and acceptance of SDF therapy for children and adults with carious lesions and/or dentinal hypersensitivity.

## METHODOLOGY

A scoping review was carried out and guided by the principles of HTA. Health technology is defined as the practical application of knowledge in the form of devices, medicines, procedures, and/or systems to improve individual and population health.<sup>16</sup> HTA involves “examining and reporting properties of a medical technology used in health care, such as safety, efficacy, feasibility, and indications for use, cost, and cost-effectiveness, as well as social, economic, and ethical consequences, whether intended or unintended.”<sup>17</sup> Scoping reviews examine the extent, range, and nature of research on a specific topic by reviewing literature of varying study designs.<sup>18</sup> Thus, this scoping review was developed to address the following objectives:

1. To review the effectiveness of SDF in preventing and arresting coronal and root carious lesions, and in reducing dentinal hypersensitivity in child and adult population groups;
2. To describe outcomes related to client/patient, parent/caregiver, and provider acceptance of SDF treatment in a dental setting;
3. To identify the indications, contraindications, and treatment protocol associated with SDF use for the prevention and treatment of coronal and root caries lesions and dentinal hypersensitivity in child and adult population groups.

The systematic search protocol received approval from the Canadian Dental Hygienists Association Silver Diamine

Fluoride Steering Committee in August 2017. Ongoing consultations on the results of the search strategy and manuscript were conducted with the steering committee until March 2018.

#### Data sources

Seven electronic databases that encompass a broad range of international literature on SDF therapies were searched: MEDLINE (biomedical sciences), EMBASE, Cochrane Library, Google Scholar, CINAHL, Web of Science, and the Latin American and Caribbean Health Sciences Literature (LILAC) database. Records from the World Health Organization International Clinical Trials Registry Platform, the clinical trial registry at the National Institute of Health, and the International Prospective Register of Systematic Reviews (PROSPERO) were also screened for relevant studies. This review was supplemented by reviewing reference lists of relevant studies and the first 200 hits from Google.

#### Search strategy

Key search terms were derived from a broad PICO framework (Table 1), and the search strategy was reviewed with a librarian at the Faculty of Dentistry, University of Toronto, Ontario, Canada. The strategy did not include restrictions on age but was limited by date (2000–2017), language (English), and to studies involving humans. Given the objectives of this scoping review, the search excluded population, comparison or outcome terms as they were assumed to limit the scope of the search. A sample search strategy is outlined in Supplementary Table 1 (available online at [www.cdha.ca/cjdh](http://www.cdha.ca/cjdh)). The full search was carried out in October 2017, followed by a second search in late November 2017. Databases were monitored until December 2017 to ensure that all relevant resources were captured for the review.

#### Screening and data extraction

Search results were imported into EndNote software and duplicate publications were removed prior to review. Two authors (JF and SS) independently reviewed abstracts for 25% of eligible studies using inclusion and exclusion criteria outlined in Table 2. The authors achieved very good agreement ( $\kappa$  0.844; CI: 0.751 to 0.87)<sup>19</sup>; the remainder of eligible abstracts and full texts were screened by the primary author (JF). Both randomized and non-randomized studies were included in order to explore the full scope of potential benefits and harms associated with SDF, including societal and client perspectives. Studies that involved application of SDF in non-humans or in therapies considered outside the scope of dental hygiene practice, such as endodontic treatment, were excluded. If no abstract was available, the source was included for full-text review. Uncertainties related to study selection were discussed and resolved in consultation with other co-authors. A justification for study exclusion at the full-text review stage was documented for each source and is provided in Supplementary Table 2 (available online at [www.cdha.ca/cjdh](http://www.cdha.ca/cjdh)). The primary author (JF) extracted data from included studies using the standardized data extraction form, with final outputs reviewed by all co-authors and members of the steering committee prior to publication.

#### Quality appraisal and data synthesis

Quality appraisals were performed by reviewing study adherence to reporting guidelines for the specific type of study design. These included the following checklists: Assessing the Methodological Quality of Systematic Reviews (AMSTAR),<sup>20</sup> Consolidated Standards of Reporting Trials (CONSORT),<sup>21</sup> Strengthening the Reporting of Observational studies in Epidemiology (STROBE),<sup>22</sup> Consolidated Health

Table 1. Silver diamine fluoride scoping review PICO framework

PICO framework	Description
Population	<ul style="list-style-type: none"> <li>• Clients/patients or parents or caregivers of clients/patients receiving treatment</li> <li>• Age groups (children, adults) receiving treatment</li> <li>• Dentition type (primary, permanent) receiving treatment</li> <li>• Tooth surface (coronal<sup>a</sup>, root surfaces) receiving treatment</li> </ul>
Intervention(s)	<ul style="list-style-type: none"> <li>• Silver diamine fluoride (SDF) at different concentrations</li> <li>• Silver nitrate and fluoride at different concentrations, if applicable<sup>b</sup></li> </ul>
Comparison	<ul style="list-style-type: none"> <li>• No treatment</li> <li>• Fluoride varnish, atraumatic restorative therapy (ART), interim restorative therapy (IRT), interim stabilization therapy (IST), and dental sealants</li> </ul>
Outcome	<ul style="list-style-type: none"> <li>• Therapeutic benefit (prevention of caries; caries arrest; reduction in dentinal hypersensitivity)</li> <li>• Safety/adverse effects</li> <li>• Client/patient-important outcomes (acceptance, cost, quality of life)</li> </ul>
Setting and context	<ul style="list-style-type: none"> <li>• Dental hygienists</li> <li>• Traditional and non-traditional practice settings (long-term care, public health, rural and remote communities)</li> </ul>

<sup>a</sup>Includes approximal surfaces

<sup>b</sup>Studies with silver nitrate and fluoride only included for non-therapeutic outcomes (e.g., client/patient or caregiver acceptance, cost-effectiveness)

Table 2. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> <li>• Years: 2000 to present</li> <li>• English language</li> <li>• Systematic reviews, randomized controlled trials (RCT), observational studies, technical reports</li> <li>• Studies involving application of SDF in a dental setting</li> <li>• Studies with at least one-week follow-up for clinical outcome measures</li> </ul>	<ul style="list-style-type: none"> <li>• Animal, in vivo, ex vivo or in vitro studies</li> <li>• Abstracts, posters or conference proceedings</li> <li>• Editorials or commentaries</li> <li>• Duplicate studies</li> <li>• Studies involving SDF application outside the scope of dental hygiene practice in Canada (e.g., restorations, endodontic treatment)</li> </ul>

Economics Evaluation Reporting Standards (CHEERS),<sup>23</sup> and CAse REport guidelines (CARE).<sup>24</sup> Quality scores were not calculated, but assessments were reviewed by all co-authors to determine study inclusion. Only one study was excluded at this stage due to unclear reporting of methods and results.<sup>25</sup>

To synthesize evidence on the effectiveness of SDF in preventing and arresting coronal and root carious lesions, and dentinal hypersensitivity in child and adult population groups, data on effect sizes were extracted from available systematic reviews, meta-analyses, and primary studies. Performing a meta-analysis was considered beyond the scope of this review. Outcomes related to client/patient, caregiver, and provider acceptance of SDF treatment in a dental setting were obtained from clinical studies that reported adverse events, client/patient or caregiver satisfaction, and ease of application. To identify the indications, contraindications, and treatment protocol associated with SDF use, data contained in the methods section of primary studies and recommendations reported from clinical guidelines were extracted. This data included reporting information on operator characteristics, clinical settings, as well as education and training requirements, when available.

## RESULTS

### Description of search results

A total of 662 sources were retrieved. After eliminating duplicate studies and screening full-text articles for eligibility ( $n = 79$ ), the authors identified 38 studies that met the criteria for inclusion (Figure 1). The 38 studies included 3 peer-reviewed policies and clinical guidelines,<sup>5,7,26</sup> 1 technical report that assessed the clinical effectiveness and cost-effectiveness of SDF,<sup>11</sup> and 5 systematic reviews that provided unique information about SDF.<sup>6,9,10,12,27</sup> The search also yielded 2 systematic reviews that were excluded as they were out of date or overlapped with other sources.<sup>28,29</sup> There were 18 unique clinical studies reported across 23 sources that were included in this review; 12 of these studies were randomized controlled trials (RCT),<sup>30-41</sup> 3 were prospective controlled clinical trials,<sup>42-44</sup> and 3 were pilot studies.<sup>25,45,46</sup> Most clinical trials or pilot studies investigated the caries arresting properties of SDF

in primary dentition<sup>31,32,34,35,38,40-42</sup> or in permanent first molars.<sup>34,43-45</sup> Other trials include 3 RCTs that investigated root caries prevention or arrest<sup>33,37,39</sup> and one RCT that investigated the effect of SDF in reducing tooth sensitivity in an adult population.<sup>30</sup> The remaining studies included in this review comprised 5 observational studies,<sup>47-51</sup> 2 economic evaluations,<sup>52,53</sup> and 1 case report.<sup>54</sup>

### Quality of included studies

Results of reporting checklists for included studies are provided in Supplementary Tables 3 to 7 (available online at [www.cdha.ca/cjdh](http://www.cdha.ca/cjdh)). The majority of the systematic reviews searched at least 2 electronic databases, but only 1 review performed an exhaustive search of grey literature.<sup>6</sup> When performed, meta-analyses did not assess for publication bias or sources of funding.<sup>30,31,33,41</sup> There were no reports of subgroup analyses to assess the variation in effect size based on SDF concentration, application frequency or risk of bias.<sup>8-10</sup>

Most RCTs did not clearly report on allocation concealment and assignment. Only 3 of the 12 RCTs provided details on the type of analyses conducted, which were intention-to-treat analyses.<sup>31,32,41</sup> Four RCTs appeared to be underpowered at the time of the final follow-up,<sup>33,36,38,39</sup> and no clinical trial provided information on how missing data were analysed. Of the 3 prospective controlled clinical trials, 2 calculated a priori sample sizes<sup>43,44</sup> but did not provide baseline demographic characteristics or reasons for loss to follow-up.<sup>42-44</sup> Thus, it is difficult to discern the quality of these clinical trials. Results from the quality appraisal checklists for observational studies, economic evaluations, and case reports revealed no major sources of bias for these studies.

### Description of outcomes

#### Clinical effectiveness of SDF

Primary studies involving the clinical application of SDF varied by recipient age, health characteristics, and country. Included studies were conducted in Hong Kong,<sup>31-34,37,39,41,42,55</sup> China,<sup>40</sup> Nepal,<sup>38</sup> Phillipines,<sup>44</sup> Cuba,<sup>43</sup> Brazil,<sup>35,45,56</sup> Peru,<sup>30,46</sup> and the United States.<sup>36</sup> Most clinical trials reported background fluoride exposure, including community water fluoride (CWF) levels. Three clinical studies in primary dentition were conducted in communities with fluoridation levels ranging from 0.03 ppm to 0.5 ppm,<sup>31,38,42,57</sup> 1 study in permanent dentition was conducted in a community with CWF at 0.09 ppm,<sup>43</sup> and 2 of the 3 studies on root surfaces were conducted at CWF levels of 0.5 ppm.<sup>33,39</sup>

*Prevention and arrest of carious lesions in primary dentition.* The majority of clinical studies assessed the effectiveness of SDF in arresting or preventing primary carious lesions (Tables 3 and 4). Study participants ranged in age from 3 to 8 years.<sup>31,32,36,38,39,41,42,47</sup> Most studies that assessed caries arrest used visual inspection and tactile detection,<sup>31,32,36,38,40-43,49</sup> but only 2 reported the use of standardized criteria,<sup>31,38</sup> such as the ICDAS.<sup>31</sup> Clinical studies on primary dentition compared SDF to sodium fluoride

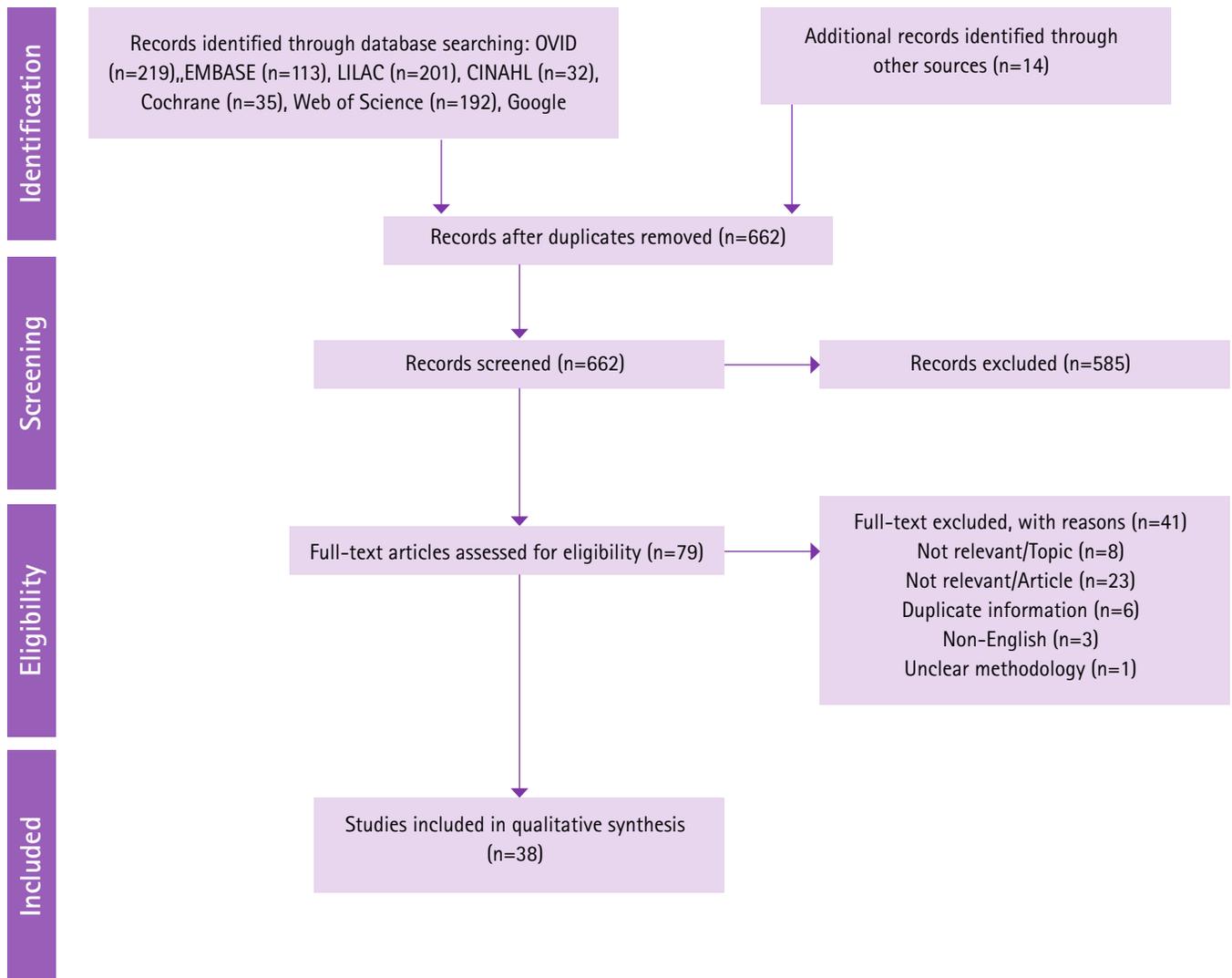


Figure 1. PRISMA flow diagram for systematic search strategy (adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med.* 2009;6(7): e1000097. doi:10.1371/journal.pmed1000097)

varnish,<sup>31,42</sup> minimally invasive restorative treatments, such as glass ionomer cement,<sup>39</sup> atraumatic restorative therapy (ART),<sup>47</sup> and no treatment.<sup>36,42</sup> The combined effect of SDF with a reducing agent was also assessed in one study, which revealed a lower proportion of study participants with black stain and similar effectiveness when adding potassium iodine as a reducing agent compared to SDF alone (93% and 90% caries arrest rate, respectively) at 30 months.<sup>38</sup> Based on results of one systematic review and one policy document,<sup>6,26</sup> SDF had more favourable results compared to fluoride varnish and ART for arresting carious lesions in primary dentition (Table 5).

#### *Prevention of carious lesions in permanent first molars.*

Two clinical trials assessed the caries prevention effects of SDF on occlusal surfaces of permanent first molars in children.<sup>34,43</sup> Llodra compared SDF to no treatment whereas Liu compared SDF to no treatment, sealant or 5% sodium fluoride varnish (NaF) for the prevention of new carious lesions.<sup>34,43</sup> Both studies used visual-tactile

detection to assess their outcome. These studies revealed superiority of sealants to SDF,<sup>34</sup> comparable findings of SDF to sodium fluoride,<sup>34</sup> and higher prevented fraction with SDF compared to no treatment.<sup>43</sup> One pilot study also measured the caries arresting effect of SDF on occlusal surfaces of first molars compared to toothbrushing and glass ionomer cement used as a sealant.<sup>45</sup> Based on a sample size of 20 teeth per group and use of bitewing radiographs to assess caries activity, Braga and colleagues found comparable caries arrest rates in all 3 groups at 30 months.<sup>45</sup> No systematic review reported results exclusively for the effect of SDF in permanent first molars or in permanent dentition.

*Prevention of root caries in adults.* Three studies assessed the effectiveness of SDF in preventing root caries in adults as an adjunct to oral hygiene instruction or in comparison to soda or sterile water.<sup>33,37,39</sup> Other comparisons were to chlorhexidine varnish and 5% NaF.<sup>37</sup> Study participants ranged in age from 65 to 85 years. Outcomes were assessed

Table 3. Overview of primary studies involving clinical application of SDF (n = 18)

	Clemens 2017 <sup>49</sup>	Duangthip 2018 <sup>31,57</sup>	Fung 2017 <sup>32,41,55</sup>	Zhi 2012 <sup>40</sup>	Chu 2002 <sup>42</sup>	Milgrom 2018 <sup>36</sup>	Yee 2009 <sup>38</sup>	dos Santos 2012 <sup>25</sup>	Mattos-Silveira 2015 <sup>35</sup>	Barreto 2017 <sup>47</sup>	Braga 2009 <sup>45</sup>	Monse 2012 <sup>44</sup>	Llodra 2005 <sup>43</sup>	Liu 2012 <sup>34</sup>	Li 2016 <sup>33</sup>	Tan 2010 <sup>37</sup>	Zhang 2013 <sup>39</sup>	Castillo 2011 <sup>30</sup>	Total
<b>Dentition type</b>																			
Primary	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓									10
Permanent											✓	✓		✓	✓	✓	✓	✓	7
Both													✓						1
<b>Tooth location</b>																			
Anterior					✓														1
Posterior									✓	✓	✓	✓		✓				✓	6
Both	✓	✓	✓	✓		✓	✓	✓					✓		✓	✓		✓	11
<b>Tooth surfaces</b>																			
Occlusal										✓	✓	✓		✓					4
Interproximal									✓	✓									2
Buccal																			1
All of the above	✓	✓	✓	✓	✓	✓	✓	✓					✓						9
Root surfaces															✓	✓	✓		3
<b>Comparison groups</b>																			
Variation of SDF treatment		✓	✓	✓	✓		✓								✓		✓		7
Fluoride varnish		✓												✓		✓			3
Chlorhexidine																✓			1
Dental sealant														✓					1
GIC dental sealant				✓					✓		✓								3
Atraumatic restorative therapy								✓		✓		✓							3
Placebo						✓			✓		✓			✓	✓	✓	✓		7
No treatment							✓					✓	✓					✓	4
No comparison	✓																		1
<b>Clinical outcomes investigated</b>																			
Caries arrest	✓	✓	✓	✓	✓	✓					✓		✓		✓		✓		10
Caries incidence							✓					✓	✓	✓		✓	✓		6
Discomfort									✓	✓									2
Reduction in pain																		✓	1
Abscess, toothache, fistula								✓											1
<b>Detection</b>																			
Visual-tactile	✓	✓	✓	✓	✓		✓				✓	✓	✓	✓	✓	✓	✓	✓	13
Visual-tactile and radiographs						✓													1
Not applicable								✓	✓	✓								✓	4
<b>Adverse effects investigated</b>																			
Black stain		✓	✓	✓	✓		✓				✓		✓		✓				8
Tooth pain/toothache			✓					✓										✓	3
Gum pain			✓			✓													2
Gum bleaching			✓			✓							✓						3

Table 3 continued...

	Clemens 2017 <sup>49</sup>	Duangthip 2018 <sup>31,57</sup>	Fung 2017 <sup>32,41,55</sup>	Zhi 2012 <sup>40</sup>	Chu 2002 <sup>42</sup>	Milgrom 2018 <sup>36</sup>	Yee 2009 <sup>38</sup>	dos Santos 2012 <sup>25</sup>	Mattos-Silveira 2015 <sup>35</sup>	Barreto 2017 <sup>47</sup>	Braga 2009 <sup>45</sup>	Monse 2012 <sup>44</sup>	Llodra 2005 <sup>43</sup>	Liu 2012 <sup>34</sup>	Li 2016 <sup>33</sup>	Tan 2010 <sup>37</sup>	Zhang 2013 <sup>39</sup>	Castillo 2011 <sup>30</sup>	Total	
Damage to gingiva																		✓	1	
Satisfaction	✓		✓	✓																3
Systemic toxicity			✓			✓														2
<b>Follow-up period</b>																				
Same day									✓	✓										2
7 days																			✓	1
14 to 21 days						✓														1
3 months	✓							✓												2
18 months		✓										✓								2
24 months				✓			✓						✓					✓		4
30 months			✓		✓						✓				✓					4
36 months													✓			✓				2

Table 4. Description of primary studies involving clinical application of silver diamine fluoride

Age group and sample size	Type of dentition	SDF brand, concentration, and frequency <sup>a</sup>	Setting	Provider	Follow-up	Clinical outcome/ Adverse effects	Reference
<b>CHILDREN</b>							
2 to 5 years old Mean = 3.6 years (+/-0.6) 30 children	Primary dentition	Advantage Arrest (38%) a. One application, with option of second application	Community clinic	Dentist	3 months	Caries arrest rate = 98.0% (CI = 95,100) • No comparison group • No adverse effects	Clemens 2017 <sup>49</sup>
3 to 4 years old Mean = 41 months (+/-4.0) 275 children	Primary dentition	Cariestop (30%) a. Every 12 months b. Three applications at weekly interval	School setting	Dentist	18 months 30 months	Caries arrest rate (30 months) a. SDF = 44% (109/246) b. SDF = 45% (97/218) NaF = 51% (95/185) • Black stain on dentine surface • No other adverse effects	Duangthip 2016 <sup>31</sup> Duangthip 2017 <sup>56</sup>
3 to 4 years old Mean = 3.8 years (SD = 0.6) 834 children	Primary dentition	Cariestop (12%) a. Every 6 months b. Every 12 months  Saforide (38%) c. Every 6 months d. Every 12 months	School setting	Clinician/ trained dentist	18 months 30 months	Mean number of arrested caries at 30 months (SD) a. 12% SDF = 2.59 (2.94) b. 12% SDF = 2.85 (2.91) c. 38% SDF = 3.20 (3.71) d. 38% SDF = 3.49 (3.27) • Black stain on dentine surfaces (36.7% to 76.3%) • Tooth/gum pain discomfort (3.7% to 7.0%) • Gum swelling (1.5% to 2.9%) • Gum bleaching (3.0% to 5.7%) • No reports of systemic toxicity	Fung 2016 <sup>41</sup> Fung 2017 <sup>32</sup> Duangthip 2017 <sup>55</sup>

Table 4 continued...

Age group and sample size	Type of dentition	SDF brand, concentration, and frequency <sup>a</sup>	Setting	Provider	Follow-up	Clinical outcome/ Adverse effects	Reference
3 to 4 years old Mean = 3.8 years (+/-0.6)  181 children	Primary dentition	Saforide (38%) a. Every 6 months b. Every 12 months	Community setting	Dentist	24 months	Caries arrest rates a. SDF(6 mo) = 90.7% b. SDF(12 mo) = 79.2% GIC = 81.8%  • Black stain on treated carious lesions	Zhi 2012 <sup>40</sup>
3 to 5 years old Mean = 4.0 years (SD = 0.8)  375 children	Primary dentition	Saforide (38%)  a. Every 12 months with excavation (exc.) b. Every 12 months no exc.	School setting	Dentist	30 months	Mean number of arrested caries (SD) a. SDF + exc. = 2.49 (0.27) b. SDF = 2.82 (0.30) 5% NaF + exc. = 1.45 (0.19) 5% NaF = 1.54 (0.27) Control = 1.27 (0.19)  • No adverse effects	Chu 2002 <sup>42</sup>
3.5 to 5.6 years old Mean = 4.8 years (+/-0.6)  55 children	Primary dentition	Advantage Arrest (38% silver; 5.5% fluoride)  a. One application	Community-based dental clinic	Dental provider	14 to 21 days	Caries arrest rate (21 days) SDF = 100% (15/29) Placebo = 2.9% (1/35)  • No gingival or soft tissue stomatitis or ulcerative lesions were identified. • Adverse events (diarrhea or stomach ache) were reported by participants in a supplemental table.	Milgrom 2017 <sup>36</sup>
3 to 9 years old Mean = 5.2 years (SD=1.2)  624 children	Primary dentition	Bees Brand (38%) a. One application with reducing agent (tea) b. One application no reducing agent  PROBEM (12%) c. One application no reducing agent	School setting	Trained primary health workers supervised by dentist	24 months	Mean number of arrested caries (SD) 38% SDF = 2.1 (0.3) 38% SDF + tea = 2.2 (0.3) 12% SDF = 1.5 (0.3) Control = 1.0 (0.2)  • Black discoloration of carious dentin	Yee 2009 <sup>38</sup>
5 to 6 years old  50 children	Primary dentition	Cariestop (30%) a. One application	University dental clinic	Not specified	3 months	• No clinical outcome reported  • No toothache, abscess or fistula reported in SDF group at 3-month follow-up	dos Santos 2012 <sup>56</sup>
5 to 7 years old  22 children	Primary dentition	Cariostatic (10%)  a. Two applications within one-week interval	University dental clinic	Dentist	30 months	• No difference in number of active caries lesion across SDF, non-treated, and GIC groups  • Black staining	Braga 2012 <sup>45</sup>
Mean = 6.29 years (+/-0.48)  373 children	Primary and permanent dentition	Fluoroplat (38%) a. Every 6 months	School setting	Not specified	36 months	• Higher number of inactive caries surfaces in SDF groups compared to control for primary and permanent teeth  • Small, mildly painful white lesion in the mucosa, which disappeared at 48 hours without treatment (3 participants)	Llodra 2005 <sup>43</sup>
3 to 10 years olds Mean = 6.56 years (+/-1.69)  141 children	Primary dentition	Cariestop (30%)  a. One application	School setting	Pediatric dentist	Same day	• Clinical outcome not reported  • No adverse effects • See Table 6	Mattos-Silveira 2015 <sup>35</sup>

Table 4 continued...

Age group and sample size	Type of dentition	SDF brand, concentration, and frequency <sup>a</sup>	Setting	Provider	Follow-up	Clinical outcome/ Adverse effects	Reference
6 to 8 years old 94 children	Primary dentition	Not specified a. One application	School setting	Not specified	Same day	<ul style="list-style-type: none"> <li>• Clinical outcome not reported</li> <li>• No adverse effects</li> <li>• See Table 6</li> </ul>	Barreto 2017 <sup>47</sup>
6 to 8 years old Mean = 6.7 years (+/- 0.7) 704 children	Permanent dentition	Saforide (38%) a. One application	School	School nurses who received one-day training; supervised by dentist	18 months	<ul style="list-style-type: none"> <li>• Greater caries increment in non-treated groups than SDF groups. Greater caries increment in SDF groups compared to dental sealant group</li> <li>• No adverse effects</li> </ul>	Monse 2012 <sup>44</sup>
Children in grades 2 and 3 Mean = 9.1 years 485 children	Permanent pit and fissure of first molars	Saforide (38%) a. Every 12 months	Portable dental chair in school setting	Dentist	24 months	<ul style="list-style-type: none"> <li>• New dentin caries compared to control (prevented fraction) SDF = 41% 5% NaF = 41% Sealant = 60%</li> <li>• Transient bitter taste</li> <li>• No adverse effects</li> </ul>	Liu 2012 <sup>34</sup>
<b>ADULTS</b>							
Mean = 43 to 44 years 126 adults	Permanent dentition	Saforide (38%) Assumed a. One application	Dental clinic	Clinician (unspecified)	7 days	<ul style="list-style-type: none"> <li>• Greater change in mean VAS score for pain in SDF group compared to controls (<math>p &lt; 0.05</math>).</li> <li>• No adverse effects</li> </ul>	Castillo 2011 <sup>30</sup>
23 to 52 years old Mean = 36.2 years 6 adults	Permanent dentition	Saforide (38%) a. One application	Dental clinic	Not specified	1 day	<ul style="list-style-type: none"> <li>• Clinical outcome not reported</li> <li>• No adverse effects</li> </ul>	Vasquez 2012 <sup>46</sup>
Mean = 72.2 years (+/-5.8) 67 adults	Permanent dentition (root surfaces)	Saforide (38%) a. Every 12 months b. Every 12 months with potassium iodide (KI)	Portable dental chair in community setting	Dentist	30 months	<ul style="list-style-type: none"> <li>• Root caries arrest rate a. SDF = 90.0% b. SDF + KI = 92.5% Control = 45.0%</li> <li>• Black stain on arrested root surface</li> <li>• No adverse effects</li> </ul>	Li 2016 <sup>33</sup>
60 to 89 years old Mean = 72.5 years (+/-5.7) 227 adults	Permanent dentition (root surfaces)	Saforide (38%) a. 3 applications every 12 months	Dental hospital	Dentist	24 months	<ul style="list-style-type: none"> <li>• Mean number of arrested root caries surfaces (SD) • OHI = 0.04 (0.02) • OHI + SDF = 0.28 (0.06) • OHI + SDF + OHE = 0.33 (0.10)</li> <li>• No adverse effects</li> <li>• Specified that follow-up was too short to support or refute possible long-term adverse effects</li> </ul>	Zhang 2013 <sup>39</sup>
Mean = 78.8 years (+/-6.2) 203 adults	Permanent dentition (root surfaces)	Saforide (38%) assumed a. Every 12 months	Portable dental chair in residential and nursing homes	Dentist	36 months	<ul style="list-style-type: none"> <li>• Risk of developing new root caries compared to oral hygiene instruction • OHI + SDF RR = 0.19 (0.07-0.46) • OHI + 5% NaF RR = 0.26 (0.10-0.63) • OHI + CHX RR = 0.27 (0.11-0.66)</li> <li>• No adverse effects</li> </ul>	Tan 2010 <sup>37</sup>

<sup>a</sup>Treatment groups distinguished by letter

Table 5. Effectiveness of silver diamine fluoride across systematic reviews and select primary studies

Indication	Reported outcomes			Quality assessment	
Caries arrest in primary dentition	Caries arrest at 30 months <sup>9</sup> (SDF vs other treatments) RR = 1.48 (1.32 to 1.66)		Caries arrest <sup>6</sup> (SDF vs fluoride or ART) <sup>a</sup> RR = 1.66 (1.41, 1.95)	Very low to low <sup>26</sup>	
Caries arrest in permanent first molars	Mean caries score at 30 months <sup>45</sup> SDF = 1.0 <sup>b</sup> GIC = 1.3 <sup>b</sup> CTT = 1.4 <sup>b</sup>	Dentin caries increment at 18 months compared to no treatment <sup>44</sup> SDF brushing group <sup>c</sup> RR = 0.71 (0.12/0.17) SDF no-brushing group <sup>c</sup> RR = 1.13 (0.09/0.08)	New dentin caries at 24 months <sup>34</sup> (SDF vs control) <sup>d</sup> RR = 0.59 PF = 41%	Mean number of inactive caries at 36 months <sup>43</sup> (SDF vs control) RR = 0.35 PF = 65%	Unclear Not assessed in existing systematic reviews <sup>9</sup>
Root caries prevention and arrest	Prevention of new caries (OHI + SDF vs OHI + placebo) <sup>37</sup> NNT = 2.5 <sup>e</sup> RR = 0.19 <sup>e</sup>  (OHI + SDF vs OHI + placebo) <sup>39</sup> NNT = 3.3 RR = 0.75  (OHI + SDF + OHE vs OHI + placebo) <sup>39</sup> NNT = 1.59 RR = 0.53		Arrest of root surface caries (OHI + SDF vs OHI + placebo) <sup>39</sup> NNT = 4.17 RR = 7.0  (OHI + SDF + OHE vs OHI + placebo) <sup>39</sup> NNT = 3.45 RR = 8.25  (OHI + SDF vs OHI + placebo) <sup>33</sup> NNT = 1.8 RR = 2.09	Unclear Not assessed in existing systematic reviews <sup>12</sup>	
Tooth sensitivity	Mean change in visual analog score for pain after 7 days <sup>30</sup> (SDF vs no treatment) Lima study site = -35.58 (-97, 12) vs 0.4 (-38,33) Cusco study site = -23.4 (-56, 24) vs -5.5 (-77, 18)			Unclear No systematic review available	

<sup>a</sup>Subgroup analysis used due to heterogeneity in silver materials studied; <sup>b</sup>all groups reported mean caries scores of 3 at baseline; <sup>c</sup>sealants were more favourable than SDF; <sup>d</sup>no difference compared to fluoride varnish, but lower PF than sealants; <sup>e</sup>the effect of SDF was more favourable than chlorhexidine or 5% sodium fluoride. RR = risk ratio: the rate of the event in the exposed (SDF) group compared to the rate in the unexposed group. PF = prevented fraction: the proportion of the total load of the disease that has been prevented by exposure to SDF. NNT = number needed to treat: The number of persons needed to be treated in order to prevent one event (e.g., decayed tooth surface).<sup>64</sup>

Table 6. Acceptance and adverse events associated with silver diamine fluoride

Aspect	Outcome
Children's reported discomfort with treatment	Approximately 22% of all children 3 to 10 years old reported some level of discomfort. SDF and control group reported less discomfort than resin infiltrant group. RR = 0.29 (SDF group compared to resin infiltrant group). <sup>35</sup>
Children's anxiety scores while receiving treatment	34% of all child participants (6 to 8 years old) reported some anxiety with ART or SDF treatment. No significant difference in anxiety levels of children treated with ART or with SDF. <sup>47</sup>
Adverse effects reported in clinical studies (randomized and non-randomized)	Black stain reported in clinical trials <sup>31-33,38,40-43,45,54,57</sup> 3 participants reported small, mildly painful white lesion in the mucosa that disappeared at 48 hours without treatment <sup>43</sup> One participant reported transient bitter taste <sup>34</sup> No reports of toothache, abscess or fistula in children 5 to 6 years old who received SDF (n = 25) <sup>56</sup>
Caregiver actual and perceived acceptance of SDF treatment	Most parents of children (age 3.6 years +/-1.0) receiving SDF treatment strongly agreed with statements about the ease of SDF application (63.3%), their comfort with discolouration of teeth (53.3%), painlessness of the process (70.0%), and taste of SDF (63.3%) <sup>49</sup> 46.6% of parents who were asked about the option of receiving SDF treatment for their children reported SDF to be unacceptable on anterior teeth, whereas most were somewhat accepting of it on posterior teeth (45.8%). There was greater acceptance by parents of children who needed treatment under general anaesthesia than those who had uncooperative or upset children. <sup>50</sup>
Dental professional perceptions of SDF treatment	Dental hygienists were asked about their perceptions of SDF use in non-traditional practice. Most dental hygienist participants felt that the advantages of SDF outweighed the disadvantages for their patient populations (88%). Most respondents felt that SDF was within the dental hygiene scope of practice (>60%). The majority of respondents were familiar with SDF but had not used the product. <sup>48</sup> The majority of graduate pediatric dentistry program directors in the US surveyed agreed, strongly agreed or very strongly agreed with concerns regarding parental acceptance (91.8%), reimbursement (73.0%), standard of care (67.5%), evidence base (63.5%), off-label use (59.4%), cost (58.1%), and adequate training (55.4%). <sup>51</sup>

**Table 7.** Overview of potential clinical indications and contraindications for SDF

	Clinical guidelines (Horst <sup>5</sup> and AAPD <sup>26</sup> )		Inclusion/exclusion criteria of primary studies	
	Indications	Contraindications	Inclusion	Exclusion
Population characteristics	<ul style="list-style-type: none"> <li>Inability to tolerate standard treatment</li> <li>Precooperative child</li> <li>Frail elder</li> <li>Individuals with severe cognitive or physical disabilities</li> <li>Dental phobias</li> <li>Patients without access to dental care</li> <li>Extreme caries risk</li> <li>Salivary dysfunction, Sjören syndrome, polypharmacy, aging, methamphetamine use</li> </ul>	<ul style="list-style-type: none"> <li>Silver allergy</li> <li>Pregnant women</li> <li>Women in their first 6 months of breastfeeding</li> <li>Stomatitis</li> <li>Desquamative gingivitis or mucositis</li> </ul>	<ul style="list-style-type: none"> <li>Generally healthy<sup>31,32,34,40,41,55,57</sup></li> <li>Elders with basic self-care ability<sup>33,37,39</sup></li> <li>Not reported</li> </ul>	<ul style="list-style-type: none"> <li>Systemic disease<sup>57</sup> or serious medical problems<sup>33,37,39</sup></li> <li>Long-term medications<sup>57</sup></li> <li>Underweight (&lt;5 kg)<sup>36</sup></li> <li>Uncooperative<sup>6,49</sup> or children with negative behaviours<sup>47</sup></li> <li>Known sensitivity to silver<sup>30</sup></li> <li>Salivary gland function significantly affected by disease, medication or treatment such as radiotherapy<sup>33</sup></li> <li>Ulceration or leukoplakia<sup>30</sup></li> </ul>
Tooth/site characteristics	<ul style="list-style-type: none"> <li>Active cavitated caries lesions</li> <li>Difficult to treat dental carious lesions</li> </ul>	<ul style="list-style-type: none"> <li>Clinical signs of pulp involvement</li> </ul>	<ul style="list-style-type: none"> <li>Enamel caries defined as ICDAS score of 2<sup>34</sup> or 3<sup>36</sup></li> <li>Active initial caries without cavitation on occlusal surfaces<sup>45</sup></li> <li>Dentin caries<sup>32,41,42,47</sup></li> <li>Active caries not involving pulp<sup>40</sup></li> </ul>	<ul style="list-style-type: none"> <li>Pulp involvement or non-vital teeth (obvious discolouration premature hypomobility)<sup>40,42</sup></li> <li>Grossly broken down, crown missing, abscess or a sinus, spontaneous or elicited pain from caries<sup>49</sup></li> <li>Hypoplastic defects, restorations or sealants<sup>45</sup></li> </ul>

**Table 8.** Reported SDF applications for treatment of coronal and root caries, and tooth sensitivity across primary studies

		Caries prevention and arrest		Root caries arrest (n = 5)	Tooth sensitivity (n = 1)	Total
		Primary dentition (n = 18)	Permanent dentition (n = 4)			
Concentration <sup>b</sup>	10% to 12%	3	1	0	0	4
	30%	4	0	0	0	4
	38%	10	3	1	1	15
	Not specified	1	0	0	0	1
Technique <sup>b</sup>	Excavation	3	1	0	0	4
	No excavation	8	0	0	0	8
	Not specified	7	3	1	1	12
Application time <sup>b</sup>	<1 minute	2	0	0	1	3
	1 minute	4	1	0	0	5
	2 minutes	4	0	0	0	4
	3 minutes	2	2	0	0	4
	Not specified	6	1	5	0	12
Number of applications <sup>b</sup>	Once	7	1	0	1	9
	More than once	11	3	0	0	14
Frequency <sup>b</sup>	Weekly	1	1	0	0	2
	3 weeks or 3 months	1	0	0	0	1
	Every 6 months	3	1	0	0	4
	Every 12 months	6	1	1	0	8
	Not applicable	7	1	0	1	9

Table 8 continued...

		Caries prevention and arrest		Root caries arrest	Tooth sensitivity	Total
		Primary dentition (n = 18)	Permanent dentition (n = 4)	(n = 5)	(n = 1)	
Provider <sup>a</sup>	Dentist/clinician	11	1	1	1	14
	Health worker	3	3	0	0	6
	School nurse	0	0	0	0	0
	Not specified	4	1	0	0	5
Setting <sup>c</sup>	Clinic	4	0	2	1	7
	Portable clinic	0	2	3	0	5
	School	6	0	0	0	6
	Community	1	0	0	0	1
	Not specified	7	0	0	0	7

<sup>a</sup>Trials reported across multiple studies recorded once; <sup>b</sup>trials including multiple SDF groups recorded separately; <sup>c</sup>trials including multiple SDF groups recorded once

by visual–tactile detection and reported by Hendre in a systematic review.<sup>12</sup> Results indicate that SDF performed more favourably, with higher prevented fraction, than chlorhexidine or 5 % NaF.<sup>12</sup> Li and colleagues also revealed similar root caries arrest rates between SDF alone and SDF with potassium iodine (KI).<sup>33</sup> Due to heterogeneity in study outcomes, no meta-analyses were performed to report the pooled effect of SDF in arresting root caries.<sup>12</sup>

**Reduction in dentinal hypersensitivity.** One study assessed the effectiveness of SDF in reducing tooth hypersensitivity on permanent cuspid and bicuspid teeth of middle-aged adults (mean age = 43 to 44 years).<sup>30</sup> Castillo and colleagues reported greater reduction in pain based on a visual analog score, in the SDF group compared to no treatment (Table 5).<sup>30</sup>

#### Safety and adverse events

All included clinical trials provided a statement regarding adverse events during the trial period; these events are listed in Table 4. Only one study provided a supplemental list of adverse events for each study participant.<sup>36</sup> Milgrom and colleagues reported moderate adverse events, including diarrhea and stomach ache, which were claimed to be unrelated to the SDF product.<sup>36</sup> One preliminary study evaluated safety and toxicity of SDF among a group of adults.<sup>46</sup> Vasquez and colleagues noted that maximum serum fluoride concentrations did not exceed those found from using fluoridated toothpaste, and concluded that SDF posed no toxic risk either from fluoride or silver exposure.<sup>46</sup> Castillo assessed damage to the gingiva as a primary outcome, and found greater prevalence of erythema, as indicated by redness with bleeding on probing, in the SDF group compared to control group at 24 hours after application to root surfaces. However, results were not statistically significant after 7 days.<sup>30</sup>

Black staining was reported as an adverse outcome of SDF application across all types of clinical trials, including studies on primary and permanent dentition, root surfaces,

and dentinal hypersensitivity (Table 4). One clinical trial evaluated adverse events as a secondary outcome, including tooth pain, gum pain, gum bleaching, and systemic toxicity, between annual and semiannual applications of SDF at 12% and 38%.<sup>55</sup> Their findings revealed a low prevalence of adverse events across all SDF groups (most less than 10%), with no report of systemic toxicity by any participant. Duangthip and colleagues reported that gum pain resolved without treatment within 2 days,<sup>32,57</sup> and a greater proportion of black stain was found in groups receiving 38% SDF (annual and semiannual applications) than in 12% SDF groups.<sup>57</sup>

#### Acceptance

**Perspectives from clients/patients and caregivers.** A total of five studies evaluated participant or caregiver acceptance either as a primary or secondary outcome (Table 6).<sup>35,47,49,50,55</sup> Of the studies that assessed participant or caregiver acceptance as a primary outcome, one randomized control trial assessed participant discomfort during SDF application in comparison to a control group,<sup>35</sup> and one cross-sectional analysis of a randomized control trial from Brazil measured anxiety levels between groups of children who received SDF or ART.<sup>47</sup> Both studies reported no difference in the levels of anxiety or discomfort between groups.<sup>35,47</sup>

Three studies assessed parental acceptance of treatment through self-reported questionnaires.<sup>49,50,55</sup> From 2 clinical studies, the majority of parents (>60%) reported satisfaction with their child's dental appearance at follow-up visits. However, anterior teeth had a lower rate of satisfaction compared to posterior teeth.<sup>49,55</sup> A cross-sectional study by Crystal and colleagues asked parents about their opinions of using SDF to treat dental caries for their children on anterior and posterior teeth.<sup>50</sup> Most parents reported higher preference for SDF use in posterior teeth, due to cosmetic concerns with black staining. No information on adult recipient perspectives of application was available.

*Perspectives from dental professionals.* Perceptions of SDF among dental professionals were assessed in 2 studies.<sup>48,51</sup> Chhokar and colleagues administered an online survey to dental hygienists in alternative practice settings (e.g., clinic care, education, and administration) in California.<sup>48</sup> Their findings revealed that most respondents did not feel clinical staining was a barrier to treatment (<15%), but parental acceptance may be an issue (50%).<sup>48</sup> In 2015, Nelson and colleagues conducted a survey of pediatric program directors in the United States to identify concerns and barriers to implementation of SDF. The majority of respondents agreed with concerns that parental acceptance, standard of care, evidence base, and reimbursement mechanisms were barriers to implementation.<sup>51</sup>

#### Cost

Two studies explored costs associated with the application of SDF in a dental setting.<sup>52,53</sup> Hansen and colleagues assessed the impact of silver nitrate and fluoride varnish on future dental care utilization and cost in the United States.<sup>52</sup> They identified higher overall dental care costs in the silver nitrate + fluoride varnish group than non-silver group.<sup>52</sup> Schwendicke and colleagues compared SDF for the prevention of root caries to no treatment, fluoride rinse or chlorhexidine varnish.<sup>53</sup> Their simulation analysis revealed that SDF was cost effective for root caries prevention compared to other treatments.

#### Description of treatment protocols

##### *Indications and contraindications*

Clinical indications and contraindications for using SDF in a dental setting were outlined in 2 clinical guidelines.<sup>5,26</sup> Indications and contraindications from North American guidelines and from inclusion and exclusion criteria identified in clinical studies are provided in Table 7. Indications for the use of SDF to arrest or prevent carious lesions include consideration for caries risk level, access to dental care, and behavioural or medical challenges with client/patient management.<sup>5,26</sup> Other clinical indications reported by Horst and from clinical trials suggest that SDF only be applied to cavitated carious lesions that do not exhibit signs of pulpal involvement.<sup>5</sup> In terms of therapeutic implications, the American Academy of Pediatric Dentistry (AAPD) has provided conditional recommendations on the use of SDF for arresting caries lesions only in primary teeth.<sup>26</sup> No recommendation for or review of the use of SDF in permanent dentition was identified in this review.

*Concentration, frequency, and application of silver diamine fluoride.* Table 8 provides an overview of clinical protocols used in primary studies. The majority of studies assessed the effect of SDF at 30% to 38% concentrations,<sup>30-37,39-44,46,49</sup> 3 studies reported across 4 articles compared or assessed SDF at 10% to 12% concentration,<sup>32,38,41,45</sup> and 1 study did not specify the concentration of SDF.<sup>47</sup> Five studies explicitly stated that they did not excavate prior to application of SDF,<sup>31,38,42,43,56</sup> and 1 study indicated that soft decayed tissues were

removed by hand excavation.<sup>40</sup> Studies that applied SDF to root surfaces of teeth did not involve excavation or prior prophylaxis.<sup>33,37,39</sup> In terms of application time, Clemens assessed application time and lesion arrest rate and found no difference in the length of application time and proportion of arrested lesions.<sup>49</sup>

In terms of frequency of SDF application, 9 studies assessed one-time application of SDF,<sup>25,30,35,36,38,44,46,47,49</sup> 4 articles reported application of SDF every 6 months,<sup>32,40,41,43</sup> 7 studies reported across 8 articles applied SDF every 12 months,<sup>31,32,34,37,39-42</sup> and 2 studies applied SDF at weekly intervals.<sup>31,45</sup> As mentioned previously, due to heterogeneity among studies, no meta-analyses have been performed to assess the effectiveness by concentration or frequency. Recommendations on the technical application of SDF were available from 2 protocols. The University of California San Francisco (UCSF) protocol for arresting caries, developed by Horst, suggests isolating and drying affected teeth prior to application, but no need for excavation,<sup>5</sup> and the AAPD suggests that clinical application should not deviate from manufacturer recommendations.<sup>7</sup>

##### *Context and training*

Most clinical studies were conducted in non-traditional practice settings such as schools,<sup>31,32,35,38,41-44,47</sup> portable clinics,<sup>33,34,37</sup> and other community settings (Table 8).<sup>40</sup> In 12 studies, SDF was applied by a dentist or clinician in a dental setting,<sup>31-37,39-42,45,49</sup> 2 studies involved application of SDF by trained school nurses or primary health workers who were supervised by a dentist,<sup>38,44</sup> and 5 studies did not specify the provider.<sup>25,30,43,46,47</sup> In terms of training requirements, school nurses received one day of training.<sup>44</sup> Results from a 2015 cross-sectional survey of pediatric dental program directors revealed that 79.7% and 25.7% of pediatric dental programs in the United States teach silver diamine fluoride through didactic or clinical courses, respectively. No other sources identified training requirements for SDF in dental practice.

## DISCUSSION

This scoping review synthesizes the research on the effectiveness of SDF, compared to other agents, in preventing or arresting caries (and reducing tooth sensitivity). Based on this synthesis, recommendations can be made for dental hygiene practice in Canada.

Research on the effectiveness, safety, and acceptance of SDF has increased over the past 20 years, which has facilitated a better understanding of the use of SDF in dentistry. Unfortunately, this review did not identify any study that assessed the effect of SDF for any indication on permanent dentition in individuals 10 to 60 years old. The authors would also like to draw attention to potential issues around the transferability of evidence to the North American context due to differences in demographics, caries risk status, and oral hygiene behaviours between populations.

The findings presented in this scoping review suggest

that SDF may be useful in managing incipient to cavitated carious lesions in primary dentition or exposed or carious root surfaces in permanent dentition. Clinical studies on the use of SDF in primary dentitions suggest that SDF may be superior to fluoride treatment in arresting caries lesions.<sup>6,9,26</sup> Due to the scarcity of research, this review could not confirm the effect of SDF in arresting coronal caries or reducing dentinal hypersensitivity in permanent dentition. In addition, due to heterogeneity in outcomes and timepoints used to assess effectiveness, the superiority of SDF over other treatment modalities such as ART or sealants using glass ionomer cement cannot be confirmed. Overall, the scope of evidence presented in this review is similar to evidence for most preventive therapies in dentistry, such as fluoride varnish, gels, and ART. In general, this research focusses on investigating the efficacy of preventive therapies in healthy children and elderly groups and seldom assesses their application in adult or special needs populations.<sup>58-61</sup>

Research on provider type and practice setting suggests that SDF may be a suitable provisional therapy in resource-limited settings. This review highlighted that SDF is a safe and acceptable therapy that can be delivered by trained and supervised non-dental personnel, such as nurses or primary care workers. This review, however, did not identify any detailed training protocols for clinicians interested in applying SDF. Currently, there are 2 clinical protocols available in North America<sup>5,7</sup>; both sources acknowledge that there is no established frequency for SDF application and insufficient evidence for the types and depths of carious lesions that can be arrested successfully.<sup>7</sup> Thus, it is expected that clinical protocols will evolve as research continues in these areas.

This review did not identify any major risks or harm related to SDF when used in healthy population groups and applied directly to carious lesions. The majority of reported adverse effects and parental concerns related to staining of treated teeth and discomfort that resolved over time.<sup>49,50,55</sup> Given the low incidence of adverse events reported in clinical trials, evidence suggests that SDF is a safe therapy for healthy individuals. However, the therapeutic benefits and risks of SDF may not be transferable to individuals excluded from clinical studies, such as individuals with compromised immune systems or other systemic conditions. For example, Lewis and colleagues suggest that SDF may not be suitable for older adults with thinner gingiva, as its application could cause gingival burn or irritation.<sup>62</sup> However, no trial has confirmed or refuted this claim. Evidence of long-term adverse effects of SDF material from longitudinal trials is limited to 3-year timeframes, which may not be long enough to support or refute long-term benefits or harms.<sup>39</sup>

The findings from this review show that SDF is not used as a replacement for the generalized application of fluoride or remineralization agents, but rather as a site-

specific application for indicated teeth. The results also do not suggest that SDF replaces any existing therapy within the scope of dental hygiene practice, but evidence supports its use as an interim therapy for managing coronal caries when permanent restorative treatment is not available. As with any therapy, providers interested in applying SDF should familiarize themselves with the indications, contraindications, benefits, and risks of using SDF as outlined in this review, and keep abreast of changes to these aspects as evidence continues to emerge. Further, providers should practise professional discretion and relay relevant information as part of the informed consent process if they intend to use SDF in practice.

Overall, there is a notable gap in research on the use of SDF in dentistry. In terms of population groups, no information is available for adolescents and young to middle-aged adults. This gap also exists in research on the effect of topical fluorides in dentistry.<sup>59</sup> As stated previously, due to inconsistencies in treatment protocols across clinical studies, there is no evidence either to support any particular application frequency, or to show the superiority of SDF over existing therapies. Therefore, this review does not provide definitive conclusions about the effect of SDF in adolescents and adults or medically compromised groups or treatment recommendations. Nonetheless, promising results among children encourage the use of SDF in population groups where definitive treatment is not readily available, when coupled with consistent monitoring until definitive treatment is available. Approval from Health Canada also provides more opportunities for its wider use in both public and private sectors.

This review suggests that more research on the effectiveness of SDF in different population groups and in comparison to other minimally invasive treatments, such as ART or interim stabilization therapy, is warranted. Further steps within the HTA framework should also be carried out to determine the economic, ethical, and social implications of adopting SDF in clinical practice. These steps include an assessment of the potential benefits and harms associated with providing SDF therapy to different client/patient groups, and whether SDF could affect later provision of care.<sup>63</sup> Finally, future research should also incorporate client/patient-important outcomes, such as function, pain/discomfort, and esthetics to better understand the impacts of SDF from the recipient's perspective.

This scoping review has some limitations. For example, the inclusion criteria were restricted to studies reported in English, and meta-analyses beyond those reported in existing systematic reviews were not performed. Despite these limitations, this scoping review uncovered a broad range of evidence on the effectiveness, safety, acceptance, and implications of SDF use in primary dentition that can be used to inform dental hygiene practice.

## CONCLUSIONS

This scoping review assessed the use of SDF for prevention

and arrest of coronal and root caries, and treatment of tooth sensitivity. Current evidence and guidelines support the use of SDF for arresting carious lesions in the primary dentition, but limited evidence is available to support the use of SDF in arresting root surface caries and reducing dentinal hypersensitivity. Based on available evidence, SDF may be a suitable therapy to add to the dental hygiene clinical armamentarium for managing carious lesions in the primary dentition. However, more research is needed to establish the frequency for SDF application and the types and depths of carious lesions that can be arrested successfully. It would also help answer practical questions related to the application and acceptance of SDF by recipients and dental providers.

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#### CONFLICTS OF INTEREST

J Farmer, S Singhal, L Dempster, and C Quiñonez were contracted by the Canadian Dental Hygienists Association as consultants on the design, research, and writing of this position paper. J Farmer was paid as a consultant for this position paper.

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