A Randomized Clinical Trial of Silver Diamine Fluoride to Arrest Early Childhood Caries in Young Children

by

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Abstract:

Objective: To investigate the effectiveness of silver diamine fluoride (SDF) to arrest early childhood caries (ECC) in very young children randomized to three different application frequency groups (regimens)

Methods: Children with active dentinal carious lesions (ICDAS 5 or 6) in primary teeth without any signs of pulpal involvement were randomized into three different application frequency groups; 1, 4, or 6 months apart. Children underwent treatment with 38% SDF at baseline visit and again at a second visit. Treated lesions were assessed at the second and third visits to determine arrest success. Participants were considered completely successful (CS) if all treated lesions were arrested and incompletely successful (IS) if at least one lesion was not arrested. Statistical analyses included descriptive and bivariate analyses. A p value ≤ 0.05 was significant.

Results: A total of 84 children with 486 carious lesions were recruited into the study with 28 children in each group. The overall proportion of completely successful treated children at visit 2 and third visit were 40% and 68% respectively. Results of McNemar's test showed a significant increase in complete success from 40% at second visit to 68% at visit 3 (p-value <0.001) across all groups for 84 study participants. Within each group, significant improvement in complete success at child-level was also noted with p-values of 0.041,0.023 and 0.004 for Regimen 1, 2 and 3 respectively. Participants in one month group showed a change of complete success from 36% at second visit to 71% at third visit (p-value 0.004). No significant differences were noted between the groups at second visit and final visit (p >0.05)

Conclusions: Findings in this study suggested that two applications of SDF at different frequencies showed similar frequency of successfully treated cases at the child level.

No difference was noted in success rates comparing three groups either at second or third visit. Results from our study were statistically insignificant when comparing the arrest rates at child level between three groups at both visits. Further analysis should investigate lesion arrest rates between the treatment groups.

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Introduction:

Early childhood caries (ECC) defined as the presence of 1 or more decayed, missing, or filled primary teeth in children < 6 years of age[3] is a global oral health concern[1,2], with recent prevalence estimates in Canada ranging from 28% to 98%.[6] The American Academy of pediatric dentistry which recognizes the unique and often virulent nature of ECC, indicates that immediate non-surgical interventions need to be implemented whenever possible. In addition, non-surgical interventions should be carried forth whenever it is possible to delay or decrease the need for dental surgery.

Restorative treatment of caries is still the predominant method of managing S-ECC. A certain challenge while treating young children is their uncooperative behavior which is age-related.[9,10] Although conscious sedation or general anesthesia in operating room are other options that can be used to treat ECC in such young population, they are both accompanied by increased cost of treatment and risks. Consequently, it is noted that restorative treatment alone does not address the underlying cause of ECC leading to high recurrent rate of forming new carious lesions. [10] Many vulnerable pediatric populations with limited access to dental care go through life with untreated ECC posing a serious health risk. [10]

The consequences of ECC are vast and include a greater risk of new carious lesions in both the primary and permanent dentitions, higher treatment costs, increased hospitalizations and emergency room visits, diminished ability to learn, loss of school days, and reduced oral health related quality of life. [4] ECC exacts a toll on children, affecting their development, school performance and behavior, and on families and society as well. [22] ECC has been associated with altered nutritional status[23], behavioral problems[24], school absences and poorer school performance.[25] The multifactorial nature

of ECC poses a challenge to identify effective prevention strategies.[8] Although primary prevention is always preferred, there were no effective non-surgical products available for secondary prevention until recently.

Recent reports have identified silver diamine fluoride (SDF) as an anti-caries agent that successfully arrests dental caries and has the potential to effectively address untreated decay in young children thereby reducing the need for rehabilitative dental surgery under GA.[11-16] One systematic review and meta-analysis reported that 38% SDF is safe and effective in arresting dentin caries in primary teeth resulting in the arrest of 81% of active caries lesions.[17] The American Dental (ADA) association practice guideline on nonrestorative treatments for carious lesions recently recommended that clinicians prioritize the use of 38% SDF solution over other products to manage cavitated carious lesions.[18] Despite this evidence, true consensus on the frequency of SDF applications in children with ECC is lacking. Furthermore, the current American Academy of Pediatric Dentistry (AAPD) Clinical Practice Guidelines on SDF urge researchers to conduct well-designed randomized clinical trials comparing the use and outcomes of SDF to arrest caries lesions in both primary and permanent teeth.[19]

While Advantage Arrest™ (38% SDF) received approval for clinical use in Canada in 2017, there has been little guidance on the frequency and duration of its application. Some proposed SDF protocols may not easily translate into dental public health clinical settings or work well in remote Indigenous communities. Their recommendations for frequent reapplication [14,17,20] is not practical or realistic in these programs or remote regions where access to dental care is limited and frequent follow-up visits may not be possible.

The aim of our study was to examine the effectiveness of SDF to arrest dental caries in very young children randomized to different application regimens. To the best of our knowledge, this study is the first randomized clinical trial (RCT) of SDF conducted in Canada for our very young population, which may aid clinicians in the decision-making process regarding SDF application for the larger benefit of patients.

Methods:

A randomized clinical trial was conducted to study the effectiveness of SDF to arrest cavitated carious lesions in primary teeth at three different application regimens. Ethics approval for this study was obtained from the University of Manitoba's Biomedical Research Board. A total of 84 participants were recruited from community clinics in Winnipeg (Access Downtown, Mount Carmel, and SMILE plus) between October 2019 and June 2021. Interested parents and caregivers were contacted by the research staff to inform them of the study objectives, eligibility criteria, and procedures. Study visits took place at one of the community-based dental clinics or the Children's Hospital Research Institute of Manitoba (CHRIM).

Children less than 72 months of age were screened by the principal investigator (RJS) to determine their eligibility for study. Inclusion criteria included each of the 84 participants meeting the International Caries Detection and Assessment System (ICDAS) 5 or 6 with caries extending into the dentin without any signs of pulpal involvement. Teeth included in the study were clinically confirmed to have soft cavitated caries lesions extending into dentin allowing for direct application of SDF. Exclusion criteria included teeth that met any of the PUFA criteria (i.e., spontaneous pain due to caries, pulp exposure, mobility, signs of pulpal infection such as abscess, fistula, or swelling). Children with silver allergy or with hereditary generalized developmental defects of enamel were excluded, as were those with severe medical issues or dental infections requiring immediate dental rehabilitation under GA.

Originally, 81 participants were recruited into the study with 2 participants being lost over time; one participant was lost after baseline visit and another one after second visit. Following this, 3 participants were recruited with a total of 84 participants who

were randomized into three groups (regimens). Group 1 was two applications of SDF four months apart, which is the protocol frequency adopted by the Winnipeg Regional Health Authority's (WRHA) Clinical Guideline on SDF. Group 2 was two applications of SDF six months apart as recommended by ADA. Group 3 involved two applications of SDF one month apart, as proposed in the AAPD's clinical practice guideline. The ADA recommends that SDF should be prioritized over 5% NaFV (sodium fluoride varnish) for nonrestorative management of cavitated lesions.[26] Thus, a control group to receive fluoride varnish was not considered as this would now be considered unethical and substandard care.

Following written informed consent from parent/ caregiver, children were randomly allocated into one of three groups using sealed envelopes to ensure random allocation at the baseline visit. During this visit, parents or caregivers completed a baseline questionnaire administered by interviewer regarding family demographics, ethnicity, dietary habits, oral hygiene routines, dental concerns including dental pain (if any) and appearance of teeth. All participants underwent a clinical dental examination with some children having radiographs taken before their enrollment into the study. Radiographs were not a part of our study protocol. Teeth meeting ICDAS 5 or 6 criteria were recorded. The location, size, hardness, color, and activity status of each eligible carious lesion was also documented in addition to calculating dmft (decayed, missing and filled primary teeth) at each visit. Following the examination, 38% SDF (Advantage arrest, Oral Science, Brossard, QC, Canada) was applied on all eligible carious lesion(s) without removal of any caries. SDF was applied with a micro brush for one minute depending on the level of patient cooperation. This was followed by wiping the treated surfaces with wet gauze or a water rinse followed by the application of 5% NaFV.

Participants returned for their second treatment visit depending on their regimen at 4 months (Regimen 1), 6 months (Regimen 2), or 1 month (Regimen 3). At this visit, their first follow up examination on previously treated teeth was completed. Lesions that were hard upon tactile probing and black in color were considered as arrested lesions. SDF was applied on previously treated lesions for one minute followed by 5%NaFV. Participants returned for their third and final visit depending on their regimen at 4 months (Regimen 1), 6 months (Regimen 2), or 1 month (Regimen 3). At this visit, a second follow up examination was completed. Parents/caregivers also completed a follow-up questionnaire administered by interviewer at this visit.

Color (yellow, brown, and black) and hardness (very soft, medium, or hard) of treated lesions as well as dmft were recorded at baseline and at each follow-up visit. Our study focussed on child level analysis with participants considered as completely successful (CS) if all treated lesions were arrested and incompletely successful (IS) if at least 1 lesion was not arrested. We used "intention to treat analysis" – those lost to follow-up were included in the analysis and classified as incompletely successful (IS). Data were entered into a REDCap database followed by saving on the secure server at CHRIM. Statistical analyses included descriptive statistics (frequencies, means, standard deviations (SD)) and bivariate analyses (Fisher's exact test for association, Pearson's Chi-squared test, McNemar's Chi-squared test and Kruskal-Wallis rank sum test). A p value ≤ 0.05 was significant.

Results:

Participant Characteristics

Baseline characteristics of participants recruited in the study are shown in Table 1. A total of 84 children (58% male, 42% female) were randomized into three groups with 28 participants in each group. The mean age of those recruited in the study was 44.0±14 months. The mean number of lesions (ICDAS 5 and 6) treated per participant was 5.7± 4.1. More than half of the participants (62%) brushed twice daily and 83% used a fluoridated toothpaste.

Child-level analysis

At the second visit, SDF treatment in 12 out of 28 participants (43%) each in the four month and six-month groups, and 10 out of 28 participants (36%) in the one-month group was deemed to be CS (Completely Successful) in that all treated lesions per child were arrested. There was no significant difference between the groups. ($p= 0.8$) using Pearson's Chi-squared test.

At the third visit, the proportion of recruited participants in each group determined to be completely successful (CS) using Pearson's Chi-squared test was 64% in the four-month group, 68% in the six-month group, and 71% in the one-month group ($p= 0.7$)

Chi-squared analysis revealed that there were no significant relationships between the frequency of complete success and treatment grouping, sex, frequency of toothbrushing, difficulty providing treatment, or use of fluoridated toothpaste at second and third visit (Table 2). Improvements in complete success of SDF treatment at the child level within and between groups was assessed (Table 3). An overall increase in complete success of SDF treatment for all 84 participants was observed between the

second visit and third visit (40% vs. 68%, p <0.001). All groups showed significant improvement in complete success following the first and second applications of SDF (Table 3). Participants in the one-month group (Regimen 3) showed much larger improvement in complete arrest (36% at second visit vs. 71% at final visit, p= 0.004 using Mc Nemar's test). Participants in the four month and six-month groups also exhibited improvement in the percentage with complete success (43% vs. 64% and, 43% vs. 68%, respectively)

Lesion-level Analysis

At baseline a total of 486 lesions (273 anterior, 213 posterior) were identified as being eligible to be treated with SDF. Overall, 149 lesions (82 anterior, 67 posterior) in children in the four-month group, 143 lesions (82 anterior, 67 posterior) in the six-month group, and 194 lesions (124 anterior, 70 posterior) in the one-month group. (Figure 1)

At the second visit, the arrest rates noted across three groups following treatment with one application of SDF (Figure 2-4) were 81.2% in four-month group (Regimen 1) (81.7% anterior, 80.6% posterior), 58.7% in the six-month group (Regimen 2) (71.6% anterior, 47.4% posterior), and 79.4% in the one-month group (Regimen 3) (86.3% anterior, 67.1% posterior). In total, 83 participants returned for the second visit, with one lost to follow-up in the six-month group.

Overall, 82 participants returned for the third and final visit; with a second participant lost to follow-up in the one-month group. The arrest rates at the final visit were 90.6% (91.5% anterior, 89.6% posterior) for the four-month group, 71.3% (70.1% anterior, 72.4% posterior) for the six-month group, and 90.7% (95.2% anterior, 82.9% posterior) for the one-month group following treatment with two applications of SDF.

Discussion:

This RCT investigated the effectiveness of using 38% SDF to arrest caries lesions in very young children with ECC randomized to different application frequency regimens. Participants were considered completely successful (CS) if all treated lesions were arrested and incompletely successful (IS) if at least one lesion was not arrested focusing primarily on results at the 'Child level'. The main outcome of this study was "complete success" of all treated lesions per child. Overall, results from our study revealed that the three proposed SDF protocols i.e., Regimen 1, 2 and 3 showed comparable frequencies of complete success at the child level.

SDF represents a simple and non-invasive agent to arrest caries in children. Our study provides essential information on success rate of using two applications of SDF at visits that are either 1 month, 4 months or 6 months apart to arrest ECC which can then be utilized to undertake additional research in area of SDF for high-risk children with ECC, such as children from disadvantaged communities, newcomer, rural, refugee groups, and First Nations and Metis communities in Canada. Results from this RCT are supported by data from one study that demonstrated effective caries arrest with biannual application of SDF than annual application.[9]. A meta-analysis of data from 8 clinical studies using 38% SDF found that the overall caries arrest rate was 81% (95% CI, 68% - 89%; $p<0.001$). [17]. Studies have found arrest rates of more than 75% with 6 monthly applications of 38% SDF supported by another systematic review from 2016 that found 86% caries arrest rate at 6 months.[9,28,17] Results from our study are consistent with another study that found arrest

rates of 93.3% with 3 monthly application of SDF *(p* value = 0.002) between two follow-up visits.[29]

An earlier clinical trial by our lab included the same criteria for complete success (CS) at child level where more than 50% (85%) of participants were determined to be CS following treatment with two applications of SDF[21] This is similar to what was found in this RCT with 68% of participants who were determined to be CS after receiving the same frequency of treatment . A study on children in Melbourne, Australia that looked at SDF protocol in children between 2-10 years of age assessed success of treatment in terms of lesions that were hard and black with no pain or infection.[30]

We used the "Intention to treat" analysis in our study allowing us to draw unbiased conclusions regarding the effectiveness of SDF in treatment of carious lesions, while also preserving the randomization by analyzing the participants in various group according to their original assigned group.[27] One of the main strengths of our study was the ability to investigate effectiveness of SDF application in a controlled manner with decreased operator bias (single operator administering treatment and recording data) and selection bias (all study participants in the study has an equal chance to be allocated to either of the three groups/regimens) making it quite robust. Our study was able to establish a causal relationship between treatment using SDF application and its effectiveness to arrest active carious lesions.

Originally our study was designed to investigate success at "Lesion Level" and one of the limitations of this study is that it only focuses on success at "Child Level". This outcome comes with its own limitations. For example, a child could have had 10 treated lesions, nine successful, but classified as "incomplete success". This type of classification could potentially minimize the benefit of SDF in that it might have prevented a child

needing treatment under GA. Defining “complete success” from a clinical viewpoint is important to avoid undermining the effect of SDF, and further analysis primarily focusing on success at the “lesion level” might prove to be a better to guide clinical decision making. To say that 10% lesion success rate in one child is equivalent to 90% success lesion arrest rate in another is not clinically applicable.

Conclusions:

Based on the results obtained in our study:

1. No significant differences in complete success of caries arrest rate were seen at child level when comparing the three regimens at second and third visit.
2. Our study did show a significant improvement in complete success from second to third visit regardless of the regimen with each group showing improved success rate at third visit indicating that treatment of carious lesions with two applications of SDF is an effective approach to arrest and manage caries in very young children.
3. Complete success may not be useful in an RCT and rather analysis should focus on the lesion level.

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Table 1: Baseline characteristics of recruited participants.

Variable	**OVERALL TOTAL** (84), No. (%), except indicated	**ONE MONTH APART-** Regimen 3 (28) No. (%), except indicated	**FOUR MONTHS APART-** Regimen 1 (28) No. (%), except indicated	**SIX MONTHS APART-** Regimen 2(28) No. (%), except indicated	**p-value**
Mean age± SD (months)	44.0 ± 14	43.0 ± 15.0	40.0± 13.0,	49.0 ± 14.0,	0.1
Sex					
Male	49 (58)	19 (68.0)	13 (46.0)	17 (61.0)	0.3
Female	35 (42)	9 (32.0)	15 (54.0)	11 (39.0)	
Dental Insurance					
Yes	58 (69.0)	20 (71.0)	19 (68.0)	19 (68.0)	>0.9
No	24 (29.0)	7 (25.0)	9 (32.0)	8 (29.0)	
Unsure	2 (2.4)	1 (3.6)	0 (0)	1 (3.60)	
Frequency of toothbrushing					
Twice daily	52 (62.0)	19 (68.0)	16 (57.0)	17 (61.0)	0.2
Once daily	24 (29.0)	5 (18.0)	9 (32.0)	10 (36.0)	
Every other day	6 (7.1)	4 (14.0)	2 (7.1)	0 (0.00)	
Seldom/rarely	2 (2.4)	0 (0.00)	1 (3.6)	1 (3.6)	
Never	0 (0.00)	0 (0.00)	0 (0.0)	0 (0.00)	
Uses fluoridated toothpaste					
Yes	70 (83.0)	24 (86.0)	24 (86.0)	22 (79.0)	0.8
No	5 (6.0)	2 (7.1)	1 (3.6)	2 (7.1)	
Unsure	9 (11.0)	2 (7.1)	3 (11.0)	4 (14.0)	
Baseline dmft, mean ± SD	6.8 ± 4.5	6.5 ± 4.4	6.6 ± 5.0	7.3 ± 4.1	0.4
No. of lesions treated per participant (ICDAS 5 and 6) mean ± SD	5.7 ± 4.1	6.4 ± 4.1	6.0 ± 4.4	5.1 ± 3.8	0.2

Table 2: Results of Fisher's exact tests to determine association between child-level factors and success of SDF treatment at second and third visit across regimens.

	Second Visit			**Third Visit**		
	Complete Success (child level) N =34	Incomplete Success (child level) N= 50	P-value	Complete Success (child level) N= 57	Incomplete Success (child level) N=27	P-value
One month Regimen 3	10 (36)	18 (64)	0.8	20 (71)	8 (29)	0.7
Four months Regimen 1	12 (43)	16 (57)		18 (64)	10 (36)	
Six months Regimen 2	12 (43)	16 (57)		19 (68)	9 (32)	
Sex						
Male	17 (50)	32 (64)		35 (61)	14 (52)	
Female	17(50)	18 (36)	0.261	22 (39)	13 (48)	0.4
Frequency of toothbrushing						
2x Daily	20 (59)	32 (64)		32 (56)	20 (74)	
<2x Daily	14 (41)	18 (36)	0.654	25 (44)	7 (26)	0.1
Difficulty providing treatment						
Yes	12 (35)	20 (40)		14 (25)	9 (35)	
No	22 (65)	30 (60)	0.819	43 (75)	17 (65)	0.4
Use of fluoridated toothpaste						
Yes	30 (88)	40 (80)		48 (84)	22 (81)	
No/Unsure	4 (12)	10 (20)	0.384	9 (16)	5 (19)	0.7

Table 3: Results of McNemar's test comparing complete success across second and third visit at child-level - Pooling all regimens and within each regimen.

COMPLETE SUCCESS	**Second Visit** No. (%)	**Third Visit** No. (%)	**p-value**
Overall Pooling all Regimens (N=84)	34 (40)	57 (68)	<0.001
One month (Regimen 3) (N= 28)	10 (36)	20 (71)	0.004
Four months (Regimen 1) (N=28)	12 (43)	18 (64)	0.041
Six months (Regimen 2) (N= 28)	12 (43)	19 (68)	0.023

Figure 1: Arrest rates overall for all lesions, anterior lesions, and posterior lesions after SDF application (treatment). Missing arrest outcome values have been counted as “not arrested”.

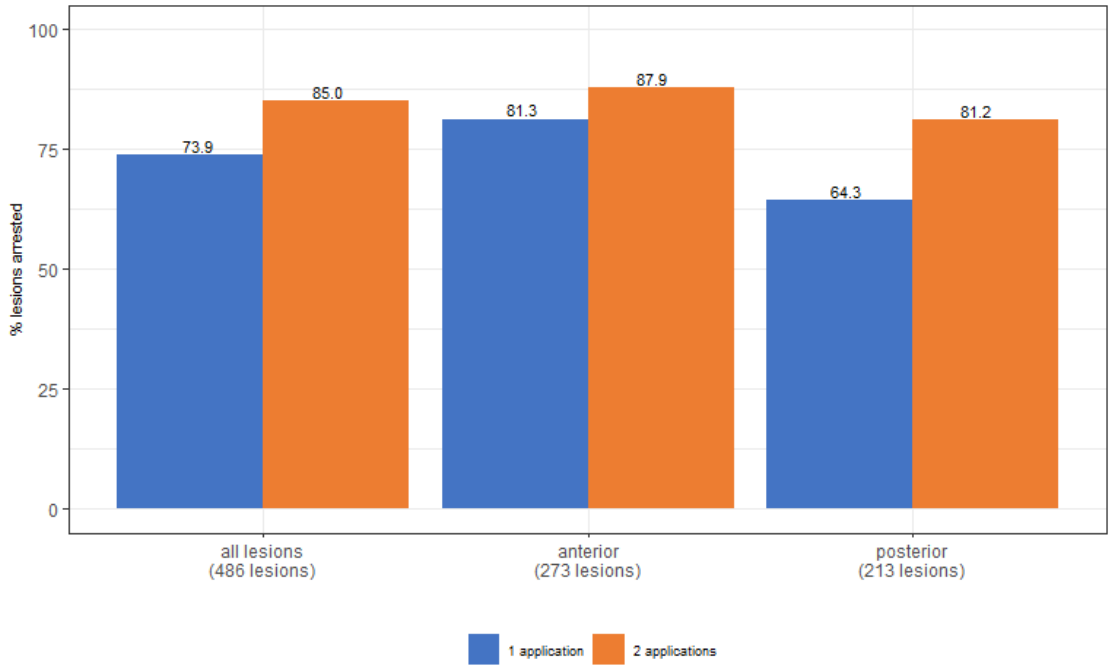


Figure 2. Arrest rates in four-month group (Regimen 1) by location and application after SDF application (treatment). Missing arrest outcome values have been counted as “not arrested”.

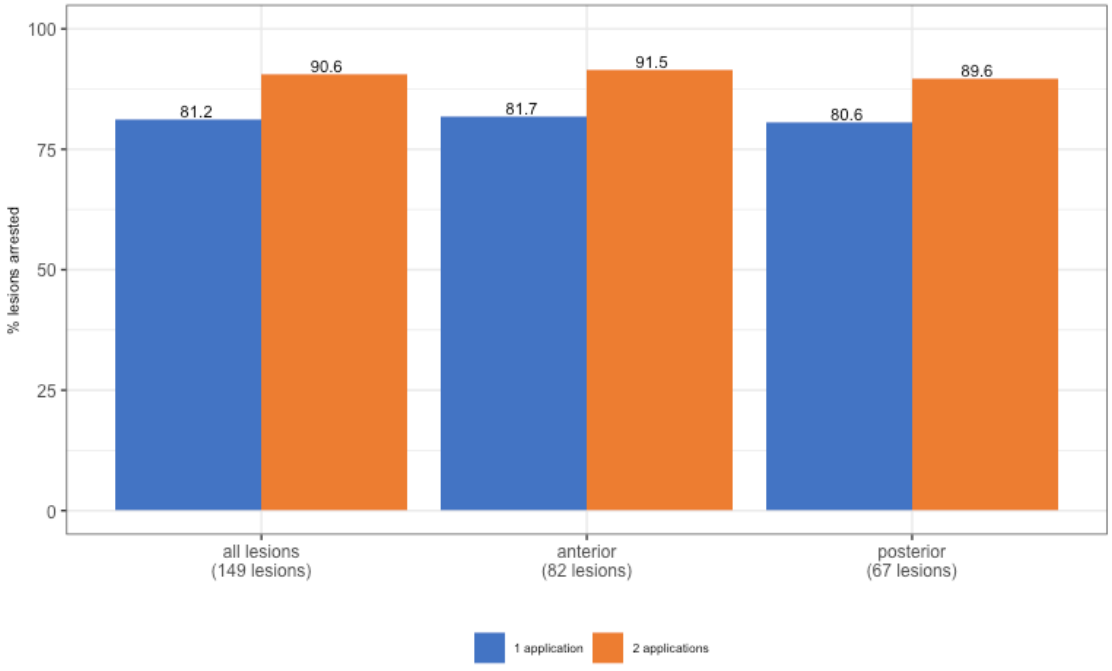


Figure 3. Arrest rates in six-month group (Regimen 2) 2 by location and application after SDF application (treatment). Missing arrest outcome values have been counted as “not arrested”.

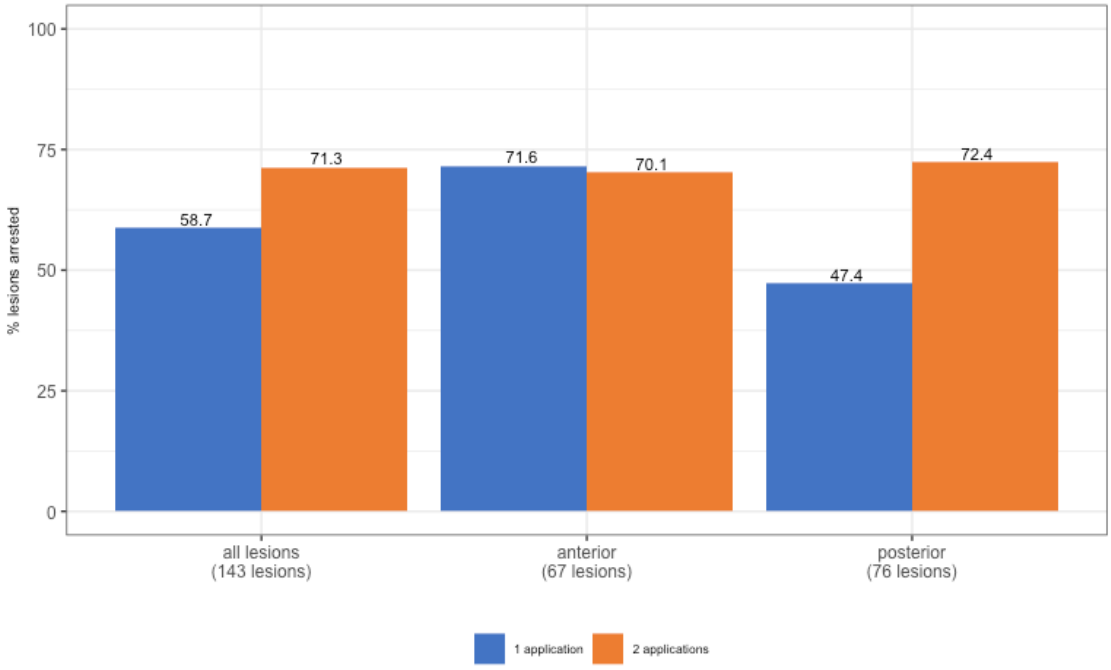
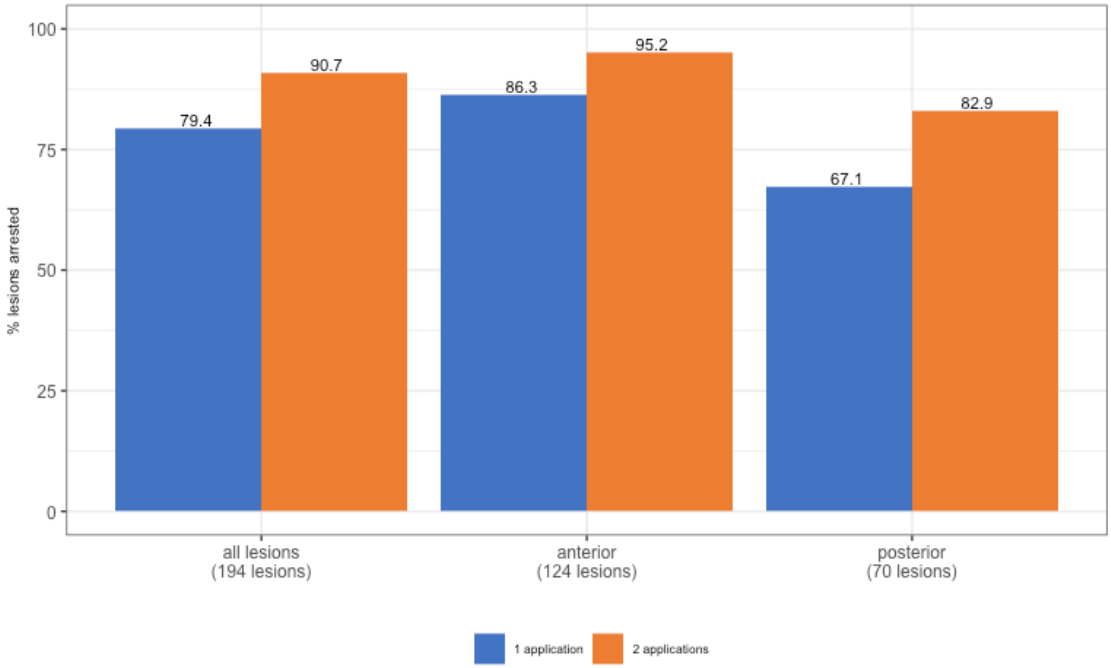


Figure 4. Arrest rates in one-month group (Regimen 3) by location and application after SDF application (treatment). Missing arrest outcome values have been counted as “not arrested”.



References:

1. Petersen PE. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century--the approach of the WHO Global Oral Health Programme. Community Dent Oral Epidemiol. 2003;31 Suppl 1:3-23. doi:10.1046/j..2003.com122.x
2. Petersen PE, Lennon MA. Effective use of fluorides for the prevention of dental caries in the 21st century: the WHO approach. Community Dent Oral Epidemiol. 2004;32(5):319-321. doi:10.1111/j.1600-0528.2004.00175.x
3. Council R. Policy on early childhood caries (ECC): Classifications, consequences, and preventive strategies. Pediatr Dent. 2018;40(6):60-62.
4. Revision L. Policy on early childhood Caries (ECC): Unique challenges and treatment options. Pediatr Dent. 2018;40(6):63-64.
5. Schroth RJ, Levi JA, Sellers EA, Friel J, Kliewer E, Moffatt MEK. Vitamin D status of children with severe early childhood caries: A case-control study. BMC Pediatr. 2013;13(1). doi:10.1186/1471-2431-13-174
6. Schroth RJ, Pang JL, Levi JA, Martens PJ, Brownell MD. Trends in pediatric dental surgery for severe early childhood caries in Manitoba, Canada. J Can Dent Assoc (Tor). 2014;80:e65.
7. Prowse S, Schroth RJ, Wilson A, et al. Diversity Considerations for Promoting Early Childhood Oral Health: A Pilot Study. Int J Dent. 2014;2014:1-10. doi:10.1155/2014/175084
8. Schroth R, Wilson A, Prowse S, et al. Looking back to move forward: understanding service provider, parent, and caregiver views on early childhood oral health promotion in Manitoba, Canada. Can J Dent Hyg. 2014;48(3):99-108.
9. Fung MHT, Duangthip D, Wong MCM, Lo ECM, Chu CH. Randomized Clinical Trial of 12% and 38% Silver Diamine Fluoride Treatment. J Dent Res. 2018;97(2):171-178. doi:10.1177/0022034517728496
10. Crystal YO, Niederman R. Silver diamine fluoride treatment considerations in children's caries management. Pediatr Dent. 2016;38(7):466-471.
11. Peng JJ, Botelho MG, Matinlinna JP. Silver compounds used in dentistry for caries management: a review. J.Dent. 2012;40(7):531-41.
12. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. J.Dent.Res. 2002;81(11):767-70.
13. Rosenblatt A, Stamford TC, Niederman R. Silver diamine fluoride: a caries "silver-fluoride bullet". J Dent Res. 2009;88(2):116-25.
14. Horst JA, Ellenikiotis H, Milgrom PL. UCSF Protocol for Caries Arrest Using Silver Diamine Fluoride: Rationale, Indications and Consent. J Calif.Dent Assoc 2016;44(1):16-28.
15. Milgrom P, Horst JA, Ludwig S, et al. Topical silver diamine fluoride for dental caries arrest in preschool children: A randomized controlled trial and microbiological analysis of caries associated microbes and resistance gene expression. J Dent 2018;68:72-78.
16. Clemens J, Gold J, Chaffin J. Effect and acceptance of silver diamine fluoride treatment on dental caries in primary teeth. J Public Health Dent. 2018;78(1):63-68.

doi:10.1111/jphd.12241
17. Gao SS, Zhao IS, Hiraishi N, et al. Clinical trials of silver diamine fluoride in arresting caries among children: a systematic review. JDR Clinical & Translational Research 2016;1(3):201-10.
18. Slayton RL, Urquhart O, Araujo MWB, et al. Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions: A report from the American Dental Association. J Am Dent Assoc. 2018;149(10):837-849.e19. doi: 10.1016/j.adaj.2018.07.002
19. American Academy of Pediatric D. Use of silver diamine fluoride for dental caries management in children and adolescents, including those with special health care needs. Pediatr Dent 2017;39(6):146-55.
20. Horst JA. Silver Fluoride as a Treatment for Dental Caries. Adv Dent Res 2018;29(1):135-4
21. Sihra R, Schroth RJ, Bertone M, et al. The Effectiveness of Silver Diamine Fluoride and Fluoride Varnish in Arresting Caries in Young Children and Associated Oral Health-Related Quality of Life. J Can Dent Assoc. 2020;86:k9
22. Casamassimo PS, Thikkurissy S, Edelstein BL, Maiorini E. Beyond the dmft. J Am Dent Assoc. 2009;140(6):650-657. doi: 10.14219/jada.archive.2009.0250.
23. Khanh LN, Ivey SL, Sokal-Gutierrez K, et al. Early childhood caries, mouth pain, and nutritional threats in Vietnam. Am J Public Health. 2015;105(12):2510-2517.
24. Williamson R, Oueis H, Casamassimo PS, Thikkurissy S. Association between early childhood caries and behaviour as measured by the child behaviour checklist. Pediatr Dent. 2008;30(6):505-509.
25. Jackson SL, Vann Jr. WF, Kotch JB, Pahel BT, Lee JY. Impact of poor oral health on children's school attendance and performance. Am J Public Health. 2011;101(10):1900-1906
26. Slayton, R. L., Urquhart, O., Araujo, M., Fontana, M., Guzmán-Armstrong, S., Nascimento, M. M., Nový, B. B., Tinanoff, N., Weyant, R. J., Wolff, M. S., Young, D. A., Zero, D. T., Tampi, M. P., Pilcher, L., Banfield, L., & Carrasco-Labra, A. (2018). Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions: A report from the American Dental Association. *Journal of the American Dental Association (1939)*, *149*(10), 837–849.e19. https://doi.org/10.1016/j.adaj.2018.07.002
27. McCoy C. E. (2017). Understanding the Intention-to-treat Principle in Randomized Controlled Trials. *The western journal of emergency medicine*, *18*(6), 1075–1078. https://doi.org/10.5811/westjem.2017.8.35985
28. Zhi QH, Lo ECM, Lin HC. Randomized clinical trial on effectiveness of silver diamine fluoride and glass ionomer in arresting dentine caries in preschool children. J Dent. 2012;40:962-967. doi:10.1016/j.jdent.2012.08.002.
29. Shrivastava, U., Barjatya, K., Ak, B. B., Vatsal, A., Shrivastava, R., Manker, A., Chand, B. R., & Juneja, P. (2021). Effectiveness and Parental Perception of Silver Diamine Fluoride toward Treatment of Dental Caries in Primary Teeth. *International journal of clinical pediatric dentistry*, *14*(6), 790–794. https://doi.org/10.5005/jp-journals-10005-1810.
30. Yawary, R., & Hegde, S. (2022). Silver Diamine Fluoride Protocol for Reducing Preventable Dental Hospitalisations in Victorian Children. *International dental journal*, *72*(3), 322–330.