Nonrestorative Treatments for Caries: Systematic Review and Network Meta-analysis
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Appendix

Methods

SEARCH STRATEGIES AND ELECTRONIC DATABASES CONSULTED

Search current to June 2017.
MEDLINE. Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

1. sodium fluoride/ or acidulated phosphate fluoride/
2. sodium flouride*.ti,ab,kf.
3. sodium fluoride*.ti,ab,kf.
4. NaF.ti,ab,kf.
5. durafluor.ti,ab,kf.
6. duraphat.ti,ab,kf.
7. Tin Fluorides/
8. stannous fluoride*.ti,ab,kf.
9. stannous flouride*.ti,ab,kf.
10. SNF.ti,ab,kf.
11. SnF2.ti,ab,kf.
12. sodium monofluorophosphate*.ti,ab,kf.
13. MFP.ti,ab,kf.
14. Acidulated Phosphate Fluoride/
15. acid* phosphate fluoride*.ti,ab,kf.
16. acid* phosphate flouride*.ti,ab,kf.
17. or/1-16
18. Xylitol/
19. xylitol*.ti,ab,kf.
20. Sorbitol/
21. sorbitol*.ti,ab,kf.
22. (glucitol or medevac or sorbilax or val or klysma sorbit).ti,ab,kf.
23. Mannitol/
24. manitol*.ti,ab,kf.
25. Erythritol/
26. erythritol*.ti,ab,kf.
27. polyol*.ti,ab,kf.
28. sugar alcohol*.ti,ab,kf.
29. or/18-28
30. Chlorhexidine/
31. chlorhexidine*.ti,ab,kf.
32. peridex.ti,ab,kf.
33. periorx.ti,ab,kf.
34. cervitec.ti,ab,kf.
35. Calcium Phosphates/
36. calcium phosphate*.ti,ab,kf.
37. ACP.ti,ab,kf.
38. casein phosphopeptide.ti,ab,kf.
39. recaldent.ti,ab,kf.
40. CPP-ACP.ti,ab,kf.
41. MI paste.ti,ab,kf.
42. calcium sodium phosphosilicate.ti,ab,kf.
43. novamin.ti,ab,kf.
44. nano hydroxyapatite.ti,ab,kf.
45. Hydroxyapatites/
46. tri-calcium phosphate.ti,ab,kf.
47. Prebiotics/
48. prebiotic*.ti,ab,kf.
49. “1.5% arginine”.ti,ab,kf.
50. Probiotics/
51. probiotic*.ti,ab,kf.
52. or/30-51
53. Dietary Carbohydrates/
54. Dietary Fiber/
55. 53 or 54
56. limit 55 to yr="1998 - 2009"
57. 52 or 56
58. SDF.ti,ab,kf.
59. Silver Nitrate/
60. silver nitrate*.ti,ab,kf.
61. advantage arrest.ti,ab,kf.
62. silver diammine.ti,ab,kf.
63. diammine silver.ti,ab,kf.
64. silver fluoride*.ti,ab,kf.
65. silver fluoride*.ti,ab,kf.
66. ammonical silver.ti,ab,kf.
67. ammoniacal silver.ti,ab,kf.
68. or/58-67
70. Lasers/
71. lasers.ti,ab,kf.
72. caries infiltration.ti,ab,kf.
73. resin infiltration.ti,ab,kf.
74. (resin adj3 (caries or infiltration)).ti,ab,kf.
75. icon.ti,ab,kf.
76. or/70-75
79. Cariostatic Agents/
80. cariostatic agent*.ti,ab,kf.
81. cariostatic effect*.ti,ab,kf.
82. cariostatic effect/
83. or/79-82
84. difluorsilane.ti,ab,kf.
85. difluorosilane.ti,ab,kf.
86. 84 or 85
87. ammonium fluoride.ti,ab,kf.
88. fluor protectos.ti,ab,kf.
89. NH4.ti,ab,kf.
90. NH 4.ti,ab,kf.
91. Sodium Bicarbonate/
92. sodium bicarbonate.ti,ab,kf.
93. sodium hydrogen carbonate.ti,ab,kf.
94. baking soda.ti,ab,kf.
95. Calcium Hydroxide/
Updated Search from Wright 2016, with date limit of January 2013 to June 2017

MEDLINE. Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:
1. "Pit and Fissure Sealants"/
2. (tetric or bitremer or fluoroshield or delton or kerr or lispro or dyract or revolution or oralis or ketac or condise).tw.
Selection of primary studies and data extraction
We also extracted the criteria used to define the outcome of arrest or reversal. If the study reported the lesions as “inactive,” “hard,” or “not progressed,” we considered them acceptable synonyms for “arrest or reversal.” Additionally, if transition scores were reported (i.e., change in ICDAS score), we only considered negative scores (i.e., lesion score changed from ICDAS 2 to 1) as “reversals” if this was possible to parse out. We did not consider the outcome of “stabilization” to be analogous to “arrest or reversal,” except if the intervention was either sealants or resin infiltration. We prioritized the extraction of radiographic data over data using visual and tactile assessment. If radiographs were used for diagnosis, we favored the most sensitive method applied in the study (digital subtraction radiography > pairwise methods > visual assessment) (Dorri et al. 2015).

Assessment of risk of bias
Two reviewers (M.P.T. and A.C.L.) used the Cochrane Risk of Bias Tool to assess the risk of bias of included studies independently and in duplicate for the domains of random sequence generation, allocation concealment, blinding of participants/personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. We used signaling questions to assign judgments of high, unclear, or low risk of bias for each domain. Reviewers discussed any disagreements until consensus was reached.

Statistical analysis
We conducted NMA to obtain estimates of the relative effectiveness of all interventions for the primary outcome by combining direct and indirect evidence. We assumed that we were estimating average relative treatment effects and their variability, and thus we chose a random-effects model. All analyses were planned a priori, anticipating the presence of a sparse network. We implemented the analysis using the package netmeta in the software R.

If studies shared similar treatment doses and/or durations as determined by the expert panel, data were combined into one node. When there was more than one follow-up time reported within a study, we chose the time that was closest to all of the others in that network. If this was not possible, we chose the longest follow-up time.

Our sparse network limited the options for analysis. We used the common heterogeneity variance assumption to estimate a single between study heterogeneity across the network, as the lack of data made it unfeasible to allow for the heterogeneity parameter to vary across the network, regardless of whether we believed that the common heterogeneity assumption was sensible. We estimated this parameter using the generalized methods of moments estimate of the between-studies variance available.
in the software package that we used (Jackson et al. 2012). In addition, we chose a frequentist approach to avoid incorporating the uncertainty about the heterogeneity parameter that is accounted for when using Bayesian random-effects models.

We assessed the assumptions of transitivity and coherence, but we did not assess goodness of fit of the network because we did not believe it was appropriate owing to the few data points of our sparse network.

We assessed global incoherence of the network using the design-by-treatment interaction model (Higgins et al. 2012). We assessed local incoherence for each loop of evidence using the back calculation method (Dias et al. 2010). We assessed intransitivity for each estimate as per GRADE guidance. We used both the assessment of local incoherence and intransitivity in the assessment of the certainty of the evidence of each network estimate.

We did not plan to conduct any sensitivity analyses to explore the effect of small studies owing to the limited amount of evidence available. In addition, the expert panel strongly believed that all studies should be considered in the analyses.

**Assessment of the certainty in the evidence**

Two reviewers made the assessments independently, and solved any disagreement by consensus. The assessment of each of the network estimates considered the following:

1) **Certainty in the direct evidence:** The certainty of this body of evidence from RCTs started as high, but serious or very serious issues of risk of bias, inconsistency, indirectness, imprecision, and publication bias could reduce the certainty (Guyatt et al. 2008). We assessed risk of bias making an overall judgment based on the risk of bias of each study providing direct evidence for the comparison of interest. We assessed inconsistency using the $I^2$ statistic, Chi-squared test, and by visual assessment of forest plots. We assessed indirectness by judging to what extent the studies answered the target question. We assessed publication bias by focusing in the comprehensiveness of our search strategy, as there were no sufficient studies to use visual or statistical methods. We assessed imprecision using the confidence interval of the direct estimates, and a threshold of clinical importance of 10%. The assessment of imprecision of the paired comparisons did not influence the certainty of the network estimates (Brignardello-Petersen et al. 2018), but it was considered in the assessment of the direct estimates.

2) **Certainty in the indirect evidence:** We assessed the certainty in the indirect evidence based on the lowest of the certainty ratings of the direct comparisons forming the first order loop that contributed the most to an indirect estimate. Then, we assessed intransitivity by assessing the presence of any effect modification in the indirect comparisons. We did this by comparing the main characteristics of the patients, intervention, comparisons, and outcome measurement between the direct comparisons forming the loop of interest. Finally, we assessed imprecision using the confidence interval of the indirect estimate and the same criteria than for the direct evidence. The assessment of imprecision of the indirect estimates did not influence the certainty of the network estimates (Brignardello-Petersen et al. 2018), but it was considered in the assessment of such estimates.

3) **Certainty in the evidence from NMAs:** We assessed the certainty in the network estimate by judging the relative contribution of the direct and indirect evidence to the network estimate. The network estimate rating was based on the source of evidence that contributed to the network estimate the most, which was judged based on a visual comparison of width of the confidence interval of the direct and indirect estimates, and their similarity to the network estimate. Then, we assessed local incoherence by comparing how similar the direct and indirect estimates were using a visual assessment and the p-value obtained using the back-calculation method; as well as a judgment of whether incoherence had an important effect in the network estimates (Brignardello-Petersen et al. 2018). Finally, we assessed imprecision using the confidence interval of the network estimate and the same criteria than for the direct estimates. (Brignardello-Petersen et al. 2018; Puhan et al. 2014).
Discussion

Implications for Practice
Caries management involves not only prevention and management of the disease process at the individual level, but once caries lesions develop, additional site-specific targeted strategies are needed at the lesion and surface level. These lesion-targeted strategies aim to promote tooth remineralization in the area of the carious lesion (e.g., fluorides), isolate the lesion mechanically from the caries-promoting biofilm, arrest it mechanically (e.g., sealants), and/or alter the conditions of the site-specific biofilm responsible for the lesion progression to a state of symbiosis with the tooth (e.g., chlorhexidine varnish). Results of this systematic review support a range of strategies that are effective at arresting and/or reversing noncavitated and cavitated carious lesions.

In the case of noncavitated carious lesions the most effective strategies will not only arrest/reverse the carious lesion, but will also help preserve tooth structure (Schwendicke et al., 2016). Therefore, nonrestorative treatment should be considered preferred method for management of these lesions. In the case of advanced cavitated carious lesions, data from this systematic review supports that 38% SDF is an effective treatment to arrest these lesions, especially when reapplied periodically every 6 months, and should be considered as an effective alternative to restorative care. For some teeth and some patients this may be all that is needed. Yet, as this treatment does not restore the missing tooth structure (which in many cases can affect the function of the tooth), and esthetically the lesion will turn black, some patients may need or desire restorative care using fillings to manage cavitated carious lesions or improve on esthetic concerns. In fact, restorative care is considered the standard of care for management of cavitated carious lesions, as restoring the cavity can not only help control the disease process (i.e., by moving the biofilm to the surface of the tooth where it is easier again for the patient to control), but can help restore tooth function. Therefore, 38% SDF can be used to arrest advanced cavitated carious lesions without the need for restorative care, and these lesions can always be restored at a later time to solve function or aesthetic issues.

Data from this systematic review also highlights the need to closely monitor lesions that are being treated in order to determine if the treatment was effective at arresting and/or reversing the lesions. Lesions might require treatment and follow up over a long period of time before radiographic or clinical methods can determine that arrest or reversal has occurred.
Brignardello-Petersen R, Mustafa, R.A., Siemieniuk, R.A.C, Hassan Murad, M., Agoritsas, T.A., Izcovich, A., Schunemann, H.J., Guyatt, G.H. 2018. Grade approach to rate the certainty from a network meta-analysis: Addressing incoherence. Submitted to Journal of Clinical Epidemiology.

Dias S, Welton NJ, Caldwell DM, Ades AE. 2010. Checking consistency in mixed treatment comparison meta-analysis. Stat Med. 29(7-8):932-944.

Jackson D, White IR, Riley RD. 2012. Quantifying the impact of between-study heterogeneity in multivariate meta-analyses. Stat Med. 31(29):3805-3820.

Schwendicke F, Frencken JE, Bjorndal L, Maltz M, Manton DJ, Ricketts D, Van Landuyt K, Banerjee A, Campus G, Domejean S et al. 2016. Managing carious lesions: Consensus recommendations on carious tissue removal. Adv Dent Res. 28(2):58-67.
APPENDIX FIGURE 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of the screening and study selection process.
## APPENDIX TABLE 1. Included studies

| Study               | Country        | RCT study design | Age: Mean (SD) or Range in Years | Dentition | Caries experience | Surface                                      | Follow-up time/s | N people (at follow-up) |
|---------------------|----------------|------------------|----------------------------------|-----------|-------------------|----------------------------------------------|------------------|-------------------------|
| Pooled Data         |                |                  |                                  |           |                   |                                              |                  |                         |
| Agrawal, 2011       | India          | Parallel         | 9-16                             | Mixed     | Noncavitated lesion | Facial/Lingual, Occlusal, and Any Surface | 12 months        | 257                     |
| Autio-Gold, 2001    | United States  | Parallel         | 3-5                              | Primary   | Noncavitated lesion | Facial/Lingual, Occlusal, and Any Surface | 9 months         | 142                     |
| Baca, 2009          | Spain          | Parallel         | Varnish: 78.24 (6.59)            | Permanent | Cavitated and noncavitated lesions | Root                                      | 12 months        | 46                      |
|                     |                |                  | Placebo: 75.64 (7.11)            |           |                   |                                              |                  |                         |
| Bakhshandeh, 2015   | Greenland      | Split-mouth      | 6.51                             | Primary   | Noncavitated lesion | Occlusal                         | 8-34 months (mean=22 months) | 47                      |
| Baysan, 2001        | United Kingdom | Parallel         | 59 (12.84)                       | Permanent | Cavitated and noncavitated lesions | Root                                      | 3 month, 6 months¹ | 186                     |
| Study | Arm (Brand name, Manufacturer, Country) | Dose/duration/frequency | Prophylaxis for all groups | Outcome reported in study |
|-------|----------------------------------------|-------------------------|---------------------------|--------------------------|
| **Pooled Data** | | | | |
| Agrawal, 2011 | 1.23% APF gel (Fluorovil, Vishal Dentocare Pvt. Ltd.; India) + Oral health education | 2 applications total (baseline and 6 months) | No | Number of active lesions that became inactive |
| | No treatment + Oral health education² | N/A | | |
| Autio-Gold, 2001 | 5% NaF varnish (Duraphat, Colgate, Palmolive) + 0.8 ppm F municipal water supply | 2 applications total (baseline and 4 months later) | Not reported | Number of active lesions that became inactive |
| | No treatment + 0.8 ppm F municipal water supply² | N/A | | |
| Baca, 2009 | 1% chlorhexidine + 1% Thymol varnish (Cervitec, Vivadent, Spain) + 0.07 ppm F municipal water supply | 7 applications total (twice in the week 1, then at 1, 3, 6, 9 and 12 months) | Not reported | Change in texture from soft to leathery or hard |
| | Placebo Varnish + 0.07 ppm F municipal water supply² | | | |
| Bakhshandeh, 2015 | Resin Infiltration (ICON, DMG Chemisch Pharmazeutische, Germany) + 5% NaF varnish (Duraphat, Woelm Pharma GmbH, Germany) | 1 application of resin infiltration (baseline); 3 total applications of varnish | No | Progression |
| | Resin Sealant (Delton, Dentsply DeTrey, Denmark) + 5% NaF varnish (Duraphat, Woelm Pharma GmbH, Germany) | 1 application of sealant (baseline); 3 total applications of varnish | | |
| | 5% NaF varnish (Duraphat, Woelm Pharma GmbH, Germany)² | 3 total applications of varnish | | |
| Baysan, 2001 | 5,000 ppm dentifrice (Prevident 5000, Colgate, Palmolive) | Brushed once a day with soft toothbrush | Not reported | Hardness |
| Study             | Method to diagnose caries                                      | Conflicts of interest   | Source funding                                      | Notes                                                                 |
|-------------------|----------------------------------------------------------------|------------------------|----------------------------------------------------|----------------------------------------------------------------------|
| Pooled Data       |                                                                 |                        |                                                    |                                                                      |
| Agrawal, 2011     | Visual assessment and probe if needed. Lesion activity by criteria given by Nyvad and colleagues | NR                     | NR                                                 |                                                                      |
| Auto-Gold, 2001   | Visual and clinical assessment: Table on page 1249 from Nyvad and colleagues | NR                     | NR                                                 |                                                                      |
| Baca, 2009        | Beighton's methods (color, texture, height, width, distance from gingival margin) - we chose "texture" because this is what is reported in most studies | No conflicts of interest | Research Group CTS-167 (Consejería de Educación de Andalucía, Spain) and projects PI020997 and PI051172 | Bitter taste was reported as an adverse event when the placebo varnish was used. |
| Bakhshandeh, 2015 | Pairwise radiographic assessment                                 | No conflicts of interest | DMG Dental                                         |                                                                      |
| Baysan, 2001      | Probe to measure hardness                                       |                        | Colgate Palmolive                                  |                                                                      |
| Study            | Country     | Design        | Median/IQR: Sealant | Test (13.04) | Median/IQR: Control | Median/IQR: Control |
|------------------|-------------|---------------|---------------------|--------------|---------------------|---------------------|
| Borges, 2010     | Brazil      | Parallel      | 16 (12-19.5)        | Permanent    | 13 (12-15)          | Control (12.53)     |
| da Silveira      | Brazil      | Parallel      | Test (13.04)        | Permanent    | Noncavitated lesion | Occlusal            | 12 months | 70 |
| Ekstrand, 2008   | Denmark     | Parallel      | 81.6 (4.3)          | Permanent    | Cavitated Lesion    | Root                | 8 months | 181 |
| Ekstrand, 2010   | Greenland   | Split-mouth   | 7.2                 | Primary      | Noncavitated lesion | Approximal          | 12 months | 39 |
| Study Year | Country | Study Design | Baseline F Level | Treatment Details | Lesion Type | Baseline | Intervention | Outcome |
|------------|---------|--------------|------------------|-------------------|-------------|----------|-------------|---------|
| 2013       | Denmark | Parallel     | 81.5 (11.6)      | Permanent Cavitated and Noncavitated Lesions | Root | 8 months | 125 |
| 2010       |         |              |                  | No treatment + Oral health education + 1,100-1,500 ppm F toothpaste | No | 1 application total (baseline) | No | Change in radiolucent area |
| 2010       |         |              |                  | Glass ionomer cement sealant (Vidrion R, SS White, Brazil) + Oral hygiene instructions + 1,100-1,500 ppm F toothpaste + Prophylaxis with pumice and water (co-intervention) + Municipal water supply | No | 1 application total (baseline) | No | Change in radiolucent area; Clinical alterations |
| 2008       |         |              |                  | 5,000 ppm dentifrice (Duraphat 5,000, Colgate Palmolive, UK) + 0.5 ppm F municipal water supply | No | Brushed twice a day with pea size amount | Sound and arrested |
| 2008       |         |              |                  | 5% NaF varnish (Duraphat Fluoride Varnish, Woelm Pharma GmbH, Germany) + 1,450 ppm dentifrice (Colgate Ultra Cavity Protection, Colgate Palmolive, UK) + 0.5 ppm F municipal water supply | No | Dental hygienist brushed elder's teeth once a month for 8 months. In between visits, participants brushed their own teeth; it is unclear how often the varnish was applied for 120 seconds | Sound and arrested |
| 2010       |         |              |                  | 5% NaF varnish (Duraphat, Woelm Pharma GmbH, Germany) + Oral hygiene instructions | No | 3 total applications (baseline, 6 months and 12 months) | No progression |
| Study          | Methodology                                                                 | Conflicts of interest | Notes                                                                 |
|---------------|-----------------------------------------------------------------------------|-----------------------|----------------------------------------------------------------------|
| Ekstrand, 2013| 5,000 ppm dentifrice (Duraphat 5,000, Colgate Palmolive, UK)                |                       | Brushed twice a day for 8 months                                      |
|               | 1.450 ppm dentifrice (Colgate Ultra Cavity Protection, Colgate Palmolive)   |                       | No                                                                    |
|               |                                                                            |                       | Arrest                                                               |
| Borges, 2010  | Exam of radiographs performed in a dark space with x2 magnifying glass      | No conflicts of interest | In the resin-sealant arm, 88.5% (23/26) of teeth experienced full retention, 7.7% (2/26) experienced partial retention, and 3.85% (1/26) experienced total loss of sealant at a 12-month follow up. |
| da Silveira   | Radiographs and assessment with a 2x magnifying glass in a dark room²; Visually assessing the presence of visible cavitation | NR                    | NR                                                                   |
|               |                                                                            |                       | Throughout the 12 month study period, 40.74% (11/26) of teeth in the GIC sealant arm resulted in total retention of the sealant, 40.74% (11/26) resulted in one sealant replacement, and 18.52% (5/27) resulted in two sealant replacements. |
| Ekstran, 2008 | Visual assessment and probing                                                | Financial support from Colgate Palmolive | Colgate Palmolive                                                   |
| Ekstran, 2010 | Radiograph², Visual assessment using ICDAS                                  | Financial support from DMG Dental | DMG Dental                                                          |
| Study            | Country  | Design     | Cavity Type | Lesion Location | Follow-up | N  |
|------------------|----------|------------|-------------|-----------------|-----------|----|
| Ekstrand, 2013   |          | Visual assessment and probing | One author of this study is a Colgate Palmolive employee |                |           |    |
| Florio, 2001     | Brazil   | Parallel   | Permanent   | Noncavitated lesion | Occlusal  | 12 months | 34 |
| Gomez, 2005      | Chile    | Split-mouth | Mixed       | Noncavitated lesion | Approximal | 24 months | 7  |
| Honkala, 2015    | Kuwait   | Split-mouth | Primary     | Noncavitated lesion | Occlusal  | 12 months | 106|
| Li, 2016         | China    | Parallel   | Permanent   | Cavitated and noncavitated lesions | Root | 12 month¹, 24 months, 30 months | 75 |
| Study | Country | Design | Intervention: | Control: | Permanent | Noncavitated lesion | Root | Time | Total |
|-------|---------|--------|---------------|----------|-----------|---------------------|------|------|-------|
| Lynch, 2000 | United Kingdom | Parallel | 59 (13) | 60 (13) | Yes | Yes | Yes | 3 months | 193 |
| Florio, 2001 |  |  | Resin modified glass ionomer sealant (Vitremer, 3M, Brazil) | 1 application total (baseline); not reapplied if material was loss | Yes | Yes | Progression and no progression |
|  |  |  | 0.2% NaF mouthrinse | Weekly |  |
|  |  |  | 5% NaF (2.26% F) varnish (Duraphat, Inpharma, Germany) + 1,500 ppm toothpaste (co-intervention) + oral health instructions (co-intervention)^2 | 3 applications total (baseline and every 6 months) | Yes |
| Gomez, 2005 |  |  | Resin sealant (Concise Sealant, 3M ESPE) + 0.6 ppm F municipal water supply | 1 application total (baseline) | No | No progression |
|  |  |  | 5% NaF varnish (Duraphat, Colgate Oral Pharmaceuticals, USA) + 0.6 ppm F municipal water supply^2 | 5 total applications (baseline and once every 6 months) |  |
| Honkala, 2015 |  |  | Resin sealant (Clinpro, 3M ESPE) + Tooth brushing instructions + Municipal water supply | Resin sealant: 1 application total (baseline) | No | Progression and no progression |
|  |  |  | 5% NaF varnish (DuraShield, Sultan Healthcare) + Municipal water supply^2 | Tooth brushing instructions: 6 months before and after application of resin sealant |  |
| Li, 2016 |  |  | 38% SDF solution (Saforide, Toyo Seyaku Kasei Co, Ltd., Japan) + Oral hygiene instructions + 1,450 ppm F toothpaste + Municipal water supply | 3 applications total (baseline and once every 12 months) | Not reported | Arrest |
| Study, Year | Solution/Instructions | Oral Hygiene | Retention | Findings |
|------------|-----------------------|--------------|-----------|----------|
| Lynch, 2000 | 38% SDF solution (Saforide, Toyo Seyaku Kasei Co, Ltd., Japan) + 2.36 mol/l potassium iodide (KI) (SIGMA-ALDRICH Co., USA) + Oral hygiene instructions + 1,450 ppm F toothpaste + Municipal water supply | Brushed once a day for one minute | Not reported | Hardness |
| Lynch, 2000 | Soda water with bitter taste + Oral hygiene instructions + 1,450 ppm F toothpaste + Municipal water supply | | | |
| Florio, 2001 | 1.1% NaF dentifrice (Prevident 5000 Plus, Colgate) | Radiographs using 5x magnification | NR | The use of a resin-modified glass ionomer sealant resulted in a 65.5% (23/35) retention rate at 12 month follow up. |
| Gomez, 2005 | 1,100 ppm dentifrice (Winterfresh Gel, Colgate) | Radiographs with 2x magnifying viewer | NR | |
| Honkala, 2015 | ICDAS | No conflicts of interest | Kuwait University (grant No. DD03/10) | Of the 345 resin-sealed occlusal surfaces 73% (252/345) were fully retained after one year follow up, where as 15.1% (52/345) experienced partial retention. |
| Study, Date        | Country          | Design  | Probe Type         | Country & Split-mouth Lesion | Tooth Site | Duration     | Mean Age |
|-------------------|------------------|---------|--------------------|-------------------------------|------------|--------------|----------|
| Li, 2016          | ICDAS            | No conflicts of interest | Research Grants Council of Hong Kong |
| Lynch, 2000       | Standard periodontal probe | NR | NR |
| Martignon, 2006   | Denmark and Colombia | Split-mouth | Colombia: median (range): 20 (15-32); Denmark: median (range): 27 (21-39) | Permanent | Noncavitated lesion | Approximal | 18 months | 72 |
| Martignon, 2010   | Colombia          | Split-mouth | 5.3 (.7) | Primary | Noncavitated lesion | Approximal | 30 months | 56 |
| Martignon, 2012   | Colombia          | Split-mouth | 21 (16-31) | Permanent | Noncavitated lesion | Approximal | 12 months¹, 24 months, 36 months | 38 |
| Meyer-Lueckel, 2012 (Paris 2010) | Germany | Split-mouth | Not reported | Permanent | Noncavitated lesion | Approximal | 36 months | 20 |
| Author                  | Country     | Design   | Treatment                                                                 | Follow-up Duration | Progression Status                                                                 |
|------------------------|-------------|----------|----------------------------------------------------------------------------|--------------------|-----------------------------------------------------------------------------------|
| Schaeken, 1991         | Netherlands | Parallel | Permanent, Noncavitated lesion, Root                                          | 12 months          | 28                                                                                |
| Sitthisettapong, 2012  | Thailand    | Parallel | Experimental: 36.9 months (2.9 months)                                      | 6 months, 12 months | 229                                                                               |
| Martignon, 2006        |             |          | Resin sealant (Gluma One Bond Adhesive, Heraeus Kulzer; 10 Danes were sealed with Concise, 3M ESPE) + Flossing instructions + 1,000-1,500 ppm F toothpaste | 1 application total (baseline) | Yes, Progression status (radiographic no change, regression, and progression) |
|                        |             |          | Control + Flossing instructions + 1,000-1,500 ppm F toothpaste¹              |                    | Not reported                                                                      |
| Martignon, 2010        |             |          | Resin sealant (Single One Bond, 3M ESPE) + Flossing advice                  | 1 application total (baseline) | Yes, Stabilization and progression                                                  |
|                        |             |          | Control + Flossing advice²                                                   |                    | Not reported                                                                      |
| Martignon, 2012        |             |          | Icon pre-product infiltration (ICON, DMG, Germany) + Flossing instructions   | 1 application total (baseline) | Not reported                                                                      |
|                        |             |          | Prime Bond NT Sealant (Dentsply, USA) + Flossing instructions               |                    | Stabilization                                                                    |
|                        |             |          | Placebo + Flossing instructions²                                            |                    |                                                                                  |
| Meyer-Lueckel, 2012    |             |          | Resin infiltration (ICON, DMG)                                              | 1 application total (baseline) | Not reported                                                                      |
| (Paris 2010)           |             |          |                                                                                  |                    | Progression of lesion depth by digital subtraction radiography (DSR)².             |
| Study                         | Treatment                                                                 | Progression of lesion depth | Study details                                                                 |
|-------------------------------|---------------------------------------------------------------------------|------------------------------|------------------------------------------------------------------------------|
| Schaeken, 1991                | 5% NaF varnish (Duraphat, Woelm, Germany) + Professional tooth cleaning and maintenance program | 4 applications total (baseline and once every three months) | Not reported | Hardness |
|                               | Control + Professional tooth cleaning and maintenance program²              |                              |                                                                              | Not reported | Hardness |
| Sithisettapong, 2012          | 10% CPP-ACP w/v paste (Tooth Mousse, GC Corporation, Japan) + Oral hygiene instructions + 1,000 ppm F toothpaste + 0.1 ppm municipal water supply | 0.4g every school day for one year | No | Regression and stabilization and progression |
|                               | Placebo + Oral hygiene instructions + 1,000 ppm F toothpaste + 0.1 ppm municipal water supply² |                              |                                                                              |              |          |
| Martignon, 2006               | Digital subtraction radiography using Compare Software by an external trained examiner²; Pair-wise visual assessment; Individual visual assessment | NR                          | Colluturo and the Universidad El Bosque                                      |              |          |
| Martignon, 2010               | Radiographs (over a light box using a Matton’s magnifying glass) scoring system from Martignon 2006 | No conflicts of interest     | NR                                                                          |              |          |
| Martignon, 2012               | Digital subtraction radiography of scanned images²; Visual score taken magnifying glass (pairwise reading of conventional radiographs) | Financial support from DMG Dental | DMG Dental                                                                  |              |          |
| Meyer-Lueckel, 2012 (Paris 2010) | DSR (digital subtraction radiography)²; lesion depth by pairwise reading of radiographs | NR                          | DMG Dental                                                                  |              |          |
| Study                        | Country | Design | Mean (SD) | tooth Type | lesion location | Time Points | Sample Size |
|------------------------------|---------|--------|-----------|-------------|----------------|-------------|-------------|
| Schaeken, 1991               | NR      | NR     | NR        | NR          | NR             | NR          | NR          |
| Sitthisettapong, 2012        | ICDAS   | No conflicts of interest | Fogarty International NIH grant #D43TW007768 |
| Altenburger, 2010            | Germany | Parallel | 25.5 (1.9) | Permanent | Noncavitated lesion | Occlusal | 3 weeks | 32 |
| Bailey, 2009                 | Australia | Parallel | 15.5 (12.3 - 18.9) | Mixed | WSL | Facial/Lingual and Any Surface | 4 weeks, 8 weeks, 12 weeks | 45 |
| Bonow, 2013                  | Brazil  | Parallel | 7-12      | Mixed | Noncavitated lesion | Facial/Lingual | 8 weeks | 59 |
| Study                | Country | Sample Type | Test | Permanent Lesions | Control Lesions | Root | Duration | Outcome |
|----------------------|---------|-------------|------|-------------------|-----------------|------|----------|---------|
| Brailsford, 2002     | England | Parallel    | Test: 85.6 (1.3) | Cavitated and noncavitated lesions | Control: 79.8 (1.4) | Root | 12 months | 78      |
| Un-pooled Data | Treatment | Comparator | Result | Outcome |
|----------------|-----------|------------|--------|---------|
| Altenburger, 2010 | 10% CPP-ACP cream (GC Tooth Mousse, GC Europe N.V., Belgium) + 1450 ppm F toothpaste | No treatment + 1450 ppm F toothpaste | N/A | Decrease in Ekstrand score (change in color and translucency) |
| Bailey, 2009 | 10% CPP-ACP w/v cream (Tooth Mousse, GC Corporation, Japan) + 900 ppm F mouthrinse + 1,000 ppm F toothpaste | Placebo + 900 ppm F mouthrinse + 1,000 ppm F toothpaste | 2 g morning and night for 12 weeks | Yes | Regression |
| Bonow, 2013 | 1.23% APF gel (DFL, Sultan Topex, Brazil) + Oral health education + NaF toothpaste + Professional tooth brushing at each appointment | Placebo + Oral health education + NaF toothpaste + Professional tooth brushing at each appointment | 9 applications total (baseline and once a week) | Not reported | Inactive Lesions |
| Brailsford, 2002 | 1% Difluorsilane varnish (Fluor-protector, Ivoclar-Vivadent) + 1% chlorhexidine, 1% thymol in ethanol/ethylacetate (88% w/w), and polyvinylbutyrol (10% w/w) varnish (Cervitec, Ivoclar-Vivadent) | 1% Difluorsilane varnish (Fluor-protector, Ivoclar-Vivadent) + Placebo gel | 5 applications total (baseline and week 6, 13, 26 and 39) | No | Improvement in texture |
| Unpooled Data | Visual assessment | No conflicts of interest | None | The use of 10% CPP-ACP daily for three weeks resulted in a 400% increase in caries arrestment (RR: 5.00, 95% CI: 0.25, 98.97) compared to 1450 ppm toothpaste daily at 3 weeks follow-up.

| Bailey, 2009 | ICDAS | NR | CRC for Oral Health Science and GC Corporation, Japan | One or more adverse events were reported for 86% of participants (n=39), no information on the arm or the nature of them. There was also one or more reported GI symptoms in the CPP-ACP cream arm.

| Bonow, 2013 | A visual-tactile examination was performed. A probe was used to gently check for surface texture and loss of tooth structure | No conflicts of interest | Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) | Patients receiving 1.23% APF gel have a 65% increased probability for arresting/reversing in the buccal/lingual surfaces compared to the placebo arm after 8 weeks of follow-up (Adjusted RR: 1.65 (95% CI: 0.69-3.96)).

| Brailsford, 2002 | Lesion width and height | NR | The South Thames regional Health Authority and varnished provided by Ivoclar-Vivadent | The use of 1% difluorsilane varnish + (1% chlorhexidine and 1% thymol) 5 times in 10 months resulted in a 40% increase in caries arrestment (RR: 1.40, 95% CI: .97, 2.00) compared to 1% difluorsilane applied at the same frequency at one year follow-up. |
| Study                          | Location | Design | Time (Years) | Tumor Type | Site | Survival Times | Number |
|-------------------------------|----------|--------|--------------|------------|------|----------------|--------|
| Duangthip, 2018b (Duangthip, 2016) | Hong Kong | Parallel | 41 months (4) | Primary | Cavitated lesion | Any Surface | 12 months, 18 months, 24 months, 30 months² | 309 |
| Duarte, 2008                  | Brazil   | Parallel | Experimental: 13.01 | Not reported | Noncavitated lesion | Any Surface | 28 Days | 170 |
| Fung, 2018 (Fung, 2016, Duangthip 2018a) | Hong Kong | Parallel | 3-4 years | Primary | Cavitated Lesion | Any Surface | 30 months | 799 |
| Hedayati-Hajikand, 2015       | Sweden   | Parallel | Experimental: 2.4 | Primary | Cavitated and noncavitated lesions | Any Surface | 12 months | 110 |
| Heidmann, 1992                | Denmark  | Parallel | 6 - 12 | Permanent | Noncavitated lesion | Any Surface | 36 months | 1,083 |
| Study                          | Intervention                                                                 | Frequency          | Outcome | Notes                                                                 |
|-------------------------------|------------------------------------------------------------------------------|--------------------|---------|----------------------------------------------------------------------|
| Duangthip, 2018b (Duangthip, 2016) | 30% SDF solution (Cariestop, Biodinamica, Brazil)                           | Once a year        | Arrest rate | Not reported                                                             |
|                               | 5% NaF varnish (Duraphat, Colgate Palmolive, USA)                            | 3 applications total (baseline, week 1, and week 2) |          |                                                                      |
| Duarte, 2008                  | 0.12% chlorhexidine digluconate + 0.05% NaF mouthrinse                       | 1 minute per day   | Reduction in active lesions | Not reported                                                             |
|                               | 0.05% NaF Rinse                                                             |                    |          |                                                                      |
| Fung, 2018 (Fung, 2016, Duangthip 2018a) | 12% SDF solution + F toothpaste + 0.5 ppm municipal water supply          | Once every 12 months | Arrest   | Not reported                                                             |
|                               | 38% SDF solution + F toothpaste + 0.5 ppm municipal water supply            | Once every 6 months |          |                                                                      |
| Hedayati-Hajikand, 2015       | 1x10 CFU ProBiora blend of three strains of probiotic bacteria (S. uberis KJ2TM, S. oralis KJ3TM, S. rattus JH145TM) wild cherry flavor sweetened with erythritol (EvoraKids, Oragenics Inc., USA) + Toothbrushing instructions + 1,100 ppm F toothpaste | | Caries increment (Δds) | No                                                                     |
|                               | Placebo chewing tablet (EvoraKids, Oragenics Inc., USA)                     |                    |          |                                                                      |
| Heidmann, 1992                | 0.2% NaF mouthrinse                                                         | Not reported       | Caries Development and progression | No                                                                     |
|                               | Water                                                                        |                    |          |                                                                      |
Black staining was reported as an adverse event. Duangthip 2016 only reports advanced lesions (ICDAS 5 and 6) while Duangthip 2018b reports moderate (ICDAS 3 and 4) and advanced (ICDAS 5 and 6) lesions.

| Study            | Methodology       | Lesion severity | Source of Funding | Adverse Events |
|------------------|------------------|-----------------|-------------------|----------------|
| Duangthip, 2018b (Duangthip, 2016) | ICDAS            | No conflicts of interest | University of Hong Kong | Black staining was reported as an adverse event. Duangthip 2016 only reports advanced lesions (ICDAS 5 and 6) while Duangthip 2018b reports moderate (ICDAS 3 and 4) and advanced (ICDAS 5 and 6) lesions. |
| Duarte, 2008     | Diagnosis was made according to the following criteria (Table 1) for non-cavitated caries previously described by Nyvad et al (1999) and Pinelli et al (2002). | NR               | FUNPESQUISTA (337/2002), Federal University of Santa Catarina, Brazil. Toothbrushes used in the study were provided by Condor (Brazil). | 85.4% of non-cavitated lesions were arrested in the 0.05% NaF mouthrinse arm compared to 85.6% of arrested lesions in the 0.05% NaF mouthrinse + 0.12% chlorhexidine arm after 28 days. |
| Fung, 2018 (Fung, 2016, Duangthip, 2018a) | Visual/tactile | No conflicts of interest | Research Grants Council of Hong Kong | Lesions treated with 38% SDF had a statistically significantly increased chance of becoming black compared to those receiving 12% SDF. Lesions treated semiannually also had a higher chance of becoming black compared to those treated annually. There was no significant difference in tooth pain, gum pain, gum swelling, or gum bleeding between the four groups; these adverse events affected a very small proportion of kids in each group. |
| Hedayati-Hajikand, 2015 | Visual assessment | No conflicts of interest | County Council, Region Skåne, Sweden. The study tablets were provided free of charge from Oragenics, FL, USA. | Out of 54 people in the probiotic tablet arm, 11% (n=5) of the enrolled patients experienced caries arrest compared to 7% (n=4) of the 56 participants in the arm that received placebo tablets after one year. |
| Heidmann, 1992   | Clinical and Radiographic assessment | NR               | Danish Dental Association | In the 0.2% NaF mouthrinse arm, 62.5% (n=270), experienced no progression of non-cavitated lesion compared to 68.5% (n=292) in the placebo mouthrinse arm. |
| Study                        | Country     | Design    | Erythritol       | Xylitol       | Treatment                        | Lesions Type | Duration | Sample Size |
|------------------------------|-------------|-----------|------------------|---------------|----------------------------------|--------------|----------|-------------|
| Honkala, 2014                | Estonia     | Parallel  | 8.6 (0.5)        | 8.2 (0.5)     | Mixed                            | Cavitated and noncavitated lesions | Any Surface | 12 months, 24 months, 36 months | 374 |
|                              |             |           |                  |               | Control: 8.1 (0.6)                |              |          |             |
| Llodra, 2005                 | Cuba        | Parallel  | 6.29 (.48)       | Mixed         | Cavitated lesions                 | Any Surface  | 36 months | 373         |
| Meyer-Lueckel, 2016          | Germany     | Split-mouth | 23 (6)          | Mixed         | Noncavitated lesion               | Approximal   | 18 months | 70          |
| Study               | Intervention Details                                                                 | Frequency | Outcomes                        | Study Details                                                                 |
|---------------------|--------------------------------------------------------------------------------------|-----------|---------------------------------|------------------------------------------------------------------------------|
| Honkala, 2014       | 0.7 g Erythritol candies (Cargill R&D Center, Europe) + Dental health education + F toothpaste | 3 candies four times per day | Not reported | Caries Development and progression |
|                     | 0.7g Xylitol candies (Cargill R&D Center, Europe) + Dental health education + F toothpaste |           |                                  |                                                                               |
|                     | 0.7g Sorbitol candies (Cargill R&D Center, Europe) + Dental health education + F toothpaste |           |                                  |                                                                               |
| Llodra, 2005        | 38% SDF (Fluoroplast, Laboratorios NaF, Argentina) + 0.2% NaF mouthrinse + Toothbrushing instructions + Dietary recommendations + 0.9 ppm municipal water supply |           | SDF: 7 total applications (baseline and once every 6 months) | Surfaces with inactive caries |
|                     | Control + 0.2% NaF mouthrinse + Toothbrushing instructions + Dietary recommendations + 0.9 ppm municipal water supply |           | Control: Not reported |                                                                               |
| Meyer-Lueckel, 2016 | Resin infiltration (ICON, DMG) + NaF varnish (co-intervention) + Oral hygiene instructions and dietary advice |           | Resin infiltration/Placebo: 1 application total (baseline) | Progression |
|                     | Placebo (Mock Treatment) + NaF varnish (co-intervention) + Oral hygiene instructions and dietary advice |           | Fluoride varnish: applied decided by the respective dentist on the basis of a 6 month recall |                                                                               |
| Honkala, 2014 | ICDAS | No conflicts of interest | Cargill R&D Center Europe (Vilvoorde, Belgium) | There was no distinction between cavitated and noncavitated lesions in the study. In the erythritol arm, 30.5% (401/1,313) of surfaces experienced a decrease in ICDAS score compared to 29.8% (456/1,531) in the arm receiving sorbitol and 28.3% (449/1,584) in the arm receiving xylitol after three years follow-up. |
| Llodra, 2005 | Visual method by explorer and flat mirror | No conflicts of interest | Local government of the Balaeric Islands | After 36 months of follow-up, on average, the 38% SDF group had 0.3 surfaces with arrested caries whereas the control group had 0.1 (P < 0.05). The children in the SDF group had a higher percentage of black stains (97%), compared with the control group, in which only 48% of the inactive lesions were black (p < 0.001). Compared with the controls, the SDF-treated children had a higher proportion of black stains in inactive lesions (p < 0.001). |
| Meyer-Lueckel, 2016 | Pairwise comparisons radiographs (stage of baseline was scored and then the score at follow-up was obtained) | No conflicts of interest | DMG Dental | Additional fluoride varnish was applied at the discretion of respective dentist during the six-month recall. Therefore, this study was removed from the network because we could not account for background fluoride varnish. However, in the resin infiltration arm, 94.6% (176/186) participants experienced no progression, compared to 68.8% (128/186) participants in the mock treatment arm (RR: 1.38, C.I. 1.24, 1.52). |
| Moberg Skold, 2005 (a) | Sweden | Parallel | 13 | Permanent | Cavitated and noncavitated lesions | Approximal | 36 months | 622 |
|------------------------|--------|----------|----|-----------|----------------------------------|-----------|-----------|-----|
| Moberg Skold, 2005 (b) | Sweden | Parallel | 13 | Permanent | Noncavitated lesion | Approximal | 36 months | 758 |
| Study | Intervention Details | Number of Applications | Frequency | Yes, according to caries risk | Caries Incidence and Progression | Study Year |
|-------|----------------------|------------------------|-----------|--------------------------------|--------------------------------|------------|
| Moberg Skold, 2005 (a) | 0.2% NaF mouthrinse (Meda AB, Sweden) + NaF varnish (co-intervention) + F toothpaste (co-intervention) + 0.1 ppm municipal water supply | 18 applications total (rinsed the first three school day of every semester) | 18 | 60 | 60 | Moberg Skold, 2005 (a) |
| | | | | | | |
| | | 36 applications total (rinsed the first and last three school days of every semester) | 36 | 60 | 60 | Moberg Skold, 2005 (a) |
| | | | | | | |
| | | 81 applications total (rinsed three consecutive days, once a month during the semester) | 81 | 60 | 60 | Moberg Skold, 2005 (a) |
| | | | | | | |
| | | Control + 0.1 ppm municipal water supply | N/A | N/A | N/A | N/A |
| Moberg Skold, 2005 (b) | 5% NaF varnish (Duraphat, Colgate, USA) + 0.1 - 0.2 ppm municipal water supply | 7 applications total (0.3 mL at baseline and once every 6 months; children also received additional NaF varnish applications at their regular dental checkups) | 7 | 60 | 60 | Moberg Skold, 2005 (b) |
| | | 9 applications total (three applications of 0.3 mL within one week, every 12 months; children also received additional NaF varnish applications at their regular dental checkups) | 9 | 60 | 60 | Moberg Skold, 2005 (b) |
| | | 24 applications total (0.3 mL at baseline and once a month for 8 months; children also received additional NaF varnish applications at their regular dental checkups) | 24 | 60 | 60 | Moberg Skold, 2005 (b) |
| | No treatment + 0.1 - 0.2 ppm F municipal water supply | Not reported; children also received additional NaF varnish applications at their regular dental checkups | Not reported | Not reported | Not reported | Not reported |
Bitewing radiographs were scored and analyzed according to Gröndahl et al. [1977] by one authorizing a light desk and a magnifying viewer

In patients receiving 0.2% NaF mouthrinse 12 times a year, 59% of caries that could have progressed were prevented compared to patients receiving six mouthrinses per year (PF=30%), 27 mouthrinses per year (PF=47%), and 20 mouthrinses per year (PF=41%).

The use of 5% NaF fluoride varnish twice a year at six month intervals resulted in a 17% increase in the chance of experiencing caries arrestment (RR: 1.17, 95% CI: 1.07, 1.27).

The use of 5% NaF fluoride varnish three times a year all in one week resulted in a 13% increase in the chance of experiencing caries arrestment (RR: 1.13, 95% CI: 1.03, 1.24).

Whereas the use of 5% NaF fluoride varnish eight times a year with one month intervals resulted in a 15% increase in the chance of experiencing caries arrestment (RR: 1.15, 95% CI: 1.06, 1.26) compared to no additional fluoride varnish. All study arms received 5% NaF varnish regularly as part of a school program.
| Study        | Country   | Study Design | N | Type      | Location | Follow-up | Case Number |
|-------------|-----------|--------------|---|-----------|----------|-----------|-------------|
| Modeer, 1984 | Sweden    | Parallel     | 14 | Permanent | Noncavitated lesion | Approximal | 36 months | 194         |
| Petersson, 1991 | Sweden   | Parallel     | 11 | Mixed     | Noncavitated lesion | Approximal | 36 months | 146         |
| Peyron, 1992  | Sweden    | Parallel     | 3 - 6 | Primary | Noncavitated lesion | Approximal | 12 months¹, 24 months | 468         |
| Study | Treatment Details | Control Details | Outcome |
|-------|-------------------|-----------------|---------|
| Modeer, 1984 | 5% NaF varnish (Duraphat, Woelm ICN Pharmaceutical, West Germany) + 0.2% NaF mouthrinse + 0.24 ppm municipal water supply | No treatment + 0.2% NaF mouthrinse + + 0.24 ppm municipal water supply | No |
| Petersson, 1991 | Fluoride varnish (Duraphat) + Oral health education + 0.1 ppm municipal water supply | Fluoride varnish (Duraphat) + Oral health education + 0.1 ppm municipal water supply | Not reported |
| Peyron, 1992 | Fluoride varnish (Duraphat, Woelm ICN Pharmaceutical, Germany) + Pumice (co-intervention) + 0.2 ppm municipal water supply | Control + 0.2 ppm municipal water supply | No |

Outcome categories: Progression, regression, and stabilization, Incidence and progression of proximal caries, Caries Progression, N/A
| Author         | Methodology                                | NR  | NR  | Description                                                                                                                                 |
|---------------|--------------------------------------------|-----|-----|---------------------------------------------------------------------------------------------------------------------------------------------|
| Modeer, 1984  | Radiograph examination and read with the aid of a magnifying viewer | NR  | NR  | The use of 5% NaF varnish (every third month for three years) and 0.2% NaF mouthrinse (every 14 days) resulted in a 4% decrease in caries arrestment (RR: .96, 95% CI: 0.51, 1.80) compared to 0.2% NaF mouthrinse (every 14 days) at 3 years follow-up. |
| Petersson, 1991 | Radiograph examination                     | NR  | NR  | Patients receiving 5% NaF varnish (Duraphat) three times a week, once a year for three years reported 116 surfaces arrested and reversed compared to 78 surfaces arrested and reversed in those receiving 5% NaF varnish (Duraphat) every six months for three years (no total number of surfaces per arm reported). |
| Peyron, 1992  | Radiograph examination                     | NR  | Patentmedelsfonden for Odontologisk Profylaxforskningsubventionen | After one year follow-up, out of 41 people in the 5% NaF varnish arm, 48.8% (n=20) of the enrolled patients with one or more superficial enamel caries lesions experienced no progression of caries lesions compared to 17.2% (n=5) of the 29 people with that did not receive 5% NaF varnish. After two years of follow-up, out of 42 people with one or more superficial enamel caries lesions receiving 5% NaF varnish, 33.3% (n=14) did not experience progression of caries lesions compared to 8.8% (n=3) of the 34 who did not receive 5% NaF varnish. |
| Study                      | Country       | Design       | Age/Duration       | Tooth Type | Lesion Type          | Site       | Follow-up Period | Sample Size |
|----------------------------|---------------|--------------|--------------------|------------|----------------------|------------|------------------|-------------|
| Trairatvorakul, 2011       | Thailand      | Split-mouth  | 13.15 (3.47)       | Permanent  | Noncavitated lesion  | Approximal | 12 months        | 26          |
| Turska-Szybka, 2016        | Poland        | Parallel     | Experimental: 3.9 (1.2) | Primary    | WSL                  | Facial/Lingual | 12 months        | 81          |
|                           |               |              | Control: 3.6 (1.4)  |            |                      |            |                  |             |
| Wallace, 1993              | United States | Parallel     | 60+ years          | Permanent  | Unclear              | Root       | 12 months, 24 months, 36 months, 48 months\(^1\) | 466         |
| Wyatt, 2014                | Canada        | Parallel     | 83 year (SD=9.54, range 54-101 years) | Permanent  | Unclear              | Root       | 24 months        | 116         |
| Study          | Intervention                                                                 | Outcome       | Control                                                                 | Outcome       |
|---------------|-----------------------------------------------------------------------------|---------------|-------------------------------------------------------------------------|---------------|
| Trairavarakul, 2011 | Glass ionomer cement sealant (Fuji VII, GC Corporation, Japan) + 1.23% APF gel + 1,000 ppm F toothpaste + <0.3 ppm municipal water supply | No            | Control + 1.23% APF gel + 1,000 ppm F toothpaste + <0.3 ppm municipal water supply² | Radiographic progression |
|                | Glass ionomer cement sealant: 1 application total (baseline)                |               | 1.23% APF gel: 2 total applications (baseline and 6 months)             |               |
|                | 1,000 ppm F toothpaste: two times daily                                     |               | 1,000 ppm F toothpaste: two times daily                                 |               |
| Turska-Szybka, 2016 | Triethylene-glycol- dimethacrylate–based resin infiltration (ICON, DMG, Germany) + 5% NaF varnish (Duraphat, Colgate Palmolive, Germany) + Oral hygiene education | No            | 5% NaF varnish (Duraphat, Colgate Palmolive, Germany) + Oral hygiene education² | WSL Arrest    |
|                | 5 applications total (baseline and once every 3 months)                     |               | 5 applications total (baseline and once every 3 months)                 |               |
| Wallace, 1993  | 1.2% APF gel (Luride, Colgate-Hoyt Laboratories, USA) + F toothpaste        | Not reported  | Control + F toothpaste²                                                 | Reversed      |
|                | 9 applications total (baseline and once every 6 months)                    |               | Once a day for the duration of the study                                |               |
| Wyatt, 2014    | 0.12% Chlorhexidine gluconate mouthrinse (Chlorhexidine gluconate 20% BP, Medisca Pharmaceutique, Canada) | Not reported  | 0.2% NaF mouthrinse (Fluorinse, Oral-B Laboratories, Canada)             | Reversal      |
|                | 0.2% NaF mouthrinse                                                         |               | Placebo mouthrinse (4% isopropyl alcohol, 0.04% peppermint essence, distilled water)² |               |
|                | Once a day for the duration of the study                                    |               |                                                                         |               |
| Study | Method | Scoring System | Fund/Company | Findings |
|-------|--------|----------------|--------------|----------|
| Trairatvorakul, 2011 | Radiographic (radiographic scoring system) by pairwise method | NR | Postgraduate Research Fund, Faculty of Dentistry, Chulalongkorn University | The use of sealants and 1.23% APF gel (at baseline and 6 months recall) resulted in a 1.950% increase in caries arrestment (RR: 20.05, 95% CI: 5.31, 79.21) compared to 1.23% APF gel (at baseline and 6 months recall) after one year of follow-up. |
| Turska-Szybka, 2016 | ICDAS | NR | NR | Of the 41 children treated with ICON RI + 2.26% (5% NaF) Duraphat fluoride varnish, 75.6% (n=31) showed no progression/continued activity of the treated spots at any examination. Of the 40 children treated with 2.26% (5% NaF) Duraphat fluoride varnish, 32.5% (n=13) of white spot lesions showed no progression/continued activity (total number of lesions not reported). |
| Wallace, 1993 | Visual tactile exam | NR | NIDR grant #ROI DE07030. Moutrinises supplied by Johnson and Johnson Dental Care Company, New Brunswick, NJ. | On average, patients receiving 1.23% APF gel had 0.10 less lesions arrested compared to those that did not receive treatment, however these results were not statistically significant (MD: -0.10; 95% CI: -0.50, 0.30). Those receiving 1.2% APF gel had on average 0.52 less lesions arrested compared to those receiving 0.05% NaF mouthrinse (MD: -0.52; 95% CI: -0.96, -0.08). |
| Wyatt, 2014 | Dental explorer used with light pressure to identify active caries lesions | NR | British Columbia Health Research Foundation Institutional Program Grant no. 212 (97-2) | On average, patients receiving 0.12% chlorhexidine mouthrinse had on 0.07 less lesions arrested compared to those that received 0.2% NaF mouthrinse, however these results were not statistically significant (MD: -0.07; 95% CI: -0.72, 0.58). Those receiving 0.12% chlorhexidine mouthrinse had on average 1.05 more lesions arrested compared to those receiving no treatment mouthrinse (MD: 1.05; 95% CI: 0.30, 1.80). |
| Study       | Country  | Study Design | Follow-up | Type of Lesion            | Surface Location | Follow-up Time | Participants |
|------------|----------|--------------|-----------|---------------------------|------------------|----------------|--------------|
| Yee, 2009  | Nepal    | Parallel     | 6 months, 12 months, 24 months | Primary Cavitated Lesion | Any Surface      | 5.2 (1.2)      | 634          |
| Zhang, 2013 | China    | Parallel     | 6 months, 12 months, 24 months, 36 months, 48 months | Permanent Cavitated and noncavitated lesions | Root             | 72.5 (5.7)     | 365          |

**Footnotes:**

1. Follow up time analyzed.
2. Positive or negative control arm (comparator).
3. Assessment method analyzed.
|                  | Intervention                                                                 | Intervention Details                                                                 | End Point Reported | Analysis |
|------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|--------------------|----------|
| **Yee, 2009**    | 38% SDF (Bee Brand Medical Dental Company, Japan) + 0.03 ppm municipal water supply | 1 application total (baseline)                                                         | Not reported       | Arrest   |
|                  | 38% SDF (Bee Brand Medical Dental Company, Japan) + Tea as a reducing agent (tannic acid by boiling 2 Meccchi tea bags) + 0.03 ppm municipal water supply |                                                                                        |                     |          |
|                  | 12% SDF (PROBEM-lab Prod. Farmaceuticos e Odontologicos, Brazil) + 0.03 ppm municipal water supply |                                                                                        |                     |          |
|                  | No intervention + 0.03 ppm municipal water supply² |                                                                                        | N/A                |          |
| **Zhang, 2013**  | 38% SDF (Saforide, Tokyo Seiyaku Kasei Co. Ltd, Japan) + Oral hygiene instructions (OHI) + 0.5 ppm municipal water supply | 2 applications total (baseline and every 12 months)                                   | Not reported       | Number of active lesions that became inactive |
| Study          | Methodology                                                                 | Conflicts of interest | Results                                                                 |
|---------------|------------------------------------------------------------------------------|-----------------------|-------------------------------------------------------------------------|
| Yee, 2009     | Sharp sickle probe with the tip gently passed over the entire surface of the cavity to detect and confirm visual evidence of caries | NR                    | - 38% SDF + tea vs No treatment: MD: 1.20, 95% CI: 0.49, 1.91           |
|               |                                                                               |                       | -12% SDF vs No treatment: MD: 0.50, 95% CI: -0.21, 1.21                 |
|               |                                                                               |                       | -38% SDF vs No treatment: MD: 1.10, 95% CI: 0.39, 1.81                  |
|               |                                                                               |                       | -38% SDF vs 12% SDF: MD: 0.80, 95% CI: -0.23, 1.43                     |
|               |                                                                               |                       | -38% SDF vs 38% SDF + Tea: MD: -0.10, 95% CI: -0.93, 0.73               |
|               |                                                                               |                       | -12% SDF vs 38% SDF + tea: MD: -0.70, 95% CI: -1.53, 0.13              |
| Zhang, 2013   | Sharp sickle probe with the tip gently passed over the entire surface of the cavity to detect and confirm visual evidence of caries | No conflicts of interest | On average, patients receiving 38% SDF + OHI + OHE had significantly more lesions arrested compared to those that only received OHI (MD: 0.29; 95% CI: 0.09, 0.49). Those that received 38% SDF + OHI, on average, had 0.24 more lesions arrested compared to those that received only OHI (MD: 0.24; 95% CI: 0.12, 0.36). When patients receiving 38% SDF + OHI + OHE were compared to those that received 38% SDF + OHI, there was not a significant difference in the average lesions arrested (MD: 0.05; 95% CI: -0.15, 0.25). |
## APPENDIX TABLE 2. Excluded studies

| Reference | Reason for Exclusion |
|-----------|----------------------|
| 1. Acevedo, A.M.M., Carolina; Rivera, Luis E.; Wolff, Mark; Kleinberg, Israel, *The inhibitory effect of an arginine bicarbonate/calcium carbonate CaviStat-containing dentifrice on the development of dental caries in Venezuelan school children*. The Journal of clinical dentistry, 2005. 16(3): p. 63-70. | Outcome reported not of interest (incidence) |
| 2. Acevedo, A.M.M., Maglynerit; Rojas-Sanchez, Fatima; Machado, Carolina; Rivera, Luis Eduardo; Wolff, Mark; Kleinberg, Israel, *Clinical evaluation of the ability of CaviStat in a mint confection to inhibit the development of dental caries in children*. The Journal of clinical dentistry, 2008. 19(1): p. 1-8. | Outcome reported not of interest (incidence) |
| 3. Achong Ra, B.D.M.F.R.J.H.G.H.I.M.A.L.W.J., *Effect of chlorhexidine varnish in caries active pediatric patients [abstract]*. Pediatric Dentistry, 1997. 19(2). | Abstract |
| 4. Achong, R.A.B., D. M.; Hildebrandt, G. H.; Feigal, R. J.; Loesche, W. J., *Effect of chlorhexidine varnish mouthguards on the levels of selected oral microorganisms in pediatric patients*. Pediatric Dentistry, 1999. 21(3): p. 169-75. | Intervention applied on a population not of interest |
| 5. Adair, S.M.X., Q., *Antibacterial and probiotic approaches to caries management*. Advances in dental research, 2009. 21(1): p. 87-9. | Proceedings from a meeting |
| 6. Agouropoulos, A.T., S.; Pandis, N.; Kavvadia, K.; Papagiannoulis, L., *Caries-preventive effectiveness of fluoride varnish as adjunct to oral health promotion and supervised tooth brushing in preschool children: a double-blind randomized controlled trial*. Journal of Dentistry, 2014. 42(10): p. 1277-83. | Mixed caries population; outcome reported not of interest (incidence) |
| 7. Akin, M.B., Faruk Ayhan, *Can white spot lesions be treated effectively?* The Angle orthodontist, 2012. 82(5): p. 770-5. | Randomization is not reported; outcome reported not of interest |
| 8. Alamoudi, N.M.H., Azza G.; Masoud, Mohamad I.; Sabbagh, Heba J.; Almushayt, Abdullah S.; Masoud, Ibrahim M., *Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs. An 18-month clinical trial*. Saudi medical journal, 2012. 33(2): p. 186-92. | Method to diagnose lesion is not acceptable |
| 9. Alexander, S.A.R., L. W., *Effects of self-applied topical fluoride preparations in orthodontic patients*. The Angle orthodontist, 2000. 70(6): p. 424-30. | Cannot construct 2x2 table; authors did not report outcome by arm |
| 10. Almeida, M.Q.d.C., Olivia Ximenes Izdiro; Ferreira, Jainara Maria Soares; Menezes, Valdenice Aparecida de; Leal, Rossana Barbosa; Sampaio, Fabio Correia, *Therapeutic potential of Brazilian fluoride varnishes: an in vivo study*. Brazilian Dental Journal, 2011. 22(3): p. 193-7. | Used 6% NaF varnish + 6% CaF<sub>2</sub>; intervention not commercially available in the United States |
| 11. Amin, H.E., *Clinical and antibacterial effectiveness of three different sealant materials*. Journal of dental hygiene : JDH, 2008. 82(5): p. 45. | Outcome reported not of interest (incidence) |
| 12. Andersson, A.S.-L., Kerstin; Hallgren, Anders; Petersson, Lars G.; Twetman, Svante, *Effect of a dental cream containing amorphous cream phosphate complexes on white spot lesion regression assessed by laser fluorescence*. Oral health & preventive dentistry, 2007. 5(3): p. 229-33. | Cannot construct 2x2 table; authors only presented total percentage of lesions at baseline and follow-up |
| 13. Andruzzioli, M.C.D.F., Giselle; Nelson-Filho, Paulo; Romano, Fabio Lourenco; Matsumoto, Mirian Aiko Nakane, *Influence of resin-modified glass ionomer and topical fluoride on levels of Streptococcus mutans in saliva and biofilm adjacent to metallic | Only surrogate outcomes were reported |
| 14. Anusavice, K.J., Efficacy of nonsurgical management of the initial caries lesion. Journal of dental education, 1997. 61(11): p. 895-905. | Not a randomized controlled trial |
|---|---|
| 15. Arruda, A.O.S.K., Ragahavendra; Inglehart, Marita R.; Rezende, Cristiane T.; Sohn, Woosung, Effect of 5% fluoride varnish application on caries among school children in rural Brazil: a randomized controlled trial. Community Dentistry and Oral Epidemiology, 2012. 40(3): p. 267-76. | Cannot construct 2x2 table; authors only reported incidence |
| 16. Asi Aminabadi, N.B., Esrafil; Pouralibaba, Firoz, The Effect of 0.2% Sodium Fluoride Mouthwash in Prevention of Dental Caries According to the DMFT Index. Journal of dental research, dental clinics, dental prospects, 2007. 1(2): p. 71-6. | Outcome reported not of interest |
| 17. Axelsson, P.K., K.; Karlsson, R.; Bratthall, D., A 30-month longitudinal study of the effects of some oral hygiene measures on Streptococcus mutans and approximal dental caries. Journal of Dental Research, 1987. 66(3): p. 761-5. | Cannot construct 2x2 table; authors only report mean progression data |
| 18. Aykut-Yelkener, A.K., Nazan; Ates, Mustafa; Ersin, Nazan; Ertugrul, Fahinur, Does casein phosphopeptide amorphous calcium phosphate provide remineralization on white spot lesions and inhibition of Streptococcus mutans? The Journal of clinical pediatric dentistry, 2014. 38(4): p. 302-6. | Outcome reported not of interest |
| 19. Baca, P.J., Pillar; Bravo, Manuel; Baca, Adela P.; Munoz, M. Jose, Caries incidence in permanent first molars after discontinuation of a school-based chlorhexidine-thymol varnish program. Community Dentistry and Oral Epidemiology, 2003. 31(3): p. 179-83. | Cannot construct 2x2 table; authors only reported incidence |
| 20. Bader, J.D.V., William M.; Shugars, Daniel A.; Gilbert, Gregg H.; Amaechi, Bennett T.; Brown, John P.; Laws, Reesa L.; Funkhouser, Kimberly A.; Makhiya, Sonia K.; Ritter, Andre V.; Leo, Michael C., Results from the Xylitol for Adult Caries Trial (X-ACT). Journal of the American Dental Association (1939), 2013. 144(1): p. 21-30. | Outcome reported not of interest |
| 21. Baeshen, H.S., Sabin; Dam, Robel; Zawawi, Khalid H.; Birkhed, Dowen, Comparison of Fluoridated Miswak and Toothbrushing with Fluoridated Toothpaste on Plaque Removal and Fluoride Release. The journal of contemporary dental practice, 2017. 18(4): p. 300-306. | Cannot construct 2x2 table; authors reported the mean change in ICDAS II score |
| 22. Bagramian, R.A., A 5-year school-based comprehensive preventive program in Michigan, U.S.A. Community Dentistry and Oral Epidemiology, 1982. 10(5): p. 234-7. | Cannot construct 2x2 table; authors only reported incidence |
| 23. Banocy, J.N., J., Effect of amine fluoride (AmF)/stannous fluoride (SnF2) toothpaste and mouthwashes on dental plaque accumulation, gingivitis and root-surface caries. Proceedings of the Finnish Dental Society. Suomen Hammaslaakariseuran toimituksia, 1991. 87(4): p. 555-9. | Outcome reported not of interest |
| 24. Banting, D.W.P., A.; Clark, D. C.; Proskin, H. M.; Schultz, M.; Perry, R., The effectiveness of 10% chlorhexidine varnish treatment on dental caries incidence in adults with dry mouth. Gerodontology, 2000. 17(2): p. 67-76. | Outcome reported not of interest |
| 25. Baseggio, W.N., Fabiana Scarpato; Davidoff, Denise Cesar de Oliveira; Nahsan, Flavia Pardo Salata; Flury, Simon; Rodrigues, Jonas Almeida, Caries-preventive efficacy and retention of a resin-modified glass ionomer cement and a resin-based fissure sealant: a 3-year split-mouth randomised clinical | Outcome reported not of interest (incidence) |
|Trial | Oral health & preventive dentistry, 2010. 8(3): p. 261-8. |
|---|---|
|26. | Bawden, J.W.G.; Holst, K.; Koch, G.; Krasse, P.; Rootzen, H. | Effect of mouthrinsing with a sodium fluoride solution in children with different caries experience. Swedish dental journal, 1980. 4(3): p. 111-7. |
| | Outcome reported not of interest (incidence) |
|27. | Bechtold, T.E.S.; Markovic, M.; Becherburg, M.; Goz, G. R. | In vivo effectiveness of enamel sealants around orthodontic brackets. Journal of orofacial orthopedics = Fortschritte der Kieferorthopadie : Organ/official journal Deutsche Gesellschaft fur Kieferorthopadie, 2013. 74(6): p. 447-57. |
| | Method to diagnose lesion is not acceptable |
|28. | Beerens, M.W.v.d.V.; van Beek, H.; ten Cate, J. M. | Effects of casein phosphopeptide amorphous calcium fluoride phosphate paste on white spot lesions and dental plaque after orthodontic treatment: a 3-month follow-up. European Journal of Oral Sciences, 2010. 118(6): p. 610-7. |
| | Intervention not of interest |
|29. | Beiruti, N.F.; Van't Hof, M. A.; Taifour, D.; Van Palenstein Helderman, W. H. | Caries-predictive effect of a one-time application of composite resin and glass ionomer sealants after 5 years. Caries Research, 2006. 40(1): p. 52-59. |
| | Outcome reported not of interest (incidence) |
|30. | Biesbrock, A.R.F.; R. V.; Bartizek, R. D.; Court, L. K.; Proskin, H. M.; Stockey, G. K. | The effect of chewing sugar-free gum after meals on clinical caries incidence. Journal of the American Dental Association (1939), 1998. 129(11): p. 1623-6. |
| | Intervention not of interest |
|31. | Benham, A.W.C.; Phillip M.; Buschang, Peter H. | Effectiveness of pit and fissure sealants in reducing white spot lesions during orthodontic treatment. A pilot study. The Angle orthodontist, 2009. 79(2): p. 338-45. |
| | Abstract |
|32. | Biesbrock, A.R.F.; R. V.; Bartizek, R. D.; Court, L. K. | Reversal of incipient and radiographic caries through the use of sodium and stannous fluoride dentifrices in a clinical trial. The Journal of clinical dentistry, 1998. 9(1): p. 5-10. |
| | Review article |
|33. | Borna, N.P.; Judy; Brown, Ronald | Remineralizing agents with casein phosphoprotein-amorphous calcium phosphate (CPP-AP) can promote white spot regression for orthodontic patients UT Cat# 2512. Texas dental journal, 2013. 130(10): p. 1030. |
| | Outcome reported not of interest (incidence) |
|34. | Borutta, A.K.; W.; Rubsam, F. | The caries-protective efficacy of 2 fluoride varnishes in a 2-year controlled clinical trial. Kariesprophylaktische Wirksamkeit zweier Fluridlacke in einer klinisch kontrollierten Zweijahresstudie., 1991. 79(7): p. 543-9. |
| | Outcome reported not of interest (incidence) |
|35. | Borutta, A.R.; G.; Hufnagl, S.; Mobius, S. | Caries prevention with fluoride varnishes among preschool children. Kariesprophylaxe mit Fluoridlacken bei Vorschulkindern., 2006. 68(11): p. 731-4. |
| | Outcome reported not of interest (incidence) |
|36. | Braga, M.M.M.; De Benedetto, M. S. | Effect of silver diammine fluoride on incipient caries lesions in erupting permanent first molars: a pilot study. Journal of dentistry for children (Chicago, Ill.), 2009. 76(1): p. 28-33. |
| | Cannot construct 2x2 table; authors reported the mean change in ICDAS II score |
|37. | Brambilla, E.T.; A.; Felloni, A.; Gagliani, M.; Malerba, A.; Strohmenger, L. | The effect of biannual applications of amine fluoride solution on caries incidence in permanent first molars: a 5-year study. International Journal of Paediatric Dentistry, 1997. 7(1): p. 9-14. |
39. Brochner, A.C., Carsten; Kristensen, Bjarne; Tranaeuf, Sofia; Karlsson, Lena; Sonnesen, Lilsette; Twetman, Svante, *Treatment of post-orthodontic white spot lesions with casein phosphopeptide-stabilised amorphous calcium phosphate*. Clinical Oral Investigations, 2011. **15**(3): p. 369-73.  
Study authors reported no statistical significance between intervention and control arm

40. Brodzikowska, A., *Fluoride and chlorhexidine varnishes in treatment of root caries [abstract]*. Journal of Dental Research, 2003. **82**(Spec Iss B): p. B.

41. Brown, J.P.A., Bennett T.; Bader, James D.; Gilbert, Gregg H.; Makhia, Sonia K.; Lozano-Pineda, Juanita; Leo, Michael C.; Chen, Chuhe; Vollmer, William M.; X. Act Trial Collaborative Group; Shugars Da, Ritter A. V. Robinson D. S. Anabtawi M. Z. Vega A. T. Radcliffe B. Vitolas B. Olivo N. Laws R. L. Funkhouser K. A. Eubanks D. J. Kirk K. Reck D. Bardsley J. Dixon A. R. Estberg E. J. Atkinson J. C. *Visual scoring of non cavitated caries lesions and clinical trial efficiency, testing xylitol in caries-active adults*. Community Dentistry and Oral Epidemiology, 2014. **42**(3): p. 271-8.

42. Bruun, C.B., J.; Hansen, K. T.; Kann, J.; Qvist, V.; Thylstrup, A., *Three-year caries increments after fluoride rinses or topical applications with a fluoride varnish*. Community Dentistry and Oral Epidemiology, 1985. **13**(6): p. 299-303.  
Not a randomized controlled trial

43. Burns, J.H., *Nano Silver Fluoride for preventing caries*. Evidence-based dentistry, 2015. **16**(1): p. 8-9.

44. Burton, J.P.D., Bernadette K.; Chilcott, Chris N.; Tagg, John R.; Thomson, W. Murray; Hale, John D. F.; Wescombe, Philip A., *Influence of the probiotic Streptococcus salivarius strain M18 on indices of dental health in children: a randomized double-blind, placebo-controlled trial*. Journal of medical microbiology, 2013. **62**(Pt 6): p. 875-84.

45. Burwell, A.K.L., L. J.; Greenspan, D. C., *Calcium sodium phosphosilicate (NovaMin): remineralization potential*. Advances in dental research, 2009. **21**(1): p. 35-9.  
Article includes animal and in-site studies

46. Cagetti, M.G.C., G.; Cocco, F.; Sale, S.; Congiu, G.; Mura, A.; Strohmenger, L.; Lingstrom, P.; Campus, G.; Italian Experimental Group on Oral, Health; Bosso M, Campus G. Cagetti M. G. Cocco F. Congiu G. Conti G. Corridone D. Lingstrom P. Mastroberardino S. Mura A. Polimeni A. Sale S. Sanna G. Strohmenger L., *Effect of Fluoridated Sealants on Adjacent Tooth Surfaces: A 30-mo Randomized Clinical Trial*. Journal of Dental Research, 2014. **93**(7 Suppl): p. 595-65S.

47. Cagliar, E., *Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial*. Journal of Dental Research, 2007. **86**(1): p. 95-95.  
Letter to the Editor

48. Cagliar, E.K., Ozgur Onder; Selvi Kuvvetli, Senem; Kavaloglu Cildir, Sule; Sandalli, Nuket; Twetman, Svante, *Short-term effect of ice-cream containing Bifidobacterium lactis Bb-12 on the number of salivary mutants streptococci and lactobacilli*. Acta Odontologica Scandinavica, 2008. **66**(3): p. 154-8.  
Only surrogate outcomes were reported

49. Cagliar, E.S., Nuket; Twetman, Svante; Kavaloglu, Sule; Ergeneli, Semra; Selvi, Senem, *Effect of yogurt with Bifidobacterium DN-173 010 on salivary mutants streptococci and lactobacilli in young adults*. Acta Odontologica Scandinavica, 2005. **63**(6): p. 317-20.  
Only surrogate outcomes were reported
| No. | Authors | Title | Journal | Year | Outcome Reported Not of Interest |
|-----|---------|-------|---------|------|----------------------------------|
| 50. | Campus, G.C., G.; Cagetti, M. G.; Bossu, M.; Sale, S.; Cocchi, F.; Conti, G.; Nardone, M.; Sanna, G.; Strohmenger, L.; Lingstrom, P.; Italian Experimental Group on Oral, Health; Bossu M, Campus G. Cagetti M. G. Caria G. P. Carta G. Cocchi F. Congiu G. Conti G. Corridone D. Lingstrom P. Mastrobernardino S. Mura A. Polimeni A. Sale S. Sanna G. Strohmenger L., | Fluoride concentration from dental sealants: a randomized clinical trial. | Journal of Dental Research, 2013. | 92(7 Suppl): p. 23S - 8S. | Outcome reported not of interest |
| 51. | Campus, G.C., Maria Grazia; Sale, Silvana; Petruzzi, Massimo; Solinas, Giuliana; Strohmenger, Laura; Lingstrom, Peter, | Six months of high-dose xylitol in high-risk caries subjects--a 2-year randomised, clinical trial. | Clinical Oral Investigations, 2013. | 17(3): p. 785-91. | Outcome reported not of interest (incidence) |
| 52. | Chambers, M.S.F., T. J.; Toth, B. B.; Lemon, J. C.; Craven, T. E.; Bouwsma, O. J.; Garden, A. S.; Espeland, M. A.; Keene, H. J.; Martin, J. W.; Sipos, T., | Erratum to “Clinical evaluation of the introral fluoride releasing system in radiation-induced xerostomic subjects. Part 2: Phase I study” (DOI:10.1016/j.oraloncology.2005.12.029). | Oral Oncology, 2007. | 43(1): p. 98-105. | Erratum |
| 53. | Chambers, M.S.M., James R.; Keene, Harris J.; Bouwsma, Otis J.; Garden, Adam S.; Sipos, Tibor; Fleming, Terence J., | Clinical evaluation of the introral fluoride releasing system in radiation-induced xerostomic subjects. Part 2: Phase I study. | Oral Oncology, 2006. | 42(9): p. 946-53. | Outcome reported not of interest |
| 54. | Chandak, S.B., Ashish; Bhardwaj, Amit; Pimpale, Jilesh; Chandwani, Manisha, | Comparative evaluation of the efficacy of fluoride varnish and casein phosphopeptide - Amorphous calcium phosphate in reducing Streptococcus mutans counts in dental plaque of children: An in vivo study. | Journal of International Society of Preventive & Community Dentistry, 2016. | 6(5): p. 423-429. | Only surrogate outcomes were reported |
| 55. | Cheng, J.C., B. W.; Cheng, N. F.; Gansky, S. A.; Featherstone, J. D. B., | Understanding treatment effect mechanisms of the CAMBRA randomized trial in reducing caries increment. | Journal of Dental Research, 2015. | 94(1): p. 44-51. | Intervention group individualized care based on risk |
| 56. | Chestnutt, I.G., | Chlorhexidine varnish has caries-reducing potential. | Evidence-based dentistry, 2006. | 7(4): p. 93. | Review article |
| 57. | Chestnutt, I.G.C., Barbara Lesley; Hutchings, Simon; Piayle, Rebecca; Pickles, Timothy; Lisles, Catherine; Kirkby, Nigel; Morgan, Maria Zeta; Hunter, Lindsay; Hodell, Ceri; Withers, Beverly; Murphy, Simon; Morgan-Trimmer, Sarah; Fitzsimmons, Deborah; Phillips, Ceri; Nuttall, Jacqueline; Hood, Kerenza, | Protocol for “Seal or Varnish?” (SoV) trial: a randomised controlled trial to measure the relative cost and effectiveness of pit and fissure sealants and fluoride varnish in preventing dental decay. | BMC Oral Health, 2012. | 12: p. 51. | Protocol |
| 58. | Chi, D.L.T., Ohnmar, Milgrom, Peter, | Cluster-randomized xylitol toothpaste trial for early childhood caries prevention. | Journal of dentistry for children (Chicago, Ill.), 2014. | 81(1): p. 27-32. | Mixed caries population; outcome reported not of interest (incidence) |
| 59. | Chu, C.H.L., E. C. M.; Lin, H. C., | Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese preschool children. | Journal of Dental Research, 2002. | 81(11): p. 767-70. | Not a randomized controlled trial |
| 60. | Chu, C.H.L., Edward C. M., | Microhardness of dentine in primary teeth after topical fluoride | Study population includes a non-random sample that was added after the initiation of the study |
| Number | Reference                                                                 | Outcome or Notes                                                                 |
|--------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| 61     | Chu, C.-H.G., Sherry Shiqian; Li, Samantha Ky; Wong, May Cm; Lo, Edward Cm, The effectiveness of the biannual application of silver nitrate solution followed by sodium fluoride varnish in arresting early childhood caries in preschool children: study protocol for a randomised controlled trial. Trials, 2015; 16; p. 426. | Study still in progress                                                              |
| 62     | Clark, D.C.S., J. W.; Quee, T. C.; Robert, G., Results of the Sherbrooke-Lac Megantic fluoride varnish study after 20 months. Community Dentistry and Oral Epidemiology, 1985. 13(2); p. 61-4. | Mixed caries population; outcome reported not of interest (incidence)               |
| 63     | Cocco, F.C., Giovanna; Cagetti, Maria Grazia; Strohmenger, Laura; Lingstrom, Peter; Campus, Guglielmo, The caries preventive effect of 1-year use of low-dose xylitol chewing gum. A randomized placebo-controlled clinical trial in high-caries-risk adults. Clinical Oral Investigations, 2017. | Authors only report prevalence                                                      |
| 64     | Cosyn, J.W.; De Rouck, Tim; Collys, Kris; Bottenberg, Peter; Matthijs, Stefan; Sabzevar, Mehran Moradi, Short-term anti-plaque effect of two chlorhexidine varnishes. Journal of clinical periodontology, 2005. 32(8); p. 899-904. | Only surrogate outcomes were reported                                               |
| 65     | Curtis, B.W.; E.; Policicino, C.; Evans, R. W.; Schwarz, E.; Sbaraini, A., The Monitor Practice Programme: is non-invasive management of dental caries in private practice cost-effective? Australian Dental Journal, 2011. 56(1); p. 48-55. | Outcome reported not of interest                                                    |
| 66     | de Amorim, R.G.L., Soraya Coelho; Bezerra, Ana Cristina Barreto; de Toledo, Orlando Aytorn, Association of chlorhexidine and fluoride for plaque control and white spot lesion remineralization in primary dentition. International Journal of Paediatric Dentistry, 2008. 18(6); p. 446-51. | Cannot construct 2x2 table                                                          |
| 67     | de Moura, M.S.d.M.S., Alexandre Henrique; Cury, Jaime Aparecido, In-vivo effects of fluoridated antiplaque dentifrice and bonding material on enamel demineralization adjacent to orthodontic appliances. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2006. 130(3); p. 357-63. | Outcome reported not of interest (incidence)                                        |
| 68     | Demito CFR, Gustavo Vivaldi; Ramos, Adilson Luiz; Bowman, S. Jay, Efficacy of a fluoride varnish in preventing white-spot lesions as measured with laser fluorescence. Journal of clinical orthodontics : JCO 2011;45(1);25-40. | Outcome reported not of interest (incidence)                                        |
| 69     | Derks, A.F., Jo; Bronkhorst, Ewald; Kuipers-Jagtman, Anne Marie; Katsaros, Christos, Effect of chlorhexidine varnish application on mutans streptococci counts in orthodontic patients. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2008. 133(3); p. 435-9. | Only surrogate outcomes were reported                                               |
| 70     | Detsomboonrat, P.T., C.; Pisamturakit, P. P., Similar 1-year caries increment after use of fluoride or non-fluoride toothpaste in infants and toddlers. Fluoride, 2016. 49(3); p. 313-326. | Mixed caries population; outcome reported not of interest (incidence)              |
| 71     | Divaris, K.P., J. S.; Slade, G. D., Surface-specific efficacy of fluoride varnish in caries prevention in the primary dentition: results of a community randomized clinical trial. Caries Research, 2013. 47(1); p. 78-87. | Mixed caries population; outcome reported not of interest (incidence)              |
| Reference                                                                 | Summary                                                                 |
|---------------------------------------------------------------------------|------------------------------------------------------------------------|
| 72. Dos Santos, V.E., Jr.; de Vasconcelos, Flavia M. N.; Ribeiro, Andrea G.; Rosenblatt, Aronita. *Paradigm shift in the effective treatment of caries in schoolchildren at risk.* International dental journal, 2012. 62(1): p. 47-51. | Intervention not of interest                                               |
| 73. Driscoll, W.S.N.-R., R.; Heifetz, S. B.; Li, S. H.; Selwitz, R. H., Evaluation of the comparative effectiveness of fluoride mouthrinsing, fluoride tablets, and both procedures in combination: interim findings after five years. Journal of public health dentistry, 1990. 50(1): p. 13-7. | Mixed caries population; outcome reported not of interest (incidence)      |
| 74. Driscoll, W.S.N.-R., R.; Selwitz, R. H.; Li, S. H.; Heifetz, S. B., A comparison of the caries-preventive effects of fluoride mouthrinsing, fluoride tablets, and both procedures combined: final results after eight years. Journal of public health dentistry, 1992. 52(2): p. 111-6. | Mixed caries population; outcome reported not of interest (incidence)      |
| 75. Du, M.C., Ning; Tai, Baojun; Jiang, Han; Li, Jing; Bian, Zhuan, Randomized controlled trial on fluoride varnish application for treatment of white spot lesion after fixed orthodontic treatment. Clinical Oral Investigations, 2012. 16(2): p. 463-8. | Method to diagnose lesion is not acceptable                                |
| 76. Du Mq, L.Q.J.H.T.B., Effect of Duraphat on enamel demineralization after fixed orthodontic treatment. 2nd Meeting of IADR Pan Asian Pacific Federation (PAPF) and the 1st Meeting of IADR Asia/Pacific Region (APR), 2009; p. 277. | Abstract from conference proceeding                                      |
| 77. Du, M.Q.; B. J.; Jiang, H.; Lo, E. C. M.; Fan, M. W.; Bian, Z., A two-year randomized clinical trial of chlorhexidine varnish on dental caries in Chinese preschool children. Journal of Dental Research, 2006. 85(6): p. 557-9. | Mixed caries population; outcome reported not of interest (incidence)      |
| 78. Duane, B., 5,000 ppm F dentifrice for caries prevention in adolescents. Evidence-based dentistry, 2012. 13(2): p. 43-4. | Commentary                                                             |
| 79. Duane, B.G., No evidence of caries reduction found in a school xylitol and erythritol lozenge programme. Evidence-based dentistry, 2011. 12(4): p. 102-3. | Review article                                                         |
| 80. Ebrahimi, M.M., Maryam; Ahrari, Farzaneh; Parisay, Iman; Jahantigh, Maliheh, The effects of three remineralizing agents on regression of white spot lesions in children: A two-week, single-blind, randomized clinical trial. Journal of clinical and experimental dentistry, 2017. 9(5): p. e641-e648. | Outcome reported not of interest                                      |
| 81. Edwards, M., Regular rinsing with chlorhexidine does not reduce caries in older adults. Evidence-based dentistry, 2009. 10(1): p. 13-4. | Review article                                                         |
| 82. Erdemir, U.S., Hande Sar; Yaman, Batu Can; Ozel, Selva; Yucel, Taner; Yildiz, Esra, Clinical comparison of a flowable composite and fissure sealant: a 24-month split-mouth, randomized, and controlled study. Journal of Dentistry, 2014. 42(2): p. 149-57. | Outcome reported not of interest (incidence)                            |
| 83. Ersin, N.K.E., Ecet, Eronat, Nesrin; Totu, Fusun Irem; Ates, Mustafa, Effectiveness of 2-year application of school-based chlorhexidine varnish, sodium fluoride gel, and dental health education programs in high-risk adolescents. Quintessence international (Berlin, Germany : 1985), 2008. 39(2): p. e45-51. | Outcome reported not of interest (incidence)                            |
| 84. Esenlik, E.U.C., E.; Bolat, E., Efficacy of a casein phosphopeptide amorphous calcium phosphate (CPP-ACP) paste in preventing white spot lesions in patients with fixed orthodontic appliances: A prospective clinical trial. European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry, 2016. 17(4): p. 274-280. | Outcome reported not of interest (incidence)                            |
85. Evans, D., *APF foam does reduce caries in primary teeth*. Evidence-based dentistry, 2007. 8(1): p. 7. Review article

86. Fadl, A.N.E., Magda M.; Dowidar, Karin L.; Mokhles, Nadia; El Tantawi, Maha M., *Effect of Tooth Mousse on Streptococcus Mutans in the Plaque of High-Caries-risk Preschool Children: A Triple-Blind, Randomized Clinical Trial*. Pediatric Dentistry, 2016. 38(4): p. 300-4. Outcome reported not of interest

87. Falony, G.H., Sisko; Runnel, Riina; Olak, Jana; Nommela, Rita; Russak, Silvia; Saag, Mare; Makinen, Pirkko-Liisa; Makinen, Kauko; Vahlberg, Tero; Honkala, Eino, *Long-Term Effect of Erythritol on Dental Caries Development during Childhood: A Posttreatment Survival Analysis*. Caries Research, 2016. 50(6): p. 579-588. Mixed caries population

88. Featherstone, J.D.B.W., J. M.; Hoover, C. I.; Rapozo-Hilo, M.; Weintraub, J. A.; Wilson, R. S.; Zhan, L.; Gansky, S. A., *A randomized clinical trial of anticaries therapies targeted according to risk assessment (caries management by risk assessment)*. Caries Research, 2012. 46(2): p. 118-29. Outcome reported not of interest

89. Feng, Y.Y., Wei; Hu, De-yu; Zhang, Yunpo; Pretty, Iain A.; Ellwood, Roger P., *Detection and prevention of early caries after fluoride dentifrice application using quantitative light-induced fluorescence in vivo*. Hua xi kou qiang yi xue za zhi = Huaxi kouqiang yixue zazhi = West China journal of stomatology, 2008. 26(6): p. 607-10. Outcome reported not of interest (incidence)

90. Ferreira, J.M.S.A., Ana Karla Ramalho; Rosa, Adriana Dias Batista; Sampaio, Fabio Correia; Menezes, Valdenice Aparecida de, *Therapeutic effect of two fluoride varnishes on white spot lesions: a randomized clinical trial*. Brazilian Oral Research, 2009. 23(4): p. 446-51. Used 6% NaF varnish + 6% CaF₂; intervention not commercially available in the United States

91. Frostell, G.B., D.; Edwardsson, S.; Goldberg, P.; Petersson, L. G.; Priwe, C.; Winholt, A. S., *Effect of partial substitution of invert sugar for sucrose in combination with Duraphat treatment on caries development in preschool children: the Malmo Study*. Caries Research, 1991. 25(4): p. 304-10. Cannot construct 2x2 table

92. Forgie, A.H.P., M.; Pine, C. M.; Pitts, N. B.; Nugent, Z. J., *A randomised controlled trial of the caries-preventive efficacy of a chlorhexidine-containing varnish in high-caries-risk adolescents*. Caries Research, 2000. 34(5): p. 432-9. Cannot construct 2x2 table; authors did not report data clearly by outcome

93. Fure, S.L., *Evaluation of different fluoride treatments of initial root carious lesions in vivo*. Oral health & preventive dentistry, 2009. 7(2): p. 147-54. Intervention not of interest

94. Gabre, P.B., D.; Gahnberg, L., *Fluoride retention of a mucosa adhesive paste compared with other home-care fluoride products*. Caries Research, 2008. 42(4): p. 240-6. Only surrogate outcomes were reported

95. Gerardu, V.A.M.B., Mark; van Loveren, Cor; Ten Cate, Jacob M., *Plaque formation and lactic acid production after the use of amine fluoride/stannous fluoride mouthrinse*. European Journal of Oral Sciences, 2007. 115(2): p. 148-52. Only surrogate outcomes were reported

96. Gizani, S.P., Georgia; Twetman, Svante; Caroni, Cris; Makou, Margarita; Papagianoulis, Lisa, *Effect of the probiotic bacterium Lactobacillus reuteri on white spot lesion development in orthodontic patients*. Caries Research, 2007. 41(6): p. 517-23. Outcome reported not of interest (incidence)
| No. | Reference                                                                                                      | Notes                                                                 |
|-----|----------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| 98  | Gokalp, S.B., Meserret, *Use of laser fluorescence in monitoring the durability and cariostatic effects of fluoride and chlorhexidine varnishes on occlusal caries: a clinical study*. Quintessence international (Berlin, Germany : 1985), 2005. 36(3): p. 183-9. | Method to diagnose lesion is not acceptable                             |
| 99  | Greig, V.C., David I., *Fluoride varnish was effective at reducing caries on high caries risk school children in rural Brazil*. Evidence-based dentistry, 2012. 13(3): p. 78-9. | Review article                                                          |
| 100 | Guclu, Z.A.A., Alev; Coleman, Nichola Jayne, *A 12-Week Assessment of the Treatment of White Spot Lesions with CPP-ACP Paste and/or Fluoride Varnish*. BioMed Research International, 2016. 2016: p. 8357621. | Used 23.3% xylitol chewing gum; intervention not commercially available in the United States |
| 101 | Gugwad, S.C.S., Preetam; Lodaya, Rahul; Bhat, Chetan; Tandon, Piyush; Choudhari, Shantanu; Patil, Shankargouda, *Caries prevention effect of intensive application of sodium fluoride varnish in molars in children between age 6 and 7 years*. The journal of contemporary dental practice, 2011. 12(6): p. 408-13. | Outcome reported not of interest (incidence)                           |
| 102 | Gupta, D.G., Rajendra Kumar, *Investigation of antibacterial efficacy of Acacia nilotica against salivary mutans streptococci: a randomized control trial*. General Dentistry, 2015. 63(1): p. 23-7. | Only surrogate outcomes were reported                                  |
| 103 | Hambire, C.U.J., Rashmi; Patil, Amol; Wani, Vaibhav R.; Kulkarni, Ankur A.; Nehete, Parag B., *Comparing the antiplaque efficacy of 0.5% Camellia sinensis extract, 0.05% sodium fluoride, and 0.2% chlorhexidine glucanate mouthwash in children*. Journal of International Society of Preventive & Community Dentistry, 2015. 5(3): p. 218-26. | Only surrogate outcomes were reported                                  |
| 104 | Hanno, A.G.A., Najiaa M.; Almushayt, Abdullah S.; Masoud, Mohammed I.; Sabbagh, Heba J.; Farsi, Najat M., *Effect of xylitol on dental caries and salivary Streptococcus mutans levels among a group of mother-child pairs*. The Journal of clinical pediatric dentistry, 2011. 36(1): p. 25-30. | Mixed caries population                                                 |
| 105 | Hardman, M.C.D., G. M.; Duxbury, J. T.; Davies, R. M., *A cluster randomised controlled trial to evaluate the effectiveness of fluoride varnish as a public health measure to reduce caries in children*. Caries Research, 2007. 41(5): p. 371-6. | Outcome reported not of interest                                       |
| 106 | Haugejorden, O.N., A., *Caries incidence after topical application of varnishes containing different concentrations of sodium fluoride: 3-year results*. Scandinavian Journal of Dental Research, 1991. 99(4): p. 295-300. | Mixed caries population                                                 |
| 107 | Haakila, G.P., S., *Effect of a varnish containing chlorhexidine and thymol (Cervitec) on approximal caries in 13- to 16-year-old schoolchildren in a low caries area*. Caries Research, 2003. 37(3): p. 185-9. | Cannot construct 2x2 table; authors only report mean progression data   |
| 108 | Hausen, H.K., S.; Seppa, L., *Application of the high-risk strategy to control dental caries*. Community Dentistry and Oral Epidemiology, 2000. 28(1): p. 26-34. | Not a randomized controlled trial                                       |
| 109 | Hausen, H.S., L.; Poutanen, R.; Niinimaa, A.; Lahti, S.; Karkkainen, S.; Pietila, I., *Noninvasive control of dental caries in children with active initial lesions. A randomized clinical trial*. Caries Research, 2007. 41(5): p. 384-91. | Intervention not of interest                                           |
| 110 | Hauser-Gerspach, I.P.-S., Victoria; Dahnhardt, Jan Eric; Meyer, Jurgen; Lussi, Adrian, *Comparison of the immediate effects of gaseous ozone and chlorhexidine gel on bacteria in cavitated carious...* | Intervention applied on a population not of interest                   |
| ID  | Reference                                                                 | Outcome Description                                                                 |
|-----|---------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| 111 | Hay, K.D.T., W. Murray, A clinical trial of the anticaries efficacy of casein derivatives complexed with calcium phosphate in patients with salivary gland dysfunction. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, 2002. 93(3): p. 271-5. | Mixed caries population                                                             |
| 112 | He, T.L., Xue; Dong, Ying; Zhang, Na; Zhong, Yisi; Yin, Wei; Hu, Deyu, Comparative assessment of fluoride varnish and fluoride film for remineralization of postorthodontic white spot lesions in adolescents and adults over a 6-month period: A single-center, randomized controlled clinical trial. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2016. 149(6): p. 810-9. | Method to diagnose lesion is not acceptable                                          |
| 113 | Hegazy, S.A.S., R. I., Antiplaque and remineralizing effects of Biorepair mouthwash: A comparative clinical trial. Pediatric Dental Journal, 2016. 26(3): p. 89-94. | Method to diagnose lesion is not acceptable                                          |
| 114 | Heidmann, J.M.A., D.; Poulsen, S.; Kirkegaard, E.; Laurbjerg, L., Development of caries in a group of Danish school-age children after cessation of systematic fluoride rinsing. Kariesudvikling hos en gruppe danske skoleborn efter ophor af systematiske flurskyllinger., 1993. 155(38): p. 2995-8. | Outcome reported not of interest (incidence)                                         |
| 115 | Heidmann, J.P., S., Comparative three-year caries protection from an aluminum-containing and a fluoride-containing toothpaste. Caries Research, 1997. 31(2): p. 85-90. | Mixed caries population                                                             |
| 116 | Heifetz, S.B.D., W. S.; Creighton, W. E., The effect on dental caries of weekly rinsing with a neutral sodium fluoride or an acidulated phosphate-fluoride mouthwash. Journal of the American Dental Association (1939), 1973. 87(2): p. 364-8. | Mixed caries population                                                             |
| 117 | Hoffman, D.A.C., Andrew E.; Rody, Wellington J., Jr.; McGorray, Susan P.; Wheeler, Timothy T., A prospective randomized clinical trial into the capacity of a toothpaste containing NovaMin to prevent white spot lesions and gingivitis during orthodontic treatment. Progress in orthodontics, 2015. 16: p. 25. | Outcome reported not of interest (incidence)                                         |
| 118 | Holm, G.B.H., K.; Mejlare, I., The caries-preventive effect of a fluoride varnish in the fissures of the first permanent molar. Acta Odontologica Scandinavica, 1984. 42(4): p. 193-7. | Cannot construct 2x2 table; authors did not clearly state which participants had caries at baseline |
| 119 | Hoszek, A.S., Isabel; Jozefowicz, Agata; Wojcieszek, Danuta; Wierzbicka, Maria; Wretlind, Katarina; Ericson, Dan, Chlorhexidine-containing glass ionomer cement. A clinical investigation on the fissure caries inhibiting effect in first permanent molars. Swedish dental journal, 2005. 29(3): p. 89-96. | Cannot construct 2x2 table; authors did not clearly state which participants had caries at baseline |
| 120 | Hu, D. Y.; Yin, W.; Li, X.; Feng, Y.; Zhang, Y. P.; Cummins, D.; Mateo, L. R.; Ellwood, R. P., A clinical investigation of the efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride, as sodium monofluorophosphate in a calcium base, on primary root caries. Journal of Clinical Dentistry, 24(Spec Iss A), A23-A31. | Used 1.5% arginine plus 1450 ppm dentifrice toothpaste; intervention not commercially available in the United States |
| 121 | Huang, G.J.R.-C., Brie; Mills, Brian E.; Shalchi, Salma; Spiekerman, Charles; Korpk, Anna M.; Starrett, Jeri L.; Greenlee, Geoffrey M.; Drangsholt, Ross J.; Matunas, Jack C., Effectiveness of Ml Paste Plus and PreviDent fluoride varnish for treatment of white spot lesions: a randomized controlled trial. | Outcome reported not of interest; authors only report mean change in percentage improvement score |
| Study Still in Progress | Cannot Construct 2x2 Table | Outcome Reported Not of Interest (Incidence) | Only Surrogate Outcomes Were Reported | Outcome Reported Not of Interest (Incidence) | Outcome Reported Not of Interest (Incidence) | Outcome Reported Not of Interest | Mixed Caries Population; Outcome Reported Not of Interest (Incidence) | Intervention Not of Interest |
|------------------------|----------------------------|---------------------------------------------|--------------------------------------|---------------------------------------------|---------------------------------------------|--------------------------------------|-----------------------------------------------|-----------------------------|
| 122. Innes, N.P.T.C., Jan E.; Speed, Chris; Douglas, Gail V. A.; Maguire, Anne; Fi, Ction Trial Collaboration; Innes Np, Clarkson J. E. Douglas G. V. Maguire A. Chadwick B. Deery C. Duggal M. Wong F. Speed C. Palmer M. Keightley A. Deverill M. Evans D. J. Freeman R. McColl E. Pitts N. B. Steen I. N. Chestnut I. Fayle S. Longbottom C. Marshman Z. Rodd H. Steele J. Treasure E. Welbury R. Laird M. Caldwell-Nichols A. Barker E. Thompson S. Philpott B. Howell B. Lais S. O'Rourke S. Mills-Ball J. Tement L. Ryan V., *The Fiction Dental Trial Protocol* - Filling Children's Teeth: Indicated or Not? *BMC Oral Health*, 2013. 13: p. 25. | 123. Irigoien-Camacho, M.E.L.-A., Maria I.; Amador-Pedraza, Yazmine; Zepeda-Zepeda, Marco A.; Villanueva-Gutierrez, Teresa; Sanchez-Perez, Leonor, *[Comparison of Varnishes and Fluoridated Toothpaste for the Prevention of Dental Caries in School Children]*. Comparacion de barnices y dentífrico con fluor en la prevencion de caries en escolares., 2015. 17(5): p. 801-814. | 124. Jenatschke, F.E., E.; Welte, H. D.; Schlagenhauf, U., Influence of Repeated Chlorhexidine Varnish Applications on Mutans Streptococci Counts and Caries Increment in Patients Treated with Fixed Orthodontic Appliances. *Journal of Orofacial Orthopedics = Fortschritte der Kieferorthopadie : Organ/Official Journal Deutsche Gesellschaft Fur Kieferorthopadie*, 2001. 62(1): p. 36-45. | 125. Jenkins, S.A., M.; Newcombe, R., Evaluation of a mouthrinse containing chlorhexidine and fluoride as an adjunct to oral hygiene. *Journal of Clinical Periodontology*, 1993. 20(1): p. 20-5. | 126. Jiang, E.M.L.; Edward Chin Man; Chu, Chun Hung; Wong, May Chun Mei, Prevention of Early Childhood Caries (Ecc) through Parental Toothbrushing Training and Fluoride Varnish Application: a 24-Month Randomized Controlled Trial. *Journal of Dentistry*, 2014. 42(12): p. 1543-50. | 127. Jiang, H.B., Z.; Tai, B. J.; Du, M. Q.; Peng, B., The Effect of a Bi-Annual Professional Application of APF Foam on Dental Caries Increment in Primary Teeth: 24-Month Clinical Trial. *Journal of Dental Research*, 2005. 84(3): p. 265-8. | 128. Jiang, H.H., Fang; Yao, Liping; Tai, Baojun; Du, Minquan, Effect of 1.23% Acidulated Phosphate Fluoride Foam on White Spot Lesions in Orthodontic Patients: a Randomized Trial. *Pediatric Dentistry*, 2013. 35(3): p. 275-8. | 129. Jiang, H.T.; Baojun; Du, MinQuan; Peng, Bin, Effect of Professional Application of APF Foam on Caries Reduction in Permanent First Molars in 6-7-Year-Old Children: 24-Month Clinical Trial. *Journal of Dentistry*, 2005. 33(6): p. 469-73. | 130. Jiang, H.T.; Baojun; Du, Min-quan; Huang, Wei; Guo, Ying, [A Two-Year Randomized Clinical Trial of 1.23% Fluoride Foam on Dental Caries Increment in Primary Teeth] Zhonghua Kou qiang yi xue za zhi = Zhonghua kouqiang yixue zazhi = Chinese Journal of Stomatolgy, 2007. 42(8): p. 456-9. | 131. Johansson, E.V.D., J. W. V.; Karlsson, L.; Andersson-Wenckert, I., Treatment Effect of Ozone and Fluoride Varnish Application on Occlusal Caries in
| Reference | Title | Journal | Year | Issue | Pages | Notes |
|-----------|-------|---------|------|-------|-------|-------|
| 132 | Joharji, R.M.A., J. O., | Prevention of pit and fissure caries using an antimicrobial varnish: 9 month clinical evaluation. | Journal of Dentistry, 2001. | 29(4) | 247-54 | Mixed caries population |
| 133 | Juarez-Lopez, M.L.A.H.-P., R. D.; Hernandez-Guerrero, J. C.; Jimenez-Farean, D.; Molina-Frechero, N., | Preventive and remineralization effect over incipient lesions of caries decay by phosphopeptic phosphate of calcium amorphous. | Revista de Investigacion Clinica, 2014. | 66(2) | 144-151 | Not a randomized controlled trial |
| 134 | Kallestal, C., | The effect of five years’ implementation of caries-preventive methods in Swedish high-risk adolescents. | Caries Research, 2005. | 39(1) | 20-6 | Mixed caries population |
| 135 | Kandelman, D.G., G., | Clinical results after 12 months from a study of the incidence and progression of dental caries in relation to consumption of chewing-gum containing xylitol in school preventive programs. | Journal of Dental Research, 1990. | 69(11) | 1771-5 | Not a randomized controlled trial |
| 136 | Karjalainen, S.E., A. L.; Ruokola, M.; Toivonen, A., | Caries development after substitution of supervised fluoride rinses and toothbrushings by unsupervised use of fluoride toothpaste. | Community Dentistry and Oral Epidemiology, 1994. | 22(6) | 421-4 | Outcome reported not of interest (incidence) |
| 137 | Karlsson, L., Lars-Erik; Trollsas, Karin; Angmar-Mansson, Birgit; Tranaeus, Sofia, | Effect of supplementary amine fluoride gel in caries-active adolescents. A clinical QLF study. | Acta Odontologica Scandinavica, 2007. | 65(5) | 284-91 | Method to diagnose lesion is not acceptable |
| 138 | Keightley, A.J.T., Greig D., | Fluoride varnish applications and caries incidence in pre-schoolers. | Evidence-based dentistry, 2014. | 15(3) | 83-4 | Review article |
| 139 | Keller, M.K.K., B. J.; Twetman, S., | Fluoride varnish or fluoride mouth rinse? A comparative study of two school-based programs. | Community dental health, 2016. | 33(1) | 23-6 | Outcome reported not of interest (incidence) |
| 140 | Keller, M.K.N.L., I.; Karlsson, I.; Twetman, S., | Effect of tablets containing probiotic bacteria (Lactobacillus reuteri) on early caries lesions in adolescents: a pilot study. | Beneficial microbes, 2014. | 5(4) | 403-7 | Method to diagnose lesion is not acceptable |
| 141 | Keltjens, H.M.S., M. J.; van der Hooven, J. S.; Hendriks, J. C., | Caries control in overdenture patients: 18-month evaluation on fluoride and chlorhexidine therapies. | Caries Research, 1990. | 24(5) | 371-5 | Outcome reported not of interest (incidence) |
| 142 | Kleber, C.J.M., J. L.; Davidson, K. R.; Putt, M. S.; Triol, C. W.; Winston, A. E., | Treatment of orthodontic white spot lesions with a remineralizing dentifrice applied by toothbrushing or mouth trays. | The Journal of clinical dentistry, 1999. | 10(1 Spec No) | 44-9 | Not a randomized controlled trial |
| 143 | Knosel, M.E., | Durability of esthetic improvement following ICON resin infiltration of multibracket-induced white spot lesions compared with no therapy over 6 months: a single-center, split-mouth, randomized clinical trial. | American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2013. | 144(1) | 86-96 | Method to diagnose lesion is not acceptable |
| ID  | Authors                                      | Title                                                                 | Journal and Volume  | Page(s) | Notes |
|-----|---------------------------------------------|----------------------------------------------------------------------|---------------------|---------|-------|
| 145 | Kolmakow, S.H., E.; Borovsky, E. V.; Kuzmina, E. M.; Vasina, S. A. | Effect of the mineralizing agent on the permanent teeth.             | The Journal of clinical pediatric dentistry, 1991. 15(3) | p. 179-87 | Intervention not of interest |
| 146 | Korkut, B.T., D.; Yanikoglu, F.; Tagtekin, D. | Clinical assessment of demineralization and remineralization surrounding orthodontic brackets with FluoreCam. | Asian Pacific journal of tropical biomedicine, 2017. 7(4) | p. 373-377 | Authors did not clearly state randomization of participants |
| 147 | Kralivaphan, P.A., C.; Triratana, T.; Mateo, L. R.; Ellwood, R.; Cummins, D.; DeVizio, W.; Zhang, Y. P. | Two-year caries clinical study of the efficacy of novel dentifrices containing 1.5% arginine, an insoluble calcium compound and 1,450 ppm fluoride. | Caries Research, 2013. 47(6) | p. 582-90 | Mixed caries population; outcome reported not of interest (incidence) |
| 148 | Kritikadatta, J.F., Chain; Abarajithan, Mohan; Kandaswamy, Deivanayagam | Remineralisation of occlusal white spot lesion with a combination of 10% CPP-ACP and 0.2% sodium fluoride evaluated using Diagnodent: a pilot study. | Oral health & preventive dentistry, 2013. 11(2) | p. 191-6 | Method to diagnose lesion is not acceptable |
| 149 | Küköle, M.P. | Changes in the appearance and form of the spots of macula cariosa alba in treatment with fluoride gel. | Folia medica, 2002. 44(1-2) | p. 64-9 | Not a randomized controlled trial |
| 150 | Küköle, M.P. | Treatment of incipient caries in children with fluoride gel. | Folia medica, 2002. 44(1-2) | p. 50-5 | Not a randomized controlled trial |
| 151 | Kumar Jena, A.P.S.; Satinder; Kumar Utreja, Ashok | Efficacy of resin-modified glass ionomer cement varnish in the prevention of white spot lesions during comprehensive orthodontic treatment: a split-mouth study. | Journal of orthodontics, 2015. 42(3) | p. 200-7 | Outcome reported not of interest (incidence) |
| 152 | Lang, N.P.R., K. | Use of oral irrigators as vehicle for the application of antimicrobial agents in chemical plaque control. | Journal of clinical periodontology, 1981. 8(3) | p. 177-188 | Only surrogate outcomes were reported |
| 153 | Lawrence, H.P.B., Darlene; Douglas, Jan; McKeown, Lynda; Switzer, Bonita; Figueiredo, Rafael; Laporte, Audrey | A 2-year community-randomized controlled trial of fluoride varnish to prevent early childhood caries in Aboriginal children. | Community Dentistry and Oral Epidemiology, 2008. 36(6) | p. 503-16 | Mixed caries population |
| 154 | Lee, W.S., Charles; Heima, Masahiro; Eggertsson, Haifstein; Ferretti, Gerald; Milgrom, Peter; Nelson, Suchitra | The effectiveness of xylitol in a school-based cluster-randomized clinical trial. | Caries Research, 2015. 49(1) | p. 41-9 | Outcome reported not of interest (incidence) |
| 155 | Legier-Vargas, K.M.-S., S. A.; Featherstone, J. D.; Gwinner, L. M. | Effects of sodium bicarbonate dentifrices on the levels of cariogenic bacteria in human saliva. | Caries Research, 1995. 29(2) | p. 143-7 | Only surrogate outcomes were reported |
| 156 | Lenkner, A.-M.H.P.; Kaisu; Hurme, Saia; Alanen, Pertti | The caries-preventive effect of xylitol/maltitol and erythritol/maltitol lozenges: results of a double-blinded, cluster-randomized clinical trial in an area of natural fluoridation. | International Journal of Paediatric Dentistry, 2012. 22(3) | p. 180-90 | Mixed caries population; outcome reported not of interest (incidence) |
| 157 | Levin, K.A.J., Colwyn M.; Wight, Christine; Valentine, Carolyn; Topping, Gail V. A.; Naysmith, Robert | Fluoride rinsing and dental health inequalities in 11-year-old children: an evaluation of a supervised school-based fluoride rinsing programme in Edinburgh. | Community Dentistry and Oral Epidemiology, 2009. 37(1) | p. 19-26 | Authors only report prevalence |
| 158 | Lexner, M.O.B., Susanne; Dahlen, Gunnar; Twetman, Svante | Microbiological profiles in saliva and supragingival plaque from caries-active | | | Outcome reported not of interest |
| Reference                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Type                                                                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|
| 159. Li, X.Z., Yisi; Jiang, Xianjun; Hu, Deyu; Mateo, Luis R.; Morrison, Boyce M., Jr.; Zhang, Yun-Po, *Randomized clinical trial of the efficacy of dentifrices containing 1.5% arginine, an insoluble calcium compound and 1450 ppm fluoride over two years.* The Journal of clinical dentistry, 2015. 26(1): p. 7-12. | Mixed caries population; outcome reported not of interest (incidence) |
| 160. Liptak LB, Nora; Twetman, Svante; Madlena, Melinda, The effect of a chlorhexidine-fluoride varnish on mutans streptococci counts and laser fluorescence readings in occlusal fissures of permanent teeth: A split-mouth study. Quintessence international (Berlin, Germany : 1985) 2016;47(9):767-73. | Mixed caries population                                                                                                           |
| 161. Liu, B.Y.L., E. C. M.; Chu, C. H.; Lin, H. C., *Randomized clinical trial on fluorides and sealants for fissure caries prevention.* Journal of Dental Research, 2012. 91(8): p. 753-8.                                                                                                    | Mixed caries population; outcome reported not of interest (incidence)                                                      |
| 162. Liu, B.Y.X., Yue; Chu, Chun Hung; Lo, Edward Chin Man, *Glass ionomer ART sealant and fluoride-releasing resin sealant in fissure caries prevention--results from a randomized clinical trial.* BMC oral health, 2014. 14: p. 54.                                                                 | Interventions not clearly stated; concentrations, brand, and manufacturers names are not reported                           |
| 163. Liu Y, R.W.Z.X.W.M.J.Q.W.W., *[Caries prevention effect of resin based sealants and glass ionomor sealants]. Zhonghua kou qiang yi xue za zhi = Zhonghua kouqiang yixue zazhi = Chinese journal of stomatology, 2014. 49(4): p. 199. | Outcome reported not of interest (incidence)                                                                                  |
| 164. Llena, C.L., A. M.; Forner, L., *CPP-ACP and CPP-ACFP versus fluoride varnish in remineralisation of early caries lesions. A prospective study.* European journal of paediatric dentistry : official journal of European Academy of Paediatric Dentistry, 2015. 16(3): p. 181-6. | Method to diagnose lesion is not acceptable                                                                                |
| 165. Llena-Puy, C., *Mi paste plus and PreviDent fluoride varnish appear no more effective than normal home care for improving the appearance of white spot lesions.* The journal of evidence-based dental practice, 2013. 13(3): p. 114-6. | Duplicate                                                                                                                      |
| 166. Llena-Puy, C., *Mi Paste Plus and PreviDent Fluoride Varnish appear no more effective than normal home care for improving the appearance of white spot lesions [commentary].* Journal of Evidence-Based Dental Practice, 2013. 13(3): p. 114. | Commentary                                                                                                                    |
| 167. Lo, O.J., J.; Torjek, C.; Xie, R.; Manaog, G.; Misner, D.; Parry, J.; Sawyer, C.; Hovan, A., *Challenging the gold standard of daily fluoride tray use for the prevention of caries in H&N radiotherapy patients.* Supportive Care in Cancer, 2012. 20: p. S120. | Abstract                                                                                                                       |
| 168. Lobo, P.L.D.d.C., C. B. M.; Fonseca, S. G. C.; de Castro, R. S. L.; Monteiro, A. J.; Fonteles, M. C.; Fonteles, C. S. R., *Sodium fluoride and chlorhexidine effect in the inhibition of mutans streptococci in children with dental caries: a randomized, double-blind clinical trial.* Oral Microbiology and Immunology, 2008. 23(6): p. 486-91. | Only surrogate outcomes were reported                                                                                          |
| 169. Lobo, P.L.D.F., Cristiane Sa Roriz; Marques, Lidia Audrey Rocha Valadas; Jamacaru, Francisco Vagnaldo Fechine; Fonseca, Said Goncalves da Cruz; de Carvalho, Cibele Barreto Mano; de Moraes, Maria Elisabete Amaral, *The efficacy of three formulations of Lippia sidoides Cham. essential oil in the reduction of salivary Streptococcus mutans in children with caries: a randomized, double-blind, controlled study.* Phytomedicine : international | Only surrogate outcomes were reported                                                                                          |
| ID  | Reference                                                                 | Notes                                                                 |
|-----|---------------------------------------------------------------------------|----------------------------------------------------------------------|
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| 173 | Machiulskienė, V.N., B.; Baelum, V., Caries preventive effect of sugar-substituted chewing gum. Community Dentistry and Oral Epidemiology, 2001. 29(4): p. 278-88. | Mixed caries population; outcome reported not of interest              |
| 174 | Machiulskienė, V.N., Bente; Baelum, Vibeke, Determinants of dropout in a community intervention trial on the caries-preventive effect of chewing gums. Journal of public health dentistry, 2002. 62(1): p. 21-7. | Mixed caries population                                               |
| 175 | Makinen, K.K.H., P. P.; Bennett, C. A.; Isokangas, P.; Isotupa, K.; Pape, H. R., Jr.; Makinen, P. L., A descriptive report of the effects of a 16-month xylitol chewing-gum programme subsequent to a 40-month sucrose gum programme. Caries Research, 1998. 32(2): p. 107-12. | Cannot construct 2x2 table; outcome was only measured in the experimental group |
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| 177 | Marinho, V., Fluoride gel inhibits caries in children who have low caries-risk but this may not be clinically relevant. Evidence-based dentistry, 2004. 5(4): p. 95. | Commentary                                                            |
| 178 | Marks, R.G.C., A. J.; Moorhead, J. E.; Cancro, L.; D'Agostino, R. B., Results from a three-year caries clinical trial comparing NaF and SMFP fluoride formulations. International dental journal, 1994. 44(3 Suppl 1): p. 275-85. | Intervention not of interest                                          |
| 179 | Mattos-Silveira, J.F., Isabela; Ferreira, Fernanda R.; Viganò, Maria E. F.; Frizzo, M. A.; Reyes, Alessandra; Novaes, Tatiane F.; Moriyama, Caroline M.; Raggio, Daniela P.; Imparato, Jose C. P.; Mendes, Fausto M.; Braga, Mariana M., New proposal of silver diamine fluoride use in arresting proximal caries: study protocol for a randomized controlled trial. Trials, 2014. 15: p. 448. | Study still in progress                                               |
| 180 | Mattos-Silveira, J.F., I.; Ferreira, F. R.; Viganò, M. E. F.; Frizzo, M. A.; Reyes, A.; Novaes, T. F.; Moriyama, C. M.; Raggio, D. P.; Imparato, J. C. P.; Mendes, F. M.; Braga, M. M., New proposal of silver diamine fluoride use in arresting proximal caries: Study protocol for a randomized controlled trial. Trials, 2015: p. no pagination. | Protocol                                                              |
| Reference | Outcome or Intervention Reported Not of Interest |
|-----------|-------------------------------------------------|
| 181. Mehta, A.P., Ganesh; Chugh, Vinay Kumar; Singh, Surjit; Halkai, Sudha; Kumar, Santosh, *Effect of light-curable fluoride varnish on enamel demineralization adjacent to orthodontic brackets: an in-vivo study*. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2015. 148(5): p. 814-20. | Outcome reported not of interest (incidence) |
| 182. Memarpour, M.F., Ebrahim; Dadanein, Shorangize; Vossoughi, Mehrdad, *Efficacy of fluoride varnish and casein phosphopeptide-amorphous calcium phosphate for remineralization of primary teeth: a randomized clinical trial*. Medical principles and practice : international journal of the Kuwait University, Health Science Centre, 2015. 24(3): p. 231-7. | Outcome reported not of interest |
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| 184. Milgrom, P.L., Kiet A.; Tut, Ohnmar K.; Mancl, Lloyd; Roberts, Marilyn C.; Briand, Kennan; Gancio, Mary Jane, *Xylitol pediatric topical oral syrup to prevent dental caries: a double-blind randomized clinical trial of efficacy*. Archives of pediatrics & adolescent medicine, 2009. 163(7): p. 601-7. | Outcome reported not of interest (incidence) |
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| 187. Mishra, R.T., Shobha; Rathore, Monika; Banerjee, Molay, *Antimicrobial Efficacy of Probiotic and Herbal Oral Rinses against Candida albicans in Children: A Randomized Clinical Trial*. International journal of clinical pediatric dentistry, 2016. 9(1): p. 25-30. | Only surrogate outcomes were reported |
| 188. Mohan, P.V.M.U.U., K. S.; Vinay, C.; Rao, R. Chandrasekhar, *In vivo comparison of cavity disinfection efficacy with APF gel, Propolis, Diode Laser, and 2% chlorhexidine in primary teeth*. Contemporary clinical dentistry, 2016. 7(1): p. 45-50. | Outcome reported not of interest |
| 189. Molina, M.X.R., F. G.; Urbina, T.; Vargas, S., *Effect of weekly mouthrinses with 0.2% neutral NaF solution on caries incidence in first permanent molars*. Efecto de enjuagatorios semanales con una solucion neutra de NaF al 0.2% en la incidencia de caries en primeros molares definitivos, 1989. 37(1): p. 176-82. | Outcome reported not of interest (incidence) |
| 190. Monse, B.H.-W., Roswiita; Mulder, Jan; Holmgren, Christopher; van Palenstein Helderman, Wim H., *Caries preventive efficacy of silver diammine fluoride (SDF) and ART sealants in a school-based daily fluoride toothbrushing program in the Philippines*. BMC oral health, 2012. 12: p. 52. | Outcome reported not of incidence |
| 191. Morgan, M.V.A., G. G.; Bailey, D. L.; Tsao, C. E.; Fischman, S. L.; Reynolds, E. C., *The anticariogenic effect of sugar-free gum containing CPP-ACP nanocomplexes on approximal caries determined* Used CPP-ACP gum; intervention not commercially available in the United States. | |
| ID | Reference                                                                 | Status/Annotation                                                                 |
|----|---------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| 192 | Muller-Bolla, M.L.-P., Laurence; Bardakjian, Hrant; Velly, Ana M., Effectiveness of school-based dental sealant programs among children from low-income backgrounds in France: a pragmatic randomized clinical trial. Community Dentistry and Oral Epidemiology, 2013. 41(3): p. 232-41. | Outcome reported not of interest (incidence)                                      |
| 193 | Munjal, D.G., Shalini; Dhindsa, Abhishek; Sidhu, Gagandeep Kaur, Sethi, Harsimran Singh, Assessment of White Spot Lesions and In-Vivo Evaluation of the Effect of CPP-ACP on White Spot Lesions in Permanent Molars of Children. Journal of clinical and diagnostic research : JCDR, 2016. 10(5): p. ZC149-54. | Not a randomized controlled trial                                                 |
| 194 | Naidu, S.T., Shobha; Nayak, Rashmi; Ratnanag, P. Venkat; Prajapati, Deepesh; Kamath, Namitha, Efficacy of Concomitant Therapy with Fluoride and Chlorhexidine Varnish on Remineralization of Incipient Lesions in Young Children. International journal of clinical pediatric dentistry, 2016. 9(4): p. 296-302. | Interventions not clearly stated; concentrations, brand, and manufactures names are not reported |
| 195 | Nascimento, M.M., The combined use of chlorhexidine and fluoride therapy can reduce the risk for dental caries. The journal of evidence-based dental practice, 2013. 13(3): p. 123-4. | Review article                                                                  |
| 196 | Nemes, J.B., J.; Wierzbicka, M.; Rost, M., Clinical study on the effect of amine fluoride/stannous fluoride on exposed root surfaces. The Journal of clinical dentistry, 1992. 3(2): p. 51-3. | Outcome reported not of interest                                                  |
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| 198 | Nordstrom, A.B., D., Preventive effect of high-fluoride dentifrice (5,000 ppm) in caries-active adolescents: a 2-year clinical trial. Caries Research, 2010. 44(3): p. 323-31. | Cannot construct 2x2 table; authors only reports mean lesion progression          |
| 199 | Nowjack-Raymer, R.E.S., R. H.; Kingman, A.; Driscoll, W. S., The prevalence of dental fluorosis in a school-based program of fluoride mouthrinsing, fluoride tablets, and both procedures combined. Journal of public health dentistry, 1995. 55(3): p. 165-70. | Outcome reported not of interest (incidence)                                      |
| 200 | Ogaard, B.A., A. Alzelius; Larsson, E.; Adolffson, U., A prospective, randomized clinical study on the effects of an amine fluoride/stannous fluoride toothpaste/mouthrinse on plaque, gingivitis and initial caries lesion development in orthodontic patients. European journal of orthodontics, 2006. 28(1): p. 8-12. | Outcome reported not of interest (incidence)                                      |
| 201 | Ogaard, B.L., E.; Glans, R.; Henriksson, T.; Birkhed, D., Antimicrobial effect of a chlorhexidine-thymol varnish (Cervitec) in orthodontic patients. A prospective, randomized clinical trial. Journal of orofacial orthopedics = Fortschritte der Kieferorthopadie : Organ/official journal Deutsche Gesellschaft fur Kieferorthopadie, 1997. 58(4): p. 206-13. | Cannot construct 2x2 table; authors reported prevalence                          |
| 202 | Ogaard, B.L., E.; Henriksson, T.; Birkhed, D.; Bishara, S. E., Effects of combined application of antimicrobial and fluoride varnishes in orthodontic patients. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its | Outcome reported not of interest (incidence)                                      |
| Citation                                                                 | Description                                      |
|------------------------------------------------------------------------|--------------------------------------------------|
| 203. O'Keefe E. 10% chlorhexidine varnish did not reduce caries in an adult population. Evidence-based dentistry 2012;13(2):45. | Commentary                                      |
| 204. Oliveira, B.H.S., M.; Carvalho, D. M.; Falcao, A.; Campos, K.; Nadanovsky, P., Biannual fluoride varnish applications and caries incidence in preschoolers: a 24-month follow-up randomized placebo-controlled clinical trial. Caries Research, 2014. 48(3): p. 228-36. | Mixed caries population; outcome reported not of interest |
| 205. Olivier, M.B., J. M.; Simard, P. L., Efficacy of APF treatments without prior toothcleaning targeted to high-risk children. Community Dentistry and Oral Epidemiology, 1992 20(1): p. 38-42. | Mixed caries population; outcome reported not of interest (incidence) |
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| 207. Oscaron, P.L.H., P.; Sjostrom, I.; Twelman, S.; Stecksen-Blicks, C., Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children. European archives of paediatric dentistry : official journal of the European Academy of Paediatric Dentistry, 2006. 7(3): p. 142-7. | Mixed caries population |
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| 210. Paraskevas, S.D., M. M.; Timmerman, M. F.; van der Velden, U.; van der Weijden, G. A., Amine fluoride/stannous fluoride and incidence of root caries in periodontal maintenance patients. A 2 year evaluation. Journal of clinical periodontology, 2004. 31(11): p. 965-71. | Intervention not of interest |
| ID   | Author(s)                                                                 | Title                                                                                                                                  | Details                                                                                           |
|------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| 211  | Pardi, V.P.; Antonio Carlos; Ambrosano, Glaucia Maria Bovi; Meneghim, Marcelo de Castro | Clinical evaluation of three different materials used as pit and fissure sealant: 24-months results. The Journal of clinical pediatric dentistry, 2005. 29(2): p. 133-7. | Outcome reported not of interest (incidence)                                                      |
| 212  | Paschos, E.K., Natascha; Huth, Karin C.; Hansson, Claia S.; Rudzki-Janson, Ingrid | Failure rate of brackets bonded with antimicrobial and fluoride-releasing, self-etching primer and the effect on prevention of enamel demineralization. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2009. 135(5): p. 613-20. | Outcome reported not of interest (incidence)                                                      |
| 213  | Pearce, E.I.C., E. W.; Suckling, G. W.                                   | Stability of fluoride levels in surface layer of normal enamel during a 21-month fluoride mouthrinsing program. Community Dentistry and Oral Epidemiology, 1980. 8(8): p. 396-400. | Cannot construct 2x2 table; authors did not clearly state which teeth had initial lesions at baseline |
| 214  | Peng, B.P., Poul Erik; Bian, Zhuan; Tai, Baojun; Jiang, Han                | Can school-based oral health education and a sugar-free chewing gum program improve oral health? Results from a two-year study in PR China. Acta Odontologica Scandinavica, 2004. 62(6): p. 328-32. | Mixed caries population; outcome reported not of interest (incidence)                            |
| 215  | Perrini, F.L.; Luca; Arreghini, Angela; Medori, Silvia; Siciliani, Giuseppe | Caries prevention during orthodontic treatment: In-vivo assessment of high-fluoride varnish to prevent white spot lesions. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2016. 149(2): p. 238-43. | Outcome reported not of interest (incidence)                                                      |
| 216  | Peters Mc, T.F.N.M.D.W.B.S.C.,                                            | Resin infiltration effects in caries-active environment [abstract]. Proceedings of the General Session of the International Association for Dental Research:, 2013: p. Abstract. | Abstract                                                                                          |
| 217  | Petersson LGM, K.; Andersson, H.; Almqvist, B.; Twetman, S.                | Effect of quarterly treatments with a chlorhexidine and a fluoride varnish on approximal caries in caries-susceptible teenagers: a 3-year clinical study. Caries Research 2000;34(2):140-3. | Outcome reported not of interest (incidence)                                                      |
| 218  | Petersson, L.G.M., Kerstin; Hakestam, Ulf; Baigi, Amir; Twetman, Svante    | Reversal of primary root caries lesions after daily intake of milk supplemented with fluoride and probiotic lactobacilli in older adults. Acta Odontologica Scandinavica, 2011. 69(6): p. 321-7. | Cannot construct 2x2 table                                                                      |
| 219  | Pitchika, V.K., Claudia J.; Andreeva, Jana; Crispin, Alexander; Hickel, Reinhard; Kuhnisch, Jan; Heinrich-Weltzien, Roswitha | Effectiveness of a new fluoride varnish for caries prevention in pre-school children. The Journal of clinical pediatric dentistry, 2013. 38(1): p. 7-12. | Not a randomized controlled trial                                                               |
| 220  | Plonka, K.A.P., M. L.; Holcombe, T. F.; Barnett, A. G.; Walsh, L. J.; Seow, W. K. | Randomized controlled trial: a randomized controlled clinical trial comparing a remineralizing paste with an antibacterial gel to prevent early childhood caries. Pediatric Dentistry, 2013. 35(1): p. 8-12. | Outcome reported not of interest (incidence)                                                      |
| 221  | Pomarico, L.V.; Michele; Maia, Lucianne Cople                            | In vivo effect of titanium tetrafluoride and sodium monofluorophosphate dentifrice on remineralization: a preliminary split-mouth clinical trial. General Dentistry, 2012. 60(4): p. e249-54. | Intervention not of interest                                                                     |
| Reference                                                                 | Description                                                                 | Outcome or Intervention |
|--------------------------------------------------------------------------|-----------------------------------------------------------------------------|-------------------------|
| Poulsen S, B.N.S.N., A comparison of retention and the effect on caries of fissure sealing with a glass-ionomer and a resin-based sealant. Community Dentistry and Oral Epidemiology, 2001. 29(4): p. 298. | | Outcome reported not of interest (incidence and retention) |
| Powell, K.R.B., P. D.; Craig, G. G., Effect of stannous fluoride treatments on the progression of initial lesions in approximal surfaces of permanent posterior teeth. Journal of Dental Research, 1981. 60(9): p. 1648-54. | Used SnF₂ dentifrice; intervention not commercially available in the United States |
| Powell, L.V.P., R. E.; Kiyak, H. A.; Hujoel, P. P., Caries prevention in a community-dwelling older population. Caries Research, 1999. 33(5): p. 333-9. | | Outcome reported not of interest (incidence) |
| Pukallus, M.L.P., Kathryn A.; Barnett, Adrian G.; Walsh, Laurence J.; Holcombe, Trevor F.; Seow, W. Kim. A randomised, controlled clinical trial comparing chlorhexidine gel and low-dose fluoride toothpaste to prevent early childhood caries. International Journal of Paediatric Dentistry, 2013. 23(3): p. 216-24. | Mixed caries population; outcome reported not of interest (incidence) |
| Pukallus, M.L.P.; Barnett, Adrian G.; Walsh, Laurence J.; Seow, W. Kim. A randomized controlled trial of a 10 percent CPP-ACP cream to reduce mutans streptococci colonization. Pediatric Dentistry, 2013. 35(7): p. 550-5. | Mixed caries population; outcome reported not of interest (incidence) |
| Quissell, D.O.B., Lucinda L.; Braun, Patricia A.; Cudei, Diana; Johs, Nikolas; Smith, Vongphone L.; George, Carmen; Henderson, William G.; Albino, Judith. Preventing caries in preschoolers: successful initiation of an innovative community-based clinical trial in Navajo Nation Head Start. Contemporary clinical trials. 2014. 37(2): p. 242-51. | Protocol |
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| Ramos-Gomez, F.J.G., Stuart A.; Featherstone, John D. B.; Hue, Bonnie; Gonzalez-Beristain, Rocío; Santo, William; Martinez, Ed; Weintraub, Jane A., Mother and youth access (MAYA) maternal chlorhexidine, counselling and paediatric fluoride varnish randomized clinical trial to prevent early childhood caries. International Journal of Paediatric Dentistry. 2012. 22(3): p. 169-79. | Mixed caries population |
| Raucci-Neto, W.d.C.-R., Larissa Moreira Spinola; Leprí, Cesar Penazzo; Faraoni-Romano, Juliana Jendiroba; Gomes da Silva, Jaciara Miranda; Palma-Dibb, Regina Guenka, Nd:YAG laser in occlusal caries prevention of primary teeth: a randomized clinical trial. Lasers in Medical Science, 2015. 30(2): p. 761-8. | Outcome reported not of interest (incidence) |
| Ravald, N.B., D., Prediction of root caries in periodontally treated patients maintained with different fluoride programmes. Caries Research, 1992. 26(6): p. 450-8. | Cannot construct 2x2 table; authors did not clearly state the outcome measure by arm |
| Rechmann, P.C., D. A.; Rechmann, B. M. T.; Le, C. Q.; Featherstone, J. D. B., In-vivo occlusal caries prevention by pulsed CO2-laser and fluoride varnish treatment - A clinical pilot study. Lasers in surgery and medicine, 2013. 45(5): p. 302-310. | Outcome reported not of interest (incidence) |
| Reed, M.W.K., J. D., A clinical evaluation of a sodium fluoride dentifrice. Pharmacology and Therapeutics in Dentistry, 1975. 2(2): p. 77-82. | Intervention not of interest |
| Rekola, M., Changes in buccal white spots during 2-year consumption of dietary sucrose or xylitol. Acta Odontologica Scandinavica, 1986. 44(5): p. 285-90. | Not a randomized controlled trial |
| 235. | Restrepo, M.B., Diego G.; Jeremias, Fabiano; Cordeiro, Rita C. L.; Magalhaes, Ana C.; Palomari Spolidorio, Denise M.; Santos-Pinto, Lourdes. Control of white spot lesion adjacent to orthodontic bracket with use of fluoride varnish or chlorhexidine gel. *TheScientificWorldJournal*, 2015. 2015: p. 218452. | Not a randomized controlled trial |
| 236. | Restrepo MB, D. G.; Jeremias, F.; Cordeiro, R. C. L.; Raveli, D. B.; Magalhaes, A. C.; Candolo, C.; Santos-Pinto, L. Control of White Spot Lesions with Use of Fluoride Varnish or Chlorhexidine Gel During Orthodontic Treatment A Randomized Clinical Trial. *The Journal of clinical pediatric dentistry* 2016;40(4):274-80. | White spot lesions were artificially induced |
| 237. | Restrepo, M.J., Fabiano; Santos-Pinto, Lourdes; Cordeiro, Rita C; Zuanon, Angela Cc. Effect of Fluoride Varnish on Enamel Remineralization in Anterior Teeth with Molar Incisor Hypomineralization. *The Journal of clinical pediatric dentistry*, 2016. 40(3): p. 207-10. | Method to diagnose lesion is not acceptable |
| 238. | Reynolds, E.C.C., F.; Shen, P.; Walker, G. D., Retention in plaque and remineralization of enamel lesions by various forms of calcium in a mouthrinse or sugar-free chewing gum. *Journal of Dental Research*, 2003. 82(3): p. 206-11. | Review article |
| 239. | Reynolds, E.C.C., F.; Cochrane, N. J.; Shen, P.; Walker, G. D.; Morgan, M. V.; Reynolds, C., Fluoride and casein phosphopeptide-amorphous calcium phosphate. *Journal of Dental Research*, 2008. 87(4): p. 344-8. | Review article |
| 240. | Ripa, L.W.L., G. S.; Sposato, A.; Rebich, T., Supervised weekly rinsing with a 0.2 percent neutral NaF solution: final results of a demonstration program after six school years. *Journal of public health dentistry*, 1983. 43(1): p. 53-62. | Not a randomized controlled trial |
| 241. | Ritter, A.V.B., J. D.; Leo, M. C.; Preisser, J. S.; Shugars, D. A.; Vollmer, W. M.; Amaechi, B. T.; Holland, J. C., Tooth-surface-specific effects of xylitol: randomized trial results. *Journal of Dental Research*, 2013. 92(6): p. 512-7. | Outcome reported not of interest (incidence) |
| 242. | Robertson, M.A.K.; Chung How; English, Jeryl D.; Lee, Robert P.; Powers, John; Nguyen, Jennifer T., *MI Paste Plus to prevent demineralization in orthodontic patients: a prospective randomized controlled trial*. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2011. 140(5): p. 660-8. | Cannot construct 2x2 table; authors did not separate data for each type of tooth |
| 243. | Rodrigues, C.R.M.D.M.; Marcela; Barros, Lucia Pereira; Grande, Rosa Helena Miranda; Myaki, Silvio Issao; Kabakura, Viviane; Miyamura, Adriana, Effect of chlorhexidine-thymol varnish on caries lesion development in first permanent molars. *The Journal of clinical dentistry*, 2008. 19(1): p. 18-21. | Outcome reported not of interest (incidence) |
| 244. | Rodriguez, G.R., B.; Faleiros, S.; Vistoso, A.; Marro, M. L.; Sanchez, J.; Urzua, I.; Cabello, R., Probiotic Compared with Standard Milk for High-caries Children: A Cluster Randomized Trial. *Journal of Dental Research*, 2016. 95(4): p. 402-7. | Mixed caries population |
| 245. | Rollings, S.G.; Louise; Borrie, Felicity; Lamont, Thomas, Small trial finds beneficial effect for MI Paste in preventing white spot lesions during orthodontic treatment. Evidence-based dentistry, 2012. 13(4): p. 117-8. | Commentary |
| 246. | Ruiken, R.T., G. J.; Konig, K.; Vogels, A.; van ’t Hof, M., Clinical cariostatic effectiveness of a NaF rinse in a low prevalence child population. Community | Mixed caries population |
| Page | Reference                                                                 | Notes                                                                                   |
|------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 57-9 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Cannot construct 2x2 table; only one arm of study is of interest                           |
| 92   | Santos, V.E.d., Jr.; Vasconcelos Filho, Arnoldo; Targino, Andrea Gadelha Ribeiro; Flores, Miguel Angel Pelagio; Galembeck, Andre; Caídas, Arnaldo Franca, Jr.; Rosenblatt, Aronita, A new "silver-bullet" to treat caries in children--nano silver fluoride: a randomised clinical trial. Journal of Dentistry, 2014. 42(8): p. 945-51. | Used nano silver fluoride; intervention not commercially available in the United States   |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Cannot construct 2x2 table; only one arm of study is of interest                           |
| 269-278 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest                                                          |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | All study participants were not randomized                                                |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | All study participants were not randomized                                                |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Cannot construct 2x2 table                                                               |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Method to diagnose lesion is not acceptable                                               |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest (incidence)                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest (incidence)                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest (incidence)                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest (incidence)                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest (incidence)                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Outcome reported not of interest (incidence)                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Mixed caries population                                                                  |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Review article                                                                          |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Commentary                                                                              |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Authors did not clearly state baseline caries status of each group at baseline            |
| 358-67 | Santamaria, R.M.I., N. P. T.; Machiulskiene, V.; Evans, D. J. P.; Splieth, C. H., Caries management strategies for primary molars: 1-yr randomized control trial results. Journal of Dental Research, 2014. 93(11): p. 1062-9. | Mixed caries population                                                                  |
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| **ECC in Urban China.** The Chinese journal of dental research: the official journal of the Scientific Section of the Chinese Stomatological Association (CSA), 2016. 19(1): p. 55-63. |                                                                                               |
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| 262. Sim, C.P.C.W., Joseph; Xu, Ying; Cheung; Yin-Bun; Soong, Yoke-Lim; Manton, David J., Anti-caries effect of CPP-ACP in irradiated nasopharyngeal carcinoma patients. Clinical Oral Investigations, 2015. 19(5): p. 1005-11. | Cannot construct 2x2 table; inconsistencies in the total number of lesions                   |
| 263. Singh, S.S., Satinder Pal; Goyal, Ashima; Utreja, Ashok Kumar; Jena, Ashok Kumar, Effects of various remineralizing agents on the outcome of post-orthodontic white spot lesions (WSLs): a clinical trial. Progress in orthodontics, 2016. 17(1): p. 25. | Method to diagnose lesion is not acceptable                                                    |
| 264. Sinha, N.G., A.; Logani, A., Shah, N., Remineralizing efficacy of silver diamine fluoride and glass ionomer type VII for their proposed use as indirect pulp capping materials - Part II (A clinical study). Journal of conservative dentistry : JCD, 2011. 14(3): p. 233-6. | Co-intervention not of interest                                                               |
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| 266. Sithisettapong, T.D., Takashi; Nishida, Yuhei; Kambara, Masaki; Phantumvanit, Prathip, Effect of CPP-ACP Paste on Enamel Carious Lesion of Primary Upper Anterior Teeth Assessed by Quantitative Light-Induced Fluorescence: A One-Year Clinical Trial. Caries Research, 2015. 49(4): p. 434-41. | Method to diagnose lesion is not acceptable                                                    |
| 267. Sjogren, K.B., D.; Rangmar, B., Effect of a modified toothpaste technique on proximal caries in preschool children. Caries Research, 1995. 29(6): p. 435-41. | Outcome reported not of interest (incidence)                                                  |
| 268. Skold, L.S., B.; Eriksson, B.; Edeland, C., Four-year study of caries inhibition of intensive Duraphat application in 11-15-year-old children. Community Dentistry and Oral Epidemiology, 1994. 22(1): p. 8-12. | Outcome reported not of interest                                                              |
| 269. Skold UML, A. M.; Rasmussson, C. G.; Birkhed, D.; Klock, B. Caries incidence in adolescents with low caries prevalence after cessation of weekly fluoride rinsing. Acta Odontologica Scandinavica 2001;59(2):69-73. | Authors did not clearly report study design used and randomization                            |
| 270. Skold-Larsson, K.S., Ola; Peterson, Lars G.; Twetman, Svante, Effect of topical applications of a novel chlorhexidine-thymol varnish formula on mutans streptococci and caries development in occlusal fissures of permanent molars. The Journal of clinical dentistry, 2009. 20(7): p. 223-6. | Outcome reported not of interest (incidence)                                                  |
| 271. Slade, G.D.B., Ross S.; Roberts-Thomson, Kaye; Leach, Amanda J.; Raye, Iris; Endean, Colin; Simmons, Bruce; Morris, Peter, Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial. Community Dentistry and Oral Epidemiology, 2011. 39(1): p. 29-43. | Mixed caries population                                                                       |
| 272. Sonesson, M.T., Svante; Bondemark, Lars, Effectiveness of high-fluoride toothpaste on enamel remineralization during orthodontic treatment a | Outcome reported not of interest (incidence)                                                  |
| Study Reference | Summary or Evidence | Notes |
|-----------------|---------------------|-------|
| 273. Souza MLRC, J. A.; Tenuta, L. M. A.; Zhang, Y. P.; Mateo, L. R.; Cummins, D.; Ellwood, R. P. | Comparing the efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride to a dentifrice containing 1450 ppm fluoride alone in the management of primary root caries. Journal of Dentistry 2013;41 Suppl 2:S35-41. | Used 1.5% arginine gel plus 1450 ppm dentifrice; intervention not commercially available in the United States. |
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| 275. Spets-Happonen, S.L., H.; Forss, H.; Kentala, J.; Alaluusua, S.; Luoma, A. R.; Gronroos, L.; Syväoja, S.; Tapaninen, H.; Happonen, P. | Effects of a chlorhexidine-fluoride-strontium rinsing program on caries, gingivitis and some salivary bacteria among Finnish schoolchildren. Scandinavian Journal of Dental Research, 1991. 99(2): p. 130-8. | Mixed caries population. |
| 276. Spiketh, C.S.H.B., Christine; Alkilzy, Mohammad; Treuner, Anja. | Efficacy of semiannual topical fluoride application in schoolchildren. Quintessence international (Berlin, Germany : 1985), 2011. 42(9): p. 753-60. | Mixed caries population. |
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| 281. Stecksen-Blicks, C.H., Pernilla Li; Twetman, Svante, Effect of xylitol and xylitol-fluoride lozenges on approximal caries development in high-caries-risk children. International Journal of Paediatric Dentistry, 2008. 18(3): p. 170-7. | Outcome reported not of interest. |
| 282. Stecksen-Blicks, C.R., G.; Oscaron, N. D.; Bergstrand, F.; Twetman, S. | Caries-preventive effectiveness of a fluoride varnish: a randomized controlled trial in adolescents with fixed orthodontic appliances. Caries Research, 2007. 41(6): p. 455-9. | Cannot construct 2x2 table; authors reported mean caries progression. |
| 283. Suetenkov, D.Y.P., A. P.; Khantonova, T. L. | Photo activated disinfection efficiency of low-intensity laser and comprehensive prevention of caries and gingivitis in adolescents using bracket system. Journal of Innovative Optical Health Sciences, 2015. 8(3): p. no pagination. | Outcome reported not of interest (incidence). |
| 284. Sundell, A.L.U., Christer; Koch, Goran, Evaluation of preventive programs in high caries active preschool children. Swedish dental journal, 2013. 37(1): p. 23-9. | Outcome reported not of interest (incidence). |
| Id | Reference                                                                 | Description                                                                 |
|----|---------------------------------------------------------------------------|------------------------------------------------------------------------------|
| 285 | Suwansingha, O.R., Praphasri, Effect of fluoride varnish on caries prevention of partially erupted permanent molar in high caries risk. The Southeast Asian journal of tropical medicine and public health, 2012. 43(3): p. 808-13. | Outcome reported not of interest (incidence)                                |
| 286 | Symington, J.M.P., Ross; Kumar, Ashish; Schiff, Robert, Efficacy of a 10% chlorhexidine coating to prevent caries in at-risk community-dwelling adults. Acta Odontologica Scandinavica, 2014. 72(7): p. 497-501. | Outcome reported not of interest (incidence)                                |
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| 289 | Tang, L.S., L.; Yuan, S.; Lv, J.; Lu, H., Effectiveness of 3 different methods in prevention of dental caries in permanent teeth among children. Shanghai kou qiang yi xue = Shanghai journal of stomatology, 2014. 23(6): p. 736-739. | Outcome reported not of interest (incidence)                                |
| 290 | Tapias, M.A.D.M, G.; Jimenez-Garcia, R.; Gonzalez, A.; Dominguez, V., Incidence of caries in an infant population in Mostoles, Madrid. Evaluation of a preventive program after 7.5 years of follow-up. International Journal of Paediatric Dentistry, 2001. 11(6): p. 440-6. | Not a randomized controlled trial                                           |
| 291 | ten Cate, J.M.C., D., Fluoride toothpaste containing 1.5% arginine and insoluble calcium as a new standard of care in caries prevention. The Journal of clinical dentistry, 2013. 24(3): p. 79-87. | Review article                                                              |
| 292 | Tickle, M.M., Keith M.; Donaldson, Michael; Killough, Seamus; O’Neill, Ciaran; Crealey, Grainne; Sutton, Matthew; Noble, Solveig; Greer, Margaret; Worthington, Helen V., Protocol for Northern Ireland Caries Prevention in Practice Trial (NIC-PiP) trial: a randomised controlled trial to measure the effects and costs of a dental caries prevention regime for young children attending primary care dental services. BMC oral health, 2011. 11: p. 27. | Protocol                                                                   |
| 293 | Tolvanen, M.L., Satu; Poutanen, Raija; Seppa, Lisa; Pohjola, Vesha; Hauser, Hannu, Changes in children’s oral health-related behavior, knowledge and attitudes during a 3.4-yr randomized clinical trial and oral health-promotion program. European Journal of Oral Sciences, 2009. 117(4): p. 390-7. | Review article                                                              |
| 294 | Torell, P.G., P. O., Fortnightly fluoride rinsing combined with topical painting of fluoride solutions containing Al-, Fe-, and Mn-ions. Scandinavian Journal of Dental Research, 1977. 85(1): p. 38-40. | Outcome reported not of interest (incidence)                                |
| 295 | Toumba, K.J.C., M. E. J., A clinical trial of a slow-releasing fluoride device in children. Caries Research, 2005. 39(3): p. 195-200. | Mixed caries population                                                      |
| 296 | Truin, G.-J.v.t.H., Martin, The effect of fluoride gel on incipient carious lesions in a low-carries child population. Community Dentistry and Oral Epidemiology, 2007. 35(4): p. 250-4. | Cannot construct 2x2 table                                                  |
| 297 | Truin, G.J.v.t.H., M. A., Caries prevention by professional fluoride gel application on enamel and dentinal lesions in low-carries children. Caries Research, 2005. 39(3): p. 236-40. | Cannot construct 2x2 table                                                  |
| 298 | Tsao, C.E.M., M. V., Does chewing sucrose-free chewing gum after meals reduce the development of carious lesions? Medical Journal of Australia, 2005. 182(2): p. 85-86. | Critical summary                                                            |
| Reference | Description | Notes |
|-----------|-------------|-------|
| 299. Tufekci, E.P., Daniel R.; Mitchell, John C.; Best, Al M.; Lindauer, Steven J., Efficacy of a fluoride-releasing orthodontic primer in reducing demineralization around brackets: an in-vivo study, American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2014. 146(2): p. 207-14. | Outcome reported not of interest (incidence) | |
| 300. Twetman, S.P., L.G., Interdental caries incidence and progression in relation to mutans streptococci suppression after chlorhexidine-thymol varnish treatments in schoolchildren. Acta Odontologica Scandinavica, 1999. 57(3): p. 144-8. | Not a randomized controlled trial | |
| 301. Twetman, S.S.-B., Christina, Effect of xylitol-containing chewing gums on lactic acid production in dental plaque from caries active pre-school children. Oral health & preventive dentistry, 2003. 1(3): p. 195-9. | Not a randomized controlled trial | |
| 302. Ueberschar, M.G., H., [Root caries incidence with regular use of AmF/SnF2 mouth rinse]; Wurzelkaries-Inzidenz unter AmF/SnF2-Mundspulung., 1991. 46(8): p. 566-8. | Intervention not of interest | |
| 303. Unal, M.O., F.; Kapdan, A.; Durer, S., A comparative clinical study of three fissure sealants on primary teeth: 24-month results. The Journal of clinical pediatric dentistry, 2015. 39(2): p. 113-9. | Outcome reported not of interest (incidence) | |
| 304. Uysal, T.A., Mihri; Ozcan, Suat; Koyuturk, Alp Erdin; Sagdic, Deniz, Effect of antibacterial monomer-containing adhesive on enamel demineralization around orthodontic brackets: an in-vivo study. American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics, 2011. 139(5): p. 650-6. | Outcome reported not of interest (incidence) | |
| 305. van der Kaaij, N.C.W.v.d.V., Monique H.; van der Kaaij, Marleen A. E.; ten Cate, Jacob M., A prospective, randomized placebo-controlled clinical trial on the effects of a fluoride rinse on white spot lesion development and bleeding in orthodontic patients. European Journal of Oral Sciences, 2015. 123(3): p. 186-93. | Intervention not of interest | |
| 306. Vashisht, R.I., Rajamani; Ramachandran, S.; Kumar, Anil; Srinivasan, Manali Ramakrishnan, Role of casein phosphopeptide amorphous calcium phosphate in remineralization of white spot lesions and inhibition of Streptococcus mutans? Journal of conservative dentistry : JCD, 2013. 16(4): p. 342-6. | Method to diagnose lesion is not acceptable | |
| 307. Vermaire, J.H.P., J. H. G.; van Herwijnen, L.; van Loveren, C., A three-year randomized controlled trial in 6-year-old children on caries-preventive strategies in a general dental practice in the Netherlands. Caries Research, 2014. 48(6): p. 524-33. | Mixed caries population | |
| 308. Vivaldi-Rodrigues, G.D., Carina Faleiros; Bowman, S. Jay; Ramos, Adisson L., The effectiveness of a fluoride varnish in preventing the development of white spot lesions. World journal of orthodontics, 2006. 7(2): p. 138-44. | Outcome reported not of interest (incidence) | |
| 309. Vogel, G.L., RE: Shen P, Cai F, Nowicki A, Vincent J, Reynolds EC (2001). Remineralization of enamel subsurface lesions by sugar-free chewing gum containing phosphopeptide-amorphous calcium phosphate. J Dent Res 80:2066-2070. Journal of Dental Research, 2002. 81(4): p. 228. | Letter to the Editor | |
| 310. Vollmer, W.M.P., Athena S.; Bader, James D.; Maupome, Gerardo; Gullion, Christina M.; Hollis, Jack F.; Snyder, John J.; Fellows, Jeffrey L.; Laws, Reesa L.; White, B. Alexander; Pacs Collaborative Protocol | |

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| Reference | Title | Abstract/Outcome |
|-----------|-------|-----------------|
| 311. Vrbic V, K.B.R.C., | Caries reduction after topical application of 4% NaF-P sub 4. Three years’ study. | Outcome reported not of interest (incidence) |
| 312. Vrbic V, K.B.R.C., | A 3 year study among Yugoslavian schoolchildren on caries reduction after topical application of 4% NaF-P sub 4. | Outcome reported not of interest (incidence) |
| 313. Wang, J.-x.Y., Yan; Wang, Xiu-jing, | Clinical evaluation of remineralization potential of casein phosphopeptide amorphous calcium phosphate nanocomplexes for enamel decalcification in orthodontics. | Outcome reported not of interest |
| 314. Wang, L.J., J.; Lu, H. F., | Efficiency of resin infiltration versus fluoride varnish for treatment of post-orthodontic white spot lesions. | Outcome reported not of interest |
| 315. Weinstein, P.S., C.; Milgrom, P., | Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition. | Cannot construct 2x2 table; authors only reported incidence |
| 316. Weintraub, J.A.R.-G., F.; Jue, B.; Shani, S.; Hoover, C. I.; Featherstone, J. D. B.; Gansky, S. A., | Fluoride varnish efficacy in preventing early childhood caries. | Outcome reported not of interest (incidence) |
| 317. Weiss, M.W., J.; Muller-Hartwich, R.; Meier, B.; Jost-Brinkmann, P. G., | Chlorhexidine in cleft lip and palate patients with multibracket appliances. Results of a prospective study on the effectiveness of two different chlorhexidine preparations in a cleft lip and palate patients with multibracket appliances. | Outcome reported not of interest (incidence) |
| 318. Wicht M.J. | Arresting root caries: Chlorhexidine-containing varnishes vs sealing therapy. (ORCA abstract). | Abstract |
| 319. Wicht, M.J.H., Rainer; Lummert, Daniel; Noack, Michael J., | Treatment of root caries lesions with chlorhexidine-containing varnishes and dentin sealants. | Cannot construct 2x2 table |
| 320. Wong, M.C.M.L., K. F.; Lo, E. C. M., | Bayesian analysis of clustered interval-censored data. | Statistical methods paper |
| 321. Wong, M.C.M.L., K. F.; Lo, Edward C. M., | Analysis of multilevel grouped survival data with time-varying regression coefficients. | Statistical methods paper |
| 322. Wright, W.T., Stephen; Anopa, Yulia; McIntosh, Emma; Wu, Olivia; Conway, David I.; Macpherson, Lorna M. D.; McMahon, Alex D., | Comparison of the caries-protective effect of fluoride varnish with treatment as usual in nursery school attendees receiving preventive oral health support through the Childsmile oral health improvement programme - the Protecting Teeth@3 Study: a randomised controlled trial. | Protocol |
| Entry | Title | Abstract/Remarks |
|-------|-------|------------------|
| 323. | Xhemnica, L.S.; D.; Roico, R.; Hysi, D. | Fluoride varnish application: a new prophylactic method in Albania. Effect on enamel carious lesions in permanent dentition. European journal of paediatric dentistry: official journal of European Academy of Paediatric Dentistry, 2008. 9(2): p. 93-6. Outcome reported not of interest (incidence) |
| 324. | Xu, X.L.; Ji Yao; Zhou, Xue Dong; Xie, Qian; Zhan, Ling; Featherstone, John D. B. | Randomized controlled clinical trial on the evaluation of bacteriostatic and cariostatic effects of a novel povidone-iodine/fluoride foam in children with high caries risk. Quintessence international (Berlin, Germany: 1985), 2009. 40(3): p. 215-23. Interventions not clearly stated; concentrations not reported |
| 325. | Yang, G.L.; Ju Hong; Wang, Jin-Hua; Jiang, Lin. | [Evaluation of the clinical effect of fluoride varnish in preventing caries of primary teeth]. Hua xi kou qiang yi xue za zhi = Huaxi kouqiang yixue zazhi = West China journal of stomatology, 2008. 26(2): p. 159-61. Outcome reported not of interest (incidence) |
| 326. | Yazicioglu, O.U. | The investigation of non-invasive techniques for treating early approximal carious lesions: an in vivo study. International dental journal, 2014. 64(1): p. 1-11. Cannot construct 2x2 table; authors only reported statistical significance among treatment and control group |
| 327. | Yin, W.H.; Fan, X.; Zhang, Y. P.; Cummins, D.; Mateo, L. R.; Pretty, I. A.; Ellwood, R. P. | A clinical investigation using quantitative light-induced fluorescence (QLF) of the anticaries efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride as sodium monofluorophosphate. The Journal of clinical dentistry, 2013. 24 Spec no A: p. A15-22. Method to diagnose lesion is not acceptable |
| 328. | Yin, W.H.; Li, X.; Fan, X.; Zhang, Y. P.; Pretty, I. A.; Mateo, L. R.; Cummins, D.; Ellwood, R. P. | The anti-caries efficacy of a dentifrice containing 1.5% arginine and 1450 ppm fluoride as sodium monofluorophosphate assessed using Quantitative Light-induced Fluorescence (QLF). Journal of Dentistry, 2013. 41 Suppl 2: p. S22-8. Method to diagnose lesion is not acceptable |
| 329. | Zanata, R.L.N.; Maria Fidelia de Lima; Pereira, Jose Carlos; Franco, Eduardo Batista; Lauris, Jose Roberto P.; Barbosa, Silvia Helena | Effect of caries preventive measures directed to expectant mothers on caries experience in their children. Brazilian Dental Journal, 2003. 14(2): p. 75-81. Outcome reported not of interest (incidence) |
| 330. | Zhan, L.C.; Chang, P.; Ngo, M.; Denbesten, P. K.; Hoover, C. I.; Featherstone, J. D. B. | Effects of xylitol wipes on cariogenic bacteria and caries in young children. Journal of Dental Research, 2012. 91(7 Suppl): p. 85S-90S. Outcome reported not of interest (incidence) |
| 331. | Zhang, D.Z.; Peng, H.; Sun, H. | Casein phosphopeptide-amorphous calcium phosphate nanocomplexes as a preventive agent for radiation caries and dental sensitivity in irradiated head and neck cancer patients. Chinese Journal of Clinical Oncology, 2014. 41(20): p. 1293-1296. Outcome reported not of interest (incidence) |
| 332. | Zhang, Q.v.t.H. | Caries-inhibiting effect of chlorhexidine varnish in pits and fissures. Journal of Dental Research, 2006. 85(5): p. 469-72. Outcome reported not of interest (incidence) |
| 333. | Zhi, Q.H.L.; Edward Chin Man; Lin, Huan Cai | Randomized clinical trial on effectiveness of silver diamine fluoride and glass ionomer in arresting dentine caries in preschool children. Journal of Dentistry, 2012. 40(11): p. 962-7. Intervention of not interest; soft decayed tissue was removed |
| 334. | Zhou, Z.Z. | Effects of topical application of immunoglobulin yolk on mutans streptococci in dental plaque, Hua xi kou qiang yi xue za zhi = Huaxi kouqiang yixue zazhi = West China journal of stomatology, 2003. 21(4): p. 295-7. Mixed caries population |
| 335. Zielinska, R.D.P., D.; Ostrowska, A.; Boltacz-Rzepkowska, E., The evaluation of caries lesion progression after infiltration with a low-viscous resin: In vivo study. Dental and Medical Problems, 2016. 53(3): p. 358-364. | Could not translate article to English |
| --- | --- |
| 336. Zimmer, S.B., M.; Seemann, R.; Witzke, S.; Roulet, J. F., The effect of a preventive program, including the application of low-concentration fluoride varnish, on caries control in high-risk children. Clinical Oral Investigations, 2001. 5(1): p. 40-4. | Outcome reported not of interest (incidence) |
| 337. Zingler, S.P., Maria; Wrede, Dirk J.; Ludwig, Bjorn; Bister, Dirk; Kneist, Susanne; Lux, Christopher J., A randomized clinical trial comparing the impact of different oral hygiene protocols and sealant applications on plaque, gingival, and caries index scores. European journal of orthodontics, 2014. 36(2): p. 150-63. | Outcome reported not of interest (incidence) |
| 338. Zotti, F.L., L.; Fontana, P.; Dalessandri, D.; Bonetti, S., Effects of fluorotherapy on oral changes caused by a vegan diet. Minerva Stomatologica, 2014. 63(5): p. 179-88. | Cannot construct 2x2 table; authors reported the net white spot lesions at follow up |
APPENDIX FIGURE 2. Risk of bias of included studies.
APPENDIX TABLE 3. Grade assessments for each network meta-analysis.

Root Network

| Treatment 1 | Treatment 2 | Risk of bias | Inconsistency | Indirectness | Publication bias | Direct Preliminary Rating | Imprecision | Direct Final Rating |
|-------------|-------------|--------------|---------------|--------------|-----------------|--------------------------|-------------|--------------------|
| 1% chlorhexidine + 1% thymol varnish | 38% SDF solution | - | - | - | - | - | - | - |
| 1% chlorhexidine + 1% thymol varnish | 38% SDF solution + potassium iodide | - | - | - | - | - | - | - |
| 1% chlorhexidine + 1% thymol varnish | 5% NaF varnish | - | - | - | - | - | - | - |
| 1% chlorhexidine + 1% thymol varnish | 5,000 ppm F (1.1% NaF) toothpaste or gel | - | - | - | - | - | - | - |
| 1% chlorhexidine + 1% thymol varnish | No treatment | Serious | None | None | Undetected | Moderate | Very Serious | Very Low |
| 38% SDF solution | 38% SDF solution + potassium iodide | Serious | None | None | Undetected | Moderate | Very Serious | Very Low |
| 38% SDF solution | 5% NaF varnish | - | - | - | - | - | - | - |
| 38% SDF solution | 5,000 ppm F (1.1% NaF) toothpaste or gel | - | - | - | - | - | - | - |
| 38% SDF solution | No treatment | Serious | None | None | Undetected | Moderate | Very Serious | Very Low |
| 38% SDF solution + potassium iodide | 5% NaF varnish | - | - | - | - | - | - | - |
| 38% SDF solution + potassium iodide | 5,000 ppm F (1.1% NaF) toothpaste or gel | - | - | - | - | - | - | - |
| 38% SDF solution + potassium iodide | No treatment | Serious | None | None | Undetected | Moderate | Very Serious | Very Low |
| 5% NaF varnish | 5,000 ppm F (1.1% NaF) toothpaste or gel | - | - | - | - | - | - | - |
| 5% NaF varnish | No treatment | Serious | None | None | Undetected | Moderate | Very Serious | Very Low |
| 5,000 ppm F (1.1% NaF) toothpaste or gel | No treatment | Serious | Serious | None | Undetected | Low | None | Low |
### Root Network (cont.)

| Common Comparator | Tmt 1 vs common comparator rating | Middle comparison | Tmt 2 vs common comparator rating | Lowest of them | Intransitivity | Indirect Preliminary Rating | Imprecision | Indirect Final Rating | Highest between direct and indirect | Starting Rating | Incoherence | Imprecision | Network rating final |
|--------------------|----------------------------------|-------------------|----------------------------------|----------------|---------------|--------------------------|-------------|--------------------------|---------------------------------|----------------|------------|------------|---------------------|
| No Treatment       | Moderate                         | Moderate          | Moderate                         | Not serious    | Moderate      | Very serious            | Very low    | Indirect                 | Moderate           | N/A          | Very Serious | Very Low             |
| No Treatment       | Moderate                         | Moderate          | Moderate                         | Not serious    | Moderate      | Very serious            | Very low    | Indirect                 | Moderate           | N/A          | Very Serious | Very Low             |
| No Treatment       | Moderate                         | Moderate          | Moderate                         | Not serious    | Moderate      | Very serious            | Very low    | Indirect                 | Moderate           | N/A          | Very Serious | Very Low             |
| No Treatment       | Moderate                         | Low               | Low                              | Not serious    | Low           | Serious                 | Very low    | Indirect                 | Low               | N/A          | Serious     | Very Low             |
| -                  | -                                | -                 | -                                | -              | -             | -                       | -           | Direct                   | Moderate           | N/A          | Very Serious | Very Low             |
| No Treatment       | Moderate                         | Moderate          | Moderate                         | Not serious    | Moderate      | Very serious            | Very low    | Indirect                 | Moderate           | N/A          | Very Serious | Very Low             |
| No Treatment       | Moderate                         | Low               | Low                              | Not serious    | Low           | Serious                 | Very low    | Indirect                 | Low               | N/A          | Very Serious | Very Low             |
| -                  | -                                | -                 | -                                | -              | -             | -                       | -           | Direct                   | Moderate           | N/A          | Very Serious | Very Low             |
| No Treatment       | Moderate                         | Low               | Low                              | Not serious    | Low           | Very serious            | Very low    | Indirect                 | Low               | N/A          | Very Serious | Very Low             |
| -                  | -                                | -                 | -                                | -              | -             | -                       | -           | Direct                   | Moderate           | N/A          | Very Serious | Very Low             |

Legend:
- Direct: Moderate
- Indirect: Moderate
- Network rating final: Very Low
Approximal Network

| Comparison                  | Direct Evidence |
|-----------------------------|-----------------|
|                            | Risk of bias    | Inconsistency | Indirectness | Publication bias | Preliminary Rating | Imprecision | Direct Final Rating |
| Treatment 1                | Treatment 2     |                |              |                  |                  |             |                    |
| 5% NaF varnish             | Resin Infiltration | -             | -            | -                | -                | -           | -                   |
| 5% NaF varnish             | Resin Infiltration + 5% NaF varnish | Serious | None | None | Undetected | Moderate | Very Serious | Very Low |
| 5% NaF varnish             | Sealant         | Serious       | None         | None             | Undetected       | Moderate    | Very Serious | Very Low |
| 5% NaF varnish             | No treatment    | -             | -            | -                | -                | -           | -                   |
| Resin Infiltration         | Resin Infiltration + 5% NaF varnish | - | - | - | - | - | - |
| Resin Infiltration         | Sealant         | Serious       | None         | None             | Undetected       | Moderate    | Very Serious | Very Low |
| Resin Infiltration         | No treatment    | Serious       | Serious      | None             | Undetected       | Low         | None       | Low |
| Resin Infiltration + 5% NaF varnish | Sealant         | -             | -            | -                | -                | -           | -                   |
| Resin Infiltration + 5% NaF varnish | No treatment | -             | -            | -                | -                | -           | -                   |
| Sealant                    | No treatment    | Serious       | Serious      | None             | Undetected       | Low         | None       | Low |
### Approximal Network (cont.)

| Common Comparator(s) | Tmt 1 vs common comparator rating | Tmt 2 vs common comparator rating | Lowest of them | Intransitivity | Indirect Preliminary Rating | Imprecision | Indirect Final Rating | Highest between direct and indirect | Starting Rating | Incoherence | Imprecision | Network rating final |
|----------------------|----------------------------------|----------------------------------|----------------|---------------|-----------------------------|-------------|-----------------------|-------------------------------------|----------------|-------------|-------------|---------------------|
| Sealant              | Moderate                         | Moderate                         | Not serious    | Moderate      | Very Serious                | Very Low    |                       | Direct                              | Moderate        | N/A          | Very Serious  | Very Low            |
| -                    | -                                | -                                | -              | -             | -                           | -           |                       | Direct                              | Moderate        | N/A          | Very Serious  | Very Low            |
| Sealant              | Moderate                         | Low                              | Not serious    | Low           | Very Serious                | Very Low    |                       | Indirect                            | Low             | N/A          | Very Serious  | Very Low            |
| Sealant, 5% NaF varnish | Moderate                        | Moderate                         | Moderate       | Not serious   | Moderate                    | Very Serious| Very Low              | Indirect                            | Moderate        | N/A          | Very Serious  | Very Low            |
| No treatment         | Moderate                         | Low                              | Not serious    | Low           | Very Serious                | Very Low    |                       | Direct                              | Moderate        | Not serious | Very Serious  | Very Low            |
| Sealant              | Moderate                         | Low                              | Not serious    | Low           | Very Serious                | Very Low    |                       | Direct                              | Moderate        | Not Serious | Serious      | Low                 |
| 5% NaF varnish       | Moderate                         | Moderate                         | Not serious    | Low           | Very Serious                | Very Low    |                       | Indirect                            | Low             | N/A          | Very Serious  | Very Low            |
| 5% NaF varnish, Sealant | Moderate                       | Moderate                         | Not serious    | Low           | Very Serious                | Very Low    |                       | Indirect                            | Low             | N/A          | Very Serious  | Very Low            |
| Resin Infiltration   | Moderate                         | Moderate                         | Not Serious    | Moderate      | Very Serious                | Very Low    |                       | Direct                              | Low             | Not serious | None         | Low                 |
### Occlusal Network

| Comparison | Direct Evidence |
|------------|----------------|
| Treatment 1 | Treatment 2 | Risk of bias | Inconsistency | Indirectness | Publication bias | Preliminary Rating | Imprecision | Direct Final Rating |
| 0.2% NaF mouthrinse | 1.23% APF gel | - | - | - | - | - | - | - |
| 0.2% NaF mouthrinse | 5% NaF varnish | Serious | None | None | Undetected | Moderate | Serious | Low |
| 0.2% NaF mouthrinse | 5% NaF varnish + Resin Infiltration | - | - | - | - | - | - | - |
| 0.2% NaF mouthrinse | Sealant | Serious | None | None | Undetected | Moderate | Serious | Low |
| 0.2% NaF mouthrinse | No treatment | - | - | - | - | - | - | - |
| 1.23% APF gel | 5% NaF varnish | - | - | - | - | - | - | - |
| 1.23% APF gel | 5% NaF varnish + Resin Infiltration | - | - | - | - | - | - | - |
| 1.23% APF gel | 5% NaF varnish + Sealant | - | - | - | - | - | - | - |
| 1.23% APF gel | Sealant | - | - | - | - | - | - | - |
| 1.23% APF gel | No treatment | - | - | - | - | - | - | - |
| 5% NaF varnish | 5% NaF varnish + Resin Infiltration | Serious | None | None | Undetected | Moderate | Serious | Low |
| 5% NaF varnish | 5% NaF varnish + Sealant | Serious | None | None | Undetected | Moderate | None | Moderate |
| 5% NaF varnish + Resin Infiltration | Sealant | Serious | None | None | Undetected | Moderate | None | Moderate |
| 5% NaF varnish + Resin Infiltration | No treatment | Serious | None | None | Undetected | Moderate | None | Moderate |
| 5% NaF varnish + Resin Infiltration | Sealant | - | - | - | - | - | - | - |
| 5% NaF varnish + Sealant | No treatment | - | - | - | - | - | - | - |
| Sealant | No treatment | Serious | None | None | Undetected | Moderate | None | Moderate |
## Occlusal Network (cont.)

| Common Comparator(s) | Tmt 1 vs common comparator rating | Middle comparison | Tmt 2 vs common comparator rating | Lowest of them | Intraneveness | Indirect Preliminary Rating | Imprecision | Indirect Final Rating | Highest between direct and indirect | Starting Rating | Incoherence | Imprecision | Network rating final |
|----------------------|----------------------------------|------------------|---------------------------------|----------------|--------------|---------------------------|-------------|--------------------------|-------------------------------|----------------|------------|------------|---------------------|
| Sealant, No treatment| Moderate                         | Moderate         | Moderate                         | Moderate       | Not serious  | Moderate                  | Serious     | Low                      | Indirect                     | Moderate       | N/A        | Serious    | Low                  |
| Sealant              | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Very serious| Very low             | Direct                        | Moderate       | Not serious | Serious    | Low                  |
| 5% NaF varnish       | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Indirect                     | Moderate       | N/A        | Not serious | Moderate             |
| 5% NaF varnish       | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Very serious| Very low             | Direct                        | Moderate       | Not serious | Serious    | Low                  |
| Sealant              | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Indirect                     | Moderate       | N/A        | Not serious | Moderate             |
| No treatment         | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Serious     | Low                      | Indirect                     | Moderate       | N/A        | Serious    | Low                  |
| No treatment, 5% NaF varnish | Moderate | Moderate         | Moderate                         | Moderate       | Not serious  | Moderate                  | Serious     | Low                      | Indirect                     | Moderate       | N/A        | Serious    | Low                  |
| No treatment, 5% NaF varnish | Moderate | Moderate         | Moderate                         | Moderate       | Not serious  | Moderate                  | Serious     | Low                      | Indirect                     | Moderate       | N/A        | Serious    | Low                  |
| No treatment         | Moderate                         | Moderate         | Moderate                         | Moderate       | Not serious  | Moderate                  | Serious     | Low                      | Indirect                     | Moderate       | N/A        | Serious    | Low                  |
| 5% NaF varnish + Sealant | Moderate | Moderate         | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Direct                        | Moderate       | Not serious | Not serious | Moderate             |
| 5% NaF varnish + Sealant | Moderate | Moderate         | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Direct                        | Moderate       | N/A        | Not serious | Moderate             |
| Sealant              | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Direct                        | Moderate       | Not serious | Not serious | Moderate             |
| 5% NaF varnish       | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Serious     | Low                      | Direct                        | Moderate       | Not serious | Serious    | Low                  |
| 5% NaF varnish       | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Indirect                     | Moderate       | N/A        | Not serious | Moderate             |
| 5% NaF varnish       | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Indirect                     | Moderate       | N/A        | Not serious | Moderate             |
| 5% NaF varnish       | Moderate                         | -                | Moderate                         | Moderate       | Not serious  | Moderate                  | Not serious | Moderate              | Indirect                     | Moderate       | N/A        | Not serious | Moderate             |
### Any surface Network (noncavitated)

#### Comparison

| Treatment 1 | Treatment 2 | Risk of bias | Inconsistency | Indirectness | Publication bias | Preliminary Rating | Imprecision | Direct Final Rating |
|-------------|-------------|--------------|---------------|--------------|------------------|-------------------|-------------|---------------------|
| 1.23% APF gel | 10% CPP-ACP Paste | - | - | - | - | - | - | - |
| 1.23% APF gel | 5% NaF varnish | - | - | - | - | - | - | - |
| 1.23% APF gel | No treatment | Serious | None | None | Undetected | Moderate | None | Moderate |
| 10% CPP-ACP Paste | 5% NaF varnish | - | - | - | - | - | - | - |
| 10% CPP-ACP Paste | No treatment | Serious | None | None | Undetected | Moderate | Serious | Low |
| 5% NaF varnish | No treatment | Serious | None | None | Undetected | Moderate | None | Moderate |

#### Indirect Evidence

| Common Comparator(s) | Tmt 1 vs common comparator rating | Middle comparison | Tmt 2 vs common comparator rating | Lowest of them | Intransitivity | Indirect Preliminary Rating | Imprecision | Indirect Final Rating | Highest between direct and indirect | Starting Rating | Incoherence | Imprecision | Network rating final |
|-----------------------|----------------------------------|-------------------|----------------------------------|----------------|---------------|-----------------------------|-------------|------------------------|-------------------------------|----------------|-------------|---------------|-------------------|
| No treatment          | Moderate                         | -                 | Moderate                         | Moderate       | Not serious   | Moderate                    | Not serious | Moderate               | Indirect                     | Moderate       | N/A         | Not serious   | Moderate          |
| No treatment          | Moderate                         | -                 | Moderate                         | Moderate       | Not serious   | Moderate                    | Serious     | Low                   | Indirect                     | Moderate       | N/A         | Serious       | Low               |
| No treatment          | Moderate                         | -                 | Moderate                         | Moderate       | Not serious   | Moderate                    | Not serious | Moderate               | Indirect                     | Moderate       | N/A         | Not serious   | Moderate          |
| -                     | -                                | -                 | -                                | -              | -             | -                           | -           | -                     | Direct                       | Moderate       | N/A         | None          | Moderate          |
| -                     | -                                | -                 | -                                | -              | -             | -                           | -           | -                     | Direct                       | Moderate       | N/A         | None          | Moderate          |

#### Network

| Highest between direct and indirect | Starting Rating | Incoherence | Imprecision | Network rating final |
|------------------------------------|-----------------|-------------|-------------|----------------------|
| Indirect                           | Moderate        | N/A         | Not serious  | Moderate             |
| Indirect                           | Moderate        | N/A         | Serious     | Low                  |
| Direct                             | N/A             | None        | Moderate     |                      |
| Direct                             | N/A             | None        | Serious     | Low                  |
| Direct                             | N/A             | None        | None        | Moderate             |

### Any surface Network (noncavitated) (cont.)
APPENDIX FIGURE 3: Network meta-analysis forest plots.
**APPENDIX TABLE 4.** Relative Risks (95% CIs) and Certainty in the Evidence for Nonrestorative treatments for the Arrest or reversal of moderate cavitated carious lesions (ICDAS 3 and 4) on Any Coronal Surface (12- to 20-mo Follow-up)

| Study: *n / n*, Surface, Follow-up | Study Arm (Dose, Duration, Frequency) | Relative Risks (95% CI), Certainty in the Evidence |
|-----------------------------------|--------------------------------------|-------------------------------------------------|
| Duangthip et al. (2016), Duangthip, Wong, et al. (2018) | 30% SDF solution (once a year, applied annually) | 30% SDF solution once a year vs. 30% SDF solution once a week, for three weeks: 30 mo, 1.00 (0.82, 1.23); Moderate (Due to serious issues of imprecision) |
| | 30% SDF solution (once a week for three weeks, not applied annually) | 24 mo, 1.03 (0.86, 1.23); Moderate (Due to serious issues of imprecision) |
| | 5% NaF varnish (once a week for three weeks, not applied annually) | 18 mo, 0.94 (0.80, 1.11); Moderate (Due to serious issues of imprecision) |
| | 12 mo, 1.02 (0.89, 1.16); Moderate (Due to serious issues of imprecision) | 12 mo, 1.02 (0.89, 1.17); Moderate (Due to serious issues of imprecision) |
| *n* – 309 people at follow-up, *n* – 649 lesions at longest follow-up | 30% SDF solution once a year vs. 5% NaF varnish once a week, for three weeks: 30 mo, 0.87 (0.71, 1.06); Moderate (Due to serious issues of imprecision) |
| Mixed (occlusal, proximal, facial/lingual) | 24 mo, 0.92 (0.76, 1.11); Moderate (Due to serious issues of imprecision) |
| 6, 12, 18, 24 and 30 mo | 18 mo, 0.89 (0.76, 1.04); Moderate (Due to serious issues of imprecision) |
| | 12 mo, 1.00 (0.87, 1.15); Moderate (Due to serious issues of imprecision) | 30% SDF solution once a week, for three weeks vs. 5% NaF varnish once a week, for three weeks: |
| | 30 mo, 0.86 (0.71, 1.05); Moderate (Due to serious issues of imprecision) | 30 mo, 0.89 (0.75, 1.07); Moderate (Due to serious issues of imprecision) |
| | 24 mo, 0.89 (0.75, 1.07); Moderate (Due to serious issues of imprecision) | 24 mo, 0.89 (0.75, 1.07); Moderate (Due to serious issues of imprecision) |
| | 18 mo, 0.89 (0.76, 1.04); Moderate (Due to serious issues of imprecision) | 18 mo, 0.89 (0.76, 1.04); Moderate (Due to serious issues of imprecision) |
| | 12 mo, 1.00 (0.87, 1.15); Moderate (Due to serious issues of imprecision) | 12 mo, 1.00 (0.87, 1.15); Moderate (Due to serious issues of imprecision) |