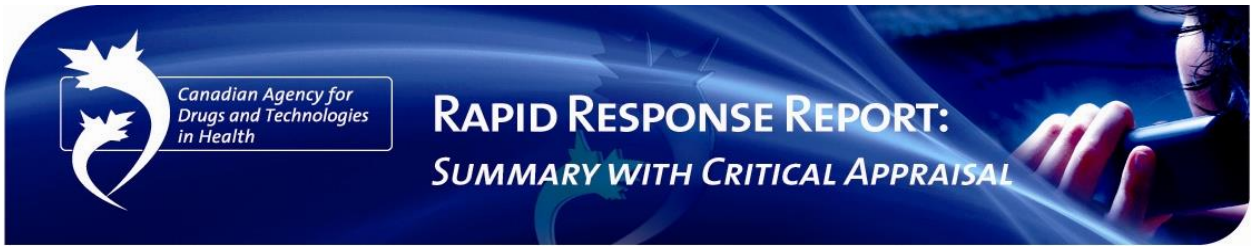

TITLE: Dental Sealants and Preventive Resins for Caries Prevention: A Review of the Clinical Effectiveness, Cost-effectiveness and Guidelines

DATE: 31 October 2016

CONTEXT AND POLICY ISSUES

Pit and fissure sealants were introduced into dental practice as far back as the 1960s.[1] Dental sealants are material that is applied into the pits and fissures of occlusal surfaces of teeth with the intention of preventing new carious lesions.[2,3] The most common materials used as dental sealants are composite resins and glass ionomers.[1,4] Pit and fissure caries account for up to 90% of all carious lesions in permanent teeth.[1,2] Development of carious lesions is multifactorial. Diet composition and bacteria present in dental plaque play a central role in caries development.[3] Sealants work by bonding to the surface of individual teeth and prevent the invasion of bacteria.[2,3] The occlusal surfaces of posterior teeth are favorable surfaces for the development of a bacteria biofilm and therefore are particularly vulnerable to caries formation.[5] There is evidence that supports the efficacy of dental sealants in the prevention of dental caries in children and adolescents. Individual trials and systematic reviews have shown that sealants prevent carious lesions in children and adolescents.[3] In 2008, the Cochrane collaboration conducted a systematic review which found that resin-based pit and fissure sealants applied to the occlusal surfaces of permanent first molars (PFM) was an effective method of preventing carious lesions in children over 54 months compared to no sealant use.[6] It has been suggested that the greatest benefit is realized by children at a high risk for caries development on permanent teeth.[3] A systematic review published in 2011 found that there was no difference in caries prevention effects of glass ionomer compared to composite resin.[7] The use of sealants to prevent caries on primary teeth is controversial and studies have demonstrated mixed results.[2,8]

Methods for optimizing the application of sealants have also been investigated in systematic reviews. Available evidence suggests that thorough tooth cleaning prior to application, tooth isolation and moisture control through the use of use of rubber dams or cotton rolls may improve sealant retention.[2]

Available economic analysis has demonstrated that there may be a cost savings associated with the application of pit and fissure sealants in children and adolescents.[3] Several professional

and governmental organizations have recommended the use of pit and fissure sealants in the prevention of dental caries in children and adolescents.[2,9,10]

The objective of this report is to review the evidence with respect to clinical effectiveness, specifically caries prevention, and cost effectiveness of dental sealants and preventative resins when applied to permanent teeth of children and adolescents.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of dental sealants and preventive resins for caries prevention when applied to permanent teeth in children?

2. What is the comparative clinical effectiveness of dental sealants and preventive resins for different tooth groups (molars, bicuspids, incisors)?

3. What is the cost-effectiveness of dental sealants and preventive resins?

4. What is the comparative cost-effectiveness of dental sealants and preventive resins when applied to different tooth groups?

5. What is the cost-effectiveness of dental sealants and preventive resins when applied at specific times after eruption and compared with no specified time interval?

6. What are the evidence-based guidelines for the use of sealants and preventive resins?

KEY FINDINGS

Three systematic reviews demonstrate that the application of dental sealants to occlusal surfaces of permanent first molars in children and adolescents prevents development of new carious lesions compared to no sealant use. There is evidence that this benefit is maintained up to 9 years. Four randomized controlled trials demonstrated conflicting results with respect to caries prevention of dental sealants compared to no dental sealants in children and adolescents. All four of these randomized controlled trials had a high risk of bias.

One systematic review of economic analyses found that dental sealants are a cost-effective intervention for caries prevention in children and adolescents.

One evidence based clinical practice guideline recommended the use of sealants on permanent molars with sound or non-cavitated occlusal surfaces in children and adolescents compared to no use of sealants. This was a strong recommendation based on moderate quality evidence.

Overall, there is good quality evidence that demonstrates caries reduction when dental sealants are applied to permanent molars in children and adolescents compared to no dental sealant application. This intervention also appears to be cost-effective.

There was no evidence that addressed the clinical or cost effectiveness of dental sealants with respect to different tooth groups or timing of application after tooth eruption.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, ECRI Institute, Canadian and major international health technology agencies, as well as a focused Internet search. Filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic studies and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and September 29, 2016.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to the selection criteria in Table 1.

Table 1: Selection Criteria

Population	Children (age 0 to 14 years) with permanent teeth
Intervention	Dental sealants and preventive resins
Comparator	No dental sealant or preventive resin use
Outcomes	Clinical effectiveness (e.g. caries reduction), cost-effectiveness, guidelines (including indications for use, timing, and tooth placement)
Study Designs	Health Technology Assessments, Systematic Reviews, Meta-analysis Randomized Controlled Trials Non-Randomized Studies Evidence-based Guidelines Economic Evaluations

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria or were published prior to 2011. Articles were also excluded if they were reported as part of an included HTA or systematic review. Evidence-based guidelines were included if they were based on systematic review methodology. Guidelines were excluded if an updated version was available for review.

Critical Appraisal of Individual Studies

Critical appraisal of a study was conducted based on an assessment tool appropriate for the particular study design. The AMSTAR checklist[11] was used to critically appraise the systematic reviews. The Cochrane Collaboration's tool for assessing risk of bias[12] was used to critically appraise the randomized controlled trials. The Newcastle-Ottawa Quality Assessment Scale[13,14] was used for non-randomized trials and the AGREE II instrument for appraisal of guidelines.[15].

For critical appraisal, a numeric score was not calculated. Instead, the strengths and limitations of the study were described.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 394 articles were identified from the electronic literature search and 32 articles from the grey literature search for a total of 426 articles; 51 were selected for full-text screening. Twelve of the full-text publications screened met the inclusion criteria. These represented 10 unique studies.

There were three systematic reviews evaluating clinical outcomes[16-19] and one systematic review of economic analysis,[20] four randomized controlled trials (RCT),[21-25] one non-randomized study,[26] and one evidence based clinical practice guideline that met the inclusion criteria for this report.[27] The systematic review by Wright and colleagues was published in duplicate.[16,17] The RCT by Muller-Bolla and colleagues published 1 year[24] and 3 year[25] clinical outcome data in separate publications.

Appendix 1 describes the PRISMA flowchart of the results of the literature review for this report.

Summary of Study Characteristics

Characteristics of the included systematic reviews, RCTs and non-randomized controlled trials and evidence-based guideline are summarized below. Additional details on the systematic reviews, RCTs and non-randomized study are detailed in Appendix 2 and 3.

<u>Systematic Reviews: Clinical Outcomes</u>

In 2016, Wright and colleagues[16,17] published a systematic review in the USA. The objective of their review was to summarize the evidence of dental sealants in the prevention of pit and fissure occlusal caries of primary and permanent molars in children, adolescents and adults. Comparators were no sealant use, fluoride varnishes, and comparison between sealant types. A total of 23 RCTs published between 1976 and 2016 with a minimum of 2 years' follow-up were included. Nine studies used a parallel design and 14 studies used a split-mouth design. In 19 of the studies sealant was applied to the PFM. Nine of the included studies compared sealant use to no sealant use. The studies in the review included children aged 3 to 16 years. The studies were conducted in a diverse group of countries in North America, Europe, South America and Asia. Children living in areas both with and without water fluoridation were included. The main outcome of this systematic review was caries incidence.

In 2015, Hou and colleagues[18] published a systematic review in China. The objective was to review the evidence for sealants (applied to PFM) in caries prevention. The comparator was no sealant application. A total of 20 RCTs published between 2002 and 2016 were included. Follow-up duration ranged from 6 months to 5 years. The studies included children and adolescents aged 6 to 20 years. The authors did not report details regarding the settings in which the included trials took place. The main outcome was caries prevention at various time points.

In 2013, Ahovuo-Saloranta and colleagues[19] published a systematic review in Finland. The primary objectives of their review were to compare sealant use with no sealant use in the prevention of caries in children and adolescents and to compare different sealant materials to one another. A total of 34 randomized or quasi-randomized studies were included; 13 studies published between 1976 and 2011 compared sealant application to PFM with no sealant application. The studies recruited children from schools and dental clinics and took place in the USA, Canada, Brazil, China, Columbia, New Zealand, Spain, Thailand, Turkey and the UK. The studies included children aged 5 to 10 years. The main outcome was caries prevention.

Systematic Reviews: Economic Outcomes

In 2016, Leo and colleagues[20] published a systematic review of economic evaluations of dental sealants. The objective of their review was to conduct a systematic review of economic evaluations of dental sealants. A total of 15 economic studies published between 1985 and 2012 were included; 13 cost-effectiveness analysis (CEA), 2 cost-benefit analysis (CBA), and one cost-utility analysis (CUA). Included studies were mainly conducted in North America, Western Europe and Australia and included children and adolescents aged 15 months to 20 years.

Randomized Controlled Trials

In 2016, Kalnina and colleagues[22] published a single center RCT in Latvia. The objective of their study was to compare ozone application with fissure sealants or fluoride varnish for the prevention of occlusal caries in permanent pre-molars in children. They compared dental sealant applied to pre-molars (bicuspids) to no sealant, fluoride varnish and ozone. A total of 122 children, all aged 10, were randomized in 2012 and were followed for 12 months. The main study outcome was incidence of caries.

In 2013, Muller-Bolla and colleagues[24,25] published a multi-center RCT with a split-mouth design in Nice, France. The objective of their study was to assess the effectiveness of a school-based dental sealant program in children from low socioeconomic background. They compared dental sealants applied to PFM to no sealant. A split mouth randomization technique was used where one tooth in a pair was randomly assigned to receive sealant and the other no sealant. This design allows for each child to serve as their own control. A total of 276 children with a mean age of 6.4 years were included and followed for up to 3 years. The main study outcomes were new carious lesions.

In 2015, Hilgert and colleagues[23] published a cluster RCT of six public primary schools in low socioeconomic areas (with fluorinated water) of Paranoá, Brazil. They compared composite resin sealants or atraumatic restorative treatment-high-viscosity glass-ionomer cement (ART-GIC) to supervised tooth brushing (STB) in children with PFM occlusal surfaces at high-caries risk. Children with PFM occlusal surfaces at low-caries risk received no intervention or STB. A total of 242 children with a mean age of 6.8 years were included and followed for up to 3 years. The main study outcome was caries prevention on PFM.

In 2012, Monse and colleagues[21] published a RCT of eight public elementary schools in the Philippines. The objective of their study was to compare the effect of a single application of an ART sealant to occlusal surfaces of permanent first molars compared to no treatment in the prevention of caries. A total of 1016 children with a mean age of 6.7 years were followed for up to 18 months. The main study outcome was new caries lesions.

Non-Randomized Study

In 2011, Baldini and colleagues[26] published a retrospective cohort study in Portugal. The objective of their study was to investigate the effectiveness of resin-based sealant and understand the influence of clinical and socioeconomic variable on caries prevention. Children were recruited in 2007 based on dental records from 2005. The dental records from 2005 documented sealant placement on the PFM or no sealant placement. A total of 277 children all born in 1997 were included and reexamined in 2007. Children were stratified into low and high caries risk based on their calculated DMFT+dmft score in 2005. The DMFT score represents the total number of teeth that are decayed, missing or filled in deciduous (primary) teeth (dmft) or permanent (DMFT) teeth. DMFT scores for permanent teeth range from 0 to 28 (or 32 if third molars are included) and dmft scores for primary teeth range from 0 to 20.[28] If the DMFT+dmft score was >0, children were classified as high risk, and if the DMFT+dmft score was = 0, they were classified as low risk. The main study outcome was DMFT increment >0 at 2 years.

Evidence-Based Guidelines

In 2016, the American Dental Association and the American Academy of Pediatric Dentistry published evidence-based clinical practice guidelines for the use of pit-and-fissure sealants.[27] The guideline panel included general and pediatric dentists, dental hygienists and health policy makers. The evidence base to support these guidelines was a systematic review conducted by Wright and colleagues in 2016,[16,17] which is also included in this Rapid Response report. The authors use a GRADE approach to assess the certainty of the evidence supporting their recommendations, which were generated by deliberation and consensus of the guideline panel.

Summary of Critical Appraisal

Strengths and limitations of the systematic reviews, RCTs, non-randomized study and evidence-based guideline are provided in Appendix 4 and 5.

Systematic Reviews: Clinical Outcomes

Overall, two of the systematic reviews were of good quality[16,17,19] and the third was of poor quality.[18] All three of the systematic reviews reported an *a priori* study design and clearly reported their research questions and inclusion criteria. Study selection was performed in duplicate in all three systematic reviews. Data abstraction was reported to be completed independently in duplicate in two of the systematic reviews.[16,17,19] A comprehensive literature search was performed in two of the systematic reviews.[16,17,19] The third systematic review[18] did not report some details of their literature search, such as contacting content experts or reviewing reference lists. One of the systematic reviews reported searching the grey literature.[16,17] One of the systematic reviews reported a comprehensive list of excluded studies[19] the other two did not.[16-18] All three systematic reviews reported a list of included studies and baseline study characteristics.[16-19] The scientific quality of the trials included in each systematic review was assessed, reported and considered when the authors formulated their conclusions in two of the systematic reviews.[16,17,19] Hou et al.[18] did undertake quality assessment of included trials, however, they reported quality as an aggregate assessment only. The methods used to combine study results were appropriate in two of the systematic reviews.[16-18] The third systematic review used a random effects model of data synthesis if four or more studies were included in the analysis and a fixed-effects model if there were fewer than three studies, regardless of the heterogeneity across trials.[19] Publication bias was considered *a priori* as part

of the statistical plan in all three of the systematic reviews.[16-19] However, there were too few studies for publication bias to be reported. Conflicts of interest were reported in two of the systematic reviews.[16,17,19] One systematic review reported conflict of interest for all of the included trials as well.[19] Hou et al.[18] did not report conflicts of interest for either the systematic review or the included studies.

Systematic Reviews: Economic Outcomes

Overall, the systematic review of economic studies[20] was of fair quality. Strengths of this systematic review were an *a priori* study design, clear research questions and inclusion criteria. Study selection and data abstraction were both performed in duplicate. A list of included studies and baseline study characteristics was reported, however, a list of excluded studies was not reported by the authors. Scientific quality of included studies was assessed, reported and considered by the authors when formulating their conclusions. The quality of the included analyses was good based on the Drummond Checklist completed by the authors, specifically in the domains of study design, analysis and interpretation. Conflict of interest was reported for the systematic review, however, it was not reported for any of the included studies. Main limitations of this systematic review were incomplete reporting of the details of the literature search as well as a description of whether the grey literature was searched. The risk of publication bias was not reported.

Randomized Controlled Trials

Overall, all four RCTs had a high risk of bias.[21-25] Three of the four were of poor quality[21-23] and one was of fair quality.[24,25] There was a high risk of selection bias in three of the RCTs.[21-23] The method of randomization and allocation concealment were not reported in two of the RCTs.[22,23] Hilgert[23] assigned two of the schools included in the cluster randomized trial to the sealant group based on availability of a dental unit at the school. Monse and colleagues[21] used a 'lottery system' to assign two schools to the no treatment group and assigned individual students to silver diamine fluoride application or ART sealant based on their number on the class register. Monse and colleagues[21] did not report allocation concealment. Muller-Bolla and colleagues[24,25] randomized participants by using an allocation sequence generated by a block of four. Blinding of study participants is challenging for an intervention such as dental sealants, as they may be visible. Because of this, blinding of the participant was assessed as 'not applicable' in keeping with the risk of bias assessment completed the Cochrane group on the same topic.[19] An attempt at blinding of outcome assessors was reported in one RCT.[21] Monse and colleagues[21] blinded outcome assessors to whether the participant received silver diamine fluoride or was compliant with daily tooth brushing. Outcome assessors were not blinded to the presence of ART sealant. Evaluation of study participants for development of new carious lesions was performed independently by two dentists in one study,[23] radiographically in one study,[22] and by 'eight calibrated examiners' in a third study.[21] The RCT by Muller-Bolla did not report the method of outcome assessment in their study.[24,25]There was a high attrition rate in two of the RCTs[21,23] Approximately one-third of study participants dropped out over a 3-year period in the cluster RCT by Hilgert[23] and colleagues. The attrition rate in the study conducted by Monse and colleagues[21] was also high with approximately one-third of the study population being lost to follow-up at 18 months and unequally distributed across treatment groups. There was a low risk of bias with respect to outcome reporting in all 4 RCTs.

Non-Randomized Study

Overall, the retrospective cohort study[26] was of fair quality. The main strengths of this study were that the included population (both exposed and unexposed) was representative of the population of interest, school aged children with permanent teeth. The exposure was ascertained by review of previous dental records, which is a reasonable method. The children were assessed to ensure that the outcome of interest was not present at the outset of the study. The presence of dental caries was assessed by a trained dentist after a calibration exercise to ensure agreement between assessors. The study follow-up time of two years is a reasonable time frame over which dental caries could develop. The main study limitations were that the cohort was derived from a single center in Latvia and the use of water fluoridation or fluoride as part of routine dental care was not reported. There was poor follow-up over the 2-year study, with less than half (44%) of the initial cohort being reassessed at 2 years. Lastly, it is unclear whether the investigators identified all important confounding variables.

Evidence-Based Guidelines

Overall, the evidence-based guideline was of good quality.[27] The main strengths of this guideline were the good quality systematic review[16,17] that provided the evidence base, the scope and purpose of the guidelines were clearly reported, guideline development included all relevant professional stakeholders and the target audience was clearly defined. The authors reported a clear mechanism for updating the guidelines every five years. The guideline recommendations were clearly and specifically reported, potential resource implications were considered and conflicts of interest and funding sources were reported. The main limitation was the omission of patients or caregivers in guideline development. It is unclear whether these guidelines underwent an independent peer review process.

Summary of Findings

The overall findings are summarized below and details are available in Appendix 6.

Clinical effectiveness of dental sealants and preventive resins for caries prevention when applied to permanent teeth in children

Systematic Reviews

Wright and colleagues demonstrated that after seven or more years of follow-up, application of sealant was associated with a significant reduction in the risk of developing carious lesions on the occlusal surfaces of permanent molars compared to no sealant use. These findings were consistent at the 2 to 3 year follow up and 4 to 7-year follow-up time points as well (Table 2). Hou et al.[18] also demonstrated a significant association between the use of resin-based pit and fissure sealant applied to PFM and caries prevention at 6 months follow-up (odds ratio [OR] 0.06, 95% confidence interval [CI] 0.01 to 0.32, P<0.0001). These findings were consistent at 1-year follow-up (OR 0.10, 95% CI 0.05 to 0.21), 2 years follow-up (OR 0.16, 95% CI 0.09 to 0.26), 3 years follow-up (OR 0.21, 95%CI 0.13 to 0.32), 4 years follow-up (OR 0.18, 95% CI 0.05 to 0.62), and 5 years follow-up (OR 0.28, 95%CI 0.20 to 0.38). Ahovuo-Saloranta and colleagues[19] found that resin based sealant prevented caries on PFM at 2 years follow-up compared to no sealant. These findings were consistent at other follow-up time points up to 9 years (Table 3). Ahovuo-Saloranta and colleagues[19] found one study that compared glass

ionomer sealant compared to no sealant and this comparison did not show a significant difference in decayed, filled permanent surfaces (DFS) at 24 months follow-up, P=0.09.

Table 2. Caries Incidence over 7 years Follow-up in Wright et al.[16,17]

Time Point	# of studies (# participants)	Caries incidence		OR (95% CI)	P-value
		Sealants n/N (%)	No sealant n/N (%)		
2 to 3 years	9 (3542)	194/1799 (10.8)	584/1743(33.5)	0.24 (0.19,0.30)	<0.00001
4 to 7 years	3 (752)	74/368 (20.1)	206/384 (53.6)	0.21 (0.10,0.44)	<0.0001
≥7 years	2 (446)	62/215 (28.8)	170/231 (73.6)	0.15 (0.08, 0.27)	<0.00001

Table 3. Caries Incidence in Resin sealant vs. no sealant in Ahovuo-Saloranta et al.[19]

Time Point	# of studies	OR (95% CI)	P-value
12 months	6	0.16 (0.08,0.30)	<0.00001
24 months	6	0.12 (0.07,0.19)	<0.00001
36 months	7	0.17 (0.11,0.27)	<0.00001
48 to 54 months	4	0.21 (0.16, 0.28)	<0.00001
5 years	1	0.31 (0.23,0.43)	<0.00001
		RR (95% CI)	
6 years	1	0.45 (0.36,0.58)	<0.00001
7 years	1	0.45 (0.34,0.59)	<0.00001
9 years	1	0.35 (0.22,0.55)	<0.0001
OR=odds ratio; **RR**=risk ratio			

Randomized Controlled Trials

Kalnina and colleagues[22] found that sealant application to permanent pre-molars (bicuspids) compared to control (no sealant) did not prevent new caries at 12 months follow-up, 0% vs. 3.5%, P=0.106. Muller-Bolla and colleagues[24,25] found a reduction in new carious lesions on PFM at 1-year follow-up with sealant compared to control (no sealant) (OR 0.26, 95% CI 0.14 to 0.49). These findings were consistent at 3 years follow-up (hazard ratio [HR] 0.38, 95% CI 0.28 to 0.52). Hilgert and colleagues[23] did not find a difference in cavitated dentine lesion-free high risk occlusal surfaces of PFM with either composite resin or high viscosity glass ionomer compared to supervised tooth brushing alone over 3 years of follow-up (P=0.59). Monse and colleagues[21] found a significant reduction in new D3 (enamel or dentin) caries at 18 months with the use of glass ionomer sealant use on PFM compared to non-treated PFM in both those with daily brushing at school (P<0.01) and those without (P<0.001).

Non- Randomized Study

Baldini and colleagues[26] found that at 2 years follow-up there was not a statistically significant difference in the development of a DMFT score >0 between no sealant use and sealant application to the PFM (OR 1.81, 95% CI 0.93 to 3.50, P=0.0767).

Comparative clinical effectiveness of dental sealants and preventive resins for different tooth groups (molars, bicuspids, incisors)

There were no studies identified that met the inclusion criteria to address this question.

Cost-effectiveness of dental sealants and preventive resins

Systematic Reviews

The systematic review of economic evaluations published by Leo et al.[20] in 2016 found that based on the results of 13 CEA, sealant application is cost-effective compared to no sealant use (willingness-to-pay threshold not specified). The two CBA found that the costs (C) of sealants were greater than the benefits (B) in the short term (B/C<1), however, the benefits outweighed the costs (B/C>1) over 10 years. The one CUA included in the systematic review was conducted in the USA and found favorable quality-adjusted tooth years, specifically for mandibular first molars based on the results of a retrospective cohort study of 6 year olds in the USA (Table 4).

Table 4. Cost-utility Analysis[20]

Tooth	Cost per QATY ($USD)
Maxillary PFM tooth 3	439.6
Maxillary PFM tooth 14	322.43
Mandibular PFM tooth 19	193.0
Mandibular PFM tooth 30	201.3
PFM=permanent first molar; **QATY**=quality adjusted tooth year; **USD**=United States Dollar	

Comparative cost-effectiveness of dental sealants and preventive resins when applied to different tooth groups

There were no studies identified that met the inclusion criteria to address this question.

Cost-effectiveness of dental sealants and preventive resins when applied at specific times after eruption and compared with no specified time interval

There were no studies identified that met the inclusion criteria to address this question.

Evidence-based guidelines for the use of sealants and preventive resins

The American Dental Association and the American Academy of Pediatric Dentistry recommends the use of sealants, compared to nonuse of sealants, on both sound occlusal surfaces and non-cavitated occlusal carious lesions on permanent molars of children and

adolescents.[27] This was a strong recommendation based on moderate quality evidence as assessed by the guidelines committee. The guidelines do not recommend one type of sealant material over another. The guidelines panel also commented that sealing permanent molars of children and adolescents is associated with a reduced cost to the health care system as it delays the need for restorative treatment. A formal economic analysis was not undertaken as part of the guidelines.

Limitations

Overall, the main limitation of the body of evidence for the use of dental sealants is the quality and poor reporting of study details. Three systematic reviews addressed the clinical effectiveness of dental sealants in the prevention of new carious lesions in children and adolescents.[16-19] The quality of the RCTs included in two of the systematic reviews was moderate.[16,17,19] Wright and colleagues[16,17] stated in their systematic review that poor quality reporting in individual trials made risk of bias assessment challenging and that allocation concealment was the most under-reported aspect of studies. Hou and colleagues[18] stated that the sample sizes of included trials was small and future research should focus on larger sample sizes and more rigorous trial design. Ahovuo-Saloranta and colleagues[19] also highlighted that one of the limitations of their systematic review was that some of the included trials were published in the 1970s.

The systematic review of economic analysis[20] did not undertake a meta-analysis, but rather provided a narrative description of economic findings of the included trials. The outcome measures used to determine benefit varied considerably across the CEA studies. Additionally, the time horizon over which the benefits of sealants surpass the costs of sealants is unclear.

All of the individual RCTs included in this report had a high risk of bias and poorly reported aspects of quality appraisal.[21-25]

Some authors have postulated that the greatest benefit for the use of sealants would be realized in children at high risk for developing carious lesions.[26] Practically, it can be difficult to identify these children as no validated clinical assessment tool exists to assist with risk stratification.[9,27] Clinically, risk stratification can be completed by a dentist taking into account tooth morphology, radiography, caries history, fluoride history and oral hygiene.[9,29].

Most of the studies included in this report applied sealants on PFM. However, there is a lack of evidence that addresses the comparative clinical or cost effectiveness of dental sealants on other tooth groups. There is also a lack of evidence to support the optimal timing of dental sealant application after tooth eruption. Variations in comparator groups as well as frequency and monitoring of routine dental care such as tooth brushing varied across studies and may lead to decreased generalizability of study results.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Evidence supporting the clinical effectiveness of dental sealants for caries prevention on occlusal surfaces of permanent teeth in children and adolescents has been consistently demonstrated across three systematic reviews.[16-19] The durability of caries prevention is also robust with a reduced risk of caries development compared to no sealant use at up to 9 years of follow-up.[19] Two of the systematic reviews were of good quality and the quality of evidence within these systematic reviews was moderate. The four RCTs included in this report

inconsistently demonstrated caries prevention with the use of dental sealants compared to no dental sealants.[21-25] Possible reasons for inconsistency in the study findings across the RCTs may be due to application of sealant to different tooth groups (PFM vs. bicuspids), different comparators across the studies (no treatment vs. supervised tooth brushing), differences in sealant type or differences in outcome assessment. In comparison to the systematic reviews, these four RCTs represent a smaller portion of the total body of literature addressing the benefit of dental sealants and all had a high risk of bias.

None of the evidence included in this report addressed the optimal timing of sealant application after eruption of permanent teeth. Three of the RCTs reported that included patients were required to have a fully erupted PRM.[21-23] It would be reasonable to postulate that sealant application should be done as early as possible after tooth eruption, prior to the onset of decay. More research is required to better characterize the optimal timing of sealant application on permanent teeth.

The majority of evidence for caries prevention of dental sealants included in this report addressed sealant applied to the occlusal surfaces of PFM. One RCT was included where sealant was applied to permanent pre-molars (bicuspids).[22] This RCT did not find a difference in the incidence of new caries at 12 months' follow-up. No studies were found that compared sealant application in one tooth group to another.

A systematic review of economic analysis[20] found that based on 13 CEA, sealant use compared to no sealant use was cost effective. One CUA found that sealant use on mandibular PFM was associated with the lower cost per quality adjusted tooth year (QATY) compared to maxillary PFM. In two CBA, the benefits begin to outweigh the costs over a long-term time horizon.

An evidence based guideline published in 2016 by the American Dental Association and American Academy of Pediatric Dentistry recommend the use of sealant compared with no use of sealant on sound occlusal surfaces and non-cavitated occlusal carious lesions in permanent molars of children and adolescents.[27] This is a strong recommendation based on moderate evidence. The evidence used to support these clinical practice guidelines is the systematic review published by Wright and colleagues.[16,17] Although the guidelines committee did not undertake a formal economic analysis, they suggest as part of their recommendation that sealing permanent molars of children and adolescents may reduce costs to the health care system.

Overall, dental sealants when applied to PFM have demonstrated consistent and durable benefit for caries prevention in children and adolescents. The majority of sealants used in the studies included in this report were composite resin. Optimal timing of application and clinical efficacy on other tooth groups remains somewhat unclear.

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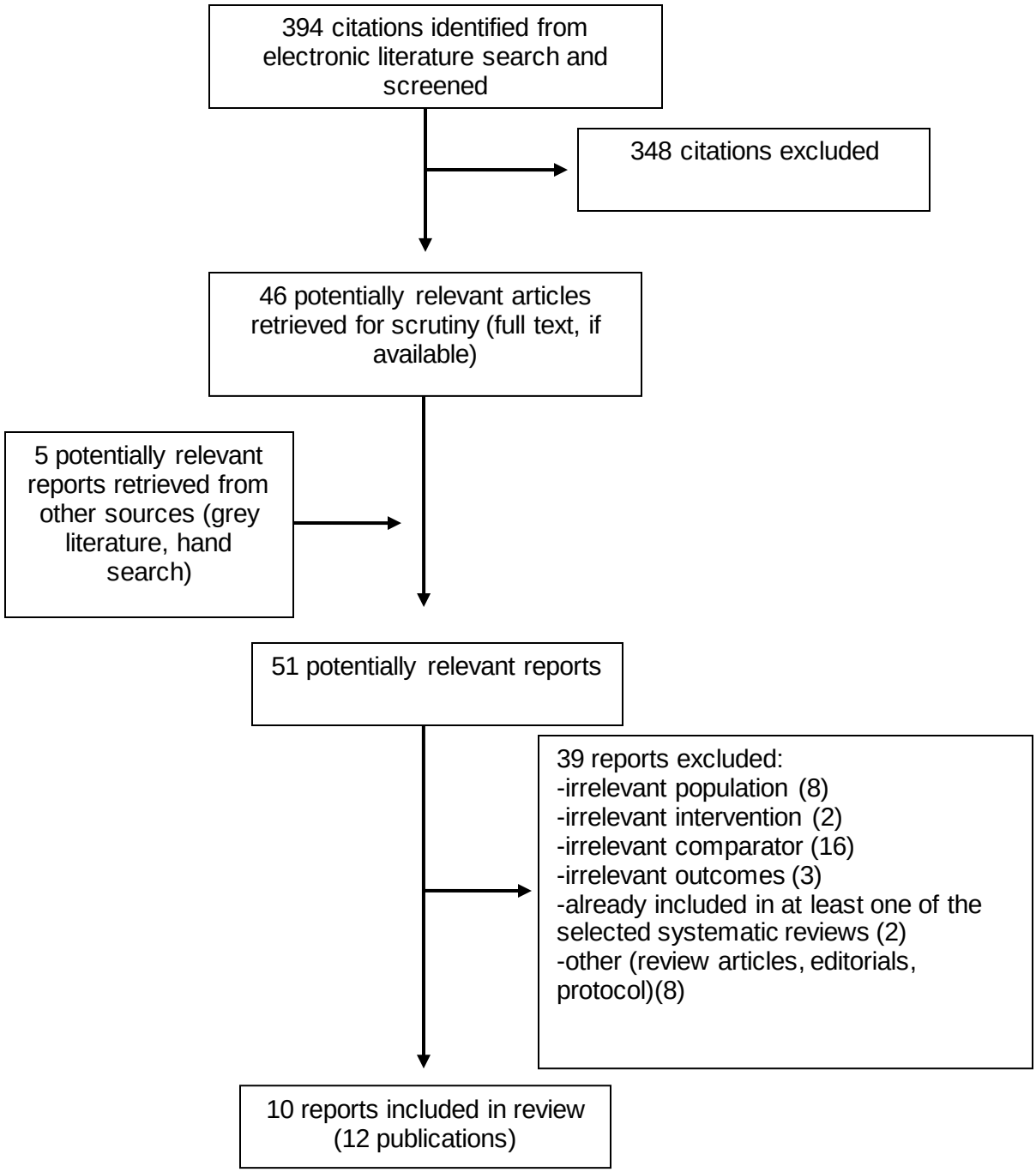
ABBREVIATIONS

AGREE	Appraisal of Guidelines for Research and Evaluation
AMSTAR	A Measurement Tool to Assess Systematic Reviews
ART-GIC	Atraumatic Restorative Treatment High-viscosity glass ionomer cement
CBA	Cost Benefit Analysis
CEA	Cost Effectiveness Analysis
CUA	Cost Utility Analysis
DFS	decayed, filled permanent surfaces
DMFT	decayed, missing or filled permanent teeth
dmft	decayed, missing or filled deciduous teeth
HTA	Health Technology Assessment
OR	Odds Ratio
PFM	Permanent First Molar
QATY	Quality Adjusted Tooth Year
RR	Risk Ratio
STB	Supervised Tooth Brushing
USA	United States of America
UK	United Kingdom

APPENDIX 1: Selection of Included Studies



APPENDIX 2. Characteristics of Included Systematic Reviews

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Clinical Outcomes
Clinical					
Wright,[16,17] 2016, USA	Systematic Review Only RCT included Min follow-up 2 years	n=23 included studies Published between 1976 and 2016 Children aged 3 to 16 years	Sealant 19/23 studies applied to PFM	No sealant Fluoride varnish Other	Caries incidence
Hou,[18] 2015, China	Systematic Review Only RCT included Follow-up: 6 months to 5 years	n=20 included studies Published between 2002 and 2013 Ages 6 to 20 years	Pit and fissure sealant (resin) applied to PFM	No sealant	Caries prevention
Ahovuo-Saloranta,[19] 2013, Finland	Systematic Review Randomized and Quasi-randomized trials included	n=34 included studies, 13 studies compared sealant vs. no sealant Published between 1976 and 2011 Ages 5 to 10 years	Sealant applied to PFM (12 studies used resin, 1 study used glass ionomer)	No sealant	Caries prevention
Economic					
Leo,[20] 2016, Italy	Systematic Review of economic evaluations	n=15 economic analysis 13 CEA 2 CBA 1 CUA Published between 1985 and 2012 Ages 15 months to 22 years	Sealant	No sealant	Cost effectiveness, cost benefit, cost-utility

RCT=randomized controlled trial; **PRM**=permanent first molar; **CEA**=cost effectiveness analysis; **CBA**=cost benefit analysis; **CUA**=cost utility analysis

APPENDIX 3: Characteristics of Included Controlled Trials

First Author, Publication Year, Country	Study Design, Length of Follow-up	Patient Characteristics, Sample Size (n)	Intervention	Comparator(s)	Clinical Outcomes
Randomized studies					
Kalnina,[22] 2016, Latvia	RCT Follow-up: 12 months	n=122 Age 10 years	Sealant applied to pre-molars (bicuspids)	Control (no sealant) Fluoride varnish Ozone	Caries
Muller-Bolla,[24,25] 2013 and 2016, France	split-mouth RCT Follow-up: 3 years	n=276 children from low-income socioeconomic backgrounds Mean Age (SD): 6.4 years (±0.4)	Resin-based sealant applied to PFM n=208 applied in 1st grade n=68 applied in 2nd grade	No sealant	New carious lesions
Hilgert,[23] 2015, Brazil	Cluster RCT Follow-up: 3 years	n=242 children from low socioeconomic areas Mean Age (SD): 6.8 years (±0.4)	Sealant (composite resin or ART-GIC) applied to high-caries risk occlusal surfaces	Daily supervised tooth brushing	Caries prevention on PFM
Monse,[21] 2012, Philippines	RCT Follow-up: 18 months	n=1016 Mean Age (SD): 6.7 years (±0.7)	ART sealant applied to occlusal surface of PFM	Control (no sealant)	New caries
Non-randomized studies					
Baldini,[26] 2011, Portugal	Retrospective Cohort study Follow-up: 2 years	n=277 HR: DMFT+dmft>0 LR: DMFT+dmft=0	Sealant applied to PFM (ART or composite resin)	No sealant	DMFT increment >0

ART-GIC=atraumatic restorative treatment-high-viscosity glass-ionomer cement; **HR**=high risk; **LR**=low risk; **RCT**=randomized controlled trial; **SD**=standard deviation; **PFM**=permanent first molar; **DMFT**=decayed, missing, filled teeth (permanent); **dmft**=decayed, missing, filled teeth (primary)

APPENDIX 4: Critical Appraisal of Included Studies

First Author, Publication Year	Strengths	Limitations
Systematic Reviews (Clinical)		
Wright,[16,17] 2016	• An a priori study design including the research question(s) and inclusion criteria was provided • Duplicate study selection and data abstraction was performed • A comprehensive literature search, including grey literature, was performed • A list of included studies and study characteristics was reported • The scientific quality of included studies was assessed, reported and considered when formulating conclusions • Methods for combining study results were appropriate • Assessment of publication bias was conducted as part of the statistical analysis • Conflict of interests for the authors of the systematic review were stated	• A list of excluded studies was not provided • Potential conflict of interest of included studies was not reported
Hou,[18] 2015	• An a priori study design including the research question(s) and inclusion criteria was provided • Duplicate study selection was performed • A list of included studies and study characteristics was reported • Individual trial quality was taken into consideration when formulating conclusions • Methods for combining study results were appropriate • Assessment of publication bias was conducted as part of the statistical analysis	• It was unclear whether duplicate data abstraction was performed • Unclear whether a comprehensive literature search was performed • Authors do not report searching the grey literature • A list of excluded studies was not provided • The authors undertook quality assessment, but did not report the quality of the individual trials, only aggregate data • Conflict of interest for neither the systematic review nor the included trials was reported
Ahovuo-Saloranta,[19] 2013	• An a priori study design including the research question(s) and inclusion criteria was provided • Duplicate study selection and data abstraction was performed • A comprehensive literature search was performed • A comprehensive list of both included and excluded studies and study characteristics was reported • The scientific quality of included	• It was unclear whether grey literature was searched • It is unclear whether the methods for combining study results were appropriate

First Author, Publication Year	Strengths	Limitations
	studies was assessed, reported and considered when formulating conclusions • Assessment of publication bias was conducted as part of the statistical analysis • Conflict of interests for the systematic review and included studies was reported	
Systematic Reviews (Economic)		
Leo,[20] 2016, Italy	• An a priori study design including the research question(s) and inclusion criteria was provided • Duplicate study selection and data abstraction was performed • A list of included studies and study characteristics was reported • The scientific quality of included studies was assessed, reported and considered when formulating conclusions • Conflict of interests for the authors of the systematic review were stated	• Details provided on the literature search were incomplete • It was unclear whether grey literature was searched • A list of excluded studies was not provided • The risk of publication bias was not assessed • Potential conflict of interest of included studies was not reported
Non-randomized Controlled Studies		
Baldini,[26] 2011	• Exposed and unexposed cohort was representative of population of interest (school aged children with permanent teeth) • Exposure was ascertained by previous dental records • Outcome of interest was not present at beginning of study • Outcome was assessed by a trained dentist and calibration exercises were undertaken • Follow-up (2 years) was long enough for the outcomes to occur	• Cohort was derived from a single center in Latvia and use of fluoride was not reported • It is unclear whether investigators controlled for important confounding variables • Less than half (44%) the initial cohort was reassessed at 2 years
Evidence-based Guidelines		
ADA, 2016[27]	• Scope and purpose of the guidelines are specifically described • Guideline development included all relevant professional stakeholders • Target audience for the guidelines is clearly defined • A rigorous methodology (systematic review) was used to	• Patients or caregivers were not included in guideline development • The guidelines do not report having gone under an independent peer review process

First Author, Publication Year	Strengths	Limitations
	search for relevant evidence, strength and limitations of the evidence are described, methods for formulating recommendations were clearly reported • A procedure is in place for updating the guidelines every 5 years • Recommendations are clear and specific • Potential resource implications of the recommendations have been considered and reported • Conflict of interest and funding sources have been reported	

APPENDIX 5: Critical Appraisal of Included Randomized Controlled Trials

First Author, Publication Year	Random sequence generation	Allocation Concealment	Blinding of participants	Blinding of outcome assessment	Incomplete Outcome Data	Selective Reporting
Kalnina,[22] 2016	H	H	NA	H	L	L
Muller-Bolla,[24,25] 2013 and 2016	L	L	NA	H	L	L
Hilgert,[23] 2015	H	H	NA	H	H	L
Monse,[21] 2012	H	H	NA	L	H	L

L=low risk of bias H=high risk of bias ?=unclear risk of bias NA=not applicable

APPENDIX 6: Main Study Findings and Authors' Conclusions

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Systematic Review (Clinical)		
Wright,[16] 2016, USA	Caries incidence 2 to 3-year f/u (9 studies, 3542 participants) Sealants vs. No Sealants 194/1799 (10.8%) vs. 584/1743 (33.5%) RRR: 76% OR (95%CI): 0.24 (0.19,0.30) P<0.00001 Caries incidence 4 to 7-year f/u (3 studies, 752 participants) Sealants vs. No Sealants 74/368 (20.1%) vs. 206/384 (53.6%) RRR: 79% OR (95%CI): 0.21 (0.10,0.44) P<0.0001 Caries incidence ≥ 7-year f/u (2 studies, 446 participants) Sealants vs. No Sealants 62/215 (28.8%) vs. 170/231 (73.6%) RRR: 85% OR (95%CI): 0.15 (0.08,0.27) P<0.00001	Moderate quality evidence suggests that use of sealants on occlusal surfaces of permanent molars reduce the incidence of carious lesions compared to control groups of participants who did not receive sealants
Hou,[18] 2015, China	Caries Prevention at 6 months (7 studies, 6022 teeth) Sealants (2996 teeth) vs. No Sealants (3026 teeth) OR (95%CI): 0.06 (0.01, 0.32); P=0.001 Caries Prevention at 1 year (17 studies, 16159 teeth) Sealants (8142 teeth) vs. No Sealants (8017 teeth) OR (95%CI): 0.10 (0.05, 0.21); P<0.00001 Caries Prevention at 2 years (15 studies, 13597 teeth) Sealants (6868 teeth) vs. No Sealants (6729 teeth) OR (95%CI): 0.16 (0.09, 0.26); P<0.00001 Caries Prevention at 3 years (13 studies, 12057 teeth) Sealants (6086 teeth) vs. No Sealants (5971 teeth) OR (95%CI): 0.21 (0.13, 0.32); P<0.00001 Caries Prevention at 4 years (3 studies, 3513	Pit and fissure sealants are an effective at preventing dental caries

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	teeth) Sealants (1837 teeth) vs. No Sealants (1676 teeth) OR (95%CI): 0.18 (0.05, 0.62); P=0.007 Caries Prevention at 5 years (2 studies, 1686 teeth) Sealants (843 teeth) vs. No Sealants (843 teeth) OR (95%CI): 0.28 (0.20, 0.38); P<0.00001	
Ahovuo-Saloranta,[19] 2013, Finland	Dentine caries (resin-based sealant vs. no sealant) 12 months (6 studies) OR (95%CI): 0.16 (0.08, 0.30); P<0.00001 24 months (6 studies, 1066 children) OR (95%CI): 0.12 (0.07, 0.19); P<0.00001 36 months (7 studies) OR (95%CI): 0.17 (0.11, 0.27); P<0.00001 48-54 months (4 studies) OR (95%CI): 0.21 (0.16, 0.28); P<0.00001 5 years (1 study) OR (95%CI): 0.31 (0.23, 0.43); P<0.00001 6 years (1 study) RR (95%CI): 0.45 (0.36, 0.58); P<0.00001 7 years (1 study) RR (95%CI): 0.45 (0.34, 0.59); P<0.00001 9 years (1 study) RR (95%CI): 0.35 (0.22, 0.55); P<0.0001 DFS Increment (glass ionomer sealant vs. no sealant) 24 months (1 study) Mean difference (95%CI): -0.18 (-0.39,0.03), P=0.09	Application of sealants to the occlusal surface of permanent first molars in children and adolescents reduces caries for up to 48 months compared to no sealant application. The evidence of efficacy of dental sealants is mainly in high risk children.
Systematic Review (Economic)		
Leo,[20] 2016, Italy	CEA: application of sealants is cost-effective compared to no application of sealant CBA: short term B/C<1, long term B/C 1 to 1.7 CUA: favorable ratio between cost and utility, especially for first permanent mandibular molars	Sealing is one of the most effective and least invasive methods of preventing pit and fissure cavities. Public (school-based) dental sealant programs are more cost effective than private programs.
Randomized Controlled Trial		
Kalnina,[22] 2016, Latvia	New caries at 12 months Sealant vs. control (no sealant)	Fissure sealant, fluoride varnish and ozone are

<table>
<tr><th>First Author, Publication Year</th><th>Main Study Findings</th><th>Authors' Conclusions</th></tr>
<tr><td></td><td>0% vs. 3.5% (6/173 occlusal surfaces); P=0.106</td><td>not significantly different in their effectiveness and are all recommended for the prevention of caries on permanent premolars in children.</td></tr>
<tr><td>Muller-Bolla,[24,25] 2013 and 2016, France</td><td>New carious lesions on PRM at 1 year
Sealant vs. Control (no sealant)
13 (3.1%) vs. 45 (10.7%)
OR (95%CI): 0.26 (0.14,0.49)

New carious lesions on PRM at 3 years
Sealant vs. Control (no sealant)
RRR: 67% HR (95%CI): 0.33 (0.24,0.46)</td><td>A school-based dental sealant program for children from low socio-economic backgrounds is effective at reducing carious lesions in PFM.</td></tr>
<tr><td>Hilgert,[23] 2015, Brazil</td><td>Cavitated Dentine Carious Lesion-free High-caries Risk Occlusal surfaces in PFM (P=0.59)
<table>
<tr><th>F/U Time (years)</th><th>CR n(%) (n=169)</th><th>STB n(%) (n=71)</th><th>ART-GIC n(%) (n=69)</th></tr>
<tr><td>0.5</td><td>1 (99.4)</td><td>0 (100)</td><td>2 (97.1)</td></tr>
<tr><td>1</td><td>3 (98.1)</td><td>1 (98.6)</td><td>2 (97.1)</td></tr>
<tr><td>2</td><td>7 (95.4)</td><td>3 (95.6)</td><td>4 (93.9)</td></tr>
<tr><td>3</td><td>12 (91.4)</td><td>3 (95.6)</td><td>6 (90.2)</td></tr>
</table>
n=number of occlusal surfaces at baseline</td><td>No difference was found between supervised tooth brushing and the application of dental sealant in the development of carious lesions in PFM over 3 years</td></tr>
<tr><td>Monse,[21] 2012, Philippines</td><td>New dentinal (D3) caries at 18 months
<table>
<tr><th colspan="2">Brushing</th><th colspan="2">Non-brushing</th></tr>
<tr><td>Non-treated (n=127)</td><td>Sealants (n=301)</td><td>Non-treated (n=544)</td><td>Sealants (n=467)</td></tr>
<tr><td>10</td><td>3</td><td>91</td><td>29</td></tr>
<tr><td colspan="2">HR(95%CI): 0.12 (0.02,0.61); P<0.01</td><td colspan="2">HR(95%CI): 0.33 (0.20,0.54); P<0.001</td></tr>
</table>
n=number of occlusal surfaces</td><td>ART sealants significantly reduce the development of new caries over 18 months</td></tr>
<tr><td colspan="3">Non-randomized studies</td></tr>
<tr><td>Baldini,[26] 2011, Portugal</td><td>DMFT increment>0 at 2 years
<table>
<tr><th>Intervention</th><th>Group</th><th>Yes, n(%)</th><th>No, n(%)</th></tr>
<tr><td>Sealed</td><td>high risk</td><td>20 (22.2)</td><td>70 (77.8)</td></tr>
<tr><td></td><td>low risk</td><td>1 (1.6)</td><td>63 (98.4)</td></tr>
<tr><td>Not sealed</td><td>high risk</td><td>22 (31.0)</td><td>49 (69.0)</td></tr>
<tr><td></td><td>low risk</td><td>4 (7.8)</td><td>47 (92.2)</td></tr>
</table>
P=0.0001

DMFT increment>0 at 2 years
Not-sealed vs. sealed:
OR (95%CI): 1.81 (0.93,3.50); P=0.0767
High risk vs. Low risk
OR (95%CI): 7.94 (3.01, 20.80); P<0.0001</td><td>Sealant placement appears to be effective in preventing development of dental caries, children at high risk who did not receive dental sealants were at higher risk of developing caries at 2 years</td></tr>
<tr><td colspan="3">CR=composite resin; ART-GIC=atraumatic restorative treatment-high viscosity glass ionomer cement; STB=supervised tooth brushing; DMFT=decayed, missing, filled teeth; OR=odds ratio; RR=risk ratio</td></tr>
</table>