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Pit and fissure sealants versus fluoride varnishes for preventing dental decay in the permanent teeth of children and adolescents (Review)

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[Intervention Review]

Pit and fissure sealants versus fluoride varnishes for preventing dental decay in the permanent teeth of children and adolescents

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ABSTRACT

Background

Most of the detected increment in dental caries among children and adolescents is confined to occlusal surfaces of posterior permanent molars. Dental sealants and fluoride varnishes are much used preventive options for caries. Although the effectiveness of sealants and fluoride varnishes for controlling caries as compared with no intervention has been demonstrated in clinical trials and summarised in systematic reviews, the relative effectiveness of these two interventions remains unclear. This review is an update of one first published in 2006 and last updated in 2010.

Objectives

Primary objective

- To evaluate the relative effectiveness of fissure sealants compared with fluoride varnishes, or fissure sealants together with fluoride varnishes compared with fluoride varnishes alone, for preventing dental caries in the occlusal surfaces of permanent teeth of children and adolescents.

Secondary objectives

- To evaluate whether effectiveness is influenced by sealant material type and length of follow-up.
- To document and report on data concerning adverse events associated with sealants and fluoride varnishes.

Search methods

We searched the following electronic databases: the Cochrane Oral Health Group Trials Register (to 18 December 2015), the Cochrane Central Register of Controlled Trials (CENTRAL) (2015, Issue 11), MEDLINE via Ovid (1946 to 18 December 2015) and EMBASE via Ovid (1980 to 18 December 2015). We also searched the US National Institutes of Health Trials Register (<http://clinicaltrials.gov>) and the World Health Organization (WHO) Clinical Trials Registry Platform for ongoing trials. We placed no restrictions on language or date of publication when searching electronic databases. We screened the reference lists of identified trials and review articles for additional relevant studies.

Selection criteria

We included randomised controlled trials with at least 12 months of follow-up comparing fissure sealants, or fissure sealants together with fluoride varnishes, versus fluoride varnishes for preventing caries in the occlusal surfaces of permanent premolar or molar teeth, in participants younger than 20 years of age at the start of the study.

Data collection and analysis

Two review authors independently screened search results, extracted data and assessed risk of bias of included studies. We attempted to contact study authors to obtain missing or unclear information.

We grouped and analysed studies on the basis of sealant material type (resin-based sealant and glass ionomer-based sealant: glass ionomer and resin-modified glass ionomer) and different follow-up periods. We calculated the odds ratio (OR) for caries or no caries on occlusal surfaces of permanent molar teeth. For trials with a split-mouth design, we used the Becker-Balagtas odds ratio. For continuous outcomes and data, we used means and standard deviations to obtain mean differences. We presented all measures with 95% confidence intervals (CIs).

We assessed the quality of the evidence using GRADE (Grades of Recommendation, Assessment, Development and Evaluation) methods.

We conducted meta-analysis using the fixed-effect model, as data from only two studies were combined. We had planned to conduct meta-analyses using a random-effects model when more than three trials were included in the meta-analysis.

Main results

In this review, we included eight trials with 1746 participants (four of the trials were new since the 2010 update). Seven trials (1127 participants) contributed to the analyses, and children involved were five to 10 years of age at the start of the trial.

Sealant versus fluoride varnish

Resin-based fissure sealants compared with fluoride varnishes

Four trials evaluated this comparison (three of them contributing to the analyses). Compared with fluoride varnish, resin-based sealants prevented more caries in first permanent molars at two-year follow-up (two studies in the meta-analysis with pooled odds ratio (OR) 0.69, 95% confidence interval (CI) 0.50 to 0.94; P value = 0.02; $I^2 = 0\%$; 358 children evaluated). We assessed the body of evidence as low quality. The caries-preventive benefit for sealants was maintained at longer follow-up in one trial at high risk of bias: 26.6% of sealant teeth and 55.8% of fluoride-varnished teeth had developed caries when 75 children were evaluated at nine years of follow-up.

Glass ionomer-based sealants compared with fluoride varnishes

Three trials evaluated this comparison: one trial with chemically cured glass ionomer and two with resin-modified glass ionomer. Researchers reported similar caries increment between study groups regardless of which glass ionomer material was used in a trial. Study designs were clinically diverse, and meta-analysis could not be conducted. The body of evidence was assessed as of very low quality.

Sealant together with fluoride varnish versus fluoride varnish alone

One split-mouth trial analysing 92 children at two-year follow-up found a significant difference in favour of resin-based fissure sealant together with fluoride varnish compared with fluoride varnish only (OR 0.30, 95% CI 0.17 to 0.55). The body of evidence was assessed as low quality.

Adverse events

Three trials (two with resin-based sealant material and one with resin-modified glass ionomer) reported that no adverse events resulted from use of sealants or fluoride varnishes. The other five studies did not mention adverse events.

Authors' conclusions

Currently, scarce and clinically diverse data are available on the comparison of sealants and fluoride varnish applications; therefore it is not possible to draw clear conclusions about possible differences in effectiveness for preventing or controlling dental caries on occlusal surfaces of permanent molars. The conclusions of this updated review remain the same as those of the last update (in 2010). We found some low-quality evidence suggesting the superiority of resin-based fissure sealants over fluoride varnish applications for preventing occlusal caries in permanent molars, and other low-quality evidence for benefits of resin-based sealant and fluoride varnish over fluoride varnish alone. Regarding glass ionomer sealant versus fluoride varnish comparisons, we assessed the quality of the evidence as very low and could draw no conclusions.

PLAIN LANGUAGE SUMMARY

Pit and fissure sealants versus fluoride varnishes for preventing dental decay in the permanent teeth of children and adolescents

Review question

This review aimed to assess whether dental sealants (or sealants together with fluoride varnishes) or fluoride varnishes are more effective for reducing tooth decay on biting surfaces of permanent back teeth in young people.

Background

Although children and adolescents have healthier teeth today than in the past, tooth decay is still a problem among some individuals and populations, and it affects a large number of people around the world. Most decay in children and adolescents is concentrated on the biting surfaces of permanent back teeth. Preventive treatment options for tooth decay include tooth brushing with a fluoride toothpaste, use of fluoride supplements (e.g. fluoride tablets) and application of dental sealants and topical fluorides at dental clinics.

Dental sealants are applied to form a physical barrier that prevents growth of bacteria and accumulation of food particles in the grooves of back teeth. Several sealant materials are available: The main types in use are resin-based sealants and glass ionomer cements. Fluoride varnishes are sticky pastes that are professionally applied to the teeth two to four times a year.

Study selection

Authors from the Cochrane Oral Health Group carried out this review of existing studies, and the evidence is current to 18 December 2015. This review is an update of one first published in 2006 and last updated in 2010.

Study characteristics

This review includes eight studies published from 1984 to 2014, in which 1746 participants were randomly assigned (1127 were included in the analyses) to receive dental sealant (or sealant together with fluoride varnish) or fluoride varnish applications, and the extent of tooth decay was compared. Participants were five to 10 years of age at the start of the trial and represented the general population.

Key results

Some evidence suggests that applying resin-based sealants to the biting surfaces of permanent back teeth in children may reduce tooth decay in the permanent teeth of children by 3.7% over a two-year period, and by 29% over a nine-year period, when compared with fluoride varnish applications. Applying resin-based sealant together with fluoride varnish to the biting surfaces of the permanent back teeth may reduce tooth decay by 14.4% over a two-year period compared with fluoride varnish alone. Effects of applying glass ionomer sealants may be similar to those seen when fluoride varnish is applied, but evidence showing the similarity between interventions is of very low quality. Three studies reported that there were no associated adverse events from sealants or fluoride varnish applications; the other studies did not mention adverse events.

Quality of the evidence

Available evidence is of low to very low quality because of the small number of included studies, and because of problems with the way in which studies were conducted. Further, most studies reported a relatively short follow-up time.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Resin-based fissure sealant compared with fluoride varnish for preventing dental caries

Resin-based fissure sealant compared with fluoride varnish for preventing dental caries

Patient or population: children and adolescents

Settings: sealant and fluoride varnish applications for school children in China, Norway and Spain

Intervention: resin-based fissure sealant applications on occlusal tooth surfaces of permanent first molars

Comparison: fluoride varnish applications on occlusal tooth surfaces of permanent first molars

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Fluoride-varnished teeth	Sealed teeth				
Dentine caries in permanent molars Follow-up: 2 years	Incidence of carious first molars (13.2%) 132 per 1000	Incidence of carious first molars (9.5%) 95 per 1000 (70 to 125)	OR 0.69 (95% CI 0.50 to 0.94)	369 children randomly assigned, 358 evaluated after 2 years (2 studies) ^{a,b}	⊕⊕⊕⊖ Low ^c	Benefits of resin sealant over fluoride varnish also found at 4 years and 9 years of follow-up ^d No adverse events of interventions reported (2 studies)

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: We are very uncertain about the estimate

^aOne split-mouth study at high risk of bias conducted in the 1980s (Raadal 1984), and one parallel-group study at unclear risk of bias conducted in 2008 (Liu 2012).

^bIn the Raadal 1984 study, fluoride rinsing programme with 0.5% NaF (sodium fluoride) solution at school.

^cDowngraded by two levels because of concerns about the applicability of the results to today's populations.

We did not downgrade evidence on the basis of overall risk of bias classifications of the two studies because these studies were otherwise well conducted even though they were not graded as having overall low risk of bias because the blinding of outcome measurement was incomplete. The incomplete blinding of outcome measurement was judged not to be a fundamental issue in assessing the quality of evidence in preventive sealant studies.

^dOne Spanish study conducted in the 1990s ([Bravo 2005](#)) with risk ratio (RR) of 0.42 (95% confidence interval (CI) 0.21 to 0.84) and RR of 0.48 (95% CI 0.29 to 0.799) at four years and nine years of follow-up, respectively. The study was assessed as having high risk of bias.

Summary of findings 2. Glass ionomer fissure sealant or resin-modified glass ionomer fissure sealant compared with fluoride varnish for preventing dental caries

Glass ionomer fissure sealant or resin-modified glass ionomer fissure sealant compared with fluoride varnish for preventing dental caries

Patient or population: children and adolescents

Settings: sealant and fluoride varnish applications for school children in Brazil and China

Intervention: glass ionomer or resin-modified glass ionomer sealant applications on occlusal tooth surfaces of permanent first molars

Comparison: fluoride varnish applications on occlusal tooth surfaces of permanent first molars

Outcomes	Impact No difference	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Dentine caries in permanent molars Follow-up: 1, 2 and 3 years	No difference in caries after 1, 2 and 3 years	3 trials (1 study with 21 evaluated children after 1 year ^a ; 2 studies with 581 evaluated children at 2 years ^b ; 1 study with 393 evaluated children at 3 years ^c)	⊕⊕⊕⊕ Very low ^d	No adverse events reported from the interventions (1 study)

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: We are very uncertain about the estimate

^aOne study with high risk of bias comparing resin-modified glass ionomer versus fluoride varnish after one year ([Florio 2001](#)).

^bThe other of the two studies at two years, with incomplete information and analyses, compared chemically cured glass ionomer versus fluoride varnish ([Ji 2007](#)). The other study actually evaluated whether additional benefit was derived by using resin-modified glass ionomer sealants and fluoride varnishes among children receiving regular oral health education ([Tagliaferro 2011](#)).

^cOne study at three years comparing chemically cured glass ionomer versus fluoride varnish, assessed as having unclear risk of bias (extensive incomplete information and analyses) ([Ji 2007](#)).

^dDowngraded because a small number of trials had high or unclear risk of bias and used different designs and follow-up times.

Summary of findings 3. Resin-based fissure sealant together with fluoride varnish versus fluoride varnish alone for preventing dental caries

Resin-based fissure sealant together with fluoride varnish compared with fluoride varnish alone for preventing dental caries

Patient or population: children and adolescents

Settings: sealant and fluoride varnish applications for school children in Germany

Intervention: resin-based fissure sealant together with fluoride varnish applications on occlusal tooth surfaces of permanent first molars

Comparison: fluoride varnish applications to occlusal tooth surfaces of permanent first molars

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Fluoride-varnished teeth	Sealed + fluoride-varnished teeth				
Dentine caries in permanent molars Follow-up: 2 years	Incidence of carious first molars (22.3%) 223 per 1000	Incidence of carious first molars (7.9%) 79 per 1000 (46 to 136)	OR 0.30 (95% CI 0.17 to 0.55)	98 children randomly assigned, 92 evaluated after 2 years (1 study) ^{a,b}	⊕⊕○○ Low ^c	No information on adverse events

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: We are very uncertain about the estimate

^aStudy conducted in the 1990s (Splieth 2001).

^bNo information on caries incidence among control teeth without treatment. Baseline caries of the study population (children five to eight years of age): mean DMFS 0.2.

^cQuality of evidence was downgraded by two levels because a single study (92 analysed participants) was conducted as early as the 1990s without information on caries incidence among control teeth without treatment, and although the study was otherwise well conducted, lack of blinding to outcome measurement caused further uncertainty about results.

BACKGROUND

Description of the condition

Dental caries is a multi-factorial chronic oral disease that affects most populations throughout the world and has been considered the most important global oral health burden (Peterson 2005). Since the 1970s, a reduction in caries prevalence has occurred in most industrialised countries; however, dental caries is still a problem for some individuals and populations, for example, in many Eastern European and South American countries, the prevalence of caries among 12-year-olds has been reported to be moderate or high (WHO 2003). A global increase in caries has been reported recently, even in countries where prevalence of caries had previously been fairly low (Bagramian 2009).

Dental caries can be explained as an interplay between specific acidogenic bacteria in the plaque biofilm, fermentable carbohydrates and tooth structure. The biofilm bacteria produce organic acids that can cause loss of minerals from the tooth surface (demineralisation). In favourable conditions, a reversal, that is, a mineral gain, is possible (remineralisation). If the demineralisation process prevails, visually detectable caries lesions occur. Development of a caries lesion is a dynamic process that may progress, stop or reverse, and assessment of the grade and activity of the lesion is challenging. The International Caries Detection and Assessment System integrates a definition of dental caries and a system to measure the caries process (ICDAS II 2008). In ICDAS II, the codes for coronal caries range from 0 to 6, depending on the severity of the lesion: codes from 0 to 3 involve a sound tooth surface to caries in enamel (with or without microcavitation); codes from 4 to 6 involve caries in dentine.

Within the mouth, occlusal surfaces of posterior teeth are the most vulnerable sites because their anatomy favours biofilm formation and retention, and the rate of occlusal caries has not fallen to the same extent as the rate of caries on smooth surfaces (Brown 1995). Most of the detected increment in dental caries among children and adolescents is confined to pit and fissure surfaces of first molars (Batchelor 2004; Brown 1995; McDonald 1992).

Description of the intervention

Dental sealants

Dental sealant is applied to a tooth surface to provide a physical barrier that prevents growth of biofilm by blocking nutrition. Although sealants were introduced for preventing caries on occlusal surfaces, they now are considered active agents in controlling and managing initial caries lesions on occlusal surfaces (Splieth 2010) and, recently, on approximal surfaces as well (Dorri 2015; Ekstrand 2012; Splieth 2010).

A resin material, bisphenol A glycidyl methacrylate (BIS-GMA), forms the basis for numerous resin-based dental sealants and composites that are now available. The effectiveness of resin-based sealants is closely related to the longevity of sealant coverage (i.e. clinical retention) (Ripa 1993). Recent reports have considered possible adverse oestrogen-like effects of resin-based materials including bisphenol A (BPA) (Azarpazhooh 2008b; Fleisch 2010; Joskow 2006). This synthetic chemical resin is widely used in the production of plastic products intended for common life but is rarely used in dental materials (ADA 2003). Current evidence suggests that people are not at risk for oestrogen-like effects

when resin-based sealants are used (ADA 2003; Azarpazhooh 2008b; Fleisch 2010).

Along with resin-based sealants, other sealant materials are available; the main type consists of glass ionomer cements (combination of silicate and polyacrylate cement system). Glassionomer cements contain fluoride and are thought to prevent caries through fluoride release over a prolonged period. Glassionomer cements may be used as the original chemically cured type or as the light cured type, which is modified with resin, for example, for rapid initiation of the curing process. Novel materials called compomers, which were introduced in the 1990s to combine benefits of resins and those of glass ionomer cements (Nicholson 2007; Ruse 1999), have also been applied as sealants. Allergic reactions to sealant materials are possible but rare.

Fluoride varnishes

The aim of topical fluoride varnish application is to treat hard tooth surfaces in such a way that caries is arrested or reversed. Fluoride acts to prevent caries in three ways: (1) by inhibiting the demineralisation and (2) promoting the remineralisation of dental enamel, and (3) by inhibiting acid formation by plaque bacteria (Shellis 1994; Ten Cate 1997). Although fluoride varnishes have a very high fluoride concentration (e.g. 22,660 ppm in Duraphat fluoride varnish), their use is considered to be safe because they have a quick-setting base, release fluoride slowly over time and require comparatively small amounts of varnish for the whole dentition (Pettersson 1993). Only a small dose of fluoride is swallowed over several hours, and risk of acute toxic reactions (e.g. nausea, vomiting) is minimal (Bawden 1998; Seppä 1999). Contact allergies to fluoride varnish due to colophony are possible but have been reported in only two cases (Chu 2006; Isaksson 1993).

Sometimes topical fluoride has been combined with sealant application to strengthen overall effectiveness in the prevention of dental caries.

Why it is important to do this review

The Cochrane Oral Health Group undertook an extensive prioritisation exercise in 2014 to identify a core portfolio of titles that were the most clinically important ones to maintain on the Cochrane Library (Worthington 2015). Consequently, this review was identified as a priority title by the paediatric dentistry expert panel (Cochrane OHG priority review portfolio).

Several systematic reviews have supported the substantial effectiveness of resin-based sealants and fluoride varnishes in preventing or controlling occlusal decay as compared with no intervention (sealant studies: Ahovuo 2013; Griffin 2008; Llodra 1993; Mejàre 2003; varnish studies: Azarpazhooh 2008a; Helfenstein 1994; Marinho 2013; Pettersson 2004). Application of sealants is more time-consuming than application of fluoride varnish, but sealants usually are applied only once, whereas fluoride varnish is applied several times, usually semi annually, depending on the caries activity of a patient. Fluoride varnish and sealant applications, although effective, are rather expensive procedures and are efficient only when children and teeth are carefully selected.

Although the effectiveness of sealants and fluoride varnishes in controlling caries as compared with no intervention has been demonstrated in clinical trials and summarised in systematic

reviews, the relative effectiveness of these two much applied measures remains unclear. The aim of this systematic review is to compare the relative effectiveness of (1) sealants and fluoride varnishes, or (2) sealants plus fluoride varnishes versus fluoride varnishes alone, for preventing dental caries in children and adolescents.

This review is an update of a review first published in 2006 and last updated in 2010, which suggested some superiority of resin-based sealants over fluoride varnishes but was based on a very small number of trials (Hiiri 2010).

OBJECTIVES

Primary objective

- To evaluate the relative effectiveness of fissure sealants compared with fluoride varnishes, or fissure sealants together with fluoride varnishes compared with fluoride varnishes alone, for preventing dental caries in the occlusal surfaces of permanent teeth of children and adolescents.

Secondary objectives

- To evaluate whether effectiveness is influenced by sealant material type and length of follow-up.
- To document and report on data concerning adverse events associated with sealants and fluoride varnishes.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) with at least of 12 months follow-up, in which fissure sealants, or fissure sealants together with fluoride varnishes, were compared with fluoride varnishes alone for preventing caries in occlusal surfaces of permanent teeth of children and adolescents. We included both parallel-group and split-mouth study designs. The unit of randomisation could be the individual, the group (e.g. school, school class) or the tooth or tooth pair.

Types of participants

Children and adolescents from the general population, younger than 20 years of age at the start of the study.

Types of interventions

- Pit and fissure sealants of all materials (except first-generation resin-based sealants) versus fluoride varnish.
- Pit and fissure sealants together with fluoride varnish versus fluoride varnish.

Intervention groups included the sealant group and the sealant plus fluoride varnish group. The control group was the fluoride varnish group.

We included studies in which applications were placed on occlusal surfaces of permanent premolar or molar teeth for the purpose of preventing caries, regardless of who did the application. Materials could be applied on sound surfaces or on enamel lesions (if scored using the ICDAS II scale, codes 0, 1, 2 and 3 were accepted). The sealant application method used in the study could consist of direct

application to the tooth surface or application after mechanical preparation of the enamel surface.

Types of outcome measures

Primary outcomes

- Incidence of dentinal carious lesions on treated occlusal surfaces of molars or premolars (yes or no).
- Changes in decayed, missing and filled (DMF) figures at surface, tooth and whole-mouth levels.
- Progression of caries lesion into enamel or dentine.

Secondary outcomes

- Time taken to apply pit and fissure sealant or fluoride varnish.
- Number of visits to the dentist for repair of sealant or fluoride varnish application.
- Adverse events and safety of sealants and fluoride varnishes.

Search methods for identification of studies

For identification of studies for this review, we developed detailed search strategies for each database searched. These were based on the search strategy developed for MEDLINE (Ovid) (see [Appendix 1](#)) but were revised appropriately for each database.

Electronic searches

We searched the following electronic databases, amending the search strategies for this 2016 update.

- Trial Register of the Cochrane Oral Health Group (to 18 December 2015) (see [Appendix 2](#)).
- Cochrane Central Register of Controlled Trials (CENTRAL) (2015, Issue 11) (see [Appendix 3](#)).
- MEDLINE via Ovid (1946 to 18 December 2015) (see [Appendix 1](#)).
- EMBASE via Ovid (1980 to 18 December 2015) (see [Appendix 4](#)).

We searched the following databases for ongoing trials.

- US National Institutes of Health Trials Register (<http://clinicaltrials.gov>) (to 18 December 2015) (see [Appendix 5](#)).
- World Health Organization (WHO) Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/default.aspx>) (to 18 December 2015) (see [Appendix 5](#)).

We placed no restrictions on the language or date of publication when searching the electronic databases.

In previous versions of this review, we also searched the following electronic databases: SCISEARCH, Cplus, INSPEC, JICST-EPLUS, NTIS, PASCAL, DARE, NHS EED, HTA and OpenSIGLE (see [Appendix 6](#)). However, we decided not to update these databases at this time because in previous versions of the review, these searches yielded no additional information.

Searching other resources

We screened the reference lists of already identified trials and review articles for additional relevant studies.

Data collection and analysis

Selection of studies

Two review authors (Anneli Ahovuo-Saloranta (AAS) and Helena Forss (HF)) independently selected papers on the basis of title, keywords and abstract, and decided on eligibility. We obtained the full text of every study considered for inclusion. If information relevant to the inclusion criteria was not available in the abstract, or if the title was relevant but the abstract was not available, we obtained the full text of the report. All information gathering and data recording were done independently, and disagreements were resolved by discussion with a third review author (Anne Hiiri (AH), Anne Nordblad (AN) or Marjukka Mäkelä (MM)).

We contacted trial authors to request additional information if the study seemed to fulfil the inclusion criteria for this review but information in the report was insufficient to allow final assessment of inclusion or exclusion.

In this review, we decided to consider only studies with a full-text report. We excluded studies reported only as abstracts because evidence has suggested discrepancies between data reported in an abstract and those provided in the final published full report, and because information on trial quality indicators is often lacking (Chokkalingam 1998; Hopewell 2006). Thus we saw that the full-text report is required to ensure reliable data extraction and assessment of risk of bias. To diminish the risk of publication bias, we contacted authors of relevant abstracts to ask whether a full-text report of the study (unpublished or published) was available.

Data extraction and management

Two review authors (AAS, HF) extracted data from all included studies in duplicate and independently. Review authors were in full agreement about excluded data, and discussion or consultation with a third review author was not needed. We attempted to contact study authors to request missing information or clarification when necessary.

We extracted the following information on study methods.

- Trial design.
- Study duration (years of follow-up).
- Year the study began.

We extracted the following characteristics of participants.

- Location where study was conducted (country and setting where participants were recruited).
- Criteria for accepting participants into the study (intact surfaces and surfaces with enamel lesion allowed).
- Age (range) and mean age at start.
- Gender.
- Baseline caries prevalence of participants (caries severity at start (average number of decayed, missing and filled deciduous teeth (dmft); decayed, missing and filled deciduous surfaces (dmfs); decayed, missing and filled permanent surfaces (DMFS) and/or decayed, filled permanent surfaces (DFS); or other measure)).
- Number of randomly assigned participants and number of teeth in treatment at study start and after follow-up.
- Number of evaluated participants.

We extracted the following characteristics of interventions.

- Intervention comparisons (sealant versus fluoride varnish, or sealant plus fluoride varnish versus fluoride varnish).
- Sealant and fluoride varnish products used in the study.
- Reapplication of sealants and frequency of fluoride varnish application.
- Information on who applied sealants and fluoride varnishes (dentist with or without assistant or dental hygienist).
- Co-interventions (e.g. background exposure to other fluoride sources (toothpaste, water, etc.)).

We extracted the following characteristics of outcomes.

- Description of outcomes.
- Description of outcome measurements.

We extracted the following additional information.

- Information related to calibration of examiners and kappa statistics.
- Sealant retention figures at follow-up.
- Funding source.
- Caries prevalence of population in study area.

Outcome information was extracted mainly as the number of dentinal carious lesions or non-carious lesions on occlusal surfaces of treatment and control teeth at different follow-up times. If a filling had been put on the occlusal surface or the tooth had been extracted as the result of caries during the study, we coded it as caries. We extracted data presented only in graphs and figures when possible. We presented data from the included studies in [Table 1](#).

In addition, we recorded caries increments as changes in DMFS/DMFT scores and as progression of caries lesions in enamel or dentine when study authors reported them. We recorded the following secondary outcomes when reported: time taken to apply pit and fissure sealant or fluoride varnish, number of visits to the dentist for repair or reapplication of sealant or fluoride varnish application and safety of sealants and fluoride varnishes.

In some studies, results were provided at more than one period of follow-up. All data were extracted at pre-selected times- at one, two, three, four, five years, etc. (annually). Analyses based on available data were carried out at these pre-selected times.

Assessment of risk of bias in included studies

Two review authors (AAS, HF) independently assessed the risk of bias of included studies. They resolved disagreements by consensus. We contacted the authors of included studies to request additional information. As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (Higgins 2011a), we assessed the following six methodological domains: random sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other sources of bias (e.g. baseline comparability). Within each domain, we judged each study as having 'low', 'high' or 'unclear' risk of bias, with the latter indicating lack of information or uncertainty over the potential for bias. See [Table 2](#) for the detailed criteria we used in our assessment.

Summary assessments of 'Risk of bias'

To draw conclusions about the overall risk of bias for caries outcomes within a study, we decided to classify the studies in three categories: studies with low, unclear or high risk of bias. We determined caries outcomes from data of the included studies (all caries data were extracted at pre-selected times - annually, at one, two, three, four, five years, etc.).

Our classification was based on the five domains that we deemed most fundamental in assessing risk of study bias: allocation concealment, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and baseline comparability.

We defined overall risk of bias categories as follows.

- Low risk of bias (plausible bias unlikely to seriously alter results) if all five fundamental domains defined above were graded as low risk of bias.
- Unclear risk of bias (plausible bias that raises some doubt about results) if one or more of the domains were graded as unclear risk of bias.
- High risk of bias (plausible bias that seriously weakens confidence in the results) if one or more domains were graded as high risk of bias.

Measures of treatment effect

We calculated odds ratios for differences in sealant and fluoride varnish groups as to whether occlusal surfaces were carious, along with appropriate standard errors and 95% confidence intervals, using [RevMan 2014](#). For split-mouth studies, we calculated odds ratios (ORs) using the Becker-Balagtas method (BB OR) outlined in [Curtin 2002](#) with R software version 3.0.1. We chose the Becker-Balagtas method because we intended to pool data from split-mouth studies and parallel-group studies in the same meta-analyses, and this method facilitated data synthesis (as outlined in the article by [Stedman 2011](#)). All included split-mouth studies presented paired data by tooth pairs, and the intraclass correlation co-efficient (ICC) (needed for BB OR calculations) could be calculated from paired data. If we had included split-mouth studies presenting data only in marginals (as parallel-group studies, not as cross-classification), we would have chosen the conservative ICC 0.05. Results of the study by [Bravo 2005](#) with clustered data are presented as risk ratios (RRs) with cluster-corrected standard errors. We requested from study authors cluster-corrected effect estimates of that study for the earlier update of this review, and we used them in this review update.

For continuous outcomes and data, we used means and standard deviations to obtain mean differences (MDs) and 95% confidence intervals (CIs).

Unit of analysis issues

In parallel-group studies and cluster-randomised studies, we chose an individual to be the unit of analysis. If clustered data were provided (e.g. several measurements per individual (e.g. more than one tooth/surface), clustering of children at school class level), we adjusted the standard errors of estimates to take clustering into account (as outlined in Section 16.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011b](#))).

In split-mouth studies, we chose a tooth pair within an individual to be the unit of analysis. In some studies, more than one pair of tooth surfaces per child might be treated. These pairs are not independent and should be analysed as 'paired data' on a per-child basis. However, data presented in these studies did not enable taking into account the dependence of tooth pairs on a per-child basis (we are unaware of any widely used methods to correct and account for dependence of the tooth pairs). This meant that confidence intervals would be slightly narrower than they should be, and this was taken into consideration when we interpreted the results.

Dealing with missing data

We contacted trial authors to retrieve missing data when necessary or feasible.

We performed analyses using an available case data analysis approach, as represented in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 ([Higgins 2011b](#)). This approach for calculating response rates uses the total number of participants for whom data were recorded for the particular outcome in question as a denominator.

In caries prevention studies, follow-up times can include several years. Studies with long follow-up have the problem of high drop-out rates, causing uncertainty in the data. The usual reason for drop-out is that children move away from the study area. We decided to include in the analyses data from all studies (regardless of drop-out rates). We assessed studies with a high drop-out rate (drop-out rate > 25% regardless of follow-up time) to be at high risk of bias. We intended to evaluate in the sensitivity analyses the effects of risk of bias grading on study results.

Assessment of heterogeneity

If a sufficient number of studies had been included in any meta-analyses, we would have assessed clinical heterogeneity by examining the characteristics of studies and the similarity between types of participants (especially baseline caries prevalence levels of populations), interventions and outcomes as specified in the criteria for included studies.

The significance of any discrepancies in estimates of treatment effects from various studies was assessed by Cochran's test for heterogeneity and by a measure of I^2 . The measure I^2 describes the percentage of variability in effect estimates that is due to heterogeneity rather than to sampling error. A value greater than 50% may be considered to represent substantial heterogeneity ([Higgins 2003](#)).

Assessment of reporting biases

If sufficient numbers of trials (more than 10) had been included in any meta-analysis, we would have assessed publication bias according to the recommendations on testing for funnel plot asymmetry provided in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 ([Sterne 2011](#)). If asymmetry was identified, we would have examined possible causes.

Data synthesis

We grouped and analysed studies on the basis of sealant material type (resin-based sealant and glass ionomer-based sealant: glass ionomer and resin-modified glass ionomer) using different follow-

up periods. We conducted meta-analyses in [RevMan 2014](#), using the generic inverse variance method with a fixed-effect or random-effects model. In meta-analyses that included two or three studies, we planned to use the fixed-effect model, and in meta-analyses with four or more studies, we planned to use the random-effects model (as recommended under 'Advice to Authors' in the Cochrane Oral Health Group Guide). We planned to pool data from studies in each comparison regardless of the risk of bias classification of these studies.

When feasible, we pooled in the same meta-analysis odds ratios from parallel-group studies and from split-mouth studies by using Becker-Balagtas odds ratios in split-mouth studies, as outlined in the article by [Stedman 2011](#).

Subgroup analysis and investigation of heterogeneity

If a sufficient number of studies had been included in any meta-analyses, we would have examined the relative effectiveness of sealants and fluoride varnishes at different caries prevalence levels. As data were insufficient, it was not possible to create subgroups for further analyses.

Sensitivity analysis

If a sufficient number of studies had been included in any meta-analyses, we would have undertaken sensitivity analyses to assess the robustness of results (for caries outcomes) by excluding studies with unclear or high risk of overall bias.

'Summary of findings' tables and assessing the quality of the evidence

We followed GRADE (Grades of Recommendation, Assessment, Development and Evaluation) methods ([GRADE 2004](#)) and used GRADEpro software to provide overall grading of the quality of evidence for caries outcomes for the following comparisons: resin-based sealant versus fluoride varnish ([Summary of findings for the main comparison](#)); glass ionomer or resin-modified glass ionomer sealant versus fluoride varnish ([Summary of findings 2](#)); and resin-

based sealant together with fluoride varnish versus fluoride varnish alone ([Summary of findings 3](#)). We assessed the quality of the body of evidence with reference to overall risk of bias of included studies at each outcome, directness of evidence, inconsistency of results, precision of estimates and risk of publication bias.

RESULTS

Description of studies

Results of the search

In this 2016 update, we used a revised search strategy in all electronic databases and searched from their respective start dates. Thus we rechecked data over all years. We retrieved the following numbers of records through searches: Cochrane Oral Health Group Trials Register (26 records), Cochrane Central Register of Controlled Trials (CENTRAL) (108 records), MEDLINE (601 records), EMBASE (490 records) and databases for ongoing trials (15 records). We had a total of 648 records after duplicates were removed. In addition to electronic searches, we found 10 potentially relevant reports in the reference lists of review articles and identified trial articles (nine records from earlier searches and one new record from this 2016 update search). Thus we considered the total number of reports to be 658.

Of these 658 records, we discarded 591 as not relevant to this review. We obtained 67 full-text reports. Of these 67 reports, we excluded 44, leaving 23 reports for final assessment. The main reasons for exclusion were as follows: Studies included only one or the other of sealant or fluoride varnish applications, other caries prevention programmes were involved in the intervention or treatments were intended to manage dentine caries.

We evaluated 23 reports in detail. We considered 12 reports representing eight individual studies as eligible for inclusion in the review. We explained the reasons for exclusion of these 10 studies with 11 reports in the [Characteristics of excluded studies](#) table. We presented this process as a flow chart in [Figure 1](#).

Figure 1. Study flow diagram

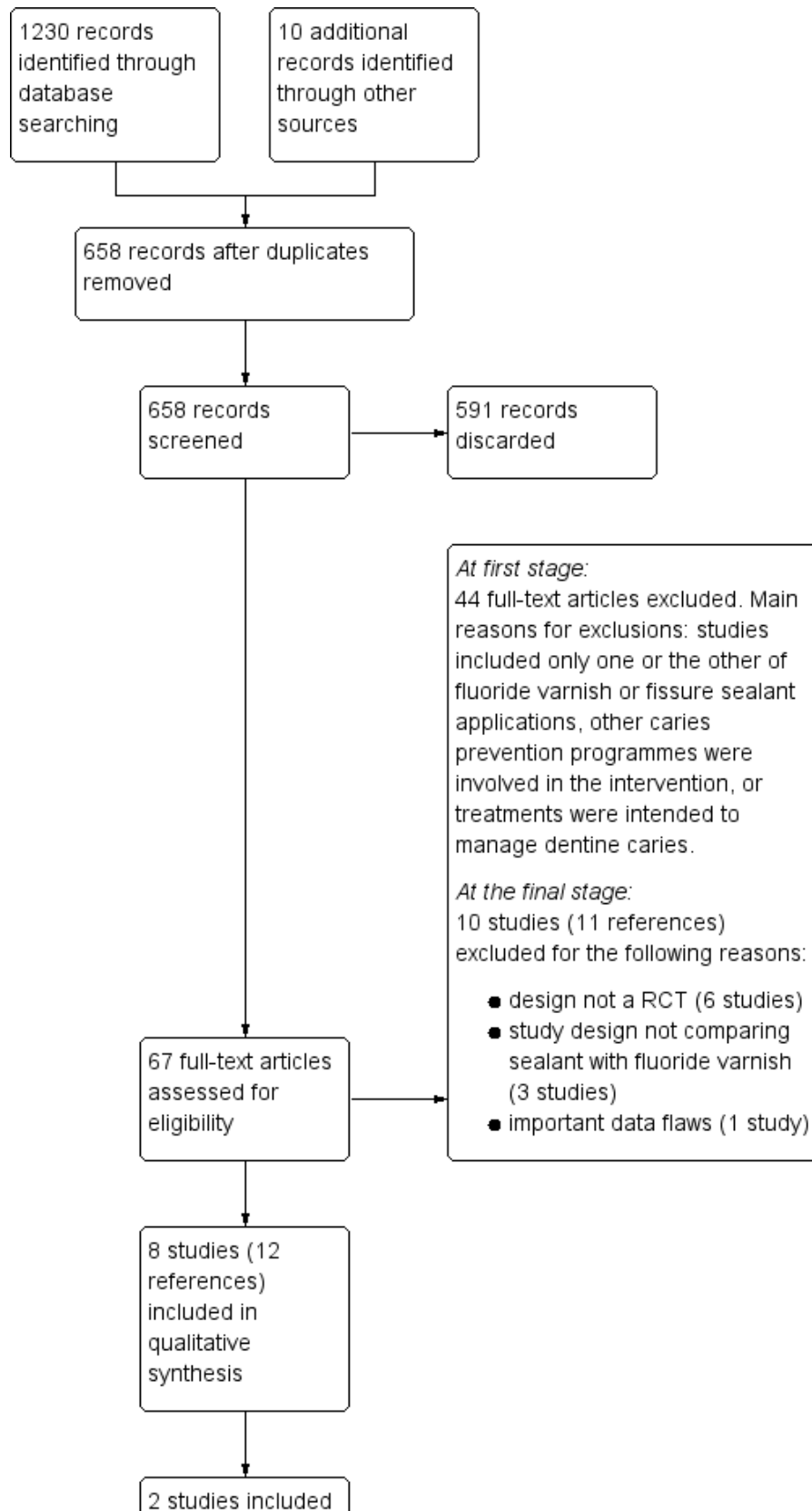
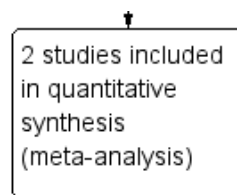


Figure 1. (Continued)



For this and previous updates, we contacted the authors of three studies to obtain additional information to assess the eligibility of studies for this review (de Oliveira 2013; Saifullina 1990; Uma 2011). One study author provided additional information (Uma 2011).

In this updated version of the review, we included four new studies (Ji 2007; Liu 2012; Salem 2014; Tagliaferro 2011) and excluded two new studies (de Oliveira 2013; Uma 2011). See [Characteristics of included studies](#) and [Characteristics of excluded studies](#).

The electronic search identified two potential ongoing trials for this review: [ISRCTN17029222](#); and [ISRCTN81071356](#). See [Characteristics of ongoing studies](#).

We applied no language restrictions and translated all non-English language reports for study assessment. Review authors could read reports in English, German and Scandinavian languages. We consulted translators to identify and assess non-English reports that had potential for inclusion (Chinese, Polish, Russian, Portuguese and Spanish).

Included studies

In total, we included eight studies in the review (Bravo 2005; Florio 2001; Ji 2007; Liu 2012; Raadal 1984; Salem 2014; Splieth 2001; Tagliaferro 2011).

Comparisons

- Pit and fissure sealants versus fluoride varnishes: resin-based fissure sealant versus fluoride varnish (n = 4) (Bravo 2005; Liu 2012; Raadal 1984; Salem 2014); glass ionomer fissure sealant versus fluoride varnish (n = 1) (Ji 2007); and resin-modified glass ionomer fissure sealant versus fluoride varnish (n = 2) (Florio 2001; Tagliaferro 2011).
 - * Tagliaferro 2011 actually evaluated whether additional benefit is derived by using sealants and fluoride varnish among children receiving regular oral health education (the evaluation was carried out separately in populations with high risk and low risk of caries).
- Pit and fissure sealant together with fluoride varnish versus fluoride varnish alone: resin-based fissure sealant plus fluoride varnish versus fluoride varnish alone (n = 1) (Splieth 2001).

Study designs

Six of the eight included studies were of parallel-group design (Bravo 2005; Florio 2001; Ji 2007; Liu 2012; Salem 2014; Tagliaferro 2011) and the other two were split-mouth studies, in which the two interventions (fissure sealant vs fluoride varnish (Raadal 1984) and fissure sealant plus fluoride varnish vs fluoride varnish alone (Splieth 2001)) were randomly allocated to teeth within a tooth pair.

Settings

Two studies were conducted in Brazil (Florio 2001; Tagliaferro 2011), two in China (Ji 2007; Liu 2012), one in Germany (Splieth 2001), one in Iran (Salem 2014), one in Norway (Raadal 1984) and one in Spain (Bravo 2005). In seven out of the eight studies, children were recruited from public dental clinics or schools. In one study, children were enrolled from private dental practice (Splieth 2001). The age range of the children over all included studies was five to 10 years.

Interventions

In all studies, sealants and fluoride varnishes were applied to occlusal surfaces of permanent first molars. Applications were done on sound surfaces (Bravo 2005; Ji 2007; Salem 2014; Tagliaferro 2011), on surfaces with enamel lesions (Florio 2001) or in the same study on sound surfaces or on surfaces with enamel lesions (Liu 2012; Raadal 1984; Splieth 2001). In Raadal 1984, surfaces with initial caries in enamel to be sealed were prepared mechanically and caries removed before sealant was applied.

The sealant material in Ji 2007 was glass ionomer; Florio 2001 and Tagliaferro 2011 used resin-modified glass ionomer; and the other five studies used resin-based sealant materials: light-polymerised resin sealant (Bravo 2005; Salem 2014; Splieth 2001), light-polymerised resin sealant with fluoride (Liu 2012) and autopolymerised resin sealant (Raadal 1984). Reapplication of sealants was reported in three studies (Bravo 2005; Salem 2014; Splieth 2001). In Bravo 2005, sealants were reapplied if partial or total loss had occurred since the previous examination after six, 12, 18, 24 and 36 months. In Salem 2014, partially and completely lost sealants were repaired or reapplied once if needed after six months. In Splieth 2001, children were examined semi annually for two years, and sealants were resealed if necessary.

Complete retention of resin-based sealants after two years varied from 43% (Salem 2014) to 81% (Splieth 2001). Bravo 2005 with longer follow-up time reported complete resin sealant retention of 63% after four years and 39% after nine years. Retention of glass ionomer sealants was also fairly high (66% complete retention after one year (Florio 2001 with resin-modified glass ionomer); 84% after two years (Tagliaferro 2011 with resin-modified glass ionomer) and 61% after three years (Ji 2007 with chemically cured glass ionomer)).

The fluoride varnish used in one study was Durafluor (Medicom Worldwide Inc., Morrisville, PA, USA) (Salem 2014), in another study Fluor Protector S (Ivoclar Vivadent Inc., Amherst, NY, USA) (Ji 2007) and in the other six studies Duraphat (Colgate Oral Pharmaceuticals, New York, NY, USA). In six studies, fluoride varnish was applied biannually only to control teeth (Florio 2001; Ji 2007; Liu 2012; Raadal 1984; Salem 2014; Tagliaferro 2011), and in one study biannually to all teeth (Splieth 2001). In Bravo 2005, Duraphat

was applied to newly erupted molars and was reapplied to all molars that had remained healthy after six, 12, 18, 24, 30, 36 and 42 months.

Co-interventions

Besides pit and fissure sealing and fluoride varnish application, studies included other co-interventions. In [Florio 2001](#), tap water was fluoridated and children received professional prophylaxis during dental examination visits. In [Raadal 1984](#), participants followed a fluoride rinsing programme at schools during follow-up, and use of fluoride tablets was recommended. [Splieth 2001](#) reported that 5% of children used fluoride tablets during the trial. Six studies reported motivation and instruction of participants towards good oral hygiene and use of fluoridated toothpaste ([Florio 2001](#); [Liu 2012](#); [Raadal 1984](#); [Salem 2014](#); [Splieth 2001](#); [Tagliaferro 2011](#)).

Two studies gave information on food (e.g. snacking habits of children). In [Splieth 2001](#), during the trial, the mean frequency of cariogenic food intake per day was 15, including a large number of sweetened drinks. In [Liu 2012](#), at study baseline, 13% of children in the sealant group and 31% in the fluoride varnish group consumed snacks twice a day or more frequently (no information was provided on snacking habits during the trial).

Caries prevalence of children at baseline

All studies except [Ji 2007](#) stated the baseline caries prevalence of the study population. The only study from the 1980s ([Raadal 1984](#)) stated that initial mean decayed, missing, filled deciduous teeth (dmft) was 4.7 (standard deviation (SD) 3.3). The three studies conducted in the 1990s stated baseline caries prevalences as follows: In [Bravo 2005](#), baseline mean decayed, filled deciduous teeth (dft) in the sealant group was 2.2 (SD 2.6), and in the varnish group 2.4 (SD 3.3); in [Florio 2001](#), mean decayed, missing, filled deciduous surfaces (dmfs) in the sealant group was 3.8 (SD 2.5), and in the fluoride varnish group 4.5 (SD 2.7); and in [Splieth 2001](#), initial mean decayed, missing, filled permanent surfaces (DMFS) was 0.2. The three studies from the 2010s stated baseline caries prevalences as follows: In [Liu 2012](#), baseline mean decayed, missing, filled deciduous teeth (dmft) in the sealant group was 3.19 (2.68) and in the varnish group 3.58 (2.25) for children eight to 10 years of age; in [Salem 2014](#), the mean dmft index for children six to seven years of age was 4.6; and in [Tagliaferro 2011](#), the baseline mean dmft index was 4.51 (2.81) for the HRS group (high-caries-risk children receiving sealants) and 4.28 (2.54) for the HRV group (high-caries-risk children receiving fluoride varnishes), and in low-caries-risk groups, dmft + DMFT was zero. In [Ji 2007](#), 21% of control teeth without treatment were decayed after three years.

Outcome measures

Seven of the included studies reported the incidence of dental carious lesions on treated occlusal surfaces of first permanent

molars in dichotomous form (yes/no). [Tagliaferro 2011](#) reported data in continuous form as mean DMF (decayed, missed and filled) increments. In addition to visual-tactile caries diagnostic methods, one of the eight studies reported the endoscopic examination to be used ([Florio 2001](#)), and two studies reported X-rays: [Florio 2001](#), digital X-rays, and [Raadal 1984](#), traditional X-rays.

Other outcomes reported were caries progression rate ([Florio 2001](#)), changes in DMF scores on a whole-mouth level ([Splieth 2001](#)) and average treatment time for sealing and varnish application ([Splieth 2001](#)). Three studies considered adverse events ([Bravo 2005](#); [Liu 2012](#); [Tagliaferro 2011](#)).

Details of all outcomes reported for each study are given in the [Characteristics of included studies](#) table.

Intra-examiner and inter-examiner agreement for caries diagnosis was stated in four studies: In [Liu 2012](#), the Kappa co-efficient for intra-examiner reliability was reported to be over 0.9, in [Salem 2014](#) about 0.8 and in [Tagliaferro 2011](#) over 0.90. Further, the study by [Bravo 2005](#) reported Kappa coefficients for intra-examiner and inter-examiner reliability greater than 0.68.

Funding source

Five of the eight studies were supported by governmental or academic sources or by independent research foundations ([Bravo 2005](#); [Florio 2001](#); [Liu 2012](#); [Salem 2014](#); [Tagliaferro 2011](#)). The other three studies did not provide information on funding.

Excluded studies

We excluded 10 studies (with 11 references) for reasons presented under [Characteristics of excluded studies](#).

Reasons for exclusion varied, and for some studies we identified several reasons for exclusion. The main reasons for exclusion were as follows: Three studies did not compare sealant with fluoride varnish; six studies clearly were not randomised or no mention was made of randomisation; and one study had important outcome data flaws.

Risk of bias in included studies

We contacted the authors of included studies to request additional information for assessment of risk of bias if information in the report was insufficient to permit final decisions. We requested additional information from seven included studies ([Bravo 2005](#); [Florio 2001](#); [Liu 2012](#); [Raadal 1984](#); [Salem 2014](#); [Splieth 2001](#); [Tagliaferro 2011](#)) but not from [Ji 2007](#) (this study was translated and data extracted by translators). 'Risk of bias' assessments for each individual study are presented in the 'Risk of bias' tables included under [Characteristics of included studies](#), and results are presented graphically by domain over all studies ([Figure 2](#)) and by individual study ([Figure 3](#)).

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

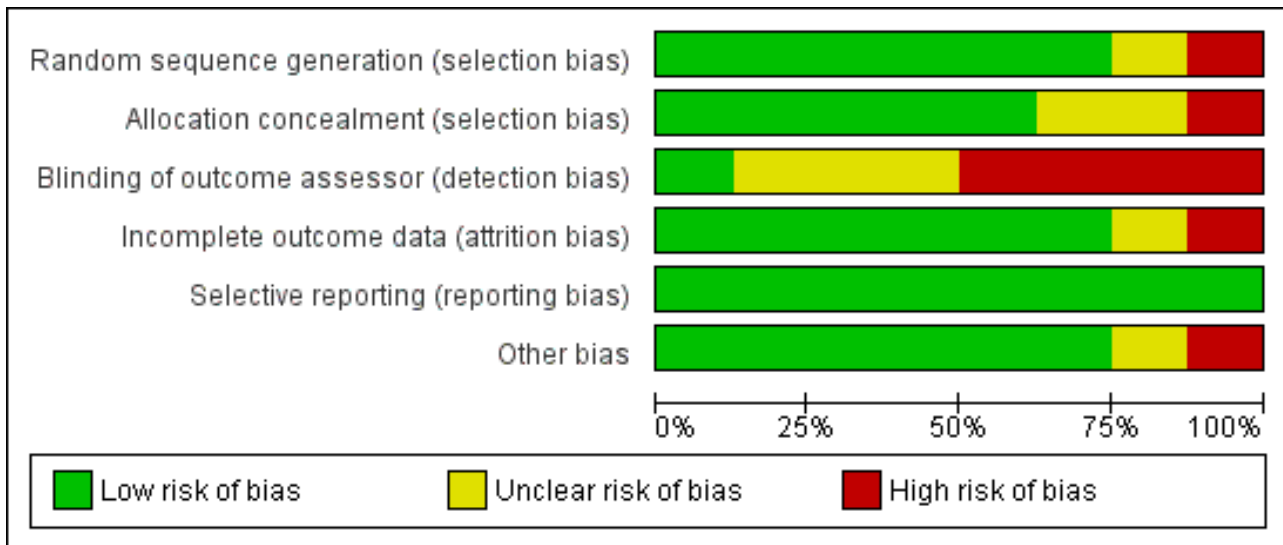


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessor (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bravo 2005	⊖	⊖	?	?	+	+
Florio 2001	+	?	⊖	⊖	+	⊖
Ji 2007	?	?	⊖	+	+	?
Liu 2012	+	+	?	+	+	+
Raadal 1984	+	+	⊖	+	+	+
Salem 2014	+	+	+	+	+	+
Splieth 2001	+	+	⊖	+	+	+
Tagliaferro 2011	+	+	?	+	+	+

Allocation

Random sequence generation was adequate, indicating low risk of bias in six studies (75%) (Florio 2001; Liu 2012; Raadal 1984; Salem 2014; Splieth 2001; Tagliaferro 2011). Random sequence was generated most often by using random numbers or tossing coins. We assessed one study in this domain as having high risk of bias (Bravo 2005) and one as having unclear risk of bias (Ji 2007).

We graded allocation concealment as having low risk of bias in five of the eight studies (Liu 2012; Raadal 1984; Salem 2014; Splieth

2001; Tagliaferro 2011). In two studies, allocation concealment remained unclear (Florio 2001; Ji 2007), and in one study, it was assessed as having high risk of bias (Bravo 2005).

Blinding

We did not address performance bias in this review (see Table 2).

We assessed blinding of outcome measurement as adequate in one of the eight studies (Salem 2014) (13%), as the study stated that the examiner was not involved in study design. Blinding of outcome

measurement was assessed as 'unclear' in three studies (38%) (Bravo 2005; Liu 2012; Tagliaferro 2011), in which forms stating children's group assignment were kept away from the examiner. In three studies, outcome assessors were not blinded (Florio 2001; Raadal 1984; Splieth 2001), and in one study, no information was provided on blinding of outcome assessors (Ji 2007), so we graded these studies as having 'high' risk of detection bias.

Incomplete outcome data

Only one study had follow-up of 12 months, and it was assessed as having high risk of bias because drop-out rates were unevenly distributed between study groups (Florio 2001). The six studies providing data at 24 months of follow-up were assessed as having low risk of bias in this domain (Ji 2007; Liu 2012; Raadal 1984; Salem 2014; Splieth 2001; Tagliaferro 2011). The only study providing data at 36 months of follow-up was assessed to be at low risk of bias in this domain (Ji 2007). The only study providing data at 48 months of follow-up was assessed to be at unclear risk of bias because no information on drop-outs was provided by study group (Bravo 2005). Bravo 2005 also measured outcomes at nine years of follow-up and was assessed to have high risk of bias in this domain (the proportion of participants assessed and included in the analysis was only 33%).

Selective reporting

All eight studies reported their pre-specified outcomes adequately so were assessed as having low risk of bias.

Other potential sources of bias

We assessed the comparability of study groups and possible co-interventions during the trial as balanced between study groups in six studies (Bravo 2005; Liu 2012; Raadal 1984; Salem 2014; Splieth 2001; Tagliaferro 2011). Two of the six studies were of split-mouth design, where conditions are the same for both teeth within a tooth pair (Raadal 1984; Splieth 2001); the other four studies were parallel-group studies (Bravo 2005; Liu 2012; Salem 2014; Tagliaferro 2011). No information on this domain was provided in Ji 2007, so the judgement was 'unclear' risk of bias. In the study by Florio 2001, groups were assessed as imbalanced at baseline, and the study was graded as having 'high' risk of bias in this domain.

Overall risk of bias was assessed as low for one study (Salem 2014), as unclear for two studies (Liu 2012; Tagliaferro 2011) and as high for five studies (Bravo 2005; Florio 2001; Ji 2007; Raadal 1984; Splieth 2001) for the five key domains of allocation concealment, blinding of outcome assessment, incomplete outcome data, selective reporting and baseline comparability of study groups (Figure 3).

Effects of interventions

See: [Summary of findings for the main comparison Resin-based fissure sealant compared with fluoride varnish for preventing dental caries](#); [Summary of findings 2 Glass ionomer fissure sealant or resin-modified glass ionomer fissure sealant compared with fluoride varnish for preventing dental caries](#); [Summary of findings 3 Resin-based fissure sealant together with fluoride varnish versus fluoride varnish alone for preventing dental caries](#)

We present a summary of main results for the following comparisons: resin-based sealant versus fluoride varnish ([Summary of findings for the main comparison](#)); glass ionomer or resin-modified glass ionomer sealant versus fluoride varnish

([Summary of findings 2](#)); and resin-based sealant together with fluoride varnish versus fluoride varnish alone ([Summary of findings 3](#)).

Results from seven studies are incorporated in this review (Bravo 2005; Florio 2001; Ji 2007; Liu 2012; Raadal 1984; Splieth 2001; Tagliaferro 2011). Although the study by Salem 2014 met the inclusion criteria, results and data (complex multi-level model with teeth nested in a child nested in a school class nested in a school) were not provided in useable form for this review (the unit of analysis was a tooth surface, but clustering of teeth and of children was not taken into account).

All studies reported data on sealant and fluoride varnish applications to occlusal surfaces of permanent first molars.

Sealant versus fluoride varnish

Primary outcome - incidence of dentinal carious lesion on treated occlusal surfaces of molars or premolars

Resin fissure sealant versus fluoride varnish

Three studies compared resin-based fissure sealant versus fluoride varnish: Two studies reported results at two years (the split-mouth study by Raadal 1984 and the parallel-group study by Liu 2012); one parallel-group study reported results at four years and nine years (Bravo 2005) (see [Table 1](#)).

At two years, the meta-analysis pooling effect estimates of Liu 2012 and Raadal 1984 found a significant benefit for resin-based sealants with an odds ratio (OR) of 0.69 (95% confidence interval (CI) 0.50 to 0.94) compared with fluoride varnish, when a fixed-effect model was used with available case data (358 evaluated participants; [Analysis 1.1](#)). We noted no statistical heterogeneity between studies (I^2 statistic = 0%), although Raadal 1984 found significant benefit for resin sealants but Liu 2012 reported that the benefit of sealants was not statistically significant. Incomplete blinding of outcome measurement led to further uncertainty surrounding results.

Bravo 2005 found a significant difference in favour of visible-light-polymerised resin sealant compared with fluoride varnish, with a risk ratio (RR) of 0.42 (95% confidence interval (CI) 0.21 to 0.84) ([Analysis 1.2](#)) and 0.48 (95% CI 0.29 to 0.79) ([Analysis 1.3](#)) at four years and nine years of follow-up, respectively. Drop-out rates were high after nine years of follow-up.

Glass ionomer fissure sealant versus fluoride varnish

Resin-modified glass ionomer fissure sealant versus fluoride varnish at one year

One small study, at high risk of bias, provided results for one year of follow-up (Florio 2001; [Table 1](#)). This study failed to find a significant difference between intervention groups, with an OR of 0.18 (95% CI 0.01 to 4.27) at one year of follow-up ([Analysis 2.1](#)). All occlusal surfaces under examination had enamel lesions before applications.

Glass ionomer fissure sealant versus fluoride varnish at two years and three years

One study with incomplete information and analyses provided results for this comparison (Ji 2007). In the statistical analyses of this study, clustering of teeth within a child was not taken into account (with adequate standard errors of estimates), and no information on numbers of children at follow-up times was

available for re-analysis of data. However, because the numbers of decayed teeth were small in both groups, we decided to report the absolute numbers of decayed tooth surfaces in sealant and fluoride varnish groups without effect estimates (ignoring the clustered data). We noted no significant differences in rates of caries development between groups (at 24 months, 11 of 321 sealed surfaces (3.4%) and 13 of 320 fluoride-varnished surfaces (4.1%) were decayed, and at 36 months, 22 of 311 (7.1%) and 24 of 320 (7.5%), respectively). The rate of caries in the control group without intervention was 14% (48/348) at 24 months and 21% (71/340) at 36 months.

Resin-modified glass ionomer cement plus oral health education versus fluoride varnish plus oral health education at two years

One study (Tagliaferro 2011) provided results for comparison of resin-modified glass ionomer cement + oral health education every three months versus fluoride varnish application biannually + oral health education every three months. The comparison was performed separately for high-caries-risk children and for low-caries-risk children. Groups to be compared were HRS (high-risk children with sealant application + oral health education) versus HRV (high-risk children with fluoride varnish application + oral health education); and LRS (low-risk children with sealant application + oral health education) versus LRV (low-risk children with fluoride varnish application + oral health education).

Investigators reported results as follows: After 24 months, the HRS group showed similar caries increment when compared with the HRV group (mean DMF (decayed, missed and filled) increments on occlusal surfaces of first permanent molars was 0.06 (SD 0.25) and 0.29 (0.68), respectively). For low-risk groups, no statistically significant differences were observed among treatments. Study authors concluded "that in a 2-year period, oral health education was sufficient to control occlusal caries in low-risk children while for high-risk children, sealant application in addition to oral health education was considered the best strategy".

Primary outcome - progression of caries lesion into enamel or dentine

One study (Florio 2001), which compared resin-modified glass ionomer fissure sealant versus fluoride varnish at one year, included only enamel caries lesions and reported arrestment of enamel caries lesions or progression into dentine with both interventions (Analysis 2.1).

Secondary outcome - number of visits to the dentist for repair of sealant or fluoride varnish application

The number of visits for repair or reapplication of sealants or fluoride varnish applications was reported directly only by Bravo 2005, for which the average number of treatment visits per child during the active phase of the programme was 2.2 (SD 1.1) (maximum 6) for children in the resin sealant group and 7.3 (SD 1.0) (maximum 8) for children in the varnish group. This difference is great because the sealant was reapplied only when partial or total loss occurred, whereas the varnish was systematically reapplied.

Secondary outcome - adverse events and safety of sealants and fluoride varnishes

Three of the included studies considered adverse events associated with sealants and fluoride varnishes (Bravo 2005; Liu 2012;

Tagliaferro 2011). Participants detected and reported no adverse events.

Sealant together with fluoride varnish versus fluoride varnish alone

Primary outcome - incidence of dentinal carious lesions on treated occlusal surfaces of molars or premolars

Resin fissure sealant plus fluoride varnish versus fluoride varnish

One split-mouth study analysed 92 children and compared resin-based fissure sealant concurrently with fluoride varnish versus fluoride varnish alone after two years (Splieth 2001); investigators found a significant difference in favour of the sealant together with fluoride varnish, with an OR of 0.30 (95% CI 0.17 to 0.55) compared with fluoride varnish alone (Table 1; Analysis 3.1). This study considered both sound occlusal surfaces and surfaces with enamel lesions. Incomplete blinding of outcome measurement caused some uncertainty in results, although the study was otherwise well conducted.

Primary outcome - changes in decayed, missing and filled (DMF) figures at whole-mouth level

Splieth 2001 reported changes in DMF figures at the whole-mouth level during this study. The mean decayed, missing and filled permanent surfaces (DMFS) score of the whole mouth in the study population increased from 0.2 to 0.6 after one year and to 1.1 after two years. Study authors reported that most caries still occurred on occlusal surfaces of first permanent molars (50.9%).

Secondary outcome - time taken to apply pit and fissure sealant or fluoride varnish

Only one study reported an average treatment time for sealing and fluoride varnish application (Splieth 2001). Total time needed for sealing and resealing of two teeth was on average 29 minutes during two years, of which most of the time was spent on initial sealants (about 17 minutes). Mean treatment time for each fluoride varnish application was under three minutes (total time during intervention: nine minutes).

DISCUSSION

Summary of main results

Effectiveness of interventions

This review found low-quality evidence for resin-based sealant, or resin-based sealant together with fluoride varnish, over fluoride varnish application for prevention of occlusal decay of permanent first molars, and very low-quality evidence for no difference between resin-modified glass ionomer or glass ionomer sealants and fluoride varnishes. Drawing conclusions on the basis of the scarce data reported in this review is complicated because of diversity in comparisons, follow-up times and sealant products, for example; thus for several outcomes, only one study was available and only one meta-analysis could be conducted. Further, it was difficult to compare caries risks of treated teeth or of children between studies because information on confounding factors (like snacking habits or use of fluoride products) and caries incidence in these populations was incomplete. Moreover, studies were conducted between the 1980s and the 2010s, and so different progression rates of caries in permanent teeth could be expected (Whelton 2004).

Sealant versus fluoride varnish

Resin fissure sealants versus fluoride varnishes

Results of the meta-analysis at two years, including one study from the 1980s (Raadal 1984) and one from the 2000s (Liu 2012), slightly favoured resin sealants over fluoride varnishes. When results are interpreted, it should be noted that the superiority of sealants noted in the Norwegian split-mouth study by Raadal 1984 may be influenced by the carry-over effect of fluoride varnish, even though this is unlikely due to a fast-setting base and a small amount of fluoride varnish applied to one or two control teeth. Further, this split-mouth study provided no information on caries incidence in control teeth without treatment and was conducted as early as 1980s. In the Chinese study conducted recently by Liu 2012, numbers of decayed tooth surfaces in all groups were, in total, rather small (at 24 months of follow-up, proportions of pit/fissure sites with dentine caries in sealant, fluoride varnish and control groups were 1.6%, 2.4% and 4.6%, respectively). Liu 2012 authors discussed that the low incidence of fissure caries in the control group without treatment may be explained in part by today's slower dental caries progression rate (Whelton 2004).

Both studies (Liu 2012; Raadal 1984) included surfaces with enamel caries lesions, in addition to sound surfaces. In the study by Raadal 1984, surfaces with enamel lesions were opened mechanically before sealant application, but researchers provided no information on the number of such surfaces included. In the study by Liu 2012, 35% of tooth sites had early-stage caries at baseline. In the study by Raadal 1984, retention of sealants after 23 months of follow-up was better (63%) than in the study by Liu 2012, which reported 46% retention of sealants. Prevalence of caries in primary teeth at baseline was reported in both studies, and it was slightly lower in Liu 2012 (baseline mean dmft 3.19 (SD 2.68) and 3.58 (2.25) in sealant group and fluoride varnish group, respectively). In Raadal 1984, the mean dmft was 4.7 (SD 3.3).

The Spanish study by Bravo 2005 (started in 1990), in which sealants were placed on sound surfaces and were reapplied when partially or totally lost during the four-year active preventive programme, found resin sealants better than fluoride varnishes at four years and nine years of follow-up. Complete sealant retention was reported at 63% at four years and 39% at nine years. The incidence of caries in the control group after nine years was 77% on occlusal surfaces, whereas 26.6% of sealant teeth and 55.8% of fluoride-varnished teeth had developed caries at nine years. Caries prevalence among primary teeth at baseline was stated as follows: mean dft in the sealant group 2.24 (SD 2.59) and in the fluoride varnish group 2.42 (SD 3.26). The total drop-out rate of Bravo 2005 at nine years of follow-up was high (67%), suggesting lack of reliability of results.

Glass ionomers and resin-modified glass ionomers versus fluoride varnishes

Three studies - one with traditional glass ionomer (Ji 2007) and two with resin-modified glass ionomer (Florio 2001; Tagliaferro 2011) - compared glass ionomer versus fluoride varnish. The small study by Florio 2001, analysing 21 children and providing only one-year data, reported no differences between resin-modified glass ionomer sealant and fluoride varnish. Retention of sealant in that study was 66%. However, Tagliaferro 2011, concluded that over a two-year period for high-risk children, sealant application in addition to oral health education was considered the best strategy. The retention rate in Tagliaferro 2011 was high (84% after 24 months). In the

third glass ionomer study by Ji 2007, numbers of decayed teeth were rather small in both treatment groups, especially after two years of follow-up (at 24 months 3.4% of sealed surfaces and 4% of fluoride-varnished surfaces were decayed; corresponding figures at 36 months were 7.1% and 7.5%). Rates of caries in control group teeth without intervention were 14% at 24 months and 21% at 36 months. Sealant retention was 60% after three years.

Sealant together with fluoride varnish versus fluoride varnish alone

The German study with split-mouth design, which compared resin sealant together with fluoride varnish versus fluoride varnish alone, found that sealant given concurrently with fluoride varnish was better than fluoride varnish alone at 24 months follow-up (Splieth 2001). Children were examined semi annually for two years, sealants were resealed if necessary and fluoride varnish was applied to all teeth at the time of examination (including the sealed tooth). Study authors reported that the study was conducted in the low-caries-risk population and that the retention rate of the sealants was high (81%). However, the mean frequency of cariogenic food intake per day was reported to be 15, including a large number of sweetened drinks. Oral hygiene was moderate.

Adverse events and safety of sealants and fluoride varnishes

Three studies assessed or considered adverse events of sealants and fluoride varnishes (Bravo 2005; Liu 2012; Tagliaferro 2011). In these studies, participants did not detect or report any adverse events.

However, some systematic reports have considered the possible oestrogen-like effects of resin-based materials including bisphenol A (BPA) (Azarpazhooh 2008b; Fleisch 2010). This synthetic chemical resin is widely used in the production of plastic products intended for common life but are rarely used as such in dental materials (ADA 2003). Dental resins include primarily BPA derivatives (e.g. bis-GMA, bis-DMA) rather than pure BPA. These derivatives can hydrolyse to BPA and can be detected transiently in saliva (Arenholt 1999; Schmalz 1999). BPA has been detected in saliva for up to three hours after application of resin sealants (Fleisch 2010). Current evidence suggests that patients are not at risk for oestrogen-like effects when sealants are used (ADA 2003; Azarpazhooh 2008b; Fleisch 2010). The American Dental Association has concluded that estimated BPA exposure from dental materials is recorded as very low compared with total estimated daily BPA exposure from food and environmental sources (ADA 2003).

Fluoride varnishes are safe for dental care when used correctly by professionals. Varnish sets rapidly when applied to teeth, and most of the sodium fluoride applied will stay on the tooth surfaces in natural resins (Chu 2006). Only a small dose of fluoride is swallowed over several hours, and risk of acute toxic reactions (such as nausea and vomiting) is minimal (Bawden 1998; Seppä 1999). Fluoride ingestion following a varnish application has been shown to have barely detectable effects on plasma fluoride concentrations. Ekstrand 1980 showed plasma fluoride peak concentrations of 3.2 to 6.3 µmol/L within two hours of Duraphat varnish application, followed by a rapid two-hour decrease. Contact allergies to fluoride varnish due to colophony are possible but have been reported in only two cases, both related to Duraphat varnish (Chu 2006; Isaksson 1993).

Overall completeness and applicability of evidence

Setting

Four of the eight included studies were conducted in the 2000s, three in the 1990s and one in the 1980s. In most studies, children were recruited from schools or public-oriented dental clinics. In only one study were children enrolled from a private dental practice (Splieth 2001). In general, these studies were conducted in well-equipped dental settings.

Diagnosis

This review compared sealants versus fluoride varnishes for prevention or control of caries, and we accepted studies with sound occlusal surfaces of molars and premolars or with enamel lesions. Four of the eight included studies reported applications only on sound surfaces (Bravo 2005; Ji 2007; Salem 2014; Tagliaferro 2011); one study only on surfaces with enamel lesions (Florio 2001); and three studies on sound surfaces or on surfaces with enamel lesions (Liu 2012; Raadal 1984; Splieth 2001). In addition to clinical-tactile caries diagnostic methods, two of the eight studies used other diagnostic methods before applications. Liu 2012 used the DIAGNOdent laser fluorescence device (KaVo Dental Corporation, Lake Zurich, IL, USA) to rule out molars with caries in dentine and fissures with potential dentine caries, and Florio 2001 reported that digital radiographic and endoscopic examinations were used to evaluate restricted enamel decay lesions.

Caries diagnosis on occlusal surfaces can, however, be challenging. Conventional visual, tactile and radiographic methods in the diagnosis of occlusal caries have not been accurate enough to identify whether a lesion extends into the dentine (McComb 2001). New technologies such as laser fluorescence methods (e.g. DIAGNOdent device) may be sensitive in detecting occlusal dental caries (Bader 2004; Twetman 2013), but the likelihood of false-positive diagnoses may increase when laser fluorescence is used rather than visual methods (Bader 2004). Regardless of the caries diagnostic method used, the condition of an occlusal surface to be sealed or varnished remains in any case somewhat unclear.

Quality of the evidence

Sealant versus fluoride varnish

Resin-based sealants versus fluoride varnishes

The body of evidence comparing resin-based sealants versus fluoride varnishes comprises three randomised studies - two studies reporting results at two years, and one at both four and nine years - and was assessed as of low quality according to GRADE (Grades of Recommendation, Assessment, Development and Evaluation) assessment criteria (Summary of findings for the main comparison). This "low" quality rating implies that further research is very likely to have an important impact on our confidence in the estimates of effects and is likely to change the estimates at each follow-up point.

The number of included trials with different designs and follow-up times is too small to permit certain conclusions. The pooled estimate of two studies slightly favoured resin sealants over fluoride varnishes at two years (with OR 0.69, 95% CI 0.50 to 0.94); these studies otherwise were well conducted, but incomplete blinding of outcome measurements can cause bias in the results. At four years and nine years, the only study of these comparisons

(with high drop-out rates) found more caries on fluoride-varnished occlusal surfaces than on resin-sealed surfaces.

The only study that showed similar effectiveness between resin sealants and fluoride varnishes was conducted in the 2000s; the other two studies (favouring sealants) were conducted earlier - in the 1980s and in the 1990s. It has been stated that the progression rate of caries in permanent teeth has recently become slower (Whelton 2004) and varies between populations, making conclusions on the quality of evidence uncertain, especially when the follow-up time is fairly short. Effectiveness of resin-based sealants is strongly related to retention of sealant, and retention depends also on follow-up time.

Glass ionomers and resin-modified glass ionomers versus fluoride varnishes

We assessed the quality of the body of evidence for glass ionomer sealants (one study with original chemically cured material, and two studies with a light curable type modified with resin) compared with fluoride varnishes as very low according to GRADE assessment criteria (Summary of findings 2). This "very low" rating implies that we are very uncertain about the estimates. Although all three studies comparing glass ionomer versus fluoride varnish reported similar results (no differences between interventions), we downgraded the evidence by three levels because of the small numbers of trials with different designs and follow-up times and assessed as having high or unclear risk of bias. Further, Tagliaferro 2011 actually evaluated whether additional benefit was derived from sealants and fluoride varnishes among children receiving regular oral health education.

Sealant together with fluoride varnish versus fluoride varnish alone

The body of evidence comparing resin-based sealant together with fluoride varnish versus fluoride varnish alone comprised one randomised study at two years, and was assessed as of low quality according to GRADE assessment criteria (Summary of findings 3). We downgraded the quality of evidence by two levels because a single study (92 analysed participants) was conducted as early as the 1990s and no information was provided on caries incidence of control teeth without treatment, and although the study was otherwise well conducted, lack of blinding of outcome measurement can cause some further uncertainty about results.

Potential biases in the review process

Study design

With a split-mouth design, fluoride varnish applied to control teeth might also impact teeth in the intervention group through saliva. However, results of a split-mouth study show that fluoride varnish application elevated fluoride concentrations of dental plaque locally in the treated teeth quadrant but fluoride concentrations were not elevated in the opposite untreated quadrant (Sköld-Larsson 2000). The carry-over effect of fluoride varnishes most probably is dose dependent, and we assessed carry-over effects on sealed occlusal surfaces to be insignificant because they have a fast-setting base and only a small amount of fluoride varnish was applied to one or two control teeth. Therefore, we decided to accept split-mouth studies into this review.

Reporting bias

We decided to consider only studies with a full-text report. We excluded studies reported only as abstracts because evidence showed discrepancies between data reported in the abstract and those provided in the final published full report, and indicated that information on trial quality indicators was often lacking (Chokkalingam 1998; Hopewell 2006). Thus we saw that the full-text report is required to ensure reliable data extraction and assessment of risk of bias. To diminish risk of publication bias, we contacted the authors of potential abstracts to ask whether a full-text report of the study (unpublished or published) was available.

Agreements and disagreements with other studies or reviews

One other systematic review has considered dental sealants versus fluoride varnishes (Neusser 2014). That review presented conclusions based on the trials (also included in this review update) of Bravo 2005, Raadal 1984 and Tagliaferro 2011, and on the previous version of this Cochrane systematic review (by Hiiri 2010). The review by Neusser 2014 concluded, "The studies and literature reviews have shown protective effects of pit and fissure sealants compared to the professional application of fluorides, particularly in children and adolescents at high caries risk. However, because of methodological flaws, the results of the RCTs should be interpreted with caution".

AUTHORS' CONCLUSIONS

Implications for practice

Although we found evidence suggesting the superiority of resin-based fissure sealants over fluoride varnishes applied to prevent occlusal caries in permanent molars, and some evidence for benefit

of resin-based sealant together with fluoride varnish over fluoride varnish alone, this evidence is of low quality. We conclude that current scarce data mean that it is not possible to reach conclusions about whether to apply sealants or fluoride varnishes on occlusal surfaces of permanent molars.

Implications for research

The number of included clinical trials was small, and more high-quality research is needed to compare the relative effectiveness of sealants versus fluoride varnishes for preventing dental decay on occlusal surfaces. With a split-mouth study design, the carry-over effect of fluoride varnish applications on the sealed teeth cannot be totally ruled out. Therefore, a parallel-group design would provide more reliable information on differences in effectiveness of sealants and fluoride varnishes. Proper documentation and description of study populations, intervention study designs, follow-up periods, drop-outs and outcomes as described in the CONSORT statement are recommended.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Bravo 2005

Methods	Trial design: cluster-randomised design, where 15 school classes were randomly assigned to 3 treatment arms. School classes were conducted at 5 primary schools, which were selected at random from a group of 21 schools. Mean number of teeth per child was 3.5 (a child was an additional cluster) Follow-up period: 9 years: 4-year caries preventive programme, plus 5 years after active programme
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Bravo 2005 (Continued)

Study was started in 1990

Participants	<p>Location: Spain, a non-fluoridated city (0.07 ppm F ion in tap water) Children were from middle or lower-middle socioeconomic status families Inclusion criteria: children with sound permanent first molars Age at baseline: 6 to 8 years (average age 7 years) Gender: girls 68% in sealant group, 47% in varnish group Baseline caries: sealant group: mean dft 2.24 (SD 2.59); fluoride varnish group: 2.42 (SD 3.26)</p> <p>Number randomly assigned: 362 (112 in sealant group; 115 in fluoride varnish group; 135 in control group) Number evaluated: 75 (37 in sealant group; 38 in fluoride varnish group; 45 in control group). Only children who (1) had at least 1 completely erupted and sound permanent molar at any period during the active programme, and (2) were examined at 4-year follow-up were included in the analysis at 9 years</p>
Interventions	<p>Comparison: resin-based sealant vs fluoride varnish Group 1: visible-light-polymerised opaque Delton Sealants were applied to completely erupted occlusal surfaces of permanent first molars by 1 dentist plus an assistant, who used portable equipment. After 6, 12, 18, 24 and 36 months, sealant was applied to molars that had not previously erupted and was replaced if partial or total loss had occurred since the previous examination Group 2: fluoride varnish (Duraphat, sodium fluoride (NaF)) Varnish was applied to partially or fully erupted occlusal surfaces of permanent first molars by 1 dentist plus an assistant, who used portable equipment. After 6, 12, 18, 24, 30, 36 and 42 months, varnish was also applied to newly erupted molars and was reapplied to all those that were still sound Group 3: control group without treatments (Only sealant and fluoride varnish groups were used in this review) Co-interventions: none reported</p>
Outcomes	<p>Sound or carious occlusal surface of molar Outcomes were assessed by a dentist. Examinations were made with an exploration probe and a flat mirror Number of visits to the dentist for repair of sealant or fluoride varnish application Adverse events</p>
Notes	<p>Inter-rater agreement: Kappa coefficients for intra-examiner and inter-examiner reliability > 0.68 in all measurements</p> <p>Sealant retention: complete sealant retention 63% at 4-year follow-up and 39% at 9-year follow-up Funding source: Spain Ministry of Education and Science. Study authors were from the university</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote from author correspondence: "Each school-class was numbered. By using a list of random numbers from a statistical book each school-class was assigned to the 3 groups. When 1 group was full of children (i.e. the sum of the children in the assigned school-classes was above the sample size needed for a group), then that group was excluded for new random assignments. The school classes allocation was not completely random, since it had some restrictions: For example, the total number of children should be at last more or less equilibrated between the three groups (thus, after the first random assignment, the following were conditional)" Comment: Randomisation procedure was not completely random
Allocation concealment (selection bias)	High risk	Comment: The non-random method used for sequence generation would likely not allow for allocation concealment

Bravo 2005 (Continued)

Blinding of outcome assessor (detection bias)	Unclear risk	<p>Quote: "A different dentist examined the subjects in a blinded fashion"</p> <p>Outcome assessor dentist did not have access to previous records (information was obtained from study authors)</p> <p>Comment: Blinding of outcome assessor was intended, but it remains unclear whether outcome assessor had information on study design</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<p>Missing data: 18% for all 3 groups combined at 4 years (drop-out rates by group not detailed)</p> <p>Comment: This domain was graded as having 'unclear' risk of bias because no information on drop-outs was provided by group at 4 years of follow-up. At 9 years of follow-up, this domain was graded as having 'high' risk of bias because proportion of participants assessed and included in the analysis was 33% (only children who had at least 1 completely erupted and sound permanent molar at any time period during the active programme, and were examined at 4-year follow-up, were included in the analysis at 9 years)</p>
Selective reporting (reporting bias)	Low risk	<p>Outcomes reported: caries response and sealant retention</p> <p>Comment: Pre-specified outcomes (in methods) were reported in a pre-specified way</p>
Other bias	Low risk	<p><i>Comparability of groups:</i></p> <p>Comment: Detailed description of demographic characteristics and caries risk level at baseline was given for groups available at 4 years and 9 years, and groups were assessed to be comparable</p> <p>Baseline mean dft in sealant group was 2.24 (SD 2.59) and in fluoride varnish group 2.42 (SD 3.26). Mean age in sealant group was 7.3 years, and in varnish group 7.6 years. Proportion of girls was 68% in sealant group and 47% in varnish group. Although proportion of girls was bigger in sealant group than in fluoride varnish group, assessment revealed that groups were in balance at baseline</p> <p><i>Co-interventions:</i></p> <p>Quote: "The children received no toothbrushing, fluoride rinse, or fluoride tablet programs"</p> <p>Comment: This domain was graded as having 'low' risk of bias because no co-interventions were included in the protocol</p>

Florio 2001

Methods	<p>Trial design: parallel-group study design, where individuals were randomly assigned to 3 treatment arms</p> <p>Follow-up: 12 months</p> <p>Study was started in 1998</p>
Participants	<p>Location: 4 public day nursery schools (families at low economic level), Brazil</p> <p>Inclusion criteria: children with first permanent molars with restricted enamel decay on occlusal surfaces</p> <p>Age at baseline: 6 years</p> <p>Baseline caries: sealant group: mean dmfs 3.8 (SD 2.5); fluoride varnish group: 4.5 (SD 2.7)</p> <p>Number randomly assigned: 34 (sealant group 12, varnish group 11, control group 11 (with total 108 teeth; mean number of teeth 3.2 per child)</p> <p>Number evaluated: 31 (10 in sealant group; 11 in fluoride varnish group; 10 in control group)</p>
Interventions	<p>Comparison: resin-modified glass ionomer fissure sealant vs fluoride varnish</p> <p>3 treatment arms</p>

Florio 2001 (Continued)

Group 1: sealant group (resin-modified glass ionomer Vitremer), applied on occlusal surfaces of first permanent molars with restricted enamel decay. No resealing
 Group 2: fluoride varnish group (Duraphat, sodium fluoride (NaF)), applied every 6 months on occlusal surfaces of first permanent molars with restricted enamel decay
 Group 3: control group

(only sealant and fluoride varnish groups were used in this review)

Co-interventions: fluoridated tap water. Children received professional prophylaxis during dental examination visits

Outcomes	Arrestment of enamel caries lesion or progression into dentine was noted at 12 months of follow-up To evaluate the caries progression rate, digital radiograph + endoscopic exam was used. Examinations were carried out by the same dentist who administered the interventions
Notes	Sealant retention: Complete sealant retention was 66% at 12 months Funding source: FAPESP/Brazil (São Paulo Research Foundation is an independent public foundation)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Table of random numbers was used Comment: Information was obtained from study authors
Allocation concealment (selection bias)	Unclear risk	No information was provided
Blinding of outcome assessor (detection bias)	High risk	No blinding of outcome assessor was performed Comment: Additional information was obtained from study authors
Incomplete outcome data (attrition bias) All outcomes	High risk	Missing data: 2/12 children (17%) in sealant group and 0/11 children (0%) in varnish group No description was given of reasons for drop-outs Comment: imbalanced groups
Selective reporting (reporting bias)	Low risk	Outcome reported: arrestment of enamel caries lesion or progression into dentine at 12 months of follow-up Comment: Pre-specified caries outcome (in methods) was reported in the pre-specified way
Other bias	High risk	<i>Comparability of groups:</i> Baseline mean dmfs was 3.8 (SD 2.5) in sealant group and 4.5 (SD 2.7) in fluoride varnish group Comment: imbalanced groups <i>Co-interventions:</i> Co-interventions in sealant and fluoride varnish groups: water supply fluoridation; professional prophylaxis during follow-up consultations; children individually informed about concepts of oral health Additional information was obtained from study authors Comment: similar co-interventions in both groups

Ji 2007

Methods	Trial design: parallel-group study design, where individuals were randomly assigned to 3 treatment arms Follow-up: 36 months
Participants	Location: Study setting was community dental clinic, and children were selected from 13 primary schools in Yangpu district of Shanghai, China Inclusion criteria: children with sound permanent first molars (caries status determined by WHO (World Health Organization) criteria) Age at baseline: range 6 to 8 years Baseline caries: not reported but 21% of control teeth without treatment were decayed after 3 years Number randomly assigned: 622 children (1016 molars, on average 1.6 teeth per child) in 3 groups: 205 children in sealant, 207 in fluoride varnish, 210 in control Number evaluated: at 24 months: 641 teeth (321 teeth in sealant group; 320 teeth in fluoride varnish group); at 36 months: 631 teeth (311 teeth in sealant group; 320 teeth in fluoride varnish group) (no information on drop-out rates of participants)
Interventions	Comparison: glass ionomer fissure sealant vs fluoride varnish 3 treatment arms Group 1: sealant group (Fuji II glass ionomer cement), applied by dentist with help of assistant. No re-sealing Group 2: silane fluoride varnish group (Fluor Protector 0.1% fluoride), applied by dentist with help of assistant, applied every half year for 3 years Group 3: control (group 1 and group 2 were considered in this review) Co-interventions: none reported
Outcomes	Sound or carious occlusal surface of molar No information was given on outcome measurement procedure
Notes	<i>Sealant retention:</i> After 24 months: retained 65%, partial retained 22%, total loss 13% After 36 months: retained 61%, partial retained 25%, total loss 14% Funding source: no information on funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "622 participants were selected from 13 primary schools, and were randomly divided into 3 groups" Comment: No information on randomisation procedure was provided
Allocation concealment (selection bias)	Unclear risk	No information was provided
Blinding of outcome assessor (detection bias)	High risk	No information was provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data by teeth: at 24 months 6/327 (1.8%) in sealant group and 15/335 (4.5%) in fluoride varnish group; and at 36 months 16/327 (4.9%) in sealant group and 15/335 (4.5%) in fluoride varnish group Comment: Although no information on drop-out rates of participants was provided, we graded this domain as having 'low' risk of bias because the drop-out rate of teeth was less than 5%

Ji 2007 (Continued)

Selective reporting (reporting bias)	Low risk	Comment: Outcomes, caries status and sealant retention were reported in a pre-specified way
Other bias	Unclear risk	<p><i>Comparability of groups:</i> No information was provided on demographic characteristics and on caries risk level at baseline</p> <p><i>Co-interventions:</i> Comment: No information was provided on co-interventions, such as frequency and methods of teeth brushing, or application of fluoride toothpaste</p>

Liu 2012

Methods	<p>Trial design: parallel-group study, 4 treatment arms (sealant, sodium fluoride varnish, silver diamine fluoride solution, placebo)</p> <p>Follow-up: 24 months</p> <p>Study started in 2008</p>
Participants	<p>Location: Children were chosen from primary schools, China</p> <p>Inclusion criteria: ≥ 1 sound permanent first molar with deep fissures or fissures with signs of early (enamel) caries viewed as wet, with opacities and discolouration, similar to ICDAS code 2 (proportion of early caries 35% of tooth sites) (clinical examinations included DIAGNOdent readings and were done by a dentist)</p> <p>Age at baseline: mean age 9.1 years (range 8 to 10 years)</p> <p>Gender: 248 boys and 253 girls</p> <p>Baseline caries: baseline mean dmft scores with SD for groups: sealant 3.19 (2.68), fluoride varnish 3.58 (2.25) (information obtained from study author)</p> <p>Number randomly assigned: 501 children (1539 molars, on average 3 teeth per child) in 4 groups: 124 children in sealant, 124 in fluoride varnish, 125 in silver diamine fluoride solution, 128 in placebo</p> <p>Number evaluated: 482 at 2-year follow-up (121 children in sealant, 116 in fluoride varnish, 121 in silver diamine fluoride solution, 124 in placebo)</p>
Interventions	<p>Comparison: resin-based fissure sealant vs fluoride varnish</p> <p>4 treatment arms</p> <p>Group 1: light-cured, fluoride-releasing resin-based sealant Clinpro Sealant (3M ESPE, St Paul, MN, USA) (applied by a dentist). No resealing</p> <p>Group 2: NaF – semi annual application of 5% sodium fluoride (NaF) varnish (Duraphat) (applied by a dentist)</p> <p>Group 3: SDF – annual application of 38% silver diamine fluoride (SDF) solution (applied by a dentist)</p> <p>Group 4: placebo control – annual application of water (applied by a dentist)</p> <p>(group 1 and group 2 were considered in this review)</p> <p>Co-interventions: 90% of toothpastes on sale contained fluoride (no systemic fluoridation in the study area)</p>
Outcomes	<p>Sound or carious occlusal surface of molar (caries in dentine ICDAS codes 4 to 6)</p> <p>Each molar was assessed at 2 sites (upper molar – mesial pit/fossa and distal-palatal groove; lower molar – occlusal fissure and buccal pit/groove). Caries incidence was reported as child level, tooth level and fissure site level</p> <p>Outcomes were assessed by the same blinded examiner using disposable mouth-mirrors attached to an intra-oral LED (light-emitting diode) light and CPI (community periodontal index) probes</p> <p>Adverse events</p>
Notes	Intra-examiner reliability: Kappa statistic over 0.9

Liu 2012 (Continued)

Sealant retention 46%

Funding source: Hong Kong Research Grants Council (study authors were from the university)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "An assistant, using computer-generated random numbers, allocated the children individually among four groups" Comment: adequate random sequence generation was provided
Allocation concealment (selection bias)	Low risk	Additional information was obtained from study author Computer-generated random number table (consisting only of numbers 1, 2, 3 and 4) was printed out and kept by a research assistant. Group allocation of participants, i.e. group 1 to group 4, followed random numbers in the random number table. Treatment was performed immediately on-site by a dentist not involved in examination of children according to group allocation while re-search assistant was present Comment: adequate allocation concealment
Blinding of outcome assessor (detection bias)	Unclear risk	Quote: "Status of the molars, including sealant retention and development of caries into dentin (ICDAS codes 4-6), was assessed every 6 mos by the same blinded examiner" Additional information obtained from study author indicated that "The record forms with group assignment information of the children were kept away from the examiner by the recorder" Comment: Blinding of outcome assessor was intended, but it remains unclear whether outcome assessor had information on study design
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data: 3/124 (2.4%) in sealant group, 7/124 (5.6%) in fluoride varnish group Comment: marginal drop-out rates
Selective reporting (reporting bias)	Low risk	Outcomes reported: caries response, sealant retention Comment: Pre-specified outcomes (in methods) were reported in pre-specified way
Other bias	Low risk	<i>Comparability of groups:</i> Quote: "Proportionately more children in the sealant group than in other groups had visited a dentist or consumed snacks once a day or less ($P < 0.05$)". (13% of children in sealant group and 31% in fluoride varnish group consumed snacks twice or more often a day) Additional information obtained from study author revealed no statistically significant differences between groups in baseline caries risk of children Mean baseline dmft scores with SD for groups: sealant 3.19 (2.68); fluoride varnish 3.58 (2.25) Comment: We decided to grade this domain as having 'low' risk of bias, although we noted differences in dental visit history and consumption of snacks between groups at baseline because baseline caries risk scores of children were similar <i>Co-interventions:</i> "No systemic fluoridation in the study area. 90% of the toothpastes on sale contained fluoride" Comment: This domain was graded as having 'low' risk of bias because no co-interventions other than fluoridated toothpaste were included in the protocol

Raadal 1984

Methods	<p>Trial design: split-mouth design, sealant tooth randomly assigned</p> <p>Follow-up: average 23 months</p>
Participants	<p>Location: Study setting was a public dental clinic in a small town in Norway</p> <p>Inclusion criteria: Children had to have 1 recently erupted homomaxillary pair of permanent first molars. Occlusal surface was sound or had initial caries in enamel</p> <p>Age at baseline: 6 to 9 years</p> <p>Gender: 62 girls, 59 boys</p> <p>Baseline caries: mean dmft 4.7 (SD 3.3)</p> <p>Number randomly assigned: 121 children with total of 210 tooth site pairs (110 in maxilla and 100 in mandible; in maxilla, mesial and distal portions of occlusal surface were treated separately)</p> <p>Number evaluated: No description of drop-outs regarding children was provided, but information provided indicates that 208 of 210 sealed sites were evaluated (meaning that 1 child or 2 children were dropped out)</p>
Interventions	<p>Comparison: resin-based fissure sealant vs fluoride varnish</p> <p>Tooth pair: occlusal surface of 1 tooth sealed with autopolymerised resin-based Concise; on occlusal surface of the other tooth of the tooth pair, fluoride varnish (Duraphat, sodium fluoride (NaF)) was applied</p> <p>No information was provided on proportions of sound surfaces and teeth with enamel lesions. Surfaces with initial caries in enamel were opened mechanically and caries removed before sealant application (Quote from the article: "In those cases where caries had progressed to the dentin, conventional cavities for amalgam fillings were prepared, and these cases were excluded from the study")</p> <p>No resealing</p> <p>Surfaces to be painted with fluoride varnish were treated every 6 months</p> <p>Co-interventions: annual information and motivation about dental care; fluoride tablets recommended; fluoride rinsing with 0.5% NaF solution at school</p>
Outcomes	<p>Sound or carious occlusal surface of molar</p> <p>Caries status was recorded using visual-tactile method and bitewings</p>
Notes	<p>Complete sealant retention 63% at 23 months</p> <p>Funding source: no information on funding</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Coin tossing. Additional information was obtained from study author Comment: Random sequence generation was adequate
Allocation concealment (selection bias)	Low risk	Comment: Random sequence was adequately concealed up until the moment of allocation by flipping a coin to allocate a particular tooth, within a tooth pair, to be sealed
Blinding of outcome assessor (detection bias)	High risk	No blinding of the outcome assessor was performed Comment: Additional information was obtained from study author
Incomplete outcome data (attrition bias) All outcomes	Low risk	Drop-out rate 1% for tooth site pairs after 23 months (no description of drop-outs was provided regarding children, but information indicates that 208 of 210 sealed sites were evaluated, meaning that 1 child or 2 children were dropped out). No reasons for drop-outs were described Comment: marginal drop-out rate

Raadal 1984 (Continued)

Selective reporting (reporting bias)	Low risk	Outcomes reported: incidence of dentinal carious lesion on treated occlusal surfaces of molars (yes or no) at 23 months of follow-up, retention Comment: Pre-specified caries outcomes (in methods) were reported in the pre-specified way
Other bias	Low risk	<i>Comparability of groups:</i> Comment: Split-mouth design, which included sound surfaces or surfaces with enamel lesions. With split-mouth designs, we saw that both surfaces within a tooth pair in any case will eventually be at equal risk for caries because of the long follow-up (regardless of whether the diagnosis consisted of a sound surface or a surface with an enamel lesion) <i>Co-interventions:</i> Annual information and motivation about dental care; fluoride tablets recommended; fluoride rinsing with 0.5% NaF solution at school Comment: split-mouth design. Conditions are the same for both teeth within a tooth pair

Salem 2014

Methods	Trial design: cluster-randomised study design, where in 12 primary schools 2 classes from each grade were randomly assigned to 2 treatment arms Follow-up: 24 months Study was started in 2009 The study was not considered in analyses of this review because results and data - complex multi-level model with teeth nested in a child nested in a school class nested in a school - were not in useable form for this review (unit of analysis was chosen to be a tooth surface, but clustering of data was not taken into account in the analyses. Study author gave the following additional information on analyses of the trial: "During study period we found that the arrangement of pupils in each class is undergoing substantial changes every year. Hence there was a combination of both groups in each class at the second year and we decided to analyse the study population at surface level")
Participants	Location: university clinic, Iran Inclusion criteria: Children had to have ≥ 1 sound (by Nyvad criteria) and newly and completely erupted first permanent molar with deep occlusal fissure Age at baseline: 6 to 7 years Gender: girls 38%, boys 62% Baseline caries: sealant group: mean dmft index 4.41 (± 0.92); fluoride varnish group: 4.76 (± 2.75) (additional information was obtained from study authors) Number randomly assigned: 400 children (sealant 200, varnish 200) with 1579 occlusal surfaces (mean number of teeth 3.9 per child) Number evaluated: 352 at 2 years (173 in sealant group, 179 in fluoride varnish group)
Interventions	Comparison: resin-based fissure sealant vs fluoride varnish 2 treatment arms Group 1: resin-based sealant (Eco Seal), applied by dentist without assistant (additional information obtained from study authors). Partially and completely lost sealants were repaired/reapplied once if needed after 6 months Group 2: sodium fluoride varnish (Durafluor, NaF 5%), applied biannually by dentist without assistant (additional information obtained from study authors) Co-interventions: All children participated in oral hygiene education sessions including restriction of sugary snacks, regular toothbrushing and toothbrush and 1450 ppm fluoride toothpaste given at every visit Fluoride concentration of water during the years 2009 to 2012 at study area was in the range of 0.45 to 0.8 ppm, on the basis of seasonal changes

Salem 2014 (Continued)

Outcomes Sound or carious occlusal surface of first molar: caries numbers for occlusal surfaces scored by Nyvad criteria. DMFT and DMFS scores reported for whole tooth surfaces
 One calibrated dentist carried out all examinations. Caries status was determined by 2 visual-tactile measures: WHO criteria (DMF) and Nyvad criteria applied

Notes Intra-examiner reliability: Kappa co-efficient for Nyvad and WHO criteria was 0.79 and 0.81, respectively
 Sealant retention: after 24 months: completely retained 43%, partial retention 46%, total loss 11%
 Funding source: granted by Institutional Review Board and Ethical Committee of Guilan University of Medical Sciences, Iran

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "In each school, one class from each grade was assigned to sealant and the other to varnish by coin tossing" Comment: Random sequence generation was adequate
Allocation concealment (selection bias)	Low risk	Quote from author correspondence: "The records were kept by dental nurses at dental clinic files. The nurses were the staff of university dental clinic and did not know the children or their dental history" Comment: Independent staff combined with cluster-randomised study design gives the impression of adequate randomisation procedure
Blinding of outcome assessor (detection bias)	Low risk	Quote from author correspondence: "The examiner was not involved in the study design and had no access to records" Comment: Blinding of outcome assessor was adequate
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data: 27/200 (13.5%) in sealant group, and 21/200 (10.5%) in fluoride varnish group Reason for drop-outs in both groups: Children moved away from the area Comment: Missing data were less than 25%, and groups were balanced in numbers and reasons for missing data
Selective reporting (reporting bias)	Low risk	Outcomes reported: caries response, sealant retention Comment: Pre-specified outcomes (in methods) were reported in pre-specified way
Other bias	Low risk	<i>Comparability of groups:</i> Information on groups was available at 2 years (additional information was obtained from study authors): Baseline mean dmft in sealant group was 4.41 (\pm 0.92) and in fluoride varnish group 4.76 (\pm 2.75). Proportion of girls was 46% in sealant group and 31% in varnish group Quote: "The majority of children reported brushing their teeth once daily and sugary snacks 1-2 times per day without significant difference between the groups" Comment: Detailed description of demographic characteristics and caries risk level was provided at baseline. Although the proportion of girls was greater in sealant group than in fluoride varnish group, we assessed that groups were balanced at baseline Co-interventions: All children participated in oral hygiene education sessions including restriction of sugary snacks and regular tooth brushing, and received toothbrush and 1450 ppm fluoride toothpaste at every visit Comment: In both groups, the same co-interventions were allowed

Splieth 2001

Methods	<p>Trial design: split-mouth design, sealant tooth randomly assigned</p> <p>Follow-up: 2 years Study was started in 1995</p>
Participants	<p>Location: a private dental practice, Germany</p> <p>Inclusion criteria: Children had to have ≥ 1 pair of equivalent first permanent molars without carious defects (occlusal surface sound or with initial lesion in enamel)</p> <p>Age at baseline: 5 to 8 years</p> <p>Baseline caries: mean DMFS 0.2</p> <p>Number randomly assigned: 98 children with 181 tooth pairs (on average 1.8 tooth pairs per child)</p> <p>Number evaluated: 92 at 2-year follow-up</p>
Interventions	<p>Comparison: resin-based fissure sealant plus fluoride varnish vs fluoride varnish alone</p> <p>Tooth pair: occlusal surface of 1 tooth sealed with visible-light activated Fissurit Transparent (VOCO GmbH, Cuxhaven, Germany); occlusal surface of the other tooth of the tooth pair applied with fluoride varnish (Duraphat, sodium fluoride (NaF))</p> <p>Fluoride varnish was applied to all teeth including the sealed tooth</p> <p>Children were examined semi annually for 2 years, sealants were resealed if necessary and fluoride varnish was applied to all teeth at examinations</p> <p>Co-interventions: Children were instructed on better oral hygiene and brushed their teeth under supervision (Mean frequency of cariogenic food intake per day was 15, including a large number of sweetened drinks. Oral hygiene was moderate)</p> <p>5% of the children used fluoride tablets during the study</p> <p>(Fluoride concentration of public water supply was 0.1 ppm)</p>
Outcomes	<p>Status of sound/caries in enamel/caries in dentine on occlusal surfaces</p> <p>Changes in DMF scores on whole-mouth level</p> <p>Average treatment time for sealing and varnish application</p> <p>Caries status was recorded by 1 experienced dentist according to WHO criteria, but without applying pressure to the explorer</p>
Notes	<p>Complete sealant retention: 81% at 24 months</p> <p>Funding source: no information on funding</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Coin tossing. Additional information was obtained from study authors Comment: Random sequence generation was adequate
Allocation concealment (selection bias)	Low risk	Comment: Random sequence was adequately concealed up until the moment of allocation by flipping a coin to allocate a particular tooth, within a tooth pair, to be sealed
Blinding of outcome assessor (detection bias)	High risk	No blinding of outcome assessor was performed Comment: Additional information was obtained from study author
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data: 6/98 (6%) after 2 years. No description of reasons for drop-outs Comment: Missing data rate < 25%
Selective reporting (reporting bias)	Low risk	Outcomes reported: status of sound/caries in enamel/caries in dentine on occlusal surfaces; changes in DMF scores on whole-mouth level; treatment time; sealant retention; costs

Splieth 2001 (Continued)

Comment: Pre-specified outcomes (in methods) were reported in the pre-specified way

Other bias	Low risk	<p><i>Comparability of groups:</i></p> <p>Comment: Split-mouth design, which included sound surfaces or surfaces with initial lesions in enamel. With split-mouth designs, we saw that both surfaces within a tooth pair in any case will eventually be at equal risk for caries because of the long follow-up (regardless of whether the diagnosis was sound surface or surface with enamel lesion)</p> <p><i>Co-interventions:</i></p> <p>The fluoride concentration of the public water supply was 0.1 ppm. 5% of children used fluoride tablets during the study. Mean frequency of cariogenic food intake per day was 15, including a large number of sweetened drinks. Oral hygiene was moderate</p> <p>Comment: split-mouth design. Conditions were the same for both teeth within a tooth pair</p>
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Tagliaferro 2011

Methods	<p>Trial design: parallel-group study, 6 randomly assigned treatment arms</p> <p>Follow-up: 24 months</p>
Participants	<p>Location: Children were from 2 public schools and lived in a low-caries-prevalence city, Brazil</p> <p>Inclusion criteria: Children had to have: (1) dmft \geq 3 and/or \geq 1 active cavitated lesion, or dmft + DMFT = 0, and (2) \geq 2 sound permanent first molars</p> <p>Age at baseline: mean age 7 years</p> <p>Gender: 52% girls, 48% boys</p> <p>Baseline caries: Mean (SD) dmft index was 4.51 (2.81) for HRS group and 4.28 (2.54) for HRV group. In low-caries-risk groups (LRS, LRV groups), dmft + DMFT was zero</p> <p>Number randomly assigned: 327 children with mean number (SD) of occlusal surfaces treated 3.47 (0.80)</p> <p>Numbers of children per group: 57 in HRC group; 57 in HRV group; 55 in HRS group; 53 in LRC group; 52 in LRV group; 53 in LRS group</p> <p>Number evaluated: 268 at 24 months (44 children in HRC group; 48 in HRV group; 47 in HRS group; 42 in LRC group; 43 in LRV group; 44 in LRS group)</p>
Interventions	<p>Comparison: resin-modified glass ionomer fissure sealant vs fluoride varnish</p> <p>6 treatment arms</p> <p>Groups 1, 2 and 3 included only high-caries-risk children</p> <p>Group 1 (HRC): control group with high-caries-risk children receiving oral health education (OHE)</p> <p>Group 2 (HRV): OHE and fluoride varnish application biannually</p> <p>Group 3 (HRS): OHE and single sealant application (resin-modified glass ionomer cement)</p> <p>Groups 4, 5 and 6 included only low-caries-risk children</p> <p>Group 4 (LRC): control group receiving oral health education (OHE)</p> <p>Group 5 (LRV): OHE and fluoride varnish application biannually</p> <p>Group 6 (LRS): OHE and single sealant application (resin-modified glass ionomer cement)</p> <p>(Only sealant and fluoride varnish groups were considered in this review: groups 2, 3, 5 and 6)</p> <p>Sealants were applied by dentist assisted by dental hygienist in dental office (sealants were applied to healthy permanent first molars). Procedure consisted of 4 stages: etching tooth surfaces with 37% phosphoric acid, primer application, ionomer application, finishing gloss application</p> <p>No resealing</p> <p>Fluoride varnish (Duraphat, sodium fluoride (NaF)) was applied by dentist assisted by dental hygienist, at schools in well-lit areas, under natural light. Duraphat was applied to occlusal surfaces of sound first permanent molars. Participants were informed to not brush their teeth or chew food for \geq 2 hours after treatment, and to consume only soft foods and liquids for 24 hours</p>

Tagliaferro 2011 (Continued)

Oral health education was carried out by dentist assisted by dental hygienist. Sessions lasting 1 hour were held every 3 months, with talks covering themes such as dental caries, dental plaque and fluoride. Oral hygiene instructions, supervised tooth brushing and dietary counselling were presented to children by means of lectures, videos, educational games and oral quizzes
Co-interventions: 93% of children used fluoridated dentifrice. Average fluoride concentration in tap water was 0.7 ppm

Outcomes Sound or carious occlusal surface of first permanent molar: Caries increment was stated as mean DMF (decayed, missing and filled) scores
One calibrated dentist carried out all examinations. Diagnosis was based on clinical examination, and no radiographs were taken at baseline or at final examinations
Adverse events

Notes Intra-examiner reliability: Kappa coefficients 0.95 (caries as cavitated lesions) and 0.90 (caries as cavitated and non-cavitated lesions)
Sealant retention: total sealant loss 16% at 24 months
Funding source: FAPESP (São Paulo Research Foundation is an independent public foundation)
Caries prevalence of population at study area: mean DMFT 1.32 for 12-years-olds

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Additional information was obtained from study authors Children were systematically allocated to each treatment group as follows: Approximately 10 children were taken from each classroom at random by a dental hygienist. The hygienist did not know the caries risk of each child. The hygienist organized the 10 children in a queue at random. (In the queue were also those children not included in the study because they did not fulfil the inclusion criteria of the study; those children were excluded after baseline examination by a dentist). The examiner (Pardi V) performed the examination of the first child in the queue, and the main researcher (Tagliaferro EP) recorded data on a specific form and classified the child as having high or low caries risk, according to pre-established criteria. After each examination day, record forms were organised according to caries risk (low or high) and sequence of examination. After this, for example, the first examined child of that day classified as having high risk of caries was systematically allocated to the control group, the second to the varnish group and the third to the sealant group, and successively. Each child was given an ID code to be used over the whole study period Comment: This domain was graded as having 'low' risk of bias because we saw that the randomisation procedure as a whole was un-systematic when noting to which treatment group each child was finally allocated
Allocation concealment (selection bias)	Low risk	Additional information was obtained from study authors The main researcher (Tagliaferro) called children for treatments as follows: Children allocated to sealant groups were brought to a clinical setting, their names and treatment group were checked and Tagliaferro applied sealants, with the help of a dental hygienist. Then, at another time, Tagliaferro went to the school, called the children allocated to varnish groups and performed varnish applications. The process of calling only children allocated to sealant or varnish groups, when sealant applications or varnish applications were performed, respectively, ensured that each child really received the intended treatment Comment: This domain was graded as having 'low' risk of bias because we saw that despite incomplete allocation concealment (the same main researcher kept the records and made the applications), the large number of children in each allotted group and the fact that implementation of each treatment was centralised gave the impression that concealment was real

Tagliaferro 2011 (Continued)

Blinding of outcome assessor (detection bias)	Unclear risk	<p>Quote: "The study was a systematically randomised, blind, controlled trial. The calibrated dentist was not aware of group assignments during evaluations"</p> <p>The examiner did not see the records used for recording interventions for each child. This information was obtained from study authors Comment: Blinding of outcome assessors was intended, but it remains unclear whether outcome assessors had information on study design</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>Missing data: 8/55 (14.5%) in HRS group, 9/57 (15.8%) in HRV group, 9/53 (17%) in LRS group, 9/52 (17.3%) in LRV group Quote: "Many individuals had moved out of the schools where the research was conducted, and some refused to take part in the final examination" Comment: Although no information was provided to explain reasons for drop-outs by group, groups (HRS vs HRV; LRS vs LRV) were assessed as balanced with each other</p>
Selective reporting (reporting bias)	Low risk	<p>Outcomes reported: caries response Comment: Pre-specified outcomes (in methods) were reported in a pre-specified way</p>
Other bias	Low risk	<p><i>Comparability of groups:</i> Quote: "At baseline, gender, age, use of fluoridated dentifrice, family income, father's and mother's education were not statistically different among the six groups" With regard to clinical variables (dmfs, dmft, DMFS, DMFT, number of occlusal surfaces being treated) at baseline, groups were reported to be balanced</p> <p>"Baseline caries experience (dmft + DMFT) was not significantly different between full participants and those lost to follow-up for HRC, HRV, and HRS groups (in the low caries risk groups, dmft + DMFT was zero)" Comment: Detailed description was given on demographic characteristics (sex, age and social class), on baseline caries risk level and on baseline condition of tooth surfaces to be treated, to assess comparability of groups also at 24 months. Groups were assessed as balanced with each other</p> <p><i>Co-interventions:</i></p> <p>All children participated in an oral education programme</p> <p>93% of children used fluoridated dentifrice Comment: In all groups, the same co-interventions were allowed</p>

dft = decayed, filled deciduous teeth
 dmfs = decayed, missing and filled deciduous surfaces
 dmft = decayed, missing and filled deciduous teeth
 DMF = decayed, missing and filled
 DMFS = decayed, missing and filled permanent surfaces
 DMFT = decayed, missing and filled permanent teeth
 ICDAS = International Caries Detection and Assessment System
 SD = standard deviation
 WHO = World Health Organization

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
de Oliveira 2013	Not an RCT (although it was reported as such)

Study	Reason for exclusion
	Children were divided into 2 groups on the basis of past caries experience. Sealants were then applied to right-side molars, and fluoride varnish to left-side molars in all children No reply to letter requesting issue of randomisation
Fischman 1977	Study design not comparing sealant vs fluoride varnish Not an RCT. Random allocation not stated
Hita 2007	Not an RCT. Study authors classified study design as quasi-experimental field trial (selection for fluoride group was randomly assigned, assignment to sealant group was not random)
Jaworska 1984	Not an RCT. Random allocation not stated Study design not clear. No contact details of study author provided for further information
Källestål 2005	Study design not comparing sealant vs fluoride varnish
Petterson 1983	Not an RCT. Commune study where children born in odd month received sealant and fluoride varnish applications on first permanent molars, and children born in even month were given only fluoride varnish applications. Clustered data (several teeth per child) but no information on number of children at baseline or at follow-up (follow-up times varied between children). Description of characteristics of children was missing
Raadal 1990	Study design not comparing sealant vs fluoride varnish Not an RCT. Random allocation not stated
Riethe 1977	Not an RCT. Random allocation not stated No contact details of study authors were given for further information
Saifullina 1990	Not an RCT. Random allocation not stated No reply to letter requesting information on the issue of randomisation
Uma 2011	Caries data remained unreliable despite additional information from study author

RCT = randomised controlled trial.

Characteristics of ongoing studies [ordered by study ID]

ISRCTN17029222

Trial name or title	Randomised trial to determine relative cost and effectiveness of pit and fissure sealants and fluoride varnishes for preventing dental decay
Methods	Prospective 2-arm randomised controlled trial
Participants	Children 6 to 7 years of age with ≥ 1 fully erupted caries-free first permanent molar
Interventions	Pit and fissure sealant vs fluoride varnish
Outcomes	Primary outcomes: (1) development of dental caries on occlusal surface of first permanent molars at 36 months; (2) cost-effectiveness
Starting date	01/06/2011
Contact information	Prof Ivor Chestnutt, Cardiff University Dental School
Notes	

ISRCTN81071356

Trial name or title	Effectiveness of fluoride varnish vs pit and fissure sealant for prevention of caries in children of primary health care
Methods	RCT, single-blinded controlled multi-centre clinical trial
Participants	Children 6 years old (on average) having ≥ 1 of the first permanent molars compatible with the application of materials, and free of clinically detectable caries (with exposed dentine) or fillings at the beginning of the study
Interventions	Resin pit and fissure sealant vs sodium fluoride varnish
Outcomes	Occlusal caries, sealant retention
Starting date	01/05/2009
Contact information	Dr Hector Rossi, Universidad de Chile, Facultad de Medicina, Santiago
Notes	

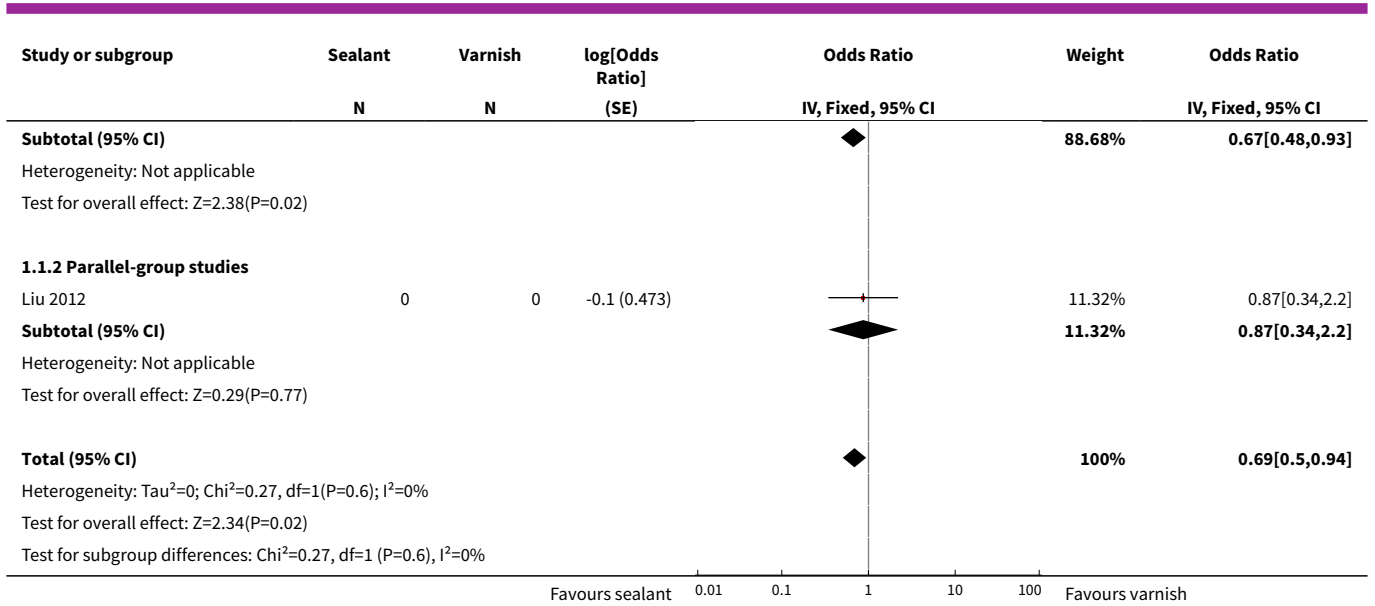
DATA AND ANALYSES

Comparison 1. Resin fissure sealant versus fluoride varnish

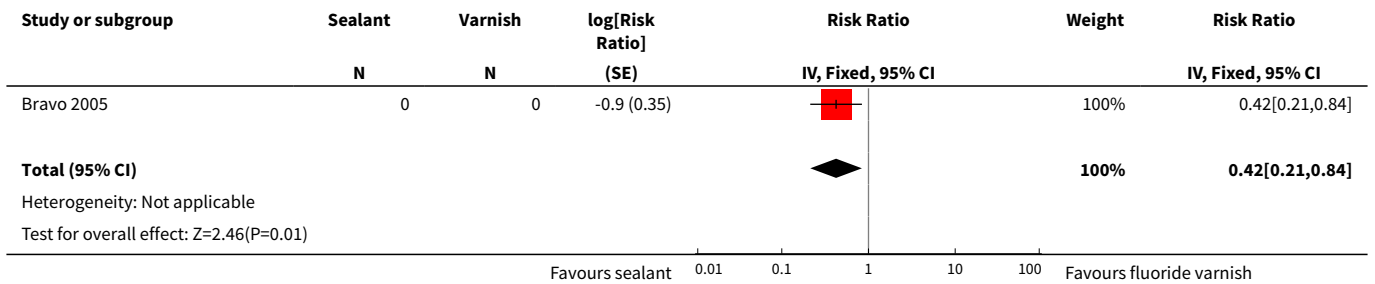
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caries at 23 to 24 months (yes/no)	2		Odds Ratio (Fixed, 95% CI)	0.69 [0.50, 0.94]
1.1 Split-mouth studies with paired data	1		Odds Ratio (Fixed, 95% CI)	0.67 [0.48, 0.93]
1.2 Parallel-group studies	1		Odds Ratio (Fixed, 95% CI)	0.87 [0.34, 2.20]
2 Caries at 4 years (yes/no)	1		Risk Ratio (Fixed, 95% CI)	0.42 [0.21, 0.84]
3 Caries at 9 years (yes/no)	1		Risk Ratio (Fixed, 95% CI)	0.48 [0.29, 0.79]

Analysis 1.1. Comparison 1 Resin fissure sealant versus fluoride varnish, Outcome 1 Caries at 23 to 24 months (yes/no).

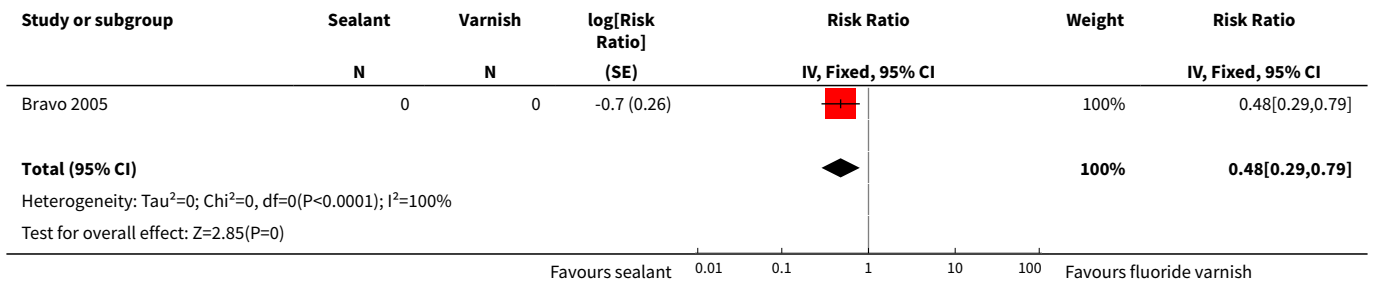
Study or subgroup	Sealant	Varnish	log[Odds Ratio] (SE)	Odds Ratio IV, Fixed, 95% CI	Weight	Odds Ratio IV, Fixed, 95% CI
	N	N				
1.1.1 Split-mouth studies with paired data						
Raadal 1984	0	0	-0.4 (0.169)		88.68%	0.67[0.48,0.93]



Analysis 1.2. Comparison 1 Resin fissure sealant versus fluoride varnish, Outcome 2 Caries at 4 years (yes/no).



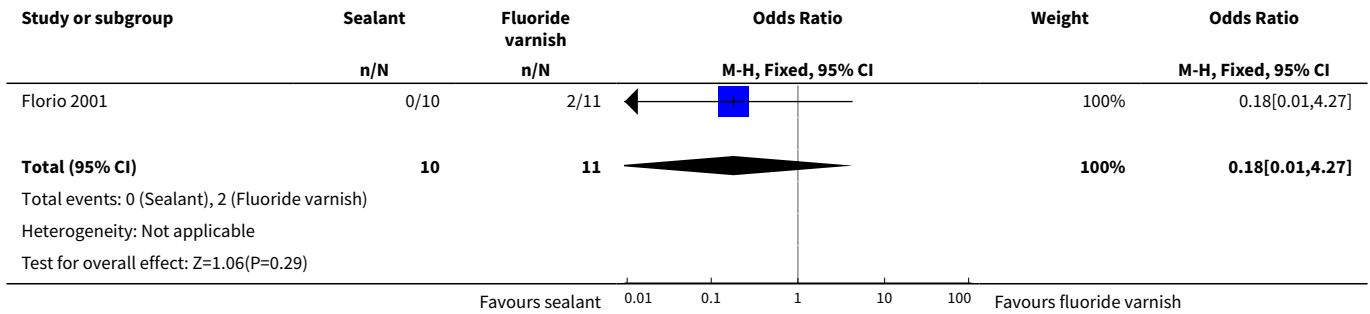
Analysis 1.3. Comparison 1 Resin fissure sealant versus fluoride varnish, Outcome 3 Caries at 9 years (yes/no).



Comparison 2. Resin-modified glass ionomer fissure sealant versus fluoride varnish

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caries at 12 months (yes/no)	1	21	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 4.27]

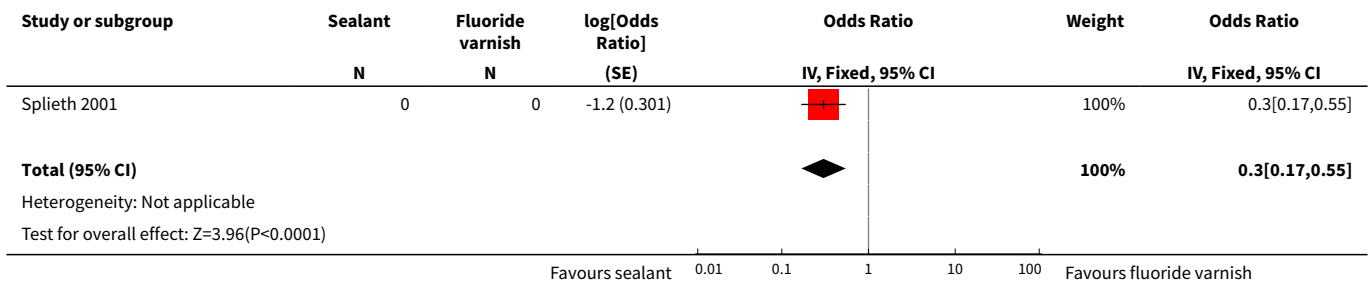
Analysis 2.1. Comparison 2 Resin-modified glass ionomer fissure sealant versus fluoride varnish, Outcome 1 Caries at 12 months (yes/no).



Comparison 3. Resin fissure sealant plus fluoride varnish versus fluoride varnish

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caries at 24 months (yes/no)	1		Odds Ratio (Fixed, 95% CI)	0.30 [0.17, 0.55]

Analysis 3.1. Comparison 3 Resin fissure sealant plus fluoride varnish versus fluoride varnish, Outcome 1 Caries at 24 months (yes/no).



ADDITIONAL TABLES

Table 1. Caries data from studies with binary outcome

RESIN FISSURE SEALANT (FS) VS FLUORIDE VARNISH (F): 23 to 24 MONTHS							
Split-mouth studies	Study	Both sound	FS sound F carious	FS carious F sound	Both carious	Proportion of decayed control tooth surfaces to total control surfaces	Becker-Balagtas marginal OR (95% CI) P value = ICC
	Raadal 1984 (sealant better)	131	31	15	31	0.30	OR = 0.67 (0.48 to 0.93) P value = 0.02 ICC 0.44
Paral-lel-group studies	Study	Description of data					OR (95% CI)
	Liu 2012 (no difference)	OR based on model of multi-level GEE logistic regression Additional information obtained from study author					OR = 0.87 (0.34 to 2.20)
POOLED							OR = 0.69 (0.50 to 0.94)
RESIN FISSURE SEALANT (FS) VS FLUORIDE VARNISH (F): 4 YEARS							
Paral-lel-group studies	Study	Description of data					RR (95% CI) P value =
	Bravo 2005 (sealant better)	Results presented as risk ratios (RRs) with cluster-corrected standard error (SE). A school class is a cluster, but several sealed and fluoride-varnished teeth were present per child. Study authors calculated cluster-corrected effect estimates when requested					RR = 0.42 (0.21 to 0.84) P value = 0.01
RESIN FISSURE SEALANT (FS) VS FLUORIDE VARNISH (F): 9 YEARS							
Paral-lel-group studies	Study	Description of data					RR (95% CI)

Table 1. Caries data from studies with binary outcome (Continued)

<p>Bravo 2005 (sealant better)</p>	<p>Results presented as risk ratios (RRs) with cluster-corrected standard error (SE). A school class is a cluster, but several sealed and fluoride-varnished teeth were present per child. Study authors calculated cluster-corrected effect estimates when requested.</p> <p>26.6% of sealant teeth and 55.8% of fluoride-varnished teeth had developed caries after 9 years (76.7% of control teeth without treatments)</p>	<p>RR = 0.48 (0.29 to 0.79) P value = 0.004</p>
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RESIN FISSURE SEALANT PLUS FLUORIDE VARNISH (FS + F) VS FLUORIDE VARNISH (F): 2 YEARS

Split-mouth studies	Study	Both sound	FS + F sound F carious	FS + F carious F sound	Both carious	Proportion of decayed control tooth surfaces to total control surfaces	Becker-Balagtas marginal OR (95% CI)
	<p>Splieth 2001 (sealant + fluoride varnish better than fluoride varnish alone)</p>	129	32	7	7	0.22	<p>OR = 0.30 (0.17 to 0.55) P value < 0.0001</p>

RESIN-MODIFIED GLASSIONOMER FISSURE SEALANT (FS) VS FLUORIDE VARNISH (F): 1 YEAR

Parallel-group studies	Study	Description of data	OR (95% CI)
	<p>Florio 2001 (no difference)</p>	<p>Clustered data (several teeth per child). Data decided to analyse at a child level (i.e. data were dichotomised - did a child have caries or not) because decayed teeth were very few. Additional information obtained from study author indicated that the two decayed surfaces in the fluoride varnish group were present in different children. Detailed data Analysis 2.1</p>	<p>OR = 0.18 (0.01 to 4.27) P value = 0.29</p>

Table 2. Criteria for 'Risk of bias' assessment

Random sequence generation (selection bias)	Was the method used to generate the allocation sequence appropriate to produce comparable groups?	We graded this domain to 'low' risk of bias if study authors described a random component in the sequence generation process (e.g. random number table, coin tossing, drawing of lots). If information about the random sequence generation process was not provided or was insufficient, we graded this domain to 'unclear' risk
Allocation concealment (selection bias)	Was the method used to conceal the allocation sequence appropriate to prevent the allocation from being known in advance of, or during, enrolment?	We graded this domain to 'low' risk of bias if study authors described adequate concealment (e.g. by means of central randomisation, or sequentially numbered, opaque and sealed envelopes) and to 'high' risk of bias if inadequate concealment was documented (e.g. alternation, use of case record numbers, date of birth or day of the week) or if allocation concealment was not used. If insufficient or no information on allocation concealment was provided, the judgement was graded 'unclear' risk
Blinding (performance bias)		We did not carry out assessment of blinding of participants and personnel in this review because we think that personnel and participants potentially knowing which of the 2 active preventive treatments a child is given is unlikely to cause bias (e.g. affect dental behaviour of a child during the trial, especially when follow-up is long (≥ 1 year in this review)).
Blinding of outcome assessment (detection bias)	Were outcome assessors blinded to the intervention a participant had received?	<p>As sealant materials are visible, blinding of the outcome assessor is possible only if a sealant has been lost. Thus outcome measurement is related to sealant retention and blinding of outcome assessor is usually impossible. On the other hand, it is difficult to assess how likely (or not likely) it is that the outcome measurement is influenced by lack of blinding of outcome assessors in preventive sealant studies.</p> <p>We decided to grade this domain as having 'low' risk of bias if study authors stated that the outcome assessor was not involved in the study design, and as having 'unclear' risk of bias if the study simply reported blinded outcome assessment or if blinding was indicated (e.g. examinations performed independently of previous records, outcome assessors not involved in applying treatments). If a trial reported nothing about blinding of outcome measurement, our judgement was 'high' risk of bias in this domain.</p>
Incomplete outcome data (attrition bias)	How complete were the outcome data for primary caries outcomes? Were drop-out rates and reasons for withdrawals reported? Were missing data imputed appropriately?	<p>In caries prevention studies, follow-up times can last several years. Studies with long follow-up have the problem of high drop-out rates causing uncertainty about data. We decided to base the judgement of this domain on caries efficacy outcome at 24 or 36 months (commonly used follow-up times in sealant studies). When both follow-up times were reported, we based our judgement on 24 months. If either of these 2 follow-up times was not reported, we based our judgement on the first caries efficacy outcome reported in the study (which in this review should be ≥ 1 year). However, the risk of bias was assessed separately and was reported in the 'Risk of bias' table for caries outcomes despite follow-up times, and the assessments were taken into account in the overall risk of bias assessment for caries outcomes within a study</p> <p>We decided to grade this domain as having 'low' risk of bias if the total proportion of missing outcome data was marginal ($< 5\%$); or if the proportion of missing outcome data was $< 25\%$ regardless of the follow-up time and groups (in parallel-group studies) were balanced in numbers for missing data; or if missing data have been imputed using appropriate methods. If no information on reasons for drop-out across intervention groups was provided, or if the proportion of missing data was documented as total proportion (5% to 25%), not by group in parallel-group studies, our judgement was 'unclear' risk. Classifying missing data $> 25\%$ as having 'high' risk of bias in all study designs was a pragmatic approach to this domain to make the judgement uniform and transparent. If several teeth</p>

Table 2. Criteria for 'Risk of bias' assessment (Continued)

		were sealed in a child's mouth (a child is a cluster), missing outcome data had to be stated (or counted) at child level (not at tooth level).
Selective reporting (reporting bias)	Were appropriate outcomes reported and were key outcomes missing?	To be included in this review, caries outcomes had to be reported. However, studies could report the outcome in different ways, for example, incidence of dentinal carious lesion on treated occlusal surfaces of molars or premolars (yes or no); changes in mean figures of decayed, missing and filled surfaces (DMFS); or progression of caries lesion into enamel or dentine. In this review, selective outcome reporting was graded as 'low' risk of bias if the study's pre-specified caries outcomes had been reported in the pre-specified way
Other sources of bias	This domain included information on comparability of intervention and control groups, and possible use of co-interventions by group	<p><i>Comparability of groups</i></p> <p>We decided to base our judgement of comparability of groups on baseline information given to groups available at follow-up times because if only information provided at the start of the study is available, it is impossible to assess whether groups are balanced with each other after follow-up time as well. The comparability of groups after follow-up is especially problematic when small studies include children with several teeth and the drop-out rate is high, even if drop-outs are balanced in numbers and reasons between groups. If no information on the groups was available at follow-up time, we decided that if the drop-out rate (regardless of follow-up time) was < 25% and drop-outs were balanced in numbers and reasons by group, our judgement would be based on information given for groups at the start of the study</p> <p>We decided to grade this domain as having 'low' risk of bias if groups were balanced in demographic characteristics (such as sex, age and social class) and in baseline caries risk level, or if possible imbalance of groups at baseline and/or after follow-up had been taken adequately into account in the analyses. If baseline characteristics in parallel-group studies were not given to groups available at follow-up and the drop-out rate was > 25%, we graded the study as having 'unclear' risk</p> <p><i>Co-interventions</i></p> <p>We decided to grade this domain as having 'low' risk of bias if groups were balanced in number and quality of co-interventions, or if no co-interventions were included in the protocol, and as having 'high' risk of bias if groups received different numbers or quality of co-interventions during the trial. If no information was provided on co-interventions, our judgement was 'unclear' risk</p>

APPENDICES

Appendix 1. MEDLINE via Ovid search strategy

1. 1. exp Fluorides, topical/
2. (fluoride\$ or fluor or "PPM F" or PPMF or APF or NAF or "Sodium F" or "Amine F" or SNF2 or "Stannous F" or "phosphat\$ F" or "acidulat\$ F" or "acidulat\$ fluor\$" or "phosphat\$ fluor\$" or fluorphosphat\$ or "amin\$ fluor\$" or "sodium\$ fluor\$" or "stannous\$ fluor\$" or SMFP or MFP or monofluor\$).mp.
3. (varnish\$ or lacquer\$ or laquer\$ or lacker\$ or lakk\$ or polyurethane\$).mp.
4. 2 and 3
5. 1 or 4
6. "Pit and fissure sealants"/
7. (fiss\$ adj6 seal\$).mp.
8. (dental adj3 seal\$).mp.
9. (compomer\$ adj4 seal\$).mp.
- 10.(composite\$ adj4 seal\$).mp.
- 11.exp Glass ionomer cements/
- 12.exp Resin cements/
- 13.("glass ionomer\$" or glassionomer\$ or "cermet cement\$" or "resin cement\$").mp.

14.or/6-13
15.5 and 14

In the previous version of this review the following search strategy was used:

1. exp TOPICAL FLUORIDES
2. topical adj6 fluoride\$.mp.
3. ((varnish\$ or lacquer\$ or laquer\$ or lakk\$ or verniz\$ or silane\$ or polyurethane\$) adj6 fluor\$).mp.
4. 1 or 2 or 3
5. exp PIT AND FISSURE SEALANTS
6. (fiss\$ adj6 seal\$).mp.
7. exp GLASS IONOMER CEMENTS
8. exp RESIN CEMENTS
9. ("glass ionomer\$" or "cermet cement\$" or "resin cement\$").mp.
10. 5 or 6 or 7 or 8 or 9
11. 4 and 10

Appendix 2. Cochrane Oral Health Group Trials Register search strategy

For this update, the Cochrane Oral Health Group's Trials Register was searched via the Cochrane Register of Studies using the search strategy below:

- 1 (fluoride* or fluor or "PPM F" or PPMF or APF or NAF or "Sodium F" or "Amine F" or SNF2 or "Stannous F" or "phosphat* F" or "acidulat* F" or "acidulat* fluor*" or "phosphat* fluor*" or fluorphosphat* or "amin* fluor*" or "sodium* fluor*" or "stannous* fluor*" or SMFP or MFP or monofluor*):ti,ab
- 2 (varnish* or lacquer* or laquer* or lacker* or lakk* or polyurethane*):ti,ab
- 3 #1 and #2
- 4 ((fissure* and seal*) or (dental and seal*)):ti,ab
- 5 ((compomer* and seal*) or (composite and seal*)):ti,ab
- 6 ("glass ionomer*" or glassionomer* or "cermet cement*" or "resin cement*"):ti,ab
- 7 #4 or #5 or #6
- 8 (#3 and #7) AND (INREGISTER)

In the previous version of this review the following search strategy was used via the Procite software:

((fluoride* AND (varnish* OR lacquer* OR laquer* or lakk* OR verniz* OR silane* OR polyurethane*)) AND (("pit and fissure sealant*" OR (fissure AND seal*) OR "glass ionomer*" OR "resin cement*" OR enamel or tooth or teeth) AND seal*))

Appendix 3. CENTRAL search strategy

- #1 [mh "Topical fluorides"]
- #2 (fluoride* or fluor or "PPM F" or PPMF or APF or NAF or "Sodium F" or "Amine F" or SNF2 or "Stannous F" or "phosphat* F" or "acidulat* F" or "acidulat* fluor*" or "phosphat* fluor*" or fluorphosphat* or "amin* fluor*" or "sodium* fluor*" or "stannous* fluor*" or SMFP or MFP or monofluor*)
- #3 (varnish* or lacquer* or laquer* or lacker* or lakk* or polyurethane*)
- #4 #2 and #3
- #5 #1 or #4
- #6 [mh ^"Pit and fissure sealants"]
- #7 ((fissure* near/6 seal*) or (dental near/6 seal*))
- #8 ((compomer* near/4 seal*) or (composite* near/4 seal*))
- #9 [mh "Glass ionomer cements"]
- #10 [mh "Resin cements"]
- #11 ("glass ionomer*" or glassionomer* or "cermet cement*" or "resin cement*")
- #12 {or #6-#11}
- #13 #5 and #12

In the previous version of this review the following search strategy was used:

- #1 FLUORIDES TOPICAL (single MeSH term)
- #2 (topical* NEXT fluoride*)
- #3 ((fluoride* or fluorine*) AND (varnish* OR lacquer* OR laquer* OR lakk* OR verniz* OR silane* OR polyurethane*))
- #4 (#1 OR #2 OR #3)
- #5 PIT AND FISSURE SEALANTS (Single MeSH term)
- #6 fissure* NEAR seal*

- #7 GLASS IONOMER CEMENTS (Explode MeSH term)
- #8 glass ionomer*
- #9 cermet cement*
- #10 RESIN CEMENTS (Single MeSH term)
- #11 resin cement*
- #12 (#5 OR #6 OR #7 OR #8 OR #9 OR #10)
- #13 #4 AND #12

Appendix 4. EMBASE via Ovid search strategy

1. Fluoride/
2. (fluoride\$ or fluor or "PPM F" or PPMF or APF or NAF or "Sodium F" or "Amine F" or SNF2 or "Stannous F" or "phosphat\$ F" or "acidulat\$ F" or "acidulat\$ fluor\$" or "phosphat\$ fluor\$" or fluorphosphat\$ or "amin\$ fluor\$" or "sodium\$ fluor\$" or "stannous\$ fluor\$" or SMFP or MFP or monofluor\$).mp.
3. (varnish\$ or lacquer\$ or laquer\$ or lacker\$ or lakk\$ or polyurethane\$).mp.
4. 1 or 2
5. 3 and 4
6. "Fissure sealant"/
7. (fiss\$ adj6 seal\$).mp.
8. (dental adj3 seal\$).mp.
9. (compomer\$ adj4 seal\$).mp.
- 10.(composite\$ adj4 seal\$).mp.
- 11."Glass ionomer"/
- 12.Resin cements/
- 13.("glass ionomer\$" or glassionomer\$ or "cermet cement\$" or "resin cement\$").mp.
- 14.or/6-13
- 15.5 and 14

In the previous version of this review the following search strategy was used:

1. exp FLUORIDES, TOPICAL
2. topical adj6 fluoride\$.mp.
3. ((varnish\$ or lacquer\$ or laquer\$ or lakk\$ or verniz\$ or silane\$ or polyurethane\$) adj6 fluor\$).mp.
4. 1 or 2 or 3
5. exp PIT AND FISSURE SEALANTS
6. (fiss\$ adj6 seal\$).mp.
7. exp GLASS IONOMER CEMENTS
8. exp RESIN CEMENTS
9. ("glass ionomer\$" or "cermet cement\$" or "resin cement\$").mp.
10. 5 or 6 or 7 or 8 or 9
11. 4 and 10

Appendix 5. US National Institutes of Health Trials Register and WHO International Clinical Trials Register Platform search strategy

varnish and sealant

Appendix 6. Search strategies of the other electronic databases searched in the previous versions of the review

OpenSIGLE (from 1980 to 2005)

((fluor*) AND (silane* OR polyurethane* OR lack* OR laquer* OR lacquer* OR varnish* OR verniz* OR vernis*))

SCISEARCH, CAPLUS, INSPEC, JICST-EPLUS, NTIS, PASCAL searched via STN Easy (to November 2009)

f fluor* AND (varnish OR lacquer* OR laquer* OR lack* OR vernis* OR verniz* OR silane* OR polyurethane*) AND (dental OR tooth OR teeth OR enamel*)

DARE, NHS EED, HTA searched via the CAIRS web interface (to November 2009)

fluor* AND silane* or polyurethane* or varnish* or lacquer* or laquer* or verniz* or vernis* or lack* or laka* AND "fissure sealant*"

or ionomer* AND dental or tooth or teeth or enamel*

WHAT'S NEW

Date	Event	Description
8 January 2016	New citation required but conclusions have not changed	<p>Conclusions remain the same as in the previous version from 2010</p> <p>The composition of the author group has been changed from the previous version of this review. The order of the authors has been changed, and Helena Forss has been added as a review author</p>
18 December 2015	New search has been performed	<p>Search strategies were amended and the search updated</p> <p>This 2016 update contains 4 new included studies involving 1277 participants (Ji 2007; Liu 2012; Salem 2014; Tagliaferro 2011), 2 new excluded studies (de Oliveira 2013; Uma 2011) and 2 new ongoing studies (ISRCTN81071356; ISRCTN17029222)</p>

HISTORY

Protocol first published: Issue 2, 2001

Review first published: Issue 4, 2006

Date	Event	Description
18 February 2009	Amended	Updated contact details for co-author
1 August 2008	Amended	Converted to new review format

CONTRIBUTIONS OF AUTHORS

Writing of the protocol - Anne Hiiri (AH), Anneli Ahovuo-Saloranta (AAS), Anne Nordblad (AN) and Marjukka Mäkelä (MM).

Study selection - AAS, Helena Forss (HF) (and AH in previous versions).

Data extraction - AAS, HF (and AH in previous versions).

Data analysis - AAS.

Writing of the review - AAS, HF, AH, AN and MM.

DECLARATIONS OF INTEREST

Anneli Ahovuo-Saloranta: none known.

Helena Forss: none known.

Anne Hiiri: none known.

Anne Nordblad: none known.

Marjukka Mäkelä: no competing interests.

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- Cochrane Oral Health Group Global Alliance, Other.

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INDEX TERMS**Medical Subject Headings (MeSH)**

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MeSH check words

Adolescent; Child; Humans