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Antibacterial agents in composite restorations for the prevention of dental caries (Review)

Pereira-Cenci T, Cenci MS, Fedorowicz Z, Azevedo M

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Antibacterial agents in composite restorations for the prevention of dental caries.
Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD007819.
DOI: [10.1002/14651858.CD007819.pub3](https://doi.org/10.1002/14651858.CD007819.pub3).

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[Intervention Review]

Antibacterial agents in composite restorations for the prevention of dental caries

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Editorial group: Cochrane Oral Health Group.

Publication status and date: Stable (no update expected for reasons given in 'What's new'), published in Issue 3, 2014.

Citation: Pereira-Cenci T, Cenci MS, Fedorowicz Z, Azevedo M. Antibacterial agents in composite restorations for the prevention of dental caries. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD007819. DOI: [10.1002/14651858.CD007819.pub3](https://doi.org/10.1002/14651858.CD007819.pub3).

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ABSTRACT

Background

Dental caries is a multifactorial disease in which the fermentation of food sugars by bacteria from the biofilm (dental plaque) leads to localised demineralisation of tooth surfaces, which may ultimately result in cavity formation. Resin composites are widely used in dentistry to restore teeth. These restorations can fail for a number of reasons, such as secondary caries, and restorative material fracture and other minor reasons. From these, secondary caries, which are caries lesions developed adjacent to restorations, is the main cause for restorations replacement. The presence of antibacterials in both the filling material and the bonding systems would theoretically be able to affect the initiation and progression of caries adjacent to restorations. This is an update of the Cochrane review published in 2009.

Objectives

To assess the effects of antibacterial agents incorporated into composite restorations for the prevention of dental caries.

Search methods

We searched the following electronic databases: the Cochrane Oral Health Group's Trials Register (to 23 July 2013), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 6), MEDLINE via OVID (1946 to 23 July 2013) and EMBASE via OVID (1980 to 23 July 2013). We searched the US National Institutes of Health Trials Register (<http://clinicaltrials.gov>), the metaRegister of Controlled Trials (www.controlled-trials.com) and the World Health Organization International Clinical Trials Registry platform (www.who.int/trialsearch) for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases.

Selection criteria

Randomised controlled trials comparing resin composite restorations containing antibacterial agents with composite restorations not containing antibacterial agents.

Data collection and analysis

Two review authors conducted screening of studies in duplicate and independently, and although no eligible trials were identified, the two authors had planned to extract data independently and assess trial quality using standard Cochrane Collaboration methodologies.

Main results

We retrieved 308 references to studies, none of which matched the inclusion criteria for this review and all of which were excluded.

Authors' conclusions

We were unable to identify any randomised controlled trials on the effects of antibacterial agents incorporated into composite restorations for the prevention of dental caries. The absence of high level evidence for the effectiveness of this intervention emphasises the need for well designed, adequately powered, randomised controlled clinical trials. Thus, conclusions remain the same as the previously published review, with no included clinical trials.

PLAIN LANGUAGE SUMMARY

Use of antibacterial substances in resin-based fillings to prevent further tooth decay (next to the filling) developing after treatment

Review question

The main question addressed by this review is how effective the use of antibacterial agents in composite (resin-based, tooth-coloured) fillings might be in preventing the development of further decay either underneath or next to the filling (secondary caries).

Background

When tooth decay (caries) has caused a cavity in a tooth a range of materials can be used as fillings. These include resin composite, glass ionomer cement, amalgam and compomers. Tooth decay that may develop next to or underneath, a filling at a later stage is a common concern in dental practice and may reduce the life span of these fillings. It is thought that including a substance that kills and prevents the growth of bacterial (also known as an antibacterial agent) in some dental fillings, for example resin composites, could help prevent the development of this secondary caries.

Study characteristics

The Cochrane Oral Health Group carried out this review of existing studies and the evidence is current up to 23 July 2013.

The review authors have not found any trials to support or disprove the effectiveness of antibacterial agents incorporated into fillings to prevent further tooth decay.

Key results

No trials were found that were suitable for inclusion in this review.

Quality of the evidence

Currently there is no evidence to support using antibacterial agents in fillings.

BACKGROUND

Description of the condition

Dental caries is a multifactorial disease in which the fermentation of food sugars by bacteria from the biofilm (dental plaque) leads to localised demineralisation of tooth surfaces, which may ultimately result in cavity formation. This process is triggered by ecological pressure (such as alteration in salivary flow or increase in sugars consumption) which results in microbiological shifts and other changes within this biofilm (Marsh 2006; Selwitz 2007).

Description of the intervention

Resin composite is a material widely used in dentistry to restore teeth. These restorations can fail for a number of reasons, from which secondary caries and restorative materials fracture represents more than 90% of the recorded failures (Demarco 2012; Hickel 2007). Caries adjacent to restorations, also described as secondary or recurrent caries, represents up 55% of the causes of failure (Brunthaler 2003; Demarco 2012; Mjör 2005; Opdam 2007). These carious lesions are mediated by biofilm accumulation at the tooth/restoration interface (Kidd 2004; Thomas 2007). To prevent a recurrence of caries and improve their longevity, attempts have been made to add antibacterial agents into composite restorative materials (Chen 2012; Imazato 2003).

How the intervention might work

Composite restorations consist of two major components: a resin composite for filling and the bonding systems to be applied to the cavity before the placement of filling materials. The incorporation of antibacterial substances in these two components would have different roles relating to the prevention of the harmful effects caused by bacteria within the biofilm covering the tooth/restoration interface. The antibacterial effects of composites for filling would be mainly relevant to inhibition of plaque accumulation on the surface of the materials and tooth around the restoration. In contrast, for bonding systems, their antibacterial effects are discussed in terms of disinfection of the cavity as well as inactivation of bacteria which could invade the adhesive interface due to microleakage (Imazato 2003). The presence of antibacterials especially in the filling material would theoretically be able to affect the initiation and progression of caries adjacent to restorations. The clinical relevance of the use of these modified materials would be a direct benefit to the patient and an indirect benefit to the health system as there would be a decreased rate of restorations repair and replacement.

Why it is important to do this review

Since the incorporation of antimicrobials could represent additional cost to the consumers or affect the mechanical properties of composites, it would be important to review the benefits and cost-effectiveness of such products in dentistry. Additionally, consumers would benefit when other possible adverse effects of these products are studied. This is an update of the Cochrane review published in 2009 (Pereira-Cenci 2009; Pereira-Cenci 2009a).

OBJECTIVES

To assess the effects of antibacterial agents incorporated into composite restorations for the prevention of dental caries.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised controlled trials (RCTs) were considered in this review.

Types of participants

Adults and adolescents in any age group with restorations in the permanent dentition and children with restorations in the primary dentition.

Types of interventions

Resin composite restorations (filling and bonding systems) containing antibacterial agents compared with composite restorations not containing antibacterial agents, considering similar materials in composition.

Types of outcome measures

Primary outcome

1. Secondary caries.

Secondary outcomes

1. Longevity of restorations, recorded by the time to failure in months. Failures included replacement of the restoration, tooth extraction, pulpotomy, or natural exfoliation adjusted extraction, these last two if primary dentition is being considered, or any inability or inadequacy to perform as expected.
2. Postoperative sensitivity, marginal adaptation, anatomic form and other clinical outcomes (tooth vitality and pulpitis) proposed to assess restoration's quality based on the US Public Health Service (USPHS) criteria and its evolution (Hickel 2007; Hickel 2010).
3. Patient's view and satisfaction with the treatment, according to the evaluation proposed by Hickel 2010.

Costs

Direct costs of interventions including financial losses to patients, evaluated by direct and indirect cost regarding materials and time to revisit the dental office.

Adverse effects

Any specific adverse effects related to any clinically diagnosed reactions to any of the active interventions would be noted.

Search methods for identification of studies

Electronic searches

For the identification of studies included or considered for this review, detailed search strategies were developed for each database to be searched. These were based on the search strategy developed for MEDLINE but revised appropriately for each database.

We searched the following databases:

- the Cochrane Oral Health Group's Trials Register (to 23 July 2013) ([Appendix 2](#));
- the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 6) ([Appendix 3](#));
- MEDLINE via OVID (1946 to 23 July 2013) ([Appendix 1](#));
- EMBASE via OVID (1980 to 23 July 2013) ([Appendix 4](#)).

No restrictions were placed on the language or date of publication when searching the electronic databases.

Searching other resources

Only handsearching done as part of the Cochrane Worldwide Handsearching Programme and uploaded to CENTRAL was included (see the [Cochrane Masterlist](#) for details of journal issues searched to date). All the references lists of the included studies were checked manually to identify any additional studies.

Trials registers

We searched the following trials registers with the following search terms: composite restorations, resins antibacterial.

- The *metaRegister* of Controlled Trials (www.controlled-trials.com) (to 1 September 2013).
- The US National Institutes of Health Ongoing Trials Register (www.clinicaltrials.gov) (to 1 September 2013).
- The World Health Organization International Clinical Trials Registry platform (www.who.int/trialsearch) (to 1 September 2013).

Data collection and analysis

Selection of studies

Two review authors (Tatiana Pereira-Cenci (TPC) and Maximiliano Sergio Cenci (MSC)) independently assessed the abstracts of studies resulting from the searches. Full copies of all relevant and potentially relevant studies, those appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision were obtained. The full text papers were assessed independently and in duplicate by two review authors and any disagreement on the eligibility of included studies was resolved through discussion and consensus or through a third party (Zbys Fedorowicz (ZF)). All irrelevant records were excluded and details of the studies and the reasons for their exclusion were noted in the [Characteristics of excluded studies](#) table in Review Manager (RevMan) 5.2 ([RevMan 2012](#)).

Data extraction and management

Although no studies were identified for inclusion in this review the following methods of data extraction, assessment of risk of bias and data management will apply for subsequent updates, and when future studies are identified.

Study details will be entered into the 'Characteristics of included studies' table in RevMan 5. The review authors (TPC and MSC) will collect independently and in duplicate outcomes data using a pre-determined form designed for this purpose. The review authors will only include data if there is an independently reached consensus, any disagreements will be resolved by consulting with a third review author (ZF).

The following details will be extracted.

- (1) Trial methods:
 - (a) method of allocation
 - (b) masking of participants, trialists and outcomes
 - (c) exclusion of participants after randomisation and proportion of losses at follow-up.

- (2) Participants:
 - (a) country of origin
 - (b) sample size
 - (c) age
 - (d) sex
 - (e) inclusion and exclusion criteria.

- (3) Intervention:
 - (a) type
 - (b) duration and length of time in follow-up.

- (4) Control:
 - (a) type
 - (b) duration and length of time in follow-up.

- (5) Outcomes:
 - (a) primary and secondary outcomes mentioned in the outcome measures section of this review.

If stated, the sources of funding of any of the included studies will be recorded.

The review authors will use this information to help them assess heterogeneity and the external validity of the trials.

Assessment of risk of bias in included studies

Two review authors (TPC and MSC) will assess the risk of bias of the selected studies independently using The Cochrane Collaboration's tool for assessing risk of bias as described in Chapter 8, section 8.5, in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). These evaluations will be compared and any inconsistencies will be discussed and resolved between the review authors.

The following domains will be assessed as 'low risk of bias', 'unclear' (uncertain risk of bias), or 'high risk of bias':

1. sequence generation;
2. allocation concealment;
3. blinding of participants and personnel;
4. blinding of outcomes assessment;
5. incomplete outcome data;
6. selective outcome reporting; and
7. other bias.

These assessments will be reported for each individual study in the 'Risk of bias' tables.

The overall risk of bias of each of the included studies will be reported according to the following:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met;
- unclear risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were assessed as unclear; or

- high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met.

Dealing with missing data

When data are not available in the printed report, or when data are unclear, we will contact the corresponding author of the study to obtain the missing data or clarification.

Assessment of heterogeneity

We plan to assess clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions and the outcomes as specified in the criteria for included studies. Statistical heterogeneity will be assessed using a χ^2 test and the I^2 statistic where I^2 values over 50% indicate moderate to high heterogeneity (Higgins 2003).

Assessment of reporting biases

If sufficient randomised controlled trials are identified, an attempt will be made to assess publication bias using a funnel plot (Egger 1997).

Data synthesis

The Cochrane Collaboration's statistical guidelines will be followed for data synthesis. The data will be analysed by TPC using RevMan 5 and reported according to Cochrane Collaboration criteria.

For continuous data the mean difference and 95% confidence intervals will be calculated. Risk ratios and their 95% confidence intervals will be calculated for all dichotomous data.

Results of clinically and statistically homogeneous trials will be pooled to provide estimates of the efficacy of the interventions only if the included studies have similar interventions received by similar participants.

For the synthesis and meta-analysis of any quantitative data we will use a fixed-effect model if there are only two or three studies, or a random-effects model if there are four or more studies. If it is established that there is significant statistical heterogeneity between the studies we will use the random-effects model with studies grouped by action.

In the event that there are insufficient clinically homogeneous trials for any specific intervention or insufficient study data that can be pooled, a narrative synthesis will be presented.

Subgroup analysis and investigation of heterogeneity

We will consider conducting subgroup analyses for different restorative materials if there are sufficient numbers of included trials.

Sensitivity analysis

If there are sufficient included studies we plan to conduct sensitivity analyses to assess the robustness of our review results by repeating

the analysis with the following adjustments: exclusion of studies with unclear or inadequate allocation concealment, unclear or inadequate blinding of outcomes assessment and completeness of follow-up.

Presentation of main results

A 'Summary of findings' table would be developed for the primary outcomes of this review using GRADEProfiler software. The quality of the body of evidence was assessed with reference to the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates, the risk of publication bias, the magnitude of the effect and whether evidence of a dose response was found. The quality of the body of evidence for each of the primary outcomes was categorised as high, moderate, low or very low.

The results of the review will be presented in a 'Summary of findings' table, with the GRADE assessment of the quality of the body of evidence.

RESULTS

Description of studies

No studies were included in this review, as we were unable to find any trials directly comparing antibacterial containing composites to other active interventions or controls.

Results of the search

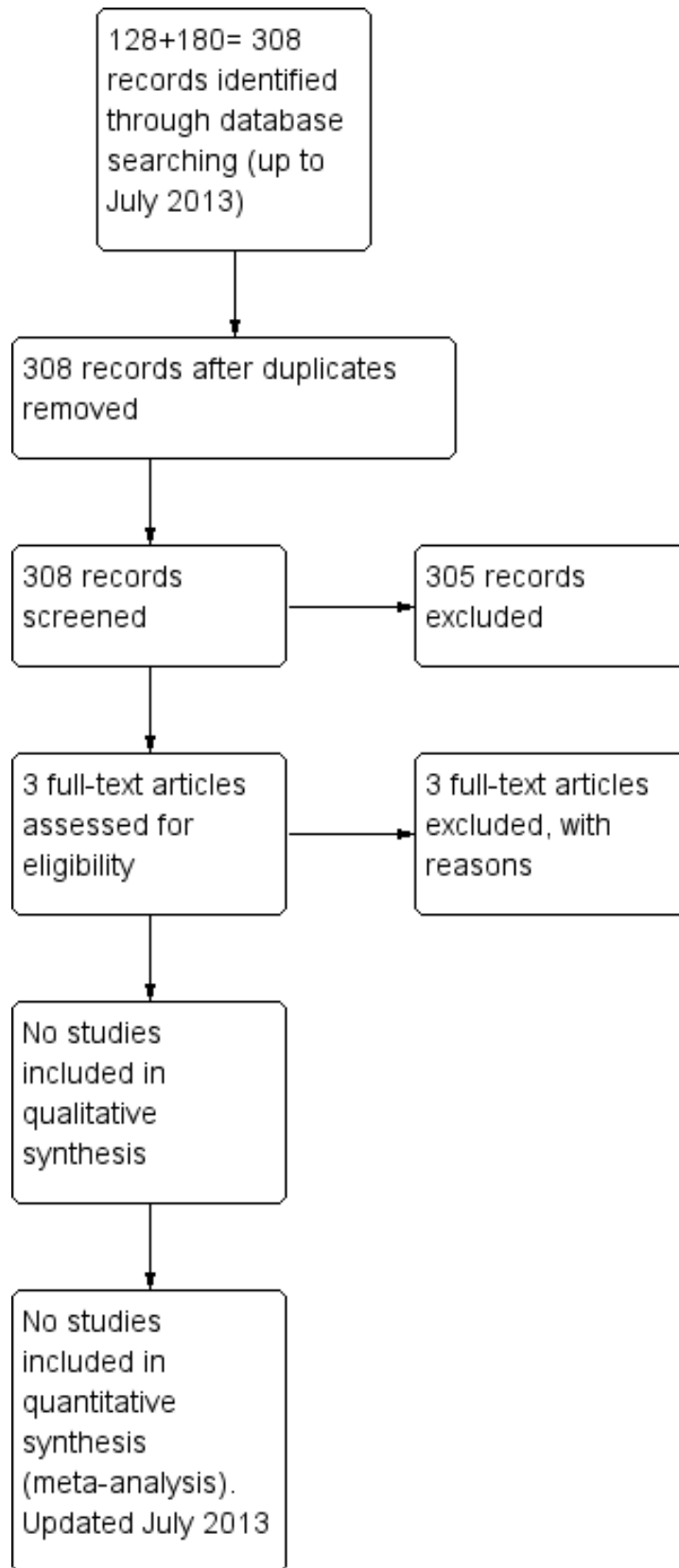
De-duplication of the search results produced 128 references to potentially eligible studies (Cochrane Oral Health Group's Trials Register 5, CENTRAL 10, MEDLINE 90, EMBASE 45). After examination of the titles and abstracts of these references, all but two were eliminated and excluded from further review. Full-text copies of the remaining studies (Ergücü 2007; Ohta 1984) in addition to five literature reviews (Busscher 2010; Chen 2012; Hannig 2012; Imazato 2003; Wiegand 2007) were obtained and then subjected to further evaluation which included an examination of their bibliographical references which provided no additional citations to potentially eligible trials. Ohta 1984 was in the Japanese language and we arranged for its translation and evaluation against our inclusion criteria but subsequently excluded it as it was ineligible.

An additional 180 references were identified in the updated searches (July 2013), 179 were excluded based on assessment of the abstracts and titles, the one remaining study (Saku 2010) was excluded after evaluation of the full text (Figure 1).

No relevant ongoing studies were identified in the searches of the trials registers.

The review authors discussed the eligibility of the potentially eligible studies, resolved any uncertainties by consensus and finally excluded all the studies (Characteristics of excluded studies table).

Figure 1. Study flow diagram.



Included studies

We retrieved a number of studies in our searches of the literature but none were eligible and therefore no trials were included in this review.

Excluded studies

We excluded all records which did not match our inclusion criteria and noted the reasons for exclusion in the [Characteristics of excluded studies](#) table.

Risk of bias in included studies

No trials were included.

Effects of interventions

None of the studies retrieved in our searches met our inclusion criteria and therefore no data were available for analysis.

DISCUSSION

New developments in dental technology, patient demands for tooth-coloured restorations and a need to find alternatives to amalgam were some reasons for the increased use of resin composite materials. An increasing number of composite restorations is placed as a routine in dental practice, and it is the most widely used direct restorative material.

Failure of composite restorations is usually attributed to the development of new caries lesions near the existing restorations. In order to prevent the development of dental caries adjacent to or underneath these restorations, antibacterial or bactericidal agents have been added to resin composite or adhesives or both, as a way to provide an adjunct treatment contributing to suppression of residual infection and increasing the survival of the restored tooth. It is important to highlight that several attempts have been made to incorporate antibacterial agents in adhesives. These antibacterial containing adhesives appear not to inhibit the progression of dental caries. The reason why antibacterial effect on adhesives is limited is probably related to the fact that it is directly proportional to the contact area between biofilm and the restorative materials. Unlike composites, dental adhesives have a limited area exposed as a thin line at the tooth-restoration interface ([Chen 2012](#)). In addition, the outcome of in vitro and randomised trials comparing the antibacterial effect of dental materials should be (the lack of) dental caries development, but the most common report is count of bacterial load ([Rolland 2011](#); [Zhang 2013](#)), which is interesting in a context of tooth cavity disinfection after partial caries removal, but probably has little impact on restorations longevity.

No randomised controlled trials on resin composite containing antibacterial agents compared to a control group were retrieved by the literature search. Therefore, it is difficult to draw conclusions to support any difference in the inhibition of caries development and progression or clinical performance of antibacterial containing resin composites and other restorations. However, this lack of evidence does not rule out the possibility of major differences on secondary caries development, longevity or postoperative sensitivity related to antibacterial containing materials.

Overall completeness and applicability of evidence

No studies were included.

Quality of the evidence

No studies were included.

Potential biases in the review process

We made every attempt to limit bias in the review process by ensuring a comprehensive search for potentially eligible studies. The authors' independent assessments of eligibility of studies for inclusion in this review minimised the potential for selection bias. The effects of language bias on the identification and selection of studies for inclusion in a systematic review is widely recognised; therefore, we ensured that language of publication was not used as an exclusion criterion.

Agreements and disagreements with other studies or reviews

We identified five literature reviews in our updated search ([Busscher 2010](#); [Chen 2012](#); [Hannig 2012](#); [Imazato 2003](#); [Wiegand 2007](#)). These reviews provided some limited background information covering a range of antibacterial restorative materials and included some detail on their possible clinical performance. However, although the reviewers undertook a search of the literature, other than reporting the use of free-text terms they gave no indication of how studies were selected or evaluated for inclusion. Therefore although the reviews were informative they cannot be considered systematic or reliable nor the basis for recommendations and guidance. Those reviews also included data from, and based their conclusions on, ex vivo studies (where the treatment was applied in vivo but the variable was measured in vitro) and further highlighted the gaps in the evidence. For instance, dental bonding systems are being tested in vitro and can inhibit invading bacteria after the placement of restoration as well as residual bacteria in the cavity ([Imazato 2003](#)). Also, the incorporation of antibacterial agents (chlorhexidine, glutaraldehyde, triclosan, silver and other nanoparticles, MDPB, chitosan, etc.) ([Chen 2012](#); [Hannig 2012](#)) and fluoride ([Wiegand 2007](#)) in dental materials may inhibit tooth demineralisation and secondary caries in vitro, and also reduce biofilm formation ([Busscher 2010](#)) but its clinical performance remains to be tested.

AUTHORS' CONCLUSIONS

Implications for practice

There is absence of evidence to support or refute the effectiveness in using antibacterial containing composites for the prevention of dental caries. However, as no data are available, the question of whether or not these antibacterial agents are effective remains unanswered. Considering that new materials containing antibacterial agents are expected to have additional costs in comparison to the currently available resin composites, the use of such materials in clinical practice cannot be justified or recommended until reliable evidence is available. Therefore, once these materials are shown to be effective at preventing dental caries, a cost-effectiveness analysis will still be required, especially in a context where patients are exposed to other preventive measures such as fluoride use. Thus, conclusions remain the same as the previously published review, with no included clinical trials.

Implications for research

In light of the disappointing results from the literature search, we strongly recommend that well-designed clinical trials of antibacterial containing resin composite restorations are undertaken and reported. High quality trials are needed to incorporate new findings into clinical practice, addressing both clinical and patient outcomes.

A review of antibacterial agents in composite restorations for the prevention of dental caries provides an example of the implications for research when no high quality eligible studies had been found. This review highlights the need for randomised controlled trials to evaluate the effects of this intervention and which can ultimately provide reliable evidence to help inform clinical decision making. Any future randomised controlled trials must be well-designed, well-conducted, and adequately delivered with subsequent

reporting, including high quality descriptions of all aspects of methodology. Reporting should conform to the Consolidated Standards of Reporting Trials (CONSORT) statement (<http://www.consort-statement.org/>) which will enable appraisal and interpretation of results, and accurate judgements to be made about the risk of bias, and the overall quality of the evidence. Although it is uncertain whether reported quality mirrors actual study conduct, it is noteworthy that studies with unclear methodology have been shown to produce biased estimates of treatment effects (Schulz 1995).

ACKNOWLEDGEMENTS

We wish to thank Anne Littlewood (Cochrane Oral Health Group) for her assistance with literature searching and the Cochrane Oral Health Group for their help in developing the protocol and conducting this review.

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CHARACTERISTICS OF STUDIES
Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ergücü 2007	Non-RCT and both groups received antibacterial bonding agent.
Ohta 1984	Non-RCT in vitro study. In Japanese translated by Ken Yaegaki.
Saku 2010	Full text confirmed resin blocks bonded to molars i.e. not composite restorations.

RCT = randomised controlled trial.

APPENDICES
Appendix 1. MEDLINE (OVID) search strategy

1. DENTAL RESTORATION, PERMANENT/
2. DENTAL CAVITY PREPARATION/
3. ((dental or tooth or teeth) and (fill\$ or restor\$ or "cavity preparation\$")).mp.
4. or/1-3
5. exp COMPOSITE RESINS/
6. (composite\$ or Bisphenol A-Glycidyl Methacrylate or compomer\$).mp.
7. or/5-6
8. exp ANTI-BACTERIAL AGENTS/
9. (antibacterial\$ or anti-bacterial\$ or antimicrob\$ or anti-microb\$ or "12-methacryloyloxydodecylpyridinium bromide\$").mp.
- 10.or/8-9
- 11.4 and 7 and 10

Appendix 2. Cochrane Oral Health Group's Trials Register search strategy

((fill* or restor*) and (composite* or compomer*) and (antibacterial* or anti-bacterial* or antimicrob* or anti-microb*))

Appendix 3. CENTRAL search strategy

- #1 DENTAL RESTORATION, PERMANENT
 #2 DENTAL CAVITY PREPARATION

#3 ((dental* or tooth or teeth) and (fill* or "cavity preparation*"))
 #4 (#1 or #2 or #3)
 #5 COMPOSITE RESINS explode all trees
 #6 (composite* or "Bisphenol A-Glycidyl Methacrylate" or compomer*)
 #7 (#5 or #6)
 #8 ANTI-BACTERIAL AGENTS explode all trees
 #9 (antibacterial* or anti-bacterial* or antimicrob* or anti-microb* or "12-methacryloyloxydodecylpyridinium bromide*")
 #10 (#8 or #9)
 #11 (#4 and #7 and #10)

Appendix 4. EMBASE (OVID) search strategy

1. DENTAL RESTORATION, PERMANENT/
2. DENTAL CAVITY PREPARATION/
3. ((dental or tooth or teeth) and (fill\$ or restor\$ or "cavity preparation\$")).mp.
4. or/1-3
5. exp COMPOSITE RESINS/
6. (composite\$ or Bisphenol A-Glycidyl Methacrylate or compomer\$).mp.
7. or/5-6
8. exp ANTI-BACTERIAL AGENTS/
9. (antibacterial\$ or anti-bacterial\$ or antimicrob\$ or anti-microb\$ or "12-methacryloyloxydodecylpyridinium bromide\$").mp.
- 10.or/8-9
- 11.4 and 7 and 10

WHAT'S NEW

Date	Event	Description
11 March 2014	Review declared as stable	This empty review will not be updated until a substantial body of evidence on the topic becomes available. If trials are conducted and found eligible for inclusion in the future, the review would then be updated accordingly.

HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 3, 2009

Date	Event	Description
12 December 2013	New citation required but conclusions have not changed	Changes to authorship. Background and methods updated. 1 new excluded study.
12 December 2013	New search has been performed	Searches updated to 23 July 2013.

CONTRIBUTIONS OF AUTHORS

Tatiana Pereira-Cenci (TPC), Maximiliano Sergio Cenci (MSC), Marina Sousa Azevedo (MSA) and Zbys Fedorowicz (ZF) were responsible for: organising the retrieval of papers, writing to authors of papers for additional information, screening search results, screening retrieved papers against inclusion criteria, appraising the quality of papers, data collection for the review, extracting data from papers and obtaining and screening data on unpublished studies.

TPC, MSC and MSA were going to enter the data into RevMan.

MSC was responsible for analysis and interpretation of the data.

All review authors contributed to writing the review.

TPC, MSC, MSA and ZF were responsible for designing and co-ordinating the review, and data management for the review. TPC and MSC conceived the idea for the review and are the guarantors for the review.

DECLARATIONS OF INTEREST

There are no financial conflicts of interest and the review authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- National Institute for Health Research (NIHR), UK.

CRG funding acknowledgement:

The NIHR is the largest single funder of the Cochrane Oral Health Group.

Disclaimer:

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health.

- Cochrane Oral Health Group Global Alliance, UK.

All reviews in the Cochrane Oral Health Group are supported by Global Alliance member organisations (British Association of Oral Surgeons, UK; British Orthodontic Society, UK; British Society of Paediatric Dentistry, UK; British Society of Periodontology, UK; Canadian Dental Hygienists Association, Canada; National Center for Dental Hygiene Research & Practice, USA; Mayo Clinic, USA; New York University College of Dentistry, USA; and Royal College of Surgeons of Edinburgh, UK) providing funding for the editorial process (<http://ohg.cochrane.org/>).

INDEX TERMS

Medical Subject Headings (MeSH)

*Dental Restoration, Permanent; Anti-Bacterial Agents [*therapeutic use]; Composite Resins [*therapeutic use]; Dental Caries [*prevention & control]

MeSH check words

Humans