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Direct composite resin fillings versus amalgam fillings for permanent or adult posterior teeth (Review)

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[Intervention Review]

Direct composite resin fillings versus amalgam fillings for permanent or adult posterior teeth

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ABSTRACT

Background

Amalgam has been the traditional material for filling cavities in posterior teeth for the last 150 years and, due to its effectiveness and cost, amalgam is still the restorative material of choice in certain parts of the world. In recent times, however, there have been concerns over the use of amalgam restorations (fillings), relating to the mercury release in the body and the environmental impact following its disposal. Resin composites have become an esthetic alternative to amalgam restorations and there has been a remarkable improvement of its mechanical properties to restore posterior teeth.

There is need to review new evidence comparing the effectiveness of both restorations.

Objectives

To examine the effects of direct composite resin fillings versus amalgam fillings for permanent posterior teeth, primarily on restoration failure.

Search methods

We searched the Cochrane Oral Health Group's Trials Register (to 22 October 2013), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 9), MEDLINE via OVID (1946 to 22 October 2013), EMBASE via OVID (1980 to 22 October 2013), and LILACs via BIREME Virtual Health Library (1980 to 22 October 2013). We applied no restrictions on language or date of publication when searching the electronic databases. We contacted manufacturers of dental materials to obtain any unpublished studies.

Selection criteria

Randomized controlled trials comparing dental resin composites with dental amalgams in permanent posterior teeth. We excluded studies having a follow-up period of less than three years.

Data collection and analysis

We used standard methodological procedures expected by The Cochrane Collaboration.

Main results

Of the 2205 retrieved references, we included seven trials (10 articles) in the systematic review. Two trials were parallel group studies involving 1645 composite restorations and 1365 amalgam restorations (921 children) in the analysis. The other five trials were split-mouth studies involving 1620 composite restorations and 570 amalgam restorations in an unclear number of children. Due to major problems with the reporting of the data for the five split-mouth trials, the primary analysis is based on the two parallel group trials. We judged all seven trials to be at high risk of bias and we analyzed 3265 composite restorations and 1935 amalgam restorations.

The parallel group trials indicated that resin restorations had a significantly higher risk of failure than amalgam restorations (risk ratio (RR) 1.89, 95% confidence interval (CI) 1.52 to 2.35, P value < 0.001 (fixed-effect model) (low-quality evidence)) and increased risk of secondary caries (RR 2.14, 95% CI 1.67 to 2.74, P value < 0.001 (low-quality evidence)) but no evidence of an increased risk of restoration fracture (RR 0.87, 95% CI 0.46 to 1.64, P value = 0.66 (moderate-quality evidence)). The results from the split-mouth trials were consistent with those of the parallel group trials.

Adverse effects of dental restorations were reported in two trials. The outcomes considered were neurobehavioral function, renal function, psychosocial function, and physical development. The investigators found no difference in adverse effects between composite and amalgam restorations. However, the results should be interpreted with caution as none of the outcomes were reported in more than one trial.

Authors' conclusions

There is low-quality evidence to suggest that resin composites lead to higher failure rates and risk of secondary caries than amalgam restorations. This review reinforces the benefit of amalgam restorations and the results are particularly useful in parts of the world where amalgam is still the material of choice to restore posterior teeth with proximal caries. The review found insufficient evidence to support or refute any adverse effects associated with amalgam or composite restorations. However, emerging research is highlighting issues around genetic susceptibility to mercury. The decision for a global phase-down of amalgam (Minamata Convention on Mercury) will restrict the future use of amalgam.

PLAIN LANGUAGE SUMMARY

Tooth-colored resin fillings compared with amalgam fillings for permanent teeth at the back of the mouth

Review question

This review, carried out by the Cochrane Oral Health Group, addressed the question of how effective tooth-colored (composite resin) fillings are compared with conventional amalgam fillings when placed directly into cavities in permanent teeth in the back of the mouth.

Background

There is controversy over the best materials to use when restoring or filling holes caused by tooth decay in permanent teeth at the back of the mouth. Amalgam fillings have been successfully used for over 150 years and are cost effective. However, their use has declined over recent years partly because of the way they look and because of the perceived risk of mercury that is used in them. Tooth-colored (composite resin) fillings are frequently used in the front teeth and also in permanent teeth at the back of the mouth.

Study characteristics

The evidence on which this review is based was up to date as of 22 October 2013. We searched scientific databases and found seven studies to include in this review comparing composite resin fillings with amalgam fillings and we included two of these studies in the main analysis. There were 3265 composite fillings and 1935 amalgam fillings but is unclear how many children these were in. The exact age of participants was also unclear in some studies; however, both children and adults with permanent teeth at the back of the mouth that required fillings were included. Study centers were located in the UK, USA, Portugal, Sweden, The Netherlands, Belgium, and Germany.

Key results

The main result including only two studies in 921 children suggests that amalgam fillings had lower failure rates than tooth-colored (composite resin) fillings used to fill holes caused by decay in permanent teeth at the back of the mouth. Further tooth decay (secondary caries) also occurred less frequently next to or under amalgam fillings compared with composite resin fillings. There was no evidence of a difference in the breaking of the two types of fillings.

The other five studies only reported the rate of failure of the fillings and the amount of further tooth decay occurring next to or under the fillings (secondary caries) and the results supported those of the two studies above.

The results suggest that tooth-colored (composite resin) fillings are almost twice as likely to fail compared with amalgam fillings when used for filling permanent teeth at the back of the mouth.

Quality of the evidence

The quality of the evidence was low to moderate. Because there was an obvious difference in the color of the fillings, it was not possible to do the comparisons 'blind' so there was, therefore, a high risk of bias.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Primary and secondary outcomes for permanent or adult posterior teeth

Patient or population: people with permanent or adult posterior teeth
Settings: outpatients
Intervention: composite
Control: amalgam

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of teeth (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Amalgam	Composite				
Failure rate Follow-up: 5-7 years	**75 per 1000**	**142 per 1000** (114 to 176)	**RR 1.89** (1.52 to 2.35)	3010 (2 studies)	⊕⊕◯◯ **low**[1,2]	Reasons for failure include secondary caries, fracture, restoration loss
Secondary caries Follow-up: 5-7 years	**57 per 1000**	**122 per 1000** (95 to 156)	**RR 2.14** (1.67 to 2.74)	3010 (2 studies)	⊕⊕◯◯ **low**[1,3]	None
Fracture of restorations Follow-up: 5-7 years	**14 per 1000**	**12 per 1000** (6 to 23)	**RR 0.87** (0.46 to 1.64)	3010 (2 studies)	⊕⊕◯◯ **low**[1,4]	None
Adverse events	*See* comments					Data were reported for neurobehavioral assessment, kidney function, psychosocial function, physical development. None of these outcomes were reported in more than 1 study. Evidence was insufficient to reach conclusions

*The basis for the **assumed risk** (e.g. the 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.

[1] Performance, detection, and selection (due to allocation concealment) bias[2] $I^2 = 87\%$[3] $I^2 = 92\%$
[4] Imprecision

BACKGROUND

Description of the condition

Dental caries (tooth decay) is a dynamic and continuous process composed of cycles of demineralization of the hard tissue of the teeth followed by cycles of remineralization. The balance between the two cycles determines the stage of the disease (ICDAS 2011). There is a close relationship between oral health and quality of life just as socioeconomic status and home environment have been shown to impact on people's oral condition (Gomes 2009; Paula 2012). Despite the great accomplishments obtained globally in oral health, caries is still a serious problem particularly among under-privileged groups in low, middle and high-income countries, affecting 60% to 90% of school children and the vast majority of adults (Costa 2012). It is also the most prevalent oral health problem in several Asian and Latin-American countries (WHO 2012).

Modern management of dental caries involves making a diagnosis to determine the person's caries risk status, followed by the application of intervention strategies focused on preventing, arresting, and possibly reversing the caries process to delay restorative treatment until it becomes absolutely necessary (Ferreira Zandona 2012). When the damage on the tooth structure is permanent, the most commonly used treatment involves cleaning the cavity and filling it with a restorative material to restore the shape and function of the tooth.

Primary caries seems to be the most frequent reason for the placement of restorations (fillings) and caries lesions are most commonly found on occlusal surfaces of posterior teeth (Nascimento 2010). Secondary caries is responsible for 60% of all replacement restorations in the typical dental practice but the association between the type of restoration materials and location of caries and the composition of the microflora has not been found to be statistically significant (Mo 2010).

Description of the intervention

The obturation and filling of occlusal cavities is an issue that has been long studied. The choice of the best material for restoring the anatomical structures that also achieves acceptable resistance to the forces of mastication is still controversial. This review compared dental amalgams and resin composites, the two main categories of dental restorative fillings used in posterior tooth restorations today.

Dental amalgams are metallic alloys. They have been predictable and inexpensive restorative materials for over 150 years. Their use and success rate have been well documented and they are the most cost-effective materials in posterior teeth restorations. However, they are declining in use in dentistry mainly due to their unesthetic appearance and concerns about their mercury content (Kelly 2004; Mitchell 2007; Roulet 1997).

Dental resin composites were developed in response to people's demands for tooth-colored restorations. Dental resin composites are particle-reinforced resins. The indications of resin composites have expanded from anterior teeth to restrict posterior restorations and even to stress-bearing posterior restorations as amalgam substitutes or amalgam alternatives (Lutz 1999). Other advantages of dental resin composite restorations include their conservative design and reparability.

The cost of placing dental amalgams (USD 12.40) is only slightly cheaper than the cost of placing composite fillings (USD 15.90) for a single restoration provided in one dental session. However, when the costs are considered in the long term, taking into consideration the differences in longevity of the two materials, Sjögren et al. calculated that the estimated cost over 10 years for a Class II restoration was USD 189.80 for amalgam fillings and USD 363.70 for a composite filling (CADTH 2012).

How the intervention might work

Dental amalgam and resin composite restorations are still the most current selection for restoring permanent molar and premolar cavities. The choice of amalgam as the preferred material to restore posterior teeth has been gradually replaced by resin composite. However, surveys and retrospective studies developed by groups of practice-based researchers differ in their conclusions about which is the material most commonly used in restorative dentistry today (Makhija 2011; Nascimento 2010).

In recent years, the field of composite dental restoratives continues to propose and achieve significant and exciting advances in resin formulation, filler loading and modification, and curing methodologies and mechanisms (Cramer 2011).

The current controversy is that amalgam restorations should be banned because of mercury toxicity. In addressing safety concerns, it is important to make the distinction between known and hypothetical risks (Rathore 2012). The truth is that a variety of potentially toxic compounds might be released from restorative dental materials (amalgam and composites) and can diffuse into the tooth pulp or gingiva reaching both saliva and circulating blood (Libonati 2011). Their adverse effects are not yet well known.

Why it is important to do this review

While the use of dental amalgam has declined (Mitchell 2007) in some parts of the world, it is still the restorative material of choice in other parts of the world. The decline is due to concerns about its mercury release in the body and environmental impact following its disposal. To achieve a balance between the environment impact of the disposal of mercury products including amalgam and its public health benefit, the Minamata Convention on Mercury

proposes a paced phase-down by national governments according to local needs (BDA 2013; UNEP 2013). The World Health Organization (WHO) further iterates that the move from amalgam would depend on quality improvement of alternative restoration materials. Since the adhesive dentistry remains one of the fastest changing fields and will most likely continue well into the next decade (McDonald 2001), there is need to provide a comprehensive update on the effects of composite materials in comparison with amalgam.

OBJECTIVES

To examine the effects of direct composite resin fillings versus amalgam fillings for permanent posterior teeth, primarily on restoration failure.

METHODS

Criteria for considering studies for this review

Types of studies

All randomized controlled trials comparing dental resin composites with dental amalgams in permanent posterior teeth (dating back to 1946) were selected, including studies with parallel group or split-mouth designs. We excluded studies that had less than a three-year follow-up period.

Types of participants

Adults or children with permanent posterior teeth suitable (i.e. with tooth decay) for resin composite or amalgam restorations or both.

Types of interventions

- Intervention: dental resin composites.
- Control: dental amalgams.

Types of outcome measures

Primary outcomes

- Failure rate (or survival rate) of the restorations.

Secondary outcomes

- Reasons for failure (according to the evaluation categories of the United States Public Health Service (USPHS), which includes color match, marginal adaptation, anatomical form, and secondary caries) and patient satisfaction. The minimum length of follow-up that was acceptable for outcomes was three years.
- Cost data (treatment time plus material costs).
- Unexpected/adverse events (as reported in included trials).

Search methods for identification of studies

Electronic searches

For the identification of studies included in, or considered for this review, we developed detailed search strategies for each database searched. We based these on the search strategy developed for MEDLINE (OVID) but revised appropriately for each database. We searched the following electronic databases:

- the Cochrane Oral Health Group's Trials Register (to 22 October 2013) (Appendix 1);
- the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 9) (Appendix 2);
- MEDLINE via OVID (1946 to 22 October 2013) (Appendix 3);
- EMBASE via OVID (1980 to 22 October 2013) (Appendix 4);
- LILACS via BIREME Virtual Health Library (1980 to 22 October 2013) (Appendix 5).

Searching other resources

Handsearching for this review was done as part of the Cochrane worldwide handsearching program, *see* the Cochrane Master List for details of the journals and issues searched to date. We checked the reference lists of all eligible trials and relevant review articles for additional studies.

We contacted the authors of unpublished studies, but did not receive any replies.

We contacted the major manufacturers of dental materials (GC and 3M ESPE) in June 2012 to obtain information on published and unpublished trials/studies that may have involved their products. We were informed that no studies comparing resin composite materials and amalgam materials had been carried out. We also contacted Ivoclar Vivident, Kerr and Dentsply at the same time but they did not reply.

Language

We placed no restrictions on language or date of publication in the databases searched.

Data collection and analysis

Selection of studies

Review authors, working independently and in duplicate, assessed the titles and abstracts resulting from the searches to identify eligible studies for this review. We obtained the full copies of possible studies and assessed them to see if they met the inclusion criteria. We directed studies on which agreement was not reached to two other review authors who also worked independently. We excluded studies until further clarification was available or if we were unable to reach a consensus. We tabulated excluded studies with reasons for exclusion (Characteristics of excluded studies table). We resolved disagreements by discussion.

Data extraction and management

The four review authors piloted specially designed data extraction forms on two papers and modified the forms before use. We resolved any disagreements by discussion. Two review authors extracted data independently and in duplicate from each study that was relevant to the specified outcomes, and sent the data forms to the other two review authors for comparison and verification. The features of the studies that we reported in the Characteristics of included studies table in the review were as follows:

1. methods - unit of randomization (participants or teeth), exclusions after randomization, unusual study design, practice setting;
2. participants - country and date of the trial, number randomized, main inclusion and exclusion criteria, losses to follow-up, stratification by age, sex, tooth type (location of the restoration), surfaces of restoration (type of cavity);
3. interventions - materials used in treatment, comparison intervention (control);
4. outcomes - failure rate (or survival rate) of the resin composite or dental amalgam restorations over time (yearly beginning from three years) with failure defined as the rating of the clinical performance greater than bravo using the assessment criteria of the USPHS guidelines, reasons of failure (secondary caries), fracture of the restoration;
5. notes - additional details relevant to that particular trial (e.g. funding sources).

Assessment of risk of bias in included studies

Two review authors undertook the assessment of risk of bias independently and in duplicate for each included study using the Cochrane 'Risk of bias' assessment tool (Higgins 2011). We assessed seven domains for each included study: sequence generation (selection bias), allocation sequence concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other potential sources of bias. The risk of bias was assessed as 'low risk', 'high risk', or 'unclear risk', with the last category indicating either lack of information or uncertainty over the potential for bias.

The Cochrane Collaboration's tool for assessing risk of bias

Domain	Support for judgment	Review authors' judgment
Selection bias.		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
Performance bias.		
Blinding of participants and personnel *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a partici-	Performance bias due to knowledge of the allocated interventions by participants and

(*Continued*)

	pant received. Provide any information relating to whether the intended blinding was effective	personnel during the study
Detection bias.		
Blinding of outcome assessment *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Detection bias due to knowledge of the allocated interventions by outcome assessors
Attrition bias.		
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors	Attrition bias due to amount, nature, or handling of incomplete outcome data
Reporting bias.		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found	Reporting bias due to selective outcome reporting.
Other bias.		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool If particular questions/entries were prespecified in the review's protocol, responses should be provided for each question/entry	Bias due to problems not covered elsewhere in the table.

After taking into account the additional information provided by the authors of the trials, we grouped the studies into the following categories:

1. low risk of bias (plausible bias unlikely to seriously alter the results);
2. unclear risk of bias if one or more of the domains are assessed as unclear;
3. high risk of bias (plausible bias that weakens confidence in the results) if one or more domains are assessed at high risk of bias.

Measures of treatment effect

For each trial, we calculated risk ratios (RR) with 95% confidence intervals (CI) for all pre-specified, dichotomous outcomes. We

calculated mean difference (MD) or standardized mean difference (SMD) for continuous data. In the case of split-mouth design studies, we aimed to calculate log risk ratio separately for each outcome.

We aimed to extract time-to-event data from each study in our review, if possible, and to express the treatment effect as a hazard ratio using survival analysis. If necessary, outcome data would have been transformed to achieve consistency of results (e.g. calculate survival rate as dichotomous data from time-to-event data at fixed time points).

Unit of analysis issues

The unit of analysis was restoration. Whenever possible, we checked the included studies for unit of analysis errors and handled if considered appropriate following the advice provided in Section 16.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

In case of missing individual data, we analyzed only available data. We performed an intention-to-treat (ITT) analysis if possible. In some cases, we contacted study authors when there was need for more information. We addressed the potential impacts of missing data on the findings of the review in the Discussion section.

Assessment of heterogeneity

We assessed heterogeneity by analyzing the point estimates and CIs on the forest plots. We assessed statistical heterogeneity using The Cochrane Collaboration's test for heterogeneity and quantified using the I^2 statistic. According to the *Cochrane Handbook for Systematic Reviews of Intervention*, I^2 values of 0% to 40% might not be important, 30% to 60% may represent moderate heterogeneity, 50% to 90% may represent substantial heterogeneity, and 75% to 100% is considerable heterogeneity (Higgins 2011). Heterogeneity was considered statistically significant if the P value was < 0.1.

Assessment of reporting biases

Only a proportion of research projects conducted are ultimately published in an indexed journal and become easily identifiable for inclusion in systematic reviews (Easterbrook 1991). Reporting biases arise when the reporting of research findings is influenced by the nature and direction of the findings of the research. We attempted to avoid time lag bias, multiple (duplicate) publication bias, and language bias by conducting a detailed sensitive search, including searching for ongoing studies. We did not restrict the search by language and non-English studies were translated by co-review authors due to their multinationality.

Data synthesis

We combined RRs for dichotomous data of the studies that were considered appropriate to be included in the meta-analysis. We intended to combine the treatment effects from split-mouth trials with those from parallel group trials where appropriate as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Elbourne 2002; Higgins 2011), but it was not possible because of poor reporting. Therefore, we treated the split-mouth trials as a subgroup so that the results could be examined either in isolation or in combination with the parallel group studies. This was particularly aimed at providing a broader view and 'bottom-line' to the review question. We used random-effects models where there were more than three studies in any meta-analysis, otherwise we used fixed-effect models.

Subgroup analysis and investigation of heterogeneity

We intended to explore the following potential sources of heterogeneity using subgroup analyses:

1. age of participants;
2. location of restoration (premolar or molar);
3. type of cavity (class I or II; stress bearing or not);
4. materials used;
5. practice setting (university based or private practice based) and operator.

However, there was not enough data available to explore the reasons of heterogeneity.

Sensitivity analysis

A sensitivity analysis was planned to examine the robustness of the meta-analysis but the number of included studies was inadequate.

Presentation of main results

We have presented a 'Summary of findings' table to show the findings of the most important outcomes (Summary of findings for the main comparison). We assessed the quality of the body of evidence by following the GRADE framework with reference to the overall risk of bias of the included studies, directness of the evidence, inconsistency of the results, precision of the estimates, risk of publication bias, and magnitude of the effect. We categorized the quality of the body of evidence for each of the outcomes as high, moderate, low, or very low.

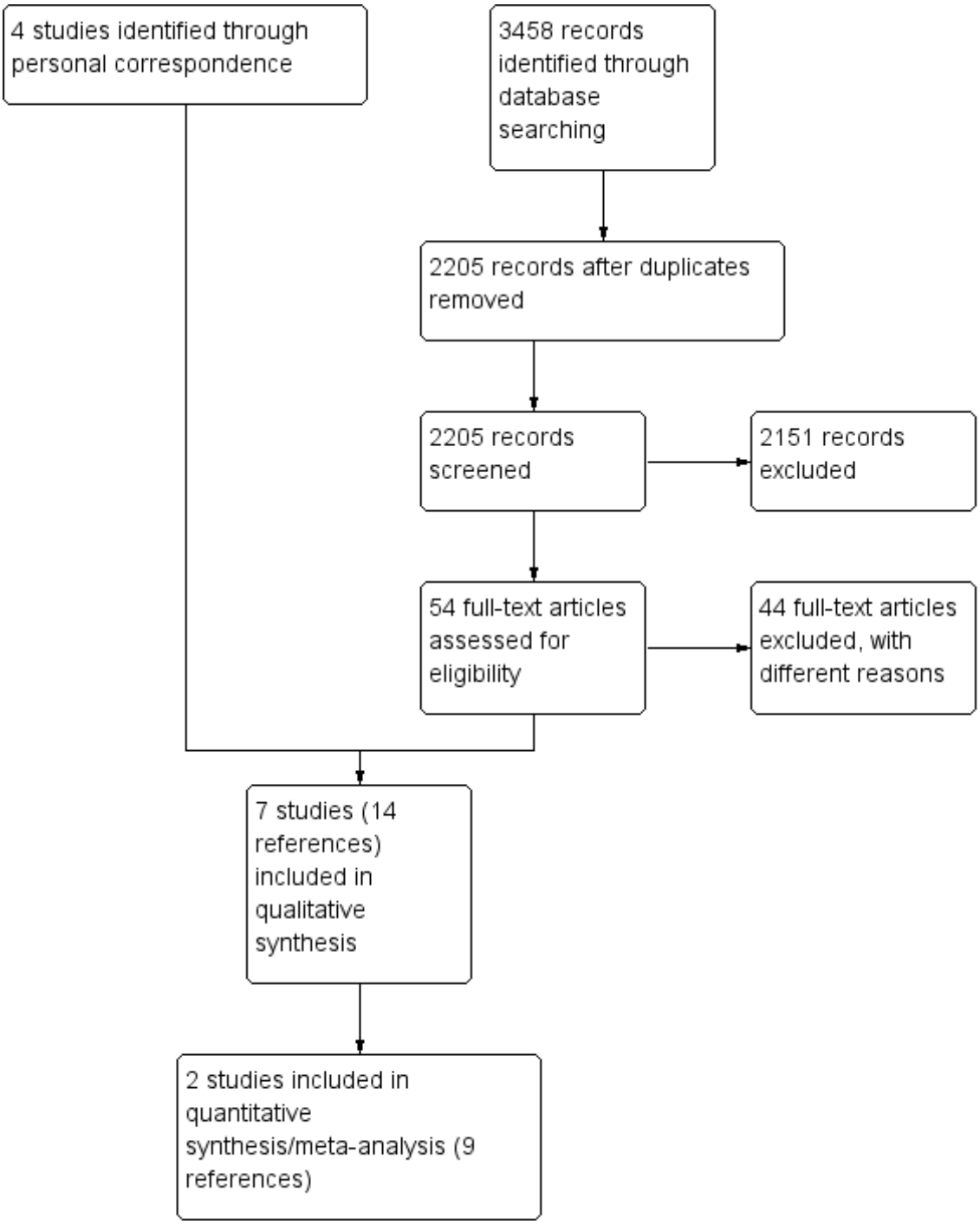
RESULTS

Description of studies

Results of the search

The search strategy retrieved 2205 references to studies after de-duplication. After examination of the titles and abstracts of these references, we considered 51 studies (54 articles) for critical appraisal. After evaluation of the full-text copies of the remaining studies, seven studies (10 articles) fulfilled the inclusion criteria. A PRISMA flow diagram illustrates the results of the search, screening, and selection of studies for inclusion (Figure 1).

Figure 1. PRISMA flow diagram of study inclusion.



Included studies

The articles obtained by bibliographic search were mostly in English and a minor proportion in German, Spanish, and Portuguese. Since the review authors were from different countries, they were able to read and translate the non-English studies. To obtain the full articles, we contacted different libraries and universities were contacted.

Characteristics of the trial designs

Seven randomized controlled trials (RCTs) that met the inclusion criteria were reported in 10 articles (Casa Pia 2007; Cunningham 1990; Hendriks 1986; Letzel 1989; NECAT 2007; Norman 1990; Robinson 1988). Two of the seven studies were parallel group trials (Casa Pia 2007; NECAT 2007), while the other five were split-mouth studies (Cunningham 1990; Hendriks 1986; Letzel 1989; Norman 1990; Robinson 1988).

The two parallel group studies reported data on two large RCTs that were developed to compare amalgam with composite to restore posterior teeth: The Casa Pia Study of Health Effects of Dental Amalgam in Children started in 1996 and was followed up for seven years (Casa Pia 2007), and The New England Children's Amalgam Trial (NECAT) conducted between September 1997 and March 2005 (NECAT 2007).

Some of the split-mouth studies reported data from a multicenter RCT designed for testing resin composite materials as a material suitable to restore posterior teeth, using amalgam restorations as positive control. The data from the split-mouth studies were not reported or analyzed in an appropriate way taking the clustering of the sites within participants into account. There were different numbers in the two groups, which makes the analysis even more problematic.

Two studies were conducted in the UK (Cunningham 1990; Robinson 1988), one in Portugal (Casa Pia 2007), one in the USA (NECAT 2007), one was a multicenter trial conducted in parts of Europe and in the USA (Letzel 1989), and the locations of two studies were not clearly reported (Hendriks 1986; Norman 1990).

Three studies were funded by the same dental industry (Letzel 1989; Norman 1990; Robinson 1988), one was funded by a research grant (Casa Pia 2007), and the other three studies did not state their funding sources (Cunningham 1990; Hendriks 1986; NECAT 2007).

Characteristics of the participants

Of the 1006 participants who took part in the two parallel group trials, data from 871 participants were analyzed. The participants were aged six to 12 years at baseline and follow-up period was five to seven years. Most of the split-mouth trials did not specify the number of participants recruited but reported data on 2190 restorations. The number of restorations varied between the five trials and ranged from 27 to 932.

Characteristics of the interventions

In the included studies, participants received amalgam restoration or composite resin restoration. In one study, participants received amalgam, compomer, or composite restoration but we have not presented the data on compomer restoration in this review (NECAT 2007).

Characteristics of outcomes

The primary outcome was failure rate. This parameter was collected and reported in all the included studies. Secondary caries was reported in six studies (Casa Pia 2007; Cunningham 1990; Hendriks 1986; NECAT 2007; Norman 1990; Robinson 1988), while fracture outcome data were reported in only two studies (Casa Pia 2007; NECAT 2007). Data on adverse outcomes were collected from participants included in the Casa Pia study and NECAT study but reported in three other articles linked to the respective primary studies. Neurobehavioral and renal function were reported in Casa Pia 2007, and psychosocial function and physical development were reported in NECAT 2007.

See Characteristics of included studies table for more information on included studies.

Excluded studies

See Characteristics of excluded studies table for further information on each excluded study.

In summary, the main reasons for exclusion after the critical appraisal of the 44 studies that had been initially identified as eligible for this review were:

- design was not randomized or controlled in the following studies: Allan 1977; Bryant 1994; Busato 1996; Cloyd 1997; Collins 1998; Eames 1974; Fukushima 1988; Hendriks 1985; Johnson 1992; Knibbs 1992; Kopperud 2012; Mjör 1993a; Mjör 1993b; Pieper 1991; Powers 1974; Prati 1988; Rowe 1989; Rytömaa 1984; Samaha 1982; Smales 1992; Tobi 1999; Van Nieuwenhuysen 2003;
- randomization was broken in one study: Welbury 1990;
- short follow-up less than specified in the protocol: Borgmeijer 1991; Kreulen 1993a; Lambrechts 1984; Leinfelder 1975; Roulet 1977; Walls 1988;
- other methodologic reasons (lack of clarity on comparison between amalgam and composite, not clear if the materials were

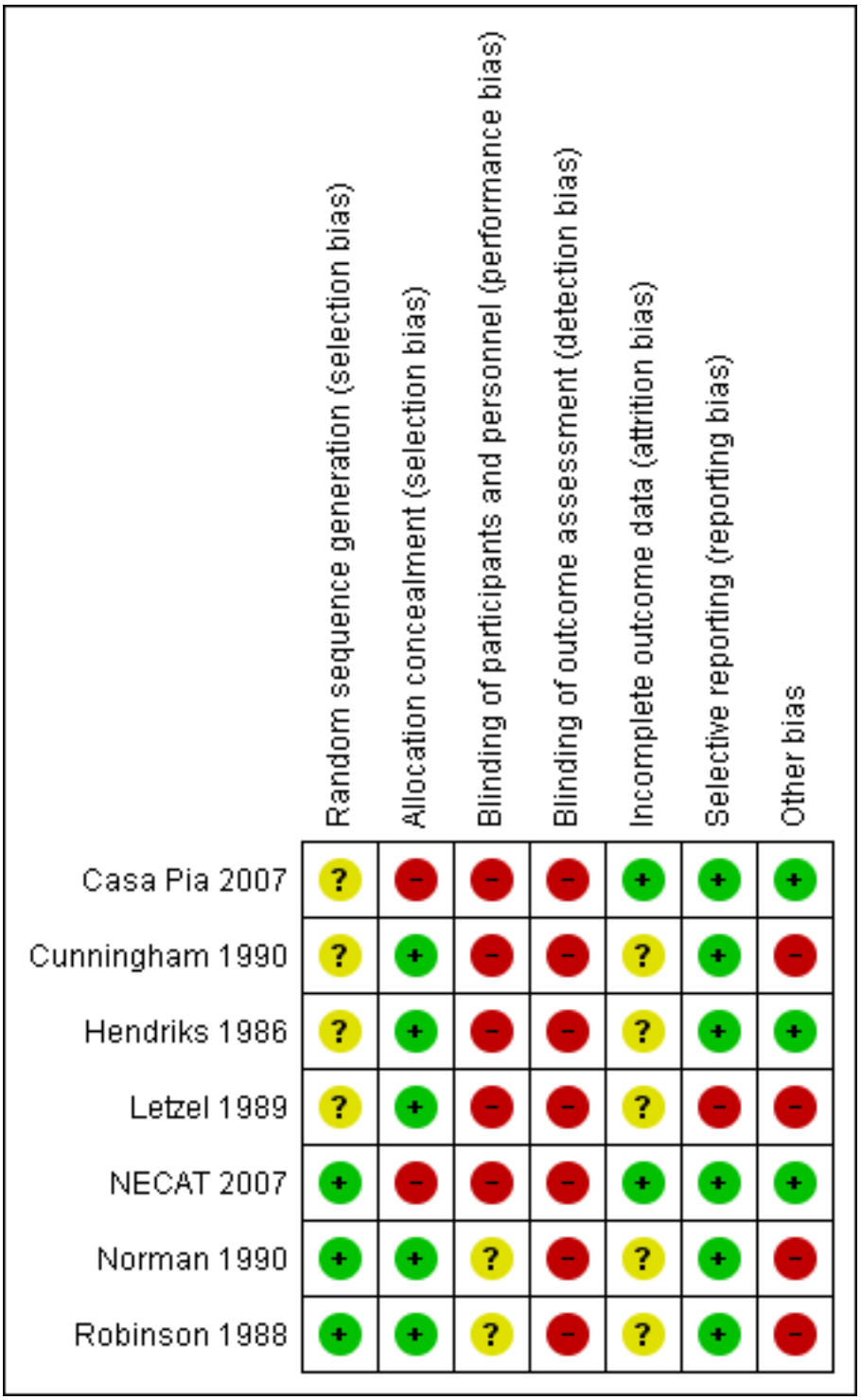
tested in permanent posterior teeth, lack of clarity on evaluation of longevity and impossibility of obtaining useful data): Bellinger 2006; Dilley 1990; Kreulen 1993b; Leinfelder 1980; Mair 1998; Mannocci 2005; Nell 1994; Roulet 1978; Shenker 2008; Smales 1992; Wilson 1996;

- contacted one study author to obtain the data of an unpublished trial (Koray n.d.). We excluded the study as the authors did not reply;
- unable to obtain the full-text article of Solano 1984 for critical appraisal.

Risk of bias in included studies

We judged all the included studies to be at high risk of bias (Figure 2). In most of the studies, bias was mainly due to lack of blinding. For the split-mouth studies in particular, it was due to failure to take clustering effect into account in the analysis.

Figure 2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.



Randomization (selection bias)

We considered three studies to be at low risk of selection bias (NECAT 2007; Norman 1990; Robinson 1988), while the other four studies were at unclear risk of bias for poor details on randomization process (Casa Pia 2007; Cunningham 1990; Hendriks 1986; Letzel 1989).

Allocation

In all the included studies, there was no indication of allocation concealment. However, we judged the five split-mouth studies to be at low risk of bias because a lack of allocation concealment would neither make a difference nor introduce bias to a split-mouth study (Cunningham 1990; Hendriks 1986; Letzel 1989; Norman 1990; Robinson 1988). We considered the two parallel studies to be at high risk of bias (Casa Pia 2007; NECAT 2007).

Blinding

We found all the studies to be at high risk of performance bias and detection bias since the nature of the intervention (dental restorations) does not allow blinding for the operators or for the participants. Even though some studies indicated that outcome assessment was carried out by evaluators independent of the operators (Norman 1990; Robinson 1988), we did not consider this to be sufficient to minimize detection bias.

Incomplete outcome data

Drop-out rates were similar in the intervention and comparator groups in the two studies we judged to be at low risk of attrition bias (Casa Pia 2007; NECAT 2007). In the other five studies that we considered to be at unclear risk of bias, an overall drop-out rate was reported (Cunningham 1990; Hendriks 1986; Letzel 1989; Norman 1990; Robinson 1988). However, we were unable to determine whether the drop-out rate was differential.

Selective reporting

The data were well documented in all but one study (Letzel 1989), which reported all data for composite resin but did not report all the amalgam data.

Other potential sources of bias

None of the split-mouth studies had clearly indicated the number of restorations per participant resulting in high risk of bias due to unit of analysis error (Cunningham 1990; Hendriks 1986; Letzel 1989; Norman 1990; Robinson 1988). In addition, Letzel 1989 reported that there were notable variations in results across the different centers involved in the trial but provided no explanation for this. The two studies that we judged to be at low risk had no other apparent biases (Casa Pia 2007; NECAT 2007).

Effects of interventions

See: **Summary of findings for the main comparison** Primary and secondary outcomes for permanent or adult posterior teeth

Due to the poor reporting of the split-mouth studies, which makes the reported data unreliable, we decided that the primary analysis should only include the two parallel group studies. We also undertook a secondary analysis of all included trials. We studied failure rate as the primary outcome, and secondary caries and fracture of the restoration as secondary outcomes. Psychosocial function, physical development, neurobehavioral assessments, and kidney function were considered to explore adverse effects of mercury release.

Failure rate

The parallel group trials both recorded failure rate in the amalgam and composite group over a period of five to seven years. In total, 1365 amalgam restorations and 1645 composite restorations were analyzed. The pooled estimate showed that composite restorations had a significantly higher risk of failure than amalgam (risk ratio (RR) 1.89, 95% confidence interval (CI) 1.52 to 2.35, P value < 0.001; fixed-effect model) (Analysis 1.1). There was indication of heterogeneity (P value = 0.005; I^2 = 87%), but, as there were only two studies, this could not be investigated. As the effect estimates for both studies were in the same direction, we decided to undertake the meta-analysis.

A subgroup analysis of the split-mouth studies also showed a similar trend with composite restorations having a higher risk of failure than amalgam restorations (RR 1.33, 95% CI 0.84 to 2.11, P value = 0.23; random-effects model) (*note* fixed-effect model displayed in forest plot as primary result is for parallel group subgroup). There was no evidence of heterogeneity (P value = 0.57; I^2 = 0%).

There was no evidence of a difference between the study design subgroups and the results of the parallel group and split-mouth trials when combined showed more precise results with composite restorations having a significantly higher risk of failure than amalgam restorations (RR 1.62, 95% CI 1.13 to 2.4, P value = 0.009; random-effects model). There was some evidence of heterogeneity (P value = 0.05; I^2 = 52%).

Secondary caries

Secondary caries was the most common reason for failure in the included studies. Meta-analysis of the parallel group studies showed

a higher risk of secondary caries in permanent posterior teeth with composite restoration compared with teeth with amalgam restoration (RR 2.14, 95% CI 1.67 to 2.74, P value < 0.001; fixed-effect model) (Analysis 1.2). Once again there was evidence of heterogeneity (P value < 0.001; I^2 = 92%), but, as there were only two studies, this could not be investigated. As the effect estimates for both studies were in the same direction, we decided to undertake the meta-analysis.

The outcome data from the split-mouth studies showed no significant difference in secondary caries when composite restorations were compared with amalgam restorations (RR 1.3, 95% CI 0.34 to 4.97, P value = 0.7; random-effects model). There was no evidence of heterogeneity (P value = 0.64; I^2 = 0%).

The combined results of the parallel group and split-mouth trials indicated an increased risk of secondary caries for composite restorations (RR 1.93, 95% CI 0.98 to 3.80, P value = 0.06; random-effects model). There was some evidence of heterogeneity (P value = 0.02; I^2 = 64%).

Fracture of the restoration

Fracture of the restorations does not seem to be a common reason for failure in the studies reporting data on fracture. There was no evidence of a difference in risk of fracture between the two materials (RR 0.87, 95% CI 0.46 to 1.64, P value = 0.66; fixed-effect model). There was no evidence of heterogeneity (P value = 0.44; I^2 = 0%).

Analysis of subgroups

One study reported failure rates separately in molars and premolars (Casa Pia 2007), but the results were not sufficient to determine whether there was an association between location of the restorations in different teeth and failure rate of restorations.

Adverse effects

Casa Pia 2007 presented trial results on the effects of mercury on the nervous system and the potential damage to the renal system in children. Some tests were carried out at baseline and at seven years after a filling placement, to explore intelligence, nerve conduction velocity, memory, attention, and visuomotor function (Additional Table 1). To study renal function, creatinine-adjusted urinary albumin levels were recorded at years one, two, three, four, five, six, and seven (Additional Table 2). According to the results, there was no statistically significant differences in measures of memory, attention, visuomotor function, or nerve conduction velocities. There were no significant group differences in creatinine-adjusted urinary albumin over the seven years of follow-up. A re-analysis of the data published in 2011, based on amalgam size and years of exposure, found a significant association between amalgam and the porphyrin biomarkers for mercury-related enzyme blockage, which suggests amalgams are a significant contributor to mercury body burden. A further investigation of a subgroup of children with genotyping assays demonstrated a genetic susceptibility to the adverse neurobehavioral effects of mercury exposure in children, predominantly in boys.

The NECAT 2007 trial focused on the effect of restorations on psychosocial function (Additional Table 3) and physical development (Additional Table 4) in children after five years of follow-up. The effect of restorations on psychosocial function was measured using two validated instruments: Child Behavior Checklist (CBCL) parent report and Behaviour Assessment for Children Self Report (BASC-SR). The degree of exposure to restorations was expressed in surface years (SY); however, no direct comparison was made between children in the composite and amalgam arm. The BASC-SR measured emotional symptoms, clinical maladjustment, school maladjustment, personal adjustment, and core syndromes such as anxiety, depression, attitude to school, and interpersonal relations. The CBCL measured competence, total problem behaviors, internalizing problems, externalizing problems, and core syndromes such as attention problems, withdrawal, anxiety/depression, delinquent behaviors, and aggression.

The authors concluded that greater exposure to composite restorations was associated with impaired psychosocial function in children whereas no adverse psychosocial outcomes were observed with greater amalgam treatment levels. No between-group comparison was reported.

The growth outcomes considered were body fat percentage, body mass index (BMI) and height. There were no statistically significant differences in physical development in children given composite and amalgam restorations.

DISCUSSION

Summary of main results

We meta-analyzed seven trials reporting outcome data on failure rate, secondary caries, fracture of restoration, and adverse effects. However, due to the poor reporting and analysis of the data from the split-mouth studies, only evidence from the two parallel group trials are presented in Summary of findings for the main comparison to inform this review. The results of the two parallel group trials suggest that composite restorations are almost twice at risk of failing, and for having secondary caries compared with amalgam restorations. There was no evidence of a difference in fracture rates between amalgam and composite restorations. Though the evidence from the two trials may be considered insufficient, they are supported by five additional split-mouth trials, which found similar results on all three outcomes. While the results of the two parallel group trials showed greater effect size, they were less precise than the pooled estimate of all seven trials. As

none of the adverse effects were reported in more than one study, the results should be interpreted with caution.

Overall completeness and applicability of evidence

The included studies were randomized controlled trials (RCTs) that compared resin composite restorations with amalgam restorations in permanent posterior teeth. Follow-up period ranged between three and seven years. We reported outcome results on failure rate, secondary caries, fracture of restorations, and adverse effects in this review. The event of a failure is reported rather than the non-event of survival. There was a limited number of studies reporting on adverse effects associated with either amalgam or compostie restorations, and the generalisability of the findings from these trials to populations other than healthy children (e.g children or adults with potential mercury-sensitive health conditions such as chronic kidney disease) is unclear. In addition, there is recent emerging research looking into genetic susceptibility to the adverse neurological effects of mercury exposure in children with effects manifested predominantly among boys. It is acknowledged that in order to complete a comprehensive systematic review of adverse events, observational studies would need to be included.This was not the focus of this review; only adverse events identified in the included trials have been reported.

We found insufficient outcome data on the cost of restorations, therefore, this outcome was not covered in the review.

The dental material industry is continuously evolving and improving the products that clinicians use. Most of the included studies were conducted in the 1990s. Some of the materials used in the studies included for the review may no longer be in use or may have been replaced by products with better mechanical properties and better resistance to wear, shrinkage, and fracture. In that case, the results of this review may not be a true reflection of the quality of new restorations that are currently in use.

Quality of the evidence

The body of evidence is based on the results of two parallel group RCTs (involving 1006 participants and 3010 restorations) supported by an additional five split-mouth RCTs. Evidence on failure rate and secondary caries were assessed as low quality due to high risk of bias and inconsistency while evidence on fracture of restoration was of moderate quality. High risk of bias was due to lack of blinding and allocation concealment. Differences in oral hygiene may have contributed to the inconsistency observed with the failure rate and secondary caries outcomes owing to age differences of participants in both trials (mean age 7.9 and 10.2 years). Inconsistency may have also resulted from the difference in adhesives used for composite restoration in the studies. The trial that found an association between composite restoration and impaired psychosocial function had reported that participants received additional composite restoration in cases where any anterior teeth needed restoration. This may have amplified the effects of composite restoration on psychosocial function.

Potential biases in the review process

There were units of analysis issues with all the studies as even the parallel group studies had more than one filling per person, and the data were analyzed without taking into account the clustering. This will mean that the confidence intervals for the effect estimates were smaller than they should be, but this effect will be very small. The effect for the split-mouth studies is unknown as there is lack of clarity in their reporting and this is why they have not been included in the primary analysis.

Agreements and disagreements with other studies or reviews

The results obtained in the process of the present systematic review are consistent with the conclusions of the systematic review performed by the Canadian Agency of Drugs and Technologies in Health (CADTH 2012), which presented safety, efficacy, and cost results. However, in the two studies in CADTH 2012 presenting efficacy data, the duration of follow-up was inadequate for inclusion in this review.

AUTHORS' CONCLUSIONS

Implications for practice

There is low-quality evidence to suggest that resin composites lead to higher failure rates and risk of secondary caries than amalgam restorations. This review reinforces the benefit of amalgam restorations and the results are particularly useful in parts of the world where amalgam is still the material of choice to restore posterior teeth with proximal caries. The review found insufficient evidence to support or refute any adverse effects amalgam or composite restorations may have on patients. However, emerging research is highlighting issues around genetic susceptibility to mercury. The decision for a global phase-down of amalgam (Minamata Convention on Mercury) will restrict the future use of amalgam.

Implications for research

This review indicates that there are higher failure rates with resin composite than amalgam restorations. The included studies date back to 2007 and composite dental restorative materials have advanced considerably since then. Since the proposed discontinuation of use of amalgam depends on quality improvement of non-

mercury-based alternative restorative materials (BDA 2013), there is need for continued focus on new research demonstrating the long-term effectiveness of the latest improved composite materials, techniques, and instruments for placing them. If future studies use a split-mouth design then it is imperative that the data are analyzed and reported appropriately taking the clustering of sites within participants into account (Lesaffre 2009).

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Casa Pia 2007

Methods	Study design: parallel group RCT Conducted in: Lisbon, Portugal Number of centers: 1 at Lisbon Faculty of Dental Medicine Recruitment period: started in 1996 Funding source: National Institute of Dental & Craniofacial Research
Participants	Inclusion criteria: children born from 1986 through 1989. At least 1 carious lesion in a permanent posterior tooth. Urinary mercury concentration less than 10 μg/L. Blood lead concentration of less than 15 μg/dL. An IQ score at least 67 on Comprehensive Test of Nonverbal Intelligence Exclusion criteria: prior exposure to dental amalgam, interference health condition Age: 8-12 years Caries risk status: unclear Location of teeth filled: 1545 permanent molars and 203 premolars Type of cavity filled: 879 Class I restorations and 869 Class II restorations Number randomized: 507 children Number evaluated: 472
Interventions	Comparison: composite versus amalgam Group A: 233 children received 892 composite restorations Group B: 239 children received 856 amalgam restorations Type of moisture control: the restorations were placed using rubber dam isolation whenever possible Duration of follow-up: 7 years
Outcomes	1. Failure rate, estimated at 7 years 2. Secondary caries, estimated at 7 years 3. Fracture of restoration, estimated at 7 years 4. Adverse sentinel health events 5. Neurobehavioral assessment of memory, attention concentration, and motor/visuomotor domains, as well as nerve conduction velocities, estimated at year 1, 2, 3, 4, 5, 6, and 7
Notes	Sample size calculation: selected to ensure adequate power for detecting 2 potential scenarios The first scenario was a small but near-uniform effect of 0.3 SD for the 3 neurobehavioral outcomes, and half of that (0.15 SD) for the nerve conduction outcome. The effect size of 0.3 SD represents a shift that would cause the proportion of abnormally low values in a normally distributed population to increase from 2.5% to 5.0%, thus doubling the proportion classified as abnormally low For the second scenario, a potential effect in only 1 of the 4 outcomes was of interest, so an effect size of 0.5 SD in the nerve conduction outcome was used, with no effects in the others A sample size of 400 (200 in each group) through 5 years of follow-up provided adequate

Casa Pia 2007 (*Continued*)

	power (97%) to detect both scenarios	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Even though the children were randomly assigned to 1 of the 2 treatment groups, the authors did not explain which method of randomization was used
Allocation concealment (selection bias)	High risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported. Due to the clinical characteristics of the interventions, blinding was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	The restorative procedures were standardized and the dentists were calibrated before starting the trial but there is no indication that assessors were blinded or different from the operators
Incomplete outcome data (attrition bias) All outcomes	Low risk	No children were missed and all of them were analyzed in the group that they were allocated by randomization
Selective reporting (reporting bias)	Low risk	Of the initial 507 children, 19 had no dental exam after baseline and 16 had no restoration to posterior teeth at baseline. 472 children (93%) were followed up for 1 years
Other bias	Low risk	No other bias apparent

Cunningham 1990

Methods	Study design: RCT of split-mouth design Conducted in: Liverpool, UK. Number of centers: 3 dentists, 1 based at Liverpool Dental Hospital, the others being general practitioners Recruitment period: not reported Funding source: unclear
Participants	Inclusion criteria: teeth requiring the treatment of Class I and Class II carious lesions Exclusion criteria: unclear Age: not reported Caries risk status: unclear

Cunningham 1990 (*Continued*)

	Location of teeth filled: not reported Type of cavity filled: O: 83 cavities, MO: 140 cavities, DO: 164 cavities, MOD: 122 cavities Number randomized: 605 cavities (Class I or Class II lesions) were randomly assigned to be restored with 2 different amalgams and 3 different composites Number evaluated: 509 restorations were reviewed
Interventions	Comparison: composite versus amalgam Group A: 309 composite restorations Group B: 200 amalgam restorations Type of moisture control: unclear Duration of follow-up: 3 years
Outcomes	1. Failures and fractures of the restorations, estimated at year 3 2. Contact points, estimated at 6, 12, 24, and 36 months 3. Gingival inflammation, estimated at 6, 12, 24, and 36 months 4. Marginal stain and caries, estimated at year 3 5. Color match, estimated at year 3
Notes	Sample size calculation: unclear

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Even though the teeth were randomly assigned to treatment groups; the authors did not explain which method of randomization was used to generate the allocation sequence
Allocation concealment (selection bias)	Low risk	There was no information about the method used to conceal the allocation sequence; however, due to the study design (split-mouth), a lack of allocation concealment was unlikely to introduce bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported. Due to the clinical characteristics of the interventions, blinding was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Due to the clinical characteristics of the interventions, blinding was not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Of the original 605 restorations, 509 could be examined at 3 years and the losses were said to have been evenly distributed across the trial arms but no data showing this. Fol-

Cunningham 1990 (*Continued*)

		low-up 84.1%
Selective reporting (reporting bias)	Low risk	All the data were well reported
Other bias	High risk	Unit of analysis error - the total number of participants was not indicated in the paper. There were 5 materials in consideration and each tooth was randomized to 1 of them but it is not really clear which is the real number of restoration per participants

Hendriks 1986

Methods	Study design: RCT of split-mouth design Conducted in: unclear Number of centers: 3 operators Recruitment period: unclear Funding source: unclear
Participants	Inclusion criteria: not reported Exclusion criteria: not reported Age: adults Caries risk status: unclear Location of teeth filled: 108 permanent molars and 124 premolars Type of cavity filled: not reported Number randomized: 242 cavities Number evaluated: 232 cavities
Interventions	Comparison: composite versus amalgam Group A: 174 composite restorations Group B: 58 amalgam restorations Type of moisture control: rubber dam Duration of follow-up: 3 years
Outcomes	Failures of restorations estimated at year 3
Notes	Sample size calculation: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The 4 materials within each series were distributed at random over the teeth selected for restoration and the participants were assigned at random to 1 of 3 operators. The authors did not explain which method of randomization was used

Hendriks 1986 (*Continued*)

Allocation concealment (selection bias)	Low risk	There was no clarification in the paper about allocation concealment; however, due to the design of the study (split-mouth) , a lack of allocation concealment was unlikely to introduce bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported. Due to the clinical characteristics of the interventions, blinding was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Due to the clinical characteristics of the interventions, blinding was not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The 3-year retrieval percentage of both the participants and restoration was 96%. However, the dropout rate was not reported by trial arm
Selective reporting (reporting bias)	Low risk	All the data were well reported
Other bias	Low risk	No other bias apparent

Letzel 1989

Methods	Study design: multicenter RCT, split-mouth design Conducted in: Liverpool (UK), London (UK), Manchester (UK), North Carolina (USA) , Indianapolis (USA), South Illinois (USA), Philadelphia (USA), Gotenburg (Sweden), Nijmegen (Netherlands), Leuven (Belgium), Louvain (Belgium), Bonn (Germany) Number of centers: 12 Recruitment period: not reported Funding source: ICI Dental Imperial Chemical Industries, Macclesfield, UK
Participants	Inclusion criteria: adults with teeth requiring posterior Class I or II restorations. Sound tooth or a sound restored tooth in proximal contact with each of the teeth were included Exclusion criteria: people who might have been unable to return for 5 years or who required special management, extensive restorative care, or cuspal replacement. Teeth requiring Class II restorations that had no proximal contact. Pairs of opposing teeth Age: adults, age not reported Caries risk status: unclear Location of teeth filled: posterior teeth Type of cavity filled: Class I and II restorations Number randomized: 447 adults, 1164 cavities Number evaluated: 338 adults, 693 cavities
Interventions	Comparison: composite versus amalgam Group A: 461 composite restorations Group B: 232 amalgam restorations

Letzel 1989 (*Continued*)

	Type of moisture control: unclear Duration of follow-up: 5 years
Outcomes	Primary outcome: failure In order to trace the causes of failure in each case, the reasons for failure were classified according to a system described by Letzel et al in 1988. This system was designed for an evaluation of the influence of experimental variables and operators on the survival rate of restorations included in controlled clinical trials of dental amalgams The system distinguishes 3 types of restoration failure: Type 1 - failures directly related to the restoration (i.e. the material and the way it is manipulated into a restoration) Type 2 - failures related to the restorative process (i.e. the result of the decision-making process of the operator) Type 3 - failures caused by external factors
Notes	Sample size calculation: not reported 12 centers were involved in the trial but the data of only 10 centers were used in this study because they complied with the condition of fully reviewing the restorations after at least 4 years

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The authors declared that randomization was done in 5 of the centers, but there is no explanation about if the sequence generation had been at random in the other centers
Allocation concealment (selection bias)	Low risk	There is no clarification in the paper about allocation concealment; however, due to the design of the study (split-mouth), a lack of allocation concealment was unlikely to introduce bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported. Due to the clinical characteristics of the interventions, blinding was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Due to the clinical characteristics of the interventions, blinding was not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The follow-up at 4 years was 76% for composite restorations. Dropout rate for amalgam was not clearly reported

Letzel 1989 (*Continued*)

Selective reporting (reporting bias)	High risk	All the data seemed to be well reported for composite but partially reported for amalgam, especially follow-up data
Other bias	High risk	There were variations in practice and dropout rate among the centers and the reason for these variations was not clearly explained. Unit of analysis error - number of restorations reported but not the number of participants per restoration

NECAT 2007

Methods	Study design: parallel group RCT Conducted in: USA Number of centers: 5 community centers from Boston and Maine, USA Recruitment period: 1997-2005 Funding source: unclear
Participants	Inclusion criteria: children fluent in English. Had 2 or more posterior teeth with dental caries. Primary and permanent teeth Exclusion criteria: had known prior or existing amalgam restorations. Had a physician diagnosed psychological behavioral, neurologic, immunosuppressive, or renal disorder Age: 6-10 years Caries risk status: not reported Location of teeth filled: posterior teeth Type of cavity filled: Class I and Class II restorations Number randomized: 534 children Number evaluated: 449 children
Interventions	Comparison: composite versus amalgam Group A: 753 composite restorations Group B: 509 amalgam restorations Type of moisture control/tooth isolation: rubber dam Duration of follow-up: 5 years. Evaluation every 6 months
Outcomes	Rate of replacement and repair of the restorations, psychosocial function (5-year follow-up), physical development (5-year follow-up)
Notes	Sample size calculation: not reported. We use only data from permanent teeth

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was stratified by geographic location (Boston/Cambridge ver-

NECAT 2007 (*Continued*)

		sus Farmington) and number of teeth with caries (2-4 versus 5 or more), using randomly permuted blocks within each of the 4 strata
Allocation concealment (selection bias)	High risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and dentists could not be blinded to treatment assignment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Due to the clinical characteristics of the interventions, blinding was not possible
Incomplete outcome data (attrition bias) All outcomes	Low risk	The follow-up at 3 years was 84% and the losses were similar in both groups
Selective reporting (reporting bias)	Low risk	All data were well reported
Other bias	Low risk	No other apparent biases

Norman 1990

Methods	Study design: RCT with split-mouth design Conducted in: unclear Number of centers: 1 Recruitment period: not reported Funding source: ICI, Imperial Chemical Industries, Macclesfield, UK
Participants	Inclusion criteria: participants in need of posterior Class I and II restorations. Maximum of 4 restorations were allowed. Selection of the teeth required that there be a sound tooth or a sound restored tooth in proximal contact to the restoration. At least a portion of the restoration was required to be in contact with an opposite tooth or restoration Exclusion criteria: not reported Age: 28-40 years Caries risk status: not reported Location of teeth filled: molars and premolars Type of cavity filled: Class I and II restorations Number randomized: 62 participants, 160 restorations Number evaluated: 123 restorations
Interventions	Comparison: composite versus amalgam Group A: 80 Occlusin composite. Light cured, highly filled hybrid posterior composite resin Group B: 43 Dispersaloy amalgam Type of moisture control: rubber dam was used to isolate the teeth Duration of follow-up: 5 years

Norman 1990 (*Continued*)

Outcomes	Primary outcomes were failure and recurrent caries Wear, marginal adaptation, anatomic form, interproximal contacts	
Notes	Sample size calculation: not reported	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	All restorations were placed by following a random selection chart for composite resins and amalgam
Allocation concealment (selection bias)	Low risk	There was no information about the method used to conceal the allocation sequence; however, due to the design of the study (split-mouth), a lack of allocation concealment was unlikely to introduce bias
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported. Due to the clinical characteristics of the interventions, blinding was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Due to the clinical characteristics of the interventions, blinding was not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The follow-up at 5 years was 80.6%. However, the dropout rate was not reported by trial arm
Selective reporting (reporting bias)	Low risk	All data were well reported
Other bias	High risk	Unit of analysis error - number of restorations reported but not the number of participants

Robinson 1988

Methods	Study design: RCT of Split-mouth design Conducted in: Guy's Hospital, London, UK Number of centers: 1 Recruitment period: not clear Funding source: ICI Dental, Macclesfield, UK

Robinson 1988 (*Continued*)

Participants	Inclusion criteria: adults who required occlusal and proximo-occlusal restorations in vital premolars and molars Exclusion criteria: mental and physical disabilities likely to prevent continued co-operation, people who would not be available for the long-term follow-up visits over the 5 years and restorations requiring cuspal replacement Age: 19-66 years Caries risk status: not reported Location of teeth filled: molars and premolars Type of cavity filled: Class I and II restorations Number randomized: 58 participants, 98 composites and 27 amalgams Number evaluated: 90 restorations
Interventions	Comparison: composite versus amalgam Group A: 70 Occlusin composite Group B: 20 Aristaloy amalgam Type of moisture control/tooth isolation used: rubber dam isolation in 82.4% of cases Duration of follow-up: 3 years
Outcomes	Failure rate in terms of the following criteria: gingival condition, interproximal contacts, color match, anatomic form, surface roughness
Notes	Sample size calculation: not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The participants were allocated to receive composite or amalgam restoration in the ratio 3:1 from a randomized table
Allocation concealment (selection bias)	Low risk	There was no information about the method used to conceal the allocation sequence; however, due to the design of the study (split-mouth), a lack of allocation concealment was unlikely to introduce bias
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported. Due to the clinical characteristics of the interventions, blinding was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Due to the clinical characteristics of the interventions, blinding was not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The follow-up at 36 month was 78.4% but it was not clear whether drop-out was balanced between the trial arms

Robinson 1988 (*Continued*)

Selective reporting (reporting bias)	Low risk	All data were well reported
Other bias	High risk	Unit of analysis error - number of restorations reported but not the number of participants

D: distal; IQ: intelligence quotient; M: mesial; MOD: mesial, occlusal, and distal; O: occlusal; RCT: randomized controlled trial; SD: standard deviation.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Allan 1977	Non-RCT. Retrospective analysis of dental records
Bellinger 2006	This study reports data of the New England Children's Amalgam Trial. As the data of permanent and temporary dentition were not informed separately, it was not possible to extract the data of permanent posterior teeth
Borgmeijer 1991	Insufficient follow-up and incomplete data
Bryant 1994	Not an RCT. No randomization
Busato 1996	Not an RCT. No randomization
Cloyd 1997	Not an RCT. No randomization
Collins 1998	Not an RCT. No randomization
Dilley 1990	It did not evaluate longevity correctly
Eames 1974	Not an RCT. No randomization
Fukushima 1988	Not an RCT. No randomization
Hendriks 1985	Not an RCT. No randomization
Johnson 1992	Not an RCT. No randomization
Knibbs 1992	Not an RCT. No randomization
Kopperud 2012	Not a randomized trial
Koray n.d.	Unpublished. The author did not respond to the request for data

(*Continued*)

Kreulen 1993a	No long-term follow-up. No caries and fracture reporting
Kreulen 1993b	The intervention did not correspond with aims of the review
Lambrechts 1984	Follow-up 18 months
Leinfelder 1975	Follow-up 24 months
Leinfelder 1980	As the study considered anterior and posterior restorations, it is difficult to be sure that the failures occurred in Class 1 and 2 restorations
Mair 1995	No data could be extracted
Mair 1998	No data could be extracted
Mannocci 2005	The intervention did not correspond with aims of the review
Mjör 1993a	Not an RCT. No randomization
Mjör 1993b	Not an RCT
Nell 1994	The intervention did not correspond with aims of the review
Pieper 1991	Not an RCT. Retrospective study
Powers 1974	Not an RCT. No randomization
Prati 1988	Not an RCT. No randomization
Roulet 1977	Follow-up 12 months
Roulet 1978	Same data as Roulet 1977
Rowe 1989	Not an RCT. No randomization
Rytömaa 1984	Not an RCT. No randomization
Samaha 1982	Not an RCT. No randomization
Shenker 2008	This study report data of the New England Children's Amalgam Trial. As the data of permanent and temporary dentition were not informed separately, it was not possible to extract the data of permanent posterior teeth
Smales 1991	Not an RCT. No randomization
Smales 1992	The intervention did not correspond with aims of the review
Solano 1984	These study data were unpublished (Master's dissertation) and could not be found for critical appraisal

(*Continued*)

Tobi 1999	Randomized at tooth level but only partially analyzed and reported
Van Nieuwenhuysen 2003	Not an RCT. No randomization
Walls 1988	Follow-up 24 month
Welbury 1990	Randomization was broken by ignoring it in 20/150 pairs of teeth
Wilson 1996	It did not compare amalgam versus composite

RCT: randomized controlled trial.

DATA AND ANALYSES

Comparison 1. Primary and secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure rate	7	5200	Risk Ratio (M-H, Fixed, 95% CI)	1.78 [1.47, 2.17]
1.1 Failure rate - parallel group studies	2	3010	Risk Ratio (M-H, Fixed, 95% CI)	1.89 [1.52, 2.35]
1.2 Failure rate - split-mouth studies	5	2190	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.90, 2.24]
2 Secondary caries	6	4036	Risk Ratio (M-H, Fixed, 95% CI)	2.11 [1.66, 2.69]
2.1 Secondary caries - parallel group studies	2	3010	Risk Ratio (M-H, Fixed, 95% CI)	2.14 [1.67, 2.74]
2.2 Secondary caries - split-mouth studies	4	1026	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.43, 5.21]
3 Fracture of restorations	2	3010	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.46, 1.64]

ADDITIONAL TABLES

Table 1. Neurobehavioral assessment

MEMORY						
Method of measurement - RAVLT memory test						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	8.1	3.7	254	8.36	2.91
At 7 years	176	9.73	2.79	172	9.65	2.86
Method of measurement - WRAML visual memory (1) WMS-III reproductions delayed (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	6.52	3.12	253	6.56	3.04
At 7 years (2)	176	32.98	6.24	172	33.02	6.24
Method of measurement - WRAMLS visual learning (1) WMS-III reproductions immediate (2)						

Table 1. Neurobehavioral assessment (*Continued*)

	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	8.14	2.75	253	7.83	2.64
At 7 years (2)	176	35.79	3.68	172	35.15	4.47
Method of measurement - RAVLT total learning test						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	37.95	9.61	253	39.09	9.98
At 7 years	176	47.36	9.48	172	46.06	9.09
ATTENTION/CONCENTRATION						
Method of measurement - Coding (1) WAIS-III digit symbol (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	8.64	3.14	253	9.04	3.14
At 7 years (2)	176	9.45	2.98	172	9.45	2.86
Method of measurement - Symbol search (1) WAIS-III symbol search (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	9.41	2.59	253	9.39	2.69
At 7 years (2)	176	9.40	2.85	172	9.77	3.08
Method of measurement - Digit span (1) WAIS-III digit span (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	7.37	2.53	253	7.4	2.73

Table 1. Neurobehavioral assessment (*Continued*)

At 7 years (2)	176	7.64	2.17	172	7.70	2.21
Method of measurement - Finger windows (1) WAIS-III spatial span (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	7.28	2.47	253	7.32	2.35
At 7 years (2)	176	9.03	2.96	172	9.34	2.99
Method of measurement - Trial A, seconds (1) Adult Trial A, seconds (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	27.69	13.05	253	27.95	12.74
At 7 years (2)	176	28.94	12.06	172	28.72	11.26
Method of measurement - Trial B, seconds (1) Adult Trial B, seconds (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	65.1	35.61	253	42.18	6.56
At 7 years (2)	176	63.84	25.5	172	65.34	25.07
Method of measurement - Stroop word						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	41.54	6.39	253	42.18	6.56
At 7 years	176	41.7	8.09	172	41.41	8.04
Method of measurement - Stroop color						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD

Table 1. Neurobehavioral assessment (*Continued*)

At treatment	254	43.03	5.62	253	44.15	6.01
At 7 years	176	41.59	8.16	172	42.67	8.14
Method of measurement - Stroop color-word						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	43.3	6.84	253	44.17	6.93
At 7 years	176	46.99	9.71	172	48.42	9.41
VISUOMOTOR						
Method of measurement - WRAVMA matching (1) WASI matrices (2)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment (1)	254	96.19	12.4	253	95.57	13.72
At 7 years (2)	176	24.44	5.33	172	24.83	5.02
Method of measurement - WRAVMA pegs (dominant)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	103.04	16.68	253	101.94	16.87
At 7 years	176	119.38	15.83	172	119.01	15.55
Method of measurement - WRAVMA pegs (non-dominant)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	106.81	15.03	253	106.18	14.64
At 7 years	176	119.38	15.83	172	119.01	15.55
Method of measurement - Standard reaction time						

Table 1. Neurobehavioral assessment (*Continued*)

	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	0.9	0.2	253	0.9	0.2
At 7 years	176	0.76	0.14	172	0.77	0.15
Method of measurement - Finger tapping (dominant)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	36.29	6.05	253	36.66	6.17
At 7 years	176	50.5	6.56	172	50.51	6.56
Method of measurement - Finger tapping (non-dominant)						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	31.33	5.37	253	32.02	5.34
At 7 years	176	44.49	6.33	172	44.48	6.34
NERVE CONDUCTION VELOCITY						
Method of measurement - Tibial, m/s						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	51.58	5.58	253	51.12	5.29
At 7 years	140	50.15	5.09	140	50.78	5.07
Method of measurement - Ulnar, m/s						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	58.75	6.51	253	59.57	6.39

Table 1. Neurobehavioral assessment (*Continued*)

At 7 years	140	57.58	6.52	140	59.26	6.41
INTELLIGENCE						
Method of measurement - CTONI						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	85	10	253	85	10
At 7 years	176	81	12	173	81	12
Method of measurement - WASI						
	Resin composite			Amalgam		
	n	Mean	SD	n	Mean	SD
At treatment	254	NA		253	NA	
At 7 years	176	92	13	173	94	14

CTONI: Comprehensive Test of Non-verbal Intelligence; RAVLT: Rey Auditory Verbal Learning Test; SD: standard deviation; WRAVMA: Wide Range Assessment of Visual Motor Abilities; WAIS-III: Wechsler Adult Intelligence Scale - Third Edition; WRAML: Wide Range Assessment of Memory and Learning; WASI: Wechsler Abbreviated Scale of Intelligence; WMS-III: Wechsler Memory Scale - Third Edition.

Table 2. Kidney function

Secondary outcome - kidney function				
Creatinine-adjusted urinary albumin levels				
	Composite		**Amalgam**	
	Mean	95% CI	Mean	95% CI
Year 1	7.4	4.2 to 12.5	7.7	3.1 to 11.5
Year 2	9.4	5.3 to 16.1	8.6	5.5 to 13.4
Year 3	9.9	6.8 to 16.7	9.0	5.5 to 17.9
Year 4	9.25	5.8 to 20.8	8.7	5.6 to 14.5

Table 2. Kidney function (*Continued*)

Year 5	8.2	5.1 to 14.3	8.0	5.4 to 12.5
Year 6	7.5	4.8 to 14.3	7.3	4.8 to 14.0
Year 7	6.8	4.4 to 13.7	6.5	4.3 to 12.3

CI: confidence interval.

Table 3. Psychosocial function

	Composite (permanent/posterior occlusal SY[a])		**Amalgam (permanent/posterior occlusal SY[a])**		**Composite versus amalgam**
	10-SY (SE[b])	**P value**	**10-SY (SE[b])**	**P value**	**P value**
BASC-SR [c] T-Score, adjusted mean					
Emotional symptoms index	1.7 (0.5)	0.002	-0.5 (0.7)	0.49	Not reported
Clinical maladjustment	1.4 (0.6)	0.02	-0.4 (0.8)	0.58	Not reported
School maladjustment	0.5 (0.7)	0.42	0.5 (0.8)	0.56	Not reported
Personal adjustment	-2.2 (0.5)	< 0.0001	0.7 (0.7)	0.35	Not reported
Anxiety	1.3 (0.6)	0.03	-1.2 (0.8)	0.13	Not reported
Depression	1.0 (0.5)	0.05	0.5 (0.7)	0.49	Not reported
Attitude to school	0.8 (0.7)	0.24	0.4 (0.9)	0.67	Not reported
Interpersonal relations	-1.5 (0.5)	0.001	0.7 (0.6)	0.25[e]	Not reported
CBCL[d] Change Score, adjusted mean					
Competence	-0.5 (0.7)	0.47	-0.3 (0.9)	0.74	Not reported
Total problem behaviors	0.1 (0.7)	0.93	-1.4 (1.0)	0.15	Not reported

Table 3. Psychosocial function (*Continued*)

Internalizing problems	0.7 (0.8)	0.37	-1.6 (1.0)	0.11	Not reported
Externalizing problems	-0.4 (0.7)	0.53	-0.9 (0.9)	0.34	Not reported
Attention problems	-0.1 (0.4)	0.75	-0.6 (0.5)	0.27	Not reported
Withdrawn	0.6 (0.4)	0.15	-0.5 (0.5)	0.33	Not reported
Anxious/depressed	0.8 (0.4)	0.07	-1.1 (0.5)	0.03	Not reported
Delinquent behaviors	0.7 (0.5)	0.16	-1.4 (0.6)	0.02	Not reported
Aggression	0.02 (0.4)	0.95	-0.05 (0.5)	0.3	Not reported

[a] SY: surface-years; [b] SE: standard error; [c] BASC-SR: Behavior Assessment for Children Self Report; [d] CBCL: Child Behavior Checklist parent report; [e] The BASC-SR scores reported in the table above reflect the scores of children aged 6-10 years. However, the BASC-SR was developed for children ≥ 8 years. Change in BASC-SR was, therefore, assessed among children aged ≥ 8 years as a subgroup. The results were similar to those for children aged 6-10 years except in the amalgam arm, where there was an association with interpersonal relations in children aged ≥ 8 years (P value = 0.03).

Table 4. Physical development

	Composite	**Amalgam**	**Composite versus amalgam**	
	5-year change (SE)	**5-year change (SE)**	**β (SE)**	**P value**
Growth outcome in girls				
Body fat percentage	8.8 (0.7)	7.7 (0.8)	0.05 (0.83)	0.95
BMI-for-age z-score	0.36 (0.06)	0.21 (0.07)	0.08 (0.12)	0.49
Height	30.7 (0.5)	31.2 (0.5)	0.77 (1.18)	0.51
Growth outcome in boys				
Body fat percentage	4.9 (0.9)	5.7 (0.9)	0.57 (0.82)	0.49
BMI-for-age z-score	0.13 (0.08)	0.25 (0.07)	-0.21 (0.23)	0.36
Height	34.4 (0.6)	33.5 (0.6)	0.48 (0.83)	0.56

BMI: body mass index; SE: standard error.

WHAT'S NEW

Last assessed as up-to-date: 22 October 2013.

Date	Event	Description
21 May 2014	Amended	Conclusions edited to reflect received feedback.

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DECLARATIONS OF INTEREST

M Graciela Rasines Alcaraz, Analia Veitz-Keenan, Philipp Sahrmann, Patrick Roger Schmidlin, Dell Davis, Zipporah Iheozor-Ejiofor: no interests to declare.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The participant inclusion criterion in the protocol was originally restricted to adults and adolescents. Tooth type (permanent posterior teeth) was considered more important as a criterion than age group, therefore, studies on children were included. Only data on permanent posterior teeth were reported in this review.

Participant satisfaction could not be analyzed as none of the randomized controlled trials had data about this variable.

Cost-effectiveness could not be calculated because of partial reporting.

In the protocol, survival rate was listed as the primary outcome but the review lists failure rate as primary outcome. Failure rate is reported in this review as a proxy for survival rate.

We aimed to minimize potential reporting biases including publication bias, time lag bias, multiple (duplicate) publication bias, and language bias by constructing a funnel plot. However, we were unable to achieve this since we had fewer than 10 studies.

Only dichotomous data were available.

The review used random-effects models unless there were fewer than four studies, when fixed-effect models were used, as this is general policy for the Cochrane Oral Health Group. The protocol stated random-effects models only.

INDEX TERMS

Medical Subject Headings (MeSH)

*Dentition, Permanent; Acrylic Resins [adverse effects; *therapeutic use]; Composite Resins [adverse effects; *therapeutic use]; Dental Amalgam [adverse effects; *therapeutic use]; Dental Caries [*therapy]; Dental Restoration Failure; Dental Restoration, Permanent [adverse effects; *methods]; Molar; Polyurethanes [adverse effects; *therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Child; Humans