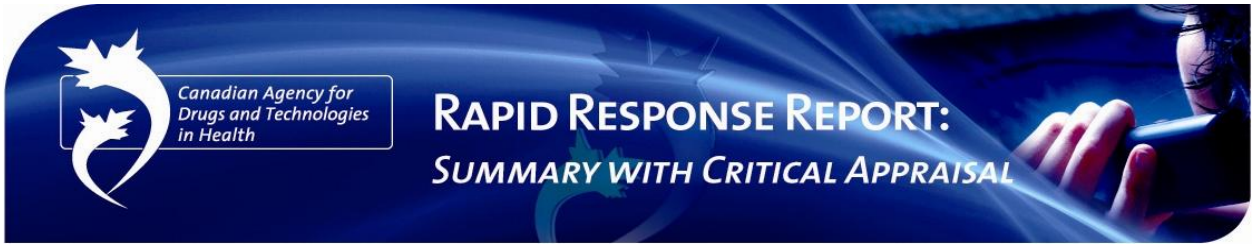


TITLE: Composite Resin and Amalgam Dental Filling Materials: A Review of Safety, Clinical Effectiveness and Cost-effectiveness

DATE: 22 June 2012

CONTEXT AND POLICY ISSUES

Dental caries is a major public health problem in most industrialized countries, affecting 60-90% of school children and the majority of adults.[1] It is a localized, progressive demineralization of the hard tissues of the crown and root surfaces of teeth.[2] Whereas very early dental caries lesions can be managed preventively to reverse the disease process, all more advanced and cavitated carious lesions must be restored by excavating the carious tissue and replacing it with an appropriate dental filling material.

For the last 150 years, the most widely used material for posterior load-bearing restorations has been silver amalgam.[3] Despite of its long history in dental practice,[4] the safety of dental amalgams has been questioned since their introduction to the dental practice. Most dental amalgams contain approximately 50% elemental mercury, a known toxic substance, which holds together the metallic constituents of the filling material. The initial safety concern was the risk of exposure to mercury vapor from the dental filling before its complete setting, and the filling was thought to be inert once it is hardened.[5] However, some reports have suggested that stress on the amalgam surface, such as the normal masticatory function, may free mercuric vapor which can then be continuously introduced into the body.[6]

Recent studies have attempted to relate the exposure to dental amalgam restorations with systemic diseases, such as multiple sclerosis and lichenoid lesions, but their results were not conclusive.[7,8]

More recent safety concerns are the risk of an environmental impact of mercury waste from dental offices.[4] Mercury from dental amalgam is commonly introduced into dental wastewater as a result of the placement of and removal of amalgam fillings.[9] The Environment Protection Agency (EPA) estimated that approximately 120,000 dental offices that use or remove amalgam in the United States discharge their wastewater exclusively to publicly owned wastewater treatment plants.[10] The use of amalgam separators in the dental clinics can potentially reduce 98.7% of the amount of amalgam expelled in the wastewater.[10] The Canadian Ministers for the Environment initiated a move to voluntary incorporation of separators according to the Canadian Environment Protection Act of 1999.[11] and published a Pollution Prevention Planning Notice in

May 2010.[12] The notice detailed the requirements to keep the mercury found in dental amalgam waste out of the environment.[13] In Ontario for example, these have been mandatory in dental offices since 2003.[13]

Tooth-colored resin composite materials are being increasingly used instead of silver amalgam, most probably due to their higher esthetic value and the increasing concerns about amalgam safety.[4] However, some factors prevent the full adoption of composite materials as an alternative for amalgams. First, the clinical longevity of amalgam fillings is thought to be superior to that of composites;[5] although a recent evidence-based review failed to draw any conclusions about filling longevity due to various limitations in the included studies.[14] A probable cause of these limitations in the review might be the inclusion of low quality trials and pooling the results from trials of heterogeneous designs, both interventional randomized controlled trials (RCTs) and observational studies, without reporting stratified results by trial design or quality. Second, the use and handling proprieties of composite are operator sensitive, and in the absence of ideal conditions and equipment, may result in more secondary caries around restored teeth and the need for more frequent replacement and repair of restorations.[5] The increased cariogenicity of composite materials, in contrast to amalgam, can also be explained by the lack of antibacterial properties and their association with a favorable environment for cariogenic and pathogenic bacterial growth.[15,16]

The higher price of composite filling is another factor that may potentially limit its use instead of amalgam. Finally, recent safety concerns have been reported relative to the exposure to bisphenol A (BPA) from dental composite.[17] BPA is a component of many plastic products; it is a potent endocrine disruptor that can mimic the effect of the female hormone estrogen.[18] Two recent studies attempted to evaluate the exposure to BPA from different dental materials that contain resin composite;[18,19] both trials reported trace amounts of BPA in the saliva and urine samples from the participants, but the exposure was considered negligible. However, the sample size and duration of the two trials limited the ability to make conclusive findings. A review of the literature about the harms from BPA products suggested that BPA might be implicated in some allergic reactions.[20] Furthermore, the environmental impact of greater use of composite (plastic) materials (office effluent, drilling pieces, particles and dust, excess or past-expiry discarded composite and resin bonding agents) is largely unknown.

In order to support the choice between dental amalgam or composite fillings, a comprehensive evaluation of the advantages and limits of each material is essential. This report will examine the evidence regarding the comparative safety, efficacy, and cost-effectiveness between amalgam fillings and resin-composite fillings when used in load-bearing areas of permanent teeth.

This report was reviewed by an expert in restorative dentistry.

RESEARCH QUESTIONS

1. What is the evidence for the safety of dental amalgams compared to resin composites when used as filling material on permanent teeth?
2. What is the evidence regarding the clinical effectiveness of dental amalgams compared to resin composites when used as filling material on permanent teeth?
3. What is the cost-effectiveness of dental amalgams compared to resin composites when used as filling materials on permanent teeth?

KEY MESSAGE

Six randomized controlled trials were identified in the reviewed literature; each research question was evaluated in two trials. There was a strong evidence of amalgam safety when used in children 6 to 10 years old. However, there was limited information to evaluate the evidence of potential harms caused by composite. There was a suggestive evidence of longer longevity of dental amalgams than composites. Although the costs reported in the review may not reflect the Canadian prices, the long-term costs of both fillings suggest a relative cheaper price of amalgam material.

METHODS

The review was based on a predefined protocol (**Appendix 1**)

Literature Search Strategy

A limited literature search was conducted on key resources including Medline, PubMed, The Cochrane Library (2012, Issue 4), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and abbreviated lists of major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and economic studies. Where possible, retrieval was limited to the human population. The electronic search was also limited to English language documents published between January 1, 2002 and April 30, 2012. The bibliographies of the retrieved health technology assessments, systematic reviews, and meta-analyses were searched manually for relevant clinical trials.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed for relevance using a predefined checklist (**Appendix 2**). Full texts of any relevant titles/abstracts were retrieved, and assessed using a screening checklist (**Appendix 3**). The final article selection was based on the inclusion criteria presented in **Table 1**.

Table 1: Selection Criteria

Population	Patients with at least one permanent tooth requiring restoration with direct filling material
Intervention	Amalgam-based filling material
Comparator	Resin composite filling material
Outcomes	**Efficacy:** restoration longevity, patient' satisfaction, prevention of recurrence of dental caries at the margin of the restoration. **Safety:** post-operative pulpal irritation and/or hypersensitivity, gingival and periodontal irritation and/or injury, effect of long-term exposure on the general health of patients, detection of the restorative material, or one of its components in other body organs or fluids, development of neuropathies, renal pathologies or immunoreactions. **Cost-effectiveness**

Study Designs	Randomized controlled trials, economic evaluation design comparing both interventions

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria. Duplicate reports of the same outcomes from the same trials were also excluded. Additionally, randomized controlled trials were excluded if they did not directly compare amalgam-based dental fillings with resin-composite filling materials. Studies evaluating filling materials on patients with mixed dentition were excluded if they did not report the results for the permanent dentition separately (or as subgroup analysis).

Critical Appraisal of Individual Studies

The methodological quality of the included studies was evaluated using the SIGN50 quality assessment tool for randomized controlled trials.[21] The internal validity was assessed with the following components: the adequacy of randomization, allocation concealment, degree of blinding, and use of intention to treat approach for analysis. For the critical appraisal of studies, a numeric score was not calculated. Instead, the strength and limitations of the study were described.

There were no cost-effectiveness studies identified for critical appraisal. With regards to the included cost studies, the reviewer evaluated the included cost studies in consultation with a health economist.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 386 potential citations were identified by the search in bibliographic database, with 354 citations being excluded during the title and abstract screening based on irrelevance to the questions of interest. The full text documents of the remaining 32 articles were retrieved. Eight additional articles were identified by the grey literature search. Of the 40 articles, 20 did not meet the inclusion criteria and were excluded, leaving 20 articles[5,22-40] that reported from six unique trials to be included in this review.[22,31,37-40] A PRISMA diagram demonstrating the study selection process is presented in **Appendix 4**.

Summary of Study Characteristics

Six trials that addressed at least one of the review questions were included in this review, included two RCTs evaluating safety of amalgam,[22,31] two RCTs comparing the efficacy of amalgam and composite,[39,40] and two economic studies evaluating and comparing the costs associated with the use of both filling materials.[37,38] Details regarding primary studies characteristics are tabulated in **Appendix 5**.

The New England Children's Amalgam trial (NECAT)[31] and the Casa Pia Children's Amalgam trial (CPCAT)[22] are two RCTs that evaluated the safety of dental amalgam fillings as compared to composite fillings. Both trials had been proposed and funded by the National Institute of Dental and Craniofacial Research (NIDCR) in the United States. The NECAT was conducted in the USA and enrolled 534 children (mean age 7.9 years) from Boston, Massachusetts and Farmington, Maine. Participants were randomized to receive either amalgam or composite for

all posterior dental fillings at baseline and at the subsequent trial visits. On the other hand, the CPCAT was conducted in Portugal and recruited 507 children (mean age 10.2 years). Both trials were planned to follow-up with the participants for five years; however, the CPCAT had an additional two-year follow-up period for 474 participants. The primary objective of both trials was to evaluate the long-term harms of amalgam; the primary outcome in the NECAT was the difference in change of the intelligence quotient (IQ) index between children in the amalgam and composite groups. The primary outcome in the CPCAT was the difference between groups in the change of neurological responses as measured by a composite of memory, attention/concentration, motor/visuo-motor, and nerve conduction velocity tests. Secondary safety outcomes in both trials included renal responses, immunological responses, and adverse health events. Efficacy comparison between the two materials was also estimated in the NECAT and CPCAT in terms of filling survival.

Efficacy of amalgam and composite dental fillings were compared in two RCTs.[39,40] Sachdeo et al.[39] (2004) published the results of a clinical trial with a two-year follow-up period. The trial randomized 133 adult patients to receive a conventional composite restoration (Tetric Ceram and Syntac II dental adhesive), an open sandwich composite technique (Prime and Bond 2.1 dental adhesive, Dyract AP compomer and Spectrum TPH composite), or Dispersalloy amalgam filling for the repair of premolars and molars. The other trial was published by Wilson et al. in 2002, and included the results of one year of patients follow-up.[40] The trial enrolled 50 adult patients who had at least one pair of similar lesions or failed restorations. Randomization was done at the tooth level, and each patient had one amalgam for each composite restoration (Z250 low-shrinkage composite). Patients were followed-up for one year for the efficacy assessment. Both trials' publications failed to specify the primary outcome or outcome measure used to evaluate efficacy of the dental filling materials. Nevertheless, there were several outcome measures defined in both trials including surface wear, marginal adaptation, anatomical form, and secondary caries.

Khairiyah et al.[37] evaluated and compared the cost of posterior dental restorations in Malaysian public dental clinics. Three materials were compared including a capsulated amalgam material, a capsulated compomer material, and a non-capsulated nano-composite resin material. The analysis was based on data collected in 2005 on 196 restorations; the total cost calculation of these restorations included the human resources, the dental material and the macro-cost (e.g., clinical attendance, facility infrastructure costs, operating and maintenance costs). Sjögren et al.[37] published the results of another cost analysis study in which they compared the long-term (10 years) cost of amalgam, composite, and glass-ionomer filling materials when used in Class II (involving the proximal surfaces) molar cavities. The estimation was based on published data about the initial costs and the median survival times for each material.

Summary of Critical Appraisal

The strength and limitations of included studies are summarized in **Appendix 6**.

Both the NECAT[30] and CPCAT[5] followed well established protocols for clinical trials. The trials estimated a priori the number of participants to be enrolled in order to achieve the desired power to support the primary outcome measure in each trial. In both trials, intention to treat analysis was used for the primary outcomes. For children who did not complete the follow-up period, the last-observation-carried-forward method was used and the effect of missing data was evaluated through a multiple imputation algorithm. Mercury exposure from other sources than dental amalgam was estimated in both trials and was adjusted for in the analysis. Due to

the nature of interventions, blinding of patients and dentists was not feasible; this might have been a source of bias because participants could have been affected by their families in a way that could impact the neurobehavioral tests. However, the NECAT attempted to reduce this source of bias by blinding the collection and analysis of data, but nothing was reported about this regard in the CPCAT publications. Another limitation for these two trials was their outcome measures; effects of mercury on the neuropsychological and renal outcomes were measured by surrogate measures, and the association between these measures and the outcomes may not reflect a real effect of amalgam mercury on the clinical patients' outcomes.

In contrast, the two efficacy trials included in this review did not have a clearly defined trial protocols.[39,40] In both trial the primary outcome or outcome measure was not designated, and the sample size was patient-inclusion driven rather than being based on a power calculation for a desired effect size. Furthermore, neither trial reported the statistical analysis type (intention to treat or others) or the method of handling missing data. Additionally, the duration of both trials was relatively short and may not have been sufficient to determine the clinical performance of filling materials which are known to survive longer than the trial duration. Another limitation for both trials might be the generalizability of the trials findings. Each trial was conducted in a single private clinic by one dental practitioner; the type of clients seen in these two clinics as well as the skills of the two dentists might not reflect what is seen in other dental care facilities.

In their cost comparison, Khairiyah et al.[38] included a comprehensive list of macro and micro costs associated with each of the three dental fillings materials. However, the analysis estimated the initial cost of new restorations per visit but did not account for differences in the survival and the need for repair of each material. The generalizability of this analysis might be questionable because the study was conducted in publicly funded healthcare facilities in Malaysia; the prices used could be negotiated and discounted prices that might not be reflective to prices in other healthcare facilities, and prices in Malaysia might not reflect what is paid for the same materials and services in western countries. Sjögren et al.[37] reported the cost paid by the patient and the social insurance of each dental filling material. Long-term cost estimation in this analysis was limited by the definition of survival time of the filling materials; the analysis defined survival as the time from restoration placement until time for its replacement but did not consider the cost associated with the restoration repair.

Summary of Findings

A summary of study findings and authors' conclusions are provided in **Appendix 7**.

<u>What is the evidence for the safety of dental amalgams compared to resin composites when used as filling material on permanent teeth?</u>

Two RCTs the NECAT[31] and CPCAT,[22] addressed the safety question of dental amalgams compared to composite filling materials. Safety outcomes are summarised under the following main themes: neurobehavioral effects, renal effects, immunological reactions, and adverse health effects.

Neurobehavioral Effects

The change (from baseline) in IQ score was the primary outcome measure in the NECAT.[31] The difference between scores of children randomized to amalgam compared to those randomized

to composite did not reach a statistically significant threshold. Furthermore, the analysis failed to demonstrate a statistically significant association between IQ scores and the degree of amalgam mercury exposure as measured by surface-year of amalgam and urinary mercury excretion.

The primary outcome in the CPCAT was a composite of memory, visuo/motor, attention/concentration and nerve conduction velocity measures. The NECAT also captured memory and visual motor tests as secondary outcome measures.[31] Both studies showed that the results of these measures did not differ, with statistical significance, between children who received amalgam and those who received composite fillings except for the nerve conduction velocity test in the CPCAT. The difference between treatments was statistically significant at year 7 only, and showed more favorable results for the amalgam group. However, these findings could not be interpreted as conclusive evidence because of the high variability over time.

Renal Effects

Urinary mercury concentration was evaluated in both trials as a measure of mercury exposure.[28,31] The results showed that children randomized to amalgam groups had statistically higher creatinine-adjusted urinary mercury concentrations than children in the composite groups. The difference between groups reached the peak at the second year at the CPCAT and continued to decline to near baseline levels by the seventh year of follow-up.[28] The difference between groups remained statistically significant at all follow-up years except for the final year.[28]

Microalbuminuria was evaluated in the NECAT and CPCAT as a measure of the renal glomerular function. Both trials reported that the difference in microalbuminuria between the treatment groups was not statistically different. Furthermore, renal tubular function was evaluated in the CPCAT using the glutathione S-transferases (α and π) concentrations in urine; results demonstrated that there were no statistically significant differences between the amalgam and composite groups.

Immunologic Reactions

The NECAT compared the distribution of lymphocytes, monocytes and neutrophils overtime between children in the amalgam and composite groups.[34] The analysis included 66 participants and was considered as an exploratory analysis rather than conclusive. Results showed that there were no statistically significant differences in the distribution of the measured white blood cells.

Adverse Health Effects

Adverse health events were defined in the CPCAT as major disease diagnosis, hospitalization, or death; however, a clear definition of adverse health events was not reported in the NECAT. The incidence of reported adverse events was similar for the amalgam and composite groups in both trials. The most common adverse events reported in the NECAT were allergy (16.9% in the amalgam group versus 17.6% in the composite group), sensory disorders (13.5% versus 10.5%), skin disorders (8.6% in both groups), psychological disorders (9.0% versus 6.7%), asthma (7.1% versus 6.4%), and migraine (6.0% versus 5.2%). There were nine adverse health events reported in the CPCAT; four events in the amalgam group and five in the composite group.

What is the evidence regarding the clinical effectiveness of dental amalgams compared to resin composites when used as filling material on permanent teeth?

Two RCTs were conducted to compare the efficacy of dental amalgam and composite dental filling materials.[39,40] The NECAT and CPCAT also reported the filling survival data for the treatment groups.[29,36]

The NECAT reported a higher rate of filling replacement for the composite fillings than for the amalgam; 14.9% versus 10.8% respectively, but the difference between groups was not statistically significant. However, the rate composite fillings that needed repair was statistically significantly higher than that for the amalgam fillings; 2.8% versus 0.4% respectively (P = 0.02).[36] The CPCAT reported a failure rate of 14.4% for the composite fillings compared to 5.6% for the amalgam.[29] The statistical significance of this finding was not reported. The risk for restoration failure due to secondary caries was statistically significantly higher in the composite group as compared to the amalgam group; the relative risk was 3.5 (95% CI 2.3 to 5.1).

Sachdeo et al.[39] reported that after two years of follow-up, the dental amalgam fillings demonstrated a statistically significant lower rate of surface wear than the two composite fillings (the conventional and the open sandwich techniques). However, the wear of two composite techniques did not differ significantly. Wilson et al.[40] demonstrated that the Z250 low shrinkage composite material did not differ significantly in its clinical performance at one year from the amalgam fillings except in the appearance measure.

What is the cost-effectiveness of dental amalgams compared to resin composites when used as filling materials on permanent teeth?

Khairiyah et al.[38] reported that the total initial cost of for a single restoration provided in one dental session was $12.40 for amalgam, $15.90 for a capsulated compomer and $13.00 for a non-capsulated composite (all prices were converted to 2012 Canadian dollars). The cost was similar for the three materials in their human resources and macro-cost components; however, the price of the filling material itself varied from $1.2 for amalgam to $4.70 for the capsulated compomer.

Sjögren et al.[37] reported that the estimated cost over ten years for a Class II amalgam filling to be $189.80, $363.70 for a composite filling, and $224.90 for a glass-ionomer filling.

Limitations

Although two included trials compared the safety of amalgam with composite dental fillings, both trials were designed to detect and evaluate harms associated with the exposure to mercury from dental amalgam. Harms related to the exposure to BPA from dental composites were not evaluated in any of the screened studies. Furthermore, safety evaluation in both trials was based mainly on surrogate outcome measures; variations in these measures might not reflect real clinical changes. Finally, results from these trials might not generalizable to adult patients because the included participants were six to ten years old at randomization. However, the choice of this particular age group was justified because children are the group receiving most restorations and are thought to be most vulnerable to the effects of mercury during their growth and development.[5]

Efficacy of amalgam and composite was compared in four trials.[5,30,39,40] Although the longevity of both materials was a secondary outcome in the NECAT and CPCAT,[5,30] filling survival results were more reliable than the results provided by Sachdeo and Wilson.[39,40] The latter two trials had methodological flaws including the absence of a clear definition of the primary outcome and the absence of power estimation. As well, these trials were limited by their follow-up periods (one and two years); this time does not allow a thorough comparison of the longevity and the need for repair between the two materials.[39,40]

The two economic evaluations were limited to cost estimation and comparison of both filling materials.[37,38] The main limitation of both studies was in the estimation of long-term cost of the dental filling; in one study the long-term cost was not estimated at all,[38] and in the other the estimation was based on the time from restoration placement until its replacement but did not include the cost of restoration repair.[37] Another potential limitation is the generalizability of the estimated costs to a Canadian context; however, while the costs reported in the review may not reflect the Canadian prices, the long-term costs of both fillings suggest a relative cheaper price of amalgam material..

Another limitation of this review was that none of the included studies evaluated the potential environmental hazard of the filling materials, particularly amalgam, nor the cost this potential hazard might engender. Dental offices may discharge amalgam mercury through the wastewater in various forms including solid and dissolved forms.[10] Dissolved mercury can be converted organic mercury (MeHg) that can reach levels toxic to humans because of its ability to bio-accumulate in fish. On the other hand, the solid mercury can be partially removed (90% to 99%) from the water treatment plans; however, the captured wastes, including solid mercury, may be incinerated or disposed of in a landfill.[10] The unbound mercury is highly volatile and can easily evaporate into the atmosphere.

In order to limit the impact of dental mercury on the environment, amalgam separators can be installed to remove amalgam waste particles in dental office discharge.[41] The use of these separators may reduce the mercury load in the wastewater up to 96%.[10] However, this may also increase the cost of using dental amalgam fillings. In 2008, the cost of purchasing and installing amalgam separators was estimated from US$ 3,078 to US$ 11,140 and the estimated annual cost ranged from US$ 1,990 to US$ 4,630.[10] Nevertheless, none of the included economic evaluations specified these costs in the analysis.[37,38]

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Within the limits of this review, the included studies provided evidence that the use of amalgam dental fillings in children did not result in different neurobehavioral, renal, or immunological outcomes compared to the use of composite. This conclusion echoes the FDA's white paper on dental amalgam.[42,43] The FDA paper provided a review of over 200 scientific articles and utilized health-based reference values for mercury exposure derived by ATSDR[44] and EPA[10] and which took into consideration even the potential for health effects in especially sensitive populations (i.e., children). The FDA Final Rule on Dental Amalgam[45] states, "*These reference values were derived using a standard risk assessment approach employing uncertainty factors, including an uncertainty factor to account for variability in sensitivity of the human population. They are considered to represent chronic or lifetime inhalation exposures that are free from adverse health outcomes and protective of human health for all individuals, including potentially sensitive populations such as children prenatally or postnatally exposed to mercury vapor." (p. 12)* The FDA's white paper reported that exposure to mercury (primarily mercury vapor) in persons with dental amalgam restorations are

not expected to exceed, except in rare cases with a very high number of amalgam surfaces, the mercury exposures observed to have adverse human health effects.[42,43]
The FDA paper concluded that the benefits of dental amalgams as a dental restorative material generally outweigh the risk of adverse health effects in the population age six and older.[43]

On the other hand, the current review revealed that further clinical research is needed to answer questions about the potential harms caused by the exposure to bisphenol A from composite materials. This is in contrast to the report of the Scientific Committee on Emerging and Newly Identified Health Risk (SCENIHR);[46] it was concluded that all dental filling materials, including amalgam and composite, are considered safe to use and they are all associated with very low rates of local adverse effects with no evidence of systemic disease. However, in its report the SCENIHR emphasized that information about the exposure, toxicity and clinical outcome for alternative materials, including composite, was less abundant than for amalgam, and the provided evidence was limited to local allergic reactions, but there were no evidence specific for harms caused by bisphenol A.[46]

The comparative efficacy evaluation suggested that amalgam fillings have a longer longevity than composite materials and less demand for repair. These results confirm the findings of a previous study by Bogacki et al.[47] who examined insurance claim data and reported that amalgam fillings require root canal treatment much less frequently than when restored with composite materials. The initial cost for placing dental amalgam is slightly cheaper than the cost for composite fillings; however, the cost difference tends to increase when taking into considerations the longevity differences of the two materials.

ACKNOWLEDGEMENTS

This report was reviewed by Dorothy McComb, B.D.S, Ms.D, FRCD(C), professor at the University of Toronto. All comments were considered when preparing the final report. The statements and conclusions in this report are those of CADTH and not of reviewers.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

REFERENCES:

1. Petersen PE, Lennon MA. Effective use of fluorides for the prevention of dental caries in the 21st century: the WHO approach. Community Dent Oral Epidemiol. 2004 Oct;32(5):319-21.

2. Lewis DW, Ismail AI. Prevention of dental caries [Internet]. In: The Canadian guide to clinical preventive health care. Ottawa: Public Health Agency of Canada. Chapter 36 [cited 2012 May 15]. Available from: http://www.phac-aspc.gc.ca/publicat/clinic-clinique/pdf/s4c36e.pdf.

3. Corbo M, Fahed E, Hershenfield S, Paige L, Panic O. Longevity of composite resin and amalgam restorations in posterior teeth: an evidence-based review of the literature [Internet]. Toronto: Faculty of Dentistry, University of Toronto; 2009. [cited 2012 May 9]. Available from: http://www.utoronto.ca/dentistry/newsresources/evidence_based/EBR09/W2EBLREPORT-2009.pdf

4. Kovarik RE. Restoration of posterior teeth in clinical practice: evidence base for choosing amalgam versus composite. Dent Clin North Am. 2009 Jan;53(1):71-6.

5. DeRouen TA, Leroux BG, Martin MD, Townes BD, Woods JS, Leitao J, et al. Issues in design and analysis of a randomized clinical trial to assess the safety of dental amalgam restorations in children. Control Clin Trials. 2002 Jun;23(3):301-20.

6. Edlich RF, Rhoads SK, Cantrell HS, Azavedo SM, Newkirk AT. Banning mercury amalgam [Internet]. Bethesda (MD): Food and Drug Administration; [cited 2012 May 8]. Available from: http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/medicaldevices/medicaldevicesadvisorycommittee/dentalproductspanel/ucm236379.pdf

7. Aminzadeh KK, Etminan M. Dental amalgam and multiple sclerosis: a systematic review and meta-analysis. J Public Health Dent. 2007;67(1):64-6.

8. Lartitegui-Sebastián MJ, Martinez-Revilla B, Saiz-Garcia C, Eguizabal-Saracho S, Aguirre-Urizar JM. Oral lichenoid lesions associated with amalgam restorations: a prospective pilot study addressing the adult population of the Basque Country [E pub ahead of print]. Med Oral Patol Oral Cir Bucal [Internet]. 2012 Feb 9 [cited 2012 May 2]. Available from: http://www.medicinaoral.com/medoralfree01/aop/17733.pdf

9. Vandeven JA, McGinnis SL. Cost-effectiveness of removing amalgam from dental wastewater. J Calif Dent Assoc. 2004 Jul;32(7):564-73.

10. United States Environmental Protection Agency. Health services industry detailed study: dental amalgam [Internet]. Washington (DC): The Agency; 2008. [cited 2012 May 9]. (EPA-821-R-08-014). Available from: http://water.epa.gov/lawsregs/lawsguidance/cwa/304m/upload/2008_09_08_guide_304m_2008_hsi-dental-200809.pdf

11. Canadian environmental protection act, 1999 [Internet]. Ottawa: Department of Justice Canada; 2012 May 31. [cited 2012 Jun 19]. Available from: http://laws-lois.justice.gc.ca/eng/acts/C-15.31/

12. Waste Reduction and Management Division, Environment Canada. Will you be affected by the new federal requirements for dental amalgam waste? Pollution prevention planning notice for dental clinics [Internet]. Ottawa: Environment Canada; 2010 May 8. [cited 2012 Jun 19]. Available from: http://www.ec.gc.ca/Publications/8A644665-940C-4527-AE7B-CC4FE2A251B6/Requirements_dental_amalgam_waste.pdf

13. Ontario regulation 196/3 made under the Dentistry Act, 1991. Amending O. reg. 205/94. Part III: amalgam waste disposal [Internet]. Toronto: Service Ontario; 2003 May 31. [cited 2012 Jun 19]. Available from: http://www.e-laws.gov.on.ca/html/source/regs/english/2003/elaws_src_regs_r03196_e.htm

14. Chadwick B, Dummer P, Dunstan F. How long do fillings last? Evidenced-Based Dentistry. 2002;3:96-9.

15. Imazato S. Antibacterial properties of resin composites and dentin bonding systems. Dent Mater. 2003 Sep;19(6):449-57.

16. Paolantonio M, D'ercole S, Perinetti G, Tripodi D, Catamo G, Serra E, et al. Clinical and microbiological effects of different restorative materials on the periodontal tissues adjacent to subgingival class V restorations. J Clin Periodontol. 2004 Mar;31(3):200-7.

17. American Dental Association. Bisphenol A and dental materials. Council on Scientific Affairs Statement [Internet]. Chicago: The Association; 2010. [cited 2012 May 7]. Available from: http://www.ada.org/1766.aspx

18. Kang YG, Kim JY, Kim J, Won PJ, Nam JH. Release of bisphenol A from resin composite used to bond orthodontic lingual retainers. Am J Orthod Dentofacial Orthop. 2011 Dec;140(6):779-89.

19. Joskow R, Barr DB, Barr JR, Calafat AM, Needham LL, Rubin C. Exposure to bisphenol A from bis-glycidyl dimethacrylate-based dental sealants. J Am Dent Assoc. 2006 Mar;137(3):353-62.

20. Ali N, Falcomer S, Li Y, Rossi P, Shainhouse T. Are there harms from Bisphenol A products? An evidence-based investigation [Internet]. Toronto: Faculty of Dentistry, University of Toronto; 2007. [cited 2012 May 9]. Available from: http://www.utoronto.ca/dentistry/newsresources/evidence_based/AreThereHarmsFromBisphenolAProducts.pdf

21. Methodology checklist 2: randomized controlled trials. In: SIGN 50: a guideline developer's handbook. Edinburgh: Scottish Intercollegiate Guidelines Network; 2008.

22. DeRouen TA, Martin MD, Leroux BG, Townes BD, Woods JS, Leitao J, et al. Neurobehavioral effects of dental amalgam in children: a randomized clinical trial. JAMA. 2006 Apr 19;295(15):1784-92.

23. Lauterbach M, Martins IP, Castro-Caldas A, Bernardo M, Luis H, Amaral H, et al. Neurological outcomes in children with and without amalgam-related mercury exposure: seven years of longitudinal observations in a randomized trial. J Am Dent Assoc. 2008 Feb;139(2):138-45.

24. Mackert JR, Jr. Randomized controlled trial demonstrates that exposure to mercury from dental amalgam does not adversely affect neurological development in children. J Evid Based Dent Pract. 2010 Mar;10(1):25-9.

25. Woods JS, Martin MD, Leroux BG, DeRouen TA, Bernardo MF, Luis HS, et al. Biomarkers of kidney integrity in children and adolescents with dental amalgam mercury exposure: findings from the Casa Pia children's amalgam trial. Environ Res. 2008 Nov;108(3):393-9.

26. Woods JS, Martin MD, Leroux BG, DeRouen TA, Bernardo MF, Luis HS, et al. Urinary porphyrin excretion in children with mercury amalgam treatment: findings from the Casa Pia Children's Dental Amalgam Trial. J Toxicol Environ Health A. 2009;72(14):891-6.

27. Geier DA, Carmody T, Kern JK, King PG, Geier MR. A significant relationship between mercury exposure from dental amalgams and urinary porphyrins: a further assessment of the Casa Pia children's dental amalgam trial. Biometals. 2011 Apr;24(2):215-24.

28. Woods JS, Martin MD, Leroux BG, DeRouen TA, Leitao JG, Bernardo MF, et al. The contribution of dental amalgam to urinary mercury excretion in children. Environ Health Perspect [Internet]. 2007 Oct [cited 2012 May 2];115(10):1527-31. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2022658/pdf/ehp0115-001527.pdf

29. Bernardo M, Luis H, Martin MD, Leroux BG, Rue T, Leitao J, et al. Survival and reasons for failure of amalgam versus composite posterior restorations placed in a randomized clinical trial. J Am Dent Assoc. 2007 Jun;138(6):775-83.

30. Children's Amalgam Trial Study Group. The Children's Amalgam Trial: design and methods. Control Clin Trials. 2003 Dec;24(6):795-814.

31. Bellinger DC, Trachtenberg F, Barregard L, Tavares M, Cernichiari E, Daniel D, et al. Neuropsychological and renal effects of dental amalgam in children: a randomized clinical trial. JAMA [Internet]. 2006 Apr 19 [cited 2012 May 2];295(15):1775-83. Available from: http://jama.ama-assn.org/content/295/15/1775.full.pdf+html

32. Barregard L, Trachtenberg F, McKinlay S. Renal effects of dental amalgam in children: the New England children's amalgam trial. Environ Health Perspect [Internet]. 2008 Mar [cited 2012 May 2];116(3):394-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2265055/pdf/ehp0116-000394.pdf

33. Bellinger DC, Trachtenberg F, Daniel D, Zhang A, Tavares MA, McKinlay S. A dose-effect analysis of children's exposure to dental amalgam and neuropsychological function: the New England Children's Amalgam Trial. J Am Dent Assoc. 2007 Sep;138(9):1210-6.

34. Shenker BJ, Maserejian NN, Zhang A, McKinlay S. Immune function effects of dental amalgam in children: a randomized clinical trial. J Am Dent Assoc [Internet]. 2008 Nov

[cited 2012 May 2];139(11):1496-505. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2908994/pdf/nihms213262.pdf

35. Bellinger DC, Trachtenberg F, Zhang A, Tavares M, Daniel D, McKinlay S. Dental amalgam and psychosocial status: the New England Children's Amalgam Trial. J Dent Res [Internet]. 2008 May [cited 2012 May 2];87(5):470-4. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2741096/pdf/nihms-65910.pdf

36. Soncini JA, Maserejian NN, Trachtenberg F, Tavares M, Hayes C. The longevity of amalgam versus compomer/composite restorations in posterior primary and permanent teeth: findings From the New England Children's Amalgam Trial. J Am Dent Assoc. 2007 Jun;138(6):763-72.

37. Sjögren P, Halling A. Long-term cost of direct class II molar restorations. Swed Dent J. 2002;26(3):107-14.

38. Khairiyah AM, Razak IA, Raja-Latifah RJ, Tan BS, Norain AT, Noor-Aliyah I, et al. Costing dental restorations in public sector dental clinics. Asia Pac J Public Health. 2009 Apr;21(2):184-95.

39. Sachdeo A, Gray GB, Sulieman MA, Jagger DC. Comparison of wear and clinical performance between amalgam, composite and open sandwich restorations: 2-year results. Eur J Prosthodont Restor Dent. 2004 Mar;12(1):15-20.

40. Wilson MA, Cowan AJ, Randall RC, Crisp RJ, Wilson NH. A practice-based, randomized, controlled clinical trial of a new resin composite restorative: one-year results. Oper Dent. 2002 Sep;27(5):423-9.

41. McManus KR, Fan PL. Purchasing, installing and operating dental amalgam separators: practical issues. J Am Dent Assoc. 2003 Aug;134(8):1054-65.

42. Food and Drug Administration. White paper: FDA update/review of potential adverse health risks associated with exposure to mercury in dental amalgam. Draft [Internet]. Silver Spring (MD): The Administration; 2006. [cited 2012 May 23]. Available from: http://www.fda.gov/medicaldevices/productsandmedicalprocedures/dentalproducts/dentalamalgam/ucm171117.htm

43. Food and Drug Administration. Addendum to the dental amalgam white paper: response to 2006 joint advisory panel comments and recommendations [Internet]. Silver Spring (MD): The Administration; 2009. [cited 2012 May 23]. Available from: http://www.fda.gov/downloads/medicaldevices/productsandmedicalprocedures/dentalproducts/dentalamalgam/ucm173908.pdf

44. Agency for Toxic Substances & Disease Registry. Public health statement [Internet]. In: Toxicological profile for mercury. Atlanta (GA): The Agency; 1999. p. 1-28 [cited 2012 May 10]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp46-c1.pdf.

45. Food and Drug Administration. 21 CFR part 872. Dental devices: classification of dental amalgam, reclassification of dental mercury, designation of special controls for dental amalgam, mercury, and amalgam alloy [Internet]. Bethesda (MD): The Administration; 2009 Nov 2. [cited 2012 May 8]. (Docket No. FDA-2008-N-0163). Available from:

http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/DentalProducts/DentalAmalgam/UCM174024.pdf

46. Scientific Committee on Emerging and Newly Identified Health Risks. The safety of dental amalgam and alternative dental restoration materials for patients and users [Internet]. Brussels (BE): European Commission; 2008. [cited 2012 May 2]. Available from: http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_016.pdf

47. Bogacki RE, Hunt RJ, del Aguila M, Smith WR. Survival analysis of posterior restorations using an insurance claims database. Oper Dent. 2002 Sep;27(5):488-92.

Appendix 1: Review Protocol

Objectives

The objective of this review is to compare the efficacy, safety and cost-effectiveness of the amalgam fillings with the resin-based fillings when used in load-bearing areas of permanent teeth.

Review Protocol and Study Selection

Studies were chosen for inclusion in the review based on the criteria in the table below.

Table #: Selection Criteria

Clinical Trial Design	Patient Population	Intervention	Comparators	Outcomes
Published RCTs	Patients with at least one permanent tooth requiring restoration with direct filling material.	Amalgam-based filling material	Resin composite filling material	<u>Efficacy</u> - Restoration longevity - Patient' satisfaction - Prevention of recurrence of dental caries at the margin of the restoration <u>Harms</u> Localized: - post operative pulpal irritation and/or hypersensitivity - gingival and periodontal irritation and/or injury Systemic: - SAE/ TEAE - Effect of longterm exposures on the general health of patients - Detection of the restorative material, or one of its components, in other body organs or fluids. - Development of neuropathies, renal pathologies, or immunoreactions

RCT=randomized controlled trial **; SAE**=severe adverse events; **TEAE**=treatment emergent adverse events;

Appendix 2: Title and abstract screening checklist

Reviewer: **Date:**

Ref ID: **First Author (year):**

1 What is the STUDY POPULATION in this article?	☐ Pediatric patients/ deciduous teeth to be restored (exclude) ☐ Pediatric patients/ mixed dentition to be restored (include) ☐ Pediatric patients/ permanent teeth to be restored (include) ☐ Adult patients (include)
2 What is the INTERVENTION?	☐ Amalgam-based filling material (include) ☐ Resin-composite filling material (include) ☐ Indirect filling material/technique (exclude) ☐ Compomer filling material (include) ☐ Resin-composite cementing material (exclude) ☐ Glass-ionomer dental material (exclude)
3 What is the TYPE OF STUDY reported in this article?	☐ Report of a clinical trial (controlled; randomized/non-randomized) (include) ☐ Meta-analyses/systematic reviews/HTAs (exclude) ☐ Report of Diagnostic trial (exclude) ☐ Report of a controlled prospective or retrospective cohort study (exclude) ☐ Report of an analytical controlled cross-sectional study (exclude) ☐ Academic/narrative review, comment, editorial, letter, note, patient handout, study design description (exclude) ☐ All other study designs (exclude) ☐ Can't decide (include)
Selection decision:	☐ **Include** ☐ **Exclude**

Appendix 3: Full text screening checklist

Reviewer: **Date:**

Ref ID: **First Author (year):**

1. **Were the included patients randomised into either amalgam or composite filling materials***?*
- ☐ Yes (include)
- ☐ No (exclude)
- ☐ Maybe (include)

2. **Is the article the PRIMARY REPORT of the FINAL OUTCOMES results from:**
- ☐ Report of a clinical trial (controlled/uncontrolled; randomized/non-randomized) (include)
- ☐ Meta-analyses/systematic reviews/HTAs (exclude)
- ☐ All other study types (exclude)
- ☐ Can't decide (include)

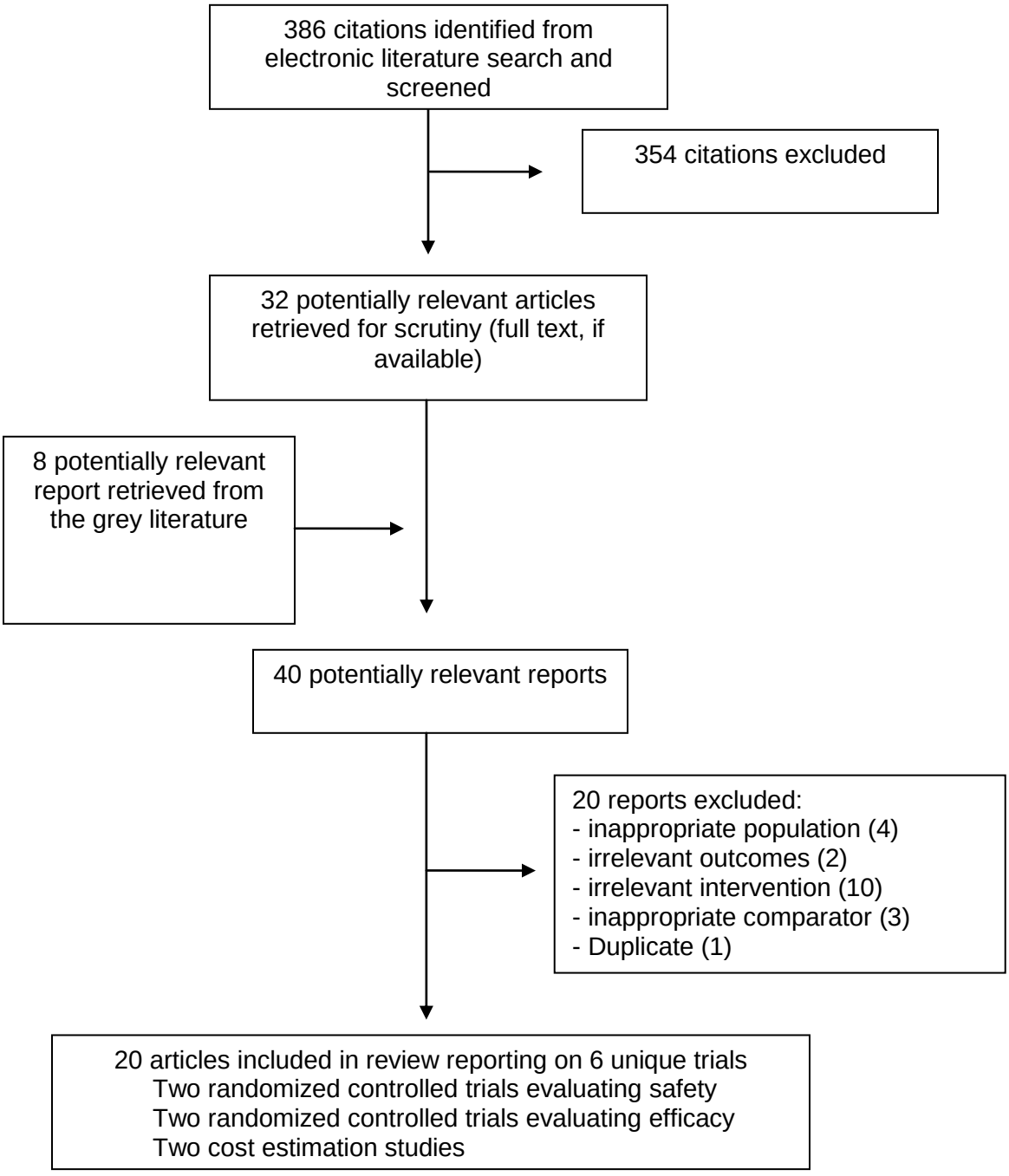
3. **What COMPARATOR is used in the study?**
- ☐ Any amalgam-based dental filling compared to any resin-composite direct dental filling material (include)
- ☐ No comparator (exclude)

4. **Include if the OUTCOME of interest in the study is one of the following:**
- ☐ Efficacy (restoration longevity, patient' satisfaction, prevention of recurrence of dental caries at the margin of the restoration) (include)
- ☐ Localized Harms (post-operative pulpal irritation and/or hypersensitivity; and gingival and periodontal irritation and/or injury) (include)
- ☐ Systemic harms (general adverse events, effect of long-term exposures on the general health of patients, detection of the restorative material, or one of its components, in other body organs or fluids; and development of neuropathies, renal pathologies, or immunoreactions) (include)
- ☐ Costs of dental filling (include)
- ☐ Cost-effectiveness (e.g. cost per case treated, cost per quality adjusted life year, cost per filling life year) (include)
- ☐ None of the above (exclude)

5. **Final Decision**
- ☐ **Include**
- ☐ **Exclude**
- ☐ **Non-English /Unable to translate**

Reason for Exclusion:
- ☐ **Inappropriate study population**
- ☐ **Not study types of interest**
- ☐ **Study description only**
- ☐ **No intervention of interest**
- ☐ **Inappropriate control group**
- ☐ **No relevant outcomes**

Appendix 4: Selection of Included Studies



Appendix 5: Characteristics of the Included Primary Studies

Randomized Controlled Trials Evaluating the Safety of Amalgam and Composite Dental Filling Materials

First Author, Publication Year, Country	Study Objectives and Design	Inclusion Criteria, Sample Size, and Patient Characteristics	Intervention, Comparator, and Study Conduct	Clinical Outcomes
The New England Children's Amalgam Trial				

Trial Design paper
The Children's Amalgam Trial Study Group, 2003[30]
 	
Main publication
Bellinger, 2006[31]
 	
Related publications
Shenker, 2008[34]
Bellinger, 2008[35]
Barregard, 2008[32]
Bellinger, 2007[33]
Soncini, 2007[36]
 	
Massachusetts and Maine, USA
	The primary objective was to assess the relative effects of amalgam and alternative (composite) restoration materials on 5-year change in IQ
	
	Randomized controlled trial
	1997-2005
		Inclusion Criteria
		• Children aged 6 to 10 years with at least 2 posterior teeth with dental caries (occlusal surface included)
		• Patients should not have previous exposure to amalgam
		• Children should not have clinical evidence of psychological, behavioural, neurological, immune-suppressive or renal disorders
		
		Sample Size
		N= 534
		
		Patient's Characteristics
		• the mean age was 7.9 years
		• 287 (53.7%) female children
		• 8 carious surfaces on primary teeth (approximate mean)
		• 2 carious surfaces on permanent teeth (approximate mean)
		• Mean IQ on WISC-III was 95.6
		• Mean Creatinine-adjusted urinary mercury concentration was 1.41 µg Hg/mL creatinine
		• During the trial, children had a mean of 15 tooth surfaces restored (approximately equal distribution to both filling material groups)
			Intervention
			• Dental composite material for all restorations at baseline and subsequently during the 5-year trial period (n=267)
			
			Comparator
			• Dental amalgam for all posterior restorations at baseline and at subsequent visits (n=267);
			
			Composite materials were used for restoration of front teeth in both groups.
			
			Conduct
			• Randomisation was stratified on geographical location and number of caries
			• Data collection and analysis were blinded
				Primary outcome
				• The mean difference between treatment arms in 5-year change in IQ
				  ○ measured by WISC-III
				Secondary outcomes (neuropsychological measures)
				• Short-term auditory memory as measured by the GMI
				• Visual-motor integration as measured by VMC
				Secondary outcomes (renal responses)
				• Renal function damage
				  ○ measured by urinary levels of creatinine-adjusted γ-GT
				• Nephrotoxicity
				  ○ measured by urinary levels of NAG
				• Renal tubular function
				  ○ measured by urinary levels of low-molecular weight protein A1M
				• Renal glomerular effects
				  ○ measured by urinary albumin in low concentrations
				Mercury exposure
				• Creatinine-adjusted urinary mercury values
				Secondary outcomes (immune functions – sub-study; N=61)
				• Total white blood cells count
				• Lymphocyte distribution
				• T-cell function
				• B-cell function
				• T-cell function methods
				• Immunoglobulin
				Secondary outcomes (Psychosocial Status – N=395)
				• Child Behavior Checklist* (parent-completed)
				• Behavior Assessment System for Children** (self-reports)
				Secondary outcomes (Filling Survival)
				• Filling replacement
				• Filling repair

Randomized Controlled Trials Evaluating the Safety of Amalgam and Composite Dental Filling Materials

First Author, Publication Year, Country	Study Objectives and Design	Inclusion Criteria, Sample Size, and Patient Characteristics	Intervention, Comparator, and Study Conduct	Clinical Outcomes
				Adverse health events
Casa Pia Children's Amalgam Trial				

Trial design paper
DeRouen, 2002[5]
 	
Main publication
DeRouen, 2006,[22]
 	
Related publications
Geier, 2011[27]
Woods, 2009[26]
Woods, 2008[25]
Lauterbach, 2008[23]
Woods, 2007[28]
Bernard, 2007[29]
 	
Lisbon, Portugal
	To assess the safety of dental amalgam restorations in children
	
	Randomized controlled trial
	1997- 2005
		Inclusion Criteria
		Students aged 8 to 10 years with at least 1 carious lesion on a permanent tooth
		
		Patients did not have previous exposure to amalgam
		
		Sample size
		N=507
		
		Patient's Characteristics
		• the mean age was 10.2 years
		• 228 (45.0%) female children
		• 16 carious surfaces (approximate mean)
		• Mean IQ on CTONI was 10.2
		• Mean Creatinine-adjusted urinary mercury concentration was 1.9 µg/g
		• During the trial, children had a mean of 18.7 tooth surfaces restored with amalgam and 21.3 restored with composite.
			Intervention
			• Treatment for dental caries using amalgam for posterior restorations (n=253)
			
			Comparator
			• Treatment for dental caries using resin composite material (n=254)
				Primary outcomes (neurological responses):
				• Memory
				  ○ measured by Rey Auditory Verbal Learning and Visual Learning tests
				• Attention/concentration
				  ○ Coding test
				  ○ Symbol search
				  ○ Digit span
				  ○ Finger window
				  ○ Stroop color word test
				• Motor/visuo-motor
				• Nerve conduction velocity
				Secondary outcomes (renal responses)
				• Renal tubular function
				  ○ measured by urinary glutathione S-transferases (GST-α and GST-π)
				Secondary outcomes (immunologic reaction)
				• Measured by urinary albumin in the low concentration range (microalbuminuria)
				Mercury exposure
				• Creatinine-adjusted urinary mercury values
				• Creatinine-adjusted urinary porphyrins†
				Adverse health events
				• Major disease diagnosis
				• Hospitalization
				• Death

A1M= alpha-1-microglobulin **; CTONI=** Comprehensive Test of Nonverbal Intelligence; γ**-GT=** gamma glutamyl -transpeptidase; **GMI=** General Memory Index (it is derived by combining a child's scores on the nine subsets of the Wide Range Assessment of Memory and Learning: Picture Memory, Design Memory, Verbal Learning, Story Memory, Finger Windows, Sound Symbol, Sentence Memory, Visual Learning, and Number/Letter Memory); **IQ=** Intelligence quotient; **NAG**= N-acetyl-beta-D-glucosaminidase**; VMC=** Visual Motor Composite (it is an overall score derived by combining a child's scores on the three subsets of the Wide Range Assessment of Visual Motor Abilities: Drawing, Matching, and Pegboard); **WISC=** Wechsler Intelligence Scale for Children

* The Child Behavior Checklist yields four global T-scores: Competence, Internalizing Behavior Problems, Externalizing Behavior Problems, and Total Problem Behaviors. Competence score is constituted form Activities, Social Adaptation and School subscales. Eight subscales contribute to behavior scores: Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behaviour and Aggression.

** The Behavior Assessment System for Children yields four global scores: Clinical Maladjustment, School Maladjustment, Personal Adjustment, and the Emotional Symptoms Index

† abnormal urine porphyrins test results may indicate liver cancer, hepatitis, lead poisoning, or porphyria

Randomized Controlled Trials Evaluating the Efficacy of Amalgam and Composite Dental Filling Materials

Study Objectives and Design	Inclusion Criteria, Sample Size, and Patient Characteristics	Intervention, Comparator, and Study Conduct	Clinical Outcomes
Sachdeo et al. 2004[39] – London, UK			
To evaluate the wear on two groups of tooth-colored Class II restorations compared to a control group of amalgam restorations. To compare the clinical performance of "open sandwich" composite restorations with a group of conventionally placed posterior composite restorations. Randomized-controlled trial – Two years follow-up	**Inclusion Criteria** • Patients were selected for inclusion if they had a premolar or molar tooth in functional occlusion but with a primary carious lesion or a pre-existing restoration in need of replacement. • The tooth was included in the study only if the resulting cavity preparation had a width not exceeding half of the bucco-palatal width of the tooth. **Sample size** N=133 patients **Patient's Characteristics** were not reported	**Intervention** • Composite restoration using a conventional technique, Tetric Ceram composite resin together with Syntac II dental adhesive (n=35) • Open sandwich technique using Prime and Bond 2.1 dental adhesive, Dyract AP compomer and Spectrum TPH composite (n=53) **Control** • Restoring teeth using dental amalgam filling material (Dispersalloy) (n=45 patients)	**There was no specific primary outcome designated in the trial publication** • Wear • Clinical performance o Occlusal and proximal contacts o Macroscopic surface texture and anatomical form o Marginal discoloration o Secondary caries o Loss of fracture of the restorations.
Wilson et al. 2002[40] – UK			
To evaluate the performance of a law-shrinking composite as an alternative to dental amalgam in the restoration of moderate-sized Class I and II cavities in premolar and permanent molars of adult patients. Randomized controlled trial – tooth level randomization – One year follow-up	**Inclusion Criteria** Patients should have a pair of similar lesions or failed restorations in vital premolar or permanent molars that required new or replacement Class I or two-surface Class II restorations of moderate size. **Sample size** N=50 patients with a total of 52 pairs of restored teeth **Patient's Characteristics** • An equal male to female patients were included • The mean age was 35 years • 17 pairs of restorations were Class I and 35 pairs were Class II	**Intervention** • Restoring teeth using Z250 low-shrinkage composite dental filling material (n=52 teeth in 50 patients) **Control** • Restoring teeth using dental amalgam filling material (Dispersalloy) (n=52 teeth in 50 patients)	**There was no specific primary outcome designated in the trial publication** • Clinical acceptability • Wear of the opposing tooth cusp • Appearance • Marginal adaptation • Anatomic form • Surface roughness • Marginal staining • Interfacial staining • Occlusal contacts • Sensitivity • Secondary caries • Patient's satisfaction o measured by the visual analogue scale

Studies Evaluating the Cost-effectiveness of Amalgam and Composite Dental Filling Materials

Study Objectives & Design	Data collection/ Assumptions	Interventions	Outcomes
Khairiyah, 2009[38] – Selangor, Malaysia			
To present data on cost per unit for amalgam restorations, tooth-colored capsulated and tooth-colored non-capsulated restorations by public dental clinics in Malaysia **Cost analysis study**	• The study included 4 clinics in 2 urban areas and 2 rural areas in Selangor – Malaysia • A pragmatic sample size of a minimum of 30 per restoration material per location was predetermined in the protocol. A total of 196 restorations were included in the analysis. • Cost calculation was estimated for one new restoration undertaken per visit (1 restoration per attendance) • The components of the calculated cost included human resources, dental materials, and the macro-cost* • Data was collected in 2005	Posterior dental fillings using one of the following materials: • capsulated amalgam material • capsulated compomer material • non-capsulated nano-composite resin material	Total and component costs for each dental filling type
Sjögren et al. 2002[37] – Sweden			

To evaluate the theoretical long-term treatment costs of direct Class II molar restorations (amalgam, composite, glass ionomer) using the MSTs derived from longevity studies conducted in the Nordic countries as time for replacement.
 	
Cost analysis study
	• Long-term (10 years) cost calculations were based on fee schedules from all (21) public dental services in Sweden. The following total** mean initial (lowest, highest) costs† were used:
	  ○ Amalgam: 95.1 (74.8, 138.6) CAD
	  ○ Composite: 121.5 (89.0, 149.9) CAD
	  ○ Glass-ionomer: 56.4 (40.5, 83.3) CAD
	• Median survival times (MST) used in the study were based on published literature in 2001. The following mean MSTs (shortest, longest) were used:
	  ○ Amalgam: 9.3 (2.0, 11.0) years
	  ○ Composite: 4.7 (1.0, 6.0) years
	  ○ Glass-ionomer: 3.0 (2.0, 4.0) years
		Class II fillings for molar teeth using one of the following materials:
		• amalgam dental filling material
		• Composite dental filling material
		• Glass-ionomer dental filling material
			The mean costs over 10 years of molar class II restorations for each dental filling type

CAD= Canadian Dollar

* Macro-cost included clinical attendance, facility infrastructure costs, operating and maintenance costs, costs of assets, vehicles and their maintenance, staff emoluments and benefits, staff training costs, mileage and toll claims, and consumables costs

** The total mean cost included the cost paid by the patient and that paid by the social insurance offices

† Costs were reported in Swedish crowns. To produce this review, these costs were converted to Canadian Dollar by using the exchange rate of May 10, 2002 (0.1521). After conversion, costs were adjusted for inflation between 2002 and 2012 (change rate 23.05%). The study reported discounted costs at 0%, 3% and 5%. The exchange and inflation rates were retrieved from Bank of Canada on May 10, 2012.

Appendix 6: Critical Appraisal of Included Studies

Critical Appraisal the Safety Studies

Strengths	Limitations
The New England Children's Amalgam Trial - The Children's Amalgam Trial Study Group, 2003[30]	
• Random assignment was made via a standardized software and encrypted files • Outcome data collection was conducted by independent investigators who were blinded with regard to treatment assignment • Sample size was calculated a priori. It was estimated that 500 participants would provide 80% power to detect a treatment-arm difference of three points in WISC-III Full Scale IQ	• Because of the nature of the trial treatments, blinding of participants and treating dentists was not feasible. Although data collection and analysis were conducted in a blinded fashion to minimize this bias, participants might have been affected by their families in a way that could impact the neurobehavioral tests. • The trial evaluated the effect of dental amalgam exposure on different outcomes. However, measures used to evaluate the exposure (surface-years of amalgam and urinary mercury excretion) were validated by using the trial data. Using trial data to validate an outcome which will be used in the analysis of data of the same trial is a methodological flaw and a source of measurement and classification biases
Casa Pia Children's Amalgam Trial - DeRouen, 2002[5]	
• The mercury exposure from dental amalgam was adjusted for exposure from other sources (i.e. elemental and environmental). • Sample size was calculated a priori. It was estimated that a minimum of 450 participants would provide 97% power to detect either scenario 1 (an effect size of 0.5 SD in each of the three neurobehavioral outcome measures and an effect size of 0.15 in nerve conduction velocity) or scenario 2 (effect size of 0.5SD in nerve velocity with no effect in the other outcome measures)	• Children in amalgam group were treated with amalgam for large restorations in posterior teeth, but they could at the same time be treated with other materials (composite, glass-ionomer or compomer) for restorations not appropriate for amalgam. Thus the two groups differed in exposure to amalgam, but they could overlap in exposure to the other materials. For this reason, harmful effects from composite could be potentially confounded by the group of children who were randomized to receive amalgam fillings but also received composite fillings for the repair of their anterior teeth. • The use of GST enzymes as surrogate measure to evaluate renal functions does not necessarily indicate permanent renal damage. These enzymes can be reversibly elevated in the presence of mercury without permanent nephritic damage.

IQ= Intelligence quotient; **SD=** standard deviation; **WISC=** Wechsler Intelligence Scale for Children

Critical Appraisal the Efficacy Studies

Strengths	Limitations
Wilson et al. 2002[40]	
• Assessment of restorations was done by two independent investigators. • Evaluation of marginal adaptation, anatomic form, surface finish and wear were assessed on die-stone replica models. The assessments were carried out blind by one investigator.	• The trial did not define a primary outcome to evaluate the performance of restorations. • There were no calculation of population size for a desired power and precision limits. • The duration of the trial was relatively short and did not permit to conclude on the clinical performance and longevity of both materials. • The generalizability of the trial findings might be questionable. One practitioner conducted all restorations, and his skills and experience might not be reflective to all dental practitioners. Furthermore, the trial population were recruited from the same dental practice, and their dental hygiene status and compliance might not be generalizable to other groups.
Sachdeo et al. 2004[39]	
• Randomization was conducted by card selection.	• Baseline patient's characteristics were not reported, and confounding factors could not be assessed. • Population size was not calculated a priori, and the trial did not evaluate the power of its findings. • The generalizability of the trial findings might be questionable. One practitioner conducted all restorations, and his skills and experience might not be reflective to all dental practitioners. Furthermore, the trial population were recruited from the same dental practice, and their dental hygiene status and compliance might not be generalizable to other groups.

Critical Appraisal the Cost Studies

Strengths	Limitations
Khairiyah et al. 2009[38]	
• Cost estimation took into consideration a comprehensive components list for the macro and micro costs	• The cost estimated might not be generalizable because the study was conducted in publicly funded clinics. In general, public health facilities have a considerable negotiation margin for prices which might not reflect the actual prices paid by private dentists. • The study did not report whether the estimation included the cost for patients, health insurance payers or both. • The cost estimation did not take into consideration the longevity of the different materials neither their need for repair and replacement.
Sjögren et al. 2002[37]	
• The analysis considered the cost paid by the patient, social insurance and the total of both.	• The cost calculation defined the mean survival time as the time from restoration placement until time for its replacement. However, it did not consider the cost associated with the restoration repair. • It was not clear whether the estimation included the associated costs of infrastructure and human resources or just the cost of the material. • The analysis defined a monetary designation of 1.0x for both amalgam and composite but 0.5x for glass ionomer. The justifications for this difference in the monetary designation was not reported or explained.

Appendix 7: Main Study Findings and Authors' Conclusions

Findings and Conclusions of the Safety Studies

Main Study Findings	First Author, Publication Year Authors' Conclusions
The New England Children's Amalgam Trial[31-34]	

• The exact follow-up rates were not reported. Approximately 75% of enrolled children had available data for the neuropsychological outcome.[31]
• **Primary outcome – Neurobehavioral (WISC-III Full-scale IQ score)**[31]
  ○ The change (SE) form baseline in IQ scores was +3.1 (0.6) in the amalgam group and +2.1 (0.6) for the composite.
  ▪ The treatment group difference in IQ change score (Amalgam - composite) was not statistically significant; 1.0 (95% CI; -0.6 to 2.5), *p*-value=0.21
  ○ The association between the Full-scale IQ scores and Amalgam mercury exposure was not statistically significant*[33]
 	
• **Secondary outcomes – Neurobehavioral (GMI and VMC)**[31,33]
  ○ The respective changes (SE) form baseline in GMI and VMC scores were +8.1 (0.7) and 3.8 (0.8) in the amalgam group and +7.2 (0.7) and 3.7 (0.8) for the composite.
  ▪ The treatment group differences change score (Amalgam - composite) was 0.9 (95% CI; -0.9 to 2.7), *p*-value=0.34 for the GMI score, and it was 0.1 (95% CI; -2.0 to 2.2), *p*-value=0.93 for the VMC score
  ○ GMI and VMC scores were not statistically significantly associated with Amalgam mercury exposure*[33]
 	
• **Secondary outcomes – Renal responses (*glomerular function*)**[31]
  ○ At year 5, 87% of the amalgam group and 90% of the composite group children had albumin detected in their urine samples.
  ▪ Albumin levels did not differ statistically significantly between treatment groups.
  ▪ The mean albumin was higher for girls than for boys. However, it was not reported if this difference was in the amalgam group only or in both groups.
 	
• **Secondary outcomes – Mercury exposure (*creatinine-adjusted urinary mercury concentration*)**[31]
  ○ After 5 years of follow-up, the mean (SD) urinary mercury concentrations in the amalgam group (0.9 (0.8) µg/g of creatinine) were higher than those in the composite group (0.6 (0.5) µg/g of creatinine).
  ▪ The reported *p*-value (<0.001) showed a statistically significant difference.
 	
• **Adverse health events**[31]
  ○ No child had a urinary mercury level greater than 20µg/g of creatinine at any time in the trial,
  ○ No child's neurological test scores consistently decreased over time,
  ○ 77 children had microalbuminuria (albumin >30mg/g creatinine) during the trial with no significant difference between treatment groups.
  ▪ Adverse health events were reported similarly in both treatment groups.
	Bellinger, 2006[31]
	
	"There were no statistically significant differences in adverse neuropsychological or renal effects observed over the 5-year period in children whose caries were restored using dental amalgam or composite materials. Although it is possible that very small IQ effects cannot be ruled out, these findings suggest that the health effects of amalgam restorations in children need not be the basis to treatment decisions when choosing restorative dental materials."

Findings and Conclusions of the Safety Studies

Main Study Findings	First Author, Publication Year Authors' Conclusions
• **Secondary outcomes – Renal responses**[32] ○ The distributions for renal markers (γ-GT, albumin and NAG) showed that there were no statistically significant differences between treatment groups. ○ The prevalence of urinary albumin >30 mg/g creatinine in year 3 or year 5 was higher in the amalgam group than in the composite group ▪ Odd Ratio = 1.8 (95% CI; 1.1 to 2.9); *p*-value=0.03 ▪ The	**Barregard, 2008**[32] "*The trial showed no effect of amalgam on renal tubular function. There was, however, an increased prevalence of MA in children treated with dental amalgam. This may reflect a casual association or it may by a chance findings. This issue should be examined further."*
• **Secondary outcome – Immunologic function**[34] ○ Changes in immunologic measurements were assessed at 5-7 days post-treatment, 6 months, 12 months and 60 months post-treatment in 66 participants. ○ The distribution of lymphocytes, monocytes and neutrophils fluctuated over time, both within and between treatment groups. ▪ No consistent or statistically significant differences were observed between the two treatment groups. ○ At 5-7 days post-treatment, it was observed that the amalgam group had a slight, but not statistically significant, decline in responsiveness of T-cells and monocytes. This trend did not persist beyond this time point.	**Shenker, 2008**[34] "*In the exploratory analysis of immune function, amalgam exposure did not cause overt immune deficits, although small transient effects were observed 5-7 days post restoration.*
• **Secondary outcome – Psychosocial Status**[35] ○ Child Behavior Checklist (parents completed) ▪ A statistically significant group differences (**favoring amalgam**) were reported for Internalizing and Total Problem Behaviors. ▪ The differences between groups did not reach a statistical significance for the Competence and Externalizing domains. ○ Behavior Assessment System for Children (self-reports) ▪ A statistically significant group differences (**favoring amalgam**) were noted for the Emotional Symptoms Index and Personal Adjustment. ▪ School and Clinical Maladjustments did not differ with statistical significance between amalgam and composite groups.	**Bellinger, 2008**[35] *"No evidence was found that exposure to mercury from dental amalgams was associated with adverse psychosocial outcomes over the five-year period following initial placement of amalgams"*
• **Secondary outcome – Filling Survival**[36] ○ Filling replacement rates showed that more composite fillings needed to be replaced than amalgam fillings did; ▪ 55 (10.8%) amalgam fillings needed to be replaced versus 112 (14.9%) composite fillings. The difference was not statistically significant (*p*-value=0.45) ▪ The main reasons for replacement were new and recurrent caries in both groups; however, the incidences for these caries were higher in the composite groups ○ The percentage of repairs was significantly higher for composites (2.8%) than for amalgam (0.4%) (*p*-value = 0.02)	**Soncini, 2007**[36] *"In posterior teeth, resin-based composite restorations had significantly higher repair rates, yet not statistically greater replacement rates, than did amalgam restorations."*

Findings and Conclusions of the Safety Studies

Main Study Findings	First Author, Publication Year Authors' Conclusions
Casa Pia Children's Amalgam Trial	
• At the fifth year of follow-up 85% of participants remained in the study, and declined to 70% through follow-up year seven. • **Primary outcome – Neurobehavioral (Memory, Visuo-motor, and Attention/Concentration)** Tests results showed small and statistically not significant differences between amalgam and composite groups. These results were consistent in the interim annual analyses and in the final analysis. (Results were reported graphically) • **Primary outcome – Neurobehavioral (nerve conduction velocity)** • Test results exhibited inconsistent treatment effects overtime. The difference between treatments was statistically significant at year 7, and showed more favorable results for the amalgam group. Because the high variability over time, these findings could not be interpreted as conclusive evidence. • **Adverse health events** **Four cases in the amalgam group** ○ 1 death due to unintentional gunshot, ○ 1 death due to hepatitis, ○ 1 case of brain aneurysm, ○ 1 case of kidney stone) **Five cases in the composite group** ○ 2 diagnosed cases of epilepsy, ○ 1 case of hyperthyroidism, ○ 1 case of asthma, ○ 1 psychiatric hospitalisation)	**DeRouen, 2006**[22] *"Children treated with dental amalgam **did not, over a 7-year follow-up period, demonstrate statistically significant differences in neurobehavioral and neurological test results**. These findings, especially in light of the observed higher treatment need in the composite treatment group 5 or more years after initial treatment, suggest that amalgam should remain a viable clinical option in dental restorative treatment."*
• **Secondary outcome – Neurobehavioral (NHS & NSS)** ○ There were slight differences between the treatment groups in the rate of participants exhibiting any NHSs, but the directions of the differences were not consistent over time, and the differences were not statistically significant in any of the years. ○ The rate of participants who exhibited one or more NSSs and the severity of these NSSs did not differ in a statistically significant manner between the treatment groups.	**Lauterbach, 2008**[23] *"The study failed to show that exposure to mercury in childhood as a consequence of treatment with amalgam restorations is associated with a higher frequency of NSSs in childhood and adolescence"*
• **Secondary outcomes – Renal responses (Renal tubular function)** ○ GST-α and GST-π concentrations were slightly higher (5% and 11% respectively) in the Amalgam group than the composite groups but the differences were not statistically significant. Overall differences between amalgam and composite groups were 1.05* (95% CI; 0.94, 1.17) for the GST-α concentration, and 1.11* (95% CI; 0.98, 1.26) for the GST-π concentration. • **Secondary outcomes – Renal responses (*glomerular function*)** ○ Albumin levels were slightly lower in the amalgam group than in the	**Woods, 2008**[25] *"Authors observed **no significant effects** of dental amalgam mercury on **measures of renal tubular or glomerular functional integrity** during a prolonged course of dental amalgam treatment in children and*

Findings and Conclusions of the Safety Studies

Main Study Findings	First Author, Publication Year Authors' Conclusions
composite, but the difference was not statistically significant ○ Overall differences between amalgam and composite groups was 0.91† (95% CI; 0.78, 1.07)	*adolescents from 9 to 18 years of age."*
• **Secondary outcomes – Mercury exposure (*creatinine-adjusted urinary mercury concentration*)** ○ The mean urinary mercury concentrations in the amalgam group increased from 1.5 µg/L at baseline to a peak of 3.2 µg/L at year 2 and then slowly declined to near baseline levels by year 7 of follow-up. ○ Increases in mean urinary mercury concentrations after amalgam treatment were larger for females than in males. Mean mercury concentrations for female amalgam group subjects reached a peak of 3.5 µg/L at year 2 and remained about 3 µg/L throughout the 7-year follow-up period. For the male amalgam group, the concentration was <3 µg/L at all years and declined to the same level as seen in the composite group by the end of follow-up. ○ Differences between treatment groups were highly significant at all follow-up years except for the final year.	**Woods, 2007**[28] *"The trial described a strong, positive correlation between mercury exposure from dental amalgam fillings and urinary mercury excretion over a 7-year longitudinal course of amalgam treatment in children. However, significant differences in urinary mercury concentrations between boys and girls with comparable levels of amalgam treatment and times since placement suggest sex-related differences in mercury handling and, possibly, susceptibility to mercury toxicity…"*
• **Secondary outcomes – Mercury exposure (*urine porphyrins*)** ○ The differences between amalgam and composite groups were not statistically significant for all measured porphyrins**. However, *5cxp, PrcP, and cP* were slightly higher in the amalgam group.	**Woods, 2009**[26] "*The trial findings described incipient increases in the urinary concentrations of porphyrins previously defined in association with HG body burden, in children and adolescents with dental amalgam Hg exposure.*
• **Secondary outcomes – Mercury exposure (*urine porphyrins*)** ○ The paper further explored the association between amalgams and urine porphyrins. ○ The analysis provided estimates of the association of urine porphyrins concentrations with cumulative exposure to dental amalgam‡. ○ The model showed that the urinary concentrations of *5cxp, PrcP, and cP* were statistically significantly correlated with the score of mercury exposure from dental amalgam.	**Geier, 2011**[27] *"The trial showed that the characteristic pattern of porphyria associated with Hg body-burden, specifically, elevated 5cxp, PrcP, and cP were significantly correlated with dental amalgam exposure in a dose-dependent fashion"*
• **Secondary outcomes – Restoration survival** ○ The analysis included 472 children and a total of 1,748 posterior restorations. ○ Overall, 177 (10.1%) restorations failed during the study period. ▪ The survival rate of the amalgam restorations was 94.4% at seven	**Bernardo, 2007**[29] *"On the bases of the results of this study and within its limitations, posterior amalgam restorations performed*

Findings and Conclusions of the Safety Studies

Main Study Findings	First Author, Publication Year Authors' Conclusions
years. ▪ The survival rate of the composite restorations was 85.5%. ▪ There were no RR or HR differences reported. ○ There were more composite restorations (77.9%) than amalgam (22.1%) failed because of secondary caries. ▪ RR was 3.5 (95% CI; 2.3 to 5.1), *p*-value <0.0001	*better than composite restorations. The difference in performance was accentuated in restorations with more than three surfaces restored and in large restorations."*

A1M= alpha-1-microglobulin**; cP=** coproporphyrin; **CTONI=** Comprehensive Test of Nonverbal Intelligence; **GMI=** General Memory Index (it is derived by combining a child's scores on the nine subsets of the Wide Range Assessment of Memory and Learning: Picture Memory, Design Memory, Verbal Learning, Story Memory, Finger Windows, Sound Symbol, Sentence Memory, Visual Learning, and Number/Letter Memory); **GST=** glutathione S-transferases; γ**-GT=** gamma glutamyl -transpeptidase; **HR=** hazard ratio **; IQ=** Intelligence quotient; **PrcP=** precopro-carboxy-porphyrin; **NAG**= N-acetyl-beta-D-glucosaminidase**; NHS=** Neurological Hard Signs (indicators to specific neural structure and, in clinical practive, are used to localize the site of lesion or dysfunction); **NSS=** Neurological Soft Signs (are subtle signs of central nervous system dysfunction that have no localizing value); **RR=** relative risk; **SE=** standard error; **VMC=** Visual Motor Composite (it is an overall score derived by combining a child's scores on the three subsets of the Wide Range Assessment of Visual Motor Abilities: Drawing, Matching, and Pegboard); **WISC=** Wechsler Intelligence Scale for Children

* Exposure was measured by surface-year of amalgam and urinary mercury excretion

** the urine porphyrins test included uro-carboxyl-porphyrin, hepta-carboxyl-porphyrin, hexa-carboxyl-porphyrin, penta-carboxyl-porphyrin, precopro-carboxyl-porphyrin, and co-proporphyrins

† exponentiated estimate of log-transformed urinary concentration in the amalgam group versus composite group (obtained from a regression model)

‡ An individual study subject's exposure was measured by counting the number of restorations using amalgam then an exposure score was computed by first giving scores of 1, 2, 3 for small, medium, or large restorations, respectively, then adding these scores for each restoration of each tooth. The exposure for each restoration done in a year were added together to form the score for that year and all subsequent years.

Findings and Conclusions of the Efficacy Studies

Main Study Findings	Authors' Conclusions
Sachdeo et al. 2004[39]	
• Differences in the amount of surface wear at the end of 2-year follow-up that there was a significantly lower rate of was recorded for the amalgam restorations as compared by the two composite groups. ○ The wear of conventional and open sandwich technique composite restorations did not differ significantly. • Clinical performance of the three groups of restorations remained satisfactory throughout the study.	*"Within the limits of the study, the results demonstrated that there was a significant difference in wear rates between amalgam and composite resin restorations with the amalgam restorations demonstrated a lower wear rate over two year period. There was no statistically significant in the wear rate between the tooth colored restorations. No statistically significant difference was recorded in the clinical performance of the restorations according to the criteria used for assessment."*
Wilson et al. 2002[40]	
• Of all restored teeth, one amalgam restoration had a fractured cusp. • Statistical analysis of data failed to reveal any statistically significant differences except in relation to appearance.	*"Results indicated that Z250, when used in conjunction with single bond adhesive system. Gave a clinically acceptable performance in Class I and II restorations of moderate size and could be considered to be an appropriate alternative to amalgam in the restoration of posterior teeth over one-year in clinical service."*

<table>
<tr><th>Main Study Findings</th><th>Authors' Conclusions</th></tr>
<tr><td colspan="2">Khairiyah et al. 2009[38]</td></tr>
<tr><td>• The Total and component cost for each dental filling material, CAD* (SD):
<table>
<tr><th>Cost component</th><th>Amalgam</th><th>TC Caps</th><th>TC Noncaps</th></tr>
<tr><td>Human resource</td><td>3.2 (1.5)</td><td>3.2 (1.6)</td><td>3.1 (1.3)</td></tr>
<tr><td>Material</td><td>1.2 (0.5)</td><td>4.7 (2.1)</td><td>1.8 (0.7)</td></tr>
<tr><td>Macro-cost</td><td>8.0 (2.8)</td><td>8.0 (2.8)</td><td>8.1 (2.8)</td></tr>
<tr><td>Total</td><td>12.4 (3.2)</td><td>15.9 (4.3)</td><td>13.0 (3.1)</td></tr>
</table></td><td>"Using amalgam restoration as the reference point, on average a posterior restoration using tooth-colored non-capsulated material costs about the same as that an amalgam restoration, whereas using tooth-colored capsulated material costs about 1.3 times as much. Hence, there are small differences in costs of using amalgam and the identified tooth-colored materials for posterior restorations, making both the latter materials feasible alternative to amalgam in cost terms."</td></tr>
<tr><td colspan="2">Sjögren et al. 2002[37]</td></tr>
<tr><td>• The mean of total** costs over 10 years for molar class II restorations by filling material were as follow, CAD† :
<table>
<tr><th>Discount rate</th><th>Amalgam</th><th>Composite</th><th>GI</th></tr>
<tr><td>0%</td><td>189.8</td><td>363.7</td><td>224.9</td></tr>
<tr><td>3%</td><td>167.6</td><td>321.9</td><td>197.8</td></tr>
<tr><td>5%</td><td>156.0</td><td>299.1</td><td>183.1</td></tr>
</table></td><td>"Amalgam Class II molar restorations had the lowest theoretical long-term cost in total, except in the scenario where the cost calculations were based on the shortest MSTs, derived from the Nordic longevity studies. Thus, in light of the study findings. Long-term costs are important to analyze in order to predict future expenses for different treatments, but also on a community level and in relation to the health from the patients point of view."</td></tr>
</table>

CAD= Canadian Dollar; **GI=** glass ionomer; **TC Caps=** capsulated tooth-colored dental filling (compomer); **TC Noncaps=** non-capsulated tooth-colored dental filling (composite)

* Costs were reported in Malaysian Ringgit. To produce this review, these costs were converted to Canadian Dollar by using the exchange rate of May 10, 2005 (0.3256). After conversion, costs were adjusted for inflation between 2005 and 2012 (change rate 14.49%). The exchange and inflation rates were retrieved from Bank of Canada on May 10, 2012

** The total included costs paid by the patient and the social insurance offices.

†Costs were reported in Swedish crowns. To produce this review, these costs were converted to Canadian Dollar by using the exchange rate of May 10, 2002 (0.1521). After conversion, costs were adjusted for inflation between 2002 and 2012 (change rate 23.05%). The study reported discounted costs at 0%, 3% and 5%. The exchange and inflation rates were retrieved from Bank of Canada on May 10, 2012.