

# Amalgam Safety and Cost-Effectiveness: An Annotated Bibliography

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### A.1 Recent policy statements and reviews from major organizations

- 1) Life Sciences Research Office. Review and analysis of literature on the health effects of dental amalgam: Executive Summary. 2003; Available at: [http://www.lsro.org/amalgam/frames\\_amalgam\\_report.html](http://www.lsro.org/amalgam/frames_amalgam_report.html). Accessed 9/15/10.
- 2) ADA. Literature Review: Dental Amalgam Fillings and Health Effects. July, 2009; Available at: <http://www.ada.org/1741.aspx>. Accessed 8/31/10.
- 3) Brownawell AM. The potential adverse health effects of dental amalgam. Toxicological Reviews 2005;24(1):1.
- 4) ADA Council on Scientific Affairs. Statement on Dental Amalgam. August, 2009; Available at: <http://www.ada.org/1741.aspx>. Accessed 9/2/10.
- 5) Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The safety of dental amalgam and alternative dental restoration materials for patients and users. 2008; Available at: [http://ec.europa.eu/health/ph\\_risk/committees/04\\_scenihhr/docs/scenihhr\\_o\\_016.pdf](http://ec.europa.eu/health/ph_risk/committees/04_scenihhr/docs/scenihhr_o_016.pdf). Accessed 9/7/10.
- 6) FDI. FDI Policy Statement: Safety of Dental Amalgam. October, 2007; Available at: <http://www.fdiworldental.org/sites/default/files/statements/English/Safety-of-dental-amalgam-2007.pdf>. Accessed 9/2/10.
- 7) World Health Organization. Policy Paper: Mercury in Health Care. August, 2005; Available at: [http://whqlibdoc.who.int/hq/2005/WHO\\_SDE\\_WSH\\_05.08.pdf](http://whqlibdoc.who.int/hq/2005/WHO_SDE_WSH_05.08.pdf). Accessed 9/15/10.
- 8) World Health Organization. Elemental mercury and inorganic mercury compounds: Human health aspects. 2003; Available at: <http://www.who.int/ipcs/publications/cicad/en/cicad50.pdf>. Accessed 9/15/10.
- 9) Rugg-Gunn AJ, Welbury RR, Toumba J, British Society of Paediatric Dentistry. British Society of Paediatric Dentistry: a policy document on the use of amalgam in paediatric dentistry. Int J Paediatr Dent 2001 May;11(3):233-238.
- 10) National Health and Medical Research Council, Australian Government. Dental Amalgam and Mercury in Dentistry - Report of an NHMRC Working Party. 2001; Available at: <http://www.nhmrc.gov.au/publications/synopses/d17syn.htm>. Accessed 9/3/10.
- 11) Health Canada. The safety of dental amalgam. 1996; Available at: [http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/pubs/dent\\_amalgam-eng.php](http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/pubs/dent_amalgam-eng.php). Accessed 9/15/10.

### A.2. Positions supported by U.S. agencies

- 12) CDC. Dental Amalgam Use and Benefits. 5/28/2010; Available at: <http://www.cdc.gov/OralHealth/publications/factsheets/amalgam.htm>. Accessed 9/24/10.

- 13) National Institutes of Health  
<http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NRY2006/PR04182006.htm>. Accessed 9/24/10.

#### **B. Recent clinical trials**

- 14) DeRouen TA, et al. Neurobehavioral effects of dental amalgam in children: a randomized clinical trial. *JAMA* 2006;295(15):1784.
- 15) Lauterbach M, Martins IP, Castro-Caldas A, 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;139(2):138.
- 16) Bellinger DC, Trachtenberg F, Barregard L, et al. Neuropsychological and renal effects of dental amalgam in children: a randomized clinical trial. *JAMA* 2006;295(15):1775-1783.
- 17) Kingman A, Albers JW, Arezzo JC, et al. Amalgam exposure and neurological function. *NeuroToxicology* 2005;26(2):241-255.

#### **C. Survival studies of amalgam and alternative materials**

- 18) 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):775-783.
- 19) Beazoglou T, Eklund S, Heffley D, Meiers J, Brown LJ, Bailit H. Economic impact of regulating the use of amalgam restorations. *Public Health Rep* 2007;122(5):657-663.
- 20) Opdam NJM, Bronkhorst EM, Loomans BAC, Huysmans MC. 12-Year survival of composite vs. amalgam restorations. *J Dent Res* 2010;89(10):1063-1067.
- 21) Simecek JW, Diefenderfer KE, Cohen ME. An evaluation of replacement rates for posterior resin-based composite and amalgam restorations in US Navy and Marine Corps recruits. *J Am Dent Assoc* 2009;140(2):200-209.
- 22) 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;138(6):763-772.
- 23) Van Nieuwenhuysen JP, D'Hoore W, Carvalho J, Qvist J. Long-term evaluation of extensive restorations in permanent teeth. *J Dent* 2003;31(6):395-405.

#### **D. U.S. Food and Drug Administration (FDA) and dental amalgam**

- 24) About Dental Amalgam Fillings. Available at:  
<http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DentalProducts/DentalAmalgam/ucm171094.htm>. Accessed: 9/22/10.
- 25) FDA. Class II Special Controls Guidance Document: Dental Amalgam, Mercury, and Amalgam Alloy. July 28, 2009; Available at:  
<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073311.htm>.

- 26) FDA. FDA Issues Final Regulation on Dental Amalgam. July 28, 2009; Available at: <http://www.fda.gov/NewsEvents/Newsroom/Pressannouncements/ucm173992.htm>. Accessed 9/22/10.
- 27) Plans to review regulation of dental amalgam. June 10, 2010; Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm215061.htm>. Accessed 7/26/10.
- 28) Dental Products Panel of the Medical Devices Advisory Committee; Notice of Meeting. 75 Federal Register 33315 (2010-06-11).
- 29) National Research Council (U.S.) Committee on Improving Risk Analysis Approaches Used by the U.S. EPA, Board on Environmental Studies and Toxicology, Division of Earth and Life Sciences. Science and Decisions: Advancing Risk Assessment. Washington, DC: National Academies Press; 2009.

**E. U.S. Environmental Protection Agency (EPA) and dental amalgam**

- 30) EPA. EPA will propose rule to protect waterways by reducing mercury from dental offices - Existing technology is available to capture dental mercury. September 27, 2010; Available at: <http://yosemite.epa.gov/opa/admpress.nsf/e77fdd4f5afd88a3852576b3005a604f/a640db2ebad201cd852577ab00634848!OpenDocument>. Accessed 9/30/2010.
- 31) ADA, NACWA, & EPA. Memorandum of Understanding on Reducing Dental Amalgam Discharges. December 23, 2008; Available at: [http://water.epa.gov/scitech/wastetech/guide/dental/upload/2008\\_12\\_31\\_guide\\_dental\\_mou.pdf](http://water.epa.gov/scitech/wastetech/guide/dental/upload/2008_12_31_guide_dental_mou.pdf). Accessed 9/30/2010.

## **A.1 Recent policy statements and reviews from major organizations:**

- (1) Life Sciences Research Office. Review and analysis of literature on the health effects of dental amalgam: Executive Summary. 2003; Available at: [http://www.lsro.org/amalgam/frames\\_amalgam\\_report.html](http://www.lsro.org/amalgam/frames_amalgam_report.html). Accessed 9/15/10.
- (2) ADA. Literature Review: Dental Amalgam Fillings and Health Effects. July, 2009; Available at: <http://www.ada.org/1741.aspx>. Accessed 8/31/10.
- (3) Brownawell AM. The potential adverse health effects of dental amalgam. *Toxicological Reviews* 2005;24(1):1.

LSRO conducted an independent review of recent scientific literature at the request of several U.S. agencies, including the NIDCR and CDC. The findings of this report were summarized in an Executive Report (1) and in a peer-reviewed article (3). The article is a concise, yet thorough, review of dental amalgam, its role as a source of elemental mercury exposure, and the known effects of this exposure. It also includes a review of human exposure to methylmercury, which occurs primarily through the consumption of fish and other contaminated seafood, and how this interrelates with exposure from dental sources. The authors discuss the nonspecific psychological and physiological effects that are sometimes attributed to dental amalgam (e.g., fatigue, depression, loss of mental acuity, etc) are not the same as adverse reactions known to occur in cases of occupational exposure. These specific, “well defined set of effects” include tremor, stomatitis, hearing loss, and renal impairment (3).

The LSRO report, along with an updated literature review by the ADA in 2009 (2), represent current, thorough reviews of the recent scientific evidence regarding dental amalgam safety. The LSRO report examined peer-reviewed publications from 1996 through 2003, and the ADA update reviewed publications from 2004 through May, 2008. The ADA’s objective was to identify new studies that addressed research gaps identified in the LSRO’s report to determine whether new information could be added to the body of knowledge regarding amalgam safety

The LSRO report concluded that recent, peer-reviewed studies “did not reveal sufficient evidence to support a causal relationship between dental amalgam restorations and human health problems” besides rare instances of allergic reaction (3). The ADA review found that several studies published between 2004 and 2008 – notably related to the New England Children’s Amalgam Trial and the Casa Pia study – demonstrated “no consistent evidence of harm”, including from use of dental amalgam in young children (2).

These reports present a detailed outline of currently available evidence, as well as major gaps in research knowledge. LSRO calls for studies of low-level exposure to mercury vapor, better designed studies of exposure to mercury vapor and its effects among dental professionals. Allergic sensitivities to mercury in dental patients are rare, but studies of potential genetic sensitivities to mercury are needed. The ADA reviewed recent research that has found no evidence of genetic susceptibility to mercury and that studies in children have no found no evidence of harm. More studies are needed to study the effects of mercury exposure in dental professionals and the secretion of mercury from breast milk.

(4) ADA Council on Scientific Affairs. Statement on Dental Amalgam. August, 2009; Available at: <http://www.ada.org/1741.aspx>. Accessed 9/2/10.

This statement cites several sources, most of which are included in this bibliography, to support their position that amalgam is a “valuable, viable and safe choice for dental patients” and the importance of ongoing research.

(5) Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The safety of dental amalgam and alternative dental restoration materials for patients and users. 2008; Available at: [http://ec.europa.eu/health/ph\\_risk/committees/04\\_scenih\\_r/docs/scenih\\_r\\_o\\_016.pdf](http://ec.europa.eu/health/ph_risk/committees/04_scenih_r/docs/scenih_r_o_016.pdf). Accessed 9/7/10.

This committee examined dental amalgam and its alternatives in regards to consumer safety and environmental effects. SCENIHR concludes that “there is no scientific evidence for risks of adverse systemic effects” in association with dental amalgam. Amalgam and alternative materials are rarely associated with local adverse effects such as allergies. The committee noted that the use of amalgam is declining, as aesthetics and minimally invasive techniques become more common.

(6) FDI. FDI Policy Statement: Safety of Dental Amalgam. October, 2007; Available at: <http://www.fdiworldental.org/sites/default/files/statements/English/Safety-of-dental-amalgam-2007.pdf>. Accessed 9/2/10.

This brief statement is similar to the SCENIHR conclusions; “there is no evidence to support an association between the presence of amalgam restorations and chronic degenerative diseases, kidney disease, autoimmune disease, cognitive function, adverse pregnancy outcomes or any non-specific symptoms.” The FDI statement includes citations from the NECAT and Casa Pia studies of amalgam restorations in children. Individual allergies to some component of amalgam are rare. Other restorative materials may have adverse effect, but this statement is not elaborated upon.

In a news release dated December 1, 2009, the FDI announced their participation in a joint meeting with the World Health Organization (WHO) and the United Nations Environmental Programme (UNEP) in November, 2009. At that meeting, FDI officials presented their position that “no ban or phase-down of mercury used in the dental profession should occur before a true alternative to dental amalgam is widely available in all countries.”<sup>1</sup>

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<sup>1</sup> FDI. FDI Participates at WHO/UNEP Meeting on Future Use of Materials for Dental Restoration. 12/1/2009; Available at: <http://www.fdiworldental.org/content/fdi-participates-whounep-meeting-future-use-materials-dental-restoration>, 9/30/2009.

(7) World Health Organization. Policy Paper: Mercury in Health Care. August, 2005; Available at: [http://whqlibdoc.who.int/hq/2005/WHO\\_SDE\\_WSH\\_05.08.pdf](http://whqlibdoc.who.int/hq/2005/WHO_SDE_WSH_05.08.pdf). Accessed 9/15/10.

The use of mercury in the healthcare industry represents a source of environmental contamination through wastewater and incineration. WHO advocates immediate development of better waste handling practices, and a long term ban on use of mercury-containing devices. Dental amalgam is cited as the major source of mercury vapor in non-industrialized settings, but is not singled out for any adverse effects other than as a source of environmental contamination.

(8) World Health Organization. Elemental mercury and inorganic mercury compounds: Human health aspects. 2003; Available at: <http://www.who.int/ipcs/publications/cicad/en/cicad50.pdf>. Accessed 9/15/10.

This lengthy report was based on the 1999 U.S. ATSDR (Agency for Toxic Substances and Disease Registry) document “Toxicological profile for mercury (update)”. Dental amalgams are discussed briefly as one of many sources of population mercury exposure. Most scientific citations regarding dental amalgam are from the 1990s.

(9) Rugg-Gunn AJ, Welbury RR, Toumba J, British Society of Paediatric Dentistry. British Society of Paediatric Dentistry: a policy document on the use of amalgam in paediatric dentistry. *Int J Paediatr Dent* 2001 May;11(3):233-238.

Improved mercury hygiene practices are called for by BSPD to reduce environmental contamination and “this is likely to be the main reason for Government action against the use of amalgam in the future”. This document provides a brief summary of actions taken by other European countries in regards to dental amalgam. The BSPD supports the position that “no restrictions should be placed upon the use of silver amalgam to restore children’s teeth”. Durability of several materials (e.g., amalgam, stainless steel crowns, composites, and glass ionomers) are compared for pediatric restorations.

(10) National Health and Medical Research Council, Australian Government. Dental Amalgam and Mercury in Dentistry - Report of an NHMRC Working Party. 2001; Available at: <http://www.nhmrc.gov.au/publications/synopses/d17syn.htm>. Accessed 9/3/10.

NHMRC recommended avoiding the use of amalgam in primary teeth. This recommendation was not derived from evidence, “but from a combination of uncertainty and application of general public and environmental health principles” that indicate a reduction of exposure to mercury where “safe and practical alternatives exist”. The report also suggested minimizing the use of amalgam in “susceptible population groups”, including children, pregnant women, and people with kidney disease.

However, it is worth noting that an Australian public information guide citing this report repeatedly states that there is no scientific evidence of harm from amalgam restorations, other than rare allergic reactions.<sup>2</sup> Information available from the Australian Dental Association website reiterates the safety of dental amalgam and opposes the replacement of amalgam restorations for any reason besides aesthetic concerns. The amalgam policy statement available from the ADA<sup>3</sup> discusses waste management concerns and does not contain any recommendations about the use of amalgam as a restorative material.

(11) Health Canada. The safety of dental amalgam. 1996; Available at: [http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/pubs/dent\\_amalgam-eng.php](http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/pubs/dent_amalgam-eng.php). Accessed 9/15/10.

Health Canada's recommendations parallel the recommendations of Australia. They also note that "current evidence does not indicate that dental amalgam is causing illness in the general population", but do assert that a small number of people may be "hypersensitive" to mercury. The government also supports the position that a total ban of amalgam is not called for, although reduced use of heavy metals is a sound environmental precaution.

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<sup>2</sup> NHMRC. Dental amalgam - filling you in: A guide to current thinking on the use of dental amalgam. Available at: [http://www.nhmrc.gov.au/files\\_nhmrc/file/publications/synopses/d18.pdf](http://www.nhmrc.gov.au/files_nhmrc/file/publications/synopses/d18.pdf). Accessed 9/15/10.

<sup>3</sup> Australian Dental Association I. Amalgam Waste Management: Policy Statement 6.11. November, 2007; Available at: [http://www.ada.org.au/app\\_cmslib/media/lib/1009/m256266\\_v1\\_policy%20statement%206.11%20amalgam%20waste%20management.pdf](http://www.ada.org.au/app_cmslib/media/lib/1009/m256266_v1_policy%20statement%206.11%20amalgam%20waste%20management.pdf). Accessed 9/30/2010.

## A.2 Positions Supported by Other U.S. Agencies

(12) CDC. Dental Amalgam Use and Benefits. 5/28/2010; Available at: <http://www.cdc.gov/OralHealth/publications/factsheets/amalgam.htm>. Accessed 9/24/10.

This fact sheet describes the components of dental amalgam and safety concerns associated with its use. The CDC refers to the LSRO literature review(1), the Casa Pia study (14, 15) and the New England Children’s Amalgam Trial(16) to support their position that there is “little evidence of any health risk”, including when used in children, and no health benefits to removing existing amalgam restorations. The CDC fact sheet state that the use of amalgam as a restorative material is declining due to reduced caries rates and the use of aesthetic alternatives.

The CDC refers to the FDA’s reclassification of dental amalgam and its role in helping consumers make informed decisions about dental amalgam restorations.

(13) NIDCR. Studies Evaluate Health Effects of Dental Amalgam Fillings in Children. 4/18/2006; Available at: <http://www.nidcr.nih.gov/Research/ResearchResults/NewsReleases/ArchivedNewsReleases/NRY2006/PR04182006.htm>. Accessed 9/24/2010.

This press release from the NIDCR/NIH announces the findings from the Casa Pia study and the NECAT(14-16), which are reported in the *Journal of the American Medical Association*. Both studies found that children who received amalgam restorations had higher urinary mercury levels, but these levels were low and were not associated with any symptoms of mercury poisoning. These two trials help fill research gaps about the safety of amalgam in children.

For a brief summary of the Casa Pia study (referred to in this document as “the Portuguese study”) and the NECAT (referred to as “the New England study”), this press release provides a concise overview of the studies’ designs and main findings.



## B. Recent clinical trials

The LSRO literature review (1,3) and its ADA update (2) offer summaries of recent studies of amalgam safety. A few publications related to major clinical trials will be summarized here.

Two recent, major clinical trials have examined amalgam safety in children: the Casa Pia study of dental amalgams in children, and the New England Children's Amalgam Trial (NECAT). The Casa Pia trial was conducted by the University of Washington and the University of Lisbon, Portugal – the main clinical site. The New England trial was conducted in two communities – one in Maine and one in Massachusetts. Both trials randomized children into two treatment groups: one group receiving amalgam posterior restorations, and one group receiving only composite restorations. The amalgam groups in both trials also received restorations of other types as indicated (i.e. for anterior restorations). Urinary mercury was used to measure mercury exposure in both trials.<sup>45</sup> Survival analyses from both studies are reviewed in a subsequent section of this bibliography – see Section C.

The Casa Pia study design and methods have been described in detail.<sup>4</sup> Findings from this study have been presented in several articles<sup>678</sup>; two major publications are summarized below (14, 15).

(15) DeRouen TA, et al. Neurobehavioral effects of dental amalgam in children: a randomized clinical trial. *JAMA* 2006;295(15):1784.

This article reports neurological and renal outcomes in a group of approximately 500 children who were randomized into amalgam and composite treatment groups. Average age of participants at baseline was approximately 10 years. The study hypothesis was that continual exposure to low levels of mercury from amalgam restorations would lead to worse neurobehavioral outcomes than in children with no history of amalgam exposure. Neurobehavioral outcomes included: memory, attention/concentration, and motor/visuomotor effects. Renal effects were assessed by measuring urinary glutathione transferase and porphyrin levels, and creatinine content. Urinary mercury levels were measured at baseline and at one-year intervals for seven years. After seven years, neurobehavioral outcomes were not significantly different between treatment groups. The authors report on nine adverse health events in both treatment groups, including deaths and major illnesses, and note that these do not demonstrate a pattern.

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<sup>4</sup> DeRouen TA, Leroux BG, Martin MD, 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;23(3):301-320.

<sup>5</sup> Children's Amalgam Trial Study Group. The Children's Amalgam Trial: design and methods. *Control Clin Trials* 2003 Dec;24(6):795-814.

<sup>6</sup> Woods JS, Martin MD, Leroux BG, et al. The contribution of dental amalgam to urinary mercury excretion in children. *Environ Health Perspect* 2007;115(10):1527-1531.

<sup>7</sup> Woods JS, Martin MD, Leroux BG, DeRouen TA, 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;108(3):393-399.

<sup>8</sup> Martin MD, Benton T, Bernardo M, et al. The association of dental caries with blood lead in children when adjusted for IQ and neurobehavioral performance. *Sci Total Environ* 2007;377(2-3):159-164.

Although neurobehavioral outcomes (including IQ) and nerve conduction performance did not differ between groups, children who were treated with dental amalgam had higher levels of urinary mercury at follow-up than children with no amalgam restorations, but levels remained within general background levels (<4 µg/L).

The authors note that this study was not designed to measure adverse outcomes related to the use of resin composite restorations – specifically, endocrine effects that have been reported as potential outcomes.

(15) Lauterbach M, Martins IP, Castro-Caldas A, 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;139(2):138.

This article describes secondary neurological outcomes assessed during the Casa Pia study. Secondary outcomes include hand tremor, along with neurological hard signs (NHSs) and neurological soft signs (NSSs), which may indicate problems with neurological development. For tremor and NHSs, outcome differences between children receiving amalgam versus composite-only varied from year to year in non-consistent directions in both groups, and were not significantly different.

Without adjusting for multiple comparisons, the authors note that NSSs were significantly less common among amalgam recipients – the opposite finding expected if mercury exposure was related to adverse effects. However, if adjustments for multiple comparisons between groups are made, this finding becomes non-significant.

To date, the Casa Pia trial has not found any adverse neurobehavioral effects associated with the constant, low levels of mercury exposure from amalgam restorations.

The design and methods used in the NECAT have been described in detail.<sup>5</sup> The findings from the NECAT have been presented in many articles<sup>9101112131415</sup>; one major publication is summarized below(16).

(16) Bellinger DC, Trachtenberg F, Barregard L, et al. Neuropsychological and renal effects of dental amalgam in children: a randomized clinical trial. *JAMA* 2006;295(15):1775-1783.

The primary outcome examined in the New England Children's Amalgam Trial was full-scale IQ, measured at baseline and after 3 and 5 years. Power calculations were used to design a study that could assess a 3-point change in IQ after 5 years. Biomarkers assessed included total mercury from urine and hair, blood lead levels, and urinary albumin levels. Hair mercury was included to control for exposure to mercury from dietary sources.

At baseline, 93% of participants had no detectable urinary mercury levels. After 5 years, 63% of the amalgam group and 45% of the composite group showed detectable urinary mercury levels. Overall, children in the amalgam group had higher mean urinary mercury levels than children in the composite group.

IQ change and change in the other neuropsychological outcomes from baseline to follow-up were not significantly different between groups. Interestingly, although not significantly different, the changes in all outcomes were favorable for the amalgam group versus the composite group. Renal function was assessed via urinary albumin and no significant differences were found between groups after five years. Adverse health events over the five-year study period were reported, and there were no significant differences in condition frequency between the two study groups.

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<sup>9</sup> Bellinger DC, Trachtenberg F, Daniel D, Zhang A, Tavares M, 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;138(9):1210-1216.

<sup>10</sup> Bellinger DC, Daniel D, Trachtenberg F, Tavares M, McKinlay S. Dental amalgam restorations and children's neuropsychological function: the New England Children's Amalgam Trial. *Environ Health Perspect* 2006;115(3):440-446.

<sup>11</sup> Barregard L, Trachtenberg F, McKinlay S. Renal Effects of Dental Amalgam in Children: The New England Children's Amalgam Trial. *Environ Health Perspect* 2007;116(3):394.

<sup>12</sup> 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* 2008;87(5):470-474.

<sup>13</sup> Maserejian NN, Trachtenberg FL, Assmann SF, Barregard L. Dental Amalgam Exposure and Urinary Mercury Levels in Children: The New England Children's Amalgam Trial. *Environ Health Perspect* 2007;116(2):256-262.

<sup>14</sup> Shenker BJ, Maserejian NN, Zhang A, McKinlay S. Immune Function Effects of Dental Amalgam in Children: A Randomized Clinical Trial. *J Am Dent Assoc* 2008;139(11):1496-1505.

<sup>15</sup> Maserejian NN, Tavares MA, Hayes C, Soncini JA, Trachtenberg FL. Prospective study of 5-year caries increment among children receiving comprehensive dental care in the New England Children's Amalgam Trial. *Community Dent Oral Epidemiol* 2009;37(1):9-18.

Overall, this study supports the findings from the Casa Pia trial: children receiving amalgam restorations had higher levels of urinary mercury, but no significant differences in neurological, behavioral, psychological, or renal function outcomes.

(17) Kingman A, Albers JW, Arezzo JC, et al. Amalgam exposure and neurological function. *NeuroToxicology* 2005;26(2):241-255.

Though not a clinical trial, findings from the U.S. Air Force Health Study are briefly discussed here. Kingman, et al., report on the prevalence of neurological signs in 1,663 U.S. military veterans and the association of these with long-term, low-dose mercury exposure from amalgam restorations. Data for this study come from the U.S. Air Force Health Study with dental examinations performed 1997-1998. Amalgam exposure was quantified by current tooth surfaces with amalgam restorations (TNAS – total number of amalgam surfaces). The number of tooth surfaces was categorized into a variable with four levels. No urinary or blood biomarkers of mercury exposure were used by this study.

No significant associations between amalgam exposure and neurological signs were found. This study was a cross-sectional study. Limitations include inability to account for past amalgam history, which may have resulted in exposure classification bias, and the inability to include biomarker measures.

### **C. Survival studies of amalgam and alternative materials**

(18) 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):775-783.

This article presents survival rates for posterior amalgam and composite restorations placed at baseline of the Casa Pia Study of amalgam safety in children. Restorations were considered failures if they needed to be replaced during the seven year study period.

After 7 years, 10% of 1,748 posterior restorations had failed. The 7-year survival rate was 94.4% for amalgams and 85.5% for composites. When the authors compared survival rates for restorations with different characteristics (i.e. size, number of surfaces), amalgam restorations performed better than composites of all types.

Restorations failed due to either secondary (recurrent) caries or fracture. Fracture failures occurred at equal proportions in amalgams and composites. Composite restorations were more likely to fail due to secondary caries than amalgams; approximately 78% of these failures occurred in composites. After adjusting for patient age, sex, tooth and restoration characteristics, the overall risk of secondary caries was 3.4 times greater in composites than in amalgams.

Given their findings, the authors conclude that posterior amalgam restorations perform better than composite ones – especially in large, multi-surface restorations.

(19) Beazoglou T, Eklund S, Heffley D, Meiers J, Brown LJ, Bailit H. Economic impact of regulating the use of amalgam restorations. *Public Health Rep* 2007;122(5):657-663.

The authors calculated costs that would be incurred if amalgam restorations were banned in various populations: the entire U.S. population, only children, or children and women of childbearing age. It was assumed that such a ban would result in an increase in the price of dental restorations due to the higher cost associated with placing composite, and a decrease in the total demand for restorations due to this increased cost. Dental insurance claim data from Delta Dental of Michigan, Ohio, and Indiana were used to estimate the number of amalgams, composites, and crowns placed nationally in 2005. ADA survey data were used to estimate average restoration costs and validate the estimates obtained from the Delta claims.

If amalgam restorations were banned only in children, the estimated first year impact would be a \$1.1 billion increase in dental expenditures, and almost \$13 billion over a 15-year period (2005 through 2020). If amalgams were banned in the entire population, the estimated first year impact would be an \$8.2 billion increase in dental expenditures, and over \$98 billion after 15 years. The authors note that the increase in restoration price (approximately \$52) for composites would place the largest strain on low-income families. A total ban on amalgam restorations would result in an estimated annual loss of service of \$15.4 million – the result of fewer restorations being placed.

(20) Opdam NJM, Bronkhorst EM, Loomans BAC, Huysmans MC. 12-Year survival of composite vs. amalgam restorations. *J Dent Res* 2010;89(10):1063-1067.

This study has major limitations that limit generalizability of its results. The authors conducted a chart review of a single general dentist to evaluate the survival rates for composite and amalgam posterior restorations. Overall, 12-year survival rates were better for composite restorations, although amalgam survival was better in patients with high caries risk.

The better survival rates for composite restorations are not surprising given the study design: the authors excluded from analysis composite restorations that were placed with a glass ionomer liner, which the authors state is associated with increased restoration failure – probably because this is used with more invasive and extensive restorations. Additionally, the dentist who placed the restorations only used composite after 1995, but prior to that period, could use either amalgam or composite for restorations. If amalgam was chosen for more extensive restorations in the earlier time period, and extensive composite restorations requiring glass ionomer liners were excluded from analysis, the findings from this study may be biased: the composite restorations included in analysis may be from teeth that were systematically chosen as less compromised at the initial time of treatment. One other characteristic of this study design limits the comparisons that can be made between amalgam and composite restorations: restorations that required replacement, repair, or extraction were all considered failure. The authors did not differentiate between types of failure.

(21) Simecek JW, Diefenderfer KE, Cohen ME. An evaluation of replacement rates for posterior resin-based composite and amalgam restorations in US Navy and Marine Corps recruits. *J Am Dent Assoc* 2009;140(2):200-209.

Overall, the design of this study limits generalizability. However, the introduction of this article provides a good review of 12 recent studies that have compared the longevity of posterior amalgam versus composite restorations. Of the 12 studies they reviewed, 9 suggested that amalgam was superior to composite, while 3 suggested that composite was equivalent or superior to amalgam. The major concerns associated with the use of composite in posterior restorations, as identified by the authors, are the increased risk of secondary caries and the shortened expected survival time versus amalgams.

This study used the dental records of 2,780 military recruits over at least a two-year period, until each participant had undergone at least two follow-up exams. Restorations that were considered clinically acceptable at baseline were followed for failure during the study period. Because this was a chart review, and composite restorations are difficult to distinguish from glass ionomers, pre-existing glass ionomer restorations were grouped with composites.

Overall, 17% of composites and 14% of amalgams required replacement during the follow-up period. After controlling for reasons for replacement, tooth and restoration characteristics, and individual caries risk, replacement rates were higher for composites than amalgams.

This study has major limitations due to the fact that there was no way of knowing when the original restorations were placed. If one group of restorations was placed earlier than another (and therefore expected to fail earlier), then the results of this survival analysis would be biased.

(22) 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;138(6):763-772.

This article evaluated the rates of replacement and repair for amalgam and composite or compomer restorations in primary and permanent teeth placed during the NECAT study. Study participants were followed from baseline for approximately five years. At baseline, children were aged 6 to 10 years, had no prior or existing amalgams, and required at least 2 posterior restorations. Restorations were repaired if they had defective margins and replaced if they developed secondary caries.

Overall, the difference in replacement rates between amalgam restorations versus composite/compomere restorations was not statistically significant. However, the survival analysis showed a widening in the gap between the two classes of materials which suggests that amalgams may perform significantly better if the follow-up time was extended. In permanent posterior teeth, composite restorations had significantly greater repairs than amalgams, but replacement rates were not significantly different.

(23) Van Nieuwenhuysen JP, D'Hoore W, Carvalho J, Qvist J. Long-term evaluation of extensive restorations in permanent teeth. *J Dent* 2003;31(6):395-405.

This prospective study compared the survival of extensive amalgam and composite restorations. Survival of these restorations was also compared with full coverage crowns. All teeth in this study had been previously restored; 60% of them had previous endodontic treatment. Restoration with a cast crown was the preferred restoration in most cases, but patients had the option of receiving a large amalgam or composite restoration.

Overall, amalgam restorations had better median survival times than composite restorations. However, crowns performed better than either large composite or amalgam restorations. Several factors were significantly associated with restoration longevity, including size of the restoration, patient age, and the use of base material – all showing a positive association with the risk of restoration failure.

#### **D. U.S. Food and Drug Administration (FDA) and dental amalgam**

(24) About Dental Amalgam Fillings. Available at: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DentalProducts/DentalAmalgam/ucm171094.htm>. Accessed: 9/22/10.

The FDA public information about amalgam fillings provides information about the benefits and potential risks of this material. Noted benefits are that this material is long-lasting and the “least expensive type of filling material”. Potential risks are related to the fact that dental amalgam contains elemental mercury which is released as mercury vapor. The FDA considers amalgam to be safe in people over age 6, based on existing clinical evidence. There is limited clinical evidence about its safety in pregnant women and children under age 6. However, FDA concludes that the estimated daily dose of mercury vapor in nursing infants and children under 6 are below levels that the EPA and CDC consider safe.

(25) FDA. Class II Special Controls Guidance Document: Dental Amalgam, Mercury, and Amalgam Alloy. July 28, 2009; Available at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073311.htm>.

(26) FDA. FDA Issues Final Regulation on Dental Amalgam. July 28, 2009; Available at: <http://www.fda.gov/NewsEvents/Newsroom/Pressannouncements/ucm173992.htm>. Accessed 9/22/10.

In July, 2009 the FDA issued new regulatory guidelines for dental amalgam. This document and the related press release describe the classification of dental amalgam as a Class II medical device (moderate risk) subject to special controls. Dental amalgam was previously not classified by the FDA as a medical device; however, its constituent materials – elemental mercury and alloy powder – had been originally classified as class I (mercury, low risk) and class II (alloy powder). This regulation also reclassified elemental mercury as Class II.

These guidelines called for product labeling that includes a warning against use of amalgam in individuals with mercury allergies, a warning to use proper ventilation when working with the material, and a statement “discussing the scientific evidence on the benefits and risk of dental amalgam, including the risks of inhaled mercury vapor” to that informed decisions could be made by patients and dentists. Labeling guidelines are described in detail in the control document (25).

Regarding the FDA classification of medical devices: Class II devices are those that are under such “special controls”. Class I devices are considered low risk and subject to “general controls”. Class I dental devices include gutta percha, facebows, and intraoral wax. Class II dental devices include composite resins, bonding agents, and dental cement. See [www.hhs.gov](http://www.hhs.gov) for more information about classification of medical and dental devices.



Dental amalgam risks that are identified in the controls document by the FDA include allergic response, mechanical failure, corrosion, contamination, improper use, and exposure to mercury (25). Risks associated with amalgam components (mercury and alloy powder) are subsets of the total risks associated with amalgam.

The FDA recommends the following statement (not shown in its entirety) be used to label amalgam regarding its use by dental professionals:

“Dental amalgam has been demonstrated to be an effective restorative material that has benefits in terms of strength, marginal integrity, suitability for large occlusal surfaces, and durability. Dental amalgam also releases low levels of mercury vapor, a chemical that at high exposure levels is well-documented to cause neurological and renal adverse health effects. Mercury vapor concentrations are highest immediately after placement and removal of dental amalgam but decline thereafter.

Clinical studies have not established a causal link between dental amalgam and adverse health effects in adults and children age six and older. In addition, two clinical trials in children aged six and older did not find neurological or renal injury associated with amalgam use.”

(27) Plans to review regulation of dental amalgam. June 10, 2010; Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm215061.htm>. Accessed 7/26/10.

This news release announced an advisory panel to be held December 14-15, 2010 to review the regulation of dental amalgam as a medical device. The meeting will focus on the use of amalgam in vulnerable populations, including pregnant women and young children. The concerns that will be addressed by this panel include ones raised by petitions about the “adequacy of the risks assessment method” used in the classification of amalgam, bioaccumulation of mercury, exposure of pediatric populations to mercury, and adequacy of clinical trials.

Links to the petitions submitted to the FDA related to this review are provided. These petitions generally call for amalgam to be either banned or designated as a Class III device. If placed into Class III, they call for amalgam use to be banned in pregnant and nursing women, young children, and other specific population groups. One petition calls for informed consent to be obtained by dentists before placing amalgam restorations. Another petition (Moms Against Mercury, et al.) calls for a risk assessment of mercury vapor based on recent EPA and NAS methods.

(28) Dental Products Panel of the Medical Devices Advisory Committee; Notice of Meeting. 75 Federal Register 33315 (2010-06-11).

This notice for an advisory committee meeting on December 14-15, 2010 includes a reference to the new risk assessment guidelines issued by the National Academy of Sciences (described in the following section).

(29) National Research Council (U.S.) Committee on Improving Risk Analysis Approaches Used by the U.S. EPA, Board on Environmental Studies and Toxicology, Division of Earth and Life Sciences. Science and Decisions: Advancing Risk Assessment. Washington, DC: National Academies Press; 2009.

This report provides recommendations to the EPA to improve their risk-analysis approaches. Risk analysis is used in public health settings to inform policy decisions, and the committee that developed this report issued near and long term recommendations to improve the risks assessment process.

This document offers a framework for risk-based decision making for problems that affect environmental conditions and includes guidelines for handling uncertainty in risk assessment (p.243).

## E. U.S. Environmental Protection Agency (EPA) and dental amalgam

(30) EPA. EPA will propose rule to protect waterways by reducing mercury from dental offices - Existing technology is available to capture dental mercury. September 27, 2010; Available at: <http://yosemite.epa.gov/opa/admpress.nsf/e77fdd4f5afd88a3852576b3005a604f/a640db2ebad201cd852577ab00634848!OpenDocument>. Accessed 9/30/2010.

The EPA has announced plans to propose a rule requiring dental offices to install amalgam separators, in order to reduce environmental discharge of amalgam. This rule is expected to be finalized in 2012; until that time, the EPA recommends dental offices to begin voluntarily installing separators.

This proposed rule follows the 2008 Memorandum of Understanding (MOU) between the EPA Office of Water, the American Dental Association, and the National Association of Clean Water Agencies (NACWA) to initiate a Voluntary Dental Amalgam Discharge Reduction Program (described below).

(31) ADA, NACWA, & EPA. Memorandum of Understanding on Reducing Dental Amalgam Discharges. December 23, 2008; Available at: [http://water.epa.gov/scitech/wastetech/guide/dental/upload/2008\\_12\\_31\\_guide\\_dental\\_mou.pdf](http://water.epa.gov/scitech/wastetech/guide/dental/upload/2008_12_31_guide_dental_mou.pdf). Accessed 9/30/2010.

This 2008 MOU provided the ADA flexibility in encouraging the voluntary use of amalgam waste best management practices (BMPs) by dental offices. These voluntary BMPs gave the dental sector “a lower priority for effluent guidelines” by the EPA, since voluntary actions can potentially achieve a significant reduction in amalgam discharge.

The MOU states that the ADA was to produce a report describing the use of amalgam separators by dentists nationally, and that the issue of regulating amalgam waste practices would be revisited by the EPA in the near future.

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