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**Editorials**

# Environmental metals and cardiovascular disease

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Metals are an important but neglected source of CV risk

Evidence on the role of environmental metals in cardiovascular disease has rapidly increased over the past two decades. In a linked article, Chowdhury and colleagues (doi:10.1136/bmj.k3435) present a comprehensive systematic review and meta-analysis of the associations between the exposure to arsenic, lead, cadmium, mercury, and copper and the risk of cardiovascular disease.**1** The first four metals were selected because of widespread population exposure and inclusion in the World Health Organization's priority list of chemicals of major public health concern. Copper was selected because of previous mechanistic links with atherosclerosis.

Analyses of data from about 350 000 people from 37 countries showed that exposures to arsenic, lead, cadmium, and copper are associated with an increased risk of cardiovascular disease incidence and mortality. This is an important call for attention to an emerging group of risk factors with a high prevalence in populations around the world.

Chowdhury and colleagues paid special attention to the dose-response effect between exposure to metals and cardiovascular disease. Most associations were linear, with no clear lower threshold for toxicity. However, the number of studies in populations with low levels of exposure remains insufficient to reach firm conclusions on the shape of the dose-response curve at low levels. This is critical information for public health authorities and should be a priority for future research.

The study reported no association between mercury exposure and cardiovascular disease. Methylmercury contamination of fish is the primary source of mercury in most populations and these null results must be interpreted carefully, given the complexity of fish intake and the large number of potential confounders of this

Experimental studies evaluating the role of metals as disruptors of redox, epigenetic, and endocrine pathways support the causal role of metals in atherosclerosis.[2][3][4] Other lines of evidence include a double blind randomized trial suggesting that chelation therapy, which increases urinary excretion of heavy metals, may provide some benefit in secondary prevention of cardiovascular disease,[5] and a genomic study reporting an association between *AS3MT*, the major gene involved in arsenic methylation and believed to influence arsenic toxicity, with cardiovascular disease.[6]

The US conducts nationally representative biomonitoring of arsenic, lead, cadmium, and mercury through regular National Health Nutrition and Examination Surveys (NHANES). These surveys document a marked reduction in population exposure to lead and cadmium (the metals monitored for longest), largely reflecting large scale public health policies on the control of tobacco, reduction of air pollution, remediation of hazardous waste, renovation of drinking water infrastructures, and banning of lead in gasoline.[7][8]

Concomitant with these reductions, cardiovascular mortality rates in the US decreased by 43% from 1988-94 to 1999-2004. [9] An analysis that accounted for traditional cardiovascular disease risk factors, showed that 32% of this reduction in cardiovascular mortality could be explained by the decline in lead and cadmium exposures.[9] The health impact of recent reductions in arsenic exposure,[10] however, has not been evaluated.

Exposure to environmental metals remains substantial because of widespread soil contamination; persistence of past uses (house paint and plumbing for lead); continuing industrial uses (plastics and batteries); and presence in tobacco and tobacco smoke, drinking water and ambient air, and dust near industrial sources and waste sites.[7][8] Cadmium content in fertilizers provide an additional exposure pathway through diet and tobacco since vegetables and grains bioconcentrate cadmium. Emerging tobacco products such as electronic cigarettes also increase metal exposure.[11] The main source of metals in electronic cigarettes seems to be the heating coil, from where metals leach into the inhaled aerosol. [11] In low and middle income countries, including many countries in Africa and Asia, exposure to high levels of arsenic and lead is still a serious threat to public health that requires urgent action.[12][13][14]

Despite widespread distribution of toxic metal contaminants, technical reports from environmental and public health agencies often disregard the mounting evidence of associated cardiovascular risk.[15][16] Similarly, metal exposures are neglected by the organizations that produce cardiovascular prevention guidelines. The evidence indicates a clear need to minimize unnecessary metal exposures.

In communities affected by disproportionate environmental and occupational exposure, surveillance systems should monitor metal biomarkers and cardiovascular disease events and implement cardiovascular disease prevention programs. Since metals are associated with cardiovascular disease even at relatively low levels of exposure, population wide strategies to minimize exposure can further contribute to overall cardiovascular prevention efforts.

# Footnotes

- Research, doi: 10.1136/bmj.k3435
- Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: none.

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