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# Ambient air pollution epidemiology systematic review and meta-analysis: A review of reporting and methods practice

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ABSTRACT

*Background:* Systematic review and meta-analysis (SRMA) are increasingly employed in environmental health (EH) epidemiology and, provided methods and reporting are sound, contribute to translating science evidence to policy. Ambient air pollution (AAP) is both among the leading environmental causes of mortality and morbidity worldwide, and of growing policy relevance due to health co-benefits associated with greenhouse gas emissions reductions.
*Objectives:* We reviewed the published AAP SRMA literature (2009 to mid-2015), and evaluated the consistency of methods, reporting and evidence evaluation using a 22-point questionnaire developed from available best-practice consensus guidelines and emerging recommendations for EH. Our goal was to contribute to enhancing the utility of AAP SRMAs to EH policy.
*Results and discussion:* We identified 43 studies that used both SR and MA techniques to examine associations between the AAPs $PM_{2.5}$, $PM_{10}$, $NO_2$, $SO_2$, CO and $O_3$, and various health outcomes. On average AAP SRMAs partially or thoroughly addressed 16 of 22 questions (range 10–21), and thoroughly addressed 13 of 22 (range 5–19). We found evidence of an improving trend over the period. However, we observed some weaknesses, particularly infrequent formal reviews of underlying study quality and risk-of-bias that correlated with lower frequency of thorough evaluation for key study quality parameters. Several other areas for enhanced reporting are highlighted.
*Conclusions:* The AAP SRMA literature, in particular more recent studies, indicate broad concordance with current and emerging best practice guidance. Development of an EH-specific SRMA consensus statement including a risk-of-bias evaluation tool, would be a contribution to enhanced reliability and robustness as well as policy utility.



## 1. Introduction

The last decade has seen a marked increase in the use of systematic review and meta-analysis (SRMA) techniques in environmental health (EH) epidemiology. SRMA provides a transparent, thorough and replicable examination of available evidence that can offset the challenges of small sample size, identify and account for bias, demonstrate where effects are consistent across studies and generalizable across populations, and highlight research gaps (Woodruff and Sutton, 2014). Provided methods used are sound, this makes SRMA a valuable tool for translating a body of science findings into recommendations for health-protective decision- and policy-making (Moher et al., 2012), through contribution to health impact assessments, burden of disease estimates, cost-benefit analysis and other approaches. Use of SRMA in EH is relatively recent compared to other fields such as clinical medicine that have refined these methods over several decades, including through the Cochrane Collaboration (Higgins and Green, 2008). This is due in part to the typical EH evidence base which – given the difficulty of conducting randomized controlled trials for environmental contaminants in human populations – is reliant on observational studies that present a number of methodological challenges to pooling findings (Dickersin, 2002). These include inability to fully control for confounders, inconsistencies across studies in exposure metrics, and differences in outcomes, populations and study designs (Woodruff and Sutton, 2011; Rooney et al., 2014).

In the mid-1990s an expert group defined recommendations for use of SRMA that addressed many of the specificities of EH observational epidemiology (Blair et al. 1995), although these were not widely adopted as a formal guideline. While no specific consensus statement for use of SRMA in EH epidemiology is currently available, the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement

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(Moher et al., 2009) and the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) Statement (Stroup et al., 2000) provide a basis for best-practice guidance. More recently, several inter-related efforts have brought about development, piloting and implementation of updated EH-specific SRMA methods. These include initiatives by the US Environmental Protection Agency (EPA) under its Integrated Risk Information System (IRIS) program (NRC 2011; NRC 2014; US EPA, 2014); by the US National Institutes of Environmental Health Sciences (NIEHS) National Toxicology Program (NTP) for its chemical assessments (Rooney et al., 2014); and by the Navigation Guide group, an interdisciplinary collaboration between academicians, practitioners, and clinicians (Woodruff and Sutton, 2011; Lam et al., 2014; Vesterinen et al. 2015) designed to improve the reliability and robustness of EH SRMAs, by incorporating risk-of-bias analysis and evaluation of strength-of-evidence.

Reviews of reporting and methods used in SRMAs have been published in several fields where the techniques are used as a means of comparing with best-practice, identifying strengths and areas for further development with a goal of enhancing the robustness and policy-utility of SRMAs (McElvenny et al. 2004; Brugha et al., 2012; Sheehan and Lam, 2015). As an example, the PRISMA statement evolved as a result of several sequential reviews of the quality of methods and reporting in the clinical medicine SRMA literature (Sacks et al. 1996; Moher et al. 1999). We had previously reviewed the methods and reporting used in 48 EH epidemiology SRMAs published over the period 1990 to mid-2013 and found a high degree of concordance with PRISMA and MOOSE guidelines and the Blair et al. (1995) recommendations; however, we also identified a number of gaps (in particular inconsistent SRMA reporting on use of exposure metrics and their comparability in underlying studies) and highlighted the need for development of EH-specific consensus SRMA guidelines (Sheehan and Lam, 2015).

Air pollution is the world's largest environmental health risk, accounting 1 in 8 deaths worldwide in 2012 (WHO, 2015a), with nearly half of the burden due to ambient, or outdoor air pollution (AAP; WHO, 2014). AAP is now also considered a leading environmental cause of lung cancer (IARC, 2013). AAP is commonly defined to include particulate matter of aerodynamic diameter $<2.5$ μm ($PM_{2.5}$) or $<10$ μm ($PM_{10}$), as well as carbon monoxide (CO), ground-level ozone ($O_3$), nitrogen dioxide ($NO_2$), and sulfur dioxide ($SO_2$). Human respiratory, cardiovascular and other health impacts of AAP have been extensively examined in epidemiological studies, and synthesized through use of SRMA, with a large number of reviews published in recent years (Cohen et al. 2005; WHO, 2014). Based in part on the AAP SRMA evidence base, the cost of AAP-related mortality and morbidity in Europe alone is estimated to exceed $1.5 trillion (WHO, 2015b).

AAP has also recently received increased policy attention because of its link to climate change. AAPs are largely emitted through burning of fossil fuels, a process that also releases carbon dioxide ($CO_2$), the largest component of greenhouse gas (GHG) emissions responsible for warming the Earth's surface and oceans and leading to climate change. Curtailing the use of fossil fuels may provide a double dividend: reduced $CO_2$ slowing the pace of global warming; as well as reduced AAPs preventing cardiovascular, respiratory and other disease (Bell et al., 2008; Haines et al., 2009). Commonly referred to as "co-benefits," these avoided costs to human health from AAP exposure can therefore also potentially play a role in underpinning policy decisions about GHG mitigation, including by providing specific dose- (or concentration)-response relationships needed to estimate likely population-wide benefits (Remais et al., 2014) as well as identify potentially vulnerable/susceptible populations. For example, based in part on such evidence anticipated AAP-related health co-benefits in Europe, the US, India and China have been shown to offset a large share of estimated GHG mitigation costs (Markandya et al., 2009; Jensen et al. 2013; Garcia-Menendez et al., 2015; Saari et al., 2015).

To our knowledge there is no recent review of the AAP SRMA literature examining its consistency with best-practice reporting and methods guidance. In order to contribute to further enhancing the utility of AAP SRMAs for the goal of health-protective policymaking, we reviewed the published SRMA literature addressing association of AAPs with adverse health outcomes in the general population, comparing methods and reporting used in practice with consensus SRMA recommendations and newly-emerging EH-specific guidance.

## 2. Methods

We searched Medline using PubMed with the pollutant search terms "ambient air pollution," "indoor air pollution," "particulate matter," "PM2.5," "black carbon," "PM10" "nitrogen dioxide," "NO2," sulfur dioxide," "SO2," "ozone," "O3," "carbon monoxide," and terms for systematic review and meta-analysis. We chose a start-date of 2009 to reflect the publication date of the PRISMA consensus reporting guidelines, a date also corresponding to a marked increase in publication of SRMAs in EH epidemiology (Sheehan and Lam, 2015). Our end-date was June 15, 2015. We did not restrict by language. We also hand-searched using reference lists.

We screened all resulting titles and abstracts and reviewed full texts of articles that met our pre-determined inclusion criteria: general, non-occupational populations, with exposure to one or more of the six commonly-measured AAP components – $PM_{2.5}$ (including black carbon), $PM_{10}$, CO, $O_3$, $NO_2$, $SO_2$ – addressing one or more health outcomes determined by study authors as adverse (including early markers of disease). To maintain the focus on AAP, we excluded SRMAs examining exposure to secondhand smoke, wildfire smoke, household or indoor sources of air pollution, PM chemical constituents, and acute poisonings. To preserve our focus on exposure-outcome association, we excluded reviews whose main outcome was effect modification or evaluation of the shape of distributions. Because our goal was to evaluate use of SRMA methods and reporting, we included only reviews for which SRMA was the main goal, and which used both SR and MA techniques; in other words, we excluded studies in which an SRMA was done as background to another study goal; and excluded SRs without MA (e.g., where available data were inadequate for a quantitative analysis), and MAs without SR (e.g., combining results across multi-center studies without an SR). We did not include studies for which only abstracts were available. Two authors (MS & JL) independently extracted data (differences were resolved by discussion and consensus), using purpose-designed data-extraction forms. Extracted data for each SRMA included: population characteristics, nature of AAP exposure, health outcomes, study designs used by underlying studies, and summary effect measures and confidence bounds, as well as responses to a questionnaire related to SRMA methods, reporting and strength of evidence evaluation.

The questionnaire included 22 items we consolidated from several sources of "good-practice" guidance for SRMAs, including the 27-item PRISMA checklist for SRMAs (Moher et al., 2009), the 35-point MOOSE consensus guidelines for SRMAs in observational epidemiology, the Blair et al. 1995 recommendations for EH SRMAs, as well as more recent emerging SRMA guidance for EH from the NTP (Rooney et al., 2014) and Navigation Guide (Woodruff and Sutton, 2014). In selecting the 22 items we aimed for a simple questionnaire that would incorporate the core recommendations in four domains: (i) SRMA article reporting, including implications of research; (ii) systematic review search, selection and extraction methods; (iii) meta-analytic statistical pooling methods and approaches to examining heterogeneity, study quality and risk of bias; and (iv) methods for evaluating the strength of evidence.

The 22 items, categorized into these four areas, include: (1) SRMA reporting (presence of six standard SRMA features including reported funding sources, table of underlying study characteristics; PRISMA study selection flow chart, forest plot of MA results by study, SRMA recommendations, and whether any SRMA guidelines were referenced); (2) systematic review literature search methods (four questions related to literature search, study selection and data extraction procedures);

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