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Review

Evaluating the application of multipollutant exposure metrics in air pollution health studies☆

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ABSTRACT

Background: Health effects associated with air pollution are typically evaluated using a single pollutant approach, yet people are exposed to mixtures consisting of multiple pollutants that may have independent or combined effects on human health. Development of exposure metrics that represent the multipollutant environment is important to understand the impact of ambient air pollution on human health.
Objectives: We reviewed existing multipollutant exposure metrics to evaluate how they can be applied to understand associations between air pollution and health effects.
Methods: We conducted a literature search using both targeted search terms and a relational search in Web of Science and PubMed in April and December 2013. We focused on exposure metrics that are constructed from ambient pollutant concentrations and can be broadly applied to evaluate air pollution health effects.
Results: Multipollutant exposure metrics were identified in 57 eligible studies. Metrics reviewed can be categorized into broad pollutant grouping paradigms based on: 1) source emissions and atmospheric processes or 2) common health outcomes.
Discussion: When comparing metrics, it is apparent that no universal exposure metric exists; each type of metric addresses different research questions and provides unique information on human health effects. Key limitations of these metrics include the balance between complexity and simplicity as well as the lack of an existing "gold standard" for multipollutant health effects and exposure.
Conclusions: Future work on characterizing multipollutant exposure error and joint effects will inform development of improved multipollutant metrics to advance air pollution health effects research and human health risk assessment.

Contents

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1. Introduction

Studies examining health effects associated with air pollution traditionally consider responses to individual pollutants, such as ozone (O_3), fine particulate matter ($PM_{2.5}$), and nitrogen dioxide (NO_2). Results of these single pollutant studies form the basis for air quality standards in the United States intended to protect public health with an adequate margin of safety under the Clean Air Act (U.S. Code, 1970). In reality, people are exposed to a combination of pollutants simultaneously, and there is uncertainty whether these pollutants act independently or in combination (in an additive, synergistic, antagonistic, or interactive manner) to affect human health. These combined effects of pollutant mixtures are likely not accounted for in traditional single pollutant health studies. Therefore, the scientific community has urged the extension of the current single pollutant risk assessment and risk management approach to account for multiple pollutants (Dominici et al., 2010; Hidy and Pennell, 2010; Johns et al., 2012; Mauderly et al., 2010; National Research Council, 2004).

Different approaches have been used to characterize independent and multipollutant exposures in epidemiologic analyses. In the past, epidemiologic studies have used co-pollutant models (e.g., including two pollutants as independent variables) to estimate health effects of single pollutants while adjusting for the concentration of additional pollutants (e.g., Tolbert et al., 2007). More recent studies, however, have developed and applied different types of multipollutant metrics (i.e., combining multiple pollutants into one variable) to represent exposure to various pollutant mixtures related to source emissions and/or specific classes of toxic pollutants. These metrics not only have the potential for providing a robust representation of multipollutant mixtures, they also reduce variable dimensions in an epidemiologic analysis that in turn can decrease effect estimate uncertainty that stems from the use of highly correlated, single pollutant exposure variables. While the development of multipollutant exposure metrics is possible, representing the multipollutant environment has been difficult considering that various pollutants are measured with different averaging times, units of measurement, and uncertainties. Furthermore, limited analysis exists on determining whether or not these advanced, multipollutant metrics capture the complex temporal or spatial patterns of personal or community-based exposure.

As multipollutant science continues to progress, it is important to identify metrics that are currently available and reveal research gaps. This article reviews existing approaches for estimating health effects of multipollutant exposure. Strengths and limitations for each approach are discussed, with attention to which approaches may be appropriate for specific aspects of multipollutant air quality health effects assessment.

2. Methodology

2.1. Study criteria

In this study, we identified and characterized different multipollutant exposure metrics used to study air pollution health effects in epidemiology and toxicology studies. We also reviewed other air quality tools, such as air quality indexes, which have utilized multipollutant approaches that can be used to inform future development of exposure metrics for use in health studies. We focused on studies that met the following criteria:

1) Focused on the development or application of a metric used to represent exposure to ambient air pollution
2) Included a metric that is constructed from ambient pollutant concentrations
3) Presented original data (i.e., excludes review articles)
4) Introduced a metric that has the potential for broad-scale application

Based on these criteria, we excluded studies that used multipollutant tools for characterizing air quality without considering an exposure or health effect aspect, and thus did not include source apportionment studies without a health or exposure component. Studies that focused on indoor or occupational air quality were excluded. We also excluded studies that used an individual pollutant as a larger indicator of a multipollutant mixture; examples include $PM_{2.5}$ as a multipollutant indicator for particle components or O_3 as a representative photochemical oxidant. Metrics that were constructed without using ambient air pollution concentrations were excluded; examples include GIS-based metrics such as location-specific annual average daily traffic counts (AADT) used to represent exposure to traffic pollution. Last, we only reviewed metrics that showed the potential for application to health studies in diverse contexts, rather than metrics developed for a specific location or situation.

2.2. Systematic review process

A comprehensive, systematic literature search following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) paradigm (Moher et al., 2009) was used to identify eligible studies/metrics to review. The PRISMA approach is a multi-stage screening process aimed at improving the transparency of reporting in scientific reviews. Fig. 1 displays the step-by-step systematic review approach used for assessing the eligibility of exposure metric studies. The first step of our systematic review involved an initial broad literature search within Web of Science and PubMed databases in April 2013 followed by an updated search in December 2013. The following search strings were used in 1) Web of Science (WOS) and 2) PubMed to identify studies relevant to multipollutant exposure and health effects.

1) Web of Science search string: (((TS = “multipollut*” OR TS = “multi-pollut*” OR TS = “apportion*”) AND (TS = “air” OR TS = “ambient”) AND TS = “health”) OR (TS = “air quality index” OR TS = “air pollution index”)) = 829 references.
2) PubMed search string: (((multipollut* OR multi-pollut* OR apportion*) AND (air OR ambient) AND health) OR (“air quality index” OR “air pollution index”)) = 390 references.

A total of 1219 studies were identified in the broad literature search. Overlapping studies identified in both WOS and PubMed literature searches were de-duplicated by removing one record from the original 1219 articles. An initial screening process was conducted on each article to select studies that met the review criteria (previously listed) based on article title and abstract. Following the initial screen, the remaining 108 articles were subjected to a full text screen to eliminate any irrelevant articles. Fourteen additional articles were identified independently outside of the search (e.g., either cited within a considered article or identified in presentations) and were included in the review. Based on our broad literature search and additional independent efforts to identify articles, a total of 53 studies were deemed eligible to review.

A relational search was also conducted to identify potentially relevant articles not found by the broad literature search. In the relational search, a computer algorithm retrieved all articles in WOS that cited any of the 53 eligible studies (either identified independently or in the broad literature search). These articles were ranked by how many of the 53 studies they cited, on the assumption that articles citing several studies were more likely to be relevant than articles citing only one study of the initial 53. References frequently citing the 53 eligible articles were subjected to initial and full text screens, similar to the approach used in the broad literature search. The algorithm was only applied to WOS, since PubMed does not provide the citation data needed for the algorithm. Three additional studies met the criteria using this search approach. Additionally, one study was identified during the peer-review process, resulting in a total of 57 articles reviewed in this paper. Additional information on “considered” and “cited” articles in this review can be found on the Health & Environmental Research

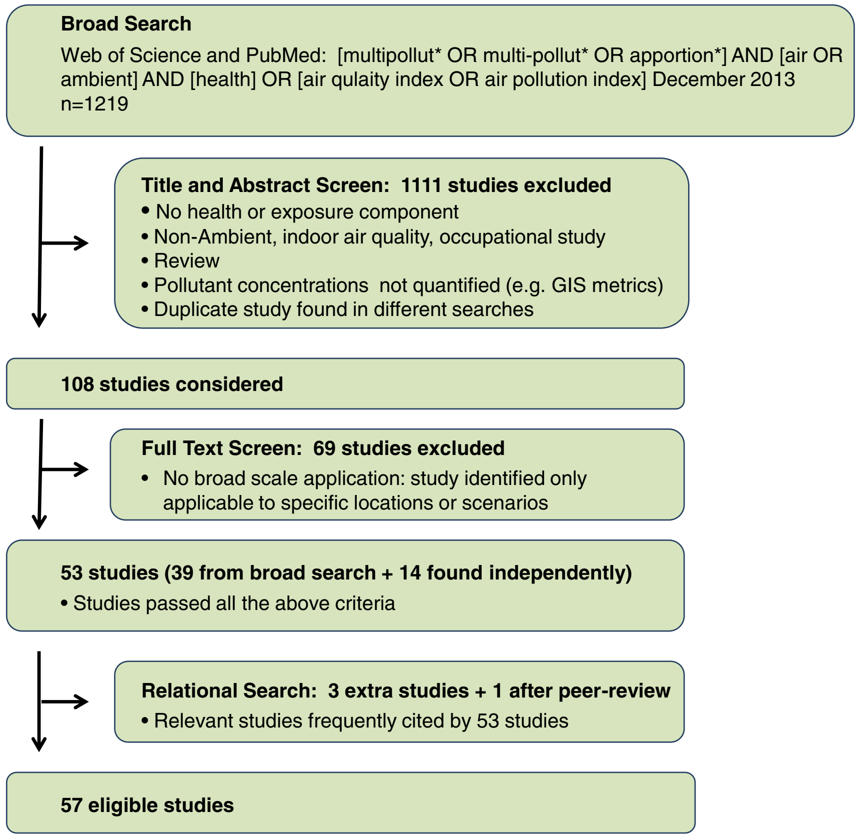

Fig. 1. Summary of literature search and review process.

Online (HERO) website (http://hero.epa.gov/index.cfm?action=litflow.viewProject&project_id=2306). HERO is an online database used by the National Center for Environmental Assessment at the U.S. Environmental Protection Agency to document literature search protocols for environmental chemical assessments and peer-reviewed journal publications.

3. Results

A variety of strategies for grouping pollutants into a multipollutant metric have been outlined in previous review papers (Hidy and Pennell, 2010; Mauderly et al., 2010). Pollutants can be grouped based on biological and/or chemical reactivity, common sources, joint atmospheric processing, and/or health effects. Conceptually, different grouping approaches apply to different scientific contexts (e.g., intervention, accountability, or epidemiology). Intervention and accountability studies are concerned with comparing different scenarios linked to changes in pollution levels, so grouping pollutants by sources may be more appropriate. Alternatively, epidemiologic studies are concerned with characterizing the relationship between exposure and health outcomes. Grouping by pollutant properties can target specific biological mechanisms associated with common health outcomes (e.g., cardiovascular effects).

Exposure metrics reviewed in this study are separated into two broad grouping paradigms based on 1) source emissions and atmospheric processes or 2) common health outcomes. For each metric, we initially discuss how it has been used in air quality or health analyses followed by a discussion of strengths and limitations. Table 1 broadly summarizes the concept, advantages, and disadvantages of each type of metric reviewed in this paper. Additionally, a table with details of key features from each study reviewed is included in the Supplemental information (Table S1).

3.1. Metrics based on source emissions or atmospheric processes

A significant portion of multipollutant research has focused on grouping pollutants based on their temporal patterns (e.g., atmospheric co-variance). This approach is predominantly used to estimate exposure to specific sources or atmospheric mixtures, assuming that pollutants with similar temporal profiles are co-emitted by common sources or undergo similar chemical and physical processes in the atmosphere. From an environmental management perspective, this approach can help identify important sources and mixtures which in turn assist the development of appropriate control strategies for air pollution mitigation. Several source-related metrics are available with varying levels of complexity, ranging from single pollutant marker species to more sophisticated multipollutant factors, clusters, or indicators. Ideally, a source-related metric should capture the spatiotemporal trends of a subset of pollutants within the source mixture.

3.1.1. Marker species

The use of single pollutant concentrations (i.e., marker species) from a central site monitor is the most basic way to represent exposure to source-related pollution. Numerous health studies have used marker species to estimate the exposures associated with major sources in urban areas, including vehicular traffic, coal-fired power plants, and crustal sources. An example of a typical marker species is nitrogen dioxide (NO_2) for traffic pollution. NO_2 is generally considered a robust marker, because it typically correlates well with the variability of traffic activity and concentrations of other constituents within the traffic mixture (Brook et al., 2007; Levy et al., 2014).

Though marker species provide adequate representation of sources in some cases, they can often oversimplify true exposure due to several limitations. First, a marker can be emitted by several sources within a sampling area and may not be specific to a sole source (Grahame and

Table 1
Available multipollutant exposure metrics.

Metric	Concept	Advantages	Disadvantages	Studies
Marker species	Using a single pollutant as a tracer or marker of a source	• Does not require advanced calculations • Relatively low uncertainty (only measurement error included)	• Simplistic representation of sources • Collinearity among single pollutants	Numerous (not reviewed in detail)
Source apportionment techniques	Groups pollutants based on their co-variability using statistical techniques or chemical transport models	• Can estimate quantitative source contribution • Useful for air quality management due to source quantification	• Analytical subjectivity • Requires advanced models • Result instability • Can require a-priori knowledge	Numerous, see review by Stanek et al. (2011)
Temporal or spatial clustering	Groups days or sites with similar pollutant mixtures using statistical technique	• Capable of assessing the entire mixture	• Analytical subjectivity • Requires advanced models • Requires a-priori knowledge • Only provides qualitative estimates	Austin et al. (2012) Gu et al. (2012) Austin et al. (2013)
Emission-based indicators	Weighted, normalized sum of source-related pollution	• Can estimate source contribution • Useful for air quality management due to source quantification • Easy to calculate	• Large uncertainties with emission inventories	Pachon et al. (2012)
Intake fraction	Ratio of pollutant mass inhaled to mass emitted; can be indicator of exposure/dose to source	• Can address changes in exposure due to emissions reduction	• Subject to uncertainties with model emissions and breathing rates	Bennett et al. (2002a,b) Levy et al. (2003) Greco et al. (2007)
Pollutant property groupings	Groups pollutant based on specific chemical properties	• Can address biological or chemical plausibility (i.e. mode of action pathways)	• Collinearity between the pollutants within the same class may be a problem • May not be related to exposure	Suh et al. (2011) Meng et al. (2013)
Mode of action	Groups pollutant based by common endpoint or key intermediate event	• Can address joint effects of pollutant mixture • Can address biological plausibility	• Collinearity among pollutants within the same class • May not be related for exposure	Ankely et al. (2010)
Health outcome-based metrics	Two pollutant mixture that best explain the association with health effects	• Address health impacts of a certain mixture • Integrates health data	• Use of p-value to determine the best mixture	Pachon et al. (2012)
Risk-based metrics	Air quality index that combines pollutants concentrations with direct or implicit epidemiologic data	• Integrates health data directly (epidemiologic results) or implicitly (through benchmark concentration values)	• Assumes an additive approach • Does not account for changes in PM composition	Stieb et al. (2005) Cairncross et al. (2007) Sicard et al. (2011) To et al. (2013) Swamee and Tyagi (1999) Kyrkilis et al. (2007) Plaia et al. (2013)

Hidy, 2004). Second, marker species may be highly reactive in the atmosphere and have complex spatial variability so that the variability of more stable pollutants within the source mixture is not captured. Such is the case with levoglucosan (a common marker for wood smoke burning) which is moderately reactive in the atmosphere and can be removed quickly from a pollutant mixture. Last, markers cannot address collinearity issues within health models, since pollutants are not combined to construct the metric.

3.1.2. Statistical techniques used to group pollutants

Recognizing the limitations of markers, a number of studies developed metrics that rely on statistical techniques to group multiple pollutants to represent a source-related mixture. In contrast to markers, multipollutant metrics can reduce the dimensionality of concentration and exposure data associated with the multipollutant environment which in turn reduces collinearity issues in health models.

3.1.2.1. Source apportionment metrics. Source apportionment has been the most widely used statistical technique to estimate exposure to air pollution sources. This technique uses mathematical relationships to identify related pollutant mixtures and quantify their impact on air quality. In particular, source apportionment combines pollutants with similar temporal patterns, resulting in a smaller set of composite orthogonal factors. By comparing components of the factors with known source profiles, the factors can frequently be used as surrogates for source-related contributions to exposure. Using these techniques, studies have observed associations between sources of air pollution and several health effects, including mortality, (Ito et al., 2006; Laden et al., 2000; Mar et al., 2000; Ozkaynak and Thurston, 1987; Thurston et al., 2005) cardiovascular and respiratory endpoints (Andersen et al., 2007; Lanki et al., 2006; Ostro et al., 2011; Sarnat et al., 2008), lung function decrements (Penttinen et al., 2006), low birth weight (Bell et al., 2010), and toxicological endpoints (Duvall et al., 2008; Maciejczyk et al., 2010; Seagrave et al., 2006; Zhang et al., 2008). More details on source apportionment results in air pollution health studies are reported by Stanek et al. (2011).

Several different receptor models exist for source apportionment analysis, each of which yields different results and requires various levels of input data. Basic receptor models, such as principal component analysis (PCA), only provide qualitative information on source categories, which limits their utility in a health study. More advanced receptor models, such as absolute PCA, positive matrix factorization (PMF), and chemical mass balance (CMB) techniques, are capable of estimating source contributions, thus, can inform investigators of the health effects due to specific concentration increments. CMB techniques and PMF require various levels of a-priori knowledge on chemical sources or measurement uncertainties, respectively. Other differences among techniques include the number of samples and the type of pollutants used as model input, which are discussed in detail by Billionnet et al. (2012). Though each technique clearly has strengths, the selection of the technique largely depends on available a-priori information and desired output.

Source apportionment can also be conducted using a chemical transport model (CTM), such as the Community Multiscale Air Quality (CMAQ) model and the Comprehensive Air Quality Model with Extensions (CAMx), which simulate pollutant concentrations over space and time. Using these models, source impacts can be quantified based on emissions associated with a particular source sector (Park et al., 2013). For example, a CTM can be initially run including the source category followed by another run removing the source; the difference between the two model runs is equivalent to the mass attributed to the source. Fann et al. (2013) used a CTM (CAMx) and a health model to indentify sources of $PM_{2.5}$ and O_3 related to total mortality across the United States during the years 2005 and 2016. They concluded that the number of deaths associated with power plants and mobile sources decreased over the study period (2005–2016). An advantage of using CTMs for source apportionment rather than a receptor model is that source impacts can be estimated across a wide spatial area with finescale resolution (e.g., 4 km × 4 km spatial resolution over regional or nationwide areas), whereas estimates from receptor models (PCA, factor analysis (FA), CMB, PMF) are restricted to the sites from which monitoring data are available.

Since many approaches exist for developing source apportionment metrics, consistency among different techniques has been an area of active research (Hopke et al., 2006; Ito et al., 2006; Thurston et al., 2005; Viana et al., 2008). In studies comparing different receptor models, specifically PCA, FA, and PMF techniques, similar sources (and their corresponding mass) are generally identified when the same pollutant dataset is used (e.g., similar pollutant species from a similar location) (Hopke et al., 2006; Thurston et al., 2005). Among the same receptor models, consistency has also been observed in health effect estimates for similar sources. Another study by Park et al. (2013) compared source impacts estimated by a receptor model (CMB) and CTM-based technique (CMAQ), which demonstrated relative consistency in source impacts between the two techniques on long temporal scales (weeks to months) and larger differences when estimating sources on a daily basis. While the literature indicates that source apportionment results generally identify similar sources, suggesting they are robust regardless of the technique employed, challenges still remain in identifying and estimating several major sources, including gasoline/diesel motor vehicle and industrial sources (Hopke et al., 2006; Sarnat et al., 2008; Viana et al., 2008).

Despite the widespread application of source apportionment by receptor models and CTMs, this technique is often criticized, because results can be subjective and unstable. Source apportionment results from receptor models are sensitive to analytical specifications, such as the number of resolved factors and pollutant input species, which are determined by the investigator (Callen et al., 2013; Xie et al., 2012a,b). Assigning source names to factors (resolved by receptor models) is also a decision by the investigator, who often uses key marker species within the factor to fingerprint sources. Results of receptor modeling analysis can also be unstable, often resulting in aberrant temporal variability in source contributions and significant levels of residual pollutant mass. In contrast, source apportionment by CTMs can lead to less daily variation that does not necessarily compare well with measurement data, but can provide spatially-resolved source impacts (Marmur et al., 2006; Park et al., 2013). To address large differences observed among different techniques, ensemble-trained apportionment techniques have been developed that merge results of several source apportionment methods (including CMB, PMF, and CTM-based methods) yielding average source factors (Lee et al., 2009). These factors have reasonable day-to-day variability and less uncertainty than factors from an individual source apportionment technique (Balachandran et al., 2012; Lee et al., 2009); however, ensemble-trained techniques require significant computational power and expertise.

3.1.2.2. Temporal and spatial clustering metrics. Cluster analysis is another statistical approach used to group pollutants based on atmospheric co-variance. In this approach, pollutant concentrations from a central site are decomposed into a series of distinct clusters. Each cluster serves as a categorical assignment that represents characteristics of a multipollutant mixture.

There are two ways cluster analysis has been applied to air quality data. Temporal clustering creates groups of days (or other time periods) with similar concentration profiles, assigning a category to each day. This categorical assignment can be used as an effect modifier in a health study to evaluate how effects of an individual pollutant (e.g., PM) vary on days with different multipollutant profiles. Alternatively, spatial clustering is used to classify geographical locations with similar multipollutant profiles. Spatial clusters can be used in conjunction with other health effect measures (e.g., risk ratios or confidence intervals) to compare the health effects of mixtures in different areas.

Few studies have employed clustering techniques in air quality and health studies. Austin et al. (2012) used k-means partitioning and hierarchical clustering to identify different PM mixtures in a dataset from Boston, MA. Hierarchical clustering was used to efficiently identify start values for the k-means algorithm. This clustering approach yields tiered results with the highest tier corresponding to the least number of clusters (to separate the data) and the lowest tier corresponding to the highest number of clusters. Elemental ratios, weather patterns, seasonal trends and particle size characteristics were used to determine the air mass origin and sources associated with each cluster. Gu et al. (2012) also performed temporal clustering to separate 96 pollutant-related variables, including different physical aspects of PM (e.g., size regimes, number concentrations, surface area characteristics) and PM chemical components, into clusters using a dataset from Augsburg, Germany.

A spatial clustering framework was developed by Austin et al. (2013) in a study investigating long-term spatial heterogeneity in $PM_{2.5}$ composition across the United States. In this study, different $PM_{2.5}$ components were averaged over a 5-year period at individual sites across the U.S. for a total of 109 monitoring sites. Sites with similar chemical profiles of $PM_{2.5}$ components (determined by X-ray fluorescence and ion chromatography) were grouped together. Common pollutant enrichment factors (EC/OC, Ni/V, SO_4^{2-}/NO_3^-, and Fe/S) were estimated at each site and used to validate and explain the rationale for different sampling site clusters. Using k-means clustering, thirty-one distinct clusters were identified corresponding to different $PM_{2.5}$ multipollutant profiles across the monitoring sites. Of the 31 spatial clusters, 21 clusters contained at least 2 monitoring sites. The distinct clusters were broadly separated into four groups representing different regional pollutant airsheds.

Compared to source apportionment, clustering may provide a more holistic approach to evaluating health risk associated with mixtures. For example, temporal clustering classifies days with different multipollutant mixtures, which include a multitude of sources within the mixture. This type of analysis allows for the evaluation of synergistic effects associated with the entire multipollutant mixture. Such evaluation is different than the capabilities of source apportionment techniques, which only allow for the assessment of effects of an individual pollutant source.

Clustering techniques, however, are also subject to limitations that influence their utility in a health study. Like source apportionment, clustering results are influenced by the number of resulting clusters and the available dataset, which are both determined by the investigator. To reduce subjectivity, previous studies provided a systematic approach employing hierarchical clustering for determining cluster number. However, further research is necessary to validate this approach. Furthermore, unlike statistical multipollutant approaches (e.g., source apportionment techniques) which yield quantitative metrics that can be used as an independent variable in a health study, cluster analysis produces discrete categories of pollutant mixtures that lend themselves to effect modification or stratified analyses. However, the potential for clusters to be used as an independent variable has yet to be explored.

3.1.3. Grouping pollutants by emissions

3.1.3.1. Emission-based indicators. Emission-based indicators also group pollutants by source, but utilize information from emission inventories, such as the National Emissions Inventory developed by the U.S. Environmental Protection Agency, rather than a statistically-based approach. Pachon et al. (2012) developed an emission-based indicator to represent exposure to mobile sources in Atlanta, GA by combining ambient concentrations of multiple traffic-related pollutants (NO_X, CO, and EC) with their annual emissions. Eq. (1) shows how Pachon et al. (2012) calculated mobile source indicators by using daily normalized concentration (C') and emissions (E_x) of each pollutant.

$$\mathrm{IMSI_{EB}} = \frac{\frac{E_{EC,mobile}}{E_{EC,total}} \times C'_{EC} + \frac{E_{NOx,mobile}}{E_{NOx,total}} \times C'_{NOx} + \frac{E_{CO,mobile}}{E_{CO,total}} \times C'_{CO}}{\frac{E_{EC,mobile}}{E_{EC,total}} + \frac{E_{NOx,mobile}}{E_{NOx,total}} + \frac{E_{CO,mobile}}{E_{CO,total}}} \tag{1}$$

Specifically, to group pollutants of varying magnitude, pollutant concentrations are normalized by their standard deviation and then weighted by their emissions derived from several databases and modeling tools (e.g., U.S. EPA National Emissions Inventory and Motor Vehicle Emissions Simulator (MOVES)). The weight of each pollutant corresponds to the fraction of emissions attributed to mobile sources.

As a part of the Pachon et al. (2012) study, multiple single pollutant markers (NO_X, CO, and EC), emission-based indicators, and source apportionment factors were evaluated as traffic surrogates. Results showed that emission-based indicators captured traffic trends during sampling periods when non-mobile sources (e.g., biomass burning) dominated urban air quality. Compared to single pollutant markers, emission-based indicators were more spatially correlated across an urban area, indicating that these metrics capture the spatial pattern of traffic over a large geographical area better than single pollutants derived from multiple sources, including non-traffic sources. In most cases, the emission-based indicators were also more strongly associated with cardiovascular endpoints in an epidemiologic analysis (Pachon et al., 2012).

Advantages of these indicators include ease of construction and the potential for improved accessibility compared to other source-related multipollutant metrics that require complex modeling and large pollutant input datasets, such as source apportionment. In addition, interpretation of emission-based indicators is more straightforward since data from specific sources are directly linked to pollutant concentrations by emissions. However, these indicators are often constrained by uncertainties in emissions inventories, especially when source emissions are erroneously reported or are highly variable across time and space.

3.1.3.2. Intake fractions. Intake fractions also use emission information, and have primarily been used as an indicator of exposure to a specific source. Intake fractions have been used for primary (Lobscheid et al., 2012; Marshall et al., 2005) and secondary pollutants (Greco et al., 2007; Levy et al., 2003); inhalation and other intake pathways such as ingestion (Bennett et al., 2002a); and for varied sources such as motor vehicles (Marshall et al., 2006), power plants (Levy et al., 2003), and dry cleaners (Evans et al., 2000).

The intake fraction (*iF*) is a dimensionless value that describes the emission-to-exposure relationship. It is defined as the fraction of a pollutant (or its precursor) emitted from a source category (e.g., mobile sources, power plants, and refineries) that is inhaled by a specified population during a given time (Bennett et al., 2002b). A generalized equation for the intake fraction is presented below (Greco et al., 2007; Marshall and Nazaroff, 2007).

$$iF_j = \frac{mass\ \ inhaled}{mass\ \ emitted} \tag{2}$$

where iF_j is the intake fraction at location j. The "*mass inhaled*" is equivalent to the pollutant mass coming from the source emissions and inhaled by the exposed population. The "*mass emitted*" is equal to the mass of pollutant emitted from a source.

Intake fraction depends primarily on three types of parameters: those that influence dilution, such as meteorology; those that reflect the proximity of people to the source, such as population density; and those that represent persistence of a pollutant in the atmosphere, such as particle size (Marshall and Nazaroff, 2007). These parameters can be measured or modeled. Measurement methods have included tracer gas experiments where chemical compounds are purposely released and measured to act as a fingerprint for a particular source (Marshall and Nazaroff, 2007). Modeling methods range from simple, one-compartment models that combine meteorological (e.g., wind speed and mixing height), demographic, and land area data (Marshall et al., 2005) to complex dispersion models (Greco et al., 2007; Levy et al., 2003).

An advantage of intake fraction is that it can be applied not only to individual pollutants but to groups of pollutants. If two pollutants are emitted from the same source and have similar fate and transport characteristics, then the intake fraction of both pollutants is the same, even if their chemical composition and mass emission rates differ (Marshall and Nazaroff, 2007). Intake fraction can also vary spatially and temporally. However, it is commonly calculated as an annual average or for a lifetime, and the spatial variability depends on the availability of spatially-resolved emissions data. The intake fraction is also subject to model uncertainties from the emissions data and assumptions about breathing rates. While the intake fraction cannot be specifically used as an independent variable for epidemiological studies, it can quantify a population's risk and provide useful information on the advantages or disadvantages of different policies and/or scenarios (e.g., emissions reductions).

3.2 Metrics based on health effects

3.2.1 Grouping pollutants by biological or physicochemical properties. Although grouping pollutants by source provides unique insight into source-based mixtures associated with health effects, this approach may combine pollutants with varying toxicities, making it challenging to evaluate the effects of more toxic groups of pollutants. Recently, grouping pollutants by chemical properties or mode of action pathways has been proposed to understand the toxicity of pollutants. While few studies have used this approach, these metrics show significant promise for future health applications.

3.2.1.1 Chemical property-based metrics. Most multipollutant metrics based on toxicity have combined pollutants by physicochemical properties (which may be related to biological reactivity). Suh et al. (2011) used this approach to investigate the effect of chemical speciation of air pollution on respiratory and cardiovascular endpoints. Over 100 pollutants were classified based on 9 chemical properties including inert, polar, aromatic, aldehyde, alkane, acidic, combustible, transition metals, and microcrystalline compounds. Using a hierarchical two-stage regression model, Suh et al. (2011) found that different chemical groups were associated with different health endpoints. For example, while respiratory hospital admissions were associated with alkane particulate species, cardiovascular endpoints were associated with transition metals.

In another study, Meng et al. (2013) investigated the association between physicochemical properties and cardiovascular disease endpoints using quantitative ion character–activity relationships. They obtained chemical health associations from the Comparative Toxicogenomics Dataset (CTD) and physicochemical properties of specific chemicals using published literature. Linear regressions were used to explore the likelihood of a relationship between physicochemical properties and cardiovascular health endpoints. Associations were found between reactive oxygen species-generating properties and cardiovascular endpoints.

These studies demonstrate that chemical property-based metrics are capable of identifying pollutant classes that have specific effects that may not have been identified using source-based approaches. This may be important for developing regulations that target the most toxic pollutants for human health. However, the use of this metric may amplify exposure and effect estimate uncertainty. Pollutant groups may be highly correlated due to similar source emissions, making it challenging to separate the effects of a single pollutant class. Pollutant groups may also not adequately represent true exposure. For example, while some pollutant classes (e.g., volatile organic compounds) are emitted by similar sources (e.g., gasoline vehicles) and probably represent exposure well, other classes (e.g., water-soluble metals) have several diverse sources (e.g., mobile and industrial), and co-exposure among these pollutants may not be likely.

3.2.1.2 Mode of action metrics. More recently, combining pollutants by mode of action pathways has received some attention (Ankely et al., 2010; National Research Council, 2004; Vinken, 2013). This approach can identify causal agents in a multipollutant mixture by linking exposure, key biological events, and a clinical outcome. For example, altered vasomotor function is considered a key biological event in the mode of action pathway leading to cardiovascular endpoints. Using this approach, the combined effects of the pollutant mixture on vasomotor function can be quantified and then extrapolated to the overall effect on the clinical outcome. Due to limited knowledge of common air pollution biological pathways, a framework for the application of these metrics is still under development. However, these metrics will likely play a critical role in revealing multipollutant interactions since other metrics cannot address such effects.

3.2.2 Health outcome-based metrics. Multipollutant outcome-based metrics have recently been developed as exposure variables in epidemiologic studies. This approach is particularly novel because it incorporates a health effect into the metric. Pachon et al. (2012) developed a series of health-based metrics, consisting of two pollutant mixtures (e.g., NO_X & EC, NO_X & CO) that is an extension of the emission-based indicator mentioned previously. The composition of the mixture was varied using a sensitivity analysis, and the association between the mixture and a cardiovascular endpoint was evaluated to determine a health-based metric. Eq. (3) demonstrates how the composition of the NO_X and EC mixture was varied in the sensitivity analysis, where the normalized concentration (C') of each pollutant is weighted by the alpha term, which was varied from 0 to 1 in Pachon et al. (2012). For example, an alpha value of 0.5 is equivalent to a 50:50 mixture of NO_x:EC (based on Eq. (3)). The mixture yielding the strongest association with health effects was defined as the health-based metric.

$$(\mathrm{NOx}\ \&\ \mathrm{EC}) = \alpha \times C'_{\mathrm{NOx}} + (1-\alpha) \times C'_{\mathrm{EC}} \tag{3}$$

Interestingly, the strongest associations with CVD were observed when pollutants were equally weighted in a two pollutant mixture, emphasizing that mixtures rather than single pollutants can more effectively explain health effects. However, questions remain regarding the appropriateness of using health information to create a metric that is then used as an explanatory variable in a health study.

3.2.3 Risk-based metrics. Another set of multipollutant metrics incorporating health information is risk communication indexes, also referred to as air quality indexes. Although these indexes are primarily used to communicate the potential risk associated with air quality, they can also be used as an exposure metric in a health model and can be used to inform the development of future exposure metrics. Currently, the AQI (developed by the U.S. Environmental Protection Agency) is the primary index used to communicate air quality risk in the U.S. (www.airnow.gov). This approach is simple and transparent, but it does not account for the potential that more than one pollutant may be contributing to health effects on a given day.

Recently, multipollutant indexes have been proposed that integrate air pollution and health effects information, either by incorporating reference concentrations, such as air quality standards, or risk information, such as epidemiologic effect estimates. Pollutants included in these indexes are typically the criteria pollutants, particularly PM, O_3, NO_2, CO, and SO_2. Air quality standards or limit values are available for these pollutants in many countries, and they are routinely included in epidemiologic analyses, so health information for these pollutants is widely available. In addition, these pollutants are major components of air pollution mixtures in many locations and can result in similar health effects (e.g., respiratory effects and mortality). Different multipollutant indexes group different pollutants based on health endpoint, location, data availability, or sensitivity analyses.

Early proposals to create multipollutant indexes involved weighting pollutant concentrations by scaling them to air quality standards developed to protect public health, then summing the scaled concentrations. To avoid the potential for overstating the risk associated with low concentrations of several pollutants, some metrics have used a power sum (e.g., root-mean-square) rather than a linear sum (Kyrkilis et al., 2007; Swamee and Tyagi, 1999). The method has been extended to account for variability in the composition of the pollutant mixture and to calculate metrics using data from multiple sites (Plaia et al., 2013; Ruggieri and Plaia, 2012). Another scaled approach has recently been proposed using satellite data for $PM_{2.5}$ and NO_2 instead of using monitoring data from a limited number of sampling sites. This satellite-based approach demonstrates the potential for constructing multipollutant metrics on a global scale (Cooper et al., 2012).

A more direct method for incorporating health information into a multipollutant index is to use effect estimates from epidemiologic studies. In this approach, pollutant concentrations are combined in an additive manner. Individual pollutant concentrations are weighted by their effect estimate to quantify the percent risk for a particular health outcome. The percent risk is summed across all pollutants to yield the overall risk attributed to the pollutant mixture. The overall risk is represented as a number on an arbitrary scale, where low and high values can represent low and high risk, respectively. This results in an epidemiology-based index that is more directly linked to a specific health endpoint than a weighted-sum index.

An example of an epidemiology-based multipollutant index is the Air Quality Health Index (AQHI) developed by Stieb et al. (2005, 2008), which serves as the primary air quality index for Canada (https://www.ec.gc.ca/cas-aqhi/default.asp?lang=En&n=065BE995-1). It is an additive method that incorporates single pollutant mortality effect estimates (as pollutant weightings) from a multi-city Canadian study of associations between mortality and short-term air pollutant concentrations. The metric was originally developed for CO, NO_2, O_3, SO_2, and $PM_{2.5}$ (Stieb et al., 2005); however, the current index includes only NO_2, O_3, and either $PM_{2.5}$ or PM_{10}. CO and SO_2 had less robust mortality associations, and little difference was found between index values calculated with and without these two pollutants, so they are no longer grouped with the other pollutants in the index. As a part of the Stieb et al. (2008) study, a sensitivity analysis was conducted to evaluate the appropriateness of using effect estimates derived from multiple cities to represent pollutant-specific health impacts in individual cities across Canada. Sensitivity analyses showed that the multi-city formulation was in good agreement with single-city epidemiologic effect estimates (Stieb et al., 2008). Other researchers have proposed similar multipollutant indexes using effect estimates from locally-conducted epidemiologic analyses to make the indexes more applicable to a specific area (Cairncross et al., 2007; Sicard et al., 2011, 2012; Wong et al., 2013).

Investigators have recently demonstrated that a multipollutant index can be used as an exposure metric in an epidemiologic model. To et al. (2013) evaluated the association between the Canadian AQHI and asthma morbidity. AQHI values were associated with asthma outpatient visits, emergency department visits, and hospital admissions in Ontario during 2003–2006. Associations were more consistently observed for the AQHI than for the individual pollutants comprising the index (NO_2, O_3, and $PM_{2.5}$), which showed variable associations across pollutants, health metrics, and lag days. Interestingly, although the AQHI is based on mortality effect estimates, associations were observed for respiratory outcomes; however, respiratory health effects have been widely reported for all three pollutants in the index (U.S. EPA, 2009, 2013). A comparison of associations between a Canadian-style AQHI (developed for Shanghai) and daily mortality and hospitalizations showed that the AQHI had stronger and more significant associations per IQR than Shanghai's API, which is a single pollutant index (Chen et al., 2013).

The multipollutant air quality indexes described here rely upon several assumptions, which although reasonable, could limit their ability to accurately represent multipollutant health risk and exposure in some situations. First, additivity of effects is presumed, and it is not yet clear whether non-additive interactions occur in reality. The metrics also do not account for differences in PM composition or air pollutant mixtures across cities. Some unknown level of uncertainty is introduced by using single pollutant effect estimates, from studies in which people were in fact exposed to a multipollutant mixture, to construct a metric to be used in locations with different air pollution mixtures, both from each other and from the mixtures in the original studies.

4. Discussion

We reviewed an extensive body of literature on multipollutant metrics that represent exposure to pollutant mixtures. These studies collectively show that pollutants can be broadly grouped into metrics based on 1) their source emission or 2) associated health outcomes, and the method used to group pollutants largely depends on the goal of the air pollution study. Source-based grouping approaches (e.g., source apportionment or emission-based indicators) are typically applied to studies interested in identifying source emissions responsible for health outcomes and developing air pollution mitigation strategies for environmental management. Conversely, health-based metrics are generally used in studies interested in determining pollutant joint effects or biological pathways linking exposure to health effects. Though each type of metric is used in vastly different research applications, both metric types are valuable and can be used to inform future multipollutant human health risk and air quality policy assessments. Research building upon the results of both health and source studies can reveal key trends in mixtures and source emissions linked to human health effects. For example, while a health-based study can identify associations between a specific class of pollutants and health effects, a source-based study can subsequently determine the source(s) from which those pollutants are emitted. Based on our review, it is apparent that no "one size fits all" metric exists; both source-based and health-based metrics are equally important in evaluating air pollution health effects.

Of the existing literature on multipollutant exposure metrics, most work has focused on the development of source-based metrics; however, the development of health-based metrics is emerging and shows potential for future applications in epidemiologic and toxicological studies. Several different types of metrics exist that represent the quantitative and qualitative aspects of a source mixture. Quantitative metrics, including marker species, source apportionment factors, and emission-based indicators, can estimate source contribution and can be used in an epidemiologic study as an exposure variable, providing a concrete sense of the effect of incremental changes in air pollution mixtures on human health. In contrast, qualitative metrics, such as temporal or spatial clusters, provide categorical information on the chemical makeup of a pollutant mixture in different geographical areas or during different time periods, and thus may be more useful as an effect modifier in an epidemiologic study. Fewer studies have developed metrics based on chemical properties, mode of action pathways or health effects, which reflects the relative lack of knowledge on common mode of action pathways of air pollutants. However, as toxicology and controlled human exposure studies continue to reveal key causal pathways and combined pollutant effects, more of these metrics will likely emerge. The use of risk communication tools, such as the AQHI, as an exposure variable in a health study shows promise for directly linking pollutant mixtures to health effects.

When comparing the utility of multipollutant metrics to single pollutant metrics, there was a clear tradeoff between complexity and simplicity. Multipollutant metrics provide unique insight on exposure to mixtures and reduce variable dimensions within a health model; however, these advantages may not outweigh their limitations. In particular, many multipollutant metrics are constructed using advanced statistical techniques (e.g., source apportionment or clustering techniques), which require significant amounts of data resources, such as data on pollutant species, measurement uncertainty, and source profiles. Such data may not be available through standard sampling networks and is difficult to obtain independently.

Multipollutant metrics also have uncertainty resulting from combining multiple pollutants with different units of measurement, measurement averaging times and measurement error, which adds additional exposure error compared to that of single pollutant metrics. In many studies, differential error is observed across multipollutant metrics, and it is unclear how uncertainty is derived or how it should be interpreted in a health study. For example, directly emitted pollutants such as NO_X and CO may show more spatial variability across an urban area than secondary pollutants such as PM and O_3. Multipollutant metrics incorporating both primary and secondary pollutants may overstate or understate variability in true exposure to the mixture and thus introduce exposure error into epidemiologic studies (Sarnat et al., 2010). In addition, there is little consistency among methods used to estimate error even when the same approach is used to group pollutants. Source apportionment techniques, for instance, use a wide array of methods to estimate error, such as bootstrapping (for PMF) (Norris and Vendantham, 2008) and effect variance quantification (for CMB) (Lee and Russell, 2007; Pachon et al., 2012), and the appropriateness of each method is ambiguous. Therefore, in considering different metrics used to represent the multipollutant environment, researchers should consider both the additional information used to construct the metrics and the potential uncertainties involved.

The question remains whether multipollutant metrics provide a better explanation of air pollution health effects than other exposure metrics. Part of this uncertainty arises from the lack of health applications for several multipollutant metrics; in addition, limitations exist in the methods used to compare metrics. Among the studies reviewed in this paper, a few have compared how single pollutant and multipollutant metrics impact the magnitude and uncertainty of effect estimates in a health study, indicating that health effect attenuation and widening of effect uncertainty are attributed to exposure misclassification. Despite the fact that multipollutant metrics add valuable information on the source and potential toxicity of a pollutant mixture, some studies show no substantial difference in effect estimates, confidence intervals, or statistical significance among multipollutant and single pollutant metrics (Pachon et al., 2012; Sarnat et al., 2008). Moreover, it is neither clear what the “true” health effect is nor does a gold standard exist for comparison. It is plausible that using a multipollutant metric could result in effect biases compared to the use of other “less precise” pollutant metrics that may not be as spatially or temporally representative of “true” exposure. Additionally, while comparing effect estimates can be used to evaluate quantitative metrics, challenges remain with assessing multipollutant metrics studies (such as pollutant clusters) used as effect modifiers in health studies.

Given the abundant interest in the health effects of air pollution mixtures, it seems clear that multipollutant science will continue to be an integral part of future air quality health effects research and human health risk assessment. Based on our review, we identified research gaps that if addressed can help facilitate the advancement of multipollutant science. The first research gap involves gaining a comprehensive understanding of how exposure error in multipollutant metrics affects the interpretation of human health data. The existing literature on this topic is sparse and only begins to address the complexity of the issue. While there is no gold standard for multipollutant exposure or health effects, characterizing the general effect of single pollutant and multipollutant metrics on the magnitude and direction of health estimates is beneficial. Past analyses have utilized simulation techniques to determine the possible consequences of exposure error on health effect estimation in a single pollutant context (Goldman et al., 2011; Zeger et al., 2000). These techniques should be extended to account for the simultaneous errors in multiple pollutants to inform the scientific community on how multipollutant metrics can be used in health studies.

Another pertinent research topic is determining the actual interactive behavior of pollutants within a mixture. Most existing metrics assume an additive effect among pollutants within a mixture, such that the effect is equal to the sum of the effect estimates of single pollutants; however, the issue is likely more complex. Pollutants may behave in a synergistic or antagonistic manner such that the combined health effect is not sufficiently captured by an additive approach. Additional work should be directed towards developing and evaluating metrics that can be used to quantify pollutant combined effects. This research effort should progress in parallel with toxicological, controlled human exposure, and panel studies targeted at addressing biological and chemical pollutant interactions within a mixture. Addressing research questions on exposure error and joint effects will help bridge the knowledge gap between multipollutant exposure and human health effects.

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References

Andersen ZJ, Wahlin P, Raaschou-Nielsen O, Scheike T, Loft S. Ambient particle source apportionment and daily hospital admissions among children and elderly in Copenhagen. J Expo Sci Environ Epidemiol 2007;17:625–36.
Ankely GT, Richard RS, Erickson RJ, Hoff DJ, Hornung MW, Johnson RD, et al. Adverse outcome pathways: a conceptual framework to supprt exotoxicology research and risk assessment. Environ Toxicol Chem 2010;29:730–41.
Austin E, Coull B, Thomas D, Koutrakis P. A framework for identifying distinct multipollutant profiles in air pollution data. Environ Int 2012;45:112–21.
Austin E, Coull BA, Zanobetti A, Koutrakis P. A framework to spatially cluster air pollution monitoring sites in US based on the PM2.5 composition. Environ Int 2013;59:244–54.
Balachandran S, Pachon JE, Hu YT, Lee D, Mulholland JA, Russell AG. Ensemble-trained source apportionment of fine particulate matter and method uncertainty analysis. Atmos Environ 2012;61:387–94.
Bell ML, Belanger K, Ebisu K, Gent JF, Lee HJ, Koutrakis P, et al. Prenatal exposure to fine particulate matter and birth weight variations by particulate constituents and sources. Epidemiology 2010;21:884–91.
Bennett DH, Margni MD, McKone TE, Jolliet O. Intake fraction for multimedia pollutants: a tool for life cycle analysis and comparative risk assessment. Risk Anal 2002a;22:905–18.
Bennett DH, McKone TE, Evans JS, Nazaroff WW, Margni MD, Jolliet O, et al. Defining intake fraction. Environ Sci Technol 2002b;36:206A–11A.
Billionnet C, Sherrill D, Annesi-Maesano I, Study G. Estimating the health effects of exposure to multi-pollutant mixture. Ann Epidemiol 2012;22:126–41.
Brook JR, Burnett RT, Dann TF, Cakmak S, Goldberg MS, Fan X, et al. Further interpretation of the acute effect of nitrogen dioxide observed in Canadian time-series studies. J Expo Sci Environ Epidemiol 2007;17:S36–44.
Cairncross EK, John J, Zunckel M. A novel air pollution index based on the relative risk of daily mortality associated with short-term exposure to common air pollutants. Atmos Environ 2007;41:8442–54.
Callen MS, Lopez JM, Mastral AM. Influence of organic and inorganic markers in the source apportionment of airborne PM10 in Zaragoza (Spain) by two receptor models. Environ Sci Pollut Res Int 2013;20:3240–51.
Chen R, Wang X, Meng X, Hua J, Zhou Z, Chen B, et al. Communicating air pollution-related health risks to the public: an application of the Air Quality Health Index in Shanghai, China. Environ Int 2013;51:168–73.
Clean Air Act. National ambient air quality standards; U.S. Code; 1970.
Cooper MJ, Martin RV, van Donkelaar A, Lamsal L, Brauer M, Brook JR. A satellite-based multi-pollutant index of global air quality. Environ Sci Technol 2012;46:8523–4.
Dominici F, Peng RD, Barr CD, Bell ML. Protecting human health from air pollution shifting from a single-pollutant to a multipollutant approach. Epidemiology 2010;21:187–94.
Duvall RM, Norris GA, Dailey LA, Burke JM, McGee JK, Gilmour MI, et al. Source apportionment of particulate matter in the US and associations with lung inflammatory markers. Inhal Toxicol 2008;20:671–83.
EPA, U.S.. Integrated Science Assessment for Particulate Matter (Final Report). U.S. Environmental Protection Agency, EPA/600/R-08/139F; 2009. [Washington, D.C.].

EPA, U.S. Integrated Science Assessment of Ozone and Related Photochemical Oxidants (Final Report). U.S. Environmental Protection Agency, EPA/600/R-10/076F; 2013. [Washington, D.C.].

Evans JS, Thompson KM, Hattis D. Exposure efficiency: Concept and application to percholorethylene exposure from dry cleaners. Journal of the Air & Waste Management Association. 2000;9:1700–3.

Fann N, Fulcher CM, Baker K. The recent and future health burden of air pollution apportioned across US sectors. Environ Sci Technol 2013;47:3580–9.

Goldman GT, Mulholland JA, Russell AG, Strickland MJ, Klein M, Waller LA, et al. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. Environ Health 2011;10.

Grahame T, Hidy G. Using factor analysis to attribute health impacts to particulate pollution sources. Inhal Toxicol 2004;16:143–52.

Greco SL, Wilson AM, Spengler JD, Levy JI. Spatial patterns of mobile source particulate matter emissions-to-exposure relationships across the United States. Atmos Environ 2007;41:1011–25.

Gu J, Pitz M, Breitner S, Birmili W, von Klot S, Schneider A, et al. Selection of key ambient particulate variables for epidemiological studies — applying cluster and heatmap analyses as tools for data reduction. Sci Total Environ 2012;435:541–50.

Hidy GM, Pennell WT. Multipollutant air quality management. J Air Waste Manage Assoc 2010;60:645–74.

Hopke PK, Ito K, Mar T, Christensen WF, Eatough DJ, Henry RC, et al. PM source apportionment and health effects: 1. Intercomparison of source apportionment results. J Expo Sci Environ Epidemiol 2006;16:275–86.

Ito K, Christensen WF, Eatough DJ, Henry RC, Kim E, Laden F, et al. PM source apportionment and health effects: 2. An investigation of intermethod variability in associations between source-apportioned fine particle mass and daily mortality in Washington, DC. J Expo Sci Environ Epidemiol 2006;16:300–10.

Johns DO, Stanek LW, Walker K, Benromdhane S, Hubbell B, Ross M, et al. Practical advancement of multipollutant scientific and risk assessment approaches for ambient air pollution. Environ Health Perspect 2012;120:1238–42.

Kyrkilis G, Chaloulakou A, Kassomenos PA. Development of an aggregate Air Quality Index for an urban Mediterranean agglomeration: relation to potential health effects. Environ Int 2007;33:670–6.

Laden F, Neas LM, Dockery DW, Schwartz J. Association of fine particulate matter from different sources with daily mortality in six US cities. Environ Health Perspect 2000;108:941–7.

Lanki T, de Hartog JJ, Heinrich J, Hoek G, Janssen NAH, Peters A, et al. Can we identify sources of fine particles responsible for exercise-induced ischemia on days with elevated air pollution? The ULTRA study. Environ Health Perspect 2006;114:655–60.

Lee S, Russell AG. Estimating uncertainties and uncertainty contributors of CMB PM2.5 source apportionment results. Atmos Environ 2007;41:9616–24.

Lee D, Balachandran S, Pachon J, Shankaran R, Lee S, Mulholland JA, et al. Ensemble-trained PM2.5 source apportionment approach for health studies. Environ Sci Technol 2009;43:7023–31.

Levy JI, Wilson AM, Evans JS, Spengler JD. Estimation of primary and secondary particulate matter: Intake fractions for power plants in Georgia. Environ Sci Tech 2003;37:5528–36.

Levy I, Mihele C, Lu G, Narayan J, Brook JR. Evaluating Multipollutant Exposure and Urban Air Quality: Pollutant Interrelationships, Neighborhood Variability, and Nitrogen Dioxide as a Proxy Pollutant. Environmental Health perspectives. 2014;122:65–72.

Lobscheid AB, Nazaroff WW, Spears M, Horvath A, McKone TE. Intake fractions of primary conserved air pollutants emitted from on-road vehicles in the United States. Atmos Environ 2012;63:298–305.

Maciejczyk P, Zhong M, Lippmann M, Chen L-C. Oxidant generation capacity of source-apportioned PM2.5. Inhal Toxicol 2010;22:29–36.

Mar TF, Norris GA, Koenig JQ, Larson TV. Associations between air pollution and mortality in Phoenix, 1995–1997. Environ Health Perspect 2000;108:347–53.

Marmur A, Park SK, Mulholland JA, Tolbert PE, Russell AG. Source apportionment of PM2.5 in the southeastern United States using receptor and emissions-based models: conceptual differences and implications for time-series health studies. Atmos Environ 2006;40:2533–51.

Marshall JD, Nazaroff WW. Intake fraction. In: Otte WR, Steinmann AC, Wallace LA, editors. Exposure analysis. Boca raton, FL: CRC Press, Taylor & Francis Group; 2007.

Marshall JD, Teoh S-K, Nazaroff WW. Intake fraction of nonreactive vehicle emissions in US urban areas. Atmos Environ 2005;39:1363–71.

Marshall JD, Granvold PW, Hoats AS, McKone TE, Deakin E, Nazaroff WW. Inhalation intake of ambient air pollution in California's South Coast Air Basin. Atmos Environ 2006;40:4381–92.

Mauderly JL, Burnett RT, Castillejos M, Ozkaynak H, Samet JM, Stieb DM, et al. Is the air pollution health research community prepared to support a multipollutant air quality management framework? Inhal Toxicol 2010;22:1–19.

Meng Q, Richmond-Bryant J, Lu S-E, Buckley B, Welsh WJ, Whitsel EA, et al. Cardiovascular outcomes and the physical and chemical properties of metal ions found in particulate matter air pollution: a QICAR study. Environ Health Perspect 2013;121:558–64.

Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic revies and meta-analysis: the PRISMA statement. PLoS Med 2009;6.

National Research Council. Air quality management in the United StatesIn: Press N.A., editor. 2004. [Washington D.C.].

Norris G, Vendantham R. EPA positive matrix factorization (PMF) 3.0. In: Agency U.E.P., editor. NC: Research Triangle Park; 2008.

Ostro B, Tobias A, Cluerol X, Alastuey A, Amato F, Pey J, et al. The effects of particulate matter sources on daily mortality: a case-crossover study of Barcelona, Spain. Environ Health Perspect 2011;119:1781–7.

Ozkaynak H, Thurston GD. Associations between 1980 U.S. mortality rates and alternative measures of airborne particle concentration. Risk Anal 1987;7:449–61.

Pachon JE, Balachandran S, Hu Y, Mulholland JA, Darrow LA, Sarnat JA, et al. Development of outcome-based, multipollutant mobile source indicators. J Air Waste Manage Assoc 2012;62:431–42.

Park SK, Marmur A, Russell AG. Environmental risk assessment: comparison of receptor and air quality models for source apportionment. Hum Ecol Risk Assess 2013;19:1385–403.

Penttinen P, Vallius M, Tiittanen P, Ruuskanen J, Pekkanen J. Source-specific fine particles in urban air and respiratory function among adult asthmatics. Inhal Toxicol 2006;18:191–8.

Plaia A, Di Salvo F, Ruggieri M, Agro G. A multisite-multipollutant air quality index. Atmos Environ 2013;70:387–91.

Ruggieri M, Plaia A. An aggregate AQI: comparing different standardizations and introducing a variability index. Sci Total Environ 2012;420:263–72.

Sarnat JA, Marmur A, Klein M, Kim E, Russell AG, Sarnat SE, et al. Fine particle sources and cardiorespiratory morbidity: an application of chemical mass balance and factor analytical source-apportionment methods. Environ Health Perspect 2008;116:459–66.

Sarnat SE, Klein M, Sarnat JA, Flanders WD, Waller LA, Mulholland JA, et al. An examination of exposure measurement error from air pollutant spatial variability in time-series studies. J Expo Sci Environ Epidemiol 2010;20:135–46.

Seagrave J, McDonald JD, Bedrick E, Edgerton ES, Gigliotti AP, Jansen JJ, et al. Lung toxicity of ambient particulate matter from southeastern US sites with different contributing sources: relationships between composition and effects. Environ Health Perspect 2006;114:1387–93.

Sicard P, Lesne O, Alexandre N, Mangin A, Collomp R. Air quality trends and potential health effects — development of an aggregate risk index. Atmos Environ 2011;45:1145–53.

Sicard P, Talbot C, Lesne O, Mangin A, Alexandre N, Collomp R. The Aggregate Risk Index: an intuitive tool providing the health risks of air pollution to health care community and public. Atmos Environ 2012;46:11–6.

Stanek LW, Sacks JD, Dutton SJ, Dubois J-JB. Attributing health effects to apportioned components and sources of particulate matter: an evaluation of collective results. Atmos Environ 2011;45:5655–63.

Stieb DM, Doiron MS, Blagden P, Burnett RT. Estimating the public health burden attributable to air pollution: an illustration using the development of an alternative air quality index. J Toxicol Environ Health A Curr Issues 2005;68:1275–88.

Stieb DM, Burnett RT, Smith-Doiron M, Brion O, Shin HH, Economou V. A new multipollutant, no-threshold air quality health index based on short-term associations observed in daily TimeSeries analyses. J Air Waste Manage Assoc 2008;58:435–50.

Suh HH, Zanobetti A, Schwartz J, Coull BA. Chemical properties of air pollutants and cause-specific hospital admissions among the elderly in Atlanta, Georgia. Environ Health Perspect 2011;119:1421–8.

Swamee PK, Tyagi A. Formation of an air pollution index. J Air Waste Manage Assoc 1999;49:88–91.

Thurston GD, Ito K, Mar T, Christensen WF, Eatough DJ, Henry RC, et al. Workgroup report: workshop on source apportionment of particulate matter health effects — intercomparison of results and implications. Environ Health Perspect 2005;113:1768–74.

To T, Shen S, Atenafu EG, Guan J, McLimont S, Stocks B, et al. The air quality health index and asthma morbidity: a population-based study. Environ Health Perspect 2013;121:46–52.

Tolbert PE, Klein M, Peel JL, Sarnat SE, Sarnat JA. Multipollutant modeling issues in a study of ambient air quality and emergency department visits in Atlanta. J Expo Sci Environ Epidemiol 2007;17:S29–35.

Viana M, Pandolfi M, Minguillon MC, Querol X, Alastuey A, Monfort E, et al. Inter-comparison of receptor models for PM source apportionment: case study in an industrial area. Atmos Environ 2008;42:3820–32.

Vinken M. The adverse outcome pathway concept: a pragmatic tool in toxicology. Toxicology 2013;312:158–65.

Wong TW, Tam WWS, Yu ITS, Lau AKH, Pang SW, Wong AHS. Developing a risk-based air quality health index. Atmos Environ 2013;76:52–8.

Xie M, Coons TL, Dutton SJ, Milford JB, Miller SL, Peel JL, et al. Intra-urban spatial variability of PM2.5-bound carbonaceous components. Atmos Environ 2012a;60:486–94.

Xie M, Hannigan MP, Dutton SJ, Milford JB, Hemann JG, Miller SL, et al. Positive matrix factorization of PM2.5: comparison and implications of using different speciation data sets. Environ Sci Technol 2012b;46:11962–70.

Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, et al. Exposure measurement error in time-series studies of air pollution: concepts and consequences. Environ Health Perspect 2000;108:419–26.

Zhang Y, Schauer JJ, Shafer MM, Hannigan MP, Dutton SJ. Source apportionment of in vitro reactive oxygen species bioassay activity from atmospheric particulate matter. Environ Sci Technol 2008;42:7502–9.

Supplemental Information for "Evaluating the Application of Multipollutant Exposure Metrics in Air Pollution Health Studies"

Table S1. Key features of 57 studies reviewed in this article

Table S1. Key features of 57 studies reviewed in this paper

Study	Exposure Metric Type	Key Features
Andersen et al. (2007)	Source Apportionment	• Identifies key PM_{10} sources in urban area using source apportionment • Finds crustal, traffic, and biomass sources are associated with adverse health outcomes
Ankely et al. (2010)	Mode of Action	• Introduces and discusses the value of Mode of Action metrics in health and toxicity studies
Austin et al. (2012)	Temporal Clustering	• Develops a method to cluster sampling days based on physicochemical properties of $PM_{2.5}$ species • Observes five types of sampling days associated with different $PM_{2.5}$ chemical composition and weather patterns
Austin et al. (2013)	Spatial Clustering	• Introduces spatial clustering of sampling sites based on similar $PM_{2.5}$ multipollutant profiles • Separates 109 sites across the US into 31 distinct site clusters based on similar chemical profiles
Balachandran et al. (2010)	Source Apportionment	• Evaluates ensemble-trained source apportionment technique that combines results of multiple receptor and chemical transport models • Demonstrates less day-to-day variability in ensemble-trained source apportionment results compared to individual apportionment methods
Bell et. al. (2010)	Source Apportionment	• Investigates the relationship between exposure to $PM_{2.5}$ sources estimated by PMF and birth weight across the US • Determines a link between low birth weight and road dust, mobile sources, and oil combustion $PM_{2.5}$ sources
Bennett et. al. (2002a)	Intake Fraction	• Extends the use of iF to multimedia pollutants with multiple exposure pathways • Finds that iF calculations provide insight into the multimedia model algorithms and help identify unusual patterns of exposure and questionable exposure model results.
Brook et al. (2007)	Marker Species	• Demonstrates NO_2 is a more robust indicator of traffic than $PM_{2.5}$ based on correlations with organic traffic

Study	Exposure Metric Type	Key Features
		species
Cairncross et al. (2007)	Risk-based	• Constructs AQHI-type air pollution index from WHO relative risk values for PM, SO_2, O_3, NO_2, and CO, using the O_3 risk value as a benchmark • Applies index to Cape Town, South Africa
Callen et al. (2013)	Source Apportionment	• Compares results of two receptor models (UNMIX, PMF) • Observes consistency among major sources identified by both receptor models
Chen et al. (2013)	Risk-based	• Constructs AQHI-type index with PM_{10} or $PM_{2.5}$ and NO_2 for Shanghai and evaluates the association between the index and daily mortality and morbidity • AQHI-type index has stronger associations with health outcomes than existing Shanghai air pollution index
Cooper et al. (2013)	Risk-based	• Constructs index using satellite data for $PM_{2.5}$ and NO_2, scaled to WHO air quality guidelines • Demonstrates potential for global-scale application of multipollutant indicators
Duvall et al. (2008)	Source Apportionment	• Evaluates association between toxicological endpoints and single pollutant markers and source apportionment results (CMB) • Identifies association between adverse toxicological endpoints and secondary sulfate and coal combustion sources
Evans et. al. (2000)	Intake Fraction	• Examines the impact of perchloroethylene emissions from dry cleaners in the United States • For many compounds, like perchloroethylene, the uncertainty inherent in the estimation of cancer potency or source emissions would dominate these small errors
Fann et al. (2013)	Source Apportionment	• Uses photochemical model (CAMx) to quantify $PM_{2.5}$ and O_3 sources in the US during 2005 and the future • Draws association between sources and morbidity during the two time periods
Grahame and Hidy (2004)	Marker Species	• Demonstrates that source identification using single pollutant marker species may be confounded due to the

Study	Exposure Metric Type	Key Features
		fact that marker species are emitted by several sources
Greco et al. (2007)	Intake Fraction	• Characterizes the relationship between mobile source emissions and subsequent $PM_{2.5}$ exposure • Long-range dispersion models with coarse geographic resolution are appropriate for risk assessments of secondary $PM_{2.5}$ or primary $PM_{2.5}$ emitted from mobile sources in rural areas, but more resolved dispersion models are needed for primary $PM_{2.5}$ in urban areas
Gu et al. (2012)	Temporal Clustering	• Uses 96 variables describing physical and chemical properties of air pollution to successfully cluster sampling days in an urban area
Hopke et al. (2006)	Source Apportionment	• Compares results of $PM_{2.5}$ source apportionment across different techniques (PCA, PMF, UNMIX, Multiple Linear Regressions) operated by different investigators • Observes general consistency in sources indentified and mass resolved among different models and investigators, with the exception of traffic and vegetative burning sources
Ito et al. (2006)	Source Apportionment	• Compares a variety of source apportionment methods (UNMIX, FA, PMF, PCA) operated by different researchers in a health study • Observes less variance across different source apportionment methods/investigators than across different source types
Kyrkillis et al. (2007)	Risk-based	• Developed aggregate index for PM_{10}, NO_2, O_3, CO, and SO_2 using a power sum with exponent 2.5 • Applied index to Athens, Greece and compared to single-pollutant index
Laden et al. (2000)	Source Apportionment	• Uses FA to identify sources of $PM_{2.5}$ for health study • Conducts FA results and health comparison in 6 different cities
Lanki et al. (2006)	Source Apportionment	• Uses PCA and multiple linear regression techniques to identify sources of $PM_{2.5}$ in urban area in a health study • Compares health effect estimates based on single pollutant

Study	Exposure Metric Type	Key Features
		and multipollutant metrics
Lee et al. (2009)	Source Apportionment	• Develops ensemble-trained source apportionment technique that combines receptor-based and chemical-transport models • Demonstrates reduced day-to-day variability and fewer zero-impact days in ensemble-trained results compared to other source apportionment techniques
Levy et al. (2003)	Intake Fraction	• Applies CALPUFF, a regional-scale dispersion model, to seven power plants to estimate emission-weighted average intake fractions of $PM_{2.5,}$ ammonium sulfate from SO_2, and ammonium nitrate from NO_X • Compares findings with those from a frequently applied source-receptor (S-R) matrix.
Levy et al. (2014)	Marker Species	• Compares mobile measurements of NO_2 to different particulate and gaseous traffic-related pollutants • Finds nitrogen oxide species, including NO_2, to be a good marker of traffic based on high spatial correlation among measured traffic species
Lobscheid et al. (2012)	Intake Fraction	• Calculates the intake fraction of conserved pollutants emitted from on-road mobile sources utilizing AERMOD for the conterminous United States • Population-weighted mean • Finds intake fractions for populous urban counties are about two orders of magnitude greater than for sparsely populated rural counties with 75% of the intake occuring in the same county as emissions.
Maciejczyk et al. (2010)	Source Apportionment	• Uses FA to identify major sources of $PM_{2.5}$ in urban area in toxicological study • Observes a strong association between metals and cellular oxidant generation
Mar et al. (2006)	Source Apportionment	• Compares source apportionment results from different receptor models (PCA, FA, PMF, UNMIX) and investigators in a health study • Observes less variation across different methods than

Study	Exposure Metric Type	Key Features
		across sources
Marmur et al. (2006)	Source Apportionment	• Compares source apportionment results from receptor-based and chemical-transport models • Demonstrates receptor models have better temporal representativeness while chemical-transport models have more spatial representativeness
Marshall et al. (2005)	Intake Fraction	• Uses three methods to estimate intake fractions for vehicle emissions in urban areas • Intake fraction varies among locations, based on factors such as meteorology, linear population density, and the spatial distribution of emissions
Marshall et al. (2006)	Intake Fraction	• Computes distributional characteristics of the inhalation intake of five pollutants for a group of ~ 25,000 people living in California's South Coast Air Basin • Accounting for microenvironmental adjustment factors, population mobility and temporal correlations between pollutant concentrations and breathing rates affects the estimated inhalation intake by 40% on average
Marshall and Nazaroff (2007)	Intake Fraction	• Illustrates the use of a simple model, the one-compartment box model, to estimate intake fraction values and compare values among sources • Provides several examples of how one might compare intake fraction values for two sources and then use this information to prioritize emission reductions.
Meng et al. (2013)	Chemical Property	• Develops new approach to associate physicochemical properties of metal pollutants with biological endpoints • Demonstrates association between health effects and solubility, ion size, oxidation potential
Ostro et al. (2011)	Source Apportionment	• Uses PMF to determine major $PM_{2.5}$ and PM_{10} sources in urban period in a epidemiologic study • Identifies a link between traffic, sulfate, and construction dust and adverse health effects
Ozkaynak and Thurston (1987)	Source Apportionment	• Uses source apportionment to determine major sources of $PM_{2.5}$ in a health study

Study	Exposure Metric Type	Key Features
		• Observes a stronger link between mortality and industrial and coal combustion compared to crustal particles
Pachon et al. (2012)	Emission-based & Health-outcome based	• Develops emission-based & health-based traffic indicators in an urban area for use in an epidemiologic analysis • Suggests that multipollutant, emission-based and health-based metrics may be more spatially representative of urban traffic impacts than single-pollutant metrics
Park et al. (2013)	Source Apportionment	• Compares $PM_{2.5}$ source apportionment results based on a receptor model (CMB) and a chemical-transport model (CMAQ) • Observes significant temporal variability in CMB, while much less temporal variations in CMAQ results
Penttinen et al. (2006)	Source Apportionment	• Uses PCA and multiple linear regressions to identify $PM_{2.5}$ sources associated with adverse health outcomes • Determines combustion sources are largely linked to negative respiratory outcomes
Plaia et al. (2013)	Risk-based	• Develops multi-site, multipollutant index for PM_{10}, NO_2, CO, and SO_2 by aggregating pollutant concentrations across sites using PCA, then aggregating across pollutants using a power sum with exponent 2 • Using simulated data, shows that method is sensitive to highly variable pollutants, particularly those at low concentrations
Ruggieri and Plaia (2012)	Risk-based	• Develops power-sum index with exponent 2 for PM_{10}, NO_2, O_3, CO, and SO_2 and a variability index to account for situations when one pollutant is much higher than the others • Combines air quality and variability indexes to clarify whether high power-sum index values are due to one or multiple pollutants
Sarnat et al. (2008)	Source Apportionment & Marker Species	• Compares $PM_{2.5}$ source exposure estimated by CMB PMF, and marker species in a epidemiologic analysis • Finds consistent results across effect estimates regardless of technique used to estimate $PM_{2.5}$ source impacts (PMF,

Study	Exposure Metric Type	Key Features
		CMB, markers)
Seagrave et al. (2006)	Source Apportionment	• Uses CMB to apportion $PM_{2.5}$ mass from multiple Southeastern US sites in a toxicological study • Observes a link between sites with contributions from vehicles and industrial sources and toxicity
Sicard et al. (2011)	Risk-based	• Develops an AQHI-type index for $PM_{2.5}$, PM_{10}, SO_2, NO_2, and O_3 using French hospital admissions data, with PM_{10} as a benchmark • Combines index with chemistry-transport model to map index values over southeastern France
Sicard et al. (2012)	Risk-based	• Develops AQHI-type index for $PM_{2.5}$, PM_{10}, SO_2, NO_2, and O_3 • Used WHO risk estimates for applying the index to Greece and the Netherlands; used French risk estimates for applying the index to southeastern France
Stieb et al. (2005)	Risk-based	• Develops AQHI by weighting pollutant concentrations by epidemiologic effect estimate, summing across pollutants, and scaling to an arbitrary scale of 1-10 • Uses mortality effect estimates from a multi-city Canadian study for CO, NO_2, O_3, SO_2, and $PM_{2.5}$
Stieb et al. (2008)	Risk-baseed	• Conducts sensitivity analyses on pollutants included in AQHI and appropriateness of using multicity effect estimates • NO_2, O_3, and $PM_{2.5}$ main drivers of index values; multicity formulation in good agreement with single-city effect estimates
Suh et al. (2011)	Chemical Property	• Develops a new approach to link chemical properties of air pollution to adverse health outcomes • Observes an association between adverse health effects and alkanes, transition metals, aromatics, and oxides
Swamee and Tyagi (1999)	Risk-based	• Analyzes methods of summing weighted pollutant concentrations to generate a multipollutant index • Suggests a power-sum method with exponent 2.5 as an

Study	Exposure Metric Type	Key Features
		intermediate approach to avoid either overstating the risk from low levels of several pollutants or understating the risk from high to moderate pollutant levels
Thurston et al. (2005)	Source Apportionment	• Compares $PM_{2.5}$ source apportioned mass across different methods (PCA, PMF, CMB, UNMIX) and investigators in a health study • Demonstrates general result consistency (identified sources and resolved mass) among different methods and investigators, with the exception of traffic and vegetative burning impacts
To et al. (2013)	Risk-based	• Evaluates association between AQHI and asthma morbidity in Ontario • Observes consistent associations between AQHI and asthma hospitalizations, despite AQHI being developed from mortality studies
Viana et al. (2008)	Source Apportionment	• Compares PM_{10} source apportioned mass across different methods (PCA, PMF, CMB) • Finds consistent results in source identification, but less consistency across resolved mass among similar sources
Vinken et al. (2013)	Mode of Action	• Discusses the utility of adverse outcome pathway (or mode of action) based metrics in toxicology studies to inform human risk assessments
Wong et al. (2013)	Risk-based	• Develops AQHI-type index for SO_2, NO_2, O_3, and PM_{10} scaled by WHO air quality guidelines • Uses relative risks for respiratory and cardiovascular hospitalizations in Hong Kong
Xie et al. (2013a)	Source Apportionment	• Compares $PM_{2.5}$ source apportionment results from different sites across an urban area • Demonstrates a degree of difference among source apportionment results across an urban area
Xie et al. (2013b)	Source Apportionment	• Compares $PM_{2.5}$ source apportionment results by PMF using different speciation datasets • Demonstrates that the number of species used in PMF can effect the number of resolved sources and mass in source

Study	Exposure Metric Type	Key Features
		categories
Zhang et al. (2008)	Source Apportionment	• Evaluates the link between PMF source apportioned $PM_{2.5}$ and ROS generation • Determines iron, soluble organic, and dust factors are related to ROS generation

PCA= Principal Component Analysis
FA = Factor Analysis
PMF = Positive Matrix Factorization
CMB = Chemical Mass Balance
CMAQ = Community Multiscale Air Quality
CAMx = Comprehensive Air Quality Model with Extensions
ROS = Reactive Oxygen Species
AQHI = Air Quality Health Index
WHO = World Health Organization