Assessing Exposure to Outdoor Air Pollution for Epidemiological Studies: Model-based and Personal Sampling Strategies

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Abstract

Epidemiologic studies have found air pollution to be causally linked to respiratory health including the exacerbation and development of childhood asthma. Accurately characterizing exposure is paramount in these studies to ensure valid estimates of health effects. Here, we provide a brief overview of the evolution of air pollution exposure assessment ranging from the use of ground-based, single-site air monitoring stations for population-level estimates to recent advances in spatio-temporal models, which use advanced machine learning algorithms and satellite-based data to accurately estimate individual-level daily exposures at high spatial resolutions. In addition, we review recent advances in sensor technology that enable the use of personal monitoring in epidemiologic studies, long-considered the ‘holy grail’ of air pollution exposure assessment. Finally, we highlight key advantages and uses of each approach including the generalizability and public health relevance of air pollution models and the accuracy of personal monitors that are useful to guide personalized prevention strategies. Investigators and clinicians interested in the effects of air pollution on allergic disease and asthma should carefully consider the pros and cons of each approach to guide their application in research and practice.
Overview of Air Pollutants and Their Relevance to Allergic Disease and Respiratory Health

Air pollution is a major contributor to the global burden of disease with increased mortality associated with exposure not only in developing countries in Africa and Asia, but also in the United States despite much stricter air quality standards.\textsuperscript{1, 2,3} Major sources of air pollution include mobile sources, i.e. traffic, and stationary sources, i.e. industrial activities.\textsuperscript{4} Major pollutants associated with health effects include particulate air pollution including particles smaller than 10 \(\mu\text{m} (\text{PM}_{10})\), 2.5 \(\mu\text{m} (\text{PM}_{2.5})\), and 0.1 \(\mu\text{m}\) (ultrafine particles, or UFP).\textsuperscript{4} Furthermore, nitrogen oxides (NO\textsubscript{x}) and volatile organic compounds (VOCs) emitted into the atmosphere can react with sunlight to form ground level ozone, a pollutant consistently associated with respiratory health.\textsuperscript{4} Epidemiologic studies worldwide consistently report a significant association between air pollutants and elevated risks of allergic and respiratory disease, with a recent study estimating that in 2015, 8–20\% of asthma emergency room visits worldwide could be attributed to ozone and 4–9\% to PM\textsubscript{2.5}.\textsuperscript{5} The objective of this brief review is to summarize recent advancements in the field of air pollution exposure assessment and highlight potential applications of both models and personal air monitoring to guide researchers and clinicians when considering the role of air pollution in their own studies or practice.

Evolution of Air Pollution Exposure Assessment for Epidemiologic Studies

Initial epidemiologic studies of air pollution included time-series studies utilizing population-level estimates of exposure.\textsuperscript{6} Following these seminal studies, cohort studies of traffic-related air pollution (TRAP) found the complex mixture of pollutants emitted from traffic sources, including UFP, diesel exhaust particles, NO\textsubscript{2}, and other pollutants, conferred specific health risks including the exacerbation of childhood asthma.\textsuperscript{7} The impact of exposure to TRAP on
development of allergic diseases is also supported by a growing number of studies.\textsuperscript{8, 9} Indeed, a recent meta-analysis found significant increased risks of developing childhood asthma for NO\textsubscript{2}, NO\textsubscript{x}, PM\textsubscript{2.5}, and PM\textsubscript{10} exposures.\textsuperscript{10} There are however studies that fail to demonstrate a positive correlation between TRAP and asthma,\textsuperscript{9} partially based on substantial variability in air pollutants measured as well as estimated levels and duration of exposure. Early studies of TRAP often relied on surrogates of exposure including proximity to major roads to estimate individual-level exposure.\textsuperscript{11} Later, land-use regression models were developed and became the standard approach to quantitatively estimate intra-urban and near-roadway TRAP exposures.\textsuperscript{12, 13} Most recently, hybrid modeling approaches utilizing a combination of satellite derived and remote sensing data, publically available geographic information, meteorology, and other data sources have been developed to estimate PM\textsubscript{2.5} and other pollutants with high spatio-temporal accuracy in the U.S. and worldwide.\textsuperscript{14-16} In addition to modeling air pollution exposures, burgeoning sensor technology has allowed for increased use of personal monitors in epidemiologic studies.\textsuperscript{17} Understanding the tradeoffs between these different exposure assessment methods is critical for designing and interpreting studies of the impact of air pollution on the development and exacerbation of allergic diseases.

**Air Pollution Exposure Prediction Models**

Epidemiological studies of the impact of air pollution on allergic diseases have traditionally relied on ambient measures collected by monitors, either for regulatory reasons (e.g., the Environmental Protection Agency’s Air Data program used to determine compliance with the National Ambient Air Quality Standards) or for a specific sampling campaign (e.g., central site monitoring performed for the formative Six Cities Study on air pollution and
Because monitoring is often prohibitively expensive, it cannot alone capture all of the spatiotemporal variability in ambient pollutants. In fact, most counties in the U.S. do not contain a regulatory air pollution monitor. To overcome this problem, exposure assessment scientists have developed methods for predicting ambient air pollution exposures where it is not measured by utilizing features of the surrounding land (e.g., traffic density or elevation), chemical transport modeling simulations, meteorological data, satellite-based measures, and more. These features are used with “ground truth” measurements in different statistical approaches ranging from simple linear regression models to complex machine learning approaches. Although each model is different with respect to its methods, features, and spatiotemporal resolution and extent, most exposure assessment models seek to maximize “predictive accuracy” – that is, accurate predictions where measurements were not made – for use in epidemiological studies.

Recent advances in utilizing data from the Earth Observing System of satellites operated by the National Aeronautics and Space Administration have allowed for incorporation of highly precise aerosol optical density data, which is a measure of the scattering of light in the atmosphere caused by aerosols. Figure 1 illustrates the predictions from one such model; the series of images represent the daily spatial surfaces of estimated PM$_{2.5}$ in Cincinnati, Ohio, USA for 14 days in June of 2010 at a resolution of 1 x 1 km. Since ambient pollutants like PM$_{2.5}$ vary with respect to space and time, these model predictions can be used to recreate daily exposures like the examples illustrated on the right side of the figure. A person’s residential address can be assigned to a latitude and longitude coordinate (called “geocoding”) and predicted air pollution exposures for their location can be averaged over time periods of interest for health studies, such as trimesters of pregnancy.
With respect to the precision of exposure assessment, relying on ambient, gridded concentration estimates can be advantageous compared to more precise estimates that incorporate individual-level characteristics and behaviors. Ambient exposure assessment models can have complete coverage of space and time within a study domain and population but are prone to measurement error; however, this measurement error is non-differential, meaning that the magnitude of error is not different depending on health outcomes. When this is the case, often termed “non-differential exposure misclassification”, this statistically means that health effect estimates can only be biased towards the null. Although it is true that increasing the precision of estimates by using personal sampling can decrease measurement error, it can also present threats to the validity of findings due to confounding by personal characteristics and behaviors. Specifically, the same types of behaviors that can cause errors in estimating personal air pollution exposure (e.g., amount of time spent outdoors, indoor-outdoor air exchange rates) also affect health outcomes (e.g. respiratory morbidity, allergic sensitivity) and so including these can create confounding pathways that do not exist when using ambient exposure assessment models. Nevertheless, these models incorporating widely available satellite data are invaluable to assign estimates of air pollution for large study populations and in locations with limited stationary sampling or other sources of air pollution data.

**The Promise of Personal Sampling**

Although exposure assessment models are useful for setting policies related to the levels of ambient air pollution, personal exposure to air pollution depends highly on individuals’ behavior and contact with pollutants in specific microenvironments. Integrating personal time-activity patterns ascertained through GPS data captured by smartphones with surface maps
produced by models as described above is one approach to improve exposure assessment.\textsuperscript{22, 23}

However, this method is unable to consider all facets of exposure and, for this reason, measuring personal exposure using wearable devices is considered the gold standard for air pollution exposure assessment.\textsuperscript{21}

Though personal sampling using time-integrated methods (e.g. using filter-based measurements conducted over 24-hours) has been conducted, technical limitations and participant burden has restricted widespread use.\textsuperscript{24, 25} More recent advances in technology, however, have produced new monitors capable of measuring time-resolved exposures (e.g. pollutant concentrations measured every 1 sec) with increased usability and decreased costs.\textsuperscript{26}

Reviews of available low and high cost personal monitors, their advantages and limitations, and technical capabilities are available.\textsuperscript{17, 27-29} Here, we briefly emphasize specific settings where personal air monitoring offers novel contributions compared to exposure assessment modeling including: 1) ascertaining the contribution and health impacts of short-term exposures compared to exposures measured or modeled over longer durations, 2) identifying specific microenvironments where elevated exposures occur, and 3) informing users of times and locations where their personal exposures are elevated with the goal of reducing personal exposures.

An important advantage to personal monitoring using real-time devices is the ability to identify the contribution of short, but elevated, exposures to air pollutants that are not captured by stationary monitoring or models. For example, time spent in transit, near diesel buses, at intersections, engaging in sports, and preparing food can result in a percentage of daily personal air pollution exposure up to 10 times higher than the percentage of time spent in these locations and activities.\textsuperscript{30-35} As shown in Figure 2, personal activities, including operating lawn and
gardening equipment, may also result in significantly elevated exposures to UFPs and other pollutants. While the health impact of these acutely elevated exposures is currently unknown, studies in both healthy and asthmatic adults have reported significant associations between short-term exposure to diesel exhaust and time spent in transit with decreased lung function and increased inflammation.\textsuperscript{36,37}

In addition, personal monitoring can be combined with global positioning satellite (GPS) and/or accelerometer data to identify specific microenvironments, including home, schools, or other locations where exposures occur. Using this approach, elevated personal exposures to black carbon, PM\textsubscript{2.5}, UFPs, and other pollutants during transit and in restaurants compared to exposures occurring in the home has been identified in multiple studies.\textsuperscript{29,33,38} Given the time spent at home, typically the home microenvironment contributes the greatest proportion of total personal daily exposure.\textsuperscript{38}

In contrast with stationary air monitoring or models to estimate air pollution exposure, personal monitors provide a depth of insight and actionable information analogous to biomonitoring. Indeed, providing individual results of personal air monitoring may be more informative than biomonitoring data given the potential to increase participants’ awareness of their exposure, identify specific locations and times of elevated exposures, and inform behavioral changes to decrease exposure and risk of adverse health outcomes. Prior studies have shown that behavioral modifications, including modifying cycling and walking routes, can significantly reduce personal exposure to UFPs, black carbon, and other pollutants.\textsuperscript{39,40} Future studies should consider how personal sampling may be utilized to reduce exposures and subsequent risk for adverse health outcomes, especially among children and adults with asthma or other conditions who may experience improved health with increased knowledge and awareness of locations and
times of highest air pollution exposure. There are, however, some limitations to personal
monitoring that must be considered including the time and training required for the patient or
subject to operate the device. While newer sensors are increasingly quiet and improved battery-
life has decreased the need for recharging batteries, maintenance of personal monitors may limit
the ability of some individuals, particularly children, to perform personal monitoring over long
periods of time. While newer, low-cost sensors are becoming available, these are often less
accurate and subject to drift then more expensive devices. In addition, the costs associated with
even the lowest-cost monitors may be prohibitive for low income households that are particularly
vulnerable to air pollution exposures and more likely to experience elevated air pollution levels.

Toward an Integrated Future of Personalized Risk Assessment and Allergic Disease
Management

Here, we have highlighted the strengths and limitations of different approaches used to estimate
exposure to air pollution. However, to fully assess the impact of air pollution on the development
of allergic diseases, these strategies need to be integrated with measurements of exposure to
common aero-allergens like pollen, which are known to coat particulate matter.\textsuperscript{41} Thus, the
nature of particulate matter differs not only by its source but also by weather conditions and
allergen present in the air.\textsuperscript{42} This is particularly relevant as particulate matter serves not only as
an allergen carrier but also importantly as an adjuvant.\textsuperscript{8} Indeed, PM$_{2.5}$ collected from measuring
stations in some areas can promote allergic airway responses that are not recapitulated by
exposure to just diesel exhaust particles.\textsuperscript{43} As outdoor pollutants are often also present indoors
and associated with common indoor pollutants like cigarette smoke, heating and cooking fumes
and other VOCs, assessing co-exposure to these air pollutants and indoor allergens (e.g. pet
dander, house dust mite, mold) should generate a comprehensive picture of environmental exposures and improve our limited understanding of their respective role and complex interplay in the development of allergic diseases.\textsuperscript{9, 44} Finally, growing evidence suggest that early exposures, including during pregnancy,\textsuperscript{45, 46} form a critical window where mitigating interventions may have the greatest impact on preventing disease development. Challenges involved in mitigating the impact of air pollution on asthma are discussed in a companion paper in this issue of the journal (Can Pollution Effects on Atopy and Asthma be Mitigated?). Information on environmental exposures coupled with symptom scores, inhaler usage and clear instructions in case of an asthma exacerbation, all integrated into mobile health applications centered on allergic diseases, is an achievable goal. For example, POLLAR (Impact of air POLLution on Asthma and Rhinitis) represent a European project of an integrated solution that tries to address the needs of patients and healthcare providers and help them better understand, prevent and treat allergic rhinitis and asthma exacerbation during high allergen and air pollution events.\textsuperscript{47} A recent comprehensive review of interactive mobile allergy and asthma smartphone applications available within the USA in 2018 point to remaining challenges.\textsuperscript{48} These promising new technologies offer a vision of a future where personal sampling solutions feeding into mobile health applications will empower patients to limit their exposure to harmful pollutants by offering actionable real time information, while allowing healthcare providers an invaluable insight into disease management.
Figure 1: A series of images representing daily spatial surfaces of estimated PM$_{2.5}$ at a resolution of 1 x 1 km in Cincinnati, Ohio, USA. Each panel represents one day in June of 2010.

Figure 2: Personal exposure to ultrafine particles during lawn mowing.

References


Figure 1
Figure 2
Journal of Allergy and Clinical Immunology Manuscript Review

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