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A multicity study of air pollution and cardiorespiratory emergency department visits: Comparing approaches for combining estimates across cities

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ABSTRACT

Determining how associations between ambient air pollution and health vary by specific outcome is important for developing public health interventions. We estimated associations between twelve ambient air pollutants of both primary (e.g. nitrogen oxides) and secondary (e.g. ozone and sulfate) origin and cardiorespiratory emergency department (ED) visits for 8 specific outcomes in five U.S. cities including Atlanta, GA; Birmingham, AL; Dallas, TX; Pittsburgh, PA; St. Louis, MO. For each city, we fitted overdispersed Poisson time-series models to estimate associations between each pollutant and specific outcome. To estimate multicity and posterior city-specific associations, we developed a Bayesian multicity multi-outcome (MCM) model that pools information across cities using data from all specific outcomes. We fitted single pollutant models as well as models with multipollutant components using a two-stage chemical mixtures approach. Posterior city-specific associations from the MCM models were somewhat attenuated, with smaller standard errors, compared to associations from time-series regression models. We found positive associations of both primary and secondary pollutants with respiratory disease ED visits. There was some indication that primary pollutants, particularly nitrogen oxides, were also associated with cardiovascular disease ED visits. Bayesian models can help to synthesize findings across multiple outcomes and cities by providing posterior city-specific associations building on variation and similarities across the multiple sources of available information.

1. Introduction

Short-term exposure to ambient air pollution has been associated with adverse health outcomes including emergency department (ED) visits, hospitalizations, and mortality due to cardiorespiratory diseases (Dominici et al., 2006; Stafoggia et al., 2013; Environmental Protection Agency, 2009; Environmental Protection Agency, 2013; Bell et al., 2004; Burnett et al., 1997). Air pollutants known to be associated with either cardiovascular (CVD) or respiratory (RD) diseases include particle pollutants, for example particulate matter < 2.5 μm in aerodynamic diameter ($PM_{2.5}$), and gaseous pollutants such as ozone (Environmental Protection Agency, 2009; Environmental Protection Agency, 2013). Associations with cardiorespiratory hospitalizations or ED visits have been identified for asthma (Strickland et al., 2010; Halonen et al., 2008), chronic obstructive pulmonary disease (COPD) (Qiu et al., 2012; Malig et al., 2015), congestive heart failure (CHF) (Wellenius et al., 2005a; Sarnat et al., 2015), and others (Darrow et al., 2014; Wellenius et al., 2005b; Malig et al., 2015), where these

Abbreviations: COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CVD, cardiovascular diseases; DF, degrees of freedom; DYS, cardiac dysrhythmia; ED, emergency department; IHD, ischemic heart disease; MCM, multicity multi-outcome; RD, respiratory diseases; URI, upper respiratory infection

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outcomes are based on specific diagnosis codes from hospital billing records. Frequently, these outcomes are combined into broad categories such as all RD ED visits, which may include ED visits for asthma, COPD, upper respiratory infection (URI), and pneumonia. However, identifying the most susceptible individuals, e.g. adults with COPD, requires understanding how associations between air pollution and health vary by specific outcome.

Multicity studies are necessary to robustly estimate air pollution associations for national regulations and also to examine effect modification across *cities* (Environmental Protection Agency, 2009). In multicity studies, previously observed differences across cities in estimated associations for total CVD and RD could potentially be driven by differences across cities in the proportion of specific outcomes, such as the proportion of pneumonia. Most previous studies of air pollution and cardiorespiratory ED visits are single-city studies that examine only a few pollutants or a few specific outcomes (Metzger et al., 2004; Peel et al., 2005). Several multicity studies conducted in Canada, California, and four U.S. cities have found significant associations between pollutants and ED visits (Stieb et al., 2009; Malig et al., 2015; Krall et al., 2017b); however the pollutant-outcome associations that were the strongest varied between studies. By examining associations in multiple cities across the U.S., we can more robustly explore how air pollution is associated with cardiorespiratory ED visits.

A challenge in conducting studies of air pollution and health is that daily counts for specific outcomes can be small, leading to greater uncertainty in estimated health associations compared with examining combined, broad cardiorespiratory categories (Winquist et al., 2012). When overdispersed Poisson time-series regression models (Ito et al., 2011; Sarnat et al., 2015; Peng et al., 2009; Ostro et al., 2006) are applied to city-specific data with short time series or with small daily health outcome counts, large effects are required in order to detect statistically significant associations due to large standard errors which are driven by the relatively small sample sizes. In multicity studies, instead of using only the data within the city to estimate associations, Bayesian approaches can borrow information across cities to estimate city-specific health associations using posterior means (Carlin and Louis, 2009).

Furthermore, it is possible that the overarching biological pathways that lead from pollution exposure to cardiorespiratory ED visits, such as those involving oxidative stress and inflammation, are similar across outcomes. Therefore, we can also consider using information for multiple *specific outcomes* as well as *cities* to improve estimates. For pollutant-outcome associations, we can compare standard time-series estimates, which do not use information for multiple cities and outcomes, with Bayesian posterior city-specific estimates, which (with the proper structure) use information for multiple cities and outcomes. This comparison can guide interpretation of uncertain time-series estimates as well as quantify potential added value in framing a more complex model. Our results identify and highlight where estimates are both uncertain and different from other estimates across cities.

Associations with cardiorespiratory ED visits also vary by *pollutant*. Some studies have found that pollutants of primary origin, such as nitrogen dioxide (NO_2) and elemental carbon (EC), were strongly associated with CVD ED visits including for myocardial infarction, heart failure (Stieb et al., 2009; Peel et al., 2007; Sarnat et al., 2015), and stroke (Villeneuve et al., 2006). For RD ED visits, associations have been identified for pollutants of both primary and secondary origin (Stieb et al., 2009; Alhanti et al., 2016; Orazzo et al., 2009; Halonen et al., 2008). While most studies have examined associations between pollution and health using a single-pollutant framework, a multi-pollutant framework may better explain some of these differences across previous studies.

As part of ongoing efforts in multicity air pollution investigations (Krall et al., 2017a, 2017b; Alhanti et al., 2016; Friberg et al., 2017; O'Lenick et al., 2017), here we estimated associations between short-term exposure to major air pollutants and cardiorespiratory ED visits in five US cities: Atlanta, GA; Birmingham, AL; Dallas, TX; Pittsburgh, PA; St. Louis, MO. In these five cities, we first estimated city-specific associations between twelve major air pollutants and specific cardiorespiratory outcomes using standard time-series regression models. Then, to combine estimated health associations across cities using data for all specific outcomes, we applied a Bayesian multicity multi-outcome (MCM) model.

2. Material and methods

2.1. Data

For each of the five cities, we obtained ED visits using electronic billing data from: the 20-county Atlanta, GA metropolitan area from 2002 to 2008; the 7-county Birmingham, AL metropolitan area from 2004 to 2008, the 12-county Dallas-Fort Worth metropolitan area from 2006 to 2008, the 3-county Pittsburgh area (including Allegheny, Washington, and Westmoreland counties) from 2002 to 2008, and the 16 counties (8 in Missouri and 8 in Illinois) in the St. Louis metropolitan area from 2002 to 2007.

ED visits were compiled based on their primary *International Classification of Diseases, 9th Revision* (ICD-9) codes (Web Appendix, Table S1). Outcomes included CHF, cardiac dysrhythmia (DYS), ischemic heart disease (IHD), and stroke for CVD ED visits and asthma and/or wheeze, COPD, pneumonia, and URI for RD ED visits. ED visits for chronic conditions such as COPD represent ED visits for exacerbations or symptoms associated with the condition. The ED visit data in this study were used in accordance with our data use agreements with the Georgia Hospital Association, the Dallas–Fort Worth Hospital Council Foundation, the Missouri Hospital Association, and individual hospitals and/or hospital systems in Birmingham and Pittsburgh. This study was conducted under approval by the Emory University Institutional Review Board; we were exempted from informed consent requirements, given the minimal risk nature of the study and the infeasibility of obtaining informed consent from individual patients for > 1.8 million billing records.

Concentrations of ozone (parts per billion, ppb), CO (parts per million, ppm), NO_2 (ppb), nitrogen oxides (NOx; ppb), SO_2 (ppb), PM_{10} ($PM < 10\,\mu m$, measured in $\mu g/m^3$), $PM_{2.5}$ ($\mu g/m^3$), and $PM_{2.5}$ chemical constituents ($\mu g/m^3$) including sulfate, nitrate and ammonium ions, OC, and EC were obtained from ambient monitoring stations located within each of the metropolitan areas. To create population-weighted average estimates of the 24-hour average (all PM measures), one-hour maximum (all gases except ozone), or the 8-hour maximum (ozone only) ambient pollution concentrations, monitor concentrations were fused with Community Multi-Scale Air Quality model estimates as described in previous work (Friberg et al., 2017; Friberg et al., 2016). The fused estimates better reflect population exposure for our large metropolitan areas compared with monitoring data alone (Friberg et al., 2017). To control for possible confounding by meteorological factors, we also obtained temperature and dew-point temperature from the National Climatic Data Center from automated surface observing stations at the major airport in each city.

2.2. Poisson time-series regression models

To estimate pollutant-outcome associations, we used the most common approach applied within the literature (Peng et al., 2009; Krall et al., 2013): we applied overdispersed Poisson time-series regression models to data from each city separately. We estimated associations with ED visits for an a priori selected exposure lag based on previous research: lag 0 exposure for CVD ED visits (Dominici et al., 2006; Sarnat et al., 2008; Metzger et al., 2004; Ye et al., 2017) and 8-day moving average exposure (mean of lag 0–7 exposure) for RD ED visits (Gass et al., 2015).

We controlled for potential confounding to be consistent with our