Environmental Research 137 (2015) 323–328

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Estimating risk of emergency room visits for asthma from personal versus fixed site measurements of NO_2

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ARTICLE INFO

Article history:
Received 8 December 2014
Received in revised form
7 January 2015
Accepted 8 January 2015
Available online 17 January 2015

Keywords:
Exposure measurement error
NO_2
Asthma
Case-crossover studies

ABSTRACT

Background: We examined the impact of data source and exposure measurement error for ambient NO_2 on risk estimates derived from a case-crossover study of emergency room visits for asthma in Windsor, Canada between 2002 and 2009.
Methods: Paired personal and fixed-site NO_2 data were available from an independent population (47 children and 48 adults) in Windsor between 2005 and 2006. We used linear regression to estimate the relationship and measurement error variance induced between fixed site and personal measurements of NO_2, and through a series of simulations, evaluated the potential for a Bayesian model to adjust for this change in scale and measurement error. Finally, we re-analyzed data from the previous case-crossover study adjusting for the estimated change in slope and measurement error.
Results: Correlations between paired NO_2 measurements were weak ($R^2 \leq 0.08$) and slopes were far from unity ($0.0029 \leq \beta \leq 0.30$). Adjusting the previous case-crossover analysis suggested a much stronger association between personal NO_2 (per 1 ppb) (Odds Ratio (OR) = 1.276, 95% Credible Interval (CrI): 1.034, 1.569) and emergency room visits for asthma among children relative to the fixed-site estimate (OR = 1.024, 95% CrI 1.004–1.045).
Conclusions: Our findings suggest that risk estimates based on fixed-site NO_2 concentrations may differ substantially from estimates based on personal exposures if the change in scale and/or measurement error is large. In practice, one must always keep the scale being used in mind when interpreting risk estimates and not assume that coefficients for ambient concentrations reflect risks at the personal level.

1. Introduction

Fixed-site monitors are often used to assign personal exposure levels in epidemiological studies of the health effects of ambient air pollution. While fixed-site monitors offer a cost-effective means of collecting exposure information for large numbers of study participants, exposure measurement error is a recognized limitation of this approach (Zeger et al., 2000). In general, the impact of exposure measurement error variance on risk estimates depends on several factors, including study design, the measurement error structure (classical or Berkson type error), and the extent of the measurement errors (Goldman et al., 2011; Thomas et al., 1993; Rhomberg et al., 2011; Zeger et al., 2000). In air pollution epidemiology, exposure measurement error often contains components of both classical and Berkson type error with the former resulting in bias toward the null and the latter resulting in little or no bias; however, both types of measurement error reduce precision (Armstrong, 1998; Sheppard et al., 2012; Zeger et al., 2000). Here we focus on the classical model, which typically leads to greater bias. Moreover, if fixed-site monitors systematically over or underestimate personal exposures, a scaling factor is required to further adjust model coefficients, since incremental changes in ambient concentrations translate into changes of a different magnitude at the personal level (Schwartz et al., 2007). Unfortunately, paired personal and fixed-site exposure data are rarely available in practice. As a result, it is usually not possible to evaluate the precise relationship between personal and fixed-site

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http://dx.doi.org/10.1016/j.envres.2015.01.006
0013-9351/

measurements in a given study, and therefore to adjust risk estimates for any change in scale or measurement error. In this study, our aim was to apply a Bayesian measurement error adjustment method that accommodates both a change in scale and measurement error variance to adjust risk estimates from fixed site values to those from personal exposures. This method was applied using paired personal and fixed-site data for ambient nitrogen dioxide (NO_2) in Windsor, Canada (Wheeler et al., 2011) along with data from a previous case-crossover study of ambient NO_2 and asthma emergency room visits in the same location (Lavigne et al., 2012). We first evaluated the method through simulations, and then applied our method to re-estimate the effect of NO_2 on asthma emergency room visits in Windsor, Canada. While the original study estimated the risk of asthma emergency room visits from fixed site NO_2 data, we estimate the effect had personal exposures been used.

2. Methods

2.1. Paired personal and fixed-site NO_2 data

Paired personal and fixed-site NO_2 data were available from participants in a previous panel study conducted in Windsor, Canada (Wheeler et al., 2011). Fixed-site data were collected at participants' homes (i.e. backyard measures) and from 2 separate fixed-site monitors operated by the Canadian National Air Pollution Surveillance (NAPS) program. This analysis focuses primarily on fixed-site NO_2 data collected from NAPS monitors; the average value of the two monitors in Windsor was used in the analyzes. All participants lived within approximately 12 km of the NAPS monitors.

All participants were non-smokers and lived in non-smoking homes, and were recruited through a school-based questionnaire distributed to elementary school children (Dales et al., 2009). Briefly, five consecutive 24-h personal NO_2 samples were collected from 47 asthmatic children (ages 9–12 years) and 48 healthy adults (children's parents) between 2005 and 2006, along with paired fixed-site measurements. All personal and backyard NO_2 measurements were collected using Ogawa passive sampling badges (Ogawa and Company). Personal NO_2 samplers were located in participants' breathing zones using a backpack that was carried (or kept nearby) for the duration of monitoring. NO_2 data from NAPS sites were collected using real-time chemiluminescence. Co-located Ogawa samplers were previously shown to correspond well with NAPs monitors in Windsor (Wheeler et al., 2011).

All adults lived in separate homes and all children lived in separate homes with the exception of two siblings. Age and sex data were not collected for adults in Windsor; children were predominantly female (77%). For simplicity, we treated all observations independently to estimate a single value for the average exposure measurement error; however, we recognize that there may be differences in measurement error between individuals. To verify this approach, we compared between- and within-cluster standard deviations in personal NO_2 exposures, which were approximately equivalent ($\sim$6 ppb), thus supporting our simplified approach. Relationships between personal and fixed-site NO_2 data were estimated separately for children and adults.

For this study, fixed-site NO_2 measurements were treated as imperfect measures of personal exposure. Sampling error in monitoring devices was ignored for both personal and fixed-site monitors as the primary objective was to evaluate the impact of using "measured" fixed-site data in place of "measured" personal data recognizing that both of these values may differ from unknown true values.

2.2. Previous case-crossover study of asthma emergency room visits and NO_2

Lavigne et al. (2012) conducted a case-crossover study of outdoor NO_2 and emergency department visits for asthma in Windsor, Ontario, Canada between April 1, 2002 and March 31, 2009. Briefly, this study included 3738 emergency room visits captured through the National Ambulatory Care Reporting System in Canada (http://www.cihi.ca/CIHI-ext-portal/internet/EN/Home/home/cihi000001). In total, approximately 33% of participants were 2–14 years of age, 40% were 15–39 years of age, and 27% were 40 years of age or older. Referent periods (3–4 per case period) were selected using a time-stratified approach (Janes et al., 2005) with reference days selected on the same day of the week, month, and year as the case. Daily mean concentrations of ambient NO_2 were calculated using fixed-site NAPS monitors in Windsor (the same monitors as above). Odds ratios and 95% confidence intervals describing the relationship between ambient NO_2 and asthma emergency room visits were estimated using conditional logistic regression adjusted for temperature, relative humidity, and daily number of influenza visits. Analyzes were conducted for all seasons combined and separately by age group for the warm (April–September) and cold (October–March) months. The strongest association between ambient NO_2 and emergency department visits was observed in the warm season for children 2–14 years of age (OR = 1.25 per 9 ppb change in NO_2, 95% CI: 1.04, 1.50). The original study was approved by the Health Canada research ethics board.

2.3. Predicting personal NO_2 exposures from fixed-site measures and covariates

Linear regression was used to predict personal NO_2 exposures from fixed-site measures. Separate models were evaluated for the warm (April–September) and cold (October–March) months and for children and adults to evaluate potential differences in the relationships between personal and fixed-site NO_2. Data for ambient temperature, relative humidity, and home indoor sources of NO_2 (i.e. presence/absence of natural gas appliances) were available for all participants from Environment Canada and participant questionnaires, respectively. These factors were evaluated in multivariable models describing the relationship between personal NO_2 exposures and fixed-site measures; however, adjusting for these factors had little impact on the relationship between personal and fixed-site NO_2 measurements. Therefore, these factors were not included in models used to estimate residual standard deviations for measurement error correction. Furthermore, as most studies do not have detailed information on factors such as gas appliance use, adjustments based on these factors may not be generally applicable. Linear regression parameters for personal and fixed-site NO_2 were estimated using STATA version 11 (StataCorp. 2009. College Station, TX: StataCorp LP).

2.4. Change of scale and measurement error correction

We used a modification of the Bayesian conditional independence model of Richardson and Gilks (1993) to adjust for measurement error. The model can be described in three stages: the first stage predicts asthma emergency visits from personal NO_2 exposure data via a conditional logistic regression model, assuming no error in NO_2. As discussed above, we assumed that the NO_2 values were independent both between and within subjects. While at first it may seem intuitive that NO_2 values within subjects may be dependent, these values are centered at individual-specific values, and separated by time. Hence it is likely that the values were uncorrelated within subjects or with correlations low