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**Biomass Burning as a Source of Ambient Fine Particulate Air Pollution  
and Acute Myocardial Infarction**

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Data and code are available upon request to the authors

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## ABSTRACT

**Background:** Biomass burning is an important source of ambient fine particulate air pollution (PM<sub>2.5</sub>) in many regions of the world.

**Methods:** We conducted a time-stratified case-crossover study of ambient PM<sub>2.5</sub> and hospital admissions for myocardial infarction (MI) in three regions of British Columbia, Canada. Daily hospital admission data were collected between 2008-2015 and PM<sub>2.5</sub> data were collected from fixed-site monitors. We used conditional logistic regression models to estimate odds ratios (ORs) describing the association between PM<sub>2.5</sub> and the risk of hospital admission for MI. We used stratified analyses to evaluate effect modification by biomass burning as a source of ambient PM<sub>2.5</sub> using the ratio of levoglucosan/PM<sub>2.5</sub> mass concentrations.

**Results:** Each 5 µg/m<sup>3</sup> increase in 3-day mean PM<sub>2.5</sub> was associated with an increased risk of MI among elderly subjects (≥ 65 years) (OR=1.06, 95% CI: 1.03, 1.08); risk was not increased among younger subjects. Among the elderly, the strongest association occurred during colder periods (<6.44 °C); when we stratified analyses by tertiles of monthly mean biomass contributions to PM<sub>2.5</sub> during cold periods, ORs of 1.19 (95%: 1.04, 1.36), 1.08 (95% CI: 1.06, 1.09), and 1.04 (95% CI: 1.03, 1.06) were observed in the upper, middle, and lower tertiles (p<sub>trend</sub>=0.003), respectively.

**Conclusion:** Short-term changes in ambient PM<sub>2.5</sub> were associated with an increased risk of MI among elderly subjects. During cold periods, increased biomass burning contributions to PM<sub>2.5</sub> may modify its association with MI.

Key words: PM<sub>2.5</sub>, biomass burning, myocardial infarction, case-crossover study

## INTRODUCTION

Ambient fine particulate air pollution (PM<sub>2.5</sub>) has a strong adverse association with cardiovascular health.<sup>1,2</sup> However, relatively few epidemiologic studies have specifically evaluated the cardiovascular health impacts of PM<sub>2.5</sub> from biomass burning<sup>3-4</sup> and further evaluation is needed.<sup>5</sup>

Biomass burning is an important source of ambient air pollution in many regions of the world and has been shown to be associated with inflammation, coagulation, and lipid peroxidation, which are important factors in the development of cardiovascular disease.<sup>3,6</sup> Moreover, exposure to wildfire smoke has been associated with increased systemic inflammation<sup>7-8</sup> and in controlled exposure settings short-term exposures to dilute wood smoke have been associated with increased arterial stiffness and decreased heart rate variability.<sup>9</sup> In addition, exposure to PM<sub>2.5</sub> from bush fires has been associated with out-of-hospital cardiac arrest.<sup>10-11</sup> Furthermore, recent evidence suggests that PM<sub>2.5</sub> from biomass burning may have increased oxidative potential<sup>12-13</sup> and may contribute to cardiovascular mortality.<sup>14</sup> However, other studies have failed to observe significant associations between short-term exposures to wood smoke and cardiac arrhythmia<sup>15</sup> or biomarkers of systemic inflammation.<sup>16</sup> Likewise, some studies have reported null associations between forest fire smoke exposure and physician visits/hospital admissions for cardiovascular outcomes.<sup>17</sup>

In this study, we examined the association between short-term changes in ambient PM<sub>2.5</sub> and hospital admissions for myocardial infarction (MI) in three regions of British Columbia, Canada impacted by biomass burning including residential wood burning (winter), forest fires (summer), and burning for land clearing (spring and autumn).

In addition, we explored potential effect modification by biomass burning as a source of ambient PM<sub>2.5</sub> using the cellulose combustion product levoglucosan as a source-specific marker.

## **METHODS**

### *Study Design and Population*

A time-stratified case-crossover design<sup>18</sup> was used to estimate the association between daily variations in ambient PM<sub>2.5</sub> and hospital admissions for acute myocardial infarction (International Classification of Diseases, 10<sup>th</sup> revision, Code I21) in three regions of British Columbia, Canada impacted by biomass burning: Prince George (population: 72,000), Kamloops (population: 85,000), and Courtenay/Comox (population: 50,000). Cases occurring between January 1, 2008 and March 31, 2015 were extracted from the Discharge Abstract Database maintained by the Canadian Institute for Health Information (CIHI) along with demographic information to describe the case population. Ambient PM<sub>2.5</sub> data for Kamloops and Courtenay were available beginning in 2010 and 2011, respectively; therefore, cases in these cities were excluded if they occurred prior to the start of PM<sub>2.5</sub> monitoring. All MI cases with residential three digit postal codes corresponding to these cities at the time of admission were eligible to be included in the analyses. Health Canada's Research Ethics Board approved this study.

### *Prospective Fixed Site Monitoring of Levoglucosan in PM<sub>2.5</sub>*

Daily mean levoglucosan data were collected prospectively in each city over a 1-year period to characterize temporal trends in the contribution of biomass burning to ambient PM<sub>2.5</sub>. These data were used to estimate monthly mean biomass burning contributions to ambient PM<sub>2.5</sub> (i.e. levoglucosan/PM<sub>2.5</sub>). Twenty-four hour mean PM<sub>2.5</sub>

concentrations (for levoglucosan analyses) were monitored in each location between January 1, 2014 and March 31, 2015 using Thermo Partisol 2025i monitors (Thermo Scientific) located at the same provincial monitoring sites where  $PM_{2.5}$  measurements were collected. Samples were collected between 7:00-7:00 to facilitate technician visits to each site. All  $PM_{2.5}$  filters underwent gravimetric analyses and were subsequently analyzed for levoglucosan by ion chromatography to provide an estimate of the daily contribution (levoglucosan/ $PM_{2.5}$ ) of biomass burning to ambient  $PM_{2.5}$ .<sup>19</sup>

Daily mean  $PM_{2.5}$  data from provincial fixed-site monitors (1 site in each city) were compiled for the entire study period (Prince George: 2008-2015; Kamloops: 2010-2015; Courtenay: 2011-2015) along with daily meteorological data and these data were used for case-crossover analyses (described below). In Prince George,  $PM_{2.5}$  data were collected using a tapered element oscillating microbalance (TEOM), whereas BAM (Beta-Attenuation Monitor) 1020 instruments were used in Kamloops and Courtenay. Daily data for ambient  $NO_2$  and  $O_3$  were also compiled for use in two-pollutant models as sensitivity analyses.

#### *Spatial Monitoring of Levoglucosan in $PM_{2.5}$*

Small-scale spatial monitoring studies were conducted in each city to characterize spatial variations in wood smoke contributions to  $PM_{2.5}$  across each region. Specifically, two weekly samples of  $PM_{2.5}$  and levoglucosan were collected each month at 8 sites located across each community between September, 2014 and March, 2015 using cascade impactors at a flow rate of 5 liters/minute. These data were used to develop linear regression models (described below) to adjust central-site measurements of  $PM_{2.5}$  (from provincial monitors) and levoglucosan (from Thermo Partisol 2025i monitors co-located

with provincial monitors) to more accurately reflect spatial variations across each region. This is an important consideration as wood smoke is known to exhibit large spatial variations.<sup>20</sup>

The locations of spatial monitoring sites were selected based on the spatial distribution of cases mapped across each region. Specifically, while we did not have access to six digit postal codes (which represent approximately one city block), CIHI provided anonymous maps of the geographic centroids of six-digit postal codes of cases which allowed us to position monitors to capture regions in which the cases lived. Moreover, using the geographic coordinates of each spatial monitoring site, CIHI identified the monitor closest to the residence of each case; therefore, spatial corrections for PM<sub>2.5</sub> and levoglucosan were based on the monitor closest to each subjects' residence. The median (interquartile range, IQR) distance between spatial monitoring sites and the centroids of six-digit postal codes was 1040 meters (IQR=623-2006 meters).

### *Statistical Analysis*

#### *Spatial Adjustment Models for Levoglucosan in PM<sub>2.5</sub>*

We used linear regression models to describe the relationship between mean levoglucosan concentrations at each of the spatial monitoring sites in each city and values measured at the central monitoring site (city-specific linear regression models are available in eTable 1; <http://links.lww.com/EDE/B172>). These models were used to adjust central-site measurements in each city to reflect spatial differences across each region. For levoglucosan, spatial adjustments were based only on the slopes of linear regression models (i.e. intercepts were assumed to be zero) as the imprecise nature of model intercepts often resulted in negative or unrealistically large values for

levoglucosan compared to fixed site values. In nearly all levoglucosan models, 95% confidence interval estimates for intercept values included the null; therefore, linear regression slopes were used as scaling factors to account for spatial differences in levoglucosan concentrations across each region.

### *Case-Crossover Analyses*

We used conditional logistic regression models to estimate odds ratios (95% confidence Intervals) describing the relationship between ambient PM<sub>2.5</sub> and the risk of MI adjusted for mean ambient temperature. We pooled data from all three cities and a cluster variance estimator was used to account for within-city correlations. We included mean temperature as a linear term in all models using the same lag times as for PM<sub>2.5</sub> (i.e. lag-0 or 3-day mean). We also examined non-linear forms (i.e. restricted cubic splines with 3 knots) for temperature but they did not improve model fit (based on Akaike information criterion values) or meaningfully change point estimates (analyses using restricted cubic splines for temperature are shown in eTable 2;

<http://links.lww.com/EDE/B172>; the linear relationship between 3-day mean temperature and MI is shown in eFigure 1; <http://links.lww.com/EDE/B172>). We also considered relative humidity as a possible covariate but it did not change model coefficients for PM<sub>2.5</sub> or improve model fit and thus we excluded it from the models we report.

The exposure periods of interest in this study included the same day as hospital admission for MI (lag-0) and the 3-day mean exposure preceding hospital admissions (including the day of admission). As the case-crossover design compares cases to themselves at different points in time it adjusts for factors that do not vary within individuals over short time-periods (e.g. age, smoking status, body mass index). In this

study, matched sets consisted of the case period (the day of myocardial infarction) and referent periods selected on the same day of the week in the same month and year as the case period (i.e. 3-4 referent periods per case). This time-stratified approach to referent selection has been shown to result in unbiased conditional logistic regression estimates in case-crossover studies.<sup>18</sup>

We first examined the relationship between PM<sub>2.5</sub> and MI for the population as a whole followed by analyses stratified by age (above or below the median value) and sex. As prospective daily levoglucosan data were only available for a single year, we did not have enough cases to use daily levoglucosan data in the main analyses. Instead, we used prospective levoglucosan data to estimate monthly mean biomass contributions to ambient PM<sub>2.5</sub> (i.e. levoglucosan/PM<sub>2.5</sub>) and conducted stratified analyses across tertiles of this parameter. We evaluated potential effect modification by biomass burning as a source of ambient PM<sub>2.5</sub> by including a first-order interaction term between PM<sub>2.5</sub> and an indicator variable for tertiles of monthly mean biomass contributions to PM<sub>2.5</sub>. We did not conduct stratified analyses by heating/non-heating season as there are important sources of biomass burning during the summer months in these locations (e.g. forest fires, burning brush). All odds ratios are expressed per 5 µg/m<sup>3</sup> increase in ambient PM<sub>2.5</sub> concentrations as this interval was approximately equal to the interquartile range of the mean difference in 3-day mean PM<sub>2.5</sub> concentrations between case and control periods. We generated concentration–response plots using restricted cubic splines with three equally spaced knots. All statistical analyses were conducted using STATA version 13 (Statacorp, College Station, TX, USA).

## Results

In total, we included 2881 cases of MI in our analyses including 504 cases from Courtenay, 885 cases from Kamloops, and 1492 cases from Prince George. Cases were predominantly male (68%) with a median age of 65 years. On average, ambient PM<sub>2.5</sub> concentrations tended to be low in all three cities (i.e. < 10 µg/m<sup>3</sup>), with higher concentrations observed during colder portions of the year (Table 1). Daily mean ambient temperatures were weakly correlated with PM<sub>2.5</sub> (r=-0.27) and levoglucosan/PM<sub>2.5</sub> (r=-0.38). Daily mean PM<sub>2.5</sub> was positively correlated with NO<sub>2</sub> (r=0.51) and inversely correlated with O<sub>3</sub> (r=-0.49); NO<sub>2</sub> and O<sub>3</sub> were also inversely correlated (r=-0.43). The ratio of daily mean levoglucosan/PM<sub>2.5</sub> was not correlated with NO<sub>2</sub> (r=0.05) but was weakly correlated with O<sub>3</sub> (r=-0.30). Correlations for 3-day mean values were similar to daily mean correlations (data not shown).

Monthly mean levoglucosan/PM<sub>2.5</sub> values are shown in Figure 1. In general, biomass burning contributions to PM<sub>2.5</sub> were higher during colder months in all three cities, consistent with residential wood burning. Courtenay had the largest biomass contributions to ambient PM<sub>2.5</sub> and seasonal differences in ambient PM<sub>2.5</sub> concentrations were most apparent in this city (Table 1). Evidence of biomass burning contributions to PM<sub>2.5</sub> were also apparent in Kamloops and Prince George during the summer months (primarily July and August) likely owing to forest fires.

City-specific linear regression models used for spatial adjustments in ambient PM<sub>2.5</sub> and levoglucosan concentrations are shown in eTable 1; <http://links.lww.com/EDE/B172>. Overall, strong positive slopes were apparent for PM<sub>2.5</sub> and levoglucosan samples collected using cascade impactors co-located with provincial

fixed-site monitors (PM<sub>2.5</sub> slope=0.78, 95% CI: 0.70, 0.86; R<sup>2</sup>=0.57; levoglucosan slope=1.03, 95% CI: 0.92, 1.15; R<sup>2</sup>=0.52). In general, the fixed site monitor in Courtenay was less representative of spatial variations across the region than monitors located in Prince George and Kamloops where R<sup>2</sup> values generally exceeded 0.7 for both PM<sub>2.5</sub> and levoglucosan (eTable 1; <http://links.lww.com/EDE/B172>).

Odds ratios describing the relationship between ambient PM<sub>2.5</sub> and hospital admissions for MI are shown in Table 2. Each 5 µg/m<sup>3</sup> increase in lag-0 or 3-day mean PM<sub>2.5</sub> concentration was associated with an increased risk of MI among elderly subjects (≥ 65 years) with slightly stronger associations observed for 3-day mean concentrations. Short-term changes in ambient PM<sub>2.5</sub> were not associated with MI among younger subjects (interaction p-value=0.032). The concentration–response relationship between 3-day mean PM<sub>2.5</sub> and hospital admissions for MI among elderly subjects is shown in Figure 2.

In general, odds ratios based on PM<sub>2.5</sub> data corrected for spatial variations across each region were slightly stronger than for uncorrected data (Table 2). This was particularly true in Courtenay where the fixed-site monitor was least representative of regional variations in PM<sub>2.5</sub>. Each 5°C increase in 3-day mean ambient temperature was also independently associated with hospital admissions for MI among elderly subjects (OR=1.10, 95% CI: 1.06, 1.14); a smaller increased risk was observed among younger subjects (OR=1.05, 95% CI: 0.98, 1.12).

Odds ratios describing the relationship between 3-day mean PM<sub>2.5</sub> concentrations and hospital admissions for MI are shown in Table 3 across tertiles of monthly mean biomass contributions to PM<sub>2.5</sub>. For the population as a whole, the strongest association

between PM<sub>2.5</sub> and MI was observed in the highest tertile of biomass contributions to PM<sub>2.5</sub>; however, the trend across tertiles was not statistically significant (p=0.519).

Among elderly subjects, the strongest association between PM<sub>2.5</sub> and MI also occurred in the highest tertile of biomass contributions to PM<sub>2.5</sub> but the trend across tertiles was not statistically significant (p=0.11).

As sensitivity analyses, we repeated the analysis for elderly subjects ( $\geq 65$  years) in Table 3 excluding Courtenay given that this city had much higher values for the proportion of levoglucosan in PM<sub>2.5</sub> compared to Kamloops and Prince George.

Excluding Courtenay did not change the trend of results across strata of biomass contributions to PM<sub>2.5</sub> using the same tertile cut points as in Table 3 (high: OR= 1.12, 95% CI: 0.97, 1.28; mid: OR=1.00, 95% CI: 0.96, 1.04; low: OR=1.04, 95% CI: 1.03, 1.04). We also re-calculated tertiles based on the distribution of monthly mean biomass contributions to PM<sub>2.5</sub> in Prince George and Kamloops and repeated the analyses among the elderly excluding Courtenay and observed a similar trend (high: OR=1.14, 95% CI: 1.00, 1.30; mid: OR=1.00, 0.96, 1.04; low: OR=1.05, 95% CI: 1.02, 1.09).

Including 3-day mean NO<sub>2</sub> or O<sub>3</sub> in the models did not dramatically change the results across tertiles of biomass contributions to PM<sub>2.5</sub> in Table 3. For example, the odds ratio among elderly subjects in the highest tertile of biomass contributions to PM<sub>2.5</sub> increased to 1.17 (95% CI: 0.96, 1.42) when NO<sub>2</sub> was included in the model and decreased to 1.12 (95% CI: 1.01, 1.24) when O<sub>3</sub> was included in the model (NO<sub>2</sub> and O<sub>3</sub> were not associated with an increased risk of MI in these models).

When analyses were examined across temperature strata (above/below the median 3-day mean temperature) the positive association between 3-day mean PM<sub>2.5</sub> and hospital

admissions for MI among elderly subjects was limited to the cold season (Table 3). Therefore, in order to determine if the risk pattern across tertiles of biomass contributions to PM<sub>2.5</sub> may be explained by temperature, we restricted our analyses to the cold period (i.e. < 6.44 °C) and again examined trends across tertiles of biomass contributions to PM<sub>2.5</sub>. The results of these analyses are shown in Table 4 and indicate increased MI risks with increasing biomass contributions to ambient PM<sub>2.5</sub>. For elderly subjects, ORs of 1.19 (95% CI: 1.04, 1.36), 1.08 (95% CI: 1.06, 1.09), and 1.04 (95% CI: 1.03, 1.06) were observed for the high, middle, and lower tertiles of biomass contributions to PM<sub>2.5</sub> (interaction p-value=0.003), respectively. Moreover, 3-day mean PM<sub>2.5</sub> concentrations (low: 6.29 µg/m<sup>3</sup>; middle: 7.58 µg/m<sup>3</sup>; high: 7.77 µg/m<sup>3</sup>) and standard deviations of mean differences between case and control days (low: 4.85 µg/m<sup>3</sup>; middle: 4.34 µg/m<sup>3</sup>; high: 4.79 µg/m<sup>3</sup>) were similar across categories of biomass contributions to PM<sub>2.5</sub>. We also observed increased risks with increased biomass contributions for younger subjects (<65 years) and for the population as a whole (interaction p-values<0.001); however, inverse associations were observed between PM<sub>2.5</sub> and MI in the low and middle tertiles for these analyses. Concentration response curves for 3-day mean PM<sub>2.5</sub> concentrations and emergency room visits for MI are shown in Figure 3 for the bottom (≤25<sup>th</sup> percentile) and top quartiles (≥75<sup>th</sup> percentile) of biomass contributions to PM<sub>2.5</sub> for elderly subjects during the cold period.

As sensitivity analyses, we re-examined the models in Table 4 for elderly subjects removing individual years from the analyses. The purpose of this analysis was to evaluate if extreme events in a given year (e.g. large forest fires) may have impacted our results. These analyses are shown in eTable 3; <http://links.lww.com/EDE/B172>; removing

individual years did not change the pattern observed in Table 4 as the greatest risks were repeatedly observed in the highest category of biomass contributions to PM<sub>2.5</sub>.

Including 3-day mean ambient NO<sub>2</sub> or O<sub>3</sub> in conditional logistic regression models did not have a meaningful impact on the magnitude of associations across strata of biomass contributions to PM<sub>2.5</sub>. For example, adding 3-day mean O<sub>3</sub> to the model for elderly subjects in Table 4 increased the odds ratio slightly in the highest tertile of biomass contributions to PM<sub>2.5</sub> (OR=1.21, 95% CI: 1.08,1.25). A similar pattern was observed when 3-day mean NO<sub>2</sub> was added to the model (OR=1.22, 95% CI: 0.96, 1.55). The pattern of increased risk with increased biomass contributions to PM<sub>2.5</sub> also remained when NO<sub>2</sub> or O<sub>3</sub> were included in the models ( $p_{\text{trend}} < 0.001$ ).

Finally, in an effort to confirm the pattern of results observed using estimated monthly mean biomass contributions to PM<sub>2.5</sub>, we conducted stratified analyses using prospective *daily* levoglucosan data (with strata based on the median value of 3-day mean levoglucosan/PM<sub>2.5</sub> during prospective monitoring). In this analysis, an odds ratio of 1.04 (95% CI: 0.98, 1.11) was observed for the lower category of biomass contributions to PM<sub>2.5</sub> whereas an odds ratio of 1.09 (95% CI: 0.99, 1.20) was observed for the upper category. This pattern is consistent with that observed for monthly data with a stronger association observed with higher biomass contributions to PM<sub>2.5</sub>; however, risk estimates were imprecise owing to the small number of cases (n=700) available during prospective monitoring.

## **Discussion**

Our findings suggest that short-term changes in ambient PM<sub>2.5</sub> are associated with an increased risk of hospital admission for myocardial infarction among elderly subjects

in areas impacted by biomass burning. Moreover, our results indicate that biomass burning contributions to ambient PM<sub>2.5</sub> may modify its association with myocardial infarction, with the largest risks occurring when biomass contributions are greatest.

Few other studies have specifically evaluated the acute cardiovascular health effects of exposure to PM<sub>2.5</sub> from biomass burning. Recently, two Australian studies reported positive associations between PM<sub>2.5</sub> from forest fires and out of hospital cardiac arrest.<sup>10-11</sup> Moreover, consistent with our findings, one of these studies also reported positive associations between ambient PM<sub>2.5</sub> and hospital admissions for MI and ischemic heart disease with stronger associations observed among older adults ( $\geq 65$  years).<sup>11</sup> Similarly, exposure to wildfire smoke from a peat bog fire in North Carolina was associated with increased emergency room visits for heart failure<sup>21</sup> and a time-series study in Seattle noted a positive association between potassium in PM<sub>2.5</sub> (a marker of biomass) and cardiovascular mortality during the cold season.<sup>22</sup> Likewise, studies in Chile<sup>23</sup> and New Zealand<sup>24</sup> reported positive associations between ambient PM<sub>10</sub> and hospital admissions for cardiovascular causes in areas impacted by biomass burning. However, at least one Canadian study did not observe an association between exposure to forest fire smoke and physician visits or hospital admissions for cardiovascular outcomes<sup>17</sup> and other studies have reported null associations between short-term changes in PM<sub>2.5</sub> and risk of myocardial infarction.<sup>25-26</sup> Reasons for these discrepancies are not clear but may relate to different sources of biomass (i.e. residential wood burning vs. forest fires) or differential impacts of exposure measurement error. In general, while the current literature is somewhat inconsistent with respect to the cardiovascular health effects of PM<sub>2.5</sub> from biomass burning, our results suggest that these emissions are

positively associated with risk of MI among elderly subjects. However, our finding of increased MI risk with increased biomass contributions to PM<sub>2.5</sub> requires further replication as the underlying biological plausibility of this observation remains unclear.

We recently reported that glutathione-related oxidative potential may modify the association between PM<sub>2.5</sub> and emergency room visits for MI with stronger associations observed in cities with PM<sub>2.5</sub> containing higher oxidative potential.<sup>27</sup> Therefore, one explanation for the observed trend of increased MI risk across tertiles of biomass contributions to PM<sub>2.5</sub> may be that the oxidative potential of PM<sub>2.5</sub> is increased when biomass contributions are greater. Indeed, at least two recent studies support this hypothesis. Specifically, Bates et al. noted that biomass burning was a strong contributor to the oxidative potential of PM<sub>2.5</sub> using the dithiolthreitol assay and also reported that dithiolthreitol activity was more strongly associated with emergency room visits for congestive heart failure than PM<sub>2.5</sub>.<sup>12</sup> In addition, Kurmi et al.<sup>13</sup> reported that wood smoke particle extracts were capable of depleting the antioxidants ascorbate and glutathione in a synthetic respiratory tract lining fluid (the same assay used above by Weichenthal et al.<sup>27</sup>). The specific chemical components explaining the increased oxidative potential of PM<sub>2.5</sub> from biomass burning have yet to be thoroughly characterized; however, Kurmi et al.<sup>13</sup> noted that metal chelators did not inhibit ascorbic acid depletion in the synthetic respiratory tract lining fluid (they did not examine the impact of metal chelators on glutathione depletion) and others have reported that semi-volatile<sup>28</sup> or polar organic components<sup>29</sup> may play an important role in the oxidative potential of wood smoke particles. Moreover, differences in particle aging and/or burning conditions may also influence wood smoke particle composition and toxicity.<sup>30</sup>

Unfortunately, we did not collect data on the oxidative potential or composition of PM<sub>2.5</sub> samples in this study and future studies should evaluate this question further. Indeed, our findings suggest that levoglucosan is likely only a marker for the components/characteristics of interest as the trend of increased risk with increased biomass contributions to PM<sub>2.5</sub> remained when Courtenay (the location with the highest levoglucosan concentrations) was removed from the analyses.

Although this study had a number of important advantages, including prospective monitoring of daily levoglucosan concentrations and spatial studies to correct for regional differences in PM<sub>2.5</sub> and levoglucosan concentrations, it is important to note several limitations. First, daily levoglucosan data were limited to a 1-year period and thus the main analyses relied on estimated monthly mean biomass contributions to PM<sub>2.5</sub>. While existing evidence suggests that the use of wood for heating (and the amount of wood used per household) has remained stable in British Columbia<sup>31</sup> over the past decade, use of monthly estimates (as opposed to daily values) likely contributed to uncertainty in our effect estimates. This error likely contained components of both classical and Berkson-type measurement error. Specifically, classical measurement error likely impacted our assessment of monthly mean levoglucosan/PM<sub>2.5</sub> values (i.e. measured values distributed around the true monthly mean) whereas Berkson type error likely resulted from the use of monthly mean values instead of daily levoglucosan data (i.e. true daily values distributed around monthly mean estimates). Non-differential misclassification of cases across tertiles of monthly mean biomass contributions to PM<sub>2.5</sub> could bias effect estimates in either direction depending on the pattern of misclassification across categories; however, this is not a likely explanation of the observed trend in MI risk across tertiles.

Alternatively, we cannot rule out the possible influence of unmeasured confounding factors that may be correlated with both PM<sub>2.5</sub> concentrations (more specifically the mean difference in PM<sub>2.5</sub> concentrations between case and control days) and MI; however, this factor would also have to be correlated with the proportion of levoglucosan in PM<sub>2.5</sub> to explain the trend in MI risk across tertiles of biomass contributions.

An additional component of exposure measurement error in our study relates to indoor exposure to PM<sub>2.5</sub> from biomass burning owing to direct emissions into the home when starting the fire or when refueling. In some cases, individual personal exposures may differ substantially from ambient PM<sub>2.5</sub> concentrations owing to indoor exposures and this likely also biased effect estimates toward the null.

Finally, as a relatively small number of cases were available, within-city effect estimates were imprecise and detailed stratified analyses within cities were not possible. However, the pattern of risk estimates across cities was consistent with the overall results as the relationship between PM<sub>2.5</sub> and MI was strongest in Courtenay which also had the largest biomass contributions to PM<sub>2.5</sub>.

In summary, our findings suggest that short-term changes in ambient PM<sub>2.5</sub> concentrations are associated with hospital admissions for MI among elderly subjects in areas impacted by biomass burning. Moreover, our results indicate that the magnitude of biomass contributions to PM<sub>2.5</sub> may modify the association between PM<sub>2.5</sub> and MI.

## References

1. Franklin BA, Brook R, Pope A. Air pollution and cardiovascular disease. *Curr Probl Cardiol* 2015; 40: 207-238.
2. Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SC Jr, Whitsel L, Kaufman JD; American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation* 2010; 121: 2331-2378.
3. Naeher LP, Brauer M, Lipsett M, Zelikoff JT, Simpson CD, Koenig JQ, Smith KR. Wood-smoke health effects: a review. *Inhal Toxicol* 2007; 19: 67-106.
4. Sigsgaard T, Forsberg B, Annesi-Maesano I, Blomberg A, Bolling A, Boman C, Jakob Bonlokke, Brauer M, Bruce N, Heroux ME, Hirvonen MR, Kelly F, Kunzli N, Lundback B, Moshhammer H, Noonan C, Pagels J, Sallsten G, Sculier JP, Brunekreef B. Health impacts of anthropogenic biomass burning in the developed world. *Eur Respir J* 2015; 46: 1577-1588.
5. Liu JC, Pereira G, Uhl SA, Bravo MA, Bell ML. A systematic review of the physical health impacts from non-occupational exposure to wildfire smoke. *Environ Res* 2015; 136: 120-132.
6. Barregard L, Sallsten G, Gustafson P, Andersson L, Johansson L, Basu S, Stigendal L. Experimental exposure to wood-smoke particles in healthy humans: effects on

- markers of inflammation, coagulation, and lipid peroxidation. *Inhal Toxicol* 2006; 18: 845-853.
7. Tan WC, Qiu D, Liam BL, Ng TP, Lee SH, van Eeden SF, D'Yachkova Y, Hogg JC. The human bone marrow response to acute air pollution caused by forest fires. *Am J Respir Crit Care Med* 2000; 161: 1213-1217.
8. Swiston JR, Davidson W, Attridge S, Li GT, Brauer M, van Eeden SF. Wood smoke exposure induces a pulmonary and systemic inflammatory response in firefighters. *Eur Respir J* 2008; 32: 129-138.
9. Unosson J, Blomberg A, Sandstrom T, Muala A, Boman C, Nystrom R, Westerholm R, Mills NL, Newby DE, Langrish JP, Bosson JA. Exposure to wood smoke increases arterial stiffness and decreases heart rate variability in humans. Part 1. *Fibre Toxicol* 2013; 10: 20.
10. Dennekamp M, Straney LD, Erbas B, Abramson MJ, Keywood M, Smith K, Sim MR, Glass DC, Del Monaco A, Haikerwal A, Tonkin AM. Forest fire smoke exposure and out of hospital cardiac arrests in Melbourne, Australia: a case-crossover study. *Environ Health Perspect* 2015; 123: 959-964.
11. Haikerwal A, Akram M, Del Monaco A, Smith K, Sim MR, Meyer M, Tonkin AM, Abramson MJ, Dennekamp M. Impact of fine particulate matter (PM<sub>2.5</sub>) exposure during wildfires on cardiovascular health outcomes. *J Am Heart Assoc* 2015; 4: e001653.
12. Bates JT, Weber RJ, Abrams J, Verma V, Fang T, Klein M, Strickland MJ, Ebel Sarnat S, Chang HH, Mulholland JA, Tolbert PE, Russell AG. Reactive oxygen

- species generation linked to sources of atmospheric particulate matter and cardiorespiratory effects. *Environ Sci Technol* 2015; doi:10.1021/acs.est.5b02967
13. Kurmi OP, Dunster C, Ayres JG, Kelly FJ. Oxidative potential of smoke from burning wood and mixed biomass fuels. *Free Radic Res* 2013; 47: 829-835.
14. Heo J, Schauer JJ, Yi O, Paek D, Kim H, Yi SM. Fine particle air pollution and mortality: importance of species sources and chemical species. *Epidemiol* 2014; 25: 379-388.
15. Langrish JP, Watts SJ, Hunter AJ, Shah AS, Bosson JA, Unosson J, Barath S, Lundback M, Cassee FR, Donadlson K, Sandstrom T, Blomberg A, Newby DE, Mills NL. Controlled exposures to air pollutants and risk of cardiac arrhythmia. *Environ Health Perspect* 2014; 122: 747-753.
16. Stockfelt L, Sallsten G, Almerud P, Basu S, Barregard L. Short-term exposure to low doses of two kinds of wood smoke does not induce systemic inflammation, coagulation or oxidative stress in healthy humans. *Inhal Toxicol* 2013; 25: 417-425.
17. Henderson SB, Brauer M, MacNab YC, Kennedy SM. Three measures of forest fire smoke exposure and their associations with respiratory and cardiovascular health outcomes in a population-based cohort. *Environ Health Perspect* 2011; 119: 1266-1271.
18. Janes H, Sheppard L, Lumley T. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. *Epidemiol* 2005; 16: 717-726.

19. Simoneit BRT, Schauer JJ, Nolte CG, Oros DR, Elias VO, Fraser MP, Rogge WF. Levoglucosan, a tracer for cellulose in biomass burning and atmospheric particles. *Atmos Environ* 1999; 33: 173-182.
20. Larson T, Su J, Baribeau AM, Buzzelli M, Setton E, Brauer M. A spatial model of urban woodsmoke concentrations. *Environ Sci Technol* 2007; 41: 2429-2436.
21. Rappold AG, Stone SL, Cascio WE, Neas LM, Kilaru VJ, Carraway MS, Szykman JJ, Ising A, Cleve WE, Meredith JT, Vaughan-Batten H, Deyneka L, Devlin RB. Peat bog wildfire smoke exposure in rural North Carolina is associated with cardiopulmonary emergency department visits assessed through syndromic surveillance. *Environ Health Perspect* 2011; 119: 1415-1420.
22. Zhou J, Ito K, Lall R, Lippmann M, Thurston G. Time-series analyses of mortality effects of fine particulate matter components in Detroit and Seattle. *Environ Health Perspect* 2011; 119: 461-466.
23. Sanhueza PA, Torreblanca MA, Diaz-Robles LA, Schiappacasse LN, Silva MP, Astete TD. Particulate air pollution and health effects for cardiovascular and respiratory causes in Temuco, Chile: a wood-smoke-polluted urban area. *J Air Waste Manage Assoc* 2009; 59: 1481-1488.
24. McGowan JA, Hider PN, Chacko E, Town GI. Particulate air pollution and hospital admissions in Christchurch, New Zealand. *Aust N Z J Public Health* 2002; 26: 23-29.
25. Levy D, Sheppard L, Checkoway H, Kaufman J, Lumley T, Koenig J, Siscovick D. A case-crossover analysis of particulate matter air pollution and out-of-hospital primary cardiac arrest. *Epidemiol* 2001; 12: 193-199.

26. Sullivan J, Sheppard L, Schreuder A, Ishikawa N, Siscovick D, Kaufman J. Relation between short-term fine particulate matter exposure and onset of myocardial infarction. *Epidemiol* 2005; 16: 41-48.
27. Weichenthal S, Lavigne E, Evans E, Pollitt K, Burnett RT. Ambient PM2.5 and risk of emergency room visits for myocardial infarction: impact of regional PM2.5 oxidative potential. Accepted by *Environ Health* March 2016.
28. Miljevic B, Heringa MF, Keller A, Meyer NK, Good J, Lauber A, Decarlo PF, Fairfull-Smith KE, Nussbaumer T, Burtscher H, Prevot AS, Baltensperger U, Bottle SE, Ristovski ZD. Oxidative potential of logwood and pellet burning particles assessed by a novel profluorescent nitroxide probe. *Environ Sci Technol* 2010; 44: 6601-6607.
29. Verma V, Polidori A, Schauer JJ, Shafer MM, Cassee FR, Sioutas C. Physicochemical and toxicological profiles of particulate matter in Los Angeles during the October 2007 southern California wildfires. *Environ Sci Technol* 2009; 43: 954-960.
30. Nordin EZ, Uski O, Nystrom R, Jalava P, Eriksson AC, Genberg J, Roldin P, Bergvall C, Westerholm R, Jokiniemi J, Pagels JH, Boman C, Hirvonen MR. Influence of ozone initiated processing on the toxicity of aerosol particles from small scale wood combustion. *Atmos Environ* 2015; 102: 282-289.
31. BC Ministry of Environment 2012. Wood Stove Inventory and Behaviour Analysis. Available :  
[http://www.bcairquality.ca/reports/pdfs/woodstove\\_inventory\\_final\\_report.pdf](http://www.bcairquality.ca/reports/pdfs/woodstove_inventory_final_report.pdf)

## Figure Legends

Figure 1. Monthly mean biomass contributions (% levoglucosan/PM<sub>2.5</sub>) to 3-day mean ambient PM<sub>2.5</sub> in Courtenay, Kamloops, and Prince George, British Columbia, Canada (2014-2015)

Figure 2. Concentration-response relationship between 3-day mean ambient PM<sub>2.5</sub> concentrations (using a restricted cubic spline with 3 knots) and hospital admissions for MI among elderly subjects ( $\geq 65$  years)

Figure 3. Concentration-response relationships between 3-day mean ambient PM<sub>2.5</sub> concentrations (using restricted cubic splines with 3 knots) and hospital admissions for MI among elderly subjects ( $\geq 65$  years) during the cold season (3-day mean temperature  $< 6.44$  °C) in the bottom ( $\leq 25^{\text{th}}$  percentile: black) and upper quartiles ( $\geq 75^{\text{th}}$  percentile: blue) of biomass contributions to ambient PM<sub>2.5</sub>.

Table 1. Descriptive data for daily air pollution concentrations

Pollutant		Overall		Cold Season (November-April)		Warm Season (May-October)	
		Mean (SD)	IQRW	Mean (SD)	IQRW	Mean (SD)	IQRW
PM <sub>2.5</sub> (µg/m <sup>3</sup> )		8.8 (7.4)	6.6	9.8 (6.6)	7.4	7.2 (8.3)	4.9
	Courtenay	9.7 (7.7)	9.3	13.1 (8.0)	11.1	4.7 (2.8)	3.8
	Kamloops	8.6 (6.1)	5.1	8.9 (4.8)	5.9	8.2 (7.5)	3.7
	Prince George	8.6 (8.0)	6.9	9.2 (6.7)	7.3	7.5 (9.6)	5.7
Levoglucosan (µg/m <sup>3</sup> )		0.3 (0.8)	0.2	0.5 (0.9)	0.4	0.06 (0.2)	0.02
	Courtenay	1.1 (1.3)	1.7	1.6 (1.3)	2.0	0.02 (0.04)	0.02
	Kamloops	0.07 (0.1)	0.07	0.09 (0.1)	0.1	0.03 (0.1)	0.01
	Prince George	0.1 (0.2)	0.09	0.1 (0.1)	0.1	0.1 (0.3)	0.05
Levoglucosan/PM <sub>2.5</sub> (%)		2.7 (5.1)	1.6	3.9 (5.9)	2.4	0.4 (0.8)	0.3
	Courtenay	9.1 (7.5)	15	13.0 (5.5)	7.2	0.6 (1.4)	0.4
	Kamloops	0.6 (0.7)	0.9	0.8 (0.8)	1.1	0.1 (0.3)	0.1
	Prince George	0.8 (0.8)	0.9	1.0 (0.8)	0.9	0.5 (0.7)	0.4
Temperature (°C)		6.4 (9.8)	13.6	0.6 (7.6)	8.4	15.5 (4.6)	6.3
	Courtenay	10.3 (5.9)	9.9	6.2 (3.4)	4.8	16.4 (3.0)	4.2
	Kamloops	9.2 (9.5)	15.3	2.9 (6.3)	8.4	18.5 (4.2)	6.5
	Prince George	3.5 (10.0)	14.1	-2.4 (7.7)	8.5	13.2 (4.1)	5.6
NO <sub>2</sub> (ppb)		9.6 (6.1)	7.2	12.1 (6.8)	9.6	6.6 (3.3)	4.1
	Courtenay	5.0 (2.5)	3.3	6.1 (2.5)	3.6	3.7 (1.6)	2.3
	Kamloops	12.6 (5.4)	7.5	14.6 (5.3)	8.1	9.3 (3.5)	4.2
	Prince George	10.6 (6.3)	7.5	13.5 (6.9)	9.8	7.2 (3.0)	3.7
O <sub>3</sub> (ppb)		19.2 (9.4)	14.1	18.7 (10.5)	17.1	19.8 (8.0)	10.6
	Courtenay	17.8 (8.4)	11.7	16.8 (9.7)	15.1	18.9 (6.6)	8.6
	Kamloops	17.7 (10.1)	17.8	14.6 (10.2)	17.9	23.0 (7.3)	8.3
	Prince George	19.9 (9.6)	14.5	20.1 (10.4)	16.4	19.6 (8.4)	11.4

IQRW, interquartile range width

Table 2. Ambient PM<sub>2.5</sub> and Hospitalization for Myocardial Infarction (per 5 µg/m<sup>3</sup> change)

Strata	n	Without Spatial Correction		With Spatial Correction	
		Odds Ratios (95% CI)		Odds Ratios (95% CI)	
		Lag-0	3-Day Mean	Lag-0	3-Day Mean
<i>All Days</i>	2833	1.01 (0.97, 1.04)	1.00 (0.95, 1.04)	1.01 (0.96, 1.07)	1.00 (0.94, 1.06)
Sex					
Men	1922	1.01 (0.99, 1.03)	0.99 (0.96, 1.03)	1.02 (0.99, 1.05)	1.00 (0.95, 1.05)
Women	912	1.00 (0.91, 1.10)	1.01 (0.94, 1.08)	1.00 (0.88, 1.14)	1.01 (0.93, 1.10)
Age <sup>a</sup>					
< 65 years	1302	0.99 (0.94, 1.03)	0.95 (0.88, 1.03)	0.99 (0.93, 1.06)	0.95 (0.86, 1.05)
≥ 65 years	1531	1.03 (1.00, 1.06)	1.05 (1.04, 1.06)	1.04 (1.00, 1.08)	1.06 (1.03, 1.08)
City					
Courtenay	488	1.01 (0.91, 1.11)	1.03 (0.92, 1.17)	1.08 (0.90, 1.30)	1.09 (0.88, 1.35)
< 65 years	152	0.95 (0.78, 1.14)	0.90 (0.71, 1.13)	1.02 (0.73, 1.44)	0.92 (0.60, 1.41)
≥ 65 years	336	1.04 (0.92, 1.16)	1.10 (0.95, 1.27)	1.12 (0.91, 1.39)	1.17 (0.91, 1.51)
Kamloops	863	1.06 (0.99, 1.13)	1.04 (0.96, 1.12)	1.07 (0.99, 1.15)	1.05 (0.96, 1.15)
< 65 years	346	1.05 (0.96, 1.14)	1.03 (0.94, 1.14)	1.07 (0.96, 1.19)	1.05 (0.93, 1.18)
≥ 65 years	517	1.07 (0.97, 1.19)	1.05 (0.94, 1.18)	1.07 (0.96, 1.20)	1.07 (0.93, 1.22)
Prince George	1482	0.99 (0.95, 1.03)	0.97 (0.93, 1.02)	0.99 (0.94, 1.04)	0.97 (0.91, 1.03)
< 65 years	804	0.97 (0.91, 1.02)	0.92 (0.85, 0.99)	0.96 (0.89, 1.03)	0.91 (0.82, 1.00)
≥ 65 years	678	1.02 (0.96, 1.08)	1.04 (0.97, 1.12)	1.02 (0.95, 1.10)	1.05 (0.96, 1.14)

All models are adjusted for mean temperature (linear term); Age strata are based on the median case age.

Table 3. Three-day mean ambient PM<sub>2.5</sub> and hospitalization for myocardial Infarction (per 5 µg/m<sup>3</sup> change) across strata of monthly mean levoglucosan/PM<sub>2.5</sub> and 3-day mean ambient temperature.

Strata	Odds Ratio (95% CI)		Odds Ratio (95% CI)			
			Age			
	n	Overall	n	< 65 years	n	≥ 65 years
Monthly mean levoglucosan/PM <sub>2.5</sub>						
High	894	1.11 (1.01, 1.22)	363	1.06 (0.98, 1.15)	531	1.15 (1.02, 1.31)
Mid	1109	0.92 (0.89, 0.94)	564	0.84 (0.82, 0.85)	545	1.00 (0.97, 1.04)
Low	854	1.05 (1.04, 1.06)	378	1.06 (1.05, 1.07)	476	1.05 (1.02, 1.09)
3-day mean temperature						
< 6.44 °C	1425	1.00 (0.96, 1.04)	676	0.90 (0.87, 0.93)	749	1.10 (1.05, 1.15)
≥ 6.44 °C	1432	1.00 (0.91, 1.10)	629	0.99 (0.90, 1.09)	803	1.01 (0.94, 1.09)

All PM<sub>2.5</sub> and levoglucosan data are corrected for spatial variations across each region. Monthly mean levoglucosan/PM<sub>2.5</sub> tertile values: High (>1.2%); Mid (>0.52-1.2%); Low (≤0.52%). All models are adjusted for mean temperature (linear term).

Table 4. Three-day mean PM<sub>2.5</sub> and hospitalization for myocardial Infarction (per 5 µg/m<sup>3</sup> change) during the cold season (3-day mean temperature < 6.44 °C) across strata of monthly mean levoglucosan/PM<sub>2.5</sub>

Strata	Odds Ratio (95% CI)		Odds Ratio (95% CI)			
			Age			
	n	Overall	n	< 65 years	n	≥ 65 years
Monthly mean levoglucosan/PM <sub>2.5</sub>						
High	584	1.14 (1.04, 1.25)	258	1.09 (1.03, 1.14)	326	1.19 (1.04, 1.36)
Mid	350	0.98 (0.90, 1.06)	161	0.86 (0.67, 1.11)	189	1.08 (1.06, 1.09)
Low	491	0.90 (0.89, 0.91)	257	0.78 (0.77, 0.79)	234	1.04 (1.03, 1.06)

All PM<sub>2.5</sub> and levoglucosan data are corrected for spatial variations across each region. Monthly mean levoglucosan/PM<sub>2.5</sub> tertile values: High (>1.5%); Mid (>0.93-1.5%); Low (≤0.93%). All models are adjusted for mean temperature (linear term).

Figure 1



**Figure 2**

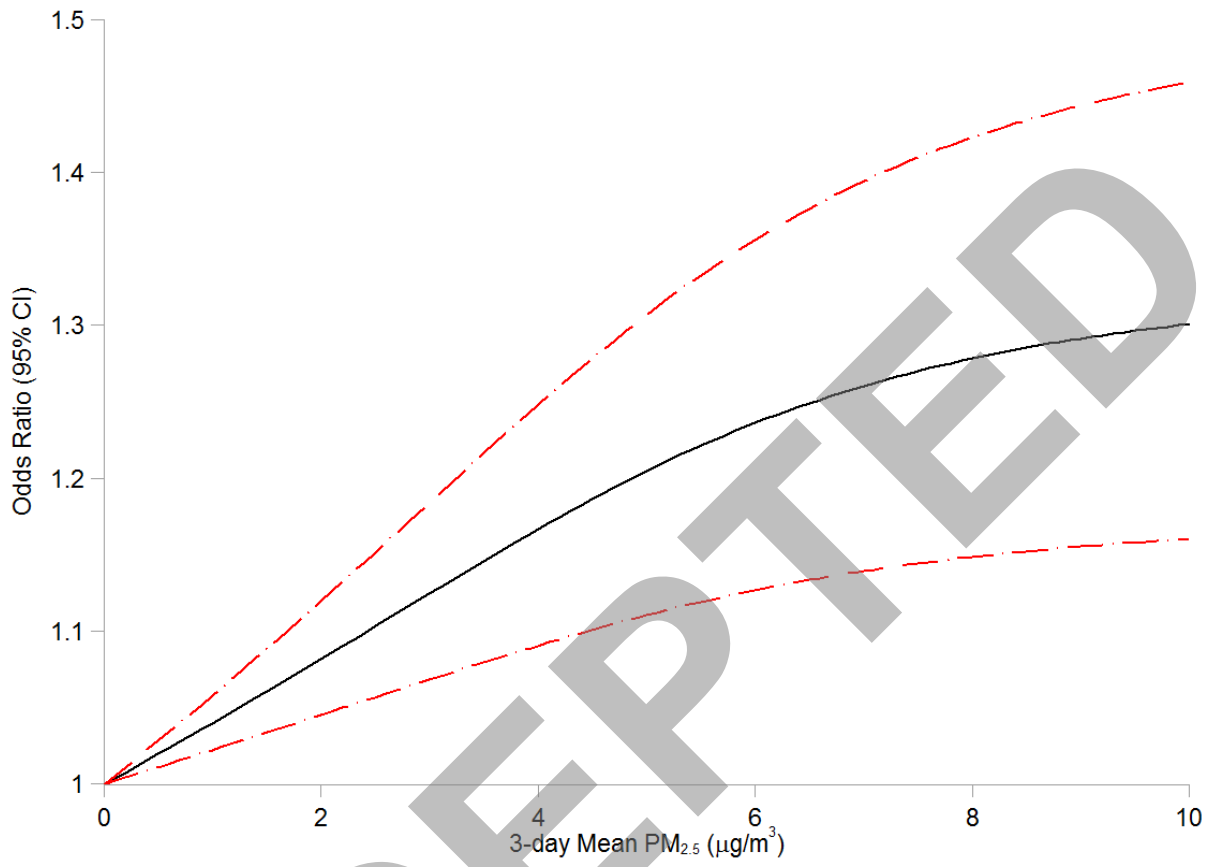


Figure 3

