OPEN

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

Scott Weichenthal,[a,b] *Ryan Kulka,*[b] *Eric Lavigne,*[b,c] *David van Rijswijk,*[b] *Michael Brauer,*[d] *Paul J. Villeneuve,*[e] *Dave Stieb,*[e] *Lawrence Joseph,*[b] *and Rick T. Burnett*[f]

Background: Biomass burning is an important source of ambient fine particulate air pollution ($PM_{2.5}$) in many regions of the world.

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

Results: Each 5 μg/m^3 increase in 3-day mean $PM_{2.5}$ 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 $PM_{2.5}$ during cold periods, 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 in the upper, middle, and lower tertiles (P_{trend} = 0.003), respectively.

Conclusion: Short-term changes in ambient $PM_{2.5}$ were associated with an increased risk of MI among elderly subjects. During cold periods, increased biomass burning contributions to $PM_{2.5}$ may modify its association with MI.

(*Epidemiology* 2017;28: 329–337)

Ambient fine particulate air pollution ($PM_{2.5}$) has a strong adverse association with cardiovascular health.[1,2] However, relatively few epidemiologic studies have specifically evaluated the cardiovascular health impacts of $PM_{2.5}$ from biomass burning[3,4] and further evaluation is needed.[5]

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.[3,6] Moreover, exposure to wildfire smoke has been associated with increased systemic inflammation[7,8] and in controlled exposure settings short-term exposures to dilute wood smoke have been associated with increased arterial stiffness and decreased heart rate variability.[9] In addition, exposure to $PM_{2.5}$ from bush fires has been associated with out-of-hospital cardiac arrest.[10,11] Furthermore, recent evidence suggests that $PM_{2.5}$ from biomass burning may have increased oxidative potential[12,13] and may contribute to cardiovascular mortality.[14] However, other studies have failed to observe significant associations between short-term exposures to wood smoke and cardiac arrhythmia[15] or biomarkers of systemic inflammation.[16] Likewise, some studies have reported null associations between forest fire smoke exposure and physician visits/hospital admissions for cardiovascular outcomes.[17]

In this study, we examined the association between short-term changes in ambient $PM_{2.5}$ 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 $PM_{2.5}$ using the cellulose combustion product levoglucosan as a source-specific marker.

Submitted 17 March 2016; accepted 30 January 2017.

From the [a]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, QC, Canada; [b]Health Canada, Air Health Science Division, Ottawa, ON, Canada; [c]Department of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Ottawa, ON, Canada; [d]University of British Columbia, Vancouver, BC, Canada; [e]Department of Health Sciences, School of Mathematics and Statistics, Carleton University, Ottawa, ON, Canada; and [f]Health Canada, Population Studies Division, Ottawa, ON, Canada.

Funded by Health Canada.

The authors report no conflicts of interest.

Data and code are available upon request to the authors.

SDC Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.epidem.com).

Correspondence: Scott Weichenthal, Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, 1020 Pins Ave. West, Montreal, QC, Canada, H3A 1A2. E-mail: scott.weichenthal@mcgill.ca.

ISSN: 1044-3983/17/2803-0329

DOI: 10.1097/EDE.0000000000000636

METHODS

Study Design and Population

A time-stratified case-crossover design[18] was used to estimate the association between daily variations in ambient $PM_{2.5}$ and hospital admissions for acute myocardial infarction (International Classification of Diseases, 10th 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 1 January 2008 and 31 March 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 $PM_{2.5}$ data for Kamloops and Courtenay were available beginning in 2010 and 2011, respectively; therefore, cases in these cities were excluded if they occurred before the start of $PM_{2.5}$ 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 $PM_{2.5}$

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 $PM_{2.5.}$ These data were used to estimate monthly mean biomass burning contributions to ambient $PM_{2.5}$ (i.e., levoglucosan/$PM_{2.5}$). Twenty-four-hour mean $PM_{2.5}$ concentrations (for levoglucosan analyses) were monitored in each location between 1 January 2014 and 31 March 2015 using Thermo Partisol 2025i monitors (Thermo Scientific, Waltham, MA) located at the same provincial monitoring sites where $PM_{2.5}$ measurements were collected. Samples were collected between 7:00 am and 7:00 am 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 $PM_{2.5}$.[19]

Daily mean $PM_{2.5}$ data from provincial fixed site monitors (one 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 eight sites located across each community between September 2014 and March 2015 using cascade impactors at a flow rate of 5 L/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 colocated 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.[20]

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 $PM_{2.5}$ 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 m (IQR = 623–2006 m).

Statistical Analysis

Spatial Adjustment Models for Levoglucosan in $PM_{2.5}$

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 with 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 $PM_{2.5}$ 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 $PM_{2.5}$ (i.e., lag-0 or 3-day mean). We also examined nonlinear forms (i.e., restricted cubic splines with three 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 $PM_{2.5}$ 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., three to four 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.[18]

We first examined the relationship between $PM_{2.5}$ 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 $PM_{2.5}$ (i.e., levoglucosan/$PM_{2.5}$) and conducted stratified analyses across tertiles of this parameter. We evaluated potential effect modification by biomass burning as a source of ambient $PM_{2.5}$ by including a first-order interaction term between $PM_{2.5}$ and an indicator variable for tertiles of monthly mean biomass contributions to $PM_{2.5}$. We did not conduct stratified analyses by heating/nonheating 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 $\mu g/m^3$ increase in ambient $PM_{2.5}$ concentrations as this interval was approximately equal to the interquartile range of the mean difference

TABLE 1. Descriptive Data for Daily Air Pollution Concentrations

	Overall		Cold Season (November–April)		Warm Season (May–October)	
Pollutant	**Mean (SD)**	**IQRW**	**Mean (SD)**	**IQRW**	**Mean (SD)**	**IQRW**
$PM_{2.5}$ ($\mu g/m^3$)	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 ($\mu g/m^3$)	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/$PM_{2.5}$ (%)	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_2 (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_3 (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 indicates interquartile range width.

in 3-day mean $PM_{2.5}$ 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).

RESULTS

In total, we included 2,881 cases of MI in our analyses including 504 cases from Courtenay, 885 cases from Kamloops, and 1,492 cases from Prince George. Cases were predominantly male (68%) with a median age of 65 years. On average, ambient $PM_{2.5}$ concentrations tended to be low in all three cities (i.e., <10 μg/m^3), with higher concentrations observed during colder portions of the year (Table 1). Daily mean ambient temperatures were weakly correlated with $PM_{2.5}$ ($r = -0.27$) and levoglucosan/$PM_{2.5}$ ($r = -0.38$). Daily mean $PM_{2.5}$ was positively correlated with NO_2 ($r = 0.51$) and inversely correlated with O_3 ($r = -0.49$); NO_2 and O_3 were also inversely correlated ($r = -0.43$). The ratio of daily mean levoglucosan/$PM_{2.5}$ was not correlated with NO_2 ($r = 0.05$) but was weakly correlated with O_3 ($r = -0.30$). Correlations for 3-day mean values were similar to daily mean correlations (data not shown).

Monthly mean levoglucosan/$PM_{2.5}$ values are shown in Figure 1. In general, biomass burning contributions to $PM_{2.5}$ were higher during colder months in all three cities, consistent with residential wood burning. Courtenay had the largest biomass contributions to ambient $PM_{2.5}$ and seasonal differences in ambient $PM_{2.5}$ concentrations were most apparent in this city (Table 1). Evidence of biomass burning contributions to $PM_{2.5}$ was 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 $PM_{2.5}$ and levoglucosan concentrations are shown in eTable 1 (http://links.lww.com/EDE/B172). Overall, strong positive slopes were apparent for $PM_{2.5}$ and levoglucosan samples collected using cascade impactors colocated with provincial fixed site monitors ($PM_{2.5}$ slope = 0.78, 95% CI: 0.70, 0.86; $R^2 = 0.57$; levoglucosan slope = 1.03, 95% CI: 0.92, 1.15; $R^2 = 0.52$). 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^2 values generally exceeded 0.7 for both $PM_{2.5}$ and levoglucosan (eTable 1; http://links.lww.com/EDE/B172).

Odds ratios describing the relationship between ambient $PM_{2.5}$ and hospital admissions for MI are shown in Table 2. Each 5 μg/m^3 increase in lag-0 or 3-day mean $PM_{2.5}$ concentration was associated with an increased risk of MI among elderly subjects (≥65 years) with slightly stronger associations

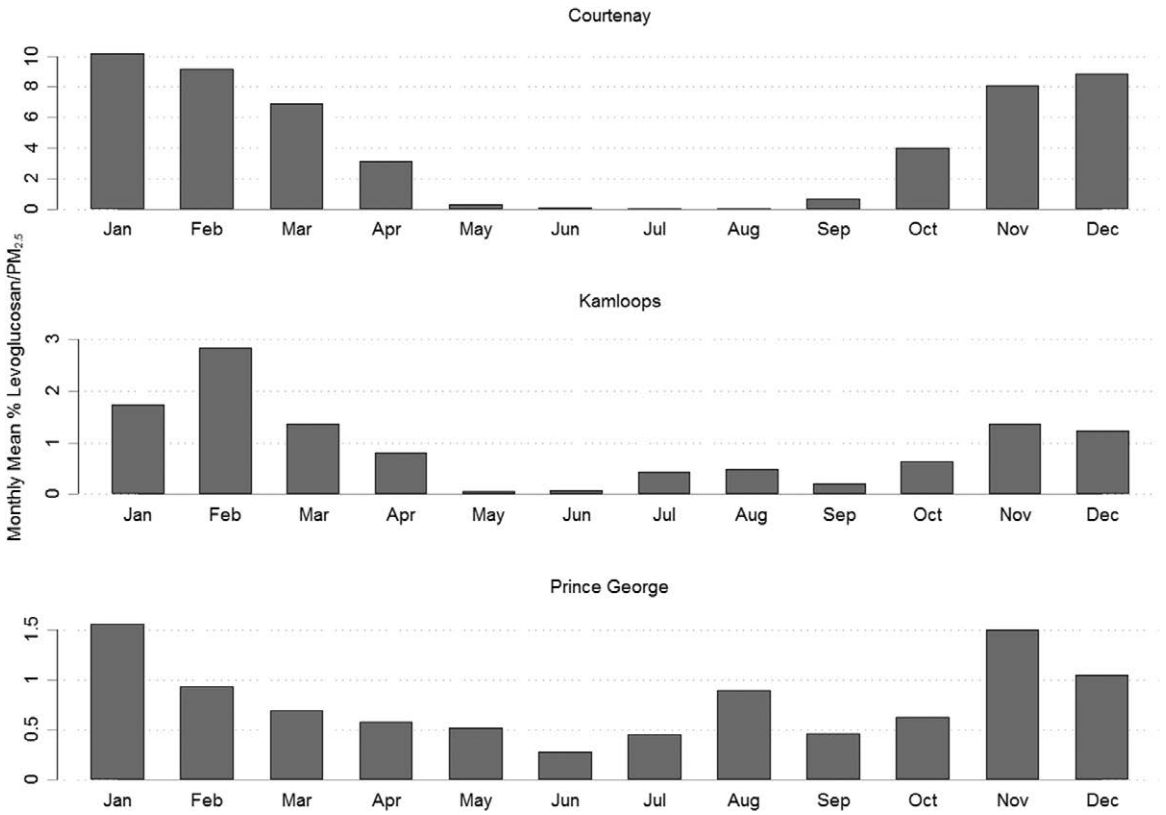

FIGURE 1. Monthly mean biomass contributions (% levoglucosan/$PM_{2.5}$) to 3-day mean ambient $PM_{2.5}$ in Courtenay, Kamloops, and Prince George, British Columbia, Canada (2014–2015).

TABLE 2. Ambient $PM_{2.5}$ and Hospitalization for Myocardial Infarction (per 5 μg/m^3 Change)

		Without Spatial Correction Odds Ratios (95% CI)		With Spatial Correction Odds Ratios (95% CI)	
Strata	**n**	**Lag 0**	**3-day Mean**	**Lag 0**	**3-day Mean**
All days	2,833	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	1,922	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					
<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	1,531	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.

observed for 3-day mean concentrations. Short-term changes in ambient $PM_{2.5}$ were not associated with MI among younger subjects (interaction P value = 0.032). The concentration–response relationship between 3-day mean $PM_{2.5}$ and hospital admissions for MI among elderly subjects is shown in Figure 2.

In general, odds ratios based on $PM_{2.5}$ 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 $PM_{2.5}$. 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 $PM_{2.5}$ concentrations and hospital admissions for MI are shown in Table 3 across tertiles of monthly mean biomass contributions to $PM_{2.5}$. For the population as a whole, the strongest association between $PM_{2.5}$ and MI was observed in the highest tertile of biomass contributions to $PM_{2.5}$; however, the trend across tertiles was not statistically significant (P = 0.519). Among elderly subjects, the strongest association between $PM_{2.5}$ and MI also occurred in the highest tertile of biomass contributions to $PM_{2.5}$ but the trend across tertiles was not statistically significant (P = 0.11).

As sensitivity analyses, we repeated the analysis for elderly subjects (≥65 years) in Table 3 excluding Courtenay given that this city had much higher values for the proportion of levoglucosan in $PM_{2.5}$ compared with Kamloops and Prince George. Excluding Courtenay did not change the trend of results across strata of biomass contributions to $PM_{2.5}$ 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 recalculated tertiles based on the distribution of monthly mean biomass contributions to $PM_{2.5}$ 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_2 or O_3 in the models did not dramatically change the results across tertiles of biomass contributions to $PM_{2.5}$ in Table 3. For example, the odds ratio among elderly subjects in the highest tertile of biomass contributions to $PM_{2.5}$ increased to 1.17 (95% CI: 0.96, 1.42) when NO_2 was included in the model and decreased to 1.12 (95% CI: 1.01, 1.24) when O_3 was included in the model (NO_2 and O_3 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 $PM_{2.5}$ and hospital admissions for MI among elderly subjects was limited to the cold season (Table 3). Therefore, to determine if the risk pattern across tertiles of biomass contributions to $PM_{2.5}$ may be explained by temperature, we restricted our analyses to the cold period (i.e., <6.44°C) and again examined trends across

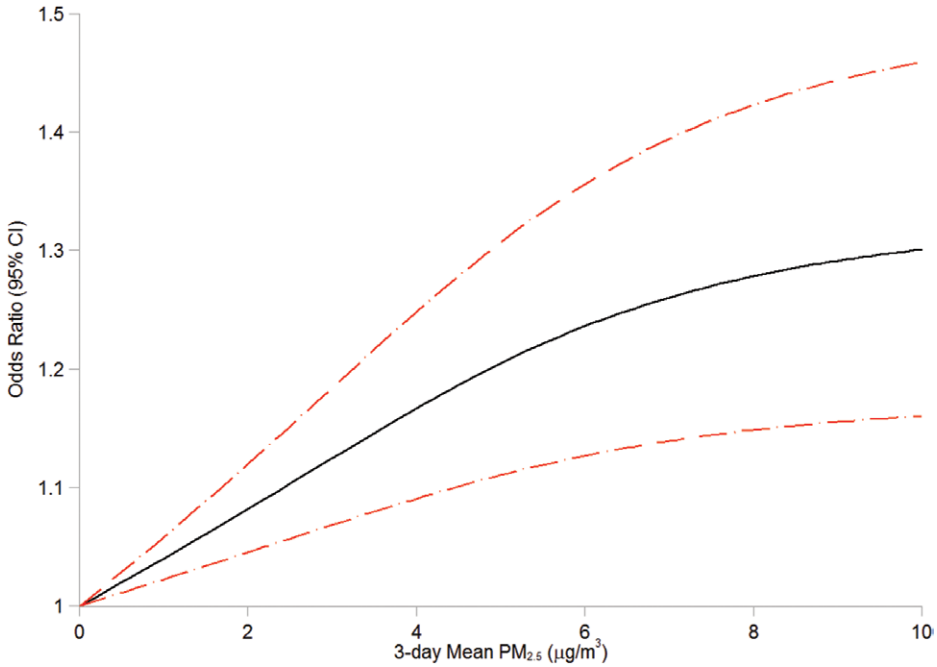

FIGURE 2. Concentration–response relationship between 3-day mean ambient $PM_{2.5}$ concentrations (using a restricted cubic spline with three knots) and hospital admissions for MI among elderly subjects (≥65 years).

TABLE 3. Three-day Mean Ambient $PM_{2.5}$ and Hospitalization for Myocardial Infarction (per 5 µg/m³ Change) Across Strata of Monthly Mean Levoglucosan/$PM_{2.5}$ and 3-day Mean Ambient Temperature

		Odds Ratio (95% CI)		Odds Ratio (95% CI)		
				Age		
Strata	n	Overall	n	<65 years	n	≥65 years
Monthly mean levoglucosan/$PM_{2.5}$						
High	894	1.11 (1.01, 1.22)	363	1.06 (0.98, 1.15)	531	1.15 (1.02, 1.31)
Mid	1,109	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 (°C)						
<6.44	1425	1.00 (0.96, 1.04)	676	0.90 (0.87, 0.93)	749	1.10 (1.05, 1.15)
≥6.44	1432	1.00 (0.91, 1,10)	629	0.99 (0.90, 1.09)	803	1.01 (0.94, 1.09)

All $PM_{2.5}$ and levoglucosan data are corrected for spatial variations across each region. Monthly mean levoglucosan/$PM_{2.5}$ tertile values: high (>1.2%); mid (>0.52%–1.2%); low (≤0.52%). All models are adjusted for mean temperature (linear term).

tertiles of biomass contributions to $PM_{2.5}$. The results of these analyses are shown in Table 4 and indicate increased MI risks with increasing biomass contributions to ambient $PM_{2.5}$. 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 $PM_{2.5}$ (interaction P value = 0.003), respectively. Moreover, 3-day mean $PM_{2.5}$ concentrations (low: 6.29 µg/m³; middle: 7.58 µg/m³; high: 7.77 µg/m³) and SDs of mean differences between case and control days (low: 4.85 µg/m³; middle: 4.34 µg/m³; high: 4.79 µg/m³) were similar across categories of biomass contributions to $PM_{2.5}$. 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 $PM_{2.5}$ and MI in the low and middle tertiles for these analyses. Concentration response curves for 3-day mean $PM_{2.5}$ concentrations and emergency room visits for MI are shown in Figure 3 for the bottom (<25th percentile) and top quartiles (≥75th percentile) of biomass contributions to $PM_{2.5}$ 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 $PM_{2.5}$.

Including 3-day mean ambient NO_2 or O_3 in conditional logistic regression models did not have a meaningful impact on the magnitude of associations across strata of biomass contributions to $PM_{2.5}$. For example, adding 3-day mean O_3 to the model for elderly subjects in Table 4 increased the odds ratio slightly in the highest tertile of biomass contributions to $PM_{2.5}$ (OR = 1.21, 95% CI: 1.08,1.25). A similar pattern was observed when 3-day mean NO_2 was added to the model (OR = 1.22, 95% CI: 0.96, 1.55). The pattern of increased risk with increased biomass contributions to $PM_{2.5}$ also remained when NO_2 or O_3 were included in the models ($P_{trend} < 0.001$).

Finally, in an effort to confirm the pattern of results observed using estimated monthly mean biomass contributions to $PM_{2.5}$, we conducted stratified analyses using prospective daily levoglucosan data (with strata based on the median value of 3-day mean levoglucosan/$PM_{2.5}$ 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 $PM_{2.5}$ 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 $PM_{2.5}$; 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 $PM_{2.5}$ 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 $PM_{2.5}$ 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 $PM_{2.5}$ from biomass burning. Recently, two Australian studies reported positive associations between $PM_{2.5}$ from forest fires and out-of-hospital cardiac arrest.[10,11] Moreover, consistent with our findings, one of these studies also reported positive associations between ambient $PM_{2.5}$ and hospital admissions for MI and ischemic heart disease with stronger associations observed among older adults (≥65 years).[11] Similarly, exposure to wildfire smoke from a peat bog fire in North Carolina was associated with increased emergency room visits for heart failure[21] and a time-series study in Seattle noted a positive association between potassium in $PM_{2.5}$ (a marker of biomass) and cardiovascular mortality during the cold season.[22] Likewise, studies in Chile[23] and New Zealand[24] reported positive associations between ambient PM_{10} 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[17] and other studies have reported null associations between short-term changes in $PM_{2.5}$ and risk of myocardial infarction.[25,26] 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 $PM_{2.5}$ 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 $PM_{2.5}$ 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 $PM_{2.5}$ and emergency room visits for MI with stronger associations observed in cities with $PM_{2.5}$ containing higher oxidative potential.[27] Therefore, one explanation for the observed trend of increased MI risk across tertiles of biomass contributions to $PM_{2.5}$ may be that the oxidative potential of $PM_{2.5}$ is increased when biomass contributions are greater. Indeed, at least two recent studies support this hypothesis. Specifically, Bates et al.[12] noted that biomass burning was a strong contributor to the oxidative potential of $PM_{2.5}$ using the dithiothreitol assay and also reported that dithiothreitol activity was more strongly associated with emergency room visits for congestive heart failure than $PM_{2.5}$. In addition, Kurmi et al.[13] 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.[27]). The specific chemical components explaining the increased oxidative potential of $PM_{2.5}$ from biomass burning have yet to be thoroughly characterized; however, Kurmi et al.[13] 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 semivolatile[28] or polar organic components[29] 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.[30] Unfortunately, we did not collect data on the oxidative potential or composition of $PM_{2.5}$ 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 $PM_{2.5}$ 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 $PM_{2.5}$ and levoglucosan concentrations, it is

TABLE 4. Three-day Mean $PM_{2.5}$ and Hospitalization for Myocardial Infarction (per 5 μg/m³ Change) During the Cold Season (3-day Mean Temperature < 6.44°C) Across Strata of Monthly Mean Levoglucosan/$PM_{2.5}$

		Odds Ratio (95% CI)		Odds Ratio (95% CI)		
				Age		
Strata	n	Overall	n	<65 years	n	≥65 years
Monthly mean levoglucosan/$PM_{2.5}$						
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 $PM_{2.5}$ and levoglucosan data are corrected for spatial variations across each region. Monthly mean levoglucosan/$PM_{2.5}$ tertile values: high (>1.5%); mid (>0.93%–1.5%); low (≤0.93%). All models are adjusted for mean temperature (linear term).

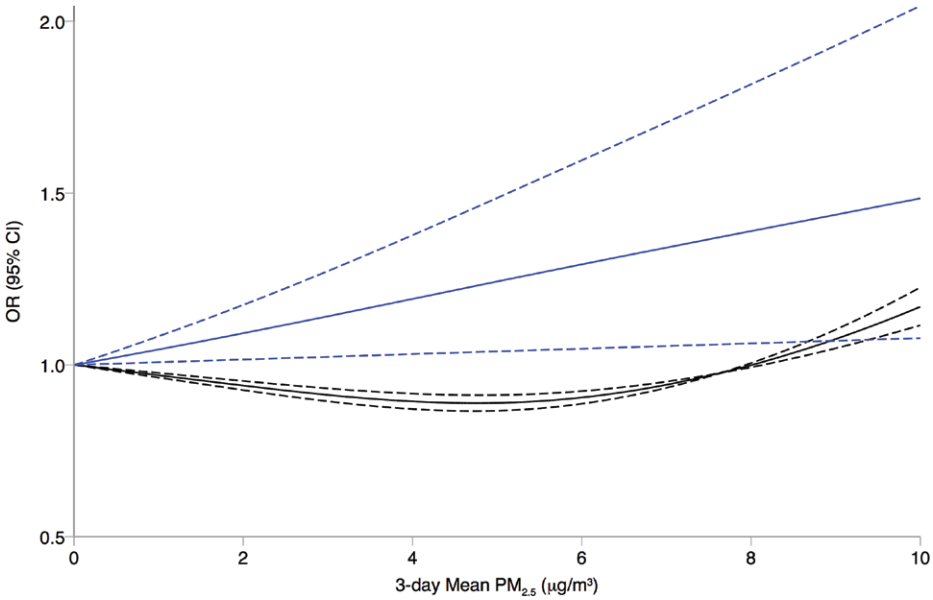

FIGURE 3. Concentration–response relationships between 3-day mean ambient $PM_{2.5}$ concentrations (using restricted cubic splines with three knots) and hospital admissions for MI among elderly subjects (≥65 years) during the cold season (3-day mean temperature < 6.44°C) in the bottom (≤25th percentile: black) and upper quartiles (≥75th percentile: blue) of biomass contributions to ambient $PM_{2.5}$.

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 $PM_{2.5}$. 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[31] 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/$PM_{2.5}$ 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). Nondifferential misclassification of cases across tertiles of monthly mean biomass contributions to $PM_{2.5}$ 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 $PM_{2.5}$ concentrations (more specifically the mean difference in $PM_{2.5}$ concentrations between case and control days) and MI; however, this factor would also have to be correlated with the proportion of levoglucosan in $PM_{2.5}$ 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 $PM_{2.5}$ 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 $PM_{2.5}$ 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 $PM_{2.5}$ and MI

was strongest in Courtenay which also had the largest biomass contributions to $PM_{2.5}$.

In summary, our findings suggest that short-term changes in ambient $PM_{2.5}$ 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 $PM_{2.5}$ may modify the association between $PM_{2.5}$ and MI.

ACKNOWLEDGMENTS

We thank the British Columbia Ministry of Environment, Dr. Paul Hasselback, Earle Plain, John Burch, Dennis Fudge, Ralph Adams, Steve Josefowich, Gail Miller, Dr. Ewa Dabek (Environment Canada), Fang Yang and Biljana Klasninovska (Canadian Institute for Health Information) for their help in conducting this study.

REFERENCES

1. Franklin BA, Brook R, Arden Pope C 3rd. Air pollution and cardiovascular disease. *Curr Probl Cardiol*. 2015;40:207–238.
2. Brook RD, Rajagopalan S, Pope CA 3rd, et al.; 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, et al. Woodsmoke health effects: a review. *Inhal Toxicol*. 2007;19:67–106.
4. Sigsgaard T, Forsberg B, Annesi-Maesano I, et al. 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, Sällsten G, Gustafson P, et al. 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, et al. The human bone marrow response to acute air pollution caused by forest fires. *Am J Respir Crit Care Med*. 2000;161(4 Pt 1):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, Sandström T, et al. Exposure to wood smoke increases arterial stiffness and decreases heart rate variability in humans. *Part Fibre Toxicol*. 2013;10:20.
10. Dennekamp M, Straney LD, Erbas B, et al. Forest fire smoke exposures 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, et al. Impact of fine particulate matter (PM2.5) exposure during wildfires on cardiovascular health outcomes. *J Am Heart Assoc.* 2015; 4: e001653.
12. Bates JT, Weber RJ, Abrams J, et al. Reactive oxygen species generation linked to sources of atmospheric particulate matter and cardiorespiratory effects. *Environ Sci Technol*. 2015;49:13605–13612.
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 specific sources and chemical species. *Epidemiology*. 2014;25:379–388.
15. Langrish JP, Watts SJ, Hunter AJ, et al. 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 chamber 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. *Epidemiology*. 2005;16:717–726.
19. Simoneit BRT, Schauer JJ, Nolte CG, et al. 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 winter woodsmoke concentrations. *Environ Sci Technol*. 2007;41:2429–2436.
21. Rappold AG, Stone SL, Cascio WE, et al. 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 analysis 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 Manag Assoc*. 2009;59:1481–1488.
24. McGowan JA, Hider RN, 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, et al. A case-crossover analysis of particulate matter air pollution and out-of-hospital primary cardiac arrest. *Epidemiology*. 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. *Epidemiology*. 2005;16:41–48.
27. Weichenthal S, Lavigne E, Evans G, Pollitt K, Burnett RT. Ambient PM2.5 and risk of emergency room visits for myocardial infarction: impact of regional PM2.5 oxidative potential: a case-crossover study. *Environ Health*. 2016;15:46.
28. Miljevic B, Heringa MF, Keller A, et al. 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, et al. 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 at: http://www.bcairquality.ca/reports/pdfs/woodstove_inventory_final_report.pdf. Accessed July 4, 2016.