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## A panel study of the acute effects of personal exposure to household air pollution on ambulatory blood pressure in rural Indian women



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#### ABSTRACT

*Background:* Almost half the world's population is exposed to household air pollution from biomass and coal combustion. The acute effects of household air pollution on the cardiovascular system are poorly characterized. We conducted a panel study of rural Indian women to assess whether personal exposures to black carbon during cooking were associated with acute changes in blood pressure.

Methods: We enrolled 45 women (ages 25–66 years) who cooked with biomass fuels. During cooking sessions in winter and summer, we simultaneously measured their personal real-time exposure to black carbon and conducted ambulatory blood pressure measurements every 10 min. We recorded ambient temperature and participants' activities while cooking. We assessed body mass index, socioeconomic status, and salt intake. Multivariate mixed effects regression models with random intercepts were used to estimate the associations between blood pressure and black carbon exposure, e.g., average exposure in the minutes preceding blood pressure measurement, and average exposure over an entire cooking session

Results: Women's geometric mean (GM) exposure to black carbon during cooking sessions was lower in winter (GM:  $40 \,\mu\text{g/m}^3$ ; 95% CI: 30, 53) than in summer (GM:  $56 \,\mu\text{g/m}^3$ ; 95% CI: 42, 76). Interquartile range increases in black carbon were associated with changes in systolic blood pressure from  $-0.4 \,\text{mm}$  Hg (95% CI: -2.3, 1.5) to  $1.9 \,\text{mm}$  Hg (95% CI: -0.8, 4.7), with associations increasing in magnitude as black carbon values were assessed over greater time periods preceding blood pressure measurement. Interquartile range increases in black carbon were associated with small decreases in diastolic blood pressure from  $-0.9 \,\text{mm}$  Hg (95% CI: -1.7, -0.1) to  $-0.4 \,\text{mm}$  Hg (95% CI: -1.6, 0.8). Associations of a similar magnitude were estimated for cooking session-averaged values.

Conclusions: We found some evidence of an association between exposure to black carbon and acute increases in systolic blood pressure in Indian women cooking with biomass fuels, which may have implications for the development of cardiovascular diseases.

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#### 1. Introduction

Household air pollution from combustion of biomass (wood, crop residues, dung) and coal for cooking are leading contributors to the global burden of disease, responsible for an estimated 3.5 million annual premature deaths (Lim et al., 2012). Over

2.8 billion people globally and 75% of Indians cook by burning biomass fuels in traditional stoves (Bonjour et al., 2013; Prasad et al., 2012; World Health Organization, 2014b). Incomplete combustion of biomass emits high concentrations of potentially toxic pollutants including particulate matter (PM), carbon monoxide, and organic compounds (e.g., formaldehyde, benzo[a]pyrene) (Naeher et al., 2007). In homes where biomass is used regularly for cooking, daily concentrations of indoor air pollutants can be 2–6 times higher (e.g., ranging from  $\sim\!50$  to  $200~\mu g/m^3$ ) than the World Health Organization's interim household air pollution

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guideline of  $35 \mu g/m^3$  (Clark et al., 2013b; World Health Organization, 2014a), although exposures below the guideline may still adversely affect health (Wellenius et al., 2012).

Exposure to household air pollution has well-documented adverse effects on the respiratory systems of children and adults (Smith et al., 2004). Of interest to the present study is that crosssectional studies in adults have shown associations with a higher prevalence of carotid atherosclerotic plaque (Painschab et al., 2013), coronary heart disease, and stroke (Lee et al., 2012) in longterm users of biomass fuels as compared with users of gaseous fuels. A small number of studies by others and us suggested an association between exposure to household air pollution and higher blood pressure (Alexander et al., 2014; Baumgartner et al., 2011; Clark et al., 2013a; McCracken et al., 2007; Shan et al., 2014). Those studies were either cross-sectional or were pre-post-studies over a period of several months. Together, those studies suggested that exposure to household air pollution may contribute to the development of hypertension and cardiovascular diseases (McCracken et al., 2012), which are the leading causes of death and disease globally and in developing countries including India (Lim et al., 2012).

To our knowledge, the acute impacts of household air pollution on blood pressure have not been investigated in longitudinal or panel studies. Many of the constituents of ambient air pollution are also found in household air pollution, and experimental studies have shown that exposure to ambient air pollution was associated with increased blood pressure within hours of exposure (Kubesch et al., 2014; Langrish et al., 2009; Urch et al., 2005). Acute changes in blood pressure may increase an individual's risk of developing adverse cardiovascular events by destabilizing preexisting atherosclerotic plaques, or by limiting normal blood flow to the heart (Brook et al., 2009). The objective of the present study was to determine whether personal exposures to black carbon, a pollutant marker of incomplete combustion from biomass, were associated with rapid changes in blood pressure among rural Indian women cooking with biomass fuels.

#### 2. Methods

We conducted a panel study among rural Indian women in which we measured their personal, real-time (1-min resolution) exposures to black carbon and assessed simultaneously their ambulatory blood pressure every 10 min during cooking sessions in winter and summer.

#### 2.1. Study site and population

This study was conducted in Hire Waddarkal, a village in the northern Koppal district of Karnataka, India (N 15°37′, *E* 76°18′). The region has a semi-arid climate and receives < 600 mm of rainfall annually. Most homes in this region use biomass for cooking (Government of India Ministry of Home Affairs, 2010), and space heating is uncommon in this temperate region where winter temperatures are generally above 16 °C and summer temperatures often exceed 40 °C (Central Ground Water Board MoWR, Government of India, 2008).

At the time of our study, the village had approximately 350 homes, with an average household comprising six family members. A typical home had 1–2 rooms such that sleeping, eating, and cooking often occurred in the same room. Most houses were constructed from a combination of natural materials including mud, dung, wood, and vegetation, and processed materials including slate, cement, concrete, and bricks. Of the working population, 75% of people were agricultural labourers, 8% participated solely in other manual labour (e.g., fishing, carpentry), and 21%

worked as both agricultural and manual labourers. Villagers reported working for about 47 h per week in addition to the 12–14 h per week spent collecting and preparing fuel wood for cooking and boiling water.

#### 2.2. Recruitment of participants

The study was conducted during the post-monsoon winter season of 2011 (October 1–November 28) and in the summer and early monsoon season of 2012 (March 28–July 12). We recruited a random selection of women from a total of 187 women who were enrolled in an ongoing cookstove evaluation study (see Supplementary material). In the larger evaluation study, women were eligible to participate if they cooked and used biomass as their main cooking fuel, used a traditional cookstove, lived in a home with 10 or fewer occupants, and were willing to pay 200 rupees (~US \$3) for a new cookstove. Women were excluded from the study if they were previous or current smokers, pregnant at enrolment, or younger than 25 years of age. If a household had more than one eligible woman, the woman who reported that she would be cooking on the measurement day was enrolled into this study.

Trained field staff introduced the study to eligible women and other household occupants. Women interested in participating were read the consent form and they provided oral informed consent. Of the 50 eligible women approached to participate in the study, five women declined to participate because they did not want to wear the air pollution monitoring devices. This study received ethical approval from St. Johns Medical College in Bangalore (#103/2011), the University of Minnesota (#1104S97992), and McGill University (#A11-M119-14B).

#### 2.3. Energy use practices

Participants cooked on vented or unvented traditional stoves (*chulas*) made of cement and mud, and sometimes cooked over an open fire (Supplementary material, Fig. S1). Some women ( $\sim$ 40%) also used a rocket stove (Chulika) obtained through enrolment in the cookstove evaluation study. All participants in our study used wood for cooking, with one home supplementing with agricultural residues and another supplementing with liquefied petroleum gas.

Cooking was typically done twice daily, with the timing and duration of cooking varying among households. Cooking in the morning started as early as 4:15 am in some households and finished around 10:00 am in others. Cooking in the evenings typically began after 4 pm and ended as late as 9 pm. In most homes, two stoves were used simultaneously to prepare a variety of foods including curries, flatbreads (e.g., roti), rice, and sambar. Additional information about participant selection, the study site, and household energy use behaviours can be found in the Supplementary material.

#### 2.4. Data collection

#### 2.4.1. Questionnaires

We administered household and individual questionnaires to elicit information on demographics, energy use behaviours, assets and incomes, exposure to environmental tobacco smoke, and individual health status (e.g., self-reported health, medication use). Field staff read the questions to participants in Kannada, the local language, and recorded their responses directly on the questionnaire. The questionnaire was developed in English from questions used in previous studies of household air pollution and health (Baumgartner et al., 2011), translated into Kannada, and then back-translated into English. After back-translation, the questionnaire was pilot-tested with English-Kannada speaking

staff at a local non-governmental organization, and with nearby villagers to ensure appropriateness of the questions and to assess whether the questions were understandable and being interpreted as intended. The field staff reworded any questions that were not being interpreted as intended and then re-tested them. The data from the questionnaire were double entered into an electronic database and the databases were compared to identify errors.

Using principle component analysis, a composite index representing socioeconomic status (SES) was constructed from data on the ownership of six household assets (chairs, mobile phones. televisions, radios, mixers, and motorcycles), the number of rooms in the home, the type of materials used for the floor, roof, and walls, and land ownership. Of the 187 households enrolled in the intervention study and included in the principle component analysis, 25 households (13%) were missing data for at least one of the 15 assets used to generate the index. Of these 25 households, 19 were missing data for one asset, 3 were missing data for 2 assets, and 3 were missing data for 3 or more assets. Missing values were imputed using average values from households with non-missing values for that asset. Asset indices are less susceptible to shortterm economic shocks and likely a better proxy of longer-term wealth among rural, subsistence populations compared with other SES metrics such as income or expenditures (Balen et al., 2010; Mohanty, 2009; Vyas and Kumaranayake, 2006).

#### 2.4.2. Anthropometric and other measurements

The staff measured women's height (centimeters), weight (kilograms), and waist circumference (centimeters) and we calculated women's body mass index [BMI; weight (kg) divided by height<sup>2</sup> (m<sup>2</sup>)]. Each participant's 24-h salt intake was assessed by weighing their household salt containers at the start and end of a 24-h period that overlapped with measurement of ambulatory blood pressure and black carbon exposure. Salt is a common additive to food, spooned into dishes during cooking. We deemed the difference between the final and initial salt weights to be the total salt used by all household members during the 24-h period. To approximate individual daily salt intake we divided the total salt used by the number of individuals in the household older than six months. This method avoids the recall bias that may be present when using 24-h dietary recall to assess salt intake (Brown et al., 2009).

#### 2.4.3. Exposure to black carbon during cooking

Women's personal exposure to black carbon was measured using battery-powered microaethelometers (microAETH Model AE-51, Magee Scientific). Participants wore the black carbon monitor in a waist pack to avoid interference with daily tasks. The inlet was clipped to the participant's shoulder to ensure that air circulating through the microAETH was drawn from the participant's breathing zone (Supplementary material, Fig. S2). A stationary microAETH was co-located at a height and distance from the cookstove that mimicked the cook's breathing zone, and was operated for a 24-h monitoring period that included the cooking session with ambulatory blood pressure measurement.

In most cases, field staff arrived at the participant's home prior to the start of a cooking session thereby allowing for variations in exposures to be captured throughout the session (e.g., while starting the fire, loading fuel, and cooking). In four of the 79 measurement sessions, the participant asked that the monitor be removed before cooking was finished.

The microAETHs were programmed to pull air through a 3 mm diameter filter at a flow rate of 50 mL per minute. The device simultaneously measured black carbon and ambient temperature each second and generated averages every minute throughout the cooking session. Minute-averaged measurements of black carbon from microAETH devices correlate highly (r=0.92) with

measurements from full-size aethalometers, and have excellent reproducibility between units (Cai et al., 2014). However, optical and electronic instrumental noise during measurement can lead to erroneous black carbon concentrations (Hagler et al., 2011). The minute-averaged black carbon measurements were thus corrected for erroneous high and low values using the U.S. EPA Optimized Noise-Reduction Averaging algorithm (United States Environmental Protection Agency, 2015). We also excluded the extremely high black carbon values (i.e., minute averages  $> 500 \,\mu\text{g/m}^3$ ; or < 3.5% of all black carbon measurements) as they may be attributable to spurious concentration "spikes", reaching upwards of 2000 µg/m<sup>3</sup>, when the monitor is exposed to mechanical shock or intense vibration, which is more likely to occur when worn during activities like cooking compared with stationary monitoring. This decision was further supported by results from the stationary black carbon monitors that were placed at a height and location similar to a cook for 24-h in kitchens in which minute-averaged concentrations were never found to exceed 500 µg/m<sup>3</sup>.

#### 2.4.4. Metrics of personal exposure to black carbon

We evaluated two metrics for exposure to black carbon that incorporated time lags that are relevant for acute effects on blood pressure (Malloy et al., 2010): (a) exposure to black carbon averaged over an increasing number of minutes prior to each blood pressure measurement, from an average of two minutes prior to blood pressure measurement to an average of 20 min, and (b) average black carbon exposure over the entirety of the cooking session prior to the last blood pressure measurement. Each of the derived black carbon exposure variables was modeled individually in the regression models.

#### 2.4.5. Ambulatory blood pressure

We measured women's ambulatory systolic and diastolic blood pressure throughout the cooking sessions. Before lighting the fire for cooking, participants were outfitted with an ambulatory blood pressure monitor (Model 90207, Spacelabs Healthcare) and blood pressure cuff worn on their left arm (Supplementary material, Fig. S2). Field staff conducted an initial resting blood pressure measurement to verify that the device was working correctly. The monitor was programmed to obtain a blood pressure measurement every 10 min. If a measurement was unsuccessful because of participant movement, the device was programmed to automatically attempt additional measurements until one was obtained. The devices were removed from the participant at the end of the cooking session.

#### 2.4.6. Activities and energy expenditure during cooking

We assessed participants' activities during each observation period because changes in physical activities can affect blood pressure (Gretler et al., 1993; Hayashi et al., 2007). A field staff member remained in the kitchen during cooking and recorded descriptions of each participant's activities (e.g., making rotis, cleaning vessels) and position (e.g., sitting, standing, walking). The information on activity was aggregated into categories according to the task and level of effort (e.g., one category included all activities related to preparing tea, a separate category included activities about roti preparation). We assigned a quantitative measure of energy expenditure [metabolic equivalent scores (METS)] to each activity using the Compendium of Physical Activities (Ainsworth et al., 2000). In instances where women were performing multiple activities at once, we selected the METS score associated with the most vigorous activity. The appropriateness of these METS assignments to the recorded tasks was verified with local Indian staff. Further detail about the categorization of activity data can be found in the Supplementary material. In addition to recording women's activities during cooking, we obtained

measurements of their heart rate using the ambulatory blood pressure monitor (Model 90207, Spacelabs Healthcare).

#### 2.5. Statistical analysis

We conducted regression analyses using linear mixed models with restricted maximum likelihood (REML) to assess whether shortterm changes in personal exposure to black carbon were associated with acute changes in systolic and diastolic blood pressure. A first order autoregressive error structure was used to account for potentially correlated error terms within individuals. All multivariate models included a random effect for each woman. Age. BMI, and ambient air temperature were included in all models as *a priori* risk factors for higher blood pressure (Brook et al., 2011; Gilberts et al., 1994; Gupta and Gupta, 2009). We then assessed confounding by other covariates (SES, living with one or more tobacco smokers, activities during cooking, time of day, season, and salt intake) by individually adding each covariate into our base models and examining the changes in the estimated regression coefficients. We included a covariate in the final model if it was an a priori risk factor or if it changed the estimate for the black carbon index by more than 10%. We also assessed effect size modification by age (i.e.,  $\geq$  50 years vs. < 50 years) and by BMI [i.e., underweight (BMI < 18.5 kg/m<sup>2</sup>) vs. not underweight (BMI  $\geq$  18.5 kg/m<sup>2</sup>)], as previous studies suggest that age and BMI may modify this association (Baumgartner et al., 2014; Clark et al., 2013a).

Non-linear associations between continuous exposure variables or covariates and blood pressure were assessed using natural cubic splines with 2, 3, 4, and 5 degrees of freedom (df). Splines allow the relationship between the independent (i.e., black carbon exposure) and dependent (i.e., blood pressure) variables to vary across levels of the independent variable. We selected smoothers having 2 and 3-df as these provided a smooth function without extraneous variability across the range. We computed the pointwise confidence intervals and plotted the fitted functions using the methods provided by Cao et al. (2006). The model assumptions of autocorrelation and normality of random effects were verified using routine regression diagnostics.

We conducted multiple sensitivity analyses. We evaluated whether our results changed with models not specifying an autoregressive structure. We also conducted our analysis without the three women who reported taking anti-hypertension medication, and evaluated the potential effect of including individual asset measures of SES (i.e., ownership of a plastic chair, motorcycle or television) in the statistical models instead of the composited values based on asset ownership. To determine if random effect models were more appropriate for the data than fixed effect models, we ran both types of models and compared the results using a Hausman test. Finally, we assessed whether adjusting for heart rate as a measure of physical activity, in place of the METS values, had an impact on our results.

#### 3. Results

#### 3.1. Characteristics of the participants

We enrolled 45 women who were between the ages of 25 and 66 years (mean: 41 years). Twelve of these women (nine in the winter, three in the summer) participated in only one season due to conflicting agricultural schedules or because they did not want to wear the monitoring devices for a second time. Five women had unusable black carbon data in one season due to equipment failure.

Table 1 shows the selected characteristics of our participants. Women's mean [ $\pm$ standard deviation (SD)] BMI and waist

 Table 1

 Selected characteristics of the study participants.

	staay participantsi		
		Minimum- maximum	Number (%)
Age (years) $(n=45)$ < 50 years old $\geq$ 50 years old	41 ± 11	25-66	33 (73.3%) 12 (26.7%)
Body mass index $(BMI, kg/m^2)^a (n=45)$ Overweight	$19.3 \pm 3.3$	12.3-28.9	3 (6.7%)
Healthy weight Underweight			22 (48.9%) 20 (44.4%)
Education (years) (n=44) Household size (n=45)	$0.6 \pm 1.8$ $6 \pm 2$	0-10 2-11	
Caste (n=44) <sup>b</sup> Other backwards caste –			6 (13.6%)
IIIA Other backwards caste – IIA			20 (45.5%)
Other backwards caste – I Scheduled tribe Scheduled caste			2 (4.6%) 2 (4.6%) 14 (31.8%)
Marital status (n=44) Currently married Widowed			37 (84.1%) 7 (15.9%)
Prevalence of asset owner- ship at the household level Television (n=45) Plastic chair (n=45) Motorcycle (n=44)			9 (20.0%) 12 (26.7%) 6 (13.6%)
Resting blood pressure (mm Hg) <sup>c</sup>			
Systolic in winter (n=45) Systolic in summer (n=41)	$108.7 \pm 17.9 \\ 109.9 \pm 16.4$	82-180 87-187	
Diastolic in winter (n=45)	$70.3 \pm 11.3$	50-100	
Diastolic in summer $(n=41)$	73.4 ± 11.5	55–117	
Ambulatory blood pressure during cooking sessions (mm Hg)			
Systolic in winter (n=42) Systolic in summer (n=37)	$119.7 \pm 16.7 \\ 114.4 \pm 14.7$	90-184 90-169	
Diastolic in winter (n=42)	$79.5 \pm 12.6$	51-121	
Diastolic in summer (n=37)	74.5 ± 11.3	54-109	

 $<sup>^</sup>a$  Using the mean of the values from both seasons; overweight: 25 < BMI < 29.9; healthy weight: 18.5 < BMI < 24.9; underweight:  $BMI < 18.5 \ (World Health Organization, 2015).$ 

circumference were  $19.3\pm3.8$  kg/m² and  $74\pm10$  cm, respectively. Five women reported a previous diagnosis of hypertension by a health professional, three of which reported taking anti-hypertension medication. Fifty-six percent of participants reported never previously having had their blood pressure measured. Forty-one percent of participants lived with at least one tobacco smoker and of these, most (89%) reported that smoking occurred both inside and outside of the home. Mean ( $\pm$  SD) daily individual salt

<sup>&</sup>lt;sup>b</sup> Some of the most socioeconomically disadvantaged groups in India; listed from highest advantage to lowest advantage based on SES and social status.

<sup>&</sup>lt;sup>c</sup> Average of the last two of three blood pressure measurements taken while seated after five minutes of quiet rest using standard protocols (Pickering et al., 2005).

intake was  $14\pm8$  g in winter, and  $12\pm8$  g in summer, although it varied considerably among participants (range in winter: 1–38 g; range in summer: 2–42 g). The average resting systolic and diastolic blood pressure among participants was 109 mm Hg and 71 mm Hg, respectively.

Of the 1010 attempted blood pressure measurements, 522 (i.e., 52%) first attempts were successful. From these, 53 initial blood pressure readings were excluded from the analysis as, based on the protocol, these measurements were collected prior to the start of exposure assessment and therefore did not have time-matched black carbon data. The number of blood pressure measurements contributed to the analyses differed among participants and by season. On average, each participant contributed 10 blood pressure measurements (range: 3–28) to the analysis. We obtained  $\sim\!6$  measurements (range: 1–19) per woman in winter and  $\sim\!5$  measurements (range: 1–13) per woman in summer.

Mean ( $\pm$  SD) systolic ambulatory blood pressure during cooking was 114.4  $\pm$  14.7 mm Hg in summer and 119.7  $\pm$  16.7 mm Hg in winter. Diastolic was 74.5  $\pm$  11.3 mm Hg in summer and 79.5  $\pm$  12.6 mm Hg in winter (Table 1).

#### 3.2. Exposure to black carbon

Women's geometric mean personal exposure to black carbon, averaged over the entire cooking session, was  $40 \,\mu g/m^3$  (95% CI: 30, 53; median: 47; range: 7–233) in winter and  $56 \,\mu g/m^3$  (95% CI: 42, 76; median: 52, range 11–399) in summer. Women cooking over open fires had considerably higher geometric mean black carbon exposure than women with chimney stoves in both seasons [53  $\,\mu g/m^3$  (95% CI: 39, 73) vs. 23  $\,\mu g/m^3$  (95% CI: 14, 37) in winter;

 $60 \ \mu g/m^3$  (95% CI: 40, 90) vs. 45  $\mu g/m^3$  (95% CI: 28, 71) in summer]. Women's activities and location within the home during the cooking session also affected their exposures (Fig. 1). The duration of a cooking session in our study was slightly longer in winter (mean:  $95 \pm 52 \ \text{min}$ ; median: 78 min) than in summer (mean:  $76 \pm 46 \ \text{min}$ ; median: 65 min).

#### 3.3. Assessment of assumptions of linearity and correlation structure

The autocorrelation coefficient (phi) values ranged from 0.2 to 0.9, with most values near 0.9, thus justifying the use of the autoregressive error structure. The residuals of the random effects for each woman were normally distributed and homoscedastic.

The models using natural cubic spline functions for age, ambient air temperature, and BMI were consistent with a linear relationship with systolic and diastolic blood pressure. Individual salt intake and SES were inconsistent with a linear response; we found upon visual inspection that splines with 2-df provided a reasonable fit.

A 3 df natural cubic spline model adequately fit the response functions for black carbon and blood pressure. Fig. 2 illustrates that a linear response did not represent the associations between systolic blood pressure and exposure to black carbon (e.g., averaged over 2–20 min, or averaged over the entire cooking session), but it could be used to represent the associations with diastolic blood pressure. We observed a non-linear association between exposure to black carbon and blood pressure in many of our models, and therefore report the change in systolic and diastolic blood pressure associated with an interquartile range (IQR; 25th–75th percentile) increase in black carbon.

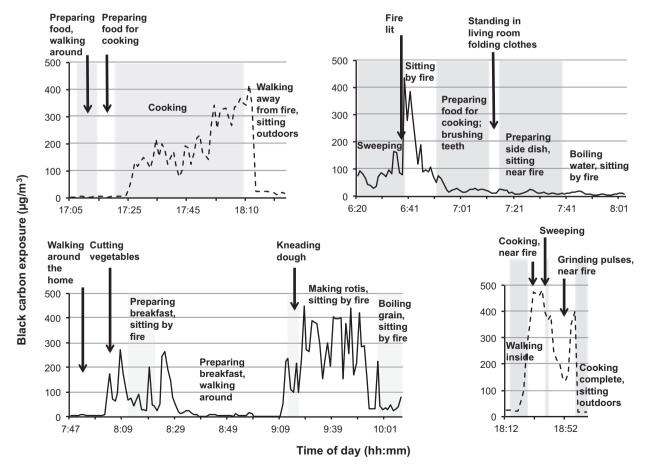


Fig. 1. Examples of time-resolved cooking session activities and real-time exposure to black carbon for four Indian women cooking with a chimney stove (black line) or open fire (dashed line). A change in shading (white or grey) indicates the time at which the field staff observed a change in the participant's activity during the cooking session.

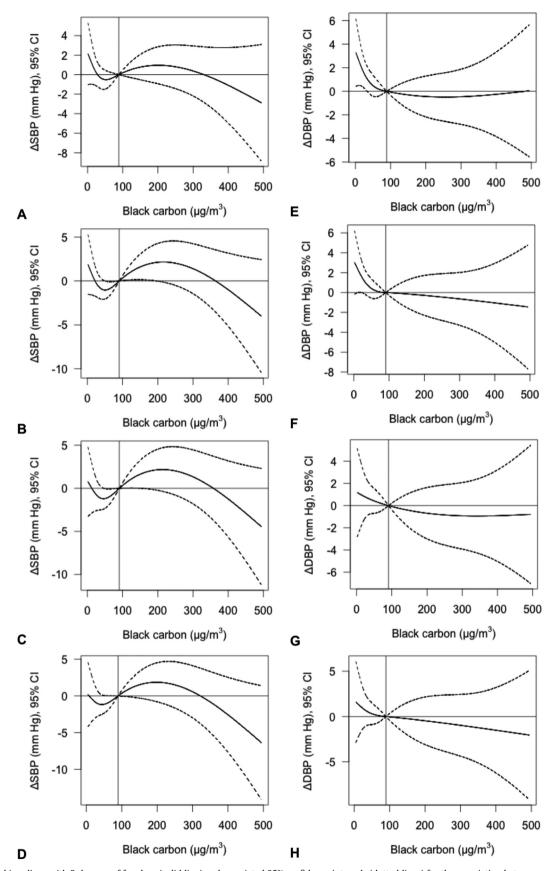
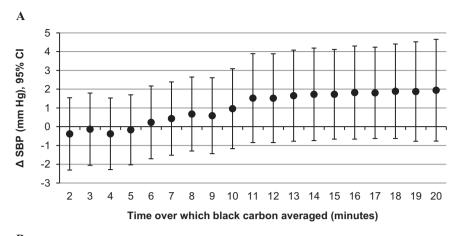


Fig. 2. Natural cubic splines with 3 degrees of freedom (solid line) and associated 95% confidence intervals (dotted lines) for the association between personal exposure to black carbon ( $\mu$ g/m³), averaged over the (A) 5 (B) 10 (C) 15 and (D) 20 min preceding blood pressure measurement, and mean change in systolic blood pressure ( $\Delta$ SBP) and averaged over the (E) 5 (F) 10 (G) 15 and (H) 20 min preceding blood pressure measurement, and mean change in diastolic blood pressure ( $\Delta$ DBP). Mean change is relative to the mean exposure (vertical line). Models are adjusted for age, BMI, time of day, SES, physical activity, salt intake, and ambient temperature.



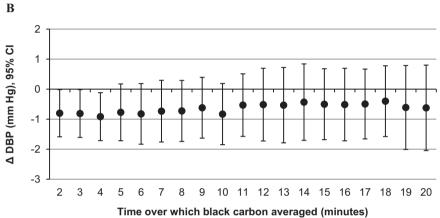


Fig. 3. Estimated change in (A) systolic ( $\triangle$ SBP) and (B) diastolic ( $\triangle$ DBP) blood pressure associated with an IQR increase in personal exposure to black carbon averaged over an increasing number of minutes prior to blood pressure measurement during a cooking session for 45 rural Indian women cooking with biomass fuels. Models are adjusted for age, BMI, time of day, SES, physical activity, salt intake, and ambient temperature.

### 3.4. Associations between black carbon exposure and acute changes in blood pressure

For each time metric, we used the numerical values of the fitted natural cubic spline functions to compute the changes in blood pressure, and 95% CIs, associated with changes in black carbon concentrations across their IQRs. The IQR value for each time metric differed by model, but most were approximately  $100 \, \mu g/m^3$ . The exact IQRs are presented in the Supplementary material, Table S2. In the multivariate models we observed a gradual increase in the magnitude of the association between personal exposure to black carbon and systolic blood pressure as the number of minutes included in the averaging period increased (Fig. 3).

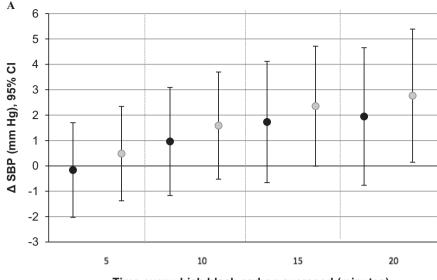
Specifically, we observed a positive association between exposure to black carbon and systolic blood pressure for averaging periods ranging from 6 to 20 min, with increases ranging from 0.2 mm Hg (95% CI:  $-1.7,\,2.2$ ) to 1.9 mm Hg (95% CI:  $-0.8,\,4.7$ ) for an IQR increase in black carbon exposure. When exposure to black carbon was averaged over five or fewer minutes prior to blood pressure measurement, an IQR increase in black carbon exposure was associated with small decreases in systolic blood pressure ranging from  $-0.4\,\mathrm{mm}$  Hg (95% CI:  $-2.3,\,1.5$ ) to  $-0.2\,\mathrm{mm}$  Hg (95% CI:  $-2.0,\,1.7$ ). For diastolic blood pressure, an IQR increase in black carbon was associated with very small decreases in blood pressure, ranging from  $-0.9\,\mathrm{mm}$  Hg (95% CI:  $-1.7,\,-0.1$ ) for a 4-min averaging period to  $-0.4\,\mathrm{mm}$  Hg (95% CI:  $-1.6,\,0.8$ ) for an 18-min averaging period.

3.5. Association between average black carbon exposure during an entire cooking session and acute changes in blood pressure

An IQR increase in black carbon (from 42 to  $165 \,\mu g/m^3$ ) was associated with an increase in systolic blood pressure of 2.6 mm Hg (95% CI: -4.1, 9.3) in the fully adjusted model (i.e., adjusted for age, temperature, BMI, SES, salt intake, time of day, and physical activity) with black carbon exposure averaged over the entire measurement period and preceding the final blood pressure measurement. In models predicting diastolic blood pressure, the same IQR increase in black carbon was associated with a small decrease in blood pressure ( $-1.4 \,\mathrm{mm}$  Hg; 95% CI: -5.9, 3.2).

#### 3.6. Sensitivity analyses

Age of the participants did not modify these associations (data not shown). Our results did not change appreciably after removing participants who reported taking anti-hypertension medications (Supplementary material, Fig. S4) or when the individual SES asset components were added to the statistical models. For all derived black carbon variables, the base models and fully adjusted models yielded very similar results both when specifying an autoregressive correlation structure and under the assumption of no time-dependent correlation structure (Supplementary material, Fig. S5). For all comparisons of the fixed vs. random effect models, a Hausman test indicated that random effect models are more appropriate for these data. We did not find evidence of effect size modification by underweight. Finally, the inclusion of heart rate



Time over which black carbon averaged (minutes)

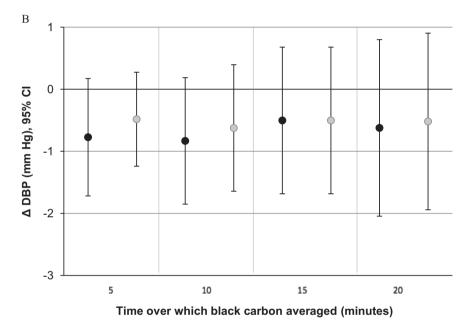


Fig. 4. Estimated change in (A) systolic (ΔSBP) and (B) diastolic (ΔDBP) blood pressure associated with an interquartile increase in personal exposure to black carbon for 45 rural Indian women cooking with biomass fuels. Main results ( ) compared with estimates when heart rate is used instead of METS to account for physical activity ( ) for 5, 10, 15 and 20-min average exposures. Models are adjusted for age, temperature, BMI, SES, activity, time of day, and salt intake.

instead of METS values to account for physical activity resulted in a similar trend but slighter stronger estimates of the association between exposure to black carbon and systolic blood pressure and slightly weaker estimates for the association with diastolic blood pressure. The inclusion of heart rate did not change our overall findings (Fig. 4).

#### 4. Discussion

Household air pollution from cooking with biomass fuels is one of the world's most widespread environmental exposures (Bonjour et al., 2013). Few studies have directly measured personal exposure to combustion-related pollutants like black carbon in settings dominated by biomass smoke (Clark et al., 2013b), or assessed its relationship with cardiovascular outcomes (Smith, 2002; Yamamoto et al., 2014). To our knowledge, this manuscript reports the first longitudinal study of the acute vascular effects of

exposure to household air pollution on blood pressure.

Women in our study were exposed to high levels of black carbon while cooking, with these exposures differing by housing characteristics such as the presence of stove chimneys as well as their activities and proximity to the stove while cooking. Their average exposure to black carbon during cooking was similar to auto-rickshaw passengers in New Delhi (geometric mean:  $42 \mu g/m^3$ ) (Apte et al., 2011), but lower than others have reported for breathing zone concentrations in rural India during cooking with unimproved stoves (128  $\mu$ g/m<sup>3</sup>) (Kar et al., 2012). Women's ambulatory systolic and diastolic blood pressure was lower in summer than in winter. Seasonal differences in blood pressure have been previously observed in Indian and other populations, and may be attributable to a range of environmental and behavioural factors for higher blood pressure that can vary seasonally including ambient or indoor temperature, diet, and physical activity (Brook et al., 2011; Modesti et al., 2013; Sega et al., 1998; van den Hurk et al., 2015).

Overall, our findings suggest that for rural Indian women cooking with biomass fuels, large increases in exposure to black carbon (i.e., an IQR, or approximately 100 μg/m<sup>3</sup> increase) are associated, within a few minutes, with small increases in systolic blood pressure. Our results support those of controlled human exposure (Bellavia et al., 2013) and observational or semi-experimental studies (Chuang et al., 2005; Kubesch et al., 2014; Langrish et al., 2009) of urban air pollution that used repeated measures of air pollution exposure and blood pressure, and suggest an association between increased exposure to air pollution and increased systolic blood pressure within minutes to hours of exposure. In a semi-experimental study among Beijing adults with metabolic syndrome (Zhao et al., 2014), hour-averaged black carbon exposure was associated with increases in blood pressure that were larger in magnitude as the calculated average included exposures further back in time. The strongest associations were observed with black carbon averages over the 10 h preceding blood pressure measurement, with a systolic increase of 0.53 mm Hg (95% CI: 0.17, 0.89) estimated per 1-µg/m<sup>3</sup> increase in 10-h average black carbon. A study in healthy young adults in Taipei found associations between PM<sub>2.5</sub> averaged over one to four hours and increases in both systolic and diastolic blood pressure (Lin et al., 2009). However, a number of studies in North America found either a weak association or no association between air pollution exposure and blood pressure within minutes to hours of exposure (Brook et al., 2002), within days of exposure (Brauer et al., 2000; Jansen et al., 2005), or observed increases for only diastolic blood pressure (Brook et al., 2009).

We observed a rather modest effect of black carbon exposure on acute changes in blood pressure compared with studies of urban air pollution, a discrepancy that may be at least partially explained by differences in population susceptibilities or the composition of air pollutants from different sources (i.e., biomass combustion vs. motor vehicles or industrial sources). The composition of pollutants from urban sources like motor vehicles may have differential health impacts than pollutants emitted from incomplete biomass combustion (Pope III and Dockery, 2006; Strak et al., 2013). In addition, our study was conducted among relatively young women (mean age=41 years), whereas most previous prospective studies of ambient air pollution and blood pressure examined responses among older participants with chronic conditions including metabolic syndrome (Zhao et al., 2014), cardiovascular diseases (Huang et al., 2012) or other health conditions (Linn et al., 1999; Rückerl et al., 2011). Finally, we assessed associations of very acute exposures whereas most other studies have assessed effects within hours to days of exposure (Brook and Rajagopalan, 2009). Cardiovascular responses within this acute time frame remain poorly understood in the context of the very high air pollution exposures experienced in settings like our study site in rural India. It remains unclear whether the cardiovascular impacts of ambient air pollution persist at the markedly higher exposure levels experienced by populations cooking with biomass fuels (McCracken et al., 2012). We are unaware of other longitudinal studies that have assessed the cardiovascular impacts of personal exposure to household air pollution. Previous cross-sectional studies, evaluating non-acute responses, have found that higher daily exposure to black carbon and other combustion-related air pollutants from biomass stoves was associated with higher systolic and diastolic blood pressure among older women in China (Baumgartner et al., 2014; Shan et al., 2014) and Peru (Peña et al., 2015). Several stove intervention studies in Latin America found that use of less-polluting cookstoves was associated with reductions in systolic (decreases of 3.1–5.9 mm Hg) and diastolic blood pressure (decreases of 1.8-1.9 mm Hg), with the largest decreases observed among older and more obese women (Alexander et al., 2014; Clark et al., 2013a; McCracken et al.,

2007). Differences in study design, methods of exposure assessment, and the use of resting blood pressure versus ambulatory blood pressure make direct comparison with our study difficult. Though the magnitudes of the observed associations in our study were small, our overall findings partially support the biological plausibility of an acute detrimental impact of exposure to household air pollution on the risk of cardiovascular events and diseases.

The mechanistic pathways linking air pollution with higher blood pressure and cardiovascular events likely depends on the timing of the effect (i.e., acute, sub-acute, and chronic) (Brook, 2005). Systemic inflammation, oxidative stress, and acute autonomic imbalance including sympathetic nervous system stimulation may trigger vascular or endothelial dysfunction (Brook et al., 2009), but it is unclear whether the rapid cardiovascular effects observed within minutes to hours of exposure and the chronic effects experienced (i.e. within days, months, or years) are driven by the same biological mechanisms (Brook, 2005). Cooking with biomass fuels is a usual daily source of exposure to black carbon and other air pollutants, and thus continued daily exposure over many years or decades may affect blood pressure rapidly through both an autonomic nervous system response and over longer timescales through oxidative stress and inflammation (Brook et al., 2009). Increased sympathetic tone has been proposed as a plausible mechanism explaining associations between ambient air pollution and acute changes in blood pressure (Brook et al., 2009); results of our study support this hypothesis. To further investigate the possibility of these different mechanisms being responsible for effects observed at different times following exposure, we would need to longitudinally assess acute changes in blood pressure over longer time periods, and we would need to replicate the results observed in our study as there is not a literature base for these types of acute vascular effects of household air pollution.

Strengths of our study include the use of minute-resolved black carbon exposure data combined with repeated blood pressure measurements that allowed us to assess an acute cause-effect relationship that is not possible in a cross-sectional study. In particular, the use of time-resolved exposure data enabled us to investigate various time-windows that may be relevant to a relationship between exposure to household air pollution and acute changes in blood pressure, and allowed for transient effects to be captured. Our direct measurements of personal exposure minimize the exposure misclassification that may occur with indirect methods. We also collected detailed information on many of the important socio-behavioural and physiological covariates that may also impact changes in blood pressure. Our use of splines to model the association between exposure to black carbon and blood pressure provided a more flexible method of estimating this relationship than would have been possible with a linear model, and may be more appropriate given the non-linear dose-response curve observed in other studies of exposure to black carbon and blood pressure (Baumgartner et al., 2014). Lastly, although it is challenging to account for all factors that may affect blood pressure in an observational study such as this, the concentrations of black carbon that we investigated exceed concentrations that would likely be considered ethical for controlled exposures in a chamber study. Conducting studies of these very high exposures to household air pollution is important, as their associations with blood pressure may not be the same as with lower concentrations, and knowledge of the exposure-response relationships is important for informing interventions.

Blood pressure is highly variable, responding to many environmental and physiological changes (Brook et al., 2011); this aspect makes it an appropriate health outcome of interest when assessing acute impacts of an environmental exposure such as black carbon. However, to accurately estimate the association between exposure to black carbon and blood pressure, factors other

than combustion-derived pollutants that acutely affect blood pressure must be adequately addressed. We attempted to account for known factors that impact blood pressure such as ambient temperature and level of activity during the cooking session. Our open-ended physical activity comments led to subsequent categorization of the activities to account for energy expenditure; this approach did not allow for unique energy expenditure values for each activity. Another potential limitation of our study is that our measurement of salt intake may not accurately reflect differential consumption by individuals in the household. While some measurement error is expected for the covariates mentioned, given the similarity between the base models and the fully adjusted models in this study, this error is unlikely to have resulted in substantial residual confounding. Further, though our study included repeated, seasonal measurements of both black carbon exposure and blood pressure, our relatively small sample size of 45 women limits the statistical power of our study.

Cardiovascular diseases are the leading causes of premature death and disease globally (Strong et al., 2005) and in India (Shokeen and Aeri, 2015). Of the estimated 1.5 million yearly premature deaths attributable to cardiovascular diseases in India, it is estimated that  $\sim$ 300,000 could be prevented through better control of high blood pressure (Gupta and Gupta, 2009), which is an independent risk factor for the development of renal and cardiovascular diseases and events including coronary heart disease and stroke (Kannel, 2000). Further, increases in systolic blood pressure at almost any level are causally associated with an increased risk of cardiovascular events and heart disease (Chobanian et al., 2003). An estimated 75% of Indians are exposed to household air pollution (Prasad et al., 2012). Thus, even a small increase in blood pressure resulting from an exposure as pervasive as household air pollution would have large population health impacts in India (Rose, 2001).

#### 5. Conclusion

This study contributes to a small number of studies of measured exposure to black carbon and is the first longitudinal study to assess the acute vascular impacts of exposure to household air pollution. We found that associations between personal exposure to black carbon and systolic blood pressure increased in magnitude as black carbon values were assessed over greater time periods preceding blood pressure measurement, but did not find an association with diastolic blood pressure. Our results suggest that changes in blood pressure may occur at very acute time-scales in response to exposure to household air pollution, potentially implicating an autonomic nervous system response. Understanding the patterns of exposure to household air pollution during cooking and examining how these exposures contribute to changes in blood pressure can inform our understanding of the long-term contribution of exposure to household air pollution to increased risk of cardiovascular diseases in India and globally.

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#### **Ethics approval**

This study received ethical approval from St. Johns Medical College in Bangalore (#103/2011), the University of Minnesota (#104S97992), and McGill University (#A11-M119-14B).

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#### Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2016.02.024.

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