

## FINAL - ID271

### STATISTICAL METHODS

#### I. General Model

To study the associations of same-day temperature and black carbon (BC) exposure with systolic blood pressure (SBP), we used generalized additive mixed models. Treating SBP as the outcome, the following general equation was used:

$$\log(Y_{it}) = \beta_0 + u_i + \beta_1 X_{1it} + \dots + \beta_k X_{kit} + \beta_{TEMP} TEMP_{it} + \beta_{BC} BC_{it} + \epsilon_{it}$$

where for participant  $i$  at visit  $t$ :  $\log(Y_{it})$  is the log-transformed SBP;  $TEMP_{it}$  and  $BC_{it}$  are same-day temperature and black carbon exposure; and  $X_{kit}$  is covariate  $k$ . To account for the highly-correlated nature of repeat measurements, we included a random intercept term,  $u_i$ , for each participant. We log-transformed SBP to ensure that our outcome was normally distributed. We then assessed whether same-day ambient temperature (TEMPC24H), BC levels (BC24H), or relative humidity (RHUM24H) had non-linear relationships with SBP using penalized splines. All models explored were fitted using the *gamm* function with a gaussian family since the outcome was continuous and normally distributed. Based on previous studies ((Auchincloss et al., 2008; Dvornch et al., 2009; Fuks et al., 2011; Rabito et al., 2020), we included the following precision variables due to their demonstrable relationships with SBP: age, race, daily alcohol intake, body mass index, cigarette smoking status, fasting blood glucose, years of education, statin medication status, physician-diagnosed diabetes mellitus, and coronary heart disease.

#### II. Effect Modification

Various effect modifiers were explored in our analysis. Firstly, we looked at whether diabetes modifies the effect of same-day BC exposure on SBP by including an interaction term between diabetes and same-day BC in one of the models, and included variables for ambient same-day temperature, sine and cosine functions of date (proxy for seasonality), and day of the week. Secondly, separate models with an interaction term between season and same-day BC/temperature were fit to test whether the associations between BC/temperature and SBP varied by warm and cold seasons. Lastly, to investigate if there were any subgroups that were particularly vulnerable to the effect of same-day BC or temperature on SBP, we included an interaction term between same-day BC or temperature and each of the following covariates as they've been shown (Gosmanova et al., 2016; Lv et al., 2018; Omvik, 1996; Santana et al., 2018; Strazzullo et al., 2007) to have a relationship with SBP: smoking status, fasting blood glucose, statin medication use, alcohol consumption, and coronary heart disease status. Race an effect modifier was excluded as we believed there were not enough subjects in each racial category to find any significant results.

#### III. Lagged Effects

To investigate if the associations between BC/temperature and SBP persisted for more than one day, we fit distributed lag models using the *gam* function from the *mgvc* package. We included three lag days for each exposure (BC or temperature) — same-day and one for each of the prior two days. As in our other

models, we adjusted for relative humidity, seasonality using sine and cosine functions of date, and day of the week. Overall effects of each exposure were derived from the sum of effects across lags.

## RESULTS

The characteristics of our study sample are displayed in Table 1. Participants in the study tended to be older with an average age across participants and visits of 73 years. The overwhelming majority of the study population was white (98%), followed by small percentages of Black and Hispanic participants. The median educational attainment of 14 years indicates the majority had obtained some college-level education. Average systolic blood pressure (SBP) among participants and across visits was 131 mmHg and average BMI was in the overweight category ( $>25$ ). Most participants did not smoke; 30% were never smokers while 66% were former, but not current, smokers. Most participants did not consume more than two alcoholic beverages per day and had fasting blood glucose levels below 110 mg/dL at visits. Overall, 39% reported taking statin medications across visits and the average prevalence of diabetes and coronary heart disease during the study was 31% and 14%, respectively.

Effect estimates from both our crude and adjusted models can be found in Table 2. All associations of the outcome with meteorological variables were estimated to be linear with 1 df. The dose-response relationships between same-day temperature and BC on SBP are depicted in Figures 1 and 2, respectively.

We found a significant, linear relationship between short-term BC exposure on systolic blood pressure in both our crude (meteorological variables only) and adjusted models. Including confounders and a priori-specified covariates in our adjusted model did not greatly change our effect estimates and, in both models, we estimate that an increase of approximately 1  $\mu\text{g}/\text{m}^3$  in short-term exposure to BC increases systolic blood pressure by approximately 1 mmHg. While an increase of 1 mmHg in systolic blood pressure might seem small, when short-term exposure to black carbon pollution is multi-fold higher (i.e., in high-traffic, densely-populated areas), there might be a much greater elevation in systolic blood pressure that does result in clinically-relevant effects. We did not find an overall significant effect of same-day temperature on systolic blood pressure.

We investigated a variety of potential interactions that might explain effect heterogeneity in the associations of same-day temperature and BC on SBP and considered an interaction significant if the p-value was  $< .05$ . Effects of significant interactions on the temperature-SBP and BC-SBP associations are displayed in Tables 3 and 4, respectively. We did not find evidence of effect modification by smoking status, fasting blood glucose, diabetes, statin use, or warm/cold season. There was evidence for effect modification of the temperature-SBP relationship by CHD and for the BC-SBP relationship by CHD and alcohol consumption.

Finally, we found significant lag effects of BC on SBP that monotonically decreased from same-day to two-day-prior exposure (i.e., more proximal exposure exhibited greater effect). The effect estimates from our distributed lag model are shown in Table 5. The summed effect across three lag days was 1.027 (95% CI: 1.010 - 1.045). We did not find evidence of lagged effects for temperature on systolic blood pressure.

## **CONCLUSION**

Same-day exposure to BC is associated with significant increases in SBP in this study population, comprised primarily of older, white males, though the clinical relevance of this finding may be dependent on the actual levels of this pollutant. As evidenced by our study results, there also appears to be lagged effects of exposure to BC. However, same-day temperature was found to be not significantly associated with SBP in our overall study population and no lagged effects were observed. CHD modified the effect of same-day temperature on SBP while CHD and alcohol consumption modified the BC-SBP association.

	Overall (N=2454)
<b>Systolic Blood Pressure (mmHg)</b>	
Mean (SD)	131 (18.0)
Median [Min, Max]	130 [77.0, 232]
<b>Age (y)</b>	
Mean (SD)	72.9 (7.45)
Median [Min, Max]	73.0 [49.0, 97.0]
<b>Race</b>	
White	2400 (97.8%)
Black	37 (1.5%)
Hispanic White	13 (0.5%)
Hispanic Black	4 (0.2%)
American Indian	0 (0%)
<b>Education (y)</b>	
Mean (SD)	14.5 (2.78)
Median [Min, Max]	14.0 [-9.00, 30.0]
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	
Mean (SD)	27.9 (4.00)
Median [Min, Max]	27.4 [16.7, 52.6]
<b>Smoking Status</b>	
Never	728 (29.7%)
Current	97 (4.0%)
Former	1629 (66.4%)
<b>Alcohol Consumption</b>	
Less than 2 drinks/day	1969 (80.2%)
Two or more drinks/day	485 (19.8%)
<b>Fasting Blood Glucose</b>	
<110 mg/dL	1743 (71.0%)
>110 & <126 mg/dL	400 (16.3%)
>126 mg/dL	311 (12.7%)
<b>Statin Use</b>	
no	1489 (60.7%)
yes	965 (39.3%)
<b>Coronary Heart Disease</b>	
no	1693 (69.0%)
yes	761 (31.0%)
<b>Diabetes</b>	
no	2119 (86.3%)
yes	335 (13.7%)

**Table 1** – Descriptive statistics of study population (*n* = 968 participants) across all clinical visits (*N* = 2454)

Exposure	Crude Model <sup>1</sup> Effect (95% CI)	Adjusted Model <sup>2</sup> Effect (95% CI)
Ambient temperature, 24 hour avg. on day of visit	0.999 (0.998, 1.000)	0.999 (0.998, 1.000)
Black carbon, 24 hour avg. on day of visit	1.017 (1.008, 1.027)***	1.015 (1.006, 1.025)**

**Table 2** – Estimated change in systolic blood pressure for a 1 µg/m<sup>3</sup> increase in same-day (24 hour) black carbon for 2454 clinical visits (n = 968 participants)

<sup>1</sup> Crude model included only meteorological variables (24h temperature, 24h black carbon, 24h relative humidity)

<sup>2</sup> Adjusted model included meteorological variables from the crude model as well as: age, race, alcohol consumption, BMI, smoking status, fasting blood glucose, educational attainment, statin use, diabetes, and coronary heart disease.

\*\*\* p < .001, \*\* p < .01

Effect Modifier	Effect Estimate <sup>1</sup>	Effect Estimate <sup>1</sup>	p-value for interaction
Coronary Heart Disease (CHD)	Not Diagnosed	Diagnosed	
	0.998	1.000	0.003

**Table 3** – Modification of the effects of same-day temperature on systolic blood pressure by coronary heart disease

<sup>1</sup> Effect estimate is the estimated increase in systolic blood pressure in mmHg associated with 1°C increase in temperature

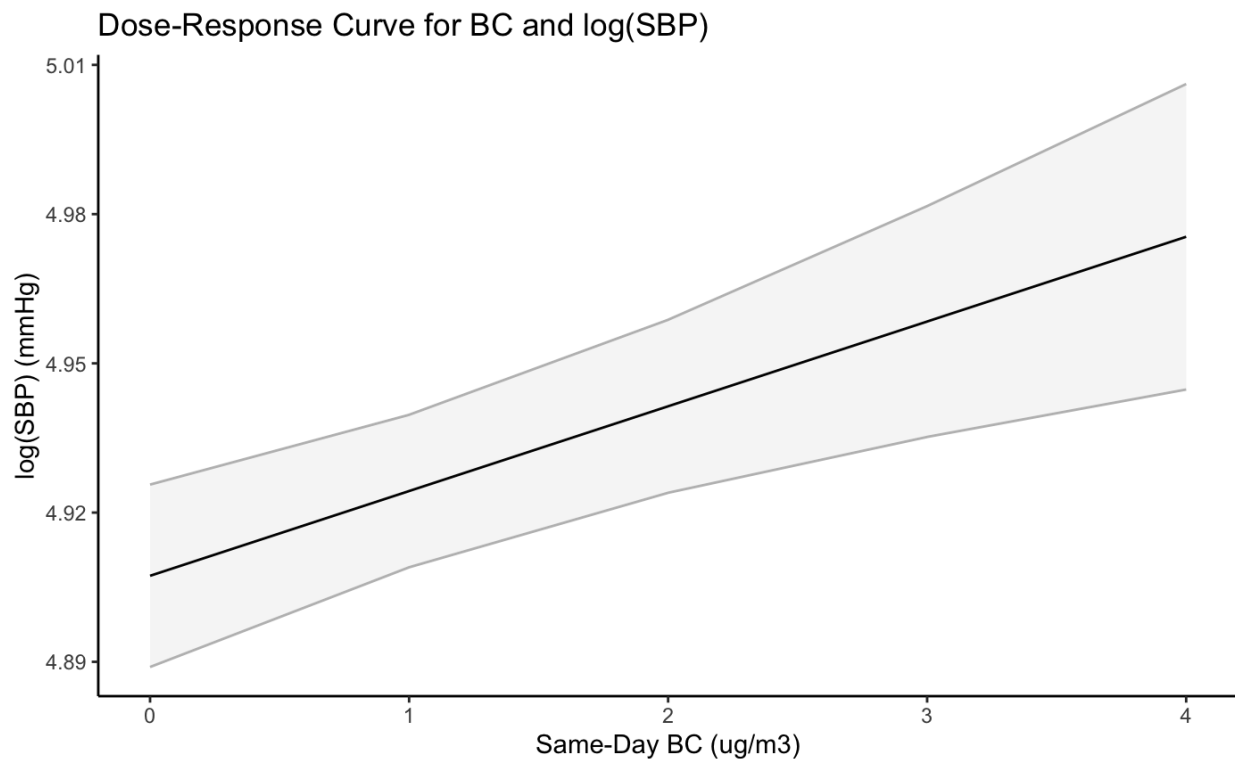
Effect Modifier	Effect Estimate <sup>1</sup>	Effect Estimate <sup>1</sup>	p-value for interaction
Alcohol Consumption	< 2 drinks/day	≥ 2 drinks/day	
	1.010	1.033	.033
Coronary Heart Disease (CHD)	Not Diagnosed	Diagnosed	
	1.008	1.031	0.010

**Table 4** – Modification of the effects of same-day (24 hour) black carbon on systolic blood pressure by alcohol consumption and coronary heart disease

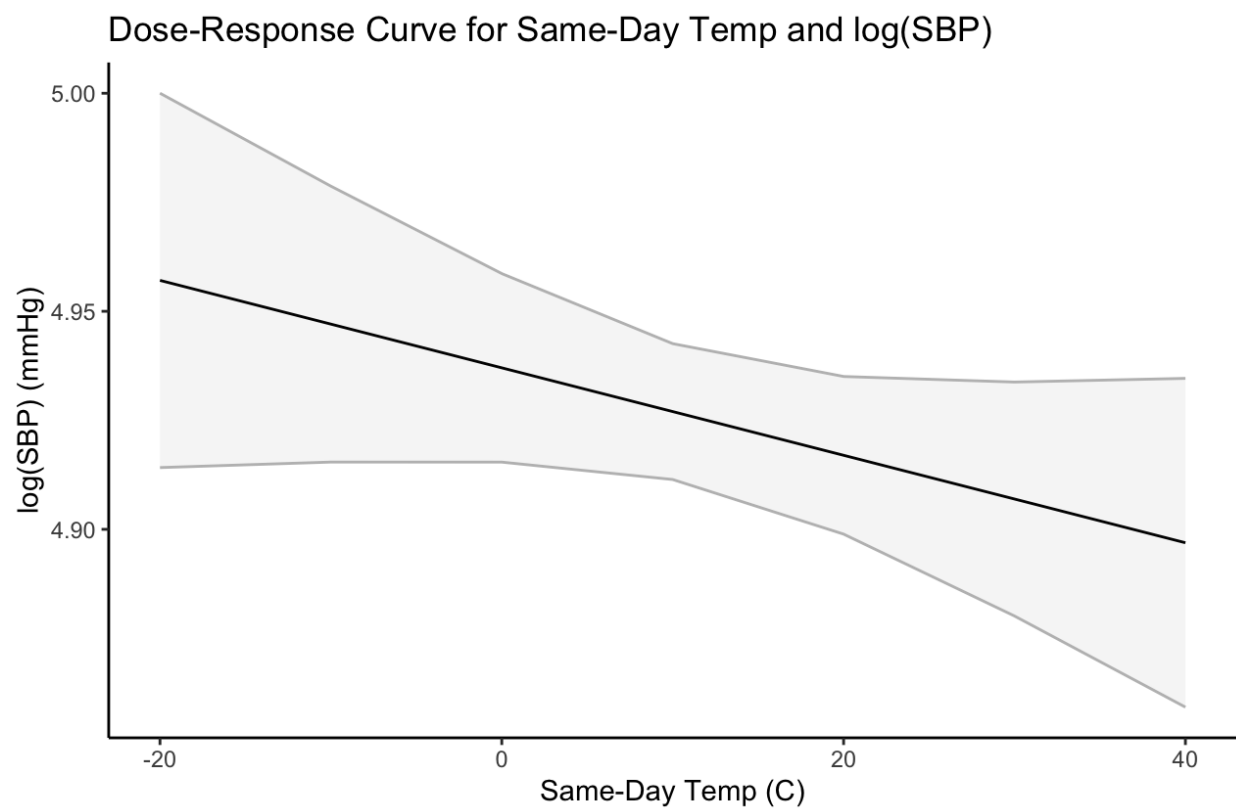
<sup>1</sup> Effect estimate is the estimated increase in systolic blood pressure in mmHg associated with 1  $\mu\text{g}/\text{m}^3$  in black carbon

Exposure	Effect (95% CI) of Same Day (Lag 0) Exposure	Effect (95% CI) of Prior Day (Lag 1) Exposure	Effect (95% CI) of 2 Days Prior (Lag 2) Exposure
Black Carbon	1.011 (0.987, 1.022)	1.010 (.999, 1.022)	1.006 (0.995, 1.018)

**Table 5** – Estimates of the lagged effects on systolic blood pressure (mmHg) for 1  $\mu\text{g}/\text{m}^3$  increase in black carbon



**Figure 1** — Dose-response relationship between same-day BC and log(SBP)



**Figure 2** — Dose-response relationship between same-day temperature and log(SBP)

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