



HAL
open science

Associations of air pollution mixtures with ambulatory blood pressure: The MobiliSense sensor-based study

Sanjeev Bista, Lia Chatzidiakou, Roderic L Jones, Tarik Benmarhnia, Nicolas Postel-Vinay, Basile Chaix

► To cite this version:

Sanjeev Bista, Lia Chatzidiakou, Roderic L Jones, Tarik Benmarhnia, Nicolas Postel-Vinay, et al.. Associations of air pollution mixtures with ambulatory blood pressure: The MobiliSense sensor-based study. *Environmental Research*, 2023, 227, pp.115720. 10.1016/j.envres.2023.115720 . hal-04225135

HAL Id: hal-04225135

<https://hal.sorbonne-universite.fr/hal-04225135>

Submitted on 2 Oct 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Associations of air pollution mixtures with ambulatory blood pressure: the MobiliSense sensor-based study

Sanjeev Bista¹, Lia Chatzidiakou², Roderic L Jones², Tarik Benmarhnia³, Nicolas Postel-Vinay⁴, Basile Chaix¹

¹ Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique IPLESP, Nemesis team, Faculté de Médecine Saint-Antoine, 27 rue Chaligny, 75012 Paris, France.

² Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK.

³ Herbert Wertheim School of Public Health and Scripps Institution of Oceanography, University of California, San Diego, 9500 Gilman Drive #0725, CA La Jolla 92093, USA.

⁴ Hypertension Unit, Hôpital Européen Georges Pompidou.

KEYWORDS

Ambulatory blood pressure
Air pollution exposure
Sensors

ABSTRACT

Air pollution is acknowledged as a determinant of blood pressure (BP), supporting the hypothesis that air pollution, via hypertension and other mechanisms, has detrimental effects on human health. Previous studies evaluating the associations between air pollution exposure and BP did not consider the effect that air pollutant mixtures may have on BP. We investigated the effect of exposure to single species or their synergistic effects as air pollution mixture on ambulatory BP. Using portable sensors, we measured personal concentrations of black carbon (BC), nitrogen dioxide (NO₂), nitrogen monoxide (NO), carbon monoxide (CO), ozone (O₃), and particles with aerodynamic diameters below 2.5 μm (PM_{2.5}). We simultaneously collected ambulatory BP measurements (30-minute intervals, N = 3319) of 221 participants over one day of their lives. Air pollution concentrations were averaged over 5 minutes to 1 hour before each BP measurement, and inhaled doses were estimated across the same exposure windows using estimated ventilation rates. Fixed-effect linear models as well as quantile G-computation techniques were applied to associate air pollutants' individual and combined effects with BP, adjusting for potential confounders. In mixture models, a quartile increase in air pollutant concentrations (BC, NO₂, NO, CO, and O₃) in the previous 5 minutes was associated with a 1.92 mmHg (95% CI: 0.63, 3.20) higher systolic BP (SBP), while 30-minute and 1-hour exposures were not associated with SBP. However, the effects on diastolic BP (DBP) were inconsistent across exposure windows. Unlike concentration mixtures, inhalation mixtures in the previous 5 minutes to 1 hour were associated with increased SBP. Out-of-home BC and O₃ concentrations were more strongly associated with ambulatory BP outcomes than in-home concentrations. In contrast, only the in-home concentration of CO reduced DBP in stratified analyses. This study shows that exposure to a mixture of air pollutants (concentration and inhalation) was associated with elevated SBP.

1. Introduction

In 2017, elevated blood pressure (BP) or hypertension was ranked among the 10 most significant contributors to global morbidity and mortality (1), resulting in 10.4 million deaths and 211.8 million disability-adjusted life-years lost that year (1). A recent report suggests that more than 30% of the world's adults have hypertension (BP \geq 140/90 mmHg) (2). It is documented that a 20 mmHg increase in systolic BP (SBP) or even a 10 mmHg increase in diastolic BP (DBP) raises the risk of cardiovascular mortality by more than two-fold (3,4). Multiple behavioral factors, including salt intake, sedentary behaviors, alcohol abuse, obesity, and environmental factors, such as ambient temperature and humidity, contribute to elevated BP (5–8). Several experimental studies have also reported (9–11) various possible mechanisms by which air pollution exposure may elevate BP, including oxidative stress, vasomotor dysfunction, altered autonomic function of the heart, induction of systemic inflammation, and endothelial dysfunction (12,13).

While numerous observational studies have assessed associations between acute exposure to air pollution and BP (14–34), the results are mixed regarding the effects of different air pollutants and exposure windows, possibly due to methodological limitations in those studies. Firstly, most large-scale air pollution studies have used outdoor stationary air pollution measurements or modeled concentrations as proxies for personal exposure, resulting in exposure misclassification and difficulties in disentangling the air pollutant effects due to multicollinearities between pollutants exacerbated by measuring them at a single point, i.e., at the stations. Moreover, most of the previous studies used a few points of clinically measured BP per person that could have been influenced by circadian rhythm or other confounders such as anxiety, diet, and physical activity. Furthermore, existing studies assessing the short-term effect of air pollution on BP outcomes relied on exposures averaged at a daily level (18,19,32–35,21–25,27,30,31), while only seven studies considered exposure at an hourly level (14–17,20,26,29). Only three of these seven hourly-level exposure studies used ambulatory BP measurements (15,26,29) [while it is known that ambulatory-measured BP is more strongly related to organ damage than isolated measurements in clinical settings (36)]. Considering short exposure windows of less than 24 hours is important because it is suggested that frequent acute increases in BP may result in hypertension (37) and other cardiovascular events in the future (38), especially among the susceptible population (39).

Ambient pollutants are highly correlated for sharing common sources (40). Therefore, individuals are usually exposed to a mixture of air pollutants rather than to a unique individual air pollution species

(41). Methods have been recently developed to consider complex chemical mixtures that can be easily adapted to study air pollution mixtures (42,43). Such approaches typically estimate a combined effect of the mixture components while considering multicollinearities and interactions between the species.

This study aims to offer insights into the mechanisms underlying the effects of air pollution on hypertension by taking advantage of state-of-the-art sensor technologies and recent developments in statistical methodologies. Notably, rapid advancement in sensor technologies enables the collection of high-resolution data on personal exposure, mobility patterns, and BP measurements for individuals. Additionally, quantile G-computation (44) offers new capabilities for estimating the effect of complex exposure mixtures on health outcomes. Using this innovative methodological framework, this study estimated the effects of acute single-pollutant species and multi-pollutant exposure [concentrations and inhaled doses of nitrogen dioxide (NO₂), nitrogen oxide (NO), carbon monoxide (CO), ozone (O₃), black carbon (BC) and fine particulate matter < 2.5 μm (PM_{2.5})] on ambulatory BP among 221 healthy adults in the Grand Paris. As little is known about the source-related health effects of air pollution, this study further aims to investigate this air pollution–BP association in different microenvironments, which could provide insight into possible health risks during daily life.

2. Methods

2.1 Study population

Data for this study come from the MobiliSense sensor-based study (45). The MobiliSense study was conducted in the Grand Paris metropolitan area, France, from May 2018 to October 2020 (first wave of the study) (45). To ensure that diversity in neighborhood conditions from the Grand Paris area would be represented in the sample, participants in the study were recruited through a two-stage stratified random sampling technique. The neighborhood sampling stage involved the random selection of local neighborhoods in the first and last quartiles of road traffic density within each quartile of area income. In the second stage, dwelling units in each pre-selected neighborhood were randomly selected in the 2013 and 2014 censuses by the National Institute of Statistics and Economic Studies. Overall, 31,970 dwellings were selected from 234 neighborhoods. The inclusion and exclusion criteria for this study are detailed elsewhere (45). In brief, our eligible participants had to be non-smoking adults from non-smoking households free of chronic heart and pulmonary diseases, living in the Grand Paris, France, and aged 30–64 years on January 1, 2016. Postal invitations to participate in the study were sent twice to the residents of the pre-selected dwellings, resulting in the recruitment of 289 participants. The sample was slightly biased toward older French citizens with higher education (46). Self-employed

people and people with stable and unstable jobs were more likely to consent than unemployed people (46).

Participants carried different sets of sensors over the 6 days of the MobiliSense study. The present analysis exclusively relies on data from day 1, where the participant's ambulatory BP was measured at a 30-minute interval from wake time to bedtime, along with the continuous monitoring of the breathing zone concentrations of several air pollutants using different personal sensors. On average, each individual contributed 15 BP measurements (range: 2, 31) over this single day of follow-up. Personal sensors used in this study are described below in detail.

2.2. Data collection and processing

2.2.1. Personal exposure to gaseous pollutants and PM_{2.5}

With well-characterized accuracy, the personal air quality monitor (PAM) integrates multiple sensors for temperature, relative humidity, gaseous pollutants, and particulate matter. Gaseous pollutants (CO, NO, NO₂, O₃) were collected at a 10 second time resolution with electrochemical sensors, whereas PM_{2.5} was measured at 1-minute intervals with an optical particle counter. The performance of the PAMs was characterized in outdoor co-locations at the end of the study, as described in Appendix 1, following the methodology described in Chatzidiakou et al. (47). These co-locations also permitted us to derive calibration equations for air pollutant concentrations, as described in Appendix 1.

2.2.2. Personal exposure to BC

Our study measured personal exposure to BC concentration with Aethalometers (MicroAeth AE51, AethLabs, CA, USA). This device has already been used in several studies (15,26,28,32,48). The device was mounted on a belt carried by the participants with the tube's inlet at the neck height to capture the BC concentration within the participants' breathing zone. The Optimized Noise Reduction Averaging (ONA) algorithm (49) was applied to 10 second measurements to correct for the erroneous high and low values of BC, taking into account filter changes. The processing steps and algorithm details have already been described in our previous publication (46).

2.2.3. Accelerometer data for physical activity

A tri-axial accelerometer, the ActiGraph wGT3X+ (50), was carried at the waist. It allowed us to monitor the participants' physical activity (51) at a 1 second resolution throughout the study. Instead of the normal filter in Actilife 6.13.3, we employed a low-frequency extension option to make the data

processing more adapted to slow-moving individuals (52). Non-wear time of the device was identified with values of the 3-axes count equal to 0 for at least 1 hour with a spike tolerance of 2 minutes of non-zero epochs, a default option in Actilife (53). The Vector Magnitude (VM) signal, as an indicator of physical activity (expressed as counts per 10 seconds), was calculated as follows:

$$VM = \sqrt{Axis1^2 + Axis2^2 + Axis3^2}$$

2.2.4. Calculation of minute ventilation and inhaled doses of pollutants

First, raw accelerometer data were used to estimate the METs (metabolic equivalent of task) at a 10 second resolution by applying the refined 2-regression model proposed by Crouter (54) in Actilife. The METs were then used to estimate the minute ventilation with the technique suggested by Johnson (55). This technique computes the ventilation rate as the product of METs with the energy conversion factor derived stochastically as a function of an individual's gender and age (Table A2 in Appendix 2).

Inhaled doses were calculated at a 10-second resolution as the cross-product of the corresponding breathing zone concentration of air pollutants ($\mu\text{g}/\text{m}^3$) and minute ventilation (56). For $\text{PM}_{2.5}$, the inhaled doses were calculated at the minute level. Our previous article described in more detail this technique for estimating inhaled doses (46).

2.2.5. Time-activity profiles

The TripBuilder Web mapping application (57) was used to process the GPS data collected at a 5-second resolution with BT-Q1000XT GPS receivers throughout the study. This application assisted us in identifying places visited by individuals, their trips, and the transport modes used in each trip. The detail of the algorithms is discussed in our previous publications (46,58,59). The start and end times of each trip stage as well as of each stay at visited places obtained from TripBuilder were cross-validated with participants during a mobility survey over the phone, enabling us to add or correct information on those trip segments or visited places that were missed by the GPS receiver. A SAS program generated a detailed timetable over the study period incorporating places visited and trips subdivided into trip stages (58), which was used in calculating the proportion of time spent in different contexts as described in section 2.2.7 below.

2.2.6. Ambulatory blood pressure

Arteriograph 24 ambulatory blood pressure monitor (TensioMed, Budapest, Hungary), a non-invasive technique, was used to monitor participants' BP. The device was set to measure BP at 30-minute

intervals during the wear time (from wake up to bedtime). This device can passively monitor the ambulatory BP with a single upper arm cuff (60). Detail on its working mechanism and validity is provided elsewhere (61).

2.2.7. *Creation of the database*

Time-varying variables such as air pollution exposure, physical activity, temperature, and relative humidity were averaged in 5-minute, 15-minute, 30-minute, and one-hour time windows prior to each ambulatory BP measurement. For example, if a participant's BP was measured at 10:00 am, then the 5-minute exposure window for that particular BP measurement would be averaging the continuously measured air pollution concentrations from 9:55 am to 10:00 am, and so on for other exposure windows. Inhaled doses were estimated as a cross-product of the mean inhaled dose ($\mu\text{g}/\text{minute}$) and the length of time (in minutes) of the corresponding exposure window. The proportion of time spent in the home, out-of-home, and in motorized and non-motorized transport (walking, biking, skateboarding, etc.) was calculated for the 5-minute to 1-hour period preceding each BP measurement, using the timestamped information on visited places and trip segments (with information on transport modes) from the detailed time table described in section 2.2.5. The non-wear time of all the devices was deleted during processing after being verified with participants. We excluded 896 BP measurements for reasons including failure of any of the devices monitoring BC, gaseous pollutants (PAM), and accelerometry or non-wear of any device mentioned above or for not participating in the mobility survey. After such exclusion, we had 3319 ambulatory BP measurements from 221 participants for analyses (Figure A2, in Appendix 3).

2.2.8. *Other covariates*

Additional potential confounding variables added to the database included age, alcohol consumption units per month, body mass index (BMI) based on measured height and weight, and gender. Moreover, annual household income was standardized by the number of units in the household, with members younger than 14 years old contributing 0.5 units. After standardization, we categorized income into three groups using the tertiles: low, middle, and high. In order to retain all the observations in the primary analyses, individuals with no information on income were coded as missing ($N = 4$). Education in our study was coded into three categories, lower than, equal to, or higher than intermediate level (Baccalauréat). Participants' employment status was classified into five categories; retired, permanent job, contract job, unemployment, and other residual categories. Place of residence was grouped into urban (main Paris city), close suburbs, and far suburbs. To control for the neighborhood socioeconomic

effect on BP, we adjusted for the per-person winsorized living standards (source: Insee, 2019) of both the residential neighborhood and the neighborhood where participants were when each BP measurement was taken, as continuous variables.

2.3. Statistical analysis

In the presence of repeated measurements per participant, Spearman's correlation was estimated for each participant separately, describing the within-person associations between air pollutants averaged over 5 minutes prior to BP measurements. In order to accurately quantify the variability of correlations across participants, the median along with the 2.5th percentile and 97.5th percentile of these within-person correlation coefficients were calculated.

2.3.1. Fixed-effect linear models

We employed fixed-effect linear models (estimating effects within individuals) to assess the relationships between air pollution exposure (concentrations and inhaled doses) and ambulatory BP, by controlling for one dummy variable related to each participant. This approach eliminates the confounding by unmeasured time-invariant person-level variables. All the models employed were multi-pollutant models, where exposures to all targeted air pollutants averaged over the same time window were added into the same model. All models controlled for time-varying confounders, including physical activity, time-activity classification, temperature, relative humidity, the living standard of the area where BP was measured, weekday vs. weekend, and hourly time trend. Natural splines were used for some covariates: short-term hourly time trend (within the day) was modeled with four degrees of freedom, while physical activity, temperature, and relative humidity were specified with three degrees of freedom based on explorations using 1 to 10 degrees of freedom (guided by the AIC, Akaike information criterion).

2.3.2. Mixture models

Quantile G-computation models available in the R software do not take into account the within-person correlation of observations and result in statistical bias when analyzing nested data as in our study. Therefore, we estimated fixed-effect quantile G-computation models to analyze the within-person association of combined air pollutant concentrations or inhaled doses (NO₂, NO, CO, O₃, and BC) with ambulatory BP, by controlling for one dummy variable related to each participant. Quantile G-computation has been recently developed as an extension of weighted quantile sum (WQS) regression by further relaxing the directional homogeneity, non-linearity, and non-additivity assumptions (62).

This method uses a quantized exposure index with empirical weights for each exposure derived from quantiles of the exposures (63). First, this method transforms the exposures into quantized versions, i.e., cutting them into categorical variables using quartiles of the exposures as cut points. Then, it fits a linear model between the transformed exposures and the outcome (63). G-computation models are capable of estimating both: a) the individual effect of per quartile increase in each exposure component (β regression coefficient), and b) the joint effect of all the exposure components (ψ) on the outcome when all of them are increased by one quartile simultaneously (44). This joint effect is the sum of all β regression coefficients of individual components in the model. In our case, the estimated coefficient ψ from the model is interpretable as the change in ambulatory BP for increasing all air pollution exposure variables by one quartile simultaneously (44). We employed a fixed-effect mixture model for each exposure window with 1000 bootstrapped samples considering the clustered nature of our data and adjusting for potential time-varying confounders using the “qgcomp” R package (64). We then replaced BC with PM_{2.5} to examine the effect of PM_{2.5} as a whole and its combined effect with other pollutants rather than just using its sub-component, BC.

2.3.3. Stratified analyses by microenvironments

To investigate changes in BP in relation to personal exposure in different microenvironments, we stratified the data into two microenvironments: when the participants spent the whole window of exposure inside at home (in-home); and alternatively when participants visited other static places than home or when they were in travel microenvironments (out-of-home) grouped due to limited observations in our relatively small sample. Those exposure windows sharing air pollution exposure from the two types of microenvironments were not considered in any of the strata. For example, even if a participant stayed at home for 55 minutes and went out for 5 minutes within a one-hour exposure window before BP measurement, this observation was entirely deleted from the analytical sample for the stratified analyses, making the total number of observations across strata less than the overall sample. As the calculated inhaled doses depend on physical activity and physical activity highly varies by type of microenvironments, we decided not to conduct this stratified analysis for inhaled doses. Stratified analyses were conducted by applying both fixed-effect linear multi-pollutant models and quantile G-computation models.

2.3.4. Sensitivity analyses

As sensitivity analyses, we developed multi-pollutant multilevel models with a random intercept at the individual level to account for repeated measurements per person and with an AR(1) first-order

continuous autoregressive structure to account for the temporal autocorrelation among residual errors within individuals (65), using the “nlme” R package (66). In addition to the covariates considered in the fixed-effect models, multilevel models were adjusted for age, sex, monthly alcohol consumption, BMI, education attainment, employment status, and the living standard of the residential area of the participant, defined in section 2.2.8. As a separate sensitivity analysis, to compare the results between linear and quantile G-computation models, we modeled air pollutant concentrations as one quartile increase rather than one natural unit increase in fixed-effect linear models.

3. Results

3.1. Characteristics of the participants

Of the 221 participants included, individuals were 56% men, and were on average 50 years old (range: 33, 67 years). Twenty-two percent lived in Paris, and the rest in the suburbs. Seventy-one percent had 3 or more years of university education, while 5% had primary or secondary level education attainment; 67% of participants had a permanent job, 2% were unemployed, 12% were retired, and 5% had unstable jobs. We had 19 participants (8%) who reported being diagnosed as hypertensive by their physician; out of them, 15 had been regularly taking anti-hypertensive medications.

We had 3319 ambulatory BP measurements from 221 participants for analyses, with each individual contributing about 15 BP measurements. Descriptive statistics on BP measurements and personal exposure to all targeted air pollutants averaged over several exposure windows are presented in Appendix Table A3. Table A4 illustrates that there was a great amount of inter-subject variability in the participant-specific correlations between air pollutant exposures, with most participants having weak correlations. NO₂ was negatively correlated with O₃ (within-subject median: -0.55). The median subject-specific correlation coefficients between NO₂ and NO, NO and O₃, O₃ and BC, and O₃ and PM_{2.5} were close to null, ranging from -0.02 to 0.04. CO and O₃ were negatively correlated with each other (median: -0.23). Other than that, all personal exposure measurements showed a weak to moderate positive correlation with each other, with the median within-subject correlation coefficients ranging from 0.1 to 0.30.

3.2. Assessment of assumptions in regression models

The variance inflation factors were below 4 for the covariates in all the models, and residuals were independent and normally distributed for linear models. The temporal autocorrelation coefficient (ϕ)

for the residuals of the multilevel models ranged from 0.09 to 0.13 for the models with SBP and from 0.10 to 0.12 for the models with DBP, justifying the need to consider the time autoregressive error structure within participants. The intra-individual correlation was about 0.50 across all the multilevel models. The individual-level random effect residuals were normally distributed.

3.3. Results from fixed-effect linear models

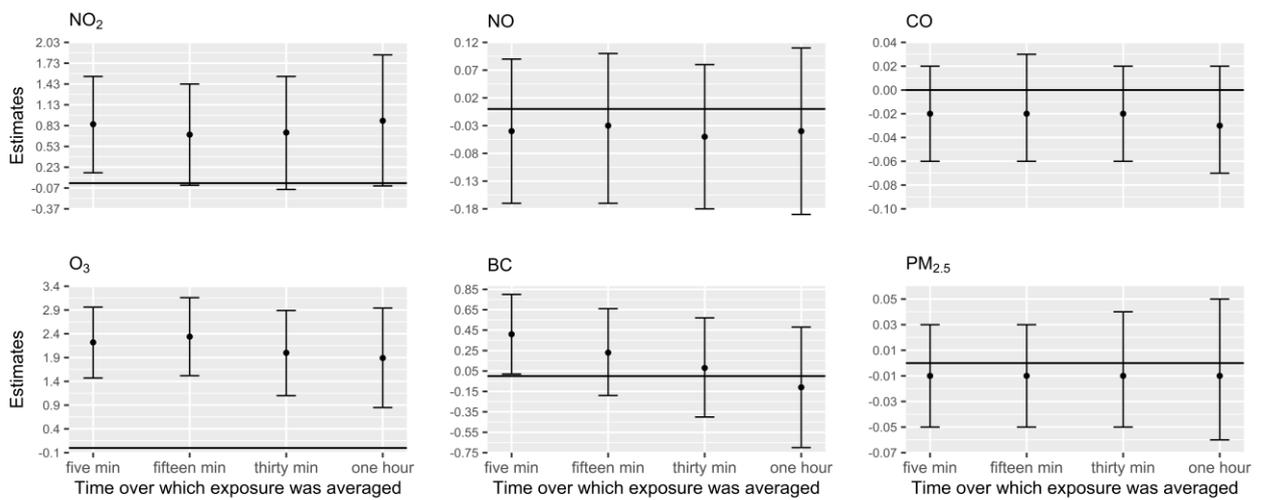
It should be noted that we only report the strongest and most noticeable associations that were documented throughout the main text, while the detail is provided in Figure 1. In multi-pollutant fixed-effect models, Figure 1, it was found that exposure to O₃ had the strongest positive association with both SBP ($\beta = 2.34$ mmHg and 95% CI: 1.53, 3.16, per 10 ppb) and DBP ($\beta = 0.71$ mmHg and 95% CI: 0.01, 1.41, per 10 ppb) over 15-minute windows. Similarly, each 10 ppb increase in NO₂ in the previous 5 minutes was associated with a 0.85 mmHg (95% CI: 0.16, 1.54) increase in SBP and a 0.61 mmHg (95% CI: 0.01, 1.21) increase in DBP. Acute exposure to BC (over 5 minutes) also increased SBP ($\beta = 0.41$ mmHg per 1 $\mu\text{g}/\text{m}^3$). Conversely, the CO concentration averaged over 5, 15, and 30 minutes was associated in a comparable negative way with DBP ($\beta = -0.05$ mmHg per 100 ppb).

Results from multi-pollutant fixed-effect models evaluating associations between inhaled doses of air pollutants and BP across all exposure windows are detailed in Appendix 5, Table A5. The associations between inhaled doses of O₃ and SBP, NO₂ and DBP, and CO and DBP were consistent with those documented for concentrations (Figure 1). A few other associations documented with concentrations in the multi-pollutant models were not retrieved with inhaled doses.

3.4. Results from mixture models

In the mixture models (Table 1), β coefficients greater than zero represent positive weights (increase in BP due to individual air pollutants), and those less than zero indicate negative weights (decrease in BP), with total positive and negative weights summing to 100%, respectively (44). The ψ estimate from the quantile G-computation is the sum of all β regression coefficients of individual air pollutants in the model, corresponding to the estimated difference in BP outcomes for one quartile increase in the

A. Systolic blood pressure (SBP)



B. Diastolic blood pressure (DBP)

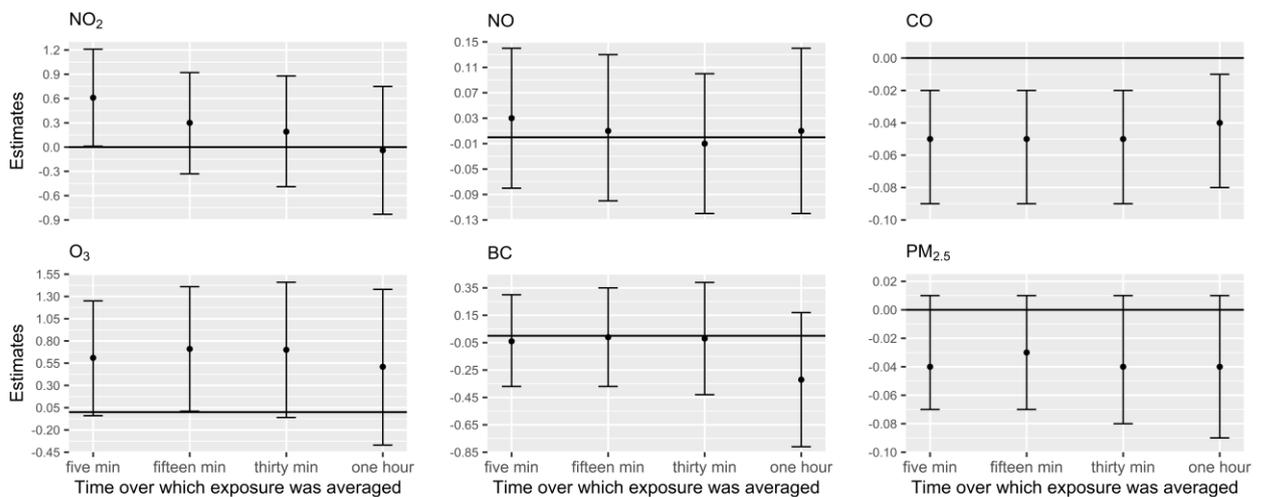


Figure 1. Associations between the personal exposure to air pollution concentrations and systolic blood pressure (SBP) (A) and diastolic blood pressure (DBP) (B). Figures represent the difference in SBP or DBP (with 95% CIs) associated with a 10-ppb increase in the personal exposure to NO₂, NO, and O₃ or 100-ppb increase in CO or 1-µg/m³ increase in BC, or 10-µg/m³ increase in PM_{2.5} averaged over 5 minutes to 1 hour preceding each BP measurement; estimates from multi-pollutant fixed-effect models.

CI: confidence interval

All models were adjusted for physical activity, temperature, relative humidity, proportion of time spent in different contexts (home, motorized vehicle and non-motorized vehicles, other places), week vs. weekend, living standard of areas where the blood pressure measurements were taken, and hourly time trend.

exposure to all targeted air pollutants simultaneously. The effect of a quartile increase in the mixture of air pollutant concentrations on SBP decreased with the increase in the exposure time window, where only the previous 5-minute [$\beta = 1.92$ mmHg (95% CI: 0.63, 3.20)] and 15-minute [$\beta = 1.64$ mmHg (95% CI: 0.38, 2.90)] windows were associated with the outcome. Similar to the results from the fixed-effect linear models, O₃ and BC were contributing strongly and positively to the joint effect, whereas CO had a consistently negative effect on SBP across all exposure windows (this also applied to DBP,

even if no overall mixture effect was detected for DBP). The results were robust to replacing BC with PM_{2.5} (Appendix 6; Table A6).

A quartile increase in the inhalation of the air pollution mixture in the previous 5-minute to 1-hour windows was associated with SBP elevations decreasing from 1.99 mmHg (95% CI: 0.89, 3.09) to 1.47 mmHg (95% CI: 0.31, 2.62) (Table 2) with increasing size of the time window considered. Similar to concentrations mixtures, O₃ and BC were positively driving the associations. Unlike concentration mixtures, thirty-minute and one-hour air pollution inhalation mixtures were associated with SBP. It is because a one-quartile increase in O₃ and BC inhalations in those exposure windows had greater effects on SBP than one quartile increase in their concentrations (comparing β coefficients across Table 1 and 2). The mixtures of concentrations and inhaled doses were found to affect only SBP, while DBP remained largely unaffected (Tables 1 and 2).

3.5. Results from stratified analyses

Our results from stratified analyses showed that out-of-home BC and O₃ concentrations had stronger associations with BP outcomes than home exposures (Appendix 7, Tables A8-A9). In contrast, only the in-home concentration of CO had a negative association with DBP. There was no detected association between the concentration of other air pollutants (NO₂, NO, and PM_{2.5}) and the BP outcomes across all the microenvironments. Results from quantile G-computation models suggest that only out-of-home air pollutant mixtures were associated with SBP (Tables A10-A11).

Table 1. Associations (95% CI) between a one quartile increase in exposure to a mixture of five air pollutants concentrations averaged over 5 minutes to 1 hour prior to each blood pressure (BP) measurement and ambulatory BP, estimated from fixed-effect quantile G-computation models*

Air pollutants	Systolic blood pressure		Diastolic blood pressure	
	Coefficient β (weightage %) ⁺	Effect of mixture ψ (95% CI)	Coefficient β (weightage) ⁺	Effect of mixture ψ (95% CI)
Five minutes				
NO ₂	0.11 (5%)		0.28 (24%)	
NO	0.33 (16%)		-0.04 (6%)	
CO	-0.13 (100%)	1.92 (0.63, 3.20)	-0.66 (94%)	0.43 (-0.66, 1.52)
O ₃	0.71 (35%)		0.32 (29%)	
BC	0.89 (44%)		0.53 (47%)	
Fifteen minutes				
NO ₂	0.07 (4%)		0.07 (8%)	
NO	0.18 (11%)		-0.07 (10%)	
CO	-0.02 (100%)	1.64 (0.38, 2.90)	-0.67 (90%)	0.11 (-0.99, 1.22)
O ₃	0.71 (43%)		0.24 (28%)	
BC	0.70 (32%)		0.55 (64%)	
Thirty minutes				
NO ₂	0.21 (14%)	1.21 (-0.11, 2.53)	0.03 (4%)	-0.17 (-1.30, 0.96)

NO	0.08 (6%)		-0.25 (25%)	
CO	-0.27 (100%)		-0.74 (75%)	
O ₃	0.63 (43%)		0.31 (37%)	
BC	0.55 (37%)		0.48 (59%)	
One hour				
NO ₂	0.40 (31%)		0.01 (8%)	
NO	0.08 (6%)		0.00 (0%)	
CO	-0.45 (100%)	0.83 (-0.44, 2.09)	-0.63 (100%)	-0.49 (-1.56, 0.58)
O ₃	0.54 (42%)		0.07 (47%)	
BC	0.26 (20%)		0.06 (45%)	

MobiliSense Study, 221 participants, 3319 BP measurements

CI: confidence interval

* Exposure to all air pollutant concentrations averaged over the same corresponding time window was included in the same model.

+ β coefficients greater than zero represent positive weights, and those less than zero indicate negative weights, with total positive and negative weights summing to 100%, respectively.

All models were adjusted for physical activity, temperature, relative humidity, proportion of time spent in different contexts (home, motorized vehicle and non-motorized vehicles, other places), week vs. weekend, living standard of areas where the BP measurements were taken, and hourly time trend.

3.6. Results from sensitivity analysis

We had almost similar conclusions from multilevel models (Appendix 8, Tables A12-A13) as we had from fixed-effect linear models. The only difference is that the magnitude of the point estimates was lower in fixed-effect models. When modeling air pollutant concentrations as one quartile increase in fixed-effect linear models (Appendix 9, Table A14), we obtained the same β coefficients (individual effect of air pollutants on BP) as from quantile G-computation models (Table 1).

4. Discussion

Hypertension is a major contributor to global mortality and morbidity. It has been suggested that air pollution effects in elevating BP may be an underlying mechanism of the consistently reported associations between air pollution and cardiovascular health outcomes (67–69). Taking advantage of recent progresses in sensor technologies and ambulatory BP measurement, this study monitored the BP levels of 221 participants as they went through their daily lives.

4.1. Main findings

Analyses were performed with multi-pollutant fixed-effect linear models as well as quantile G-computation techniques considering both concentrations and inhaled doses over various short-term time windows. The linear associations between O₃ and SBP, and CO and DBP were consistently documented for concentrations and inhaled doses.

Confirming the results from the fixed-effect linear models, quantile G-computation models also showed that air pollution mixtures in terms of concentrations and inhaled doses elevated BP. However, the associations were observed only for SBP, with shorter exposure windows having a stronger effect. The mixture was not found to be associated with DBP, while in the fixed-effect linear multi-pollutant models, some associations were documented for DBP (with NO₂ and O₃, although weaker than for SBP). This may be due, to some extent, to the strong negative effect of CO on DBP, which canceled the association with the mixture. Findings from the fixed-effect linear as well as G-computation models confirm that O₃ and BC were the most significant effect contributor for SBP, while CO may lower SBP. We estimated the effect of inhaled doses on BP because using breathing zone concentrations relies on the assumption of a uniform breathing rate, neglecting the fact that the amount of air pollutants inhaled depends on the ventilation rate (70). Also, in our previous publication (46), we have demonstrated that air pollution inhalation is not directly proportional to the breathing zone concentrations as it is also dependent on the concurrent ventilation rates. This reasoning might explain the inconsistency in our study regarding the associations of concentration and inhalation mixtures with SBP in 30-minute and 1-hour exposure windows.

The higher magnitude of point estimates obtained from multilevel models compared to those from fixed-effect models, even though they led to similar conclusions, could be understood with the logic that multilevel models account for both within and between participant effects, whereas the fixed-effect model only estimates within-person effects.

Previous research has suggested several physiological mechanisms for inhaled air pollution short-term and long-term effects on BP (71–74). Although it reported weaker associations in magnitude than ours, a cross-sectional study concluded that concentrations of ambient O₃ in the 3-5 lag hours increased BP (17). Several other quasi-experimental (18,28) and observational studies (19,21,26) confirmed the association considering 24-hour averaged O₃ concentration. Some potential mechanisms linking O₃ and increased BP are elevated levels of oxidative stress, serotonin-induced vasoconstriction, and decreased acetylcholine-induced vasodilation (75). Past studies have reported mixed findings regarding the short-term effect of NO_x (NO + NO₂) on BP (17–19,23–25).

Table 2. Associations (95% CI) between a one quartile increase in inhaled doses mixture of five air pollutants cumulated over 5 minutes to 1 hour prior to each blood pressure (BP) measurement and ambulatory BP, estimated from fixed-effect quantile G-computation models*

Air pollutants	Systolic blood pressure		Diastolic blood pressure	
	Coefficient β (weightage %) ⁺	Effect of mixture ψ (95% CI)	Coefficient β (weightage %) ⁺	Effect of mixture ψ (95% CI)
Five minutes				
NO ₂	0.11 (5%)		0.32 (21%)	
NO	0.17 (7%)		-0.22 (22%)	
CO	-0.44 (100%)	1.99 (0.89, 3.09)	-0.77 (78%)	0.51 (-0.40, 1.41)
O ₃	1.37 (48%)		0.77 (51%)	
BC	0.98 (40%)		0.41 (28%)	
Fifteen minutes				
NO ₂	0.01 (1%)		0.04 (5%)	
NO	0.33 (19%)		-0.18 (17%)	
CO	-0.30 (100%)	1.43 (0.31, 2.54)	-0.88 (83%)	-0.22 (-1.14, 0.71)
O ₃	0.89 (51%)		0.32 (38%)	
BC	0.50 (29%)		0.48 (57%)	
Thirty minutes				
NO ₂	-0.12 (31%)		0.01 (1%)	
NO	0.25 (13%)		-0.16 (14%)	
CO	-0.28 (69%)	1.57 (0.42, 2.71)	-0.97 (86%)	-0.24 (-1.24, 0.77)
O ₃	1.08 (55%)		0.58 (64%)	
BC	0.63 (32%)		0.31 (34%)	
One hour				
NO ₂	0.19 (11%)		-0.01 (2%)	
NO	-0.04 (24%)		0.03 (15%)	
CO	-0.13 (76%)	1.47 (0.31, 2.62)	-0.81 (98%)	-0.59 (-1.55, 0.37)
O ₃	1.03 (63%)		0.08 (34%)	
BC	0.43 (26%)		0.12 (51%)	

MobiliSense Study, 221 participants, 3319 BP measurements

CI: confidence interval

* Inhalation of all air pollutants cumulated over the same corresponding time window was included in the same model.

⁺ β coefficients greater than zero represent positive weights, and those less than zero indicate negative weights, with total positive and negative weights summing to 100%, respectively.

All models were adjusted for physical activity, temperature, relative humidity, proportion of time spent in different contexts (home, motorized vehicle and non-motorized vehicles, other places), week vs. weekend, living standard areas where the BP measurements were taken, and hourly time trend.

Previous studies have documented acute elevations in BP associated with higher daily PM_{2.5} levels (34,35), while other studies reported null associations (32,33). One study assessing exposures to 5 cook stove conditions documented that short-term exposure (30 minutes) to PM_{2.5} had a decreasing effect on SBP; however, at 24 hours after exposure, SBP was elevated by 2 to 3 mmHg across the exposure groups compared to the control group (76). This study found no association with DBP for any time point and condition. Exposure sources in this study were very different from emission sources in our study. It is understood that air pollutants from urban sources such as motor engines may produce distinct health effects than the air pollutants from incomplete biomass combustion (77).

Past studies demonstrated a stronger association between PM_{2.5} concentration and BP than with gaseous pollutants, while our study showed that acute effects on BP were greater for gaseous pollutants

and BC. Therefore, suggestive evidence from our study indicates that the source of PM and its varying chemical composition might affect the toxicity of the mixture and the resulting health effects. Evidence supporting the longer-term effects of PM_{2.5} on BP is more convincing. Thus, longer exposure windows (over an entire day or even more) might be required to find a relationship between PM_{2.5} and BP. However, it should also be noted that some studies reported that breathing zone BC concentration averaged over short periods (5 minutes to 1 hour) did not affect SBP and DBP (15,20,26,29).

Our study showed that an increase in CO concentrations decreased DBP, which is concordant with a previous study investigating the adverse effect of ambient CO concentration on resting BP (17). Another study also reported that ambient CO concentration at a 0-day to 14-day lag reduced DBP but did not affect SBP (78). CO is produced from the incomplete combustion of carbon. Experimental studies have suggested that a decrease in BP by concentrated CO may be due to vasorelaxation (reduction in tension of the blood vessel walls) in the cerebrovascular circulation (79). According to an animal study, CO exposure leads to arterial hypotension and reduced systemic vascular resistance (80). Furthermore, a human study also observed that acute CO exposure was responsible for reduced peripheral resistance (81).

The major reason that may explain the inconsistencies between our findings and previous studies is the time frame, 5 minutes to 1 hour before measurement, which is much more acute compared to previous short-term studies considering hourly (15–17,28) and day lag models (30,34,35,82). Another potential explanation is that most of them used ambient air pollution levels measured at the nearest station (24,33,34,83) or modeled air pollution levels (22,25,84) as a proxy for breathing zone concentrations. Several studies have highlighted that personal exposure to air pollutants may induce different responses in humans than exposure to background ambient pollutants due to variations in sources and chemical compositions (17,85,86). In addition, unlike past studies, we have taken into account five other air pollutants while estimating the independent effect of each air pollutant on BP. Moreover, almost all past studies used resting BP, whereas our study totally relied on ambulatory measurements.

The level of air pollution exposure varies substantially across microenvironments due to the variation in the distribution of air pollution sources (e.g., lower exposure to vehicle emissions while at home or in green spaces). This variation in sources might explain the effect modification by microenvironments in our stratified analyses. For instance, BC concentration had a stronger effect on SBP in out-of-home (transport/places other than home) contexts than in in-home microenvironments. One potential reason

is that exposure to transport-related emissions has a stronger effect on BP than exposure from home-based sources because of the differences in chemical composition and toxicological profile (71,87).

4.2. Strengths and limitations

The major strength of our study is the use of personal sensors for monitoring the breathing zone concentrations of various air pollutants and meteorological conditions, as well as the data on highly resolved time activity-location patterns of individuals generated from the post-processing of GPS receiver and mobility survey data. Our study relied on ambulatory measurements of BP. It is believed that ambulatory BP can capture slight variations in BP and minimize the effect of other factors on measurements by virtue of intensive recording in real-time contexts, making ambulatory BP readings more reliable than clinical measurements (88).

We applied a new approach to assessing the combined effect of air pollution mixture on ambulatory BP across several exposure windows. However, due to the lack of studies that have applied mixture modeling methods in estimating the effect of air pollution on BP, and thus the inability to compare our findings with those obtained from other studies, our results must be interpreted with caution.

Our paper is the first to evaluate the association between inhaled doses of air pollutants and BP. We took advantage of the repeated BP measurements per participant along with the continuous monitoring of personal air pollution exposure and attempted to estimate associations that were as close as possible to causal relationships through proper consideration of time ordering of data and adjustment for time-varying confounders.

A limitation of our study was the lack of statistical power to test the association by isolating only the transport microenvironment. Furthermore, the wide range of confidence intervals of the effect estimates associating concentrations mixtures with SBP, especially in the in-home microenvironment, further adds to the limitation. Future studies may overcome this limitation to investigate whether microenvironments act as an effect modifier or not in the association between air pollution exposure and BP. As another limitation, in our study, the calculation of inhaled doses involved several approximations, such as first estimating the ventilation rate from body acceleration and then using that ventilation rate to calculate the inhaled doses, which likely introduced intrinsic error in estimated doses and resulted in non-differential misclassification. It is well understood that this sort of non-differential misclassification in exposure biases the effect estimates toward the null. This may explain why some weak associations of some air pollutants documented with their concentrations were not replicated

while modeling their inhaled doses. Finally, given that the concentrations of air pollutants in our study were much lower compared to highly polluted countries such as in Asia, findings from our research may not be directly generalizable to people exposed to a higher level of air pollution. Still, they could potentially apply to other European countries with lower air pollution levels.

4.3. Conclusion

This continuous monitoring study found that very short-term simultaneous exposure (in terms of concentrations or inhaled doses) to air pollutants (NO₂, NO, CO, O₃, and BC) was positively associated with SBP. O₃ and BC drove the main effect increasing SBP. Interventions targeting a reduction of air pollution exposure in daily life contexts could potentially reduce the future burden of hypertension. Future research relying on multiple days of BP measurements, along with personal monitoring of air pollutants and potential confounders, will be useful to better understand the association between air pollutants (individually or as a mixture) and BP outcomes. For example, it will allow researchers to examine whether all individuals are sensitive to air pollutants or whether there is between-individual variability in this blood pressure sensitivity and if so why. A better understanding of the environmental triggers of blood pressure increases in the different microenvironments may provide the scientific underpinning to reduce acute blood pressure responses resulting in the long-term incidence of hypertension and cardiovascular risk.

CRedit authorship contribution statement

Sanjeev Bista: Data processing, conception of methodology, statistical analysis, interpreted the results and wrote original draft. **Lia Chatzidiakou:** Conception of methodology, data processing, writing – review & editing. **Roderic L Jones:** Data processing, conception of methodology, writing – review & editing. **Tarik Benmarhnia:** Statistical analysis, conception of methodology, writing – review & editing. **Nicolas Postel-Vinay:** writing – review & editing. **Basile Chaix:** Project conception, conception of methodology, development of overall research plan, study oversight, funding acquisition, writing – review & editing and supervision.

Corresponding author: Sanjeev Bista

Declaration of competing interest

The authors have no relevant financial or non-financial interests to disclose.

Acknowledgment

This work was supported by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement 647000, 2014 ERC Consolidator grant, MobiliSense project). The funding institution had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

References

1. Stanaway JD, Afshin A, Gakidou E, Lim SS, Abate D, Abate KH, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Stu. *Lancet* [Internet]. 2018 Nov;392(10159):1923–94. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673618322256>
2. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global Disparities of Hypertension Prevalence and Control. *Circulation* [Internet]. 2016 Aug 9;134(6):441–50. Available from: <https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.115.018912>
3. Lewington S. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* [Internet]. 2002 Dec;360(9349):1903–13. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673602119118>
4. Choi Y-J, Kim S-H, Kang S-H, Yoon C-H, Lee H-Y, Youn T-J, et al. Reconsidering the cut-off diastolic blood pressure for predicting cardiovascular events: a nationwide population-based study from Korea. *Eur Heart J* [Internet]. 2019 Mar 1;40(9):724–31. Available from: <https://academic.oup.com/eurheartj/article/40/9/724/5232599>
5. Brook RD, Weder AB, Rajagopalan S. “Environmental Hypertensionology” The Effects of Environmental Factors on Blood Pressure in Clinical Practice and Research. *J Clin Hypertens* [Internet]. 2011 Nov;13(11):836–42. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1751-7176.2011.00543.x>
6. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* [Internet]. 2018 Sep 1;39(33):3021–104. Available from: <https://academic.oup.com/eurheartj/article/39/33/3021/5079119>
7. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Pr. *Hypertension* [Internet]. 2018 Jun;71(6). Available from: <https://www.ahajournals.org/doi/10.1161/HYP.0000000000000065>
8. Forman JP. Diet and Lifestyle Risk Factors Associated With Incident Hypertension in Women. *JAMA* [Internet]. 2009 Jul 22;302(4):401. Available from: <http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2009.1060>
9. Bellavia A, Urch B, Speck M, Brook RD, Scott JA, Albetti B, et al. DNA Hypomethylation, Ambient Particulate Matter, and Increased Blood Pressure: Findings From Controlled Human Exposure Experiments. *J Am Heart Assoc* [Internet]. 2013 May 20;2(3). Available from: <https://www.ahajournals.org/doi/10.1161/JAHA.113.000212>
10. Urch B, Silverman F, Corey P, Brook JR, Lukic KZ, Rajagopalan S, et al. Acute Blood Pressure Responses in Healthy Adults During Controlled Air Pollution Exposures. *Environ Health Perspect* [Internet]. 2005 Aug;113(8):1052–5. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.7785>
11. Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F. Inhalation of Fine Particulate Air Pollution and Ozone Causes Acute Arterial Vasoconstriction in Healthy Adults. *Circulation* [Internet]. 2002 Apr 2;105(13):1534–6. Available from: <https://www.ahajournals.org/doi/10.1161/01.CIR.0000013838.94747.64>
12. Mills NL, Donaldson K, Hadoke PW, Boon NA, MacNee W, Cassee FR, et al. Adverse cardiovascular effects of air pollution. *Nat Clin Pract Cardiovasc Med* [Internet]. 2009 Jan 25;6(1):36–44. Available from: <http://www.nature.com/articles/ncpcardio1399>
13. Mills NL, Törnqvist H, Robinson SD, Gonzalez MC, Söderberg S, Sandström T, et al. Air Pollution and Atherothrombosis. *Inhal Toxicol* [Internet]. 2007 Jan 20;19(sup1):81–9. Available from: <http://www.tandfonline.com/doi/full/10.1080/08958370701495170>
14. Rabito FA, Yang Q, Zhang H, Werthmann D, Shankar A, Chillrud S. The association between short-term residential black carbon concentration on blood pressure in a general population sample. *Indoor Air* [Internet]. 2020 Jul 18;30(4):767–75. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/ina.12651>
15. Delfino RJ, Tjoa T, Gillen DL, Staimer N, Polidori A, Arhami M, et al. Traffic-related Air Pollution and Blood Pressure in Elderly Subjects With Coronary Artery Disease. *Epidemiology* [Internet]. 2010 May;21(3):396–404. Available from: <https://journals.lww.com/00001648-201005000-00019>
16. Floyd CN, Shahed F, Ukah F, McNeill K, O’Gallagher K, Mills CE, et al. Acute Blood Pressure-Lowering Effects of Nitrogen Dioxide Exposure From Domestic Gas Cooking Via Elevation of Plasma Nitrite Concentration in Healthy Individuals. *Circ Res* [Internet]. 2020 Aug 28;127(6):847–8. Available from: <https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.120.316748>

17. Choi Y-J, Kim S-H, Kang S-H, Kim S-Y, Kim O-J, Yoon C-H, et al. Short-term effects of air pollution on blood pressure. *Sci Rep* [Internet]. 2019 Dec 30;9(1):20298. Available from: <http://www.nature.com/articles/s41598-019-56413-y>
18. Day DB, Xiang J, Mo J, Li F, Chung M, Gong J, et al. Association of Ozone Exposure With Cardiorespiratory Pathophysiologic Mechanisms in Healthy Adults. *JAMA Intern Med* [Internet]. 2017 Sep 1;177(9):1344. Available from: <http://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2017.2842>
19. Choi J-H, Xu Q-S, Park S-Y, Kim J-H, Hwang S-S, Lee K-H, et al. Seasonal variation of effect of air pollution on blood pressure. *J Epidemiol Community Heal* [Internet]. 2007 Apr 1;61(4):314–8. Available from: <https://jech.bmj.com/lookup/doi/10.1136/jech.2006.049205>
20. Pun VC, Ho K. Blood pressure and pulmonary health effects of ozone and black carbon exposure in young adult runners. *Sci Total Environ* [Internet]. 2019 Mar;657:1–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0048969718348204>
21. Chuang K-J, Yan Y-H, Cheng T-J. Effect of Air Pollution on Blood Pressure, Blood Lipids, and Blood Sugar: A Population-Based Approach. *J Occup Environ Med* [Internet]. 2010 Mar;52(3):258–62. Available from: <https://journals.lww.com/00043764-201003000-00004>
22. Schwartz J, Alexeeff SE, Mordukhovich I, Gryparis A, Vokonas P, Suh H, et al. Association between long-term exposure to traffic particles and blood pressure in the Veterans Administration Normative Aging Study. *Occup Environ Med* [Internet]. 2012 Jun;69(6):422–7. Available from: <https://oem.bmj.com/lookup/doi/10.1136/oemed-2011-100268>
23. de Paula Santos U, Braga ALF, Giorgi DMA, Pereira LAA, Grupi CJ, Lin CA, et al. Effects of air pollution on blood pressure and heart rate variability: a panel study of vehicular traffic controllers in the city of São Paulo, Brazil. *Eur Heart J* [Internet]. 2005 Jan 1;26(2):193–200. Available from: <http://academic.oup.com/eurheartj/article/26/2/193/491482/Effects-of-air-pollution-on-blood-pressure-and>
24. Zeng X-W, Qian Z (Min), Vaughn MG, Nelson EJ, Dharmage SC, Bowatte G, et al. Positive association between short-term ambient air pollution exposure and children blood pressure in China—Result from the Seven Northeast Cities (SNEC) study. *Environ Pollut* [Internet]. 2017 May;224:698–705. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0269749116318747>
25. Bilenko N, Rossem L van, Brunekreef B, Beelen R, Eeftens M, Hoek G, et al. Traffic-related air pollution and noise and children’s blood pressure: Results from the PIAMA birth cohort study. *Eur J Prev Cardiol* [Internet]. 2015 Jan 18;22(1):4–12. Available from: <http://journals.sagepub.com/doi/10.1177/2047487313505821>
26. Zhao X, Sun Z, Ruan Y, Yan J, Mukherjee B, Yang F, et al. Personal Black Carbon Exposure Influences Ambulatory Blood Pressure. *Hypertension* [Internet]. 2014 Apr;63(4):871–7. Available from: <https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.113.02588>
27. Liu C, Fuertes E, Tiesler CMT, Birk M, Babisch W, Bauer C-P, et al. The associations between traffic-related air pollution and noise with blood pressure in children: Results from the GINIplus and LISApplus studies. *Int J Hyg Environ Health* [Internet]. 2014 Apr;217(4–5):499–505. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1438463913001375>
28. Weichenthal S, Hatzopoulou M, Goldberg MS. Exposure to traffic-related air pollution during physical activity and acute changes in blood pressure, autonomic and micro-vascular function in women: a cross-over study. *Part Fibre Toxicol* [Internet]. 2014 Dec 9;11(1):70. Available from: <http://particleandfibretoxicology.biomedcentral.com/articles/10.1186/s12989-014-0070-4>
29. Norris C, Goldberg MS, Marshall JD, Valois M-F, Pradeep T, Narayanswamy M, et al. A panel study of the acute effects of personal exposure to household air pollution on ambulatory blood pressure in rural Indian women. *Environ Res* [Internet]. 2016 May;147:331–42. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0013935116300640>
30. Jansen KL, Larson T V., Koenig JQ, Mar TF, Fields C, Stewart J, et al. Associations between Health Effects and Particulate Matter and Black Carbon in Subjects with Respiratory Disease. *Environ Health Perspect* [Internet]. 2005 Dec;113(12):1741–6. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.8153>
31. Baumgartner J, Zhang Y, Schauer JJ, Huang W, Wang Y, Ezzati M. Highway proximity and black carbon from cookstoves as a risk factor for higher blood pressure in rural China. *Proc Natl Acad Sci* [Internet]. 2014 Sep 9;111(36):13229–34. Available from: <https://pnas.org/doi/full/10.1073/pnas.1317176111>
32. Mirowsky JE, Peltier RE, Lippmann M, Thurston G, Chen L-C, Neas L, et al. Repeated measures of inflammation, blood pressure, and heart rate variability associated with traffic exposures in healthy adults. *Environ Heal* [Internet]. 2015 Dec 15;14(1):66. Available from: <http://ehjournal.biomedcentral.com/articles/10.1186/s12940-015-0049-0>
33. Ibald-Mulli A, Timonen KL, Peters A, Heinrich J, Wölke G, Lanki T, et al. Effects of particulate air pollution

- on blood pressure and heart rate in subjects with cardiovascular disease: a multicenter approach. *Environ Health Perspect* [Internet]. 2004 Mar;112(3):369–77. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.6523>
34. Wu S, Deng F, Huang J, Wang H, Shima M, Wang X, et al. Blood Pressure Changes and Chemical Constituents of Particulate Air Pollution: Results from the Healthy Volunteer Natural Relocation (HVNR) Study. *Environ Health Perspect* [Internet]. 2013 Jan;121(1):66–72. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1104812>
 35. Baumgartner J, Schauer JJ, Ezzati M, Lu L, Cheng C, Patz JA, et al. Indoor Air Pollution and Blood Pressure in Adult Women Living in Rural China. *Environ Health Perspect* [Internet]. 2011 Oct;119(10):1390–5. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1003371>
 36. Mancia G, Parati G. Ambulatory Blood Pressure Monitoring and Organ Damage. *Hypertension* [Internet]. 2000 Nov;36(5):894–900. Available from: <https://www.ahajournals.org/doi/10.1161/01.HYP.36.5.894>
 37. Timothy DJ, Kannan S, Schulz AJ, Keeler GJ, Mentz G, House J, et al. Acute Effects of Ambient Particulate Matter on Blood Pressure: Differential Effects across Urban Communities. *Hypertension* [Internet]. 2009 May 1 [cited 2021 Nov 10];53(5):853. Available from: [/pmc/articles/PMC3593813/](https://pubmed.ncbi.nlm.nih.gov/12802026/)
 38. Clement DL, De Buyzere ML, De Bacquer DA, de Leeuw PW, Duprez DA, Fagard RH, et al. Prognostic Value of Ambulatory Blood-Pressure Recordings in Patients with Treated Hypertension. *N Engl J Med* [Internet]. 2003 Jun 12 [cited 2021 Nov 10];348(24):2407–15. Available from: <https://pubmed.ncbi.nlm.nih.gov/12802026/>
 39. Tofler GH, Muller JE. Triggering of acute cardiovascular disease and potential preventive strategies. *Circulation* [Internet]. 2006 Oct [cited 2021 Nov 10];114(17):1863–72. Available from: <https://pubmed.ncbi.nlm.nih.gov/17060396/>
 40. Brunekreef B, Holgate ST. Air pollution and health. *Lancet* [Internet]. 2002 Oct;360(9341):1233–42. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673602112748>
 41. Goldberg MS. On the interpretation of epidemiological studies of ambient air pollution. *J Expo Sci Environ Epidemiol* [Internet]. 2007 Dec 14;17(S2):S66–70. Available from: <http://www.nature.com/articles/7500629>
 42. Sun Y, Li X, Benmarhnia T, Chen J-C, Avila C, Sacks DA, et al. Exposure to air pollutant mixture and gestational diabetes mellitus in Southern California: Results from electronic health record data of a large pregnancy cohort. *Environ Int* [Internet]. 2022 Jan;158:106888. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0160412021005134>
 43. Li R, Hou J, Tu R, Liu X, Zuo T, Dong X, et al. Associations of mixture of air pollutants with estimated 10-year atherosclerotic cardiovascular disease risk modified by socio-economic status: The Henan Rural Cohort Study. *Sci Total Environ* [Internet]. 2021 Nov;793:148542. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0048969721036147>
 44. Keil AP, Buckley JP, O'Brien KM, Ferguson KK, Zhao S, White AJ. A Quantile-Based g-Computation Approach to Addressing the Effects of Exposure Mixtures. *Environ Health Perspect* [Internet]. 2020 Apr;128(4):047004. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/EHP5838>
 45. Chaix B, Bista S, Wang L, Benmarhnia T, Dureau C, Duncan DT. MobiliSense cohort study protocol: do air pollution and noise exposure related to transport behaviour have short-term and longer-term health effects in Paris, France? *BMJ Open* [Internet]. 2022 Mar 31;12(3):e048706. Available from: <https://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2021-048706>
 46. Bista S, Dureau C, Chaix B. Personal exposure to concentrations and inhalation of black carbon according to transport mode use: The MobiliSense sensor-based study. *Environ Int* [Internet]. 2022 Jan;158:106990. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0160412021006152>
 47. Chatzidiakou L, Krause A, Popoola OAM, Di Antonio A, Kellaway M, Han Y, et al. Characterising low-cost sensors in highly portable platforms to quantify personal exposure in diverse environments. *Atmos Meas Tech* [Internet]. 2019 Aug 30 [cited 2020 Aug 4];12(8):4643–57. Available from: <https://amt.copernicus.org/articles/12/4643/2019/>
 48. Louwies T, Nawrot T, Cox B, Dons E, Penders J, Provost E, et al. Blood pressure changes in association with black carbon exposure in a panel of healthy adults are independent of retinal microcirculation. *Environ Int* [Internet]. 2015 Feb;75:81–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0160412014003286>
 49. Hagler GSW, Yelverton TLB, Vedantham R, Hansen ADA, Turner JR. Post-processing Method to Reduce Noise while Preserving High Time Resolution in Aethalometer Real-time Black Carbon Data. *Aerosol Air Qual Res* [Internet]. 2011 Oct [cited 2020 May 3];11(5):539–46. Available from: <http://www.aaqr.org/doi/10.4209/aaqr.2011.05.0055>
 50. ActiGraph Corporation 2013. ActiGraph wGT3X-BT user manual [Internet]. Available from: http://actigraphcorp.com/wp-content/uploads/2015/04/wGT3X-BT_UsersManual_RevD_Q3_2014.pdf

51. Metcalf BS, Curnow JSH, Evans C, Voss LD, Wilkin TJ. Technical reliability of the CSA activity monitor: The EarlyBird Study. *Med Sci Sports Exerc* [Internet]. 2002 [cited 2020 Aug 7];34(9):1533–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/12218751/>
52. WANNER M, MARTIN BW, MEIER F, PROBST-HENSCH N, KRIEMLER S. Effects of Filter Choice in GT3X Accelerometer Assessments of Free-Living Activity. *Med Sci Sport Exerc* [Internet]. 2013 Jan [cited 2020 Aug 5];45(1):170–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/22895373/>
53. TROIANO RP, BERRIGAN D, DODD KW, MÂSSE LC, TILERT T, MCDOWELL M. Physical Activity in the United States Measured by Accelerometer. *Med Sci Sport Exerc* [Internet]. 2008 Jan;40(1):181–8. Available from: <http://journals.lww.com/00005768-200801000-00025>
54. Crouter SE, Kuffel E, Haas JD, Frongillo EA, Bassett DR. Refined two-regression model for the actigraph accelerometer. *Med Sci Sports Exerc* [Internet]. 2010 May [cited 2020 Aug 5];42(5):1029–37. Available from: <http://pubmed.ncbi.nlm.nih.gov/20811855/>
55. Johnson T. A GUIDE TO SELECTED ALGORITHMS, DISTRIBUTIONS, AND DATABASES USED IN EXPOSURE MODELS DEVELOPED BY THE OFFICE OF AIR QUALITY PLANNING AND STANDARDS. 2002.
56. Apparicio P, Gelb J, Carrier M, Mathieu M-È, Kingham S. Exposure to noise and air pollution by mode of transportation during rush hours in Montreal. *J Transp Geogr* [Internet]. 2018 Jun [cited 2020 May 24];70:182–92. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0966692317308451>
57. Wolf J, Oliveira M, Thompson M. Impact of Underreporting on Mileage and Travel Time Estimates: Results from Global Positioning System-Enhanced Household Travel Survey. *Transp Res Rec J Transp Res Board* [Internet]. 2003 Jan 1;1854(1):189–98. Available from: <http://journals.sagepub.com/doi/10.3141/1854-21>
58. Chaix B, Benmarhnia T, Kestens Y, Brondeel R, Perchoux C, Gerber P, et al. Combining sensor tracking with a GPS-based mobility survey to better measure physical activity in trips: public transport generates walking. *Int J Behav Nutr Phys Act* [Internet]. 2019 Dec 7;16(1):84. Available from: <https://ijbnpa.biomedcentral.com/articles/10.1186/s12966-019-0841-2>
59. Chaix B, Kestens Y, Duncan S, Merrien C, Thierry B, Pannier B, et al. Active transportation and public transportation use to achieve physical activity recommendations? A combined GPS, accelerometer, and mobility survey study. *Int J Behav Nutr Phys Act* [Internet]. 2014 Dec 27;11(1):124. Available from: <http://ijbnpa.biomedcentral.com/articles/10.1186/s12966-014-0124-x>
60. Corrigendum to: 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* [Internet]. 2019 Feb 1;40(5):475–475. Available from: <https://academic.oup.com/eurheartj/article/40/5/475/5137110>
61. Horváth IG, Németh Á, Lenkey Z, Alessandri N, Tufano F, Kis P, et al. Invasive validation of a new oscillometric device (Arteriograph) for measuring augmentation index, central blood pressure and aortic pulse wave velocity. *J Hypertens* [Internet]. 2010 Oct;28(10):2068–75. Available from: <https://journals.lww.com/00004872-201010000-00015>
62. Snowden JM, Rose S, Mortimer KM. Implementation of G-Computation on a Simulated Data Set: Demonstration of a Causal Inference Technique. *Am J Epidemiol* [Internet]. 2011 Apr 1;173(7):731–8. Available from: <https://academic.oup.com/aje/article-lookup/doi/10.1093/aje/kwq472>
63. Carrico C, Gennings C, Wheeler DC, Factor-Litvak P. Characterization of Weighted Quantile Sum Regression for Highly Correlated Data in a Risk Analysis Setting. *J Agric Biol Environ Stat* [Internet]. 2015 Mar 24;20(1):100–20. Available from: <http://link.springer.com/10.1007/s13253-014-0180-3>
64. Keil AP, Buckley JP, O'Brien KM, Ferguson KK, Zhao S, White AJ. Quantile G-Computation [R package qgcomp version 2.10.1]. *Environ Health Perspect* [Internet]. 2022 Dec 7 [cited 2022 Dec 8];128(4). Available from: <https://cran.r-project.org/package=qgcomp>
65. Goldstein H, Healy MJR, Rasbash J. Multilevel time series models with applications to repeated measures data. *Stat Med* [Internet]. 1994 Aug 30;13(16):1643–55. Available from: <https://onlinelibrary.wiley.com/doi/10.1002/sim.4780131605>
66. CRAN - Package nlme [Internet]. [cited 2022 Jun 2]. Available from: <https://cran.r-project.org/web/packages/nlme/index.html>
67. Laden F, Schwartz J, Speizer FE, Dockery DW. Reduction in Fine Particulate Air Pollution and Mortality. *Am J Respir Crit Care Med* [Internet]. 2006 Mar 15;173(6):667–72. Available from: <http://www.atsjournals.org/doi/abs/10.1164/rccm.200503-443OC>
68. Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, et al. Long-Term Exposure to Air Pollution and Incidence of Cardiovascular Events in Women. *N Engl J Med* [Internet]. 2007 Feb;356(5):447–58. Available from: <http://www.nejm.org/doi/abs/10.1056/NEJMoa054409>
69. Chen H, Goldberg MS, Burnett RT, Jerrett M, Wheeler AJ, Villeneuve PJ. Long-Term Exposure to Traffic-Related Air Pollution and Cardiovascular Mortality. *Epidemiology* [Internet]. 2013 Jan;24(1):35–43.

- Available from: <https://journals.lww.com/00001648-201301000-00006>
70. Dons E, Laeremans M, Orjuela JP, Avila-Palencia I, Carrasco-Turigas G, Cole-Hunter T, et al. Wearable Sensors for Personal Monitoring and Estimation of Inhaled Traffic-Related Air Pollution: Evaluation of Methods. *Environ Sci Technol* [Internet]. 2017 Feb 7;51(3):1859–67. Available from: <https://pubs.acs.org/doi/10.1021/acs.est.6b05782>
 71. Brook RD, Urch B, Dvonch JT, Bard RL, Speck M, Keeler G, et al. Insights Into the Mechanisms and Mediators of the Effects of Air Pollution Exposure on Blood Pressure and Vascular Function in Healthy Humans. *Hypertension* [Internet]. 2009 Sep 1 [cited 2021 Jul 30];54(3):659–67. Available from: <https://www.ahajournals.org/doi/abs/10.1161/HYPERTENSIONAHA.109.130237>
 72. Brook RD, Weder AB, Rajagopalan S. “Environmental Hypertensionology” The Effects of Environmental Factors on Blood Pressure in Clinical Practice and Research. *J Clin Hypertens* [Internet]. 2011 Nov;13(11):836–42. Available from: <http://doi.wiley.com/10.1111/j.1751-7176.2011.00543.x>
 73. Brook RD, Rajagopalan S, Pope CA, Brook JR, Bhatnagar A, Diez-Roux A V., et al. Particulate Matter Air Pollution and Cardiovascular Disease. *Circulation* [Internet]. 2010 Jun;121(21):2331–78. Available from: <https://www.ahajournals.org/doi/10.1161/CIR.0b013e3181d8bece1>
 74. Brook RD. You are what you breathe: Evidence linking air pollution and blood pressure. *Curr Hypertens Rep* [Internet]. 2005 Nov;7(6):427–34. Available from: <http://link.springer.com/10.1007/s11906-005-0037-9>
 75. Paffett ML, Zychowski KE, Sheppard L, Robertson S, Weaver JM, Lucas SN, et al. Ozone Inhalation Impairs Coronary Artery Dilatation via Intracellular Oxidative Stress: Evidence for Serum-Borne Factors as Drivers of Systemic Toxicity. *Toxicol Sci* [Internet]. 2015 Aug;146(2):244–53. Available from: <https://academic.oup.com/toxsci/article-lookup/doi/10.1093/toxsci/kfv093>
 76. Fedak KM, Good N, Walker ES, Balmes J, Brook RD, Clark ML, et al. Acute Effects on Blood Pressure Following Controlled Exposure to Cookstove Air Pollution in the STOVES Study. *J Am Heart Assoc* [Internet]. 2019 Jul 16;8(14). Available from: <https://www.ahajournals.org/doi/10.1161/JAHA.119.012246>
 77. Strak M, Hoek G, Godri KJ, Gosens I, Mudway IS, van Oerle R, et al. Composition of PM Affects Acute Vascular Inflammatory and Coagulative Markers - The RAPTES Project. Cormier SA, editor. *PLoS One* [Internet]. 2013 Mar 13;8(3):e58944. Available from: <https://dx.plos.org/10.1371/journal.pone.0058944>
 78. Khajavi A, Tamehri Zadeh SS, Azizi F, Brook RD, Abdi H, Zayeri F, et al. Impact of short- and long-term exposure to air pollution on blood pressure: A two-decade population-based study in Tehran. *Int J Hyg Environ Health* [Internet]. 2021 May;234:113719. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1438463921000341>
 79. A. Sutherland B, C. Harrison J, M. Nair S, A. Sammut I. Inhalation Gases or Gaseous Mediators As Neuroprotectants for Cerebral Ischaemia. *Curr Drug Targets* [Internet]. 2013 Jan 1;14(1):56–73. Available from: <http://openurl.ingenta.com/content/xref?genre=article&iissn=1389-4501&volume=14&issue=1&spage=56>
 80. Penney DG. Hemodynamic response to carbon monoxide. *Environ Health Perspect* [Internet]. 1988 Apr;77:121–30. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.8877121>
 81. Heistad DD, Wheeler RC. Effect of carbon monoxide on reflex vasoconstriction in man. *J Appl Physiol* [Internet]. 1972 Jan 1;32(1):7–11. Available from: <https://www.physiology.org/doi/10.1152/jappl.1972.32.1.7>
 82. Hoffmann B, Luttmann-Gibson H, Cohen A, Zanobetti A, de Souza C, Foley C, et al. Opposing Effects of Particle Pollution, Ozone, and Ambient Temperature on Arterial Blood Pressure. *Environ Health Perspect* [Internet]. 2012 Feb;120(2):241–6. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.1103647>
 83. Chuang K-J, Yan Y-H, Cheng T-J. Effect of Air Pollution on Blood Pressure, Blood Lipids, and Blood Sugar: A Population-Based Approach. *J Occup Environ Med* [Internet]. 2010 Mar;52(3):258–62. Available from: <http://journals.lww.com/00043764-201003000-00004>
 84. Curto A, Wellenius GA, Milà C, Sanchez M, Ranzani O, Marshall JD, et al. Ambient Particulate Air Pollution and Blood Pressure in Peri-urban India. *Epidemiology* [Internet]. 2019 Jul;30(4):492–500. Available from: <https://journals.lww.com/00001648-201907000-00005>
 85. Padró-Martínez LT, Patton AP, Trull JB, Zamore W, Brugge D, Durant JL. Mobile monitoring of particle number concentration and other traffic-related air pollutants in a near-highway neighborhood over the course of a year. *Atmos Environ* [Internet]. 2012 Dec;61:253–64. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1352231012006760>
 86. Brook RD, Bard RL, Burnett RT, Shin HH, Vette A, Croghan C, et al. Differences in blood pressure and vascular responses associated with ambient fine particulate matter exposures measured at the personal versus community level. *Occup Environ Med* [Internet]. 2011 Mar 1;68(3):224–30. Available from: <https://oem.bmj.com/lookup/doi/10.1136/oem.2009.053991>
 87. Auchincloss AH, Diez Roux A V., Dvonch JT, Brown PL, Barr RG, Daviglus ML, et al. Associations between Recent Exposure to Ambient Fine Particulate Matter and Blood Pressure in the Multi-Ethnic Study

- of Atherosclerosis (MESA). *Environ Health Perspect* [Internet]. 2008 Apr;116(4):486–91. Available from: <https://ehp.niehs.nih.gov/doi/10.1289/ehp.10899>
88. Hu J, Xue X, Xiao M, Wang W, Gao Y, Kan H, et al. The acute effects of particulate matter air pollution on ambulatory blood pressure: A multicenter analysis at the hourly level. *Environ Int* [Internet]. 2021 Dec;157:106859. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0160412021004840>