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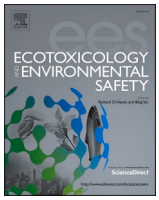

Does personalization in exposure assessment change ambient air pollution exposure-response relationships? A panel study

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ABSTRACT

Accurate exposure assessment is crucial to understand linkages between ambient air pollution and cardiopulmonary disease. Air quality monitors (AQM) are widely used, but do not account for personal behaviors. We compare the exposure-response relationships between ambient air pollution ($PM_{2.5}$ and O_3) and cardiopulmonary biomarkers in a panel study using both stationary AQM and Exposure Model for Individuals (EMI). Participants (n = 28) underwent 3–5 sessions totaling 134 visits. Participants underwent spirometry and blood sampling. $PM_{2.5}$ and O_3 concentrations were calculated for each visit (lag0) and 4 preceding days (lag1–4) using AQM and EMI. A mixed-effects model was applied to examine the associations between exposure and outcomes. AQM and EMI were strongly correlated for $PM_{2.5}$ ($\rho = 0.89$) and moderately correlated for O_3 ($\rho = 0.46$). Exposure-response relationships for $PM_{2.5}$ were similar, with $PM_{2.5}$ associated with increased oxLDL at lag1 (12.2 % (95 %CI: 4.5, 20.2) AQM, 17.9 % (95 %CI: 8.1, 27.8) EMI), increased vWF at lag0 (4.27 % (95 %CI: 0.15, 8.39) AQM, 7.12 % (95 %CI: 2.57, 11.67) EMI) and decreased vWF at lag3 −6.5 % (95 %CI: −11.4, −1.6) AQM, −5.6 % (95 %CI: −10.6, −0.7) EMI) and lag4 (-5.4 % (95 %CI: −10.2, −0.7) AQM, −6.7 % (95 %CI: −12.1, −1.3) EMI). O_3 showed more variability, with positive associations with vWF at lag0 (12.9 % (95 %CI: 6.1, 19.7) AQM, −2.77 % (95 %CI: −8.1, 2.6) EMI) and D-dimer at lag1 27.0 % (95 %CI: 0.9, 53.0) AQM, −6.86 % (95 %CI: −26.3, 12.6) EMI), for AQM only, and negative associations with tPA at lag3 for EMI only (-10.0 % (95 %CI: −21.5, 1.4) AQM, −11.2 % (95 %CI: −19.6, −2.8) EMI). Our findings suggest that exposure-response associations to short-term $PM_{2.5}$ and oxLDL and markers of coagulation are consistent between the AMQ and EMI methods, implying increased risk for cardiovascular disease. For O_3, AQM and EMI were less consistent, highlighting the challenges of estimating and modeling O_3 exposure.

1. Introduction

Ambient air pollution is a major environmental health risk factor that confers a large burden of disease (Cohen, 2017; Malashock, 2022), including increased risk of respiratory disease, cardiovascular disease, diabetes mellitus, low birth weight, and all-cause mortality (Schraufnagel, 2019). To understand and quantify the health effects caused by air pollution, it is critical to accurately estimate air pollution exposure (National Research Council, 2012). The gold standard of air pollution exposure assessment is personal air monitoring, in which high quality, portable monitors measure pollutant concentrations as individuals move through various microenvironments (Larkin and Hystad, 2017). While this approach more realistically accounts for individual variation, personal air monitoring is limited by cost of monitors, scale at which monitors can be deployed, and other logistic and methodological challenges (Larkin and Hystad, 2017). Instead of direct measurement,

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many epidemiologic and panel studies rely on measurements from stationary air quality monitors to serve as proxies for exposure (Yu et al., 2024). There are, however, several criticisms with this approach, first, federal and state air quality monitors are limited in their distribution, thus coverage, particularly away from urban centers, can be limited. Second, data from stationary monitors assumes homogeneity in an airshed and cannot account for time spent in various microenvironments, such as proximity to busy roadways, which may confer greater exposure. Finally, in the US, individuals spend roughly 87 % of their time in an indoor environment (Klepeis, 2001), and thus the utilization of ambient air quality monitors data may result in overestimation of ambient air pollution.

A method that has been used to account for some of these limitations in stationary monitors is the incorporation of more personalized modeling. One such model, called the Exposure Model for Individuals (EMI), couples ambient air monitor data with a microenvironment-based multi-tiered exposure model. Specifically, EMI links data from a nearest ambient air monitor with a mechanistic air exchange rate (AER) model, a mass-balance $PM_{2.5}$ and O_3 building infiltration model, and a GPS-based microenvironment classification (MicroTrac) model to determine outdoor concentrations (Tier 1), residential air exchange rates (Tier 2), building infiltration factors (Tier 3), indoor concentrations (Tier 4), personal exposure factors (Tier 5), and personal exposures (Tier 6) (Breen, 2019). The incorporation of ambient air quality data with the multi-tiered model that accounts for building-specific infiltration of ambient air pollutants, and time spent indoors and outdoors provides a more personalized approach to the estimation of individual air pollution exposure.

Despite advances in the modeling of ambient air pollution exposure, to date, few studies have directly compared how the usage of stationary air quality monitors or model-estimated air pollution exposure effect exposure-response relationships (Yu et al., 2024). Moreover, among studies that compare estimation models and stationary monitors, the primary outcome has typically been mortality (Yu et al., 2024). Thus, there is limited data on the exposure-response relationships between common air pollutants and readily obtainable biological markers.

In the present study, we compare how the usage of stationary air quality monitor (AQM), and EMI model exposure assessments perform when investigating exposure-response relationships for both $PM_{2.5}$ and O_3 and cardiopulmonary outcomes in participants enrolled in a panel study.

2. Methods

2.1. Study design

The study protocols, procedures, and participant demographics have been described in more detail elsewhere (Tong, 2022), briefly 28 healthy participants between the ages of 25 and 55 years old were recruited from the region surrounding the U.S. Environmental Protection Agency (EPA) Human Studies Facility (HSF) in Chapel Hill, North Carolina. These participants were part of a larger clinical trial evaluating the effects of omega-3 and omega-6 fatty acids on cardiopulmonary outcomes from ambient air pollution exposure (Tong, 2022). For this analysis, the low omega-3 group was solely used as they more accurately reflect the general US populace in terms of omega-3 status and fish consumption (Papanikolaou et al., 2014). Summary statistics for study participants are listed in Table 1. Participants visited the EPA HSF for two consecutive weekdays for three to five sessions, separated by at least 7 days, amounting to a total of 134 visits. On the first day, the participant was provided a GPS data logger (model BT-Q1000XT; Qstartz, International, Taipei, Taiwan), which they carried for the next 24 h. Various clinical measurements were collected at baseline and the following day. At each visit, participants were tested for spirometry and venous blood was collected. Participants gave informed consent and study protocol was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill and the U.S. EPA and registered at ClinicalTrials.gov (Identifier: NCT02921048).

Table 1
Summary statistics of Study Participants.

Characteristic	Study Participants ($n = 28$)
Age, yr	37 ± 8
BMI, kg/m^2	24.9 ± 3.3
Sex	
Female	18 (64.3 %)
Male	10 (35.7 %)
Race	
White	19 (67.9 %)
African American	9 (32.1 %)
Marital status	
Single	13 (46.4 %)
Married	12 (42.9 %)
Separated/divorced	3 (10.7 %)
Education	
Graduate degree	9 (32.1 %)
College degree	16 (57.1 %)
High school/trade school	3 (10.7 %)

Input data for EMI were obtained from the participants for their home building characteristics, and street addresses for home and work. Daily questionnaires were used to collect occupant behavior related to building operation, including indoor temperature, open windows and doors, and operating window fans. The GPS data loggers were used to collect continuous participant locations. Before each 24-hour deployment of the GPS data logger, the GPS memory was cleared using QTravel software (version 1.2; Qstartz International, Taipei, Taiwan) and the battery was fully charged. The GPS was programmed to sample every 5 s and to collect the date, time, position (latitude, longitude), speed, number of satellites used, and position dilution of precision (dimensionless value that indicates accuracy of GPS position due to the satellite geometry) (Breen, 2014). The sampled data were stored in the GPS memory during the 24-hour sampling period, and then downloaded and stored in a text file for the MicroTrac model described in the Supplemental Materials.

2.2. Air pollution exposure assessment

Hourly $PM_{2.5}$ and O_3 concentrations derived from a central air quality monitor (Millbrook NCore) located in Raleigh, NC approximately 44 km (27 miles) from the HSF were used to calculate AQM exposure metrics: 24-hour average ambient concentration for $PM_{2.5}$ and a daily maximum 8-hour concentration for O_3, for each visit (lag0) and the 4 days preceding the visit (lag1–4), as well as a 5-day moving average (5MA). Hourly measurements of air temperature and relative humidity were also acquired from the Milbrook NCore.

In addition to the AQM, we modeled personal exposures using EMI (Breen, 2019), which was previously developed, evaluated, and applied in other panel studies (Breen, 2020; Breen et al., 2018; Breen, 2014; Breen, 2015; Breen et al., 2010). The details on the EMI model are provided in the Supplemental Materials. Briefly, hourly exposure metrics for $PM_{2.5}$ and O_3 were calculated based on hourly air quality monitor concentrations, meteorological data, residential building characteristics and operating conditions, and time spent in different microenvironments. From these hourly exposure estimates, we determined EMI exposure metrics: 24-h average exposure for $PM_{2.5}$ and a daily maximum 8-h exposure for O_3, for each visit (lag0) and the 4 days preceding the visit (lag1–4), as well as a 5-day moving average (5MA).

2.3. Lung function and biomarker measurements

Biological outcomes have been described in more detail elsewhere (Tong, 2022), briefly lung function was measured via spirometry using a 10.2-L dry seal digital spirometer (SensorMedics). The largest value

from at least three qualified maneuvers was selected for forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), and FEV_1/FVC ratio as per American Thoracic Society guidelines (Miller, 2005). Lung function in all participants was measured by using one dedicated spirometer and was measured by the same technician to minimize variability. Venous blood samples were stored at −80°C before biomarker analysis. All measures were taken at the same time of day to minimize circadian variation. Plasma levels of ox-LDL (oxidized low-density lipoprotein), von Willebrand Factor (vWF), D-dimer, and tissue plasminogen activator (tPA) were measured by using commercial enzyme-linked immunosorbent assay (ELISA) kits.

2.4. Statistical analysis

Spearman correlation coefficients were calculated for the agreement between AQM and EMI exposure metrics for both $PM_{2.5}$ and O_3. A linear-mixed effect model with participant specific random intercepts was applied to examine the associations between air pollutants and health outcomes and assess differences in effect estimates. A two-pollutant model was used and the effects of immediate exposure, lag0, and days preceding measurement (lag1–4) and well as a 5MA were separately modelled. The model was adjusted a priori for body mass index (BMI), age, race, sex, and glutathione-S-transferase μ-1 (GSTM1) status, marital status, and educational attainment. BMI and age were incorporated as continuous variables, sex was categorized using binary sex categorization (male/female) of "sex assigned at birth", GSTM1 status was dichotomous (presence or absence of GSTM1 gene). Race included the following categories: White, Black, Asian. Marital status was stratified as "single", "married", "seperated/divorced". Education was stratified as "graduate degree", "college degree", "high school/ trade school". Relative humidity and temperature corresponding to the air pollution lag were included as covariates and seasonal trends were adjusted for using a natural cubic spline. Effect estimates are presented as the percent change and 95 % confidence interval from the mean of health outcome per interquartile increase in air pollutant. All analyses were performed by using R (version 4.1.3, R Foundation for Statistical Computing) and the packages "lme4" and "splines."

3. Results

The AQM and EMI exposure metrics for both $PM_{2.5}$ and O_3, are shown in Table 2. The ambient air pollution concentrations taken during the study period were below the National Ambient Air Quality Standards (NAAQS) 24-hour $PM_{2.5}$ standard of 35 μg/m^3 (National Ambient Air Quality Standards (NAAQS) for PM, 2024) and the NAAQS O_3 8-hour average of 70 ppb (National Ambient Air Quality Standards (NAAQS) for Ozone, 2015). The mean values for AQM metrics are higher than for the EMI exposure metrics, as expected, as the EMI uses the ambient air pollutant concentrations from AQM as a starting point and subsequently models infiltration and exposure. Fig. 1 depicts the Spearman correlation coefficients between the AQM and EMI exposure metrics. For $PM_{2.5}$, the AQM and EMI were highly correlated, with a Spearman correlation coefficient of 0.89. For O_3, we observed a moderate correlation of 0.46 between the AQM and EMI exposure metrics. Next, we compared these two exposure methods on the associations between ambient air pollution and pulmonary function and cardiovascular markers. Full data tables across pollutants and exposure methods and stratified by sex can be found in the Supplemental Materials.

3.1. $PM_{2.5}$ exposure and health outcomes

$PM_{2.5}$ was associated with a small increase in FVC at lag0 for AQM (1.18 %, 95 %CI: 0.23–2.13) and EMI (1.33 %, 95 %CI: 0.16–2.51) (Fig. 2A). Similarly, $PM_{2.5}$ was associated with a small increase in FEV_1 at lag0 for AQM (1.03 %, 95 %CI: 0.03–2.04) and EMI (1.24 %, 95 %CI: 0.01–2.48) (Fig. 2B). The association between $PM_{2.5}$ and FEV_1/FVC ratio was null at all lags. Additionally, $PM_{2.5}$ was associated with an increase in ox-LDLs at lag 1 for AQM (12.24 %, 95 %CI: 4.26–20.21) and for EMI (17.94 %, 95 %CI: 8.07–27.82), and 5MA for AQM (9.03 %, 95 %CI: 1.04–17.01) (Fig. 2C). We also observed a positive association between vWF and $PM_{2.5}$ for lag0 for both AQM (4.27 %, 95 %CI: 0.15–8.39) and EMI (7.12 %, 95 %CI: 2.57–11.67) (Fig. 2D). Finally, we observed a negative association between $PM_{2.5}$ and vWF at lag3 for AQM (-6.48 %, 95 %CI: −11.41 to −1.55) and EMI (-5.63 %, 95 %CI: −10.58 to −0.68) and lag4 for AQM (-5.43 %, 95 %CI: −10.16 to −0.69) and EMI (-6.72 %, 95 %CI: −12.12 to −1.32) (Fig. 2D). The associations between $PM_{2.5}$ and D-dimer and tPA were null (Supplemental Materials, Figure?).

3.2. O_3 exposure and health outcomes

In contrast to $PM_{2.5}$, O_3 was not associated with changes in either FVC or FEV_1. However, O_3 was associated with a decrease in FE1/FVC ratio at lag3, but only when measured by AQM (-1.2 %, 95 %CI: −2.12 to −0.27) compared to no change in EMI (-0.01 %, 95 %CI: −0.78–0.76) (Fig. 3A). O_3 exposure was not associated with changes in oxLDLs, however we did observe an association between O_3 and vWF at lag0 measured by AQM (12.87 %, 95 %CI: 6.05–19.7) (Fig. 3B). In contrast, when O_3 was measured by EMI, the association was null (-2.77 %, 95 % CI: −8.13–2.59). Similarly, O_3 was associated with increased D-dimer at lag1 when measured by AQM (26.99 %, 95 %CI: 0.93–53.04) (Fig. 3C), but was null when measured via EMI (-6.86 %, 95 %CI: −26.31–12.6). tPA showed a negative association with O_3 at lag3 only when measured by EMI (-11.17 %, 95 %CI: −19.57 to −2.76) although AQM also trended down (-10.04 %, 95 %CI: −21.48–1.39) (Fig. 3D).

4. Discussion

The goal of this study was to evaluate how usage of a stationary air quality monitor (AQM) and the more personalized Exposure Model for Individuals (EMI) perform when estimating the exposure-response relationship to $PM_{2.5}$ and O_3 on cardiopulmonary biomarkers. AQM and EMI exposure metrics displayed a strong positive correlation for $PM_{2.5}$, with average EMI exposure roughly 64 % of the average AQM estimate. In contrast, we observed a moderate positive correlation for O_3, with the average EMI exposure approximately 25 % of the average AQM estimate. As EMI is derivative of AQM, we expected a positive correlation for both pollutants, however the agreement for $PM_{2.5}$ was particularly robust. Furthermore, we observed consistent associations between short-term $PM_{2.5}$ exposure and health endpoints with both exposure assessment methods. Specifically, we observed a positive association between $PM_{2.5}$ and oxidized low-density lipoprotein (oxLDL) at lag1. The oxidation of lipoproteins, including the generation of oxLDL, occurs as a byproduct of oxidative stress, as such, circulating oxLDLs are a marker of systemic oxidative stress and an established

Table 2
Summary statistics of AQM and EMI exposure metrics on visit days.

Metric	Pollutant	n	Missing (%)	Mean	SD	Min	P25	Median	P75	Max	IQR
AQM	$PM_{2.5}$ (μg/m^3)	133	0.8	9.9	3.8	1.8	7.4	9.2	11.9	22	4.4
EMI	$PM_{2.5}$ (μg/m^3)	114	13.9	6.3	2.5	2.4	4.6	5.9	7.8	14.5	3.2
AQM	O_3 (ppb)	134	0.0	42.3	10.6	17	35	42.5	49.8	68	14.8
EMI	O_3 (ppb)	112	19.6	10.8	6.0	2.0	6.4	9.6	14.3	31.1	7.9

AQM = air quality monitor-based exposure metric, EMI = Exposure Model for Individuals based exposure metric.

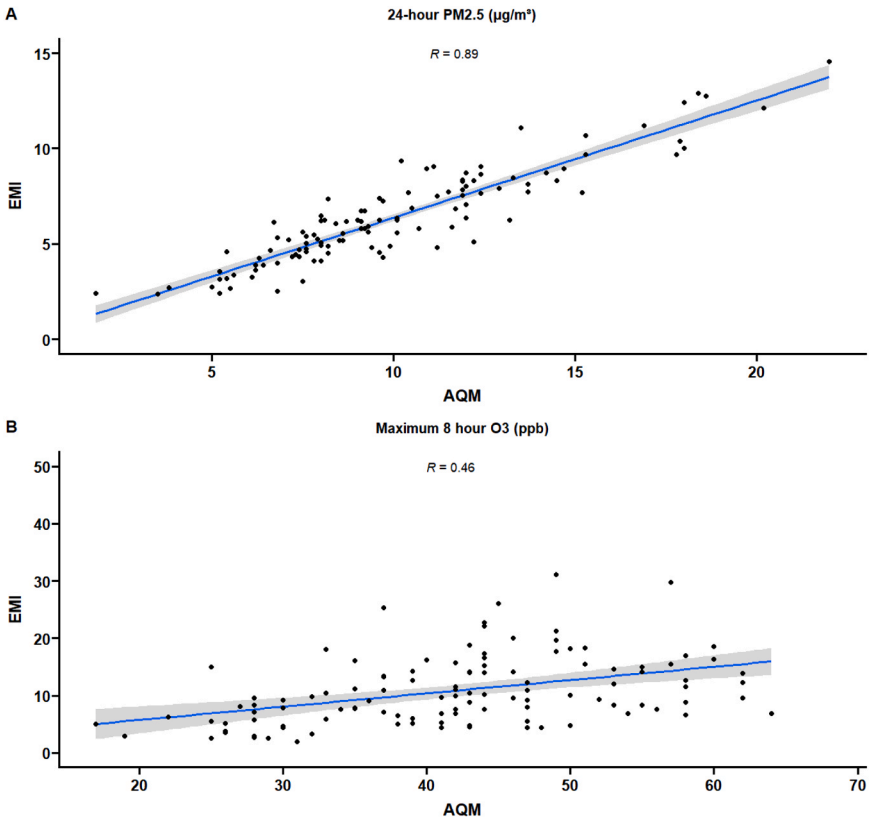

Fig. 1. Correlation plot (with Spearman's rho) of air pollution exposure metrics for all participant visits (n = 134). $PM_{2.5}$ (A) is shown as 24-hour average concentration (µg/m^3). Ozone (B) is shown as the maximum 8-hour concentration (ppb). AQM = Air Quality Monitor based exposure metric, EMI = Exposure Model for Individuals based exposure metric.

marker for atherosclerosis (Gradinaru et al., 2015). OxLDLs are mechanistically involved in all stages of atherosclerotic disease progression (Hong et al., 2023) and they promote expression of adhesion molecules on the endothelium, inhibit nitric oxide signaling, induce endothelial dysfunction, promote inflammation and foam cell formation (Poznyak et al., 2021). OxLDLs in plasma have been previously found to be positively associated with roadway proximity and with carbon load in airway macrophages among individuals with diabetes (Jacobs, 2011). Animal models have also demonstrated a link between $PM_{2.5}$ and oxLDLs, specifically mice exposed to ambient levels of $PM_{2.5}$ and fed a high fat diet displayed elevated oxLDLs in serum (Chen, 2024). However, to our knowledge this is the first instance of a linkage between $PM_{2.5}$ and elevated oxLDLs among otherwise healthy individuals. In addition to oxLDL, we further observed associations between $PM_{2.5}$ and levels of vWF, with a positive association at lag0 and a negative association at lag3 and lag4. vWF is normally tightly regulated and constitutively produced and released, maintaining a balance between clotting and bleeding (Xiang and Hwa, 2016). During endothelial injury, additional vWF is released, where it can bind platelets, promoting their adhesion and aggregation (Hantrakool et al., 2022). vWF can also bind and stabilize Factor VIII, promoting the coagulation cascade (Cortes et al., 2020). The binding of platelets with vWF promotes release of platelet granules, which contain a wide range of products including additional vWF and other adhesive glycoproteins (Yun et al., 2016). Short term $PM_{2.5}$ exposure, even at relatively low levels have been shown to be associated with increased vWF (Liang, 2020). Furthermore, elevated vWF is associated with risk of cardiovascular disease (Xiang and Hwa, 2016). The biphasic response, with an increase at lag0 and subsequent decrease at lag3 and lag4 days should be interpreted with caution, but we speculate it may be indicative of acute endothelial injury, most evident at lag0, followed by down-regulation of vWF or consumption of vWF via platelet adhesion and aggregation, which would lead to an inverse association at later lags (Liang, 2020). Lastly, we observed an association between $PM_{2.5}$ and increased FVC and FEV_1 at lag0 for both AQM and EMI. The increase in pulmonary function was unexpected, as short-term exposure to $PM_{2.5}$ is associated with pulmonary function declines (Dales et al., 2009; Edginton et al., 2019; Zhou, 2022). The increase was small, corresponding to about a 1 % increase in lung function, and transient, as the associations at later lags were null. Of interest, the pulmonary function outcomes displayed similar temporal trends with vWF. Conventionally, elevated vWF is thought to be associated with reduced lung function, however the majority of these findings occur among populations with severe lung impairments (Langholm, 2020). In contrast, in a controlled human exposure study to low levels of $PM_{2.5}$, particle exposure resulted in decrements in both FEV_1 and vWF (Wyatt et al., 2020), similar to our findings at later lag days. While these findings hint at a potential relationship, additional research will be required to tease out associations between PM2.5 exposure and interrelated biomarkers. Taken together, these data indicate that in our study region, AQM and EMI perform similarly for the evaluation of short-term $PM_{2.5}$ exposure associated health outcomes. Additionally, these findings imply that low levels of ambient $PM_{2.5}$ exposure are associated with risk of atherosclerosis and endothelial injury as evidenced by the changes of circulating oxLDL and vWF.

In contrast to $PM_{2.5}$, the associations between short-term O_3 exposure and health outcomes were dependent on the exposure assessment method. We observed a negative association between O_3 and FEV_1/FVC ratio only when measured by AQM. Similarly, we observed perturbations in hemostatic regulation, specifically elevated levels of vWF and D-dimer when O_3 was measured using AQM. In contrast, we observed a negative association between O_3 and tissue plasminogen activator (tPA) when O_3 was measured with EMI, although AQM trended in the same direction, with similar effect estimates. These biomarkers are interrelated, as vWF is released during endothelial activation and binds fibrin,

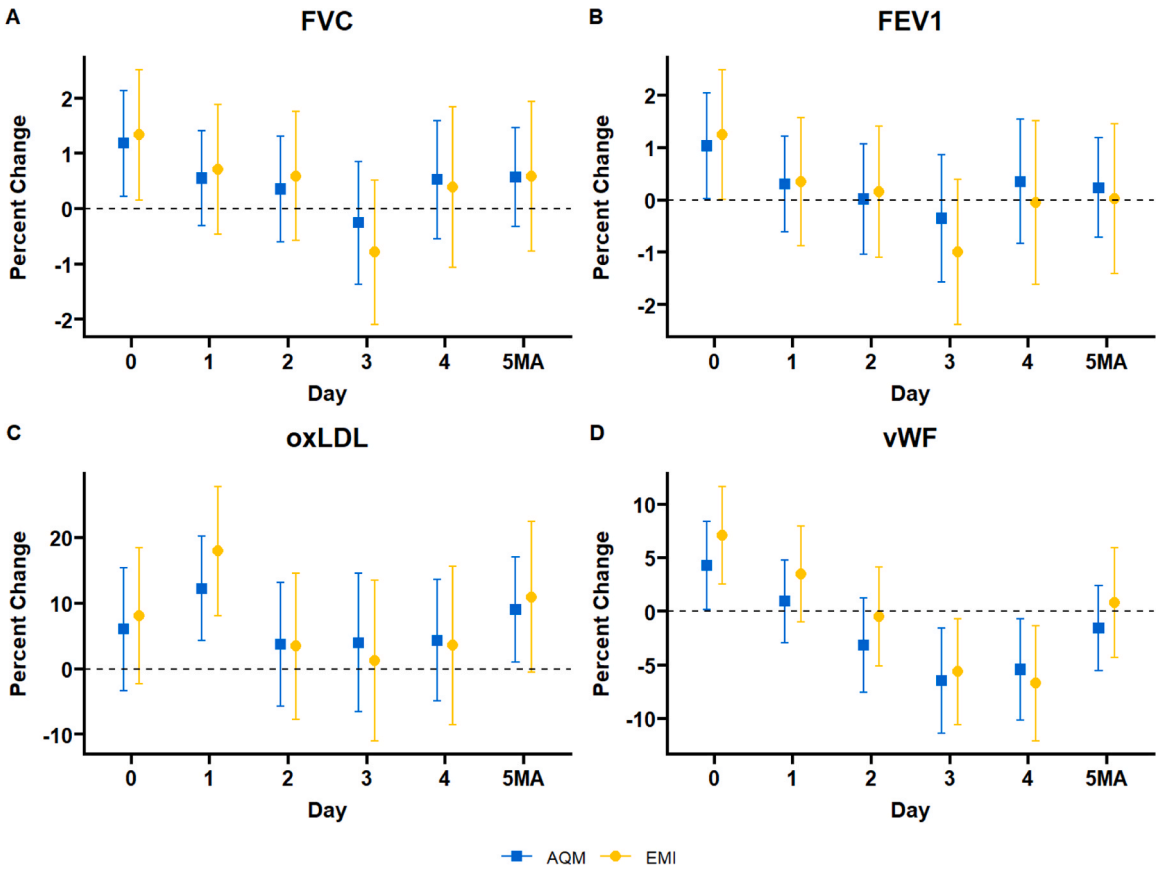

Fig. 2. Associations between short-term $PM_{2.5}$ exposure and cardiopulmonary markers. $PM_{2.5}$ was associated with an increase in FVC at lag0 for both AQM and EMI (A) and an increase in FEV_1 at lag0 both AQM and EMI (B). $PM_{2.5}$ was associated with an increase in oxLDL at lag1 for both AQM and EMI (C) and at 5MA for AQM. $PM_{2.5}$ was associated with increase in vWF at lag0 AQM and EMI (D) and a decrease at lag3 and lag4. Effect estimates are presented as the percent change and 95 % confidence interval from the mean of health outcome per interquartile increase in air pollutant. FEV_1 = Forced Expiratory Volume in 1 s, FVC = Forced Vital Capacity, oxLDL = oxidized low-density lipoprotein, vWF= von Willebrand Factor, tPA = tissue plasminogen activator, AQM = Air Quality Monitor, EMI = Exposure Model for Individuals.

which is involved in blood clotting (Reininger, 2008). TPA is a protease involved in the fibrinolysis process, promoting the breakdown of fibrin, which leads to fibrin degradation products, including D-dimer. Together, these biomarkers indicate activated endothelium (vWF), decreased fibrinolysis (tPA), and the presence of blood clots (D-dimer), thus linking O_3 exposure to altered hemostasis. These findings are similar to those reported by us and others after controlled human exposure to ozone, specifically increased coagulation, and decreased fibrinolysis, including decreased tPA and elevated D-Dimer (Devlin et al., 2012; Kahle, 2015; Niu, 2022). While the overall exposure-response relationships point to altered hemostasis, there were considerable discrepancies between exposure-response relationships depending on the measurement tool used. We postulate that these differences are driven primarily by how O_3 infiltration is modeled in EMI, as well as the relationship between ambient O_3 and O_3-secondary reaction products. Since AQM does not account for personal behaviors, such as spending time indoors, AQM is prone to overestimating personal O_3 exposure. EMI, on the other hand, accounts for time spent indoors in part by applying an infiltration factor to the outdoor concentration. Neither measurement accounts for the contribution of O_3 infiltration on the production of O_3-reaction products. O_3 lost to secondary reactions during infiltration is not innocuous and has biological relevance. O_3 can react with lipids from skins oils, such as squalene, generating secondary volatile organic compounds (VOCs) (Coffaro and Weisel, 2022). It can also react with VOCs present in the indoor environment from varied sources such as paints, carpets, furniture, cleaning products, personal care products, and cooking emissions (Davies, 2023; Nazaroff, 2006). The resulting reaction products are diverse and often lacking in toxicological data, however several products of ozonolysis have been demonstrated to induce adverse health effects (Coffaro and Weisel, 2022; Zhou et al., 2023). Furthermore, the indoor concentration of secondary compounds generated by O_3 has been shown to be strongly correlated with ambient O_3, displaying similar temporal trends and peaks even at low O_3 ambient concentrations (Liu et al., 2021). Curiously, certain biomarkers have been shown to respond differently to O_3 versus O_3 generated secondary compounds (He, 2023). One of note is vWF, which was demonstrated to be positively associated with personal O_3 exposure (both indoor and outdoor) but negatively associated with O_3 reaction products (He, 2023). Similar to these data, we observed a positive association with vWF and ambient O_3 measured by AQM, but a negative trend when measured by EMI. Such findings underscore the complex relationships between outdoor O_3 concentration, indoor O_3 concentration, and O_3 reaction products, and may in part explain variations observed between AQM and EMI measures and health outcomes. Indoor air O_3 concentrations, while highly dependent on ambient concentrations, track better with personal exposure (Kim and Rohr, 2021). While our study was not designed to investigate the contribution of indoor versus outdoor exposure, indoor air quality remains an important variable when considering exposure assessment and thus a limitation of the present study.

Overall, we demonstrate a strong agreement between the AQM and EMI for $PM_{2.5}$ when assessing associations between short-term $PM_{2.5}$ exposure and health endpoints. These findings echo the findings of a meta-analysis which demonstrated consistency in the risk estimates for

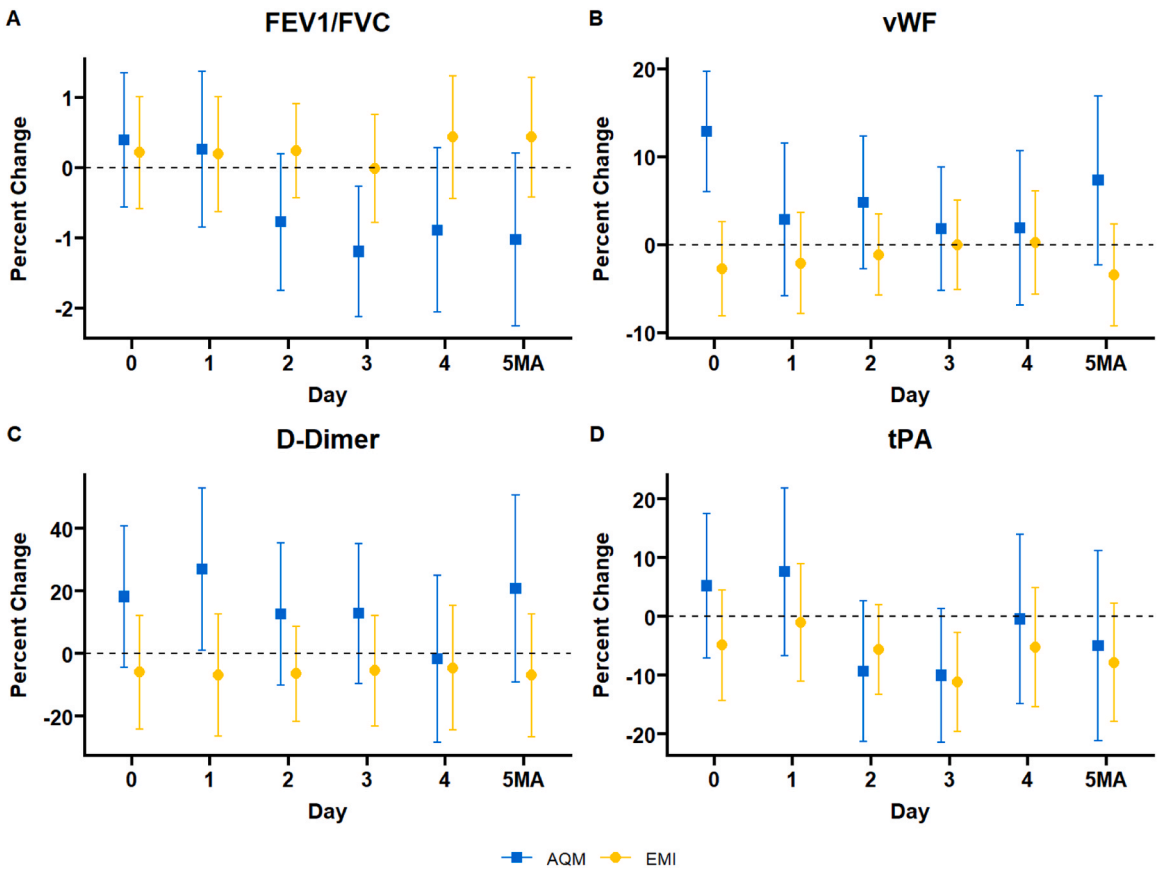

Fig. 3. Associations between short-term O_3 exposure and cardiopulmonary markers. O_3 was negatively associated with FEV_1/FVC at lag3 for AQM only (A). O_3 positively associated with vWF at lag0 for AQM only (B). O_3 was further associated with an increase in D-Dimer at lag2 for AQM only (C). O_3 was negatively associated with tPA at lag3 for EMI only (D). Effect estimates are presented as the percent change and 95 % confidence interval from the mean of health outcome per interquartile increase in air pollutant. FEV_1/FVC = the ratio of FEV_1 over FVC, vWF= von Willebrand Factor, tPA = tissue plasminogen activator, AQM = Air Quality Monitor, EMI = Exposure Model for Individuals.

mortality after $PM_{2.5}$ exposure for both model-estimated and station-observed $PM_{2.5}$ (Yu et al., 2024). In future studies, it will be advantageous to incorporate additional tools that can be used to increase confidence in the air pollution estimates, such as remote-sensing products, the usage of more widely distributed low-cost ambient monitors networks, or personal monitoring. While the addition of each of these tools has merits, they do not completely address the challenge of modeling exposure with regards to behaviors, indoor environments, and microenvironments, all of which modify exposure concentration and delivered dose. Nonetheless, despite limitations in both models used, we find that for $PM_{2.5}$, the overall direction and association of the exposure-response relationship remains consistent.

In contrast to $PM_{2.5}$, the two methods for O_3 exposure showed only moderate agreement. O_3 exposure-response relationships were generally null, with the AQM showing more associations than EMI. Additionally, the two models did not show agreement when assessing associations between O_3 and health endpoints. Additional research, including the deployment of low-cost O_3 monitors, may be needed to better investigate the discrepancies between the two exposure assessment methods as well as examine the role of infiltration and O_3-secondary reactions on biomarkers. To conclude, in our study area, both AQM and EMI performed similarly for the assessment for exposure-response relationships to $PM_{2.5}$ and demonstrate associations between $PM_{2.5}$ exposure and elevated oxLDL, implying increased oxidative stress. In contrast, AQM and EMI showed limited agreement for the assessment for exposure-response relationships to O_3 but overall show markers of altered hemostasis. Future studies should consider the importance of both O_3 exposure and the production of O_3 reaction products estimating effects of exposure on biomarkers.

CRediT authorship contribution statement

Siqi Zhang: Software, Methodology, Data curation. **Haiyan Tong:** Writing – review & editing, Supervision, Project administration, Investigation, Conceptualization. **Jairus Pulczinski:** Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Vlad Isakov:** Writing – review & editing, Software, Methodology. **Alexandra Schneider:** Writing – review & editing, Conceptualization. **Michael Breen:** Writing – review & editing, Software, Methodology, Investigation. **Miyuki Breen:** Methodology, Investigation. **Robert Devlin:** Supervision, Conceptualization. **James Samet:** Investigation, Conceptualization. **Ana Rappold:** Supervision, Project administration. **David Diaz-Sanchez:** Supervision, Project administration, Conceptualization.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

https://catalog.data.gov/dataset/pisces-dataset-impact-of-dietary-omega-3-fa-on-the-association-between-exposure-to-ambient.

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