Science of the Total Environment 870 (2023) 161874

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Relationship between traffic-related air pollution and inflammation biomarkers using structural equation modeling

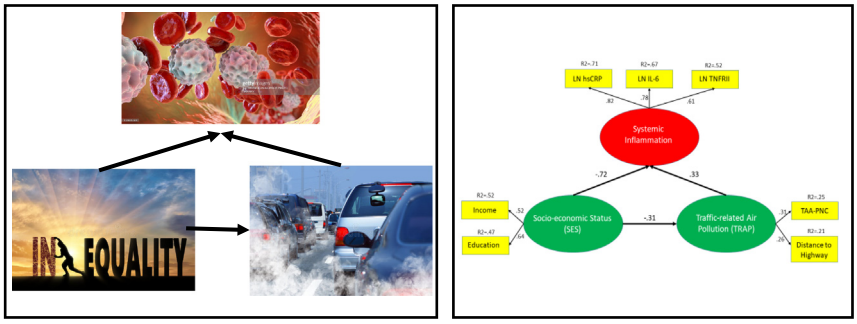
Kevin J. Lane [a,*], Jonathan I. Levy [a], Allison P. Patton [b], John L. Durant [c], Wig Zamore [d], Doug Brugge [e]

[a] Department of Environmental Health, Boston University School of Public Health, Boston, MA, United States of America
[b] Health Effects Institute, Boston, MA, United States of America
[c] Department of Civil and Environmental Engineering, Tufts University, Medford, MA, United States of America
[d] Somerville Transportation Equity Partnership, Somerville, MA, United States of America
[e] Department of Public Health Sciences, University of Connecticut School of Medicine, Farmington, CT, United States of America

HIGHLIGHTS

- Traffic-related air pollution increases inflammation, with both represented by many markers.
- Structural equation models use multiple metrics to better elucidate associations.
- We assessed associations of air pollution and socioeconomic status with inflammation.
- IL-6, CRP and TNFRII in blood were used in a latent construct of inflammation.
- Association was larger for latent inflammation construct than individual biomarkers.

GRAPHICAL ABSTRACT



ARTICLE INFO

Editor: Pavlos Kassomenos

Keywords:
C-reactive protein
Inflammation
Micro-environment
Particle number concentration
Ultrafine particles
Structural equation modeling

ABSTRACT

Background: Evidence suggests that exposure to traffic-related air pollution (TRAP) and social stressors can increase inflammation. Given that there are many different markers of TRAP exposure, socio-economic status (SES), and inflammation, analytical approaches can leverage multiple markers to better elucidate associations. In this study, we applied structural equation modeling (SEM) to assess the association between a TRAP construct and a SES construct with an inflammation construct.

Methods: This analysis was conducted as part of the Community Assessment of Freeway Exposure and Health (CAFEH; N = 408) study. Air pollution was characterized using a spatiotemporal model of particle number concentration (PNC) combined with individual participant time-activity adjustment (TAA). TAA-PNC and proximity to highways were considered for a construct of TRAP exposure. Participant demographics on education and income for an SES construct were assessed via questionnaires. Blood samples were analyzed for high sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and tumor necrosis factor-α receptor II (TNFRII), which were considered for the construct for inflammation. We conducted SEM and compared our findings with those obtained using generalized linear models (GLM).

Results: Using GLM, TAA-PNC was associated with multiple inflammation biomarkers. An IQR (10,000 particles/cm^3) increase of TAA-PNC was associated with a 14 % increase in hsCRP in the GLM. Using SEM, the association between the TRAP construct and the inflammation construct was twice as large as the associations with any individual inflammation

Abbreviations: TRAP, traffic-related air pollution; SEM, structural equation modeling; UFP, ultrafine particles; PNC, particle number concentration; TAA, time-activity adjusted; CRP, C-reactive protein; IL-6, interleukin-6; TNFRII, tumor necrosis factor-α receptor II; SES, socioeconomic status; CAFEH, The Community Assessment of Freeway Exposure and Health; CBPR, community-based participatory research; TAPL-1, Tufts Air Pollution Monitoring Laboratory.

* Corresponding author at: Boston University School of Public Health, 715 Albany Street, Talbot Building, Boston, MA 02118, United States of America.
E-mail addresses: klane@bu.edu (K.J. Lane), jonlevy@bu.edu (J.I. Levy), apatton@healtheffects.org (A.P. Patton), john.durant@tufts.edu (J.L. Durant), brugge@uchc.edu (D. Brugge).

http://dx.doi.org/10.1016/j.scitotenv.2023.161874
Received 24 October 2022; Received in revised form 6 January 2023; Accepted 24 January 2023
Available online 27 January 2023

biomarker. SES had an inverse association with inflammation in all models. Using SEM to estimate the indirect effects of SES on inflammation through the TRAP construct strengthened confidence in the association of TRAP with inflammation. *Conclusion:* Our TRAP construct resulted in stronger associations with a combined construct for inflammation than with individual biomarkers, reinforcing the value of statistical approaches that combine multiple, related exposures or outcomes. Our findings are consistent with inflammatory risk from TRAP exposure.

1. Introduction

Extensive evidence indicates that living near highways and major roadways and corresponding exposure to traffic-related air pollution (TRAP) are associated with adverse health outcomes (HEI, 2010; HEI, 2022). Ultrafine particles (UFP, <100 nm in aerodynamic diameter), a component of TRAP, are elevated near traffic corridors, and there is increasing evidence that exposure to UFP contributes to these health risks (Berklein et al., 2021; Brugge et al., 2018; Downward et al., 2018; Ostro et al., 2015; Ohlwein et al., 2019; SAB, 2018; Weichenthal et al., 2017; HEI, 2022). That said, there remains substantial uncertainty regarding UFP-related health effects and the extent to which UFP serves as a surrogate for other TRAP constituents. This is principally because of the spatiotemporal variability of UFP concentrations and the associated problem of exposure error.

Better elucidating the health effects of TRAP and the contribution from UFP requires reductions in exposure error and improvements in characterization of outcomes. Exposure error likely biases associations toward the null in many studies. Multiple strategies have been used to improve UFP exposure assignment (Apte et al., 2017; Breen et al., 2014; Minet et al., 2018; Simon et al., 2018), including leveraging information on the microenvironments where people spend time throughout the day. For example, in our study showing associations of individually assigned UFP exposures with biomarkers of inflammation, we found that adjustment for time activity in addition to incorporation of body mass index (BMI) and race/ethnicity led to more interpretable exposure-response curves (Lane et al., 2015; Lane et al., 2016). However, ambient UFP is only one marker of TRAP, and few studies have simultaneously considered incorporation of multiple covariates reflective of TRAP exposure and multiple covariates reflective of inflammation, which could provide more robust insight than analyses of individual covariates while avoiding issues of multiple comparison.

Here we reanalyze data from the Community Assessment of Freeway Exposure and Health (CAFEH) study, a cross-sectional study evaluating associations between TRAP and multiple inflammation biomarkers, using structural equation modeling (SEM). SEM is a combination of path analysis, factor analysis, and linear regression that allows for evaluation of both direct and indirect effects of variables (path analysis) and development of latent constructs of correlated variables (factor analysis) (Tomarken and Waller, 2005). Thus, SEM allows simultaneously considering multiple pathways by which risk factors might be associated with measures of health. In this context, SEM allows us to test whether or not related variables, in this case multiple markers of TRAP exposure and inflammation, load onto (i.e., are sufficiently correlated within factor analysis) latent constructs. If an inflammatory biomarker construct results in stronger associations than individual biomarkers, or if a TRAP construct results in stronger associations than individual pollutants such as UFP, it would further support our hypothesis that TRAP is associated with inflammation.

2. Methods

2.1. Study design and population data

The CAFEH study is community-based participatory research (CBPR) and has been described in detail previously (Fuller et al., 2013b; Lane et al., 2013; Lane et al., 2015; Patton et al., 2014a; Patton et al., 2015). Briefly, the study is a cross-sectional design in which we recruited participants from three sets of geographic areas paired to include demographically similar populations living in near-highway and urban-background (>1 km from highways) neighborhoods over the course of one year each per paired areas. We stratified recruitment by distance to a major highway (Interstate-93) in and near Boston, MA to maximize exposure contrast to UFP; strata were 0–100 m, 100–400 m, and > 1 km. All participant recruitment and health outcome measurements were conducted in September 2009 through July 2013.

Random samples were drawn by enumerating all addresses in the study areas, and were supplemented with smaller convenience samples to meet enrollment targets. We recruited participants at their homes where they signed informed consent forms. Consented participants were then administered a questionnaire that collected basic demographics (including age, sex, race or ethnicity), information on potential confounders (including income, education, smoking, occupation), and hourly time activity for two recent days, which has been shown to be predictive of longer-term time activity (Panis, 2010). The protocol was approved by the Tufts University IRB.

Participants who completed the in-home survey were invited to attend field clinics at which biological data were collected. Blood samples were drawn and analyzed for high sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and tumor necrosis factor alpha receptor II (TNFRII) using research and clinical grade laboratory assays (described elsewhere) (Fuller et al., 2013b). BMI was calculated from height and weight as measured using research-grade instruments.

Highly resolved geocoding was conducted at the parcel level with orthophoto correction for single and multi-family homes, while residential unit correction was conducted for participants in large public housing facilities (Lane et al., 2013). Euclidean distance from nearest highway was calculated for each participant's geocoded residential position using the Massachusetts Department of Transportation road network layer (Lane et al., 2013). The Euclidean distance measure was used in the SEM models.

2.2. Exposure assessment

Here we present in brief a summary of the PNC monitoring, modeling and exposure assignment, with more details provided in Supplemental Text 1 and elsewhere (e.g., Padró-Martínez et al., 2012; Patton et al., 2015; Lane et al., 2015).

In the same years as recruitment, we collected air pollution data with the Tufts Air Pollution Monitoring Laboratory (TAPL-1), a modified recreational vehicle outfitted with multiple air monitoring instruments, including a condensation particle counter (Model 3775, TSI, Shoreview, MN) that measures UFP as particle number concentration (PNC, 4–3000 nm). TAPL-1 was equipped with a Garmin GPS V and driven on fixed routes in the study areas. Routes were designed to collect data near homes of all participants and driving times were scheduled to include all days of the week, hours including early morning through late evening, and all seasons. Data for times when self-sampling of TAPL-1 exhaust was likely (i.e., when TAPL-1 was stopped or moving slowly downwind relative to wind speed) were removed during quality control. The resulting data sets showed higher PNC near the highway and major roadways as well as higher PNC during colder weather, as expected (Padró-Martínez et al., 2012; Patton et al., 2014b).

Land use data and hourly traffic and meteorology were used as variables to build hourly predictive regression models of PNC measured for each study area. Model building led to four models of natural log transformed PNC: two models for the pairs of near-highway and urban-background neighborhoods that were monitored on the same days and one each for a near-highway and an urban background neighborhood that were more distant from each other and therefore monitored on different days. Variables

used in the regression models included highway side (east or west), distance to highway, distance to nearest major road, wind speed and direction, temperature, day of week, and highway traffic volume and speed. Models included different sets of variables based on their predictive value. We found that neighborhood-specific models performed better in the individual neighborhoods than a more general modeling approach (Patton et al., 2015).

Hourly individualized exposure of each participant was assigned based on modeled ambient PNC levels after adjustment for where study participants typically spent each hour of the day (time-activity adjusted PNC, hereafter TAA-PNC). Modeled ambient PNC at the residence (a majority of participant time) was used for time indoors and outdoors at home because paired measurements made at a subset of the homes showed effective infiltration of UFP (Fuller et al., 2013a). Time spent at work was assigned the mean of modeled concentrations at all near-highway participant residences for high traffic exhaust exposure jobs and urban background levels for low traffic exhaust exposure jobs. Time on highways was assigned modeled values at the edge of the highway. Exposures during time spent in other locations were assigned as urban background levels because this is the most common exposure in the metropolitan area (Lane et al., 2016). Annual average TAA-PNC values were used for the epidemiological analyses reported in this paper.

2.3. Statistical analysis

As the values for hsCRP, IL-6 and TNFRII were not normally distributed, we log-transformed them for all analyses, after which point they approximated a normal distribution. We used generalized linear models (GLMs) to test the independent association of log-transformed hsCRP, IL-6 and TNFRII (hereafter referred to as hsCRP, IL-6 and TNFRII) with TAA-PNC. GLMs were adjusted for age (years), gender (female, male), BMI (kg/m^2), smoking status (current, former, never), and race or ethnicity (detailed below). These variables are all known to be cardiovascular disease risk factors and/or predictors of some of our biomarkers of interest (Lane et al., 2016). The study participants (N = 408) included a large non-Hispanic White population and a large Chinese and Vietnamese population, with more limited numbers for other racial/ethnic groups. Therefore, we grouped race/ethnicity into non-Hispanic White, East Asian (Chinese and Vietnamese), and other (African American, Haitian Creole, Hispanic, Latino, Indian, Pakistani and Native American).

To develop our SEM, we included the adjustment covariates listed above to facilitate comparison with the GLMs. Beyond these covariates, we limited the dataset to significant independent predictors of one or more biomarkers of inflammation and used a Pearson's test for correlation as well as associations observed in previous analyses (Lane et al., 2015; Lane et al., 2016) to identify predictors for the latent constructs for TRAP, socioeconomic status (SES), and inflammation. We then examined the association between latent TRAP, SES, and inflammation using a SEM. SEMs consist of two stages: a measurement model, which shows the relationships between latent constructs of TRAP, SES, and inflammation and their predictors; and a structural model, which we used to examine the association between each latent construct.

We examined the sensitivity of our findings to the potential role of SES by developing two models, both of which were adjusted for the same covariates. In one model, we allowed SES alone to contribute directly to inflammation. In the second model, we allowed SES to contribute directly to inflammation and indirectly through the TRAP construct. We then compared the associations and model fit.

Effect-size estimates were reported for an inter-quartile range (IQR) increase in TRAP or TAA-PNC. Model fit was compared using the Akaike information criterion (AIC) and root mean square error (RMSE). All statistical analyses were performed using SAS (Statistical Analysis Software, Cary, North Carolina) version 9.3.2. SEM was conducted using Proc Calis to determine path loadings, *p*-values between latent variables, and the individual variables contributing to the latent variables.

3. Results

The majority of the study population was female, above the age of 60 years, overweight or obese, and current or former smokers (Table 1). Non-Hispanic White and East Asian participants constituted 42 % and 40 % of the population, respectively. East Asians were heavily concentrated in the paired near highway and urban areas where participants were recruited in the final year of recruitment. We previously reported that being older or a current or former smoker was associated with higher levels of all inflammation biomarkers (Lane et al., 2016). BMI (in kg/m^2), when divided into underweight (≤18.5), normal (18.6–24.9), overweight (25–29.9) and obese (≥30) categories, had a non-monotonic relationship with each biomarker of inflammation, with lower levels for normal weight than for underweight or overweight/obese participants. East Asian participants had lower median levels of all biomarkers than non-Hispanic White participants and the other race or ethnicity category (Corlin et al., 2014). Of note, all underweight participants were East Asian while all obese participants were non-Asian. Gender was associated with a minor difference for IL-6, but not for hsCRP and TNFRII.

In our SEM, the inflammation construct was explained by hsCRP, IL-6 and TNFRII with each pair of variables having a Pearson's correlation above 0.4 (Supplemental Table 1). Income and education had a Pearson's correlation of 0.46 and were used to predict the SES construct. The latent construct TRAP was predicted by TAA-PNC and distance to highway as a proxy for exposure to other air pollutants, such as NO_2 and black carbon that are also elevated near highways (Karner et al., 2010).

Table 2 presents the associations from the two SEMs of the TRAP and SES constructs on the inflammation construct adjusted for age, gender, BMI, smoking status, and race/ethnicity. SEM 1 was designed to examine the independent effects of TRAP and SES on inflammation. SEM 2 allowed SES to directly contribute to inflammation and indirectly contribute through the TRAP pathway. Fig. 1 compares the two SEMs graphically.

Both SEMs resulted in positive associations of the latent construct for TRAP as well as TAA-PNC with the inflammation construct composed of hsCRP, IL-6 and TNFRII. Adjustment for BMI had the largest effect on

Table 1
Population characteristics (n = 408).

Characteristic	n	% or mean ± SD
Age (years, mean ± SD)	408	61 ± 13
BMI (kg/m^2, mean ± SD)	408	27.4 ± 6.8
Underweight (<18.5)	14	3 %
Normal weight (18.5–24.9)	168	41 %
Overweight (25–29.9)	117	29 %
Obese (30+)	109	27 %
City/neighborhood		
Near highway (≤500 m)		
Somerville	100	24 %
Dorchester/South Boston	90	22 %
Chinatown	133	32 %
Urban background (≥1000 m)		
Somerville	25	6 %
Dorchester/South Boston	20	5 %
Malden	40	10 %
Sex		
Female	238	58 %
Male	170	42 %
Smoking		
Current	83	20 %
Former	126	31 %
Never	199	49 %
Educational attainment		
<High school diploma	136	34 %
High school diploma	123	30 %
Undergraduate	99	24 %
Graduate school	50	12 %
Race/ethnicity		
White non-Hispanic	173	42 %
East Asian	162	40 %
Other	73	18 %

Table 2
SEM outputs for the independent and joint effects between TRAP, SES and inflammation.

Model	Latent construct & predictors (1)	Partial R^2	Variance (*p*-val)	Latent construct & predictors (2)	Partial R^2	Variance (*p*-val)	Latent construct & predictors (3)	Partial R^2	Variance (*p*-val)
SEM 1	TRAP		0.27 (0.07)	SES		−0.64 (<0.01)	Inflammation		
	TAA-PNC	0.223	0.31 (0.11)	Education	0.51	0.27 (<0.01)	hsCRP	0.67	0.76 (<0.01)
	Distance to highway	0.19	0.16 (0.08)	Income	0.38	0.30 (<0.01)	IL-6	0.59	0.68 (0.02)
							TNFRII	0.41	0.55 (0.02)
SEM 2	TRAP		0.33 (0.03)	SES		−0.72 (<0.01)	Inflammation		
	TAA-PNC	0.25	0.34 (0.06)	Education	0.52	0.64 (<0.01)	hsCRP	0.71	0.82 (<0.01)
	Distance to Highway	0.21	0.26 (0.09)	Income	0.47	0.52 (<0.01)	IL-6	0.67	0.78 (<0.01)
							TNFRII	0.52	0.61 (<0.01)

Fig. 1. Structural equation models of the independent (top SEM 1) and joint (bottom SEM 2) associations of TRAP and SES with inflammation.

Table 3
Comparison of the association between an IQR increase (10,000 particle/cm^3) in time-activity adjusted particle number concentration (TAA-PNC) and LN hsCRP or the inflammation latent construct using three models: 1) GLM, 2) SEM with TRAP independent of SES (SEM 1), and 3) SEM with linked pathways between SES and TRAP (SEM 2).

Model	Measure	hsCRP	Inflammation
GLM	β	14.0 %	NA
	AIC	405.4	NA
	RMSE	1.04	NA
	R^2	0.12	NA
SEM 1	β	28.2 %	29 %
	AIC	45.7	176
	RMSE	0.14	0.16
	R^2	0.24	0.19
SEM 2	β	34.1 %	29 %
	AIC	26.2	139
	RMSE	0.13	0.11
	R^2	0.27	0.32

All models adjusted for age, gender, BMI, smoking status and race.

these associations, followed by smoking status. Age, gender and education had marginal effects on the associations, but were retained in adjusted models because they are known cardiovascular disease risk factors. Additional adjustment by race/ethnicity increased the TAA-PNC β-estimates and strength of association for hsCRP, IL-6 and TNFRII.

The association between the TRAP construct and inflammation was greater, and the overall model fit slightly improved with the comparative fit index increasing from 0.91 to 0.93, when SES contributed to inflammation through the TRAP construct (Fig. 1, bottom). However, including SES as a mediation step resulted in a minimal increase in the effect of TAA-PNC on the inflammation construct. We tested another model (results not shown) that included a smoking construct consisting of both individual and environmental tobacco smoke (ETS, from exposures in the residence and workplace). However, the smoking variables were not independent predictors of hsCRP, IL-6 and TNFRII, nor was the construct found to meaningfully contribute to inflammation in our SEM.

Table 3 compares the association between TAA-PNC and hsCRP using a GLM that includes the same predictors as the SEM models as covariates. Also shown are both of the SEM models with hsCRP as the outcome variable which allows for comparisons of association and model fit. An IQR [10,000 particles/cm^3] increase in TAA-PNC was associated with a 14 % increase in hsCRP in the GLM, an association that more than doubled in both of the SEMs. Overall model fit was substantially improved in the SEMs compared to the GLM, with decreases in both AIC and RMSE.

4. Discussion

Using SEMs, we found that a latent construct for inflammation, which incorporated concentrations of three blood biomarkers (IL-6, CRP and TNFRII), had a moderate and positive association with a latent construct for TRAP that included time-activity adjusted PNC (UFP) exposures. Further, the latent construct for inflammation was strongly inversely associated with SES, and inclusion of a pathway between SES and TRAP strengthened the association between TRAP and inflammation. This suggests that TRAP, based primarily on UFP exposure, in conjunction with individual attributes associated with SES, could have combined effects on inflammation.

Critically, using SEM, we found associations that were approximately double those estimated through identically-structured GLM, reinforcing the value of modeling approaches that account for the complex relationships among covariates and leverage insights from multiple related exposure and outcome variables. These findings thus strengthen our confidence in associations between TRAP/UFP and inflammation.

Our construct for inflammation that uses three blood markers of inflammation likely not only reflects a more robust statistical approach, but is consistent with biologically plausible pathways. It is established that "inflammasomes" drive concentrations of IL-1 family cytokines and some gasdermins. IL-1, in turn, drives downstream inflammation biomarkers such as CRP and IL-6. It makes sense that a construct like ours which combines inflammation biomarkers would better capture inflammation derived from upstream activation than would individual biomarkers.

The NLRP3 inflammasome (nucleotide-binding oligomerization domain-like receptor [NLR] family pyrin domain-containing 3) is of particular interest for two reasons: 1) Among the 21 human inflammasomes only NLRP3 integrates inflammatory responses; and 2) NLRP3 is known to be activated by many types of particles, both endogenous and exogenous. UFP, which can cross biological barriers, such as cell membranes, are a prime candidate for being an additional activator of this inflammasome. There is a need for further research to investigate the early stages of activation of this pathway directly.

The primary limitation of our analysis is that the CAFEH study was cross-sectional, which limits causal interpretation. However, we note that the associations we observed strengthened and became more monotonic when we reduced exposure error through gold standard geocoding, correcting for time activity of study participants and adjusting for confounders (Lane et al., 2015; Lane et al., 2016). Here we reported additional strengthening of associations when we combined the inflammation biomarkers as well as multiple TRAP covariates into single constructs in SEM models. These findings are all consistent with reducing exposure and outcome error, which otherwise tend to bias results toward the null.

An additional limitation is that there was likely residual exposure misclassification because our ambient models and time activity adjustments explain some, but not all exposure variation assigned to study participants. We also did not assess the role of respiratory rate, which would also affect personal exposure (Corlin et al., 2018). Finally, we did not model or assess exposure to air pollutants other than UFP that are elevated near highways (Patton et al., 2014b). We did include distance to highway as a surrogate for other pollutants that are elevated next to highways and that may be patterned differentially from UFP. However, multiple near-highway pollutants should be modeled and assigned explicit exposures in future epidemiology studies.

Our study suggests several lines of future research. First, there is a need for epidemiological studies that directly assess the association between TRAP exposure, ideally including high-resolution estimates of UFP and other pollutants with consideration of activity patterns, and activation of inflammasomes. Second, some of the challenges of high-resolution exposure assessment still need to be addressed. Our current approach of developing finely resolved models of PNC as an indicator of UFP (20 m × 20 m) with personal time-activity adjustments may not be viable for all studies due to the substantial resources required to build high resolution ambient models of PNC and to collect personal data from all study participants.

Finally, given the importance of SES gradients near major roadways, the role of SES in TRAP and UFP epidemiology requires further attention. Broadly, we recommend the use of SEM in settings with exposures that may have multi-directional contributions and outcomes that can be used to measure different aspects of physiological pathways that may not be testable in a one-way causal model.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2023.161874.

Ethics approval and consent to participate

The protocol was approved by the Tufts University IRB (Protocol 8468) and participants were consented at their residence prior to entry into the study.

Consent for publication

Not applicable.

Funding

Funding was provided by the National Institute of Environmental Health Sciences (NIEHS) (Grant Nos. ES015462, ES026980 and ES030289).

CRediT authorship contribution statement

Dr. Lane – Conducted the statistical analysis and was the lead author of the manuscript.

Dr. Levy – Advised on statistical analysis and contributed to the writing of the manuscript.

Dr. Patton – Developed the UFP models and contributed to writing of the manuscript.

Dr. Durant – Oversaw the field UFP monitoring, model development and contributed to writing of the manuscript.

Mr. Zamore – Advised on analysis and writing of the manuscript.

Dr. Brugge – Is principal investigator on the CAFEH study, advised on the analysis and contributed to writing of the manuscript.

Data availability

The data that support the findings of this study are available on request from the corresponding author Kevin J. Lane. The data are not publicly available due to containing information that could compromise research participant privacy/consent.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Doug Brugge reports financial support was provided by the National Institute of Environmental Health Sciences (NIEHS).

Acknowledgments

We are grateful to the CAFEH Steering Committee and the great help from our community partners. Funding for CAFEH was provided by the National Institute of Environmental Health Sciences (NIEHS) (Grant Nos. ES015462, ES026980 and ES030289). The contents of this article do not necessarily reflect the views of HEI, or its sponsors, nor do they necessarily reflect the views and policies of the EPA or motor vehicle and engine manufacturers.

References

Apte, J.S., Messier, K.P., Gani, S., Brauer, M., Kirchstetter, T.W., Lunden, M.M., Hamburg, S.P., 2017. High-resolution air pollution mapping with Google street view cars: exploiting big data. Environ. Sci. Technol. 51 (12), 6999–7008. https://doi.org/10.1021/acs.est.7b00891.

Berklein, F., Finley, A., Zamore, W., Brugge, D., M, C., 2021. A scoping review of published research on ultrafine particle exposure and health outcomes. Ambient Combustion Ultrafine Particles and Health. Nova Science Publishers, pp. 255–298.

Breen, M.S., Long, T.C., Schultz, B.D., Crooks, J., Breen, M., Langstaff, J.E., Cao, Y., 2014. GPS-based microenvironment tracker (MicroTrac) model to estimate time–location of individuals for air pollution exposure assessments: model evaluation in Central North Carolina. J. Exposure Sci. Environ. Epidemiol. 24 (4), 412–420. https://doi.org/10.1038/jes.2014.13.

Brugge, D., Berklein, F., Yao, Q., Turner, A., Zamore, W., Chung, M., 2018. An evidence map of ultrafine epidemiology. Paper Presented at the ETH Conference on Combustion Generated Nanoparticles, Zurich.

Corlin, L., Woodin, M., Hart, J.E., Simon, M.C., Gute, D.M., Stowell, J., Brugge, D., 2018. Longitudinal associations of long-term exposure to ultrafine particles with blood pressure and systemic inflammation in puerto rican adults. Environ. Health 17 (1), 1–11. https://doi.org/10.1186/s12940-018-0379-9.

Corlin, L., Woodin, M., Thanikachalam, M., Lowe, L., Brugge, D., 2014. Evidence for the healthy immigrant effect in older chinese immigrants: a cross-sectional study. BMC Public Health 14 (1), 1–8. https://doi.org/10.1186/1471-2458-14-603.

Downward, G.S., van Nunen, E.J., Kerckhoffs, J., Vineis, P., Brunekreef, B., Boer, J.M., van der Schouw, Y.T., 2018. Long-term exposure to ultrafine particles and incidence of cardiovascular and cerebrovascular disease in a prospective study of a dutch cohort. Environ. Health Perspect. 126 (12), 127007. https://doi.org/10.1289/EHP3047.

Fuller, C.H., Brugge, D., Williams, P.L., Mittleman, M.A., Lane, K., Durant, J.L., Spengler, J.D., 2013. Indoor and outdoor measurements of particle number concentration in near-highway homes. J. Exposure Sci. Environ. Epidemiol. 23 (5), 506–512. https://doi.org/10.1038/jes.2012.116.

Fuller, C.H., Patton, A.P., Lane, K., Laws, M.B., Marden, A., Carrasco, E., Durant, J.L., 2013. A community participatory study of cardiovascular health and exposure to near-highway air pollution: study design and methods. Rev. Environ. Health 28 (1), 21–35. https://doi.org/10.1515/reveh-2012-0029.

HEI, 2010. Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. HEI Special Report 17. HEI Boston, MA.

HEI Panel on the Health Effects of Long-Term Exposure to Traffic-Related Air Pollution, 2022. Systematic Review and Meta-analysis of Selected Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. Special Report 23. Health Effects Institute, Boston, MA.

Karner, A.A., Eisinger, D.S., Niemeier, D.A., 2010. Near-roadway air quality: synthesizing the findings from real-world data. Environ. Sci. Technol. 44 (14), 5334–5344. https://doi.org/10.1021/es100008x.

Lane, K.J., Kangsen Scammell, M., Levy, J.I., Fuller, C.H., Parambi, R., Zamore, W., Brugge, D., 2013. Positional error and time-activity patterns in near-highway proximity studies: an exposure misclassification analysis. Environ. Health 12 (1), 1–14. https://doi.org/10.1186/1476-069X-12-75.

Lane, K.J., Levy, J.I., Scammell, M.K., Patton, A.P., Durant, J.L., Mwamburi, M., Brugge, D., 2015. Effect of time-activity adjustment on exposure assessment for traffic-related ultrafine particles. J. Exposure Sci. Environ. Epidemiol. 25 (5), 506–516. https://doi.org/10.1038/jes.2015.11.

Lane, K.J., Levy, J.I., Scammell, M.K., Peters, J.L., Patton, A.P., Reisner, E., Brugge, D., 2016. Association of modeled long-term personal exposure to ultrafine particles with inflammatory and coagulation biomarkers. Environ. Int. 92, 173–182. https://doi.org/10.1016/j.envint.2016.03.013.

Minet, L., Liu, R., Valois, M.-F., Xu, J., Weichenthal, S., Hatzopoulou, M., 2018. Development and comparison of air pollution exposure surfaces derived from on-road mobile monitoring and short-term stationary sidewalk measurements. Environ. Sci. Technol. 52 (6), 3512–3519. https://doi.org/10.1021/acs.est.7b05059.

Ohlwein, S., Kappeler, R., Kutlar Joss, M., Künzli, N., Hoffmann, B., 2019. Health effects of ultrafine particles: a systematic literature review update of epidemiological evidence. Int. J. Public Health 64 (4), 547–559. https://doi.org/10.1007/s00038-019-01202-7.

Ostro, B., Hu, J., Goldberg, D., Reynolds, P., Hertz, A., Bernstein, L., Kleeman, M.J., 2015. Associations of mortality with long-term exposures to fine and ultrafine particles, species and sources: results from the California teachers study cohort. Environ. Health Perspect. 123 (6), 549–556. https://doi.org/10.1289/ehp.1408565.

Padró-Martínez, L.T., Patton, A.P., Trull, J.B., Zamore, W., Brugge, D., Durant, J.L., 2012. 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. 61, 253–264. https://doi.org/10.1016/j.atmosenv.2012.06.088.

Panis, L.I., 2010. New directions: air pollution epidemiology can benefit from activity-based models. Atmos. Environ. 44 (7), 1003–1004. https://doi.org/10.1016/j.atmosenv.2009.10.047.

Patton, A.P., Collins, C., Naumova, E.N., Zamore, W., Brugge, D., Durant, J.L., 2014. An hourly regression model for ultrafine particles in a near-highway urban area. Environ. Sci. Technol. 48 (6), 3272–3280. https://doi.org/10.1021/es404838k.

Patton, A.P., Perkins, J., Zamore, W., Levy, J.I., Brugge, D., Durant, J.L., 2014. Spatial and temporal differences in traffic-related air pollution in three urban neighborhoods near an interstate highway. Atmos. Environ. 99, 309–321. https://doi.org/10.1016/j.atmosenv.2014.09.072.

Patton, A.P., Zamore, W., Naumova, E.N., Levy, J.I., Brugge, D., Durant, J.L., 2015. Transferability and generalizability of regression models of ultrafine particles in urban neighborhoods in the Boston area. Environ. Sci. Technol. 49 (10), 6051–6060. https://doi.org/10.1021/es5061676.

Environmental Protection Agency Scientific Advisory BoardAB, 2018. https://yosemite.epa.gov/sab/sabproduct.nsf/0/932D1DF8C2A9043F852581000048170D/$File/PM-1STERD-OCT2018.PDF Retrieved from https://yosemite.epa.gov/sab/sabproduct.nsf/0/932D1DF8C2A9043F852581000048170D/$File/PM-1STERD-OCT2018.PDF.

Simon, M.C., Patton, A.P., Naumova, E.N., Levy, J.I., Kumar, P., Brugge, D., Durant, J.L., 2018. Combining measurements from mobile monitoring and a reference site to develop models of ambient ultrafine particle number concentration at residences. Environ. Sci. Technol. 52 (12), 6985–6995. https://doi.org/10.1021/acs.est.8b00292.

Tomarken, A.J., Waller, N.G., 2005. Structural equation modeling: strengths, limitations, and misconceptions. Annu. Rev. Clin. Psychol. 1, 31–65. https://doi.org/10.1146/annurev.clinpsy.1.102803.144239.

Weichenthal, S., Bai, L., Hatzopoulou, M., Van Ryswyk, K., Kwong, J.C., Jerrett, M., Lu, H., 2017. Long-term exposure to ambient ultrafine particles and respiratory disease incidence in in Toronto, Canada: a cohort study. Environ. Health 16 (1), 1–11. https://doi.org/10.1186/s12940-017-0276-7.