Published in final edited form as:

J Expo Sci Environ Epidemiol. 2018 June ; 28(4): 371–380. doi:10.1038/s41370-018-0025-1.

Contribution of the in-vehicle microenvironment to individual ambient-source nitrogen dioxide exposure: the Multi-Ethnic Study of Atherosclerosis and Air Pollution

Marnie F. Hazlehurst, MS¹, Elizabeth W. Spalt, MS¹, Tyler P. Nicholas, MS¹, Cynthia L. Curl, PhD², Mark E. Davey, MBA¹, Gregory L. Burke, MD³, Karol E. Watson, MD⁴, Sverre Vedal, MD¹, and Joel D. Kaufman, MD^{1,5,6}

¹Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA

²Department of Community and Environmental Health, Boise State University, Boise, ID, USA

³Division of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA

⁴Department of Medicine/Cardiology, University of California Los Angeles, Los Angeles, CA, USA

⁵Department of Medicine, University of Washington, Seattle, WA, USA

⁶Department of Epidemiology, University of Washington, Seattle, WA, USA

Abstract

Exposure estimates that do not account for time in-transit may underestimate exposure to traffic-related air pollution, but exact contributions have not been studied directly. We conducted two-week monitoring, including novel in-vehicle sampling, in a subset of the Multi-Ethnic Study of Atherosclerosis and Air Pollution cohort in two cities. Participants spent the majority of their time indoors and only 4.4% of their time (63 min/day) in-vehicle, on average. The mean ambient-source NO₂ concentration was 5.1 ppb indoors and 32.3 ppb in-vehicle during drives. On average, indoor exposure contributed 69% and in-vehicle exposure contributed 24% of participants' ambient-source NO₂ exposure. For participants in the highest quartile of time in-vehicle (1.3 hrs/day), indoor and in-vehicle contributions were 60% and 31%, respectively. Incorporating infiltrated indoor and measured in-vehicle NO₂ produced exposure estimates 5.6 ppb lower, on average, than using only outdoor concentrations. The indoor microenvironment accounted for the largest proportion of ambient-source exposure in this older population, despite higher concentrations of NO₂ outdoors and in vehicles than indoors. In-vehicle exposure was more influential among participants who drove most and for participants residing in areas with lower outdoor air pollution. Failure to characterize exposures in these microenvironments may contribute to exposure misclassification in epidemiologic studies.

Users may view, print, copy, and download text and data-mine the content in such documents, for the purposes of academic research, subject always to the full Conditions of use: http://www.nature.com/authors/editorial_policies/license.html#terms

Corresponding author. Joel Kaufman, joelk@uw.edu, 4225 Roosevelt Way NE, Suite 302, Seattle, WA 98105.

Supplementary information is available at the Journal of Exposure Science and Environmental Epidemiology's website.

Conflict of interest: The authors declare no conflict of interest.

Keywords

traffic-related air pollution; microenvironment; in-vehicle exposure

INTRODUCTION

Accurate exposure assessment remains a central challenge in large epidemiologic studies investigating the health effects of ambient air pollution exposure. Long-term monitoring at the individual level is not feasible on such a scale and thus studies rely on surrogate measures to estimate individual exposure to air pollution. Typical measures include city-wide averages based on centrally located monitors, distance from residences to the nearest major roadways, or modeled outdoor concentrations at residences.^{1–8} However, environmental exposures such as air pollution can vary greatly among different microenvironments.^{9–12} People spend the majority of their time indoors and thus the indoor microenvironment is particularly important.^{13–16} To better account for this microenvironment, the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) improved estimates of individual exposure by developing and incorporating modeled particulate infiltration into residences.^{17–20} Yet even these improved estimates including indoor exposures do not account for another potentially important microenvironment: inside motor vehicles.

Concentrations of traffic-related air pollution (TRAP) can be much higher on the roadway and inside motor vehicles than at residential locations.^{21–23} Despite the limited time spent in-vehicle relative to indoors, exposures in this microenvironment may comprise a large proportion of individual exposure to air pollution,^{24,25} and if so, exposure estimates not accounting for time spent in-transit may underestimate exposure to TRAP. Though TRAP includes mixtures of many pollutants, nitrogen dioxide (NO₂) is often used as a surrogate marker of TRAP. NO₂ is also of interest because it is designated by the US EPA as a criteria air pollutant and is associated with a number of health effects including cardiovascular disease.^{26,27}

Given the challenge of accurate exposure assessment and the potential impact of in-vehicle exposures, the primary aim of this study was to quantify the contribution of time spent in the in-vehicle microenvironment to individual exposure to ambient source NO₂. We hypothesized that, although most participants spend only a small portion of their time in-transit, the in-vehicle microenvironment may still substantially contribute to overall exposure to NO₂, and that the magnitude of this contribution may vary by factors such as city and season. We conducted monitoring campaigns with air pollution sampling and intensive time-location assessment to test this hypothesis.

METHODS

A subset of the MESA Air cohort participated in two-week monitoring campaigns. These campaigns were conducted during summer and winter in Winston-Salem, NC in 2013 (n=64) and in Los Angeles, CA in 2014 (n=64). During each monitoring campaign, samplers

were deployed over the course of six consecutive days and then collected after two weeks of monitoring.

Study population

Selection and recruitment of the MESA Air cohort has been described in detail elsewhere.^{19,28} Briefly, MESA Air is an ancillary study to the Multi-Ethnic Study of Atherosclerosis (MESA), which enrolled participants aged 45–84 who were free of recognized cardiovascular disease at baseline (2000–2002). MESA targeted four racial/ethnic groups for inclusion: white, black, Hispanic, and Chinese. The 128 participants included in this in-vehicle study met the following criteria: previously consented to be contacted about participating in monitoring studies, English-speaking, reported owning and driving a car as their primary mode of transportation, reported driving on average at least 30 minutes per day, non-smoking, not living with any smokers, and not planning to spend multiple nights away from home during the sampling period. All study participants gave informed written consent before data collection and all of the participating centers' institutional review boards approved the study.

Outdoor concentrations of NO₂

Residential indoor and outdoor, in-vehicle, and personal air monitoring was conducted to measure concentrations of NO₂ in each microenvironment. Two-week integrated samples were collected using Ogawa passive samplers (Ogawa & Co., Pompano Beach, FL) and analyzed using ion chromatography.

Ambient-source indoor concentrations of NO₂

As we were interested solely in the ambient-source portion of indoor air pollution, we used a literature-derived estimate of infiltration to estimate the proportion of the outdoor NO₂ concentration that infiltrates inside the residence. This indoor to outdoor (I/O) ratio includes a city- and season-specific air exchange rate (AER), a building fabric filtration factor (f)⁹ of 1.00 which reflects the ability of gases to penetrate the building envelope due to natural ventilation, and a decay rate of NO₂ (K)¹⁰ of 0.99 h⁻¹, and is calculated using:

$$I/O = (AER \times f)/(K + AER)$$

Based on the literature, AERs of 0.81 and 0.36 were used in Winston-Salem for winter and summer, respectively.²⁹ AERs of 0.61 and 1.13 were used in Los Angeles for winter and summer, respectively.³⁰ The literature-derived ratios were compared to the observed indoor to outdoor ratio in homes with no reported indoor sources of NO₂.

Indoor sources of NO₂ such as gas appliances and relevant housing characteristics such as the presence of an attached garage were collected via questionnaire at the start of each monitoring period. Measured residential indoor concentrations of NO₂ in homes with no reported indoor sources were only used to calculate an observed indoor-outdoor ratio (n=8 and n=5 in winter and summer in Winston-Salem, respectively, and n=2 in winter in Los Angeles).

In-vehicle concentrations of NO₂

A novel in-vehicle sampler was also placed in each participant's primary vehicle. Participants were instructed to open the in-vehicle sampler before driving and close the sampler at the conclusion of their drive, so the sampler was only open while the participant was in the vehicle. Additionally, participants were asked to take the sampler with them if they traveled in a different vehicle.

These novel samplers sealed tightly when closed, and were designed to minimize empty space while still providing room for the passive air samplers to be exposed when the housing of the sampler was open. Given these design considerations, 350 mL of dead space remained inside the canister upon closure. The Ogawa sampler inside of the canister continued to sample the NO₂ from the trapped air in this dead space until all NO₂ was consumed. This was confirmed using laboratory tests with known levels of NO₂, which indicated that the Ogawa badge was absorbing NO₂ from the air inside the canister after the canister was closed (Table S3). To account for this additional sampling occurring upon each closure of the canister, we calculated an effective sampling rate assuming a high affinity of the sorbent for NO₂ (see equation in supplement). This simplified sampling rate assumed concentration independence and was calculated using the molecular weight of NO₂ and molar volume of air at standard temperature and pressure and assuming a relative humidity of 43%. Given the 350 mL volume of air trapped in the canister, we estimated that it would take 40.2 minutes for all of the NO₂ to be absorbed. When calculating NO₂ vehicle concentrations, the aggregate sampling time included this additional sampling time for each opening and closure of the canister.

Two-week time-location measurements

During each of the sampling periods, participants were asked to complete two methods of intensive location tracking: carrying a GPS unit and filling out Time-Location Diaries (TLDs). Participants were instructed to carry a customized 747ProS GPS Data Logger unit (G&V Global Tech Co., LTD, Taipei City, Taiwan) whenever they left the house. Participants were also instructed to fill out a TLD providing specific location information categorizing locations as home indoors, home outdoors, other indoors, other outdoors, and in-vehicle, throughout each day of the monitoring period. Time-location patterns measured by these two methods were integrated to capitalize on their respective strengths.³¹ GPS data were used to classify time as in-vehicle, at home, or in other locations, and time at home and in other locations was further divided into indoor and outdoor using proportions reported in the TLDs. Ultimately, the analysis of GPS and TLD data yielded a single estimate of time spent in each of three types of microenvironments: indoors, outdoors, and in-vehicle.

Additionally, participants provided information on the TLDs about transit-related activities such as traffic conditions, road type, and open vehicle windows. Specific information about the make, model, and year of the primary and secondary vehicles was collected via questionnaire at the start of each monitoring period.

Data Analysis

Overall individual exposure to ambient-source NO₂ was calculated by summing exposures from three microenvironments—indoors, outdoors, and in-vehicle—using a simple time-weighted model.

$$\text{Total Individual Exposure} = \text{Exposure}_{\text{outdoor}} + \text{Exposure}_{\text{indoor}} + \text{Exposure}_{\text{vehicle}}$$

$$\text{Exposure}_{\text{outdoor}} = (t_{\text{outdoor}} * [\text{NO}_2]_{\text{outdoor}}) / t_{\text{total}}$$

$$\text{Exposure}_{\text{indoor}} = (I/O * t_{\text{indoor}} * [\text{NO}_2]_{\text{outdoor}}) / t_{\text{total}}$$

$$\text{Exposure}_{\text{vehicle}} = (t_{\text{vehicle}} * [\text{NO}_2]_{\text{vehicle}}) / t_{\text{total}}$$

The proportional contributions of each of the three microenvironments to overall individual exposure to ambient-source NO₂ were compared with a focus on the relative importance of the in-vehicle environment.

RESULTS

Characteristics of the subset of MESA Air participants who participated in each two-week monitoring campaign, as well as characteristics of the entire MESA Air cohort, are shown in Table 1. Each subset included a similar proportion of female participants as the entire cohort, except for the Los Angeles summer campaign, which included a higher proportion of male participants. Chinese-Americans were under-represented in the monitoring subset, in part because Chinese-Americans were not recruited in Winston-Salem in the overall cohort. The median age was lower in the Los Angeles subset than in the Winston-Salem subset.

Only a small number of homes did not have NO₂ sources identified during each monitoring campaign (n=8 and n=5 in winter and summer in Winston-Salem, respectively, and n=2 in winter in Los Angeles); no homes during the Los Angeles summer campaign had zero indoor NO₂ sources identified. However, even with these small sample sizes, the observed I/O ratios were similar to the literature-based ratio in both cities (Table 2). The literature-based I/O ratios used in this analysis were 0.45 in winter and 0.27 in summer in Winston-Salem, and 0.38 in winter and 0.53 in summer in Los Angeles. The mean observed I/O ratios for without indoor sources were 0.43, 0.37, and 0.49 during monitoring in winter and summer in Winston-Salem and winter in Los Angeles, respectively. In contrast, the mean observed I/O ratios for homes with indoor sources ranged from 1.2 during the winter monitoring in Los Angeles to 2.6 during the summer monitoring in Winston-Salem.

Concentrations of NO₂ were highest in-vehicle and lowest indoors during each monitoring campaign, while participants spent the majority of their time indoors and on average only 4 to 5% (approximately 1 hr/day) of their time in a motorized vehicle (Table 3). As expected,

NO₂ concentrations were on average higher in Los Angeles compared to Winston-Salem and tended to be higher outdoors during the winter campaigns than the summer campaigns. Average in-vehicle concentrations of NO₂ ranged from 23.0 ppb in summer in Winston-Salem to 38.2 ppb in winter in Los Angeles. The average time per trip was similar across cities (28 minutes). Participants drove on average 27% percent of their trips on major roads (defined as freeways, expressways, highways, or toll roads), and 21% percent of their trips in heavy traffic, with participants in Los Angeles reporting driving more on major roads and in heavy traffic than participants in Winston-Salem.

The indoor microenvironment contributed the highest proportion of individual exposure to ambient-source NO₂ (Figure 1) compared to the other two microenvironments monitored in this study, ranging from 53% in Winston-Salem in the summer to 75% in Los Angeles in the winter. However, the in-vehicle microenvironment contributed a larger proportion of exposure than the outdoor microenvironment, overall: 21%, 40%, 17%, and 18% from the in-vehicle microenvironment on average in Winston-Salem in the winter and summer, and Los Angeles in the winter and summer, respectively. Among participants who drove at least 1.3 hours per day (i.e. the highest quartile of time in-vehicle in this sample) during the sampling period, the in-vehicle microenvironment contributed a larger proportion than among those participants who drove less (Figure 2). For these participants, in Winston-Salem in the winter and summer, and in Los Angeles in the winter and summer, the average contribution of the in-vehicle microenvironment to the overall exposure was 34%, 56%, 23%, and 21%, respectively.

Estimates of total ambient-source NO₂ exposure using only outdoor NO₂ concentrations were highest compared to estimates incorporating ambient-source indoor or in-vehicle concentrations (Table 4). Estimates using infiltrated indoor concentrations in addition to outdoor concentrations were on average 6.4 ppb lower (standard deviation 3.8 ppb) than estimates using only outdoor concentrations. Incorporating both infiltrated indoor and measured in-vehicle concentrations resulted in exposure estimates on average 5.6 ppb lower (standard deviation 4.0 ppb) than estimates using only outdoor concentrations. Larger absolute differences in the exposures calculated using information from indoor and in-vehicle microenvironments compared to those only using outdoor concentrations, were observed in winter compared to summer and in Los Angeles compared to Winston-Salem. Among the participants in the highest quartile of time spent in-vehicle (at least 1.3 hrs/day in this sample), incorporating in-vehicle exposures resulted in higher estimates than among those who drove less.

We also conducted a sensitivity analysis in which we used lower and higher AER values from the literature.^{29,30,32} The contribution of indoor infiltration of ambient NO₂ to overall exposure ranged from an average of 53% during summer in Winston-Salem using the lowest AER to an average of 84% during winter in Los Angeles using the highest AER (see Table S2). Even with the lowest AER, the indoor contribution to total exposure remained higher on average than the in-vehicle contribution.

DISCUSSION

Using novel in-vehicle samplers deployed concurrently with indoor and outdoor monitors, this study demonstrated the importance of the in-vehicle and indoor microenvironments for accurate exposure characterization. The in-vehicle microenvironment, on average, contributed more to overall exposure to NO₂ than the outdoor microenvironment. However, exposure indoors to NO₂ originating outdoors accounted for the majority of ambient-source NO₂ exposure within this older population.

A limited number of studies have investigated the role of the in-vehicle microenvironment in overall exposure,³³ with some relying on modeled commute exposures rather than measured in-vehicle concentrations.³⁴ A study in Barcelona found that in-vehicle exposures may contribute up to 24% of overall NO₂ exposure, even for participants spending on average only 6% of time in-vehicle,³⁵ which is a similar finding to the current study. The in-vehicle microenvironment may contribute to measurement error in exposure assessment, particularly among those who travel most and in areas where the outdoor levels of air pollution are generally low.^{33,36}

Indoor concentrations were the largest contributor to overall individual exposure, particularly in the city with the highest outdoor concentrations, and thus focus on improved estimation of ambient-source indoor exposures is warranted. Studies in a variety of U.S. cities have examined the effect of various housing characteristics on AERs^{29,30,37,38} and I/O ratios of NO₂,³⁹ and report AERs ranging from 0.36 h⁻¹ in North Carolina during the summer²⁹ to 1.92 h⁻¹ in Michigan during the summer.³⁰ In a sensitivity analysis, variation in AER altered the proportion of overall exposure due to the indoor microenvironment, though even with the lowest AER the mean contribution of the indoor microenvironment remained greater than 50%. Differences in AER are attributed to meteorological conditions including wind speed, indoor versus outdoor temperature differences, and humidity, as well as housing ventilation choices such as open windows versus air conditioning.^{29,30,37} Such characteristics may be important to consider in further characterizing air pollution exposure variability to reduce measurement error.

While some evidence suggests that ignoring in-vehicle exposure may contribute to bias in epidemiologic studies,^{40–42} others have found only a small contribution from the in-vehicle microenvironment and suggest that the indoor microenvironment may be the most important source of measurement error in air pollution epidemiology.^{43,44} Epidemiologic studies have most often used modeled outdoor concentrations at the residential location, which may overestimate overall exposure as shown in the current study. Future studies may reduce bias by accounting for exposure magnitude and variability related to the indoor and in-vehicle microenvironments.

The measurement error contributed to epidemiological studies by ignoring high exposures from in-vehicle microenvironments could bias results. If exposure assessment systematically underestimates variation in exposure across study participants, the main effect would be over-estimation of the concentration-response slope. If exposure assessment misclassifies exposure in a random way, the effect will typically (although not always) be biased toward

the null and underestimation of uncertainty in the concentration-response relationship. If the misclassification is correlated with the outcome or other predictors of outcome, the effect may be confounded and could be either over- or under-estimated. It is difficult to predict which of these is most likely.⁴⁵

The in-vehicle concentrations measured in this study (overall median two-week NO₂ concentration: 30.4 ppb) are consistent with near-roadway regulatory monitoring in California; no near-roadway sites have been established in Winston-Salem. Specifically, at the designated near-roadway regulatory site in Los Angeles County, which was intentionally located near a major roadway with heavy traffic, the annual average NO₂ concentration in 2015 was 23.9 ppb.⁴⁶

The concentrations measured in this study are also consistent with prior literature examining NO₂ concentrations inside of vehicles. However, most studies of adults utilized occupational settings such as patrol cars⁴⁷ and taxis,^{33,48–50} or scripted drive protocols.^{23,51} Furthermore, only a small number of these studies were conducted in North America.^{21,23,47,51} The earliest of these studies, conducted in Raleigh, NC in 1988, reported a median in-vehicle NO₂ concentration of 43.1 ppb during scripted drives in both the morning and evening rush hour.²¹ In patrol cars during 3pm to 12am shifts in and around Raleigh, NC, the median concentration was 22.2 ppb.⁴⁷ The median NO₂ concentration measured inside the vehicle during scripted drives primarily on the New Jersey Turnpike during morning commute hours was 20.6 ppb⁵¹ and in three Canadian cities during three hour commutes was 39.0 ppb.²³ Most prior studies monitored NO₂ for a limited amount of time (e.g. only during rush hour or only during some shifts) or on small number of days. Our study builds upon this literature by implementing in-vehicle monitoring in a population—selected for reasons other than occupational exposures—who were instructed to go about their usual activities (un-scripted) over a two-week period in two distinct cities.

While this study expanded on prior work to understand the influence of in-vehicle exposures by implementing a novel sampling campaign, it was also subject to several limitations. First, this population is a sample of older adults, only about half of whom are employed, and thus their driving habits, time-location patterns, and exposures while driving may limit generalizability to younger populations. Second, limitations in the passive sampling equipment due to the unscripted nature of this study and requirement for ease of use by participants, required additional post-hoc adjustments to calculate in-vehicle concentrations of air pollutants. We assumed that the in-vehicle NO₂ concentration at the end of each trip was equal to the trip average, though it is possible that this assumption was not correct in each case. The adjustments also assumed a concentration-independent sampling rate within the closed in-vehicle sampler and thus are likely an oversimplification. Third, we used NO₂ as a marker for the suite of potential air pollutants associated with traffic proximity. It is possible that NO₂ is not a perfect indicator. For example, non-reactive pollutants such as carbon monoxide or volatile organic compounds such as 1,3 butadiene, may have higher contributions from in-vehicle exposures.

Even given the limitations mentioned above, this study deployed a novel sampling design to measure NO₂ as a marker of TRAP in an older population with well-characterized time-

activity patterns. In-vehicle concentrations were relatively similar across cities, but outdoor and infiltrated indoor concentrations varied substantially. Therefore, resulting in-vehicle exposures made up a larger proportion of overall NO₂ exposure in the city with lower outdoor air pollution levels and lower air exchange rates (i.e., in Winston-Salem, compared to Los Angeles). This study suggests that while in-vehicle exposure is an important component of overall individual-level NO₂ exposure, overall exposure in this older population is largely determined by ambient-source exposure inside the residence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This publication was developed under a STAR research assistance agreement, No. RD831697 (MESA Air), and RD83479601-01 (UW CCAR), awarded by the U.S Environmental Protection Agency and NIH NIEHS R01ES023500 (SPIROMICS Air). It has not been formally reviewed by the EPA. The views expressed in this document are solely those of the authors and the EPA does not endorse any products or commercial services mentioned in this publication.

References

1. Dockery DW, Pope CA 3rd, Xu X, Spengler JD, Ware JH, Fay ME, et al. An association between air pollution and mortality in six U.S. cities. *N Engl J Med.* 1993; 329:1753–1759. [PubMed: 8179653]
2. 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.* 2007; 356:447–458. [PubMed: 17267905]
3. Pope CA 3rd, Burnett RT, Thun MJ, Calle EE, Krewski D, Thurston GD, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA.* 2002; 287:1132–41. [PubMed: 11879110]
4. Hoek G, Brunekreef B, Goldbohm S, Fischer P, Van Den Brandt PA. Association between mortality and indicators of traffic-related air pollution in the Netherlands: A cohort study. *Lancet.* 2002; 360:1203–1209. [PubMed: 12401246]
5. Ostro B, Lipsett M, Reynolds P, Goldberg D, Hertz A, Garcia C, et al. Long-term exposure to constituents of fine particulate air pollution and mortality: Results from the California Teachers Study. *Environ Health Perspect.* 2010; 118:363–369. [PubMed: 20064787]
6. Gehring U, Heinrich J, Kramer U, Grote V, Hochadel M, Sugiri D, et al. Long-term exposure to ambient air pollution and cardiopulmonary mortality in women. *Epidemiology.* 2006; 17:545–51. [PubMed: 16755270]
7. Rosenlund M, Berglund N, Pershagen G, Hallqvist J, Jonson T, Bellander T. Long-term exposure to urban air pollution and myocardial infarction. *Epidemiology.* 2006; 17:383–390. [PubMed: 16699471]
8. Puett RC, Hart JE, Yanosky JD, Paciorek C, Schwartz J, Suh H, et al. Chronic fine and coarse particulate exposure, mortality, and coronary heart disease in the Nurses' Health Study. *Environ Health Perspect.* 2009; 117:1697–1701. [PubMed: 20049120]
9. Dimitroulopoulou C, Ashmore M, Byrne M, Kinnersley R. Modelling of indoor exposure to nitrogen dioxide in the UK. *Atmos Environ.* 2001; 35:269–279.
10. Yamanaka S. Decay Rates of Nitrogen Oxides in a Typical Japanese Living Room. *Environ Sci Technol.* 1985; 18:566–570.
11. Lee K, Xue J, Geyh AS, Özkaynak H, Leaderer BP, Weschler CJ, et al. Nitrous acid, nitrogen dioxide, and ozone concentrations in residential environments. *Environ Health Perspect.* 2002; 110:145–149.

12. Lee K, Levy JI, Yanagisawa Y, Spengler JD, Billick IH. The Boston residential nitrogen dioxide characterization study: classification and prediction of indoor NO₂ exposure. *J Air Waste Manag Assoc.* 1998; 48:736–742. [PubMed: 9739626]
13. Graham SE, McCurdy T. Developing meaningful cohorts for human exposure models. *J Expo Anal Environ Epidemiol.* 2004; 14:23–43. [PubMed: 14726943]
14. Leech JA, Nelson WC, Burnett RT, Aaron S, Raizenne ME. It's about time: a comparison of Canadian and American time-activity patterns. *J Expo Anal Environ Epidemiol.* 2002; 12:427–432. [PubMed: 12415491]
15. US EPA. U.S. EPA Exposure Factors Handbook 2011 Edition (Final Report). Washington, DC: 2011. <https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252>
16. US EPA. Descriptive Statistics Tables from a Detailed Analysis of the National Human Activity Pattern Survey (NHAPS) Data. Las Vegas, NV: 1996.
17. Allen RW, Adar SD, Avol E, Cohen M, Curl CL, Larson T, et al. Modeling the residential infiltration of outdoor PM_{2.5} in the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *Environ Health Perspect.* 2012; 120:824–830. [PubMed: 22534026]
18. Cohen MA, Adar SD, Allen RW, Avol E, Curl CL, Gould T, et al. Approach to estimating participant pollutant exposures in the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *Environ Sci Technol.* 2009; 43:4687–4693. [PubMed: 19673252]
19. Kaufman JD, Adar SD, Allen RW, Barr RG, Budoff MJ, Burke GL, et al. Prospective study of particulate air pollution exposures, subclinical atherosclerosis, and clinical cardiovascular disease: The Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *Am J Epidemiol.* 2012; 176:825–37. [PubMed: 23043127]
20. Kaufman JD, Adar SD, Barr RG, Budoff M, Burke GL, Curl CL, et al. Association between air pollution and coronary artery calcification within six metropolitan areas in the USA (the Multi-Ethnic Study of Atherosclerosis and Air Pollution): a longitudinal cohort study. *Lancet.* 2016; 6736:1–9.
21. Chan CC, Ozkaynak H, Spengler JD, Sheldon L. Driver exposure to volatile organic compounds, CO, ozone, and NO₂ under different driving conditions. *Env Sci Technol.* 1991; 25:964–972.
22. Westerdahl D, Fruin S, Sax T, Fine PM, Sioutas C. Mobile platform measurements of ultrafine particles and associated pollutant concentrations on freeways and residential streets in Los Angeles. *Atmos Environ.* 2005; 39:3597–3610.
23. Weichenthal S, Van Ryswyk K, Kulka R, Sun L, Wallace L, Joseph L. In-vehicle exposures to particulate air pollution in Canadian Metropolitan areas: The urban transportation exposure study. *Environ Sci Technol.* 2015; 49:597–605. [PubMed: 25469563]
24. Baxter LK, Dionisio KL, Burke J, Ebelt Sarnat S, Sarnat JA, Hodas N, et al. Exposure prediction approaches used in air pollution epidemiology studies: key findings and future recommendations. *J Expo Sci Environ Epidemiol.* 2013; 23:654–9. [PubMed: 24084756]
25. Ragettli MS, Tsai MY, Braun-Fahrlander C, de Nazelle A, Schindler C, Ineichen A, et al. Simulation of population-based commuter exposure to NO₂ using different air pollution models. *Int J Environ Res Public Health.* 2014; 11:5049–5068. [PubMed: 24823664]
26. Kunzli N, Kaiser R, Medina S, Studnicka M, Chanel O, Filliger P, et al. Public-health impact of outdoor and traffic-related air pollution: A European assessment. *Lancet.* 2000; 356:795–801. [PubMed: 11022926]
27. Frampton MW, Boscia J, Roberts NJ, Azadniv M, Torres A, Cox C, et al. Nitrogen dioxide exposure: effects on airway and blood cells. *Am J Physiol Lung Cell Mol Physiol.* 2002; 282:L155–L165. [PubMed: 11741827]
28. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, et al. Multi-Ethnic Study of Atherosclerosis: Objectives and design. *Am J Epidemiol.* 2002; 156:871–881. [PubMed: 12397006]
29. Breen MS, Breen M, Williams RW, Schultz BD. Predicting residential air exchange rates from questionnaires and meteorology: Model evaluation in central North Carolina. *Environ Sci Technol.* 2010; 44:9349–9356. [PubMed: 21069949]
30. Isaacs K, Burke J, Smith L, Williams R. Identifying housing and meteorological conditions influencing residential air exchange rates in the DEARS and RIOPA studies: development of

distributions for human exposure modeling. *J Expo Sci Environ Epidemiol*. 2013; 23:248–258. [PubMed: 23443234]

31. Hazlehurst MF, Spalt EW, Curl CL, Davey ME, Vedal S, Burke GL, et al. Integrating data from multiple time-location measurement methods for use in exposure assessment: the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *J Expo Sci Environ Epidemiol*. 2017:1–6.
32. Sherman M, McWilliams J. Air Leakage of U.S. Homes: Model Prediction. 2007
33. Son B, Yang W, Breyse P, Chung T, Lee Y. Estimation of occupational and nonoccupational nitrogen dioxide exposure for Korean taxi drivers using a microenvironmental model. *Environ Res*. 2004; 94:291–296. [PubMed: 15016597]
34. de Nazelle A, Seto E, Donaire-Gonzalez D, Matamala J, Nieuwenhuijsen MJ, Jerrett M. Improving estimates of air pollution exposure through ubiquitous sensing technologies. *Environ Pollut*. 2014:92–99.
35. de Nazelle A, Fruin S, Westerdahl D, Martinez D, Ripoll A, Kubesch N, et al. A travel mode comparison of commuters' exposures to air pollutants in Barcelona. *Atmos Environ*. 2012; 59:151–159.
36. Gurram S, Stuart AL, Pinjari AR. Impacts of travel activity and urbanicity on exposures to ambient oxides of nitrogen and on exposure disparities. *Air Qual Atmos Heal*. 2015; 8:97–114.
37. Yamamoto N, Shendell DG, Winer aM, Zhang J. Residential air exchange rates in three major US metropolitan areas: Results from the Relationship among Indoor, Outdoor, and Personal Air Study 1999–2001. *Indoor Air*. 2010; 20:85–90. [PubMed: 19874401]
38. Breen MS, Burke JM, Batterman SA, Vette AF, Godwin C, Croghan CW, et al. Modeling spatial and temporal variability of residential air exchange rates for the Near-Road Exposures and Effects of Urban Air Pollutants Study (NEXUS). *Int J Environ Res Public Health*. 2014; 11:11481–11504. [PubMed: 25386953]
39. Lee JY, Ryu SH, Kim CH, Bae G-N, et al. Indoor-to-outdoor pollutant concentration ratio modeling of CO₂, NO₂, and lung-deposited nanoparticles. *Atmos Pollut Res*. 2016; doi: 10.1016/j.apr.2016.02.007
40. Setton E, Marshall JD, Brauer M, Lundquist KR, Hystad P, Keller P, et al. The impact of daily mobility on exposure to traffic-related air pollution and health effect estimates. *J Expo Sci Environ Epidemiol*. 2011; 21:42–48. [PubMed: 20588325]
41. Williams R, Jones P, Croghan C, Thornburg J, Rodes C. The influence of human and environmental exposure factors on personal NO₂ exposures. *J Expo Sci Environ Epidemiol*. 2012; 22:109–15. [PubMed: 21540887]
42. Stroh E, Rittner R, Oudin A, Ardö J, Jakobsson K, Björk J, et al. Measured and modeled personal and environmental NO₂ exposure. *Popul Health Metr*. 2012; 10:10. [PubMed: 22681784]
43. Ragettli MS, Phuleria HC, Tsai M-Y, Schindler C, de Nazelle A, Ducret-Stich RE, et al. The relevance of commuter and work/school exposure in an epidemiological study on traffic-related air pollution. *J Expo Sci Environ Epidemiol*. 2015; 25:474–81. [PubMed: 25492241]
44. Baxter LK, Burke J, Lunden M, Turpin BJ, Rich DQ, Thevenet-Morrison K, et al. Influence of human activity patterns, particle composition, and residential air exchange rates on modeled distributions of PM_{2.5} exposure compared with central-site monitoring data. *J Expo Sci Environ Epidemiol*. 2013; 23:241–247. [PubMed: 23321856]
45. Sheppard L, Burnett RT, Szpiro AA, Kim S, Jerrett M, Iii CAP, et al. Confounding and exposure measurement error in air pollution epidemiology. 2012:203–216.
46. South Coast AQMD. 2016 Air Quality Management Plan. 2016. <http://www.aqmd.gov/docs/default-source/clean-air-plans/air-quality-management-plans/2016-air-quality-management-plan/final-2016-aqmp/final2016aqmp.pdf?sfvrsn=15>
47. Riediker M, Williams R, Devlin R, Griggs T, Bromberg P. Exposure to particulate matter, volatile organic compounds, and other air pollutants inside patrol cars. *Environ Sci Technol*. 2003; 37:2084–2093. [PubMed: 12785511]
48. Lewné M, Plato N, Gustavsson P. Exposure to particles, elemental carbon and nitrogen dioxide in workers exposed to motor exhaust. *Ann Occup Hyg*. 2007; 51:693–701. [PubMed: 17921238]
49. Farrar D, Dingle P, Tan R. Exposure to nitrogen dioxide in buses, taxis, and bicycles in Perth, Western Australia. *Bull Environ Contam Toxicol*. 2001; 66:433–438. [PubMed: 11443303]

50. Zagury E, Le Moullec Y, Momas I. Exposure of Paris taxi drivers to automobile air pollutants within their vehicles. *Occup Environ Med.* 2000; 57:406–410. [PubMed: 10810130]
51. Patton AP, Laumbach R, Ohman-Strickland P, Black K, Alimokhtari S, Lioy PJ, et al. Scripted drives: A robust protocol for generating exposures to traffic-related air pollution. *Atmos Environ.* 2016; 143:290–299.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.

Percent contribution of each microenvironment—indoor, outdoor, and in-vehicle—to overall individual exposure to ambient-source NO₂ during each monitoring campaign in Winston-Salem (A) and Los Angeles (B). Gray boxes show the 25th percentile to 75th percentile, the horizontal black bar shows the median, the whiskers show either the minimum or 1.5 times the interquartile range below 25th percentile and either the maximum or 1.5 times the interquartile range above the 75th percentile, and points are outliers.

Figure 2.

Percent contribution of each microenvironment—indoor, outdoor, and in-vehicle—to overall individual exposure to ambient-source NO₂ during each monitoring campaign in Winston-Salem (A) and Los Angeles (B), only for those participants who drove on average at least 1.3 hours per day (i.e. in the highest quartile of time spent in-vehicle, n=38) during the study period. Gray boxes show the 25th percentile to 75th percentile, the horizontal black bar shows the median, the whiskers show either the minimum or 1.5 times the interquartile range below 25th percentile and either the maximum or 1.5 times the interquartile range above the 75th percentile, and points are outliers.

Table 1

Characteristics of the MESA Air cohort and the subset of participants who completed two-week monitoring.

Characteristic	Winston-Salem, NC ¹		Los Angeles, CA ²		Entire MESA Air Cohort ^{3,4} (n=4 920)
	Winter (n=46)	Summer (n=47)	Winter (n=47)	Summer (n=46)	
<i>Sex, n (%)</i>					
Female	25 (54)	23 (51)	24 (51)	19 (41)	2 625 (53)
Male	21 (46)	24 (49)	23 (49)	27 (59)	2 295 (47)
<i>Race/Ethnicity, n (%)</i>					
White	20 (43)	21 (45)	14 (30)	15 (33)	2 055 (42)
Black	26 (57)	26 (55)	9 (19)	5 (15)	1 285 (26)
Chinese	0 (0)	0 (0)	3 (6)	7 (11)	541 (11)
Hispanic	0 (0)	0 (0)	21 (45)	19 (41)	1 039 (21)
<i>Age,⁴ n (%)</i>					
45–54	1 (2)	1 (2)	2 (4)	2 (4)	77 (2)
55–64	9 (20)	14 (30)	21 (45)	16 (34)	1 616 (33)
65–74	18 (39)	19 (40)	16 (34)	21 (45)	1 569 (32)
75–84	15 (33)	12 (26)	8 (17)	6 (13)	1 300 (26)
85+	3 (7)	1 (2)	0 (0)	1 (2)	358 (7)
<i>Median Age⁴</i>	72	69	65	67	69
<i>Age Range⁴</i>					
	54 – 89	54 – 89	54 – 83	54 – 90	53 – 94
<i>Employed,^{4,5} n (%)</i>					
	18 (40)	25 (56)	27 (57)	27 (59)	2 158 (44)

¹Monitoring completed in 2013.

²Monitoring completed in 2014.

³Includes participants in Winston-Salem, NC; Los Angeles, CA; Baltimore, MD; New York City, NY; Chicago, IL; and St. Paul, MN.

⁴ At MESA Exam 5 in 2010–2012.

⁵ Employed outside of the home.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

Observed (mean $\pm$ standard deviation) and literature-based indoor to outdoor (I/O) ratios of NO₂ for each monitoring campaign.

City	Season	N ¹	Observed I/O ratio	Literature-based ² I/O ratio
Winston-Salem	Winter	8	0.43 $\pm$ 0.07	0.45
	Summer	5	0.37 $\pm$ 0.24	0.27
Los Angeles	Winter	2	0.49 $\pm$ 0.02	0.38
	Summer	0	-	0.53

¹Number of participants with no identified indoor sources of NO₂ whose measured NO₂ concentrations were used to calculate the observed I/O ratio.

²Using AERs from Breen *et al* (2010) for Winston-Salem and from Isaacs *et al* (2013) for Los Angeles.^{29,30}

Table 3

Mean $\pm$ standard deviation of NO₂ concentration and percent of time spent in each of three microenvironments—indoors, outdoors, and in-vehicle—during four monitoring campaigns.

City	Season	Microenvironment		
		Indoor ¹	Outdoor	In-vehicle ²
<i>NO₂ Concentration (ppb)</i>				
Winston-Salem	Winter	4.1 ± 1.1	9.3 ± 2.5	30.8 ± 12.8
	Summer	1.4 ± 0.7	5.0 ± 2.8	23.0 ± 14.0
Los Angeles	Winter	7.9 ± 1.7	20.7 ± 4.5	36.6 ± 18.6
	Summer	6.7 ± 1.5	12.6 ± 2.8	38.2 ± 15.0
<i>% Time</i>				
Winston-Salem	Winter	94 ± 4	2 ± 3	4 ± 2
	Summer	92 ± 6	4 ± 4	4 ± 3
Los Angeles	Winter	91 ± 6	4 ± 5	5 ± 2
	Summer	89 ± 8	7 ± 7	4 ± 2

¹Indoor ambient-source NO₂ was calculated using the measured outdoor concentration and literature-based I/O ratio.

²In-vehicle concentrations account for additional sampling time due to air trapped in sampler upon closure.

Table 4

Total individual ambient-source NO₂ exposure calculated using three methods: concentrations measured outdoors only; concentrations outdoors and infiltrated indoors; and concentrations outdoors, infiltrated indoors, and measured in-vehicle.

City and Season	Method	Individual Ambient-Source NO ₂ Exposure (ppb) ¹		
		Overall (N=151)	<1.3 hrs/day driving ² (N=113)	1.3 hrs/day driving ² (N=38)
<i>Winston-Salem</i>				
Winter	O	9.2 ± 2.5	9.4 ± 2.5	8.1 ± 2.7
	O+I	4.5 ± 1.3	4.6 ± 1.2	4.2 ± 1.3
	O+I+V	5.2 ± 1.2	5.2 ± 1.3	5.3 ± 0.8
Summer	O	5.0 ± 2.8	5.3 ± 3.0	4.1 ± 1.5
	O+I	1.6 ± 0.9	1.7 ± 0.9	1.5 ± 0.5
	O+I+V	2.4 ± 1.0	2.2 ± 0.9	2.9 ± 1.3
<i>Los Angeles</i>				
Winter	O	20.7 ± 4.5	20.8 ± 4.6	20.3 ± 4.5
	O+I	9.0 ± 2.2	8.8 ± 2.3	9.3 ± 2.1
	O+I+V	9.6 ± 2.1	9.4 ± 2.2	10.1 ± 1.8
Summer	O	12.6 ± 2.8	12.6 ± 3.0	12.5 ± 2.4
	O+I	7.3 ± 1.7	7.3 ± 1.9	7.5 ± 1.4
	O+I+V	8.3 ± 1.8	8.3 ± 2.1	8.3 ± 1.1

Abbreviations: O = outdoor concentrations only; O+I = outdoor and infiltrated indoor concentrations; O+I+V = outdoor, infiltrated indoor, and measured in-vehicle concentrations.

¹Summary statistics are mean ± standard deviation.

²Participants in the highest quartile of time spent in-vehicle (75th percentile=1.3 hours/day) were compared to those who drove less.