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Blood Pressure Effect of Traffic-Related Air Pollution

A Crossover Trial of In-Vehicle Filtration

Michael T. Young, MPH, PhD; Karen Jansen, MS; Kristen E. Cosselman, PhD, MPA; Timothy R. Gould, MSE; James A. Stewart, MSCE; Timothy Larson, MSCE, PhD; Coralynn Sack, MD, MPH; Sverre Vedal, MD, MSc; Adam A. Szpiro, ScM, PhD; and Joel D. Kaufman, MD, MPH

Background: Ambient air pollution, including traffic-related air pollution (TRAP), increases cardiovascular disease risk, possibly through vascular alterations. Limited information exists about in-vehicle TRAP exposure and vascular changes.

Objective: To determine via particle filtration the effect of on-roadway TRAP exposure on blood pressure and retinal vasculature.

Design: Randomized crossover trial. (ClinicalTrials.gov: NCT05454930)

Setting: In-vehicle scripted commutes driven through traffic in Seattle, Washington, during 2014 to 2016.

Participants: Normotensive persons aged 22 to 45 years ($n = 16$).

Intervention: On 2 days, on-road air was entrained into the vehicle. On another day, the vehicle was equipped with high-efficiency particulate air (HEPA) filtration. Participants were blinded to the exposure and were randomly assigned to the sequence.

Measurements: Fourteen 3-minute periods of blood pressure were recorded before, during, and up to 24 hours after a drive. Image-based central retinal arteriolar equivalents (CRAEs) were measured before and after. Brachial artery diameter and gene expression were also measured and will be reported separately.

Results: Mean age was 29.7 years, predrive systolic blood pressure was 122.7 mm Hg, predrive diastolic blood pressure was 70.8 mm Hg, and drive duration was 122.3 minutes (IQR, 4 minutes). Filtration reduced particle count by 86%. Among persons with complete data ($n = 13$), at 1 hour, mean diastolic blood pressure, adjusted for predrive levels, order, and carryover, was 4.7 mm Hg higher (95% CI, 0.9 to 8.4 mm Hg) for unfiltered drives compared with filtered drives, and mean adjusted systolic blood pressure was 4.5 mm Hg higher (CI, −1.2 to 10.2 mm Hg). At 24 hours, adjusted mean diastolic blood pressure (unfiltered) was 3.8 mm Hg higher (CI, 0.02 to 7.5 mm Hg) and adjusted mean systolic blood pressure was 1.1 mm Hg higher (CI, −4.6 to 6.8 mm Hg). Adjusted mean CRAE (unfiltered) was 2.7 μm wider (CI, −1.5 to 6.8 μm).

Limitations: Imprecise estimates due to small sample size; seasonal imbalance by exposure order.

Conclusion: Filtration of TRAP may mitigate its adverse effects on blood pressure rapidly and at 24 hours. Validation is required in larger samples and different settings.

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Traffic-related air pollution (TRAP) exposure is recognized as a risk factor for cardiovascular disease and other health effects. It has been proposed that the relationship between air pollution exposure and cardiovascular disease is mediated through inflammation and autonomic dysregulation (1). In vivo studies have shown atherosclerotic changes in response to controlled exposure (2–4). Experimental research in humans primarily relies on controlled laboratory exposures with limited generalizability.

In our prior controlled-exposure research, using diesel exhaust as a proxy for TRAP exposure, we observed alterations in blood pressure during and up to 24 hours after exposure (5–7). These and other experimental results suggest acute effects of TRAP-like exposures, but the exposure concentrations typically used in these studies better reflect occupational exposures and are higher than typical concentrations in ambient on-roadway air. In addition, the chemical components and particulate size of the mixtures used are not exact replications of on-roadway ambient air pollution.

TRAP is a complex air pollution mixture generated by roadway sources (vehicle exhaust and brake and tire wear). Pollutants that are commonly measured to characterize TRAP have higher concentrations near roadways and include ultrafine particles; black carbon; oxides of nitrogen; carbon monoxide (CO); carbon dioxide (CO_2); and, to a lesser extent, particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) (8). TRAP is the major source of air pollution contrasts within U.S. metropolitan areas.

In the United States, the average travel time to work for commuters was more than 27 minutes in 2019 (9). Time in traffic is associated with higher pollution exposures and has been observationally associated with increased cardiovascular risk. One study found increased odds of myocardial infarction shortly after exposure to traffic (10), but the observational design was unable to conclusively implicate TRAP in this effect due to the co-occurring traffic exposures of psychological stress and noise.

Scripted commute studies, in which volunteers are driven through traffic, are a novel approach to assess the health effects of air pollution in a realistic setting (11). To

See also:

Web-Only
Supplement

determine real-world acute changes in both blood pressure and retinal arteriolar diameter in response to on-roadway TRAP compared with filtered air, we conducted a double-blind crossover trial of passenger compartment filtration in rush-hour motor vehicle traffic.

METHODS

Design Overview

The trial was a randomized crossover trial of in-vehicle filtration during a scripted commute. Participants were randomly assigned to the order of exposures, and participants and the study coordinator were blinded to exposure status. Drives occurred during the period from November 2014 to July 2016.

The protocol was finalized before study initiation and was not modified except as described in this article. Although this environmental intervention study was not a typical clinical trial as usually contemplated by trial registration programs at the time, we did initiate registration of this protocol with ClinicalTrials.gov (NCT05454930), concurrent with study onset. Because of challenges in adapting a nonpharmaceutical intervention to the ClinicalTrials.gov system, publication of the protocol initially occurred in July 2015 but was subsequently reset by the Protocol Registration and Results System, leading to the appearance of an unregistered trial. Ultimately these issues were resolved and the trial registration was completed, though not before completion of data collection.

Settings and Participants

Participants were recruited in Seattle, Washington, through flyers posted on the University of Washington campus as well as through the research recruitment site of the University of Washington Institute of Translational Health Sciences. Inclusion criteria required that participants be aged 18 to 49 years. Participants were screened to confirm that they did not have hypertension, asthma, diabetes, hypercholesterolemia, cardiovascular disease, or any chronic medical conditions based on self-reported medical history, spirometry, fasting glucose level, lipid levels, and electrocardiography. Participants were excluded if they were taking antihypertensive medications, and those who were recruited were screened via blood pressure measurement to confirm that they were normotensive at recruitment. To determine blood pressure at screening, we used 3 readings measured 1 minute apart with an arm cuff (Omron HEM-907XL) after participants sat for 5 minutes. The average of the last 2 measurements was used to determine eligibility (inclusion criteria were ≥90/60 and ≤131/86 mm Hg).

In addition, at screening, potential volunteers were tested for a common genotypic single-nucleotide polymorphism (SNP) in the irritant receptor gene TRPV1 (rs8065080). We selected 16 participants for the trial such that there were approximately equal numbers of participants in each allele group of the SNP. We had previously identified this SNP as a modifier of the effect of diesel exhaust exposure on blood pressure (6).

Our initial protocol for the scripted commute trial called for 24 participants, each with 2 drive sessions (1 filtered and 1 unfiltered). After an additional consultation with our external scientific advisory committee (ESAC) but before recruitment, the protocol was modified (institutional review board modification was filed in October 2014) to have 3 drive sessions (1 filtered and 2 unfiltered) per participant, resulting in a reduction in the sample size from 24 (2 drives each) to 16 (3 drives each). This was the protocol that ultimately was followed.

Sixteen participants initiated the drive protocol, although complete outcome data for the blood pressure end points are available for only 13 participants due to failure to collect adequate outcome data (1 participant had Raynaud syndrome, which made taking readings using the fingertip blood pressure sensor impossible) and data loss on the measurement device ($n = 2$). Retinal images were collected on all drives in all participants.

The Human Subjects Division of the University of Washington approved participant consent forms and the study protocol.

Randomization and Intervention

On each study day, a participant was driven through rush-hour Seattle traffic for 2 hours following a preplanned route (**Supplement Figure 1**, available at Annals.org). These drives occurred 3 times for each participant, and each drive was separated by at least 3 weeks. Pairs of adjacent drives for the same participant took place between 21 and 218 days apart. On 1 drive day, the vehicle was equipped with 2 filtration devices: a commercially available car cabin air filter (FRAM Fresh Breeze model CF10743), and a home high-efficiency particulate air (HEPA) cleaner and active carbon air purifier (Whirlpool Whispure 510), which was placed in the front seat with air directed toward the participant using a purpose-built vent and diffuser. On 2 days, on-road air was entrained into the cabin through the vehicle's factory air vents with filter elements removed from both units. An overview of the randomization, sequences, and washout periods is shown in **Figure 1**.

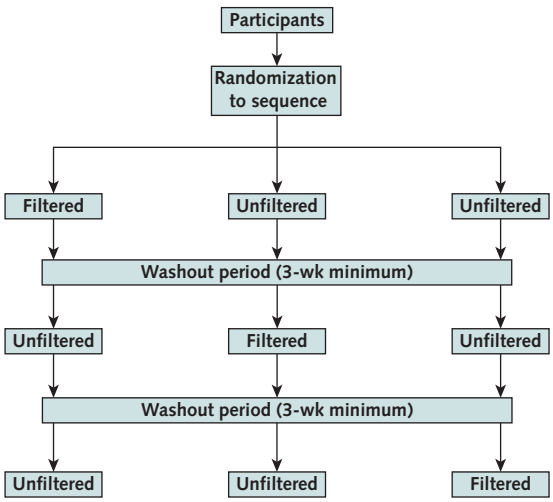
The order of the filtered and unfiltered days was randomized before initiation of recruitment by generating values from a discrete uniform distribution corresponding to 1 of the 3 possible sequences (filtered–unfiltered–unfiltered, unfiltered–filtered–unfiltered, unfiltered–unfiltered–filtered) for each participant. Randomization was not designed to guarantee an equal number of sequences and was not blocked with respect to genotype or other factors.

All drives occurred on Monday through Thursday, with a planned start time of 9:30 a.m. and a duration of 2 hours. As described earlier, each participant had multiple drive days. These days were not constrained to be on the same day of the week, but no drives were scheduled on holidays. Drives occurred during all seasons of the year.

The vehicle was the same for each drive (Dodge Grand Caravan), and the driver was the same for all drives except one. The vehicle's windows were always closed, and the car's HVAC system was set so that recirculation was off. The air conditioning was always on, and heat was adjusted to maintain a comfortable temperature.

Participants received instructions to fast beginning at 10:00 p.m. the night before each study drive and again beginning at 10:00 p.m. after the drive (because additional

Figure 1. Overview of randomization. Participants were randomly assigned to a sequence, with at least a 3-week washout period between drives. Each drive occurred separately.



measurements were collected at 24 hours after the drive). Participants received a predetermined lunch shortly after each drive. This lunch was designed by the research kitchen and included a turkey and Swiss cheese sandwich, chips, milk, and an apple. Dietary restrictions were accommodated such that if a participant received a substitution, that substitution was the same for all of that participant's drives. Specifically, vegetarians received a chickpea sandwich instead of a turkey sandwich. Participants who did not consume dairy did not receive cheese or milk.

Blinding

Participants and the study coordinator were blinded to exposure status. Research technicians set the exposure status ahead of time via removal or installation of filters and were responsible for monitoring in-vehicle exposure levels during the drive. These research technicians did not interact with the study participant. To assess the effectiveness of blinding, each day participants were asked whether they believed filtration was used, whether they thought no filtration was used, or whether they did not know.

Adherence

Because the intervention was controlled by the technician, nonadherence is not strictly relevant in this design. However, we were interested in assessing the effectiveness of filtration to determine the extent to which filtration altered in-vehicle exposure concentrations. To assess the effectiveness of filtration, we performed continuous in-vehicle exposure measurement during drives. The exposure instruments were situated on a platform at the rear of the drive vehicle, and the sample inlet for these instruments was connected to a manifold, the inlet to which was located near the breathing zone of the study participant. This was the case for all drives.

We measured in-vehicle particle count via a TSI P-Trak 8525, black carbon with an AethLabs microAeth AE51, $PM_{2.5}$ via a Radiance Research M903 nephelometer, and nitrogen dioxide (NO_2) with an Aerodyne Research cavity attenuated phase shift monitor. Nephelometry-based measurements of the particle scattering coefficient of light (bscat) were converted to $PM_{2.5}$ mass based on a conversion factor specific to the Seattle-Duwamish monitoring site (an area traversed in the study drive) and adjusted for the wavelength used by the M903 nephelometer. The equation that was used was $(28.6 \times [10\,000 \times \text{bscat}]) + 2.6$, where bscat was in units of reciprocal meters.

Outcomes and Follow-up

The primary prespecified outcomes in our protocol were blood pressure, brachial artery diameter, retinal arteriolar diameter, and gene expression. Of these, we focus here on blood pressure because it is the only one that has direct clinical relevance. It is also the only one with a long time series of measurements, including repeated measurements during the drive and the following day. Central retinal arteriolar equivalent (CRAE) is also reported in this article. Other outcomes will be reported separately.

Blood pressure measurements were taken at the finger using a pulse waveform device (Finometer Pro Model-1 [Finapres Medical Systems]) for 3-minute periods. Pulse waveform measurement of blood pressure allows for beat-to-beat pressure assessment and has been validated for physiologic research (12). We selected a finger pulse waveform device because the continuous beat-to-beat approach permits continuous physiologic assessment throughout the drive and is more robust to vibrations and noise from driving compared with brachial artery devices that use discrete auscultatory or oscillometric measurement. The protocol for measurement of blood pressure was designed to increase consistency across all measurement periods. Specifically, the seat in the vehicle and the seat used for postdrive measurements were always set to the same angle. This angle was checked every day using a goniometer. Measurements were always taken on the right hand, and during the measurement periods, participants were directed to place their feet flat on the floor.

We recorded these 3-minute measurement periods of continuous blood pressure at 14 prespecified times throughout the day. One measurement period was taken immediately before the drive at approximately 9:30 a.m., 9 measurement periods were taken during the 2-hour drive, 3 measurement periods were after the drive on the same day, and a single measurement period was taken 24 hours after drive initiation. These measurement times were initiated manually by the study coordinator according to a schedule defined in relation to minutes since the start of the drive (5, 15, 30, 45, 60, 75, 90, 105, 120, 150, 300, 420, and 1440 minutes). Beat-to-beat blood pressure measurements were averaged separately over each 3-minute measurement period (**Supplement Table 1**, available at Annals.org).

Retinal photographs were taken 30 minutes before and 30 minutes after the 2-hour drive period. The photographs were taken using a digital nonmydriatic retinal camera (Canon CR6-45nm), and CRAE values were calculated

using IVAN (Interactive Vessel Analyzer) software (University of Wisconsin) (13).

Statistical Analysis

The originally proposed controlled-exposure design included a sample size assessment for different end points. Sample sizes were chosen empirically on the basis of results from previously conducted controlled-exposure studies. Specifically, we had observed alterations in brachial artery diameter, finding a 0.11-mm (95% CI, 0.02 to 0.18 mm) decrease in response to diesel exhaust exposure compared with filtered air in a sample of 22 persons (14). On the basis of these results, we chose a sample size of 24 participants and 48 sessions. Subsequently, the design of this experiment changed, based on revised requirements from the U.S. Environmental Protection Agency (EPA) (see the Role of the Funding Source section). We did not update the sample size assessment because the number of sessions was fixed on the basis of allocated resources. On the advice of our ESAC, we modified the protocol to include 2 unfiltered drives and 1 filtered drive per participant to capitalize on expected variation in ambient exposure on unfiltered days while keeping the total number of drive sessions constant at 48. Again, the sample size assessment was not updated because the number of drives was fixed on the basis of the resources available.

We estimated the effect of roadway air pollutants (unfiltered air) on blood pressure at each time interval using a single mixed-effects model per outcome. The model was specified with an interaction between exposure (filtered vs. unfiltered) and categorical measurement time, with a main effect for categorical measurement time. We also adjusted for predrive blood pressure measurement, drive order (categorical), participant (as a fixed effect; categorical), and carryover (defined as the preceding exposure value) (15). We included a term for drive day as a random intercept (because there were 2 unfiltered days) nested within each participant. The entire time course of blood pressure response was of interest, so we report all measured time points from a fully saturated model. Additional details on model formulation are provided in the statistical appendix (see the **Supplement**, available at Annals.org).

The effect of unfiltered days on CRAE was estimated using a slightly altered model. Because CRAE was collected exactly twice on each day (before and after the drive), we fit a model without interaction by time and without a random effect for day within participant.

We performed a χ^2 test on perception of filtration against actual exposure status. In addition, we performed a sensitivity analysis on the blood pressure results in which we also adjusted for season.

Role of the Funding Source

This study was part of the University of Washington Center for Clean Air Research, which was overseen by an ESAC. The primary funder of the center, the EPA, had ex

Table 1. Characteristics of Participants, by Drive Sequence*

Characteristic	Filtered-Unfiltered-Unfiltered		Unfiltered-Filtered-Unfiltered		Unfiltered-Unfiltered-Filtered	
	Initiated Trial ($n = 6$)	Complete Data Available ($n = 4$)	Initiated Trial ($n = 2$)	Complete Data Available ($n = 2$)	Initiated Trial ($n = 8$)	Complete Data Available ($n = 7$)
Age, *y*						
Mean (SD)	30.2 (8.0)	29.3 (7.8)	25.0 (2.8)	25.0 (2.8)	30.5 (9.1)	30.7 (9.9)
Median (IQR)	29.5 (13.3)	29.0 (12.8)	25.0 (2.0)	25.0 (2.0)	27.5 (10.5)	26.0 (14.0)
Gender, % *(n)*						
Male	50.0 (3)	50.0 (2)	50.0 (1)	50.0 (1)	62.5 (5)	57.1 (4)
Female	50.0 (3)	50.0 (2)	50.0 (1)	50.0 (1)	37.5 (3)	42.9 (3)
Average time between drives, *d*						
Mean (SD)	31.8 (8.0)	33.8 (7.8)	30.0 (2.8)	30.0 (2.8)	53.0 (9.1)	47.8 (9.9)
Median (IQR)	29.3 (3.3)	31.0 (7.3)	30.0 (5.0)	30.0 (5.0)	40.3 (31.8)	38.5 (18)
Predrive systolic blood pressure, *mm Hg*						
Mean (SD)	–	115.6 (9.7)	–	117.7 (7.8)	–	128.2 (11.0)
Median (IQR)	–	116.3 (9.0)	–	117.7 (5.5)	–	122.5 (19.3)
Predrive diastolic blood pressure, *mm Hg*						
Mean (SD)	–	70.3 (11.4)	–	67.1 (4.1)	–	72.1 (6.3)
Median (IQR)	–	70.8 (18.9)	–	67.1 (2.9)	–	73.7 (7.3)
CRAE, *μm*						
Mean (SD)	169.1 (9.7)	171.9 (9.7)	159.8 (31.1)	159.8 (31.1)	162.2 (10.7)	161.9 (11.5)
Median (IQR)	170.1 (11.0)	172.0 (9.4)	159.8 (22.0)	159.8 (22.0)	163.8 (12.9)	163.4 (15.0)

CRAE = central retinal arteriolar equivalent.
* Sixteen participants initiated the trial, but blood pressure data were unavailable for some or all drives for 3 participants, resulting in an analytic sample of 13 for the blood pressure analysis (denoted as "complete data available").

Table 2. Characteristics of Drives for the 13 Participants in the Blood Pressure Analysis, by Filtration Status

Characteristic	Filtered (n = 13 Drives)	Unfiltered (n = 26 Drives)
Season, % (*n*)		
Winter	7.7 (1)	30.1 (8)
Spring	46.2 (6)	23.1 (6)
Summer	30.1 (4)	15.4 (4)
Fall	15.4 (2)	30.8 (8)
Day, % (*n*)		
Monday	23.0 (3)	19.2 (5)
Tuesday	38.4 (5)	46.2 (12)
Wednesday	15.4 (2)	3.8 (1)
Thursday	23.1 (3)	30.8 (8)
Drive duration, *min*		
Mean (SD)	121.9 (3.7)	122.5 (4.0)
Median (IQR)	120.0 (2.0)	120.0 (4.8)
Drive start time (9:30 a.m. target), % (*n*)		
≤10 min from target	84.6 (11)	84.6 (22)
>10 and ≤30 min from target	7.7 (1)	15.4 (4)
>30 and <60 min from target	7.7 (1)	0 (0)

officio representation on the ESAC. The funder had no role in data collection, analysis, interpretation, or writing of the study reports. The study was modified from its original design as a controlled-exposure study at the request of the EPA, and the study as conducted was proposed as an alternate approach by the center investigators and, after modifications to the protocol, was approved by the ESAC. All authors were provided complete access to the data, and all authors share responsibility for the decision to submit the manuscript for publication.

Results

Study Sample and Randomization

The mean age was 29.7 years (range, 22 to 45 years). The mean predrive blood pressures were 122.7 mm Hg (IQR, 22.4 mm Hg) for systolic pressure and 70.8 mm Hg (IQR, 14.6 mm Hg) for diastolic pressure. The mean drive duration was 122.3 minutes (IQR, 4 minutes). The sample sizes were approximately equal by gender (male, $n = 9$; female, $n = 7$) and by TRPV1 (rs8065080) allele groups (C/T alleles, $n = 4$; C/C alleles, $n = 6$; T/T alleles, $n = 6$). Three participants were excluded from the blood pressure analysis. For 1 participant, blood pressure could not be measured via the finger pulse waveform device because the participant had Raynaud syndrome. Two participants were excluded due to data loss when blood pressure data were inadvertently overwritten on the Finapres device.

Different numbers of participants received each drive sequence, and we observed modest imbalances by age and blood pressure with respect to drive sequence (Table 1). Mean systolic blood pressures by sequence were 115.6, 117.7, and 128.2 mm Hg, with some imbalance also occurring in diastolic blood pressure. Drive characteristics, including season, day of week, duration, and start time, are summarized by filtration status in Table 2. We observed imbalance in filtration status by season; for example, winter drives accounted for 1 of 13 filtered drives and 8 of 26 unfiltered drives.

Filtration and In-Cabin Measurements

Filtration was highly effective for particles (Figure 2 and Table 3). The drive-average particle number count (PNC) was reduced by 86%. The average $PM_{2.5}$ concentration was reduced by 60%, and black carbon was reduced by 86%. Filtration was ineffective for gases: NO_2 concentrations were reduced by 19%, and CO and CO_2 were effectively unaltered. Correlations between pollutants are presented in Supplement Figure 2 (available at Annals.org).

Effect of Filtration on Blood Pressure and CRAE

Raw mean blood pressure values generally showed decreases from the predrive measures in both groups, with larger decreases in the filtered group (Table 4; Supplement Figures 3 and 4, available at Annals.org). The peak effect from the statistical analysis was observed at 1 hour after the start of the drive for both systolic and diastolic blood pressure (Figure 3). Diastolic blood pressure at 1 hour, after adjustment for predrive levels, drive order, participant, and carryover, was on average 4.7 mm Hg higher (CI, 0.9 to 8.4 mm Hg) in unfiltered drives than in filtered drives. Adjusted systolic blood pressure was on average 4.5 mm Hg higher (CI, −1.2 to 10.2 mm Hg) in unfiltered drives compared with filtered drives. At approximately 24 hours, adjusted diastolic blood pressure was on average 3.8 mm Hg higher (CI, 0.02 to 7.5 mm Hg), and systolic blood pressure was 1.1 mm Hg higher (CI, −4.6 to 6.8 mm Hg). Adjusted mean CRAE was 2.7 μm wider (CI, −1.5 to 6.8 μm) on unfiltered days than on filtered days.

We found no carryover effect, with t values of 0.24 for diastolic blood pressure, −0.93 for systolic blood pressure, and 0.30 for CRAE. For the survey on perception of filtration, participants responded "do not know" for 26 out of 39 drives and were ineffective at correctly guessing exposure ($\chi^2 = 0.17$ and $\nu = 1$ for days where participants did guess). Results were robust to adjustment for season (Supplement Table 2, available at Annals.org).

Discussion

In our small crossover trial of in-vehicle filtration of TRAP, we found that drives in vehicles with unfiltered TRAP resulted in net increases in blood pressure of more than 4.5 mm Hg compared with drives with in-vehicle filtration, although estimates were imprecise and the CIs for the increases included zero at various time points. Changes in blood pressure occurred rapidly, peaked within 60 minutes, and persisted over 24 hours. In-vehicle filtration of TRAP did not alter CRAE.

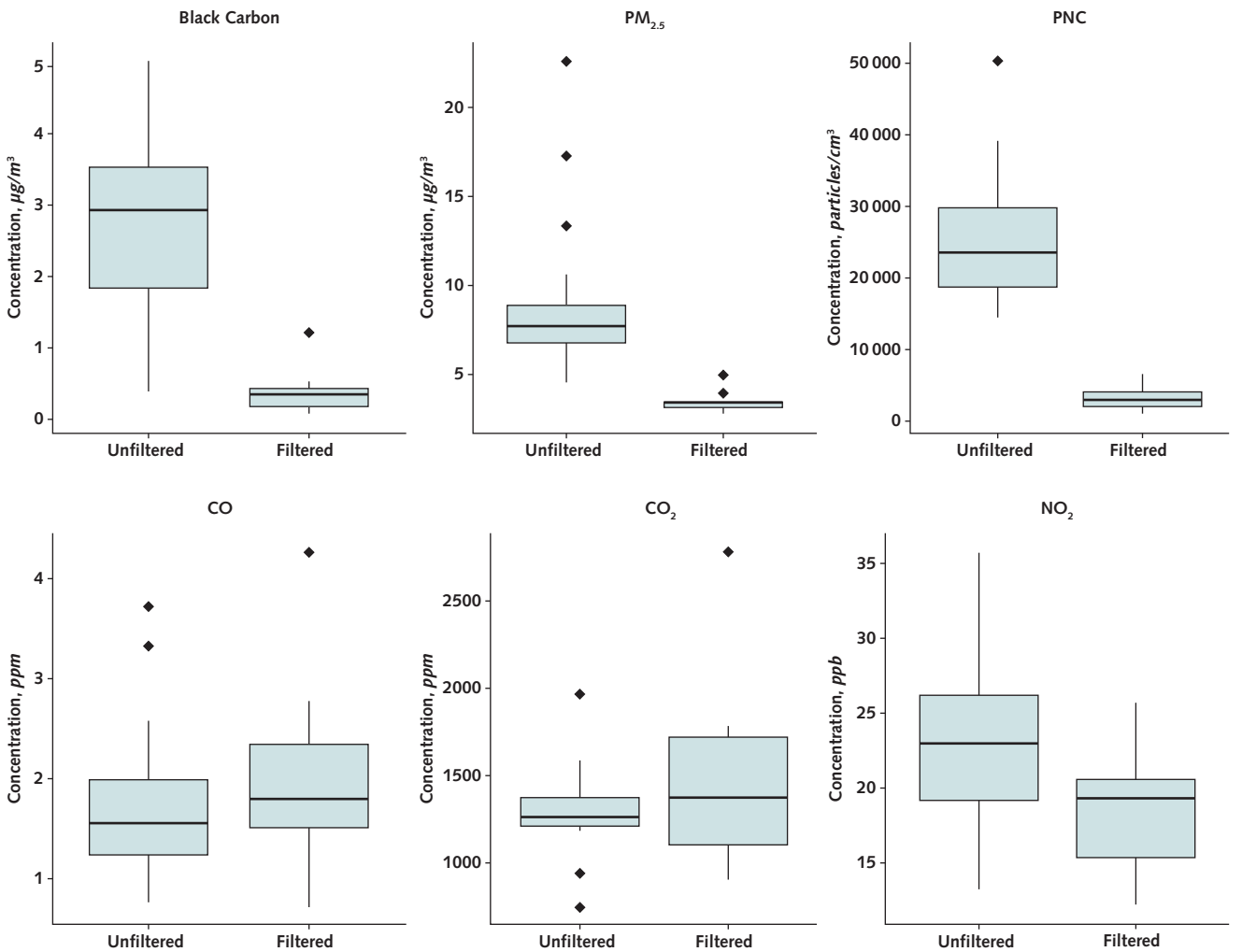
Interest in filtration research designs has been increasing (16). Most filtration studies are set in the home, where ambient air pollution levels are relatively low (17, 18), and fewer studies are set near roadways. A crossover trial of filtration of TRAP set in rooms near a roadway found a 2.8-mm Hg change in blood pressure at 20 minutes for a PNC of 30 000 particles/cm^3 ($n = 77$) (17), motivating an upcoming trial of the effect of residential filtration on

blood pressure (19). Randomized crossover studies found that facemasks decreased on-roadway blood pressure, although the unblinded designs limit interpretability (n = 15 and 24) (20, 21). A randomized crossover trial of TRAP also found blood pressure effects but relied on an unblinded location for exposure (n = 28) (22). A randomized crossover on-roadway study of facemasks was blinded via sham control; this study found differences in exhaled nitric oxide and in one arterial stiffness indicator (n = 15) (23).

Our study may be unique in studying the effect of in-vehicle filtration on blood pressure. A prior study using a randomized sham-controlled crossover design assessed the acute effects of in-vehicle filtration on heart rate and found increases in high-frequency heart rate variability, but it did not report postexposure blood pressure (n = 48) (11). Our current study extends to a real-world setting our previous controlled-exposure laboratory findings. With a controlled exposure of freshly generated, diluted, aged diesel exhaust, we found blood pressure changes similar in magnitude to those in the current study (4.4–mm Hg increase when 30- and 90-minute readings were combined [CI, 1.1 to 7.7 mm Hg]) (n = 45) (5). This study had considerably higher $PM_{2.5}$ mass concentrations (200 $\mu g/m^3$), but PNC was on the same order of magnitude (53 000 particles/cm^3), suggesting the importance of PNC (which generally reflects the smallest particles [ultrafine particles]). The time response of blood pressure in the present study is consistent with prior studies, where we identified changes at 60 minutes (5–7) and 24 hours (7) after the start of exposure.

Air pollution–induced changes in blood pressure are believed to be partly due to autonomic alterations (1). Our prior diesel exhaust study found that blood pressure response is modified by an α-1 adrenergic blockade (n = 20) (7). In addition, the irritant receptor TRPV1 may partially mediate air pollution–induced autonomic alterations (6, 24). We examined CRAE to assess microvasculature effects because arterioles are key resistance vessels.

Figure 2. Effectiveness of filtration.



The figure shows the distribution of drive-average (2-hour duration in traffic) pollutant measurements in Seattle, Washington, comparing filtered and unfiltered days. CO = carbon monoxide; CO_2 = carbon dioxide; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter <2.5 µm in diameter; PNC = particle number count; ppb = parts per billion; ppm = parts per million.

Table 3. Distribution of Drive-Average (2-Hour Duration) Pollutant Measurements*

Pollutant	Unfiltered		Filtered	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
PNC, *per cm*^{3}	25 204.6 (8740.8)	23 648.3 (18 790.6–29 758.5)	3405.9 (1824.9)	3023.5 (2289.4–4086.9)
$PM_{2.5}$, $\mu g/m^3$	8.7 (4)	7.7 (6.9–8.9)	3.5 (0.6)	3.4 (3.2–3.5)
Black carbon, $\mu g/m^3$	2.8 (1.3)	2.9 (1.9–3.6)	0.4 (0.3)	0.3 (0.2–0.4)
NO_2, *ppb*	22.9 (5.1)	22.9 (19.2–26.2)	18.6 (4.4)	19.4 (15.5–20.6)
CO, *ppm*	1.7 (0.8)	1.5 (1.2–2)	2 (1)	1.8 (1.5–2.3)
CO_2, *ppm*	1314.4 (282.8)	1269 (1215.1–1387.1)	1491.2 (534.3)	1374.9 (1115.9–1724.3)

CO = carbon monoxide; CO_2 = carbon dioxide; NO_2 = nitrogen dioxide; $PM_{2.5}$ = particulate matter <2.5 μm in diameter; PNC = particle number count; ppb = parts per billion; ppm = parts per million.
* Drives had 815 measurements (at 10-second frequency) on average, each resulting in a single ~2-hour average. Pollution data were available for 37 of the 39 drives in the analytic sample. The SDs correspond to the distribution of 2-hour averages, not for measurements at the raw sampling frequency.

However, retinal vessels are atypical in that they lack autonomic innervation and are regulated through local factors (25), which may explain the divergent results.

The ineffectiveness of the studied filtration system for gaseous pollutants implicates the particle component of TRAP in observed effects. We were unable to distinguish specific causal pollutants because filtration reduced all measures of particulates, although $PM_{2.5}$ was least reduced. Ultrafine particles (measured as particulate count) and black carbon are not regulated under EPA standards or World Health Organization air quality guidelines. Concentrations of $PM_{2.5}$ were consistently below current U.S. regulatory limits. These results suggest the potential for particle filtration to mitigate the acute effects of air pollution exposure and justify further research into the effects of filtration in other acute and long-term exposure settings.

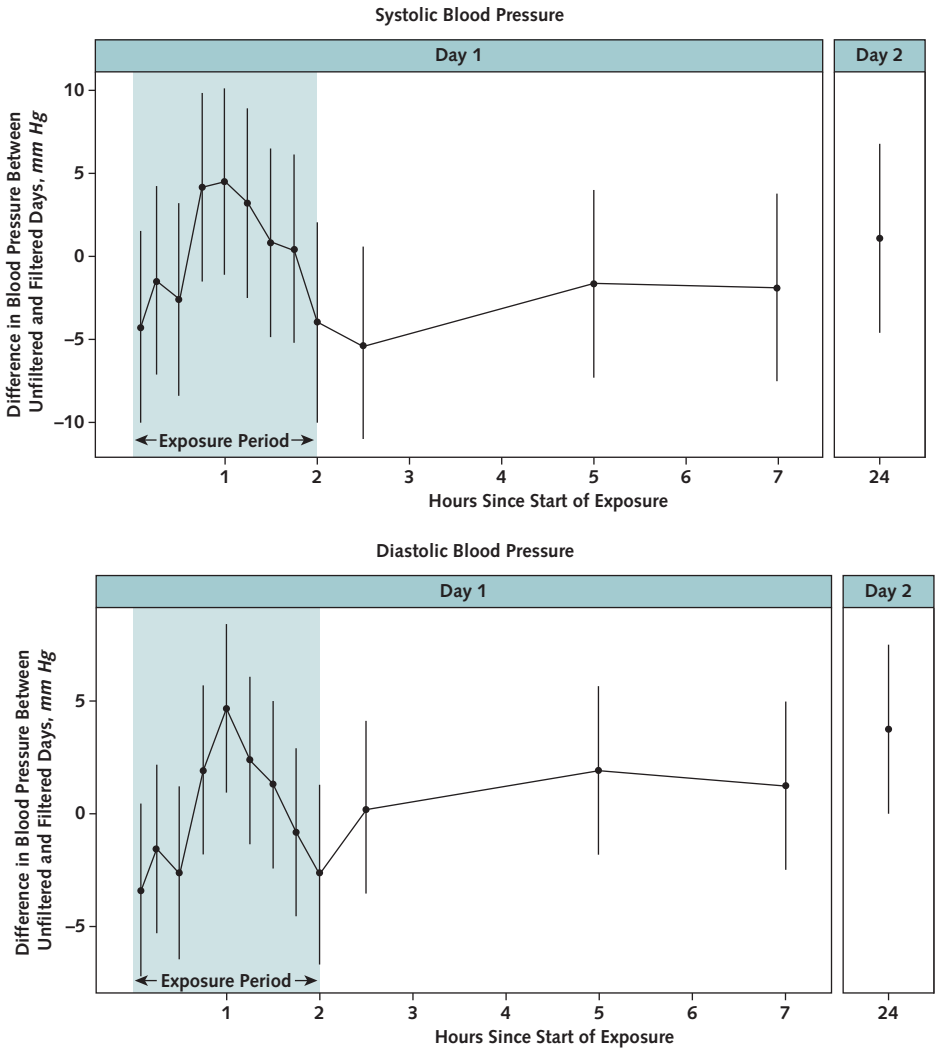
Several limitations should be considered when interpreting our results. Blood pressure measured using finger pulse waveforms may more strongly reflect specific hemodynamic changes than conventional brachial artery measurement, although good estimates of brachial blood pressure can be reconstructed from measurements taken using Finapres devices. The equipment in this study dates from 2014 to 2016, although it reflects current filtration and measurement technology and on-road pollution

Table 4. Raw Blood Pressure Values and Changes From Predrive Values*

Time	Systolic Blood Pressure (95% CI), *mm Hg*				Diastolic Blood Pressure (95% CI), *mm Hg*			
	Raw Value		Change From Predrive Value		Raw Value		Change From Predrive Value	
	Filtered	Unfiltered	Filtered	Unfiltered	Filtered	Unfiltered	Filtered	Unfiltered
Predrive	124.7 (116.7 to 132.6)	121.7 (115.2 to 128.3)	–	–	72.8 (67.8 to 77.8)	69.8 (65.9 to 73.6)	–	–
5 min	119.3 (111.9 to 126.6)	115.0 (109.7 to 120.4)	−4.0 (−7.4 to −0.5)	−6.7 (−11.7 to −1.7)	72.3 (67.6 to 76.9)	68.1 (64.5 to 71.8)	0.0 (−3.8 to 3.9)	−1.6 (−3.8 to 0.5)
15 min	119.2 (111.0 to 127.3)	117.1 (112.6 to 121.5)	−5.5 (−10.7 to −0.3)	−4.7 (−9.9 to 0.6)	71.7 (67.4 to 76.1)	69.2 (65.9 to 72.5)	−1.1 (−5.0 to 2.8)	−0.6 (−3.3 to 2.1)
30 min	122.0 (114.5 to 129.4)	118.3 (114.7 to 122.0)	−3.1 (−8.8 to 2.6)	−3.4 (−8.8 to 2.0)	73.9 (68.9 to 78.9)	70.1 (67.4 to 72.9)	0.6 (−4.0 to 5.3)	0.4 (−2.7 to 3.4)
45 min	116.1 (109.8 to 122.4)	119.5 (114.6 to 124.4)	−8.5 (−14.7 to −2.4)	−2.4 (−8.3 to 3.5)	70.1 (66.4 to 73.7)	71.2 (67.8 to 74.7)	−2.7 (−6.7 to 1.2)	1.0 (−2.3 to 4.3)
60 min	112.6 (105.3 to 120.0)	116.5 (112.0 to 121.0)	−12.1 (−19.6 to −4.5)	−5.2 (−12.2 to 1.8)	66.6 (62.5 to 70.8)	70.4 (67.1 to 73.6)	−6.2 (−12.2 to −0.1)	0.6 (−3.0 to 4.2)
75 min	116.0 (109.8 to 122.1)	118.6 (114.2 to 122.9)	−8.7 (−13.6 to −3.8)	−3.2 (−9.9 to 3.6)	70.4 (66.1 to 74.7)	71.8 (68.6 to 75.1)	−2.4 (−7.9 to 3.2)	2.1 (−1.6 to 5.8)
90 min	116.6 (111.0 to 122.1)	117.0 (113.0 to 121.0)	−8.1 (−14.9 to −1.3)	−5.3 (−11.7 to 1.2)	70.2 (66.3 to 74.1)	70.7 (68.2 to 73.2)	−2.6 (−8.0 to 2.8)	0.8 (−2.6 to 4.2)
105 min	118.1 (111.2 to 125.1)	118.0 (113.7 to 122.2)	−6.6 (−12.4 to −0.8)	−3.8 (−10.4 to 2.8)	72.6 (68.1 to 77.0)	70.8 (67.9 to 73.6)	−0.2 (−5.0 to 4.6)	1.0 (−2.5 to 4.5)
120 min	120.7 (112.0 to 129.3)	114.0 (109.2 to 118.9)	−6.1 (−14.2 to 2.1)	−6.8 (−13.9 to 0.2)	73.7 (67.2 to 80.1)	69.1 (66.1 to 72.2)	−0.5 (−6.4 to 5.4)	−0.6 (−4.9 to 3.7)
150 min	121.3 (114.9 to 127.8)	116.2 (111.6 to 120.7)	−3.5 (−10.4 to 3.4)	−5.6 (−11.2 to 0.0)	69.3 (64.3 to 74.4)	69.4 (65.8 to 72.9)	−2.8 (−7.6 to 2.1)	−0.4 (−4.3 to 3.4)
300 min	119.6 (110.4 to 128.7)	117.3 (112.9 to 121.6)	−5.1 (−14.3 to 4.0)	−4.5 (−10.4 to 1.5)	67.0 (61.8 to 72.2)	68.0 (64.4 to 71.5)	−5.8 (−8.7 to −2.8)	−1.8 (−5.7 to 2.1)
420 min	121.1 (113.4 to 128.7)	118.6 (113.6 to 123.5)	−3.6 (−11.9 to 4.7)	−3.2 (−8.7 to 2.3)	70.9 (65.5 to 76.4)	71.2 (67.6 to 74.8)	−1.9 (−6.5 to 2.8)	1.4 (−2.1 to 5.0)
1440 min	112.0 (104.8 to 119.3)	112.5 (106.6 to 118.5)	−12.6 (−23.6 to −1.6)	−9.2 (−16.8 to −1.6)	65.7 (60.7 to 70.7)	68.5 (65.0 to 72.0)	−7.1 (−11.4 to −2.9)	−1.3 (−5.3 to 2.7)

* Direct comparison of treatment-specific CIs from this table does not reflect the within-participant study design and statistical adjustments accounted for in the main results.

Figure 3. Effect of unfiltered traffic-related air pollution on blood pressure.



The figure shows modeled estimates and 95% CIs of blood pressure comparing unfiltered days with filtered days, with adjustment for predrive blood pressure. Models were estimated using data from 39 drives by 13 participants.

characteristics. Our study was small, included healthy participants, and had genotype-stratified recruitment, all of which limit generalizability. The small sample size and long periods between drives meant that randomization did not balance all time-varying variables, such as season, leading to potential confounding. A sensitivity analysis that adjusted for season did not appreciably alter the results, but further research is needed to confirm our findings in different settings and larger populations. Finally, the clinical implications of transient changes in blood pressure are not well understood, and further research is also needed to determine whether these changes might contribute to acute risk for cardiovascular disease events or long-term vascular alterations.

In conclusion, in a realistic on-road exposure trial, we found that, compared with filtered TRAP exposure, unfiltered exposure may result in net increases in blood pressure that occur and peak within 60 minutes and are sustained at 24 hours, suggesting that the effects of air pollution on blood pressure may be reduced with effective cabin air filtration. Our study reinforces existing literature suggesting that traffic-derived particulate matter may be implicated in hypertension.

From Department of Environmental and Occupational Sciences, University of Washington, Seattle, Washington (M.T.Y., K.J., K.E.C., S.V.); Department of Civil and Environmental Engineering, University of Washington, Seattle, Washington (T.R.G.); Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington (J.A.S.); Department of Civil and Environmental Engineering and Department of Environmental and Occupational Sciences, University of Washington, Seattle, Washington (T.L.); Department of Medicine and Department of Environmental and Occupational Sciences, University of Washington, Seattle, Washington (C.S.); Department of Biostatistics, University of Washington, Seattle,

Washington (A.A.S.); and Department of Environmental and Occupational Sciences, Department of Medicine, and Department of Epidemiology, University of Washington, Seattle, Washington (J.D.K.).

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Corresponding Author: Joel D. Kaufman, MD, MPH, University of Washington, 4225 Roosevelt Way NE, Suite 100, Seattle, WA 98105; e-mail, joelk@uw.edu.

Author contributions are available at Annals.org.

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Author Contributions: Conception and design: K. Jansen, K.E. Cosselman, T.R. Gould, J.A. Stewart, A.A. Szpiro, J.D. Kaufman.
Analysis and interpretation of the data: M.T. Young, K.E. Cosselman, T. Larson, C. Sack, A.A. Szpiro, J.D. Kaufman.
Drafting of the article: M.T. Young, J.D. Kaufman.
Critical revision for important intellectual content: M.T. Young, K. Jansen, C. Sack, A.A. Szpiro, J.D. Kaufman.
Final approval of the article: M.T. Young, K. Jansen, K.E. Cosselman, T.R. Gould, J.A. Stewart, T. Larson, C. Sack, S. Vedal, A.A. Szpiro, J.D. Kaufman.
Provision of study materials or patients: K. Jansen, J.A. Stewart.
Statistical expertise: M.T. Young, A.A. Szpiro.
Obtaining of funding: S. Vedal, J.D. Kaufman.
Administrative, technical, or logistic support: K. Jansen, J.A. Stewart, T. Larson, J.D. Kaufman.
Collection and assembly of data: K. Jansen, K.E. Cosselman, T. R. Gould, J.A. Stewart, J.D. Kaufman.