Using sensors to investigate the acute effect of traffic-related air pollution in different commuting modes

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Abstract

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The contribution of transportation to ambient particulate matter (PM) has increased since 2000 in China. Over this time, Chinese cities have grown rapidly in size, population, car ownership and daily commute distance. These changes have led to increased travel times, exposures to traffic-related air pollution (TRAP) and combined uses of transportation modes during daily commutes. This dissertation aims to explore the health impacts of TRAP exposure for different commuting modes, evaluate a possible intervention to mitigate the adverse effects of TRAP in traffic, and investigate the relationships between built environment factors and travel behaviors for adults in Chengdu, China.

First, portable sensors were employed to characterize TRAP and noise exposures in different transportation modes, neighborhoods and seasons in Chengdu. The study found that car trips exposed people to the lowest TRAP and noise levels compared to other modes (i.e., cycling, riding buses, and riding subways).

Second, a randomized double-blind crossover intervention experiment was conducted among 21 healthy adults, where each subject travelled on a scripted route repeatedly for two hours using different transportation modes. Subjects used portable positive pressure respirators in half of the trips and wore sham respirators in the other half of the trip. TRAP exposure was recorded during each trip and cardiorespiratory health outcomes were measured immediately before and after trips. The study showed traveling by bus, subway or walking was associated with increased heart rate and decreased lung function as compared to riding in a personal motor vehicle. Increased black carbon and PM with aerodynamic diameter less than 1.0 μm (PM_1) exposures were associated with elevated airway inflammation and decreased lung function, respectively. However, the study found no significant differences in cardiorespiratory health outcomes between subjects wearing effective respirators and those using sham respirators for two hours in traffic.

Third, a commute survey was conducted in Chengdu to ask for home addresses, work locations and time respondents spent in multi-modal commuting. The non-linear relationships between built environment factors extracted from a Geographic Information System and time spent in different transportation modes were explored. Finally, a health impact assessment was performed for TRAP exposure and physical activity to evaluate the impact of multi-modal commuting under potential built environment changes on cardiovascular diseases mortality for employed urban residents in Chengdu. The study found that home-work distance was the most important factor in determining time spent in different travel modes. The health impact assessment showed that generally, commuting under the policy of garden city and easier access to public transit would be beneficial for cardiovascular health of residents. However, a longer home-work distance was estimated to lead to excess cardiovascular diseases mortality due to increased TRAP exposure and reduced physical active in daily commutes.

Overall, these studies in Chengdu, China suggest that active and public transportation exposes commuters to higher TRAP levels. For interventions at the individual level, wearing a novel positive pressure respirator to reduce TRAP exposure during commutes may not improve the cardiorespiratory health among healthy adults. For policy interventions, the planning policy of garden city and TOD would potentially benefit population health for employed urban residents in Chengdu. However, future planning policies are needed to reduce pollutant concentrations and to address the job-housing mismatch in Chinese cities to reduce commuting distances and to protect population health.

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CHAPTER 1. INTRODUCTION

1.1 BACKGROUND

Globally, more than 54 % people live in urban areas [1], and this percentage is estimated to reach 68 % in 2050 [2]. Urban residents not only spend increased time in traffic with the sprawl of urban area, they are also exposed to disproportionately high levels of air pollution in traffic as compared to other microenvironments [3,4]. Traffic is a major source of air pollution in urban areas [5]. Traffic-related air pollution (TRAP) comes from the emissions of motor vehicles that result from fossil fuel combustion, and consists of mixtures of air pollutants, including NO, NO_2, NOx, CO, and particulate matter (PM).For example, globally, 25% of urban ambient PM with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) is estimated to come from traffic [5]. People who spend time in traffic are exposed to tailpipe emissions from vehicle traffic, non-tailpipe emissions (such as brake and tire wear), as well as noise that together, may have adverse effects on health and well-being.

The health impact of ambient air pollution has been studied globally. Ambient air pollution exposures have been associated with respiratory and cardiovascular diseases outcomes [6-10], adverse birth outcomes [11-14], diabetes [15-17], and cognitive performance [18-21]. Based on 2017 global estimates, ambient air pollution contributed to 147 million (95% CI: 132-162 million) disability-adjusted life-years (DALYs), and was the fifth-ranked environmental risk factor attributable to global burden of diseases in East Asia [22]. An increasing number of studies have explored the health effects of TRAP recently [23-28]. However, there is still controversy over whether the observed effects are due to air pollution exposure from traffic, and if the effects are confounded by factors such as noise and socioeconomic characteristics [29]. From a public health perspective, it is of great importance to understand how much TRAP urban commuters are exposed to, what health effects are induced by TRAP exposures in different commuting modes, and whether there is a way to reduce TRAP exposure and related adverse health effects for urban commuters.

1.2 Specific Aims

Figure 1 illustrates a conceptual model that provides a broad context for the research aims of this dissertation. Although the dissertation does not cover all of the topics illustrated in the figure, it allows for the reader to understand the specific contributions of this research.

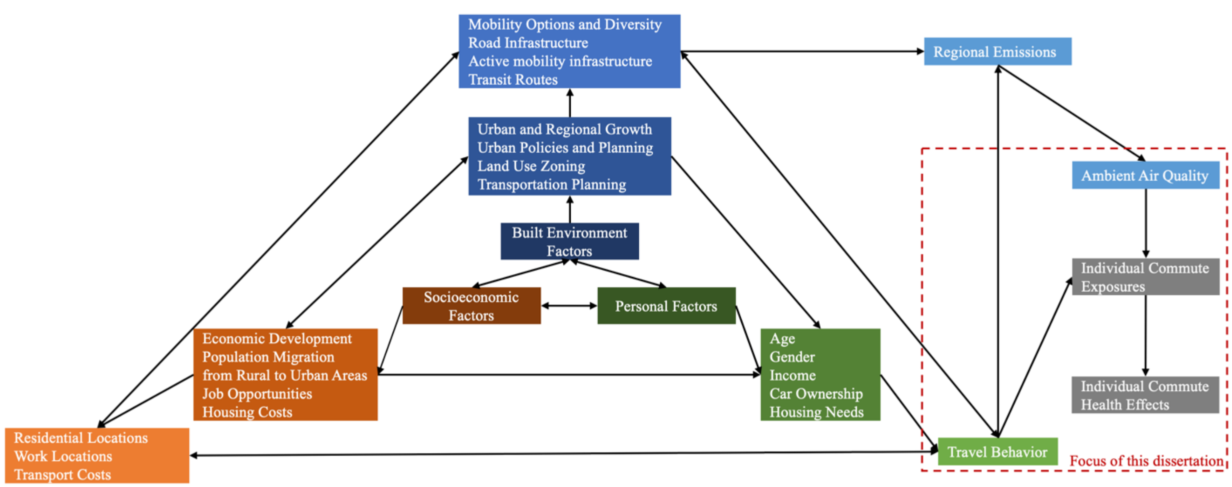

Figure 1. Conceptual model of acute health effects from personal exposures to traffic related pollution during urban commuting

As urban development occurs, urban and surrounding regional land use evolves. The economic and employment opportunities that exist in urban centers may motivate population migration from rural areas into the city, creating other societal needs, such as needs for housing, transportation, food, energy, services, etc. To meet these needs, urban planning and social policies may shape the evolving land use and neighborhood characteristics of the urban area. For example, land use zoning attempts to create compatible land uses, which can separate commercial areas, from industrial, residential and natural areas. The separation of areas through land use policies creates the need for a well-designed urban and regional transportation system. The transportation options that exist within the city should be considered within the context of connectivity with regional transportation options, so that the city is not isolated, but allows for transport of people, goods, and services between the urban core, and the surrounding suburban and rural areas, as well as between cities.

As described earlier, modern transportation systems allow for multiple modes, yet there are underlying factors that affect the feasibility and practicality of these modes too. Road infrastructure, car ownership, and vehicle operating costs may affect personal car use. Transit routes and cost may affect the use of public transit options. Home-work distances and infrastructure for safe walking and bicycling may affect active mobility. Similarly, various factors, such as congestion and limitations of other modes, may be motivating innovation options, such as shared mobility options.

The overall transportation system, and the population's choices and uses of the various mobility options, each of which may be associated with pollutant emissions. Often urban planning is focused on reducing regional emissions. For example, reducing the numbers of personal car trips by encouraging people to take public transit may reduce roadway congestion, reduce the emissions from individual vehicles, yet still allow the public to travel using zero/low emission options such as electric or hybrid buses and subways. Moreover, encouraging people to take active modes of travel, not only reduces roadway congestion and pollution emissions, but potentially provides an opportunity for physical activity, which is important for public health. Regional transportation emissions and air quality issues are typically studied at the aggregate population or region/city/neighborhood level.

While a well-designed transportation system has the potential reduce urban air pollution from mobile sources, there are still open questions about how at the individual-level, a person's mobility choices might affect their own acute cardiorespiratory health. This dissertation is focused on these questions, namely quantifying the exposures to pollution that a person experiences in certain transportation modes, whether these exposures are associated with certain acute health effects, whether these exposures and health effects could be mitigated at the personal level. There is, however one study in this dissertation that examines travel behavior, and attempts to link urban planning concepts to mode choice, exposure, and health effects.

The overarching goal of this dissertation is to quantify the impact of air pollution exposures for different transportation modes on cardiorespiratory health in Chengdu, China. Chengdu is the capital city of Sichuan Province in southwest China, and represents many of the transportation opportunities and challenges facing cities in low and middle-income countries (LMICs). The objective of the dissertation is to test hypotheses that (1) TRAP exposures vary by transportation mode, (2) TRAP exposures experienced in different travel modes are associated with short-term cardiorespiratory health effects, (3) the use of a personal protective respirators can reduce acute adverse effects of TRAP exposure and (4) built environment factors affect employees' commute choices as well as population health. These hypotheses were tested through the following specific aims:

Aim 1 (Chapter 2): Characterize variations in TRAP and noise levels experienced in different modes of transportation in Chengdu, China. Linear models were developed to explain variations in $PM_{2.5}$, BC and noise by season, neighborhood, and travel modes based on repeatedly measurements for scripted trips.

Aims 2 and 3 below, were based on a randomized double-blind crossover intervention study, where a group of healthy volunteers traveled with effective or sham respirators using different transportation modes on a scripted route. TRAP concentrations were recorded continuously using portable sensors during each trip, and selected measures of cardiovascular and respiratory health were measured before and after each trip.

Aim 2 (Chapter 3): Relate the TRAP exposure in different modes of transportation to short-term cardiorespiratory health effects. The associations between TRAP exposures and blood pressure (BP), heart rate (HR), fractional exhaled nitric oxide (FeNO), and lung function measured by spirometry were assessed, after controlling for potential confounders (*e.g.*, temperature, relative humidity, noise, perceived stress, physical activity).

Aim 3 (Chapter 4): Evaluate the effect of wearing a positive pressure respirator during intra-city travel on exposures and cardiorespiratory health, in the same subjects from Aim 2. The effectiveness of the respirator to reduce PM exposure was evaluated in a laboratory experiment. Then, health outcomes measured before and after each trip were compared within-subject between sham and effective respirator trips.

Aim 4 (Chapter 5): Investigate the impact of the built environment features on time spent in a mixture of commuting modes (multi-modal commuting). Machine learning algorithms (Random Forest) and mediation analysis (G-computation) were used to examine relationships between built environment and time spent in different modes of transportation. Additionally, a health impact assessment was performed to estimate changes in cardiovascular mortality attributable to $PM_{2.5}$ and physical activity levels during daily commuting with potential changes in the built environment in Chengdu.

The remainder part of Chapter 1 presents systematic reviews of studies that have examined TRAP variations between different transportation modes, and cross-over studies that have explored the acute effect of TRAP on human health.

1.3 TRAFFIC-RELATED AIR POLLUTION EXPOSURES IN TRANSPORTATION

Studies in different countries have investigated the variation of air pollution concentrations for several modes of transportation. Existing studies have mostly focused on particulate matter exposures (*e.g.,* $PM_{2.5}$, BC) and have largely been conducted in Europe to compare air pollution exposures for different transportation modes, including driving a car, riding a subway, tram or bus, as well as active transportation (walking and cycling).

A literature search was performed in PubMed for relevant studies using the following combination of keywords: “traffic related air pollution”, “transportation AND air pollution”, “transportation mode OR travel mode”, “exposure”, with no restrictions on publication date. In addition, relevant studies were retrieved from Web of Science, as well as the reference lists of the identified studies. After removing duplicated publication records, remaining studies were assessed for inclusion by two reviewers who independently followed the inclusion and exclusion criteria in Table 1. The two reviewers discussed and resolved issues that arose during the screening process. This process resulted in a pool of 60 eligible studies for the systematic review. The selection process is shown in detail in Figure 1, in accordance with preferred reporting items for systematic reviews and meta- analyses (PRISMA) guidelines.

Table 1. Screening criteria for studies investigating TRAP exposures in different transportation modes.

Inclusion criteria
Road traffic related air pollution Peer reviewed articles Written in English
Exclusion criteria
No on road TRAP measurements (water or air traffic, TRAP measured at indoor or outdoor places near road) Reviews and protocol

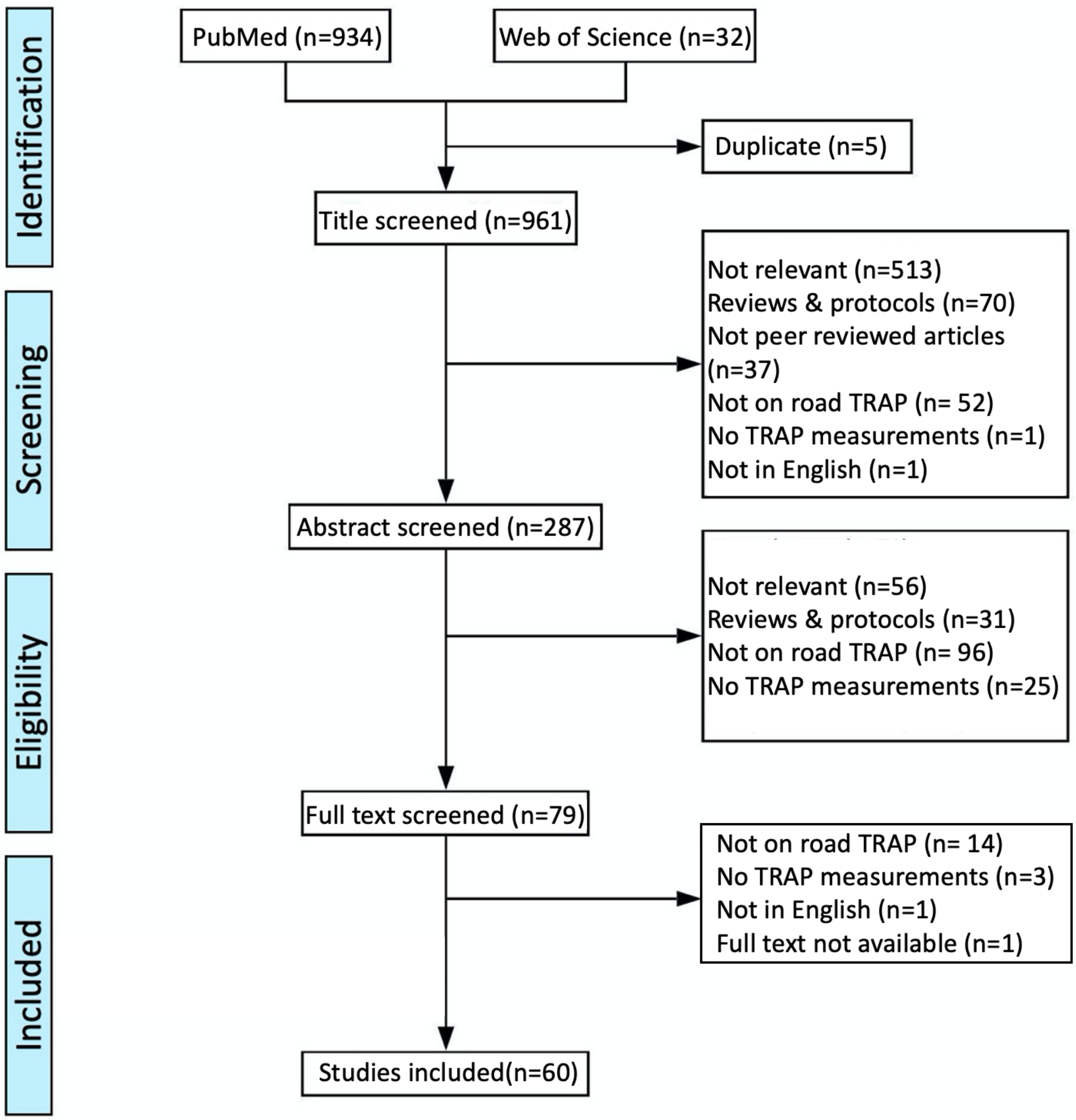

Figure 2. Preferred reporting items for systematic reviews and meta- analyses (PRISMA) diagram for exposure studies

1.3.1 Findings from Europe

Most of European studies showed that traveling in a car is associated with the highest level of air pollution exposure, including exposures to $PM_{2.5}$, BC, CO and VOC (*e.g.* benzene) [30-33]. Other studies investigated exposures to particles with different aerodynamic diameters during commuting, and found that bus trips resulted in the highest concentrations of larger particles including PM_{10} and coarse particles ($PM_{2.5}$-PM_{10}), while exposures to submicron (PM_1), fine particles ($PM_{2.5}$) and UFP levels were higher in car than with other modes of transportation [34-36].

However, some studies found that active modes of transportation involve greater exposure than others. For example, a study in London found that commuters using a walking mode were exposed to 4.7 times higher coarse particle mass ($PM_{2.5}$-PM_{10}), 2.2 times higher fine particle mass (PM_1-$PM_{2.5}$) and 1.9 times higher very fine particle mass ($<PM_1$) and 1.4 times higher UFP number concentration than those driving [37]. Another study of three cities reported that PM and BC concentrations were generally higher during biking than during driving cars with closed windows [38].

Despite the inconsistencies between studies finding greater/lesser exposure for active vs non-active transit modes, studies including an estimation of inhalation dose of air pollutants during time in transportation led to the consistent conclusion that individuals inhaled the highest levels of air pollution when using active transportation and lowest levels while driving a car compared to other transportation modes mainly because of the reduced commute time [37,39] and inhalation rate (minute ventilation) [31,33,34] when driving a car.

1.3.2 Findings from the United States

Similar studies were conducted in the United States, and reported inconsistent results for the relative exposures of different transportation modes. The Fort Collins Commuter Study measured BC, $PM_{2.5}$, UFP number concentrations during cycling and driving, and found air pollutant levels were higher when cycling than when driving [40]. A different study in Salt Lake City monitored $PM_{2.5}$ concentrations when cycling, walking, driving, riding a bus and riding a light-rail train. This study found the highest and lowest mean $PM_{2.5}$ concentrations were both measured during driving, but with windows closed (5.20 μg/m^3) and with windows open (15.21 μg/m^3), respectively. The study also estimated that the inhalation dose during commuting was highest for walking, followed by cycling, and lowest when driving with windows closed [41]. However, a New York study comparing $PM_{2.5}$ exposures in car, subway and for walking reported that the fine particle levels did not differ among the three commuting modes (21.4, 30.6 and 26.5 μg/m^3 respectively) [42].

1.3.3 Findings from Asia

Several Asian studies measured air pollution exposures in roadway transport and railway transport of intra-city commuting. A Beijing study compared exposures during walking, riding buses and taking the subway, and found that the highest UFP number concentrations and $PM_{2.5}$ mass concentrations occurred during the subway trips, while walking had the highest particulate polycyclic aromatic hydrocarbons (particulate-PAHs) concentrations compared to others [43]; another study in Guangzhou measured higher VOC levels in roadway transport than railway transport (*e.g.*, average of benzene concentrations ranged from 4.8 to 6.1 μg/m^3 in roadway transports vs. 3.0–3.8 μg/m^3 in railway transports) [44]. For roadway transport, CO levels were found to be higher in taxis than in buses or during walking [45-47], while $PM_{2.5}$ concentrations were found to be lowest when riding taxis than walking and riding buses[47]. Consistent with studies in Europe and the United States, research that considered inhaled dose found that the lowest dose was associated with individuals traveling in cars [47].

1.3.4 Factors impacting pollutant levels

Some studies explored factors affecting exposure levels for different modes of transportation, including travel routes, travel time, ventilation, fuel types and meteorological conditions. One of the most studied factors is the travel route during cycling. Studies of cyclists traveling on different routes consistently found that cyclists were exposed to higher air pollution levels on high-traffic routes than on low-traffic routes [30,34,40,46,48-50]. These studies often characterized routes based on distance from roadway vehicle traffic (*e.g.*, cycle path vs. traffic roadside) and high vs. low intersection density.

Studies also found that commuting time of day and season also affect air pollution exposures in traffic. A study in Northwest China found that morning commutes resulted in approximately 40 % higher $PM_{2.5}$ exposures of cyclists, while higher UFP levels were observed in the afternoon and evening commutes compared to the morning commutes (18,502 vs. 18,342 particles/cm^3) [50]. In terms of seasonal differences, $PM_{2.5}$ and UFP exposures during cycling were clearly higher in autumn months than summer months. Another study investigating in-vehicle $PM_{2.5}$ and CO exposures during car driving reported that afternoon non-peak hour commutes only exposed passengers to slightly lower air pollution levels compared to evening peak hour commutes [44]. However, the effects of commuting time on air pollution exposures may be related to variations of traffic volumes and may differ between studies in different cities.

Various vehicle-related factors were found to affect exposure. For example, ventilation was shown to influence air pollution exposure during commutes, with natural ventilation (i.e., open windows) inducing increased PM, but reduced CO levels during car and bus trips, while mechanical ventilation (*e.g.*, air conditioning system, filtration system) decreasing PM but increasing CO levels [41,44,51]. This may because that the vehicle filtration system and closing of windows potentially makes the cabin a different microenvironment from pollutant concentrations outside of the cabin in the street (*e.g.*, vehicle emissions). However, one study reported that the difference in CO levels between buses running with closed windows (air-conditioned) and opened (non-air-conditioned) was not statistically significant [46]. This inconsistency would possibly be explained by variations in air exchange, such as the frequency of doors open under operation, the ventilation system's intake of fresh air, and because vehicle filtration may not reduce gas pollutants.

Another vehicle-related factor that was found to impact exposure is fuel type (i.e., diesel, gasoline and electricity). Zuurbier et al. measured particle number counts (PNC), $PM_{2.5}$ and PM_{10} mass concentration, and soot levels in diesel buses, electric buses, gasoline-fueled cars and diesel-fueled cars in the Netherlands [34]. Results from the study showed diesel buses had significantly higher PNC (32%) and soot (46%) levels than electric buses, while gasoline-fueled cars had higher soot concentrations than diesel-fueled cars. Another study in Europe compared commuters' exposure to air pollution in electric-powered and diesel-powered trains, and found diesel-powered trains exposed travelers to approximately 35-fold, 6-fold, 8-fold, 3-fold, twice and 6 times higher of UFP, BC, NO_x, NO_2, $PM_{2.5}$ and benzo(a)pyrene than traveling in electric-powered trains, respectively [52].

Meteorological factors were also explored in different studies. Mostly studies reported that higher wind speed was associated with lower air pollution exposure [30,53]; whereas, another study found instead of wind speed, temperature was negatively associated with $PM_{2.5}$ concentrations while temperature and relative humidity explained variations in UFP levels during commuting [50].

1.3.5 Summary of exposure findings

In summary, studies comparing personal exposures for different modes of transportation have found inconsistent results, especially for the comparison of air pollution levels during driving vs. walking/cycling. However, when considering traveling time and minute ventilation, commuters tend to inhale more air pollutants during active transport than riding a car. Additionally, air pollution exposures during transportation are determined by different factors, including travel behavior (route, time, etc.), vehicle characteristics (fuel types, ventilation conditions, etc.) as well as environmental factors (temperature, relative humidity, wind speed, etc.).

1.4 Crossover studies investigating health effects of traffic-related air pollution

An increasing number of studies have evaluated the health effects of short-term exposure to traffic-related air pollution during commuting. A systematic review was conducted to summarize existing cross-over studies investigating short-term health effects of traffic-related air pollution exposure in commuting. A crossover study is a longitudinal study where study participants receive a sequence of different treatments or exposures. That is, the participants switch throughout to all the treatment or exposure groups after a washout period.

A literature search was performed in PubMed for relevant studies using the following combination of keywords: "traffic related air pollution", "transportation AND air pollution", "transportation mode OR travel mode", "short-term health effect", and "cross-over study OR intervention study OR panel study", with no restrictions on publication date. In addition, relevant studies were retrieved from Web of Science, as well as the reference lists of the identified studies (extended search). After removing duplicated publication records, remaining studies were assessed for inclusion by two reviewers who independently followed the inclusion and exclusion criteria in Table 2. The two reviewers discussed and resolved issues that arose during the screening process. This process resulted in a pool of 32 eligible studies for the systematic review. The selection process is shown in detail in Figure 3, in accordance with Preferred reporting items for systematic reviews and Meta- Analyses (PRISMA) guidelines.

Table 2. Screening criteria for studies investigating health effect of TRAP exposures.

Inclusion criteria
Road traffic related air pollution
Short-term health effects
Cross-over studies
Peer reviewed articles
Written in English
Full text available online
Exclusion criteria
No road TRAP measurements (water or air traffic, TRAP measured at indoor or outdoor places near road)
Long-term exposure and health studies
Not human health studies (animal/in vitro/in vivo experiment, no human health measurements)
Reviews and protocol
Qualitative analysis
Occupational exposures

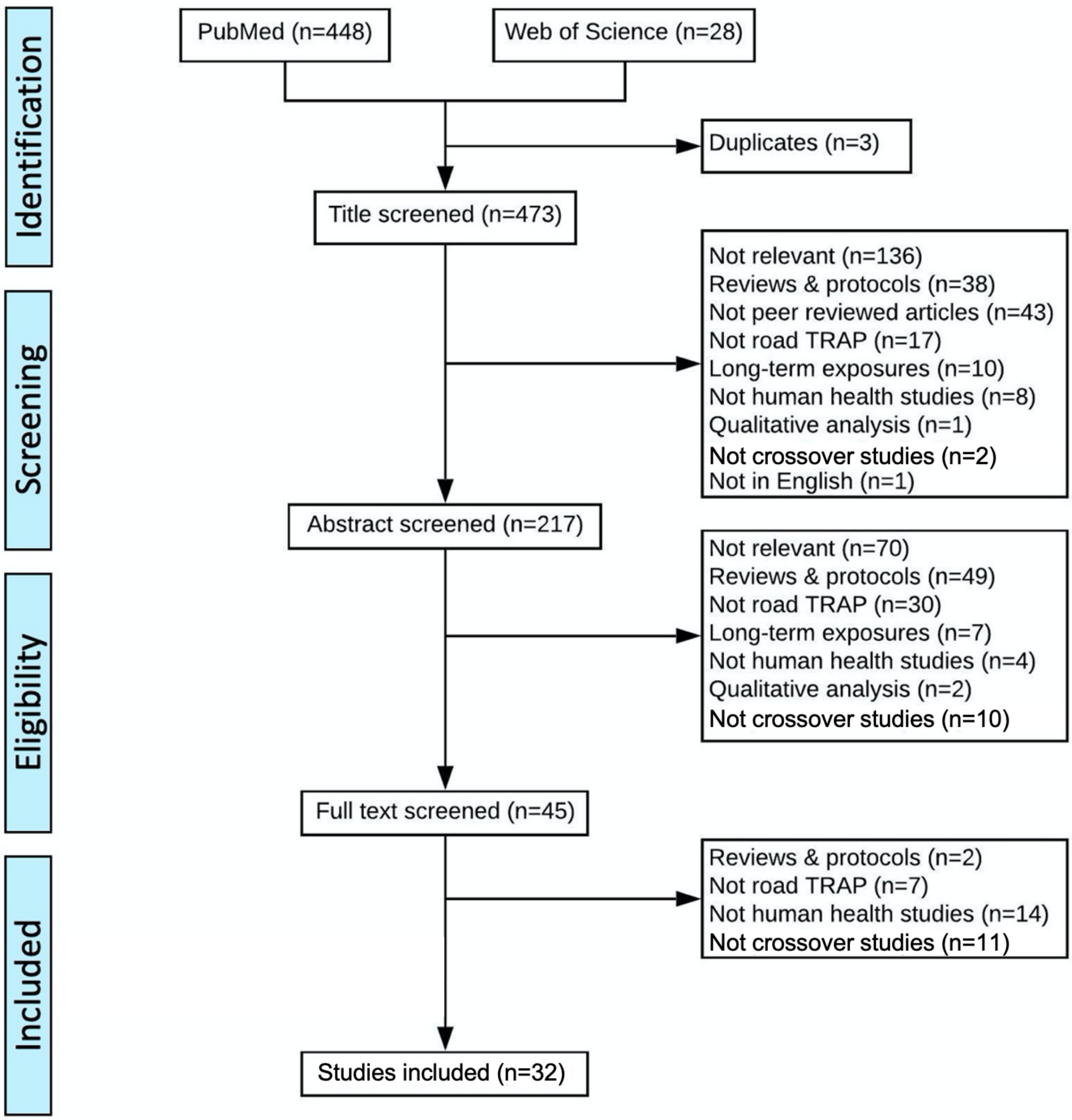

Figure 3. Preferred reporting items for systematic reviews and meta- analyses (PRISMA) diagram for health effect studies

Data were extracted systematically from each study using a pre-designed standard data collection form. The details of each study were tabulated, including title, journal, author(s), year of publication, study location, study design, population (sample size and subject characteristics), study settings, exposure duration, measured TRAP, outcome assessment, statistical methods, and main results. Due to heterogeneity in the study settings and measured outcomes, the results were analyzed using a narrative synthesis rather than a quantitative synthesis.

A total of 13 out of the 32 crossover studies were controlled exposure experiments in laboratory settings (i.e., exposure chambers). Controlled exposure experiments (i.e., chamber studies) and real-life exposures studies are listed in Table 3 and Table 4, respectively.

1.4.1 Crossover designed controlled exposure experiments

A total of 13 studies were conducted in chambers with controlled exposures (Table 3). Eleven of the chamber studies investigated the health effects of diesel exhaust (controlled for $PM_{2.5}$ mass concentrations) compared to filtered air exposures, while the remaining two studies estimated changes in health biomarkers after exposure to different levels of CO and NO_2.

1.4.1.1 Gaseous pollutants

The study exploring the health effects of one-hour NO_2 exposures on patients with stable coronary heart disease reported null associations for all the health outcomes measured (FeNO, lung function, heart rate, blood pressure, leucocyte coping capacity and, and time-domain and frequency-domain of HRV parameters) [54]. However, these null results may be biased since all the patients were taking regular medication during the study, which could interfere the effect of NO_2 exposures. The study exploring the health effects of CO among healthy adults found that the increment in CO concentrations was correlated with decreased diastolic blood pressure (DBP) and increased degree of self-reported drowsiness, failure in focusing and fatigue [55]. However, the study exposed subjects to increasing levels of CO in chronological order with a wash-out period of only 60 min. The reported effects of CO may be results of cumulative exposure of the series level exposure of CO and the effect on fatigue may be partly due to the repeated tests.

1.4.1.2 Particles

1.4.1.2.1 Particles and inflammation

Among crossover studies exposing subjects to different levels of $PM_{2.5}$ (diesel exhaust vs. filtered air), the most common health outcomes measured were inflammatory responses. Four out of five studies reporting systemic inflammation found non-significant associations between 60 min or 120 min of diesel exhaust exposures and different inflammatory markers for healthy subjects from immediately after exposure to 24 hours after exposure [56-59]. However, a Seattle study having healthy adults exposed to diesel exhaust (at 200 $\mu g/m^3$ of $PM_{2.5}$) for 2 hours, reported small but significant increases in different inflammatory biomarkers after 5 hours (matrix metalloproteinase-9, IL-1beta, IL-6 and IL-10) and 20 hours (E-selectin, intercellular adhesion molecule-1, vascular cell adhesion molecule-1, and myeloperoxidase) after exposure [60]. The subjects in the Seattle study were resting during exposure, whereas subjects in the other 4 studies reporting null association were performing moderate physical exercise (minute ventilation of around 15 or 20 $L/min/m^2$ body surface area) on bicycle ergometers during exposure. It is possible that physical activity moderated the association between TRAP exposures and systemic inflammation.

1.4.1.2.2 Particles and vasomotor dysfunction

Three crossover studies explored the associations between diesel exhaust and vasomotor dysfunction. The studies conducted in Seattle and Sweden recruited healthy subjects for the experiments and found adverse health effects of diesel exhaust on arterial vasoconstriction: the

Seattle study reported significant reduction in brachial artery diameter (20.09 mm, 95% CI: 20.01, 20.17) at 30 min after the 2 hours exposure to diesel exhaust at rest (200 μg/m^3 of $PM_{2.5}$) compared to filtered air exposure, and also found the modification effect of genotypes (AGTR1 and TRPV1) [61]; the Swedish study found cycling intermittently for 60 min in diesel exhaust (300 μg/m^3 of $PM_{2.5}$) attenuated the vasodilatation to acetylcholine, bradykinin, sodium nitroprusside, and verapamil at 6 hours post-exposure, compared to filtered air exposures [56]. Another study in the UK enrolled 20 male patients with stable coronary artery disease to cycle intermittently for 60 min in diesel exhaust (300 μg/m^3 of $PM_{2.5}$) and filtered air in a randomized order and showed that diesel exhaust exposures did not aggravate preexisting vasomotor dysfunction. However, this result may be biased because patients in the UK study were taking regular medication that were known to influence endothelial vasomotor function [62].

1.4.1.2.3 Particles and other health outcomes

Controlled exposure studies have investigated the effects of diesel exhaust exposures on lung function, fibrinolytic function, HRV, blood count, postural stability and neurodegeneration. Limited evidence was found for diesel exhaust exposure and lung function [57,63,64]. Two studies investigated the association between exposures to diesel exhaust and fibrinolytic function and found reduction of tissue plasminogen activator at 6 hours following the 60 min intermittent cycling in diluted diesel exhaust (300 μg/m^3 of $PM_{2.5}$) for both healthy and male coronary artery disease patients [56,62]. Two hours of diesel exhaust inhalation at 200 μg/m^3 resulted in increased high frequency (HF) power of HRV comparing to filtered air exposure (**Δ** = 0.33, 95% CI: 0.01, 0.7) and decreased low frequency and high frequency ratio (LF/HF) (**Δ** = -0.74, 95% CI: -1.2, -0.2); whereas, the effect only existed at 1 hour post-exposure, and was not observed at other times up to 20 hours after the exposure [65].

For blood count, 2-hour exposure to diesel exhaust was found to be significantly associated with increased hematocrit at 7 hours post exposure in both healthy and metabolic syndrome subjects, with a stronger association in the latter group; however, diesel exhaust elicited increased platelet count at 22 hours following exposure in only the healthy subject group [60].

One Canadian study measured postural stability using Balance Error Scoring System (BESS) before and after 120 min exposure to diesel exhaust for 28 healthy participants; no significant association was seen between diesel exhaust exposure and postural stability [66].

In addition, a study analyzed neurotoxicity of diesel from the same trial by measuring astrocytic protein S100b, the neuronal cytoplasmic enzyme neuron-specific enolase, and serum brain-derived neurotrophic factor; still, no associations were found between diesel exhaust exposures and brain damage [58]. It is possible that acute diesel exhaust exposure was insufficient to induce changes in the neuro-cognitive spectrum, as the impact of TRAP exposures on central nervous system may occur through a chronic, "multiple-hit" mechanism [66].

1.4.1.3 Physical activity

There is increasing interest in the trade-offs between the potentially adverse effects of TRAP exposures and health benefits of physical activity. A few Canadian studies investigated the modification effects of exercise on diesel exhaust exposure in chamber experiments. One study explored the effect of diesel exhaust on cycling performance as well as cardiorespiratory health. The study recruited 8 healthy endurance-trained males and exposed them to diesel exhaust (300 $\mu g/m^3$ of $PM_{2.5}$) or filtered air for 60 min followed by a 20 km cycling time trial. In contrast to the non-significant effect of TRAP exposures on lung function reported by other studies, the study reported that compared to filtered air exposure, diesel exposures induced decrement in FEV1 and increment in heart rate during the cycling time trial. However, no association was found for diesel exhaust exposure and cycling performance represented by time used to cover the 20 km distance [63]. The other 2 studies were based on the same experiment design with 18 recreationally active males performing high-intensity cycling, low intensity cycling and resting in either diesel exhaust (300 μg/m^3 of $PM_{2.5}$) or filtered air for 45 min. No sign of increment in systemic inflammatory markers [59], or difference on lung function and autonomic effects [64] were found following exercising in diesel exhaust compared to filtered air.

1.4.1.4 Strengths and limitations

The strength of the controlled exposure experiments is in the ability to infer causality. The crossover design studies allow each study participant to act as his or her own control, and are able to identify within- and between-subject variations. Except for one study in Korea investigating adverse effects of CO [55], all the others randomized the order of exposure, and most had double-blinded participants and research staff (except the UK study addressing NO_2 is single-blinded [54]). The randomized double-blind design with a long period (1-9 weeks) of wash-out avoided possible carryover effects between exposure conditions and unconscious information bias. In addition, these studies employed strict controls to eliminate bias. For example, some studies had each subject performing trials at the same time of day to control the diurnal variations of different health markers [59,61-65]; other studies controlled the temperature and humidity of the exposure chamber to account for the meteorological factors on both exposure and health outcomes [56,60]; some studies required participants to maintain the same pre-test transportation mode and route to minimize variations of TRAP exposure prior each trial

[58,59,61,63,64,66]; and most studies asked participants to refrain from specific food/drinks or medication/vitamin supplementation before all the trials [56,58-64,66] or provided meals with the same food content and quantity to participants during trials [60] to avoid the confounding of diet on biomarkers.

One limitation for these chamber studies is that study participants were not exposed to real-life TRAP exposures. Although some studies had subjects intermittently cycling to mimic the physical activity level in real-world exposures in transit, differences exist in TRAP components, psychological stress, noise levels, meteorological factors, and exposure position between chamber studies (controlled exposure studies) and real-life exposures. As such, these studies are limited in the ability to generalize results to real-world commuting scenarios. As described above, most of the studies controlled $PM_{2.5}$ concentrations in the exposure chamber and investigated the association between fine particles and different health outcomes. However, variations may exist in other unmeasured pollutants (*e.g.*, NO) that are potentially responsible for adverse health effects [62,65]. Relatively small sample sizes pose another limitation in these resource-intensive studies. Such controlled exposure studies measured multiple health outcomes and are limited in statistical power due to small affordable sample size and feasibility issues, particularly for rare outcomes. For example, some studies were powered based on one of the health outcomes measured and may inadequately powered for other endpoints [54,59,64].

Table 3. Summary of controlled exposure experiments.

Study	Study area	Population	Exposure duration	Statistical methods	Health outcomes	Effects (↑↓↔) *
Peretz, 2008 [65]	Seattle, USA	A total of 16 (3 healthy and 13 MetS) adults aged 18-49, not smoking ≥ 6 mo, with normal spirometry, no history of ongoing medical care for heart diseases, hypertension, asthma, diabetes, hypercholesterolemia or other chronic conditions	120 min (9am-11am)	paired t-tests, and ANOVA	HRV	↑↓ (frequency domain) ↔ (time domain)
Krishnan, 2013 [60]			120 min	paired t-tests	complete blood count and differential count inflammatory cytokines endothelial adhesion molecules	↑ (hematocrit), ↑ platelet (healthy subjects), ↔ (WBC, neutrophils, lymphocytes or erythrocytes) ↑ (matrix metalloproteinase-9, IL-1β, IL-6, IL-10) ↑ (sE-selectin, sICAM-1, and sVCAM-1)
Sack, 2016 [61]		21 healthy non-pregnant adults aged 18-49, not currently smoking, with BMI ≤ 27kg/m^2, normal fasting blood sugar, and brachial artery images optimal for analysis	120 min in the morning	linear mixed-effect models	BAd	↓
Giles, 2012 [63]	Vancouver, Canada	8 endurance-trained non-smoking males with no history of cardiorespiratory diseases	60 min	paired t-tests, and ANOVA	heart rate lung function VO2, VCO2, VE, VT, FB, and SpO2	↓ ↓(FEV1) ↔
Cliff, 2016 [58]		28 non-smoking, non-pregnant healthy subjects aged 19-49, with no co-existing medical conditions or medications, could spoke & read in English, not having a	120 min	ANOVA	IL-6, TNF-α, the astrocytic protein S100b, NSE, and serum BDNF	↔

Curran, 2018 [66]		moderate-to-high degree of claustrophobia and implanted metal interfering with fMRI		linear mixed-effect models	postural stability	↔
Giles, 2018 [64]	Vancouver, Canada	18 recreationally active males who were non-smokers and were free from cardiorespiratory diseases	30 min	ANOVA	lung function FeNO HRV symptoms plasma norepinephrine	↔ ↑ ↑ ↓ ↑ (throat and chest symptoms) ↑
Giles, 2019 [59]					complete blood count endothelial adhesion molecules	↔ ↓ (sICAM-1), ↔ (sVCAM-1, sP-Selectin and sE-Selectin)
Mills, 2007 [62]	UK	20 not currently smoking men with stable coronary artery disease, with no occupational exposure to air pollution, prior myocardial infarction (>6 mo), asthma, angina pectoris, arrhythmia, diabetes, uncontrolled hypertension, renal or hepatic failure, and were able to achieve Bruce protocol stage 2	60 min (8am-9am)	2-tailed Student's t-tests	ST-segment depression vasomotor dysfunction t-PA	↑ ↔ ↓
Barath, 2010 [56]	Sweden	18 healthy non-smoking males aged 21-30 with normal lung function, were free from symptoms of respiratory tract infections ≥ 6 weeks prior to and during the study	60 min	2-way ANOVA and 2-tailed Student's t-tests	blood pressure heart rate baseline forearm blood flow after exposure vasodilatation t-PA systemic inflammation biomarkers (peripheral blood leukocyte, neutrophil and	↔ ↔ ↔ ↓ ↓ ↔

					platelet counts, plasma concentrations of TNF-a, IL-6, sP-selectin, sICAM-1, CD40L and CRP)	
Muala, 2014 [57]	Sweden	30 non-smoking healthy subjects	60 min	McNemar's Chi-square tests, Wilcoxon's signed-rank tests, and ANOVA	symptoms lung function inflammation biomarkers (IL6, TNF-α, sP-selectin, sICAM-1, and CD40L)	↑ ↔ ↔
Scaife, 2012 [54]	Aberdeen, UK	18 non-smoking patients aged <80, with stable CHD, reduced LV systolic function, on cardiac rate, rhythm and HRV indices and leucocyte coping capacity, and were not taking beta blockers,	60 min	paired t-tests and Wilcoxon's signed-rank tests	FeNO lung function blood pressure heart rate HRV LCC	↔ ↔ ↔ ↔ ↔ ↔
Lee, 2017 [55]	Seoul, South Korea	29 non-smoking adults who were free from cardiorespiratory disease, and with no occupational TRAP exposures	45 min	one-way ANOVA, Wilcoxon's signed-rank tests and Friedman tests	symptoms COHb levels blood pressure	↑ (drowsiness, failure in focusing and fatigue) ↑ ↓ (DBP)

* Effects marked as ↑ indicate positive associations, ↓ indicate negative associations, and ↔ indicate insignificant associations found in in studies. Abbreviations: MetS (metabolic syndrome), ANOVA(analysis of variance), WBC (white blood cell), sE-Selectin (soluble E-Selectin) , BAd (brachial artery diameter), VO_2 (oxygen consumption), VCO_2 (carbon dioxide production), VE (minute ventilation), VT (tidal volume), FB (breathing frequency), SpO_2 (oxyhemoglobin saturation), fMRI (functional magnetic resonance imaging), S100b (S100 calcium binding protein B), NSE (neuron-specific enolase), BDNF (brain-derived neurotrophic factor), sP-Selectin (soluble Platelet-Selectin), t-PA (tissue plasminogen activator), CD40L (CD40 ligand, a.k.a. CD154), CHD (coronary heart disease), LV (left ventricular), LCC (leucocyte coping capacity), COHb (carboxyhemoglobin), DBP (diastolic blood pressure).

1.4.2 Crossover designed real-life exposure studies

1.4.2.1 TRAP and symptoms

A total of 19 crossover studies were conducted in real-world scenarios (Table 4). Four studies in Australia and the UK recorded self-reported symptoms before, after, and in exposures. A UK study among mild to moderate asthmatic adults showed insignificant differences in self-reported symptoms after participants walked for two hours on London's busiest shopping street (Oxford Street) or in a traffic-free park (Hyde Park) [67]. A similar study in the UK had healthy participants, chronic obstructive pulmonary disease (COPD) patients, and ischemic heart disease (IHD) patients walk for two hours on Oxford Street and in Hyde Park as well, but found COPD patients reported more cough, sputum, shortness of breath, and wheeze after exposure to increased TRAP (walking down Oxford Street vs. in Hyde Park) [68]. For healthy individuals, an Australian study with 38 participants found more reports of eye and chest symptoms after two hours exposure at a heavily trafficked location (positive control) than other locations, and an increment in the report of "dry nose" after two hours exposure at the downwind location of a tunnel ventilation stack after the road tunnel opened than before the tunnel opened [69]. Another Australian study recruited 35 healthy frequent bicycle commuters to complete workday commutes on their typical commuting routes and alternative routes of lower proximity to motorized traffic; the results also showed significantly decreased frequency of in-commute nasopharyngeal irritation when switching from typical route to alternation routes [48]. Although, these studies found potential associations between TRAP exposures and self-reported symptoms among either cardiorespiratory diseases patients or healthy subjects, the results might be biased because (1) participants could not be blinded in all of these four studies, (2) symptoms were all self-reported, and (3) the reported difference on symptoms could be induced by other factors like traffic-related noise.

1.4.2.2 TRAP and respiratory health

More than half of the 19 studies measured lung function as one of the outcomes of interest and reported inconsistent results. In contrast to null associations between TRAP exposures and lung function (measured by spirometry) reported in some studies [48,69-71], others found significant associations between TRAP exposures and lung function among both healthy individuals and asthma/ IHD/ COPD patients [67,68,72-75]. Among studies that found adverse effects of TRAP exposure on lung function, most reported significant decreases in lung function measured by FEV1 and FVC, while a few studies found that TRAP exposures induced a reduction in small airway markers, including mean forced expiratory flow at 25% to 75% of forced vital capacity (FEF25–75) [72] and mid-expiratory flow at 25% lung volume (MEF25) [74]. These studies mostly identified adverse effects of particles ($PM_{2.5}$, PM_1, UFP) on lung function, and a few showed that other components of TRAP, including copper [73] and NO_2 [68] were negatively associated with impaired lung function. However, most of these studies failed to control physical activity levels of subjects during exposure [48,67-70,74,75], which may impact the inhaled dose of TRAP and also lung function directly.

Two studies in Spain investigated effect modification of physical activity during transportation on the relationships between TRAP exposures and lung function [71,76]. Both studies had healthy volunteers participating in four exposure scenarios, including combinations of the exposure status (a. low TRAP environment in a pedestrian friendly park or b. high TRAP environment on a pedestrian overpass of a main transit roadway with a high volume of diesel powered motorized traffic) and the physical activity status (a. rest or b. intermittent exercise as 15 min intermittent cycle ergometry; 50-70% of their maximum heart rate estimated by age and sex). One study with 28 subjects completing the four exposure sessions found that the intermittent physical activity independently increased lung function as compared to rest, all the measured pollutants (BC, UFP, NO_x, PM_{10}, $PM_{2.5}$, PM_{coarse}) had null associations with lung function, and limited evidence for the interaction between TRAP and physical activity for lung function [71]. However, the other study with 30 subjects found physical activity and PM_{coarse} exposures were both independently associated with lung function immediately after and 7 hours after exposure, and physical activity reduced the negative impact of particulate matter exposure on lung function while TRAP exposure reduced the positive effect of physical activity on lung function ($p_{interaction} < 0.05$) [76]. Although these two studies were designed to avoid diurnal variation of health markers (exposure scenarios all happened between 8am and 10am) and to minimize pre-test exposures (volunteers arrived at the study site before morning rush hour), both studies could not blind volunteers to different exposure scenarios that may introduce unconscious information bias.

Airway inflammation, often noninvasively measured by FeNO, is another common health outcome of interest in studies investigating short-term effect of TRAP exposures. Positive associations between 60-120 min excessive exposures to TRAP (including PM_{coarse}, $PM_{2.5}$, EC and Cu) and increased airway inflammation were reported in studies among healthy adults [69,71-73,77]. In contrast, one study in Belgium had healthy volunteers cycling for 20 min either near a major bypass road or in a room with filtered air, and found null associations between cycling site, $PM_{2.5}$ or UFP and FeNO [78]. An Austrian study having healthy students walk for 1 hour along a busy road or in a park found increased particle exposure was significantly associated with reduced FeNO immediately after and 1 hour after the walk [74]. Though previous studies showed conflicting results on the circadian rhythmicity of FeNO [73,79,80], the diurnal variations of FeNO may confound the associations between short-term TRAP exposure and airway inflammation, which may explain the counter-intuitive results reported by the Austrian study. Additionally, the very brief (20 min) exposure to TRAP in the Belgian study may be insufficient to induce airway inflammation among healthy individuals.

1.4.2.3 TRAP and cardiovascular health

HRV (as a marker for cardiac autonomic regulation) was the most studied cardiovascular outcome in these studies, followed by heart rate and blood pressure. Consistent with results from controlled exposure chamber studies, most crossover designed studies with real-life exposure scenarios reported significant associations between TRAP exposures and HRV indices among healthy subjects. One study in Denmark found subjects had increased LF of HRV after commuting on diesel-powered trains for three days compared to three-day commuting on electric-powered trains [75], while another study in Beijing found decreased HF of HRV among healthy college students after traveling approximately four hours on subways compared to traveling on the same subway line with respirators and/or headphones [81]. Studies estimating health effects of different air pollutants showed significant associations of UFP, $PM_{2.5}$, PM_{10} with frequency-domain components of HRV [72,81], and associations of $PM_{2.5}$, NO_2, and O_3 with time-domain components of HRV[72,82]; also, the regional $PM_{2.5}$ exposures prior to the study test day modified the association between TRAP exposures and HRV[82]. Only one study found limited evidence of an association between $PM_{2.5}$ exposure during walking and HRV [74]. However, this study measured HRV by electrocardiograph (ECG) devices when subjects were walking, which may introduce motion artifacts to the ECG signals.

Some of these real-life exposure studies measured heart rate and blood pressure as outcomes of interest but showed inconsistent results. For heart rate, a Beijing study had healthy college students traveling on a subway line for approximately 4 hours, and showed decreased heart rate when students traveled on subways wearing respirators and/or headphones compared to when they traveled without any interventions [81]. However, the London study of both healthy subjects and chronic diseases patients found no differences in heart rate between walking on busy street or in a park among all of the subject groups (health, COPD, and IHD) [68]. This same study found positive associations between 2 hours of TRAP exposure and SBP among the COPD group 5 hours as well as the IHD patients at 26-hour post-exposure (no association was found among healthy subjects) [68]. An Austrian study showed that increased level of $PM_{2.5}$ during walking was significantly related to increased SBP among healthy individuals [74]. However, it is worth noting that the blood pressure was measured during commuting with ambulatory blood pressure monitoring in the Austrian study rather than in the sitting position.

A few studies focused on the adverse effects of TRAP exposures on vascular function. A study measured reactive hyperemia-mediated vasodilation and nitroglycerin-induced vasodilation for healthy adults after each 3-day exposure in diesel-powered trains or electric-powered trains during daily commutes; the results showed no associations between diesel exposure and microvascular dysfunction [75]. Since there were no baseline measurements for subjects in the design and no adjustment for potential confounders in the analyses, the results may be biased by the daily variations of health markers and other confounding factors. Two other studies measured flow-mediated vasodilation and arterial stiffness (pulse wave velocity and augmentation index) after 20 min and 120 min exposure to TRAP respectively, and both found a significant adverse effect of TRAP exposures on vascular health [68,82,83]. In particular, the study in London measured pulse wave velocity and augmentation index for three groups of subjects (healthy, COPD and IHD group) before and after walking along a busy road or in a park. In all of the 3 groups, subjects had lower pulse wave velocity and augmentation index up to 26-hour after the walk in the park compared to the walk on the road; the stratified analyses reveal that NO_2 and UFP was associated with arterial stiffness for COPD patients while BC and UFP was associated with arterial stiffness [68].

1.4.2.4 TRAP and systemic inflammation

The effect of TRAP exposure on systemic inflammation has been evaluated in many of these studies. While most controlled exposure experiments found null associations between TRAP and systemic inflammation, cross-over designed real-life exposure studies report conflicting results. Some studies found increased level of systemic inflammations markers (*e.g.*, interleukin, tumor necrosis factor alpha, acute phase proteins, cell adhesion molecules, differential cell count and myeloperoxidase) in blood samples at 30 min to 8 hours after 20 min-120 min exposures to increased TRAP among healthy and asthmatic populations [67,71,73,78]. However, a study in Denmark collected blood samples from subjects after each 3-day exposure sessions on diesel-powered trains or electric-powered trains in daily commute and found unaltered levels of CRP and serum amyloid A [75]. As mentioned earlier, the results may be biased by the daily variations of biomarkers and other confounding factors because of lacking baseline health measurements and information on potential confounders. An Australian study measured inflammatory cells in sputum at 3 hours after the 2-hour TRAP exposure and also found null associations between TRAP and systemic inflammation [48]. It is possible that the outcome (inflammatory cells in sputum) is not as sensitive as other biomarkers to changes in TRAP concentrations, and may have different response time to TRAP exposures. Additionally, counter to expectation, negative associations between $PM_{2.5}$ inhalation doses and IL-10 and neutrophils were found in a Dutch study, where blood inflammation biomarkers at 6-hour after 2-hour exposure in transit were analyzed [84]. Related to inflammation, two studies investigated the short-term effect of TRAP exposures on coagulation. The same Dutch study found unexpected negative associations between increased $PM_{2.5}$ exposures and decreased factor VII. Since it was not clear whether a wash-out period was included or whether the order of exposures for different commuting modes were randomized in the Dutch study, it was difficult to determine the reliability of their results for systemic inflammation and coagulation. Also, because there was no information about other components of TRAP (*e.g.*, NO_2, CO), the counter-intuitive findings of the Dutch study may be confounded by the gaseous pollutants. A Belgian study reported insignificant differences in platelet function between 20 min cycling near a major road versus in a room with filtered air [78]. This null association may be explained by the brief exposure to TRAP, which may have been insufficient to induce changes in coagulation.

1.4.2.5 TRAP and oxidative DNA damage

Two studies in Denmark explored the effect of short-term TRAP exposure and oxidative DNA damage (both measured by DNA strand breaks and FPG-sensitive sites in peripheral blood mononuclear cells). One study recruited 15 healthy adults to cycle 20 km in traffic or in a clean room; results showed 4-fold increase in the level of FPG-sensitive sites after cycling in traffic compared to cycling in the clean room [85]. Another study enrolled 29 healthy volunteers to commute on diesel-powered or electric-powered trains for 3 consecutive days and analyzed oxidative DNA damages at the end of each 3-day exposure scenario; similarly, higher levels of

DNA strand breaks were found after commuting by diesel-powered trains for 3 days than riding electric-powered trains [75].

1.4.2.6 Metabolomics

Only one study applied metabolomic methods to detect associations between TRAP exposure and metabolites and to identify possible metabolic pathways and mechanisms underlying the adverse effect of TRAP on human health. The study employed untargeted analysis by a liquid chromatography with high resolution mass spectrometer (LC-HRMS) to analyze metabolite features in venous blood from 45 subjects with or without asthma before and 8-hour after 120 min commute in cars. After adjusting for potential confounders and false discovery rates, the study identified 494 and 220 unique metabolic features associated with at least 3 pollutants in the negative and positive ionization modes, respectively; the study also identified 5 metabolic pathways predominantly associated with xenobiotic-mediated oxidative stress and acute inflammatory response significantly perturbed across different pollutant models; and finally the study annotated 45 metabolic features, 92% of which were endogenous metabolites related to oxidative stress, inflammatory responses, and nucleic acid damage and repair and hypothesize that TRAP may perturbate the arginine metabolome [86]. Findings from the study reveal possible mechanisms of TRAP toxicity, and support future use of the untargeted metabolomic methods in investigating adverse health effect of TRAP exposure.

1.4.2.7 Limitations

The difference between crossover studies with real-life exposure and controlled exposure experiments (chamber studies) is that in most cases, study participants could not be blinded for different exposure sessions. In most studies, large variations of TRAP exposure levels were realized by picking exposure locations with distinct characteristics in term of traffic, like the assignment of busy roads vs. parks/clean rooms [67-69,71-74,76,78,82,85,86], or the assignment of different commuting routes with varying proximity to traffic and the assignment of different transportation modes. The lack of blinding, and thus the psychological factor of participants' perception of differences between exposure sessions may introduce bias into health measurements. However, some studies leveraged facial masks to allow variations of TRAP exposure while blinding the study volunteers. For example, the study in Tianjin used powered air purifying respirators (PAPRs) with either sham or effective filters to expose subjects to different levels of TRAP [77]. Such study design could be a useful way to blind study participants in real-life exposure studies.

Another difference from the chamber experiments is that additional efforts are needed to control for the confounding effect of noise. Study participants exposed at various locations with different TRAP levels are normally exposed to different levels of noise as well. For example, locations with high level of TRAP concentrations tend to be closer to busy traffic, where traffic-related noise would also be higher than, or the sound characteristics might differ from low TRAP locations (*e.g.,* parks). While a few studies had noise as an exposure of interest [68,74,81], only one study measured noise levels simultaneously with TRAP exposure and further adjusted for noise levels in data analyses [73].

Finally, there is a trade-off between measuring the subsequent effects of TRAP exposures and strict controls for potential confounders. As a crossover study focuses on short-term health effects of exposures, and most studies are designed to expose subjects to TRAP for 60 min-120 min to mimic the normal daily commuting time, the acute effect of short-term TRAP exposures on health measured in these studies is transient. Some markers may respond to TRAP exposures in a few minutes, while others may show changes at several hours after the exposure. Therefore, timing is an important issue for measuring changes in biomarkers. Many studies measured health markers multiple times from immediately after to 24 hours after the exposure to identify the time lag of effects and capture changes in different markers. However, when collecting markers from participants several hours after the exposure, it is infeasible to control potential confounders in real-life exposure studies as strictly as they may be controlled in chamber experiments. Thus, these markers measured in later time-points may be biased by potential exposures in subjects' daily life. For example, many of these studies measured or collected biomarkers 6 or 8 hours after the exposure but with limited information on other exposures or potential confounders for the period between the end of the exposure and later health measurements [67,68,71,73,74,76,77,84,86]. While subjects were in the real-world instead of in an experimental setting, biomarkers collected several hours or even in the next day would be impacted by many different factors, including other sources of exposure, diet, mood, sleep, etc.

Table 4. Summary of real-life exposure studies

Study	Study area	Population	Exposure duration	Statistical methods	Health outcomes	Effects (↑↓↔) *
Vinzents, 2005 [85]	Copenhagen, Denmark	15 healthy non-smoking subjects	mean cycling time of 93 ± 15 min from Mar. to Jun., 2003	linear mixed-effect models	oxidative DNA damage (strand breaks and oxidized purines)	↑ (FPG-sensitive sites)
McCreanor, 2007 [67]	London, UK	60 adults with either mild (n=31) or moderate (n=29) asthma	120 min (10:30am-12:30pm) on weekdays between Nov. and Mar. from 2003 to 2005	linear mixed-effect models	lung function FeNO exhaled breath condensate (pH) respiratory symptoms inflammation biomarkers in sputum (total and differential cell counts, IL-8, myeloperoxidase, and eosinophil cationic protein)	↓ (FEV1, and FVC) ↔ ↑ ↔ ↑ (myeloperoxidase)
Jacobs, 2010 [78]	Antwerp, Belgium	38 non-smoking subjects aged 18-65 years, cycling to work ≥ twice/week, who were not taking antiplatelet therapy	20 min	linear mixed-effect models	FeNO inflammation biomarkers (blood cell counts, differential leukocyte counts, IL-6, Clara cell protein, and platelet function)	↔ ↑ (blood neutrophils) ↔ (IL-6, platelet function, Clara cell protein and number of blood leukocytes)
Cutrufello, 2011 [83]	Scranton, USA	16 healthy, non-asthmatic, non-smoking male collegiate athletes	20 min	ANOVA and Pearson's correlation	total work accumulated (kJ) FMD pulmonary vasoconstriction (PAP)	↓ ↓ ↑

Weichenthal, 2011 [72]	Ottawa, CA	42 healthy non-smoking adults not exposed to tobacco smoke in home and not take medications for cardiorespiratory conditions	60 min (11:30am-12:30pm) on weekdays from May to Sep. 2010	linear mixed-effect models	lung function HRV FeNO	↑ (FEF25-75, FEV1) ↓ ↑ ↑
Zuurbier, 2011 [84]	Arnhem, the Netherland	34 healthy non-smoking office workers aged 18-56, living close (< 20 min) to the starting point of exposure	120 min during morning rush hour on 47 weekdays from Jun. 2007 to Jun. 2008	linear mixed-effect models	inflammation biomarkers (CRP, IL6, IL8, IL10, TNFα, CC16, and blood cell count) blood coagulation markers (PT, APTT, platelets, fibrinogen, factor VII, and vWF)	↓ (IL10, neutrophils) ↔ (CC16) ↓ (factor VII)
Cowie, 2012 [69]	Sydney, Australia	36 non-smoking, non-pregnant volunteers who were able to walk for 2 h and had sense of smell	120 min (2 periods of 20 min walking and 2 periods of 10 min rest interlaced)	PCA and linear mixed-effect models	lung function FeNO symptoms	↔ ↑ ↑ (eye, nose, and chest symptoms)
Jarjour, 2013 [70]	Berkeley, USA	15 healthy regular cyclists (≥ once/week) aged 23-48, not current smoking, with no cardiorespiratory and other chronic conditions	8am–10am on weekdays from Apr. to Jun 2011	Paired t-tests	lung function	↔
Cole-Hunter, 2013 [48]	Brisbane, Australia	35 healthy adults not smoking > 1 yr, with commute cycle routes of high proximity to traffic, no history of cardiopulmonary disease, and recent respiratory infection (symptoms > 2 weeks)		linear mixed-effect models	symptoms lung function inflammatory cell in sputum (total cell counts and differential cell counts)	↑ (nasopharyngeal irritation) ↔ ↔

Weichenthal, 2014 [82]	Montreal, CA	53 healthy non-smoking non-pregnant women aged 18-45, not taking heart or anti-hypertensive medications, and able to complete 2 h of moderate exercise on bicycles	120 min (approximately 11am-1pm) in the summer of 2013	linear mixed-effect models	HRV microvascular function blood pressure	↑ ↓ ↓ (RHI) ↑ (SBP, DBP)
Kubesch, 2015 [71]	Barcelona, Spain	28 healthy, non-pregnant adults aged 18-60, not smoking ≥ 1 year, not taking any medication and not suffering from any chronic illness	120 min during morning rush hour (8am-10am)	linear mixed-effect models	lung function FeNO blood cell count inflammation markers in serum (IL-1b, IL-6, IL-8, IL-10 and TNFα)	↔ ↑ ↑ (neutrophil count) ↑ (leucocytes)
Matt, 2016 [76]		30 healthy adults with the above criteria			lung function	↓ (FEV1, and FVC)
Sinharay, 2018 [68]	London, UK	age-matched (aged ≥ 60) healthy subjects (40), stable IHD patients (39) or stage 2 COPD patients (40), who had been clinically stable ≥ 6 mo, abstained from smoking ≥12 mo and taking medications as recommended by patients' doctors	120 min (11am–1pm) from Oct. 2012 to Jun. 2014;	hierarchical proportional odds analyses with a random effect and linear mixed-effect models	symptoms, lung function resistance of the R5 and R20 blood pressure arterial stiffness (PWV and augmentation index)	↑ (COPD subjects) ↓ (FEV1 and FVC in COPD subjects) ↑ (COPD subjects) ↓ (SBP in COPD subjects), ↑ (SBP in IHD subjects) ↑
Yang, 2018 [81]	Beijing, China	39 healthy non-smoking college students with no cardiorespiratory diseases, not taking any medicine, and having fit factor >100 in fit test of respirator wearing	approximately 9am–1pm in Thursdays and weekends from Mar. to May, 2017	linear mixed-effect models	HRV heart rate ST segment elevation blood pressure	↓ (HF) ↑ ↑ ↔

Golan, 2018 [73]	Atlanta, USA	ACE-2: 60 young (aged 18–39) adults (30 with asthma, 30 without asthma) recruited with the same criteria of ACE-1#	120 min during morning rush hour (7am-9am)	linear mixed-effect models	lung function FeNO inflammation biomarkers (hs-CRP, IL-1β, IL- 6, IL-8, TNF-α, sICAM- 1, and sVCAM-1	↓ (FEV1, FVC) ↑ ↑
Liang, 2019 [86]					metabolic features from untargeted analysis	↑ (inflammatory and oxidative stress related metabolites)
Moshammer, 2019 [74]	Vienna, Austria	24 healthy, non-smoking students	60 min	linear mixed-effect models	lung function FeNO HRV blood pressure	↓ (MEF25) ↓ ↔ ↑ (SBP)
Andersen, 2019 [75]	Copenhagen, Denmark	29 healthy, non-smoking, and non-pregnant adults	3 consecutive days (6 h/day) from May to Nov. 2017	linear mixed-effect models	lung function microvascular function HRV inflammation biomarkers (CRP and SAA) DNA damage in PBMCs (DNA strand breaks and FPG-sensitive sites) urinary excretion of PAH metabolites	↓ (FEV1, PEF) ↔ ↑ (LF) ↔ ↑ (DNA strand breaks) ↔
Han, 2019 [77]	Tianjin, China	39 healthy, non-smoking, non-alcohol-addicted university students	120 min during the rush hour (7:30am–9:30 am)	linear mixed-effect models	FeNO	↑

* Effects marked as ↑ indicate positive associations, ↓ indicate negative associations, and ↔ indicate insignificant associations found in in studies.
#ACE-1 inclusion criteria can be found in Table 1.
Abbreviations: FPG (formamidopyrimidine glycosylase), FMD (flow-mediated vasodilation, PAP (pulmonary arterial pressure), CC16 (Clara cell protein 16), FEF25–75 (mean forced expiratory flow at 25% to 75% of forced vital capacity), PT (prothrombin time), APTT (activated partial thromboplastin time), vWF (von Willebrand factor), RHI (reactive hyperemia index), IHD (ischemic heart disease), COPD (chronic obstructive pulmonary disease), R5 and R20 (respiratory tract at 5 and 20 Hz), PWV(pulse wave velocity), hs-CRP (high-sensitivity C-reactive protein), MEF25 (mid-expiratory flow at 25% lung volume), SAA (Serum amyloid A), PBMC (peripheral blood mononuclear cell), PEF (peak expiratory flow), PAH (polycyclic aromatic hydrocarbon).

1.4.3 Future directions

In general, as compared to the crossover real-life exposure studies, the crossover designed controlled exposure experiments provide stronger evidence for causality due to strict control of potential confounders. However, controlled exposure experiments (i.e. chamber studies) have limited generalizability compared to crossover designed real-life exposure studies. This is because TRAP exposures in a lab setting differ from real-world TRAP exposures in terms of co-exposures to noise, weather, psychological stress, physical activity levels, etc.

With an increasing number of studies of the short-term health effects of TRAP exposure, a few aspects could be considered in future crossover studies, especially for crossover studies under real-life exposure settings. There is increasing interest in understanding the trade-offs between beneficial effects of physical activity in transportation and adverse effects of TRAP exposure, and yet only a few studies have investigated the interaction between physical activity and TRAP exposures on short-term health changes. As physical activity directly impacts human health, future studies could include physical activity as a covariate to evaluate its modification effect on the relationship between TRAP exposure and short-term health effects. Furthermore, future studies could also leverage activity data to calculate TRAP inhaled doses at the individual level to account for the indirect impact of physical activity on health. The TRAP inhalation doses would also be a closer measure of the internal exposure of TRAP to minimize exposure misclassification bias in health effects assessment.

Real-life exposure studies could also benefit from additional information on stress, noise and meteorological factors as they are important factors impacting health. Though existing studies measured health markers before and after each exposure session to control for potential confounders other than the TRAP exposure, most of them failed to control for the confounding effects of noise and psychological stress subjects experienced during the study. In contrast with controlled exposure studies conducted in the experimental chamber settings, the psychological stress, noise levels and meteorological conditions (*e.g.*, temperature, relative humidity, wind speed) vary in different real-world exposure sessions. Thus, lacking information on these important confounders would lead to biased estimates for the health effects of TRAP exposures.

Most existing randomized crossover real-life exposure studies were not able to blind the participants, and thus, health effect estimates might be confounded by unconscious information bias. A few studies have used a PAPR with filters to deplete a specific pollutant in the air, and to estimate the health effect of that pollutant. Such a design of wearing effective versus sham respirator during TRAP exposures would be useful in future studies as a practical way to blind participants and to tease out the health effect of a particular pollutant from bias due to demand characteristics or the placebo effect. However, wearing a typical PAPR designed to protect workers from occupational exposures in public in transit is inherently different exposure scenario than real-life.

TRAP exposures under real-life settings consist of mixtures of air pollutants, including both particles (*e.g.*, UFP, $PM_{2.5}$, PM_{10}, BC) and gases (*e.g.*, NO_2, NO_x, CO). However, most existing studies measured only personal exposure to particles as the surrogate for TRAP. Thus, the estimates of health effect of particles in traffic may be biased as the study cannot rule out the effect of gaseous pollutants on health. Future studies can monitor both particles and gaseous pollutants simultaneously for study participants using newly developed portable sensors to tease out the health impact of particular pollutants exposed in traffic.

In addition, the average level of air pollution concentrations was commonly used to represent personal TRAP exposures in health effect assessment studies. Considering the various ways to characterize and quantify noise exposures and HRV, alternative exposure and outcome metrics, including the median, standard deviation, range, maximum levels, and other novel metrics can be explored in future studies. As recent regulations of ambient air pollution are based on the daily or 8-hour averages, existing health effect assessment studies used the average level of air pollution with the hypothesis that increased average level of air pollution leads to higher risk of diseases or death. However, air pollution exposure peaks may be more associated with the triggering of adverse acute health outcomes. It would be useful to explore alternative exposure metrics using the continuous individual air pollution monitoring data from air sensors used in crossover studies to better characterize short-term TRAP exposures in health effect studies.

Finally, as most studies have found transient and clinically insignificant changes in health markers among healthy participants, future studies may focus more on susceptible populations such as children, the elders and patients with chronic diseases, to better understand whether short-term exposure to excessive TRAP induce clinically meaningful effect on health.

Chapter 2. EXPOSURES TO AIR POLLUTION AND NOISE FROM MULTI-MODAL COMMUTING IN A CHINESE CITY

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2.1 ABSTRACT

Background: Modern urban travel includes mixtures of transit options, which potentially impact individual pollution exposures and health. This study aims to investigate variations in traffic-related air pollution and noise levels experienced in traffic in Chengdu, China.

Methods: Real-time $PM_{2.5}$, black carbon (BC), and noise levels were measured for four transportation modes (car, bus, subway, and shared bike) on scripted routes in three types of neighborhoods (urban core, developing neighborhood, and suburb). Each mode of transportation in each neighborhood was sampled five times in summer and winter, respectively. After quality control, mixed effect models were built for the three pollutants separately.

Results: Air pollutants had much higher concentrations in winter. Urban Core had the highest $PM_{2.5}$ and BC concentrations across seasons compared to the other neighborhoods. The mixed effect model indicated that, as compared to biking, car commutes were associated with lower $PM_{2.5}$ (-34.4 μg/m^3; 95% CI: -47.5, -21.3), BC (-2016.4 ng/m^3; 95% CI: -3383.8, -648.6), and noise (-9.3 dBA; 95% CI: -10.5, -8.0) levels; subway commutes had lower $PM_{2.5}$ (-11.9 μg/m^3; 95% CI: 47.5, -21.3), but higher BC (2349.6 ng/m^3; 95% CI: 978.1, 3722.1) and noise (3.0 dBA; 95% CI: 1.7, 4.3) levels.

Conclusion: Personal exposure to air pollution and noise vary by season, neighborhood, and transportation modes. Exposure models accounting for environmental, meteorological, and

behavioral factors, and duration of mixed mode commuting may be useful for health studies of urban traffic microenvironments.

Keywords: multi-modal commuting; traffic related air pollution; noise; personal monitoring

2.2 INTRODUCTION

Urban mobility is changing. With economic growth and urbanization, individuals are no longer constrained to a single transportation mode. Commuting can include private, public, and shared options, physically active and non-active options, as well as combinations of mode types, such as walking, bicycling, and trips by car, bus, light rail, and train. Changes in urban mobility can potentially alter numerous population health determinants through physical activity levels, stress, access to resources, transportation-related costs, and time, as well as exposures to air pollution, noise, and other environmental stressors [87-90]. Moreover, the impacts associated with mobility changes may differentially affect certain populations based on income and residential location [91-94]. Thus, access to commute options is becoming an important environmental and social justice issue [95].

Air pollution concentrations have been found to be disproportionately high in high-traffic cities around the world. In cities such as Hong Kong [96], Montreal, Toronto, and Vancouver [97], and Los Angeles [98], significantly higher pollutant exposures have been found in transport microenvironments. The Multi-Ethnic Study of Atherosclerosis study reported that in-vehicle exposure contributed 24% of participants' ambient-source NO_2 exposure on average in Winston-Salem and Los Angeles [4]. In a study from Europe, similar results have been found, where despite a small proportion of daily time being routinely spent on intra-city transit (usually no more than 1.5–2 hours per day), commuters can receive up to 30% of their inhaled daily dose of black carbon (BC), and approximately 12% of their daily $PM_{2.5}$ personal exposure during their regular journeys [3]. In light of these findings and the absence of similar studies done in China, it is of great importance to estimate pollution exposures during transportation for Chinese cities. Transportation is also the major source of noise in cities [99]. For example, the measured time-weighted noise levels for the subway in New York city reached 80 decibels (dBA) to 90 dBA, with peaks of 106 dBA [100]. Both air pollution and noise has been related to various adverse health effects in humans. Previous studies document various adverse health effects of air pollution, including respiratory disease, cardiovascular systems, and birth outcomes. Also, excessive noise exposure has been related to annoyance, sleep disturbance, cardiovascular diseases, mental disorder, and children's cognition. Thus, transportation has significant effects on the environment and health.

Personal pollution intake is related to commuting choices due to variations in exposure levels in microenvironment, minute ventilation, as well as commuting time. For example, biking is oftentimes recommended as an active commuting mode and non-emission choice. However, cyclists may experience increased air pollution exposure because of their higher minute ventilation. To date, available evidence linking pollution exposures and health effects for different commuting choices is limited. Understanding the relationship between the choices commuters make and their exposures may be key to reducing exposures by informing behavior and adapting urban infrastructure.

Chengdu is a megacity in the Sichuan Basin, southwest China, with a 2016 population of around 14 million. As the capital of Sichuan province, Chengdu is the only megacity in the western part of China, with 72% of it being urbanized [101]. Located in the bottom of the Sichuan Basin, air pollution is a major concern because the province suffers from acidic rain and frequent haze events due to low wind speed and relatively high humidity [102]. The topography surrounding Chengdu, with Longquan Mountain to the east and Qionglai Mountain to the west, hinders the dispersion of locally produced pollutants and causes high levels of pollution, especially under certain weather conditions [103].

To date, a few studies have measured traffic-related air pollution in Beijing and Shanghai. However, none of these have characterized the potential for differences in noise exposures by transit mode and exposures between different commuting neighborhoods. With rapid development in recent decades, Chengdu has been experiencing changes in urban mobility options as populations confront traffic congestion. The city operates mature private and public transportation systems. Car ownership and private car use have grown considerably. As one indicator of the growth, according to the Traffic Management Bureau of the Public Security Ministry of China, the car ownership in Chengdu witnessed a ten-fold increase in the last decade, reaching 4.94 million at the end of 2017, and second only to Beijing in terms of mainland cities in China [104]. For public transportation, the Chengdu Public Transport Group Co., Ltd., reported that Chengdu had a total of 668 bus routes, with more than 1.5 billion passenger trips having been taken in 2017 [104]. The metro system, introduced in 2010, now includes 6 lines. The nearly 200-km length system served 2.14 million passenger trips on average per day in 2017 [105]. Shared bicycle use has also been booming in Chinese cities since its introduction in 2014. Formerly called the "kingdom of bicycles," Chengdu is a bike-friendly city because of its flat terrain. With more than 1.3 million shared bikes in the city, Chengdu ranks first according to reports from both Mobike and Ofo—two of the biggest companies in the Chinese shared bicycle market—with the longest average distance of 2.3 km per ride and the highest riding index (a combined indicator of riding distance and time per user) compared to other Chinese cities. Although the city has a large population and an extensive and complex traffic system, transit-related noise and air pollution exposures have not been well characterized in Chengdu.

The current study aimed to characterize variations in personal traffic-related pollution exposures ($PM_{2.5}$, black carbon (BC), and noise) for different transportation modes and different neighborhoods using scripted trips in summer and winter in Chengdu.

2.3 METHODS

2.3.1 Neighborhood, Routes and Modes

Chengdu is the capital city of Sichuan province in Southwest China. The weather in the city is humid (with annual average of relative humidity around 80%). The dominant wind direction in Chengdu is Northeast, with daily average wind speed of 1.1 m/s to 1.6 m/s. Similar to other major cities in China, Chengdu consists of five ring roads (from the inner city to the outside are named as the first ring road, second ring road, and up to the fifth ring road) that divide the city in terms of land use and population density. In Chinese cities, the oldest and densest areas of the city typically lie within the first few ring roads, and the addition of ring roads over time reflect the growth of the city, with suburban areas developed principally for residences or new businesses. From Chengdu's city center to the suburbs, three representative neighborhoods were chosen for comparison: a neighborhood in the central city (Urban Core), one between the second and third ring road (Developing Neighborhood), and another outside the fourth ring road (Suburb) (Figure 4). The Urban Core is the economic center and traffic hub of the city, where shopping malls and office blocks are clustered. The Developing Neighborhood is an example of a historically industrial area that was outside of the city, but is now in transition from an area that previously supported a dismantled steel plant to a new residential neighborhood. With high traffic flow on the second ring road, which is a major urban thoroughfare, there are also several construction sites along the road, which reflects the development that is occurring in this neighborhood. The selected Suburb is located in the center of Longquan district. It covers the southeast suburban area of Chengdu, and is the east entrance to the city, with a population of 0.66 million in 2016. Although it is principally a residential area, truck traffic is not unusual during the day, although trucks are not allowed to enter the third ring road between 7 am and 10 pm.

Image 1: https://img1.qunarzz.com/travel/d7/1807/e5/414ab47f2ca500b5.jpg_r_720x480x95_045083cb.jpg
Image 2: http://imgs.soufun.com/viewimage/news/2015_07/07/65/9/hd/006871964000/900x600.jpb
Image 3: https://i2.kknews.cc/SIG=25gipf3/4860004054777sqo9o5.jpg

Figure 4. Map of the three sampling neighborhoods in Chengdu City.

Four modes—car, bus, subway, and shared bike—were sampled within each neighborhood as they represent the four main transportation options in Chengdu. One main travel route was chosen for each of the three neighborhoods (three routes in total). The selection criteria for the routes considered:

(a) Identifying a route that was approximately 2–3 km in distance. To make each mode of transportation feasible and based on the reported average distance per ride of the shared bike of 2.3 km [106], the three routes were designed to be no more than 3 km in distance.

(b) The four trip modes were possible for each route. To make the exposure measures comparable between modes, and not entirely due to routing differences, all modes were ensured to be possible for each route.

The final selected scripted routes were: in the Urban Core, a route from the People's Park subway station to the Chunxi Road subway station (2.4 km); in the Developing Neighborhood, a route from the Tazishan Park subway station to the Dongda Road subway station (2.8 km); and in the chosen Suburb, a route from the Longping Road subway station to the Longquan subway station (2.1 km).

2.3.2 Exposure Measurements

For each of the three neighborhood routes, trips were repeated by research staff in both the summer (August 2017) and winter (December 2017) seasons. For each season, five trips were conducted for each of the four modes (i.e., 20 trips in each season for each neighborhood route; 5 trips × 4 modes × 2 seasons × 3 neighborhood routes = 120 trips in total). The trips in each neighborhood and mode included both weekdays and weekends, morning and afternoon, and rush hour as well as off-peak hours. All the routes were travelled in both directions between 9 am and 4 pm. In the summer and winter sampling campaigns, noise levels and air pollution concentrations were simultaneously measured by portable monitors. For safety, and to make it easier to manage multiple instruments, each trip was monitored by two to four researchers traveling together, carrying different instruments. $PM_{2.5}$ was measured by an optical particle counter, the Portable University of Washington Particle

(PUWP) monitor (University of Washington, Seattle, WA, USA), which collects 12 readings per minute (an estimate of $PM_{2.5}$ mass concentration and particle count concentrations for 6 size bins from 0.3 to 10 um based on the volume-fixed chamber); BC was monitored by the microAeth AE51 (AethLabs, San Francisco, CA, USA), set at a flow rate of 100 ml/min and time base of 30 seconds (30 seconds per reading); and noise level was recorded by the NoisePro DLX Dosimeter (3M, St. Paul, MN, USA), with 1-second measurements. Research staff also carried a Bluetooth GPS data logger BT 335 (GlobalSat, Chino, CA, USA) during each trip in order to record the start and end times and to confirm the actual travel route for each trip. Before the monitoring campaign, the flow rate of AE51 was checked, which was off by less than 1%. Thus, no additional flow calibration was performed for the AE51. Additionally, before and after each trip, the NoisePro DLX dosimeter was calibrated against the Quest QC-20 calibrator (3M, St. Paul, MN, USA). Clocks in all of the instruments were synchronized before sampling campaigns, and inlets for the instruments were fixed on the shoulder or the backpack strap of research staff to measure breathing zone concentrations. For subway trips, exposures were delineated as the period from entering a subway station entrance to leaving the exit at a subsequent station; and similarly, for each bus trip, from the arrival at the start bus station to the exit at the subsequent end station. After each trip, measurements were immediately downloaded from all instruments and safely archived as separate files for later data analyses. After the data extraction, the BC data was checked for the flow, and both the $PM_{2.5}$ and BC data was checked for zero readings to detect any instrumental failure during the monitoring.

2.3.3 Statistical Analysis

Recorded data for $PM_{2.5}$, BC, and noise levels for each trip were extracted from the raw data files in each instrument. Multiple quality control measures were utilized to evaluate the raw data files to ensure an acceptable level of data quality. First, an optimized noise-reduction algorithm (ONA) was used to reduce noise in real-time BC data obtained, which accounts for changes in sensitivity of the measurement related to changes in filter attenuation [107]. The ONA BC data were used in subsequent analyses. Observations with missing values for any pollutant were also removed (25 missing data points for $PM_{2.5}$, 208 missing data for BC, and no missing data for noise). $PM_{2.5}$ measurements with corresponding $PM_{0.3}$ counts equal to 0 were considered unreliable and were removed (353 data points were removed out of 16,543). Finally, $PM_{2.5}$ measurements larger than 1,000 $\mu g/m^3$ and BC measurements larger than 100,000 ng/m^3 were considered outliers and were removed as well (18 outliers for $PM_{2.5}$, and 6 outliers for BC). After the quality control processes, 1-minute averages of $PM_{2.5}$ were computed from the PUWP monitor data. All of the exposure data were then stratified by season, neighborhood, mode of transportation, days of the week (workdays/weekends), and hours of the day (data was grouped into 2-hour chunks as 9:00–10:59, 11:00–12:59, 13:00–14:59, 15:00–16:59, and 17:00–18:59) for descriptive analysis. One-minute average data were collected for all three pollutants and merged for each minute of sampling to calculate pairwise Spearman’s correlation coefficients.

With repeated measurements and different background pollutants levels in each trip, linear mixed models were applied to explain variations in each traffic-related pollution by season, neighborhood, and travel modes. Separate multivariable mixed effect regression models were estimated with each single pollutant as the dependent variable (1-minute average $PM_{2.5}$, 30-second BC, and 1-second noise), with season, neighborhood, and mode as fixed effects independent variables, and with trip as a random effect (random intercept). Days of the week (workdays and weekend) and hours of the day (grouped into 2-hour chunks) were also added into models as fixed effects to adjust for various pollutant distributions in different days and hours. Additional single-pollutant multivariable linear mixed models were established to account for potential interactions between transportation modes and different types of neighborhoods. All data processing and statistical analyses were performed in R 3.5.2 (http://www.R-project.org/) (R Foundation for Statistical Computing, Vienna, Austria).

2.4 RESULTS

A time-series plot for $PM_{2.5}$ and BC raw data (raw measurement before ONA smoothing) for a single day is shown in Figure 5 and shows the variations in different exposures that commuters experience as they transition between transportation modes within a multi-modal travel (each segment of the multi-modal travel represents a ~3km trip on the scripted routes). Looking at some of the demarcated modes (e.g., bus and subway), the exposures are not constant, but can vary during an entire trip, and within modes of the trip. Also, the high levels of $PM_{2.5}$ observed during lunch (not during a trip) illustrates the potential importance of exposures that occur in other microenvironments, and suggests that certain indoor microenvironments can contribute substantially to cumulative PM exposure. Furthermore, the figure shows that the correlations that may exist between $PM_{2.5}$ and BC are not immediately obvious from a single day of monitoring, even with repeated measures. Furthermore, it is noteworthy that the BC raw data measured by the aethalometer was noisy, with many negative values. Thus, all the statistical analyses were based on ONA smoothed BC data.

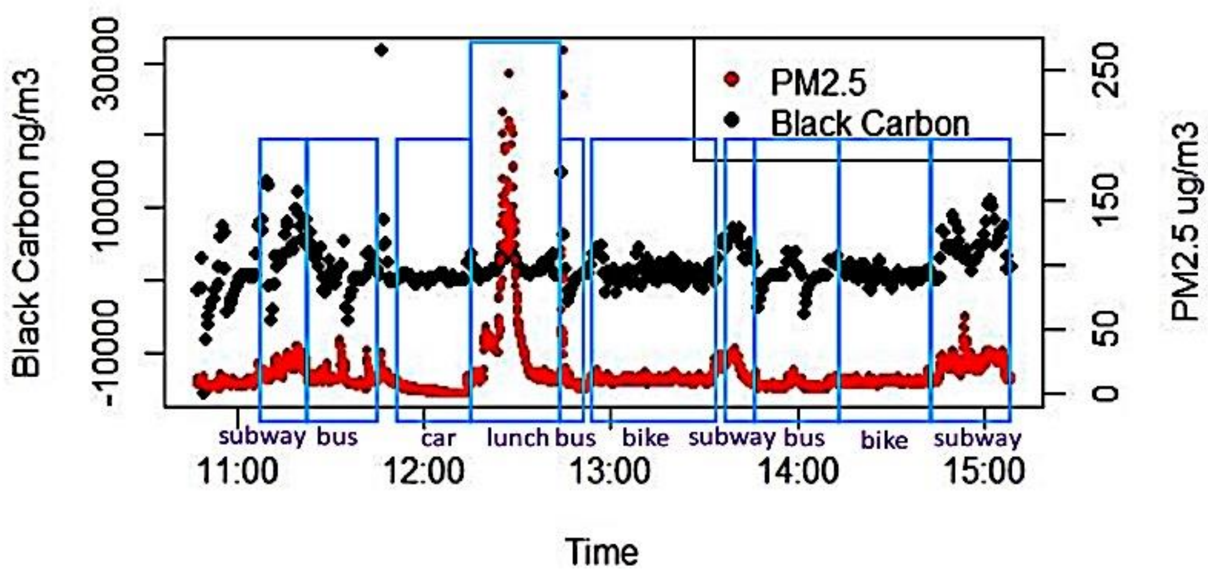

Figure 5. Time-series plot for PM2.5 and BC raw data (before ONA smoothing) in one day.

Descriptive statistics of the three pollutants based on all 120 trips across the summer and winter seasons are summarized in Table 5. $PM_{2.5}$ and BC had much higher concentrations ($p < 0.05$) in the winter than the levels in summer ($PM_{2.5}$ median: 123 vs. 33.6 μg/m^3, BC median: 8916.5 vs. 1896.3 ng/m^3); however, noise levels were slightly higher in the summer time (within and across neighborhoods). In terms of the spatial distribution, the urban core neighborhood had the highest median $PM_{2.5}$ and BC concentrations across seasons. In the summer time, the suburban area had the lowest $PM_{2.5}$ and BC levels, while in the winter time, the lowest $PM_{2.5}$ and BC levels were recorded in the developing neighborhood. Noise levels were roughly the same in the three neighborhoods (within and across seasons). Since days of the week and hours of the day have great impacts on the distribution of pollutants, the data was also summarized by workday/weekend and hour of the day as well (Table A1). All the pollutants ($PM_{2.5}$, BC, and noise) had higher levels on weekends than on workdays.

Table 6 summarizes the correlations between $PM_{2.5}$, BC, and noise in different neighborhoods and seasons. All of the pollutants were positively correlated with each other, except for $PM_{2.5}$ and noise measured in Developing Neighborhood in the winter time ($\rho = -0.11$) and BC and noise measurements in the Urban Core across seasons ($\rho = -0.05$). $PM_{2.5}$ and BC were strongly correlated with each other in the urban core ($r = 0.84$) and suburban ($r = 0.86$) neighborhoods across seasons. $PM_{2.5}$ and BC had a slightly stronger correlation in the summer ($\rho = 0.67$) than in the winter ($\rho = 0.64$) across neighborhoods. In general, noise had weak correlations ($\rho <0.4$) between $PM_{2.5}$ and BC.

Table 5. Summary of exposures during trips by season and neighborhood.

Pollutants	Urban Core			Developing Neighborhood			Suburb			All Area		
	N[1]	Median (Mean)[2]	IQR (SD)[3]	N[1]	Median (Mean)[2]	IQR (SD)[3]	N[1]	Median (Mean)[2]	IQR (SD)[3]	N[1]	Median (Mean)[2]	IQR (SD)[3]
Summer												
$PM_{2.5}$ (μg/m^3)	246	38.4	11.8	337	38.7	15.1	243	10.9	15.3	826	33.6	26.3
BC (ng/m^3)	581	2410	3620	471	1890	3490	477	895	3040	1530	1900	3570
Noise (dBA)	20171	72.8	7.7	14551	72.6	6.0	14489	72.8	6.7	49211	72.7	6.9
Winter												
$PM_{2.5}$ (μg/m^3)	370	178	79.8	289	91.0	25.0	185	157.0	97.5	844	123.0	98.0
BC (ng/m^3)	1014	12000	8380	782	5140	4080	398	10200	6620	2194	8920	8350
Noise (dBA)	30291	72.3	6.3	23487	72.4	6.4	11953	72.8	7.5	65731	72.4	6.6
All Seasons												
$PM_{2.5}$ (μg/m^3)	707	95	144	535	63.0	52.6	428	47.5	130.2	1670	57.0	90.9
BC (ng/m^3)	1595	8590	11000	1253	4160	5380	875	5060	9240	3723	5920	8660
Noise (dBA)	50462	72.5	6.9	38038	72.5	6.2	26442	72.8	7.0	114942	72.6	6.7

[1] N is the number of measurements for each pollutant.

[2] For $PM_{2.5}$ and BC, the median was recorded; for noise, the mean was recorded.

[3] For $PM_{2.5}$ and BC, the interquartile rang (IQR) was recorded; for noise, the standard deviation was recorded.

Table 6. Correlations between PM2.5, BC, and noise during trips by season and neighborhood.

Pollutants	Urban Core			Developing Neighborhood			Suburb			All Areas		
Summer												
	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise
$PM_{2.5}$	1	0.57	0.32	1	0.80	0.18	1	0.63	0.29	1	0.67	0.28
BC	-	1	0.25	-	1	0.34	-	1	0.35	-	1	0.39
Noise	-	-	1	-	-	1	-	-	1	-	-	1
Winter												
	Urban Core			Developing Neighborhood			Suburb			All Areas		
	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise
$PM_{2.5}$	1	0.51	0.03	1	0.12	-0.11	1	0.53	0.38	1	0.64	0.02
BC	-	1	0.16	-	1	0.33	-	1	0.18	-	1	0.16
Noise	-	-	1	-	-	1	-	-	1	-	-	1
All seasons												
	Urban Core			Developing Neighborhood			Suburb			All Areas		
	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise	$PM_{2.5}$	BC	Noise
$PM_{2.5}$	1	0.84	0.01	1	0.55	0.06	1	0.86	0.17	1	0.81	0.06
BC	-	1	-0.05	-	1	0.29	-	1	0.20	-	1	0.12
Noise	-	-	1	-	-	1	-	-	1	-	-	1

Table 7. Summary of multivariable mixed effects model results.

Variables	$PM_{2.5}$ (μg/m^3)			BC (ng/m^3)			Noise (dBA)		
	Estimate	**95% CI**	**SE**	**Estimate**	**95% CI**	**SE**	**Estimate**	**95% CI**	**SE**
Intercept	51.7	37.8, 65.5	7.3	3834.5	2360.8, 5313.2	774.7	74.0	72.7, 75.2	0.6
Bike	reference			reference			reference		
Bus	-8.1	-21.4, 5.2	7.0	-895.9	-2268.9, 476.5	723.8	1.8*	0.5, 3.0	0.7
Car	-34.4*	-47.5, -21.3	6.9	-2016.4*	-3383.8, -648.6	719.9	-9.3*	-10.5, -8.0	0.6
Subway	-11.9	-25.1, 1.3	7.0	2349.6*	978.1, 3722.1	723.2	3.0*	1.7, 4.3	0.7
Suburb	reference			reference			reference		
Urban core	18.8*	6.5, 31.1	6.5	1939.4*	650.8, 3219.3	676.5	0.0	-1.1, 1.2	0.6
Developing Neighborhood	3.3	-9.1, 15.6	6.5	-114.1	-1407.3, 1177.6	680.5	0.3	-0.9, 1.5	0.6
Summer	reference			reference			reference		
Winter	110.9*	108.3, 113.5	1.3	6251.6*	5913.6, 6593.5	174.0	-1.3*	-1.3, -1.2	0.0

∗ Statistically significant based on the 95% CI; all the multivariable models were adjusted for neighborhood, season, days of the week (weekends/workdays), and hours of the day.

The three pollutants were observed to vary by modes of transportation (Table A2, Figure A1 in the appendix). In the summer, riding a car exposed people to the lowest median $PM_{2.5}$ (8.4 $\mu g/m^3$), median BC (211.5 ng/m^3), and mean noise levels (62.3 dBA), while riding a subway was the most polluted mode of transportation for all three pollutants (median $PM_{2.5}$: 43.1 $\mu g/m^3$, median BC: 7616.0 ng/m^3, mean noise: 76.1 dBA). In the winter time, biking had the highest median $PM_{2.5}$ (179.0 $\mu g/m^3$) and median BC (10,979.5 ng/m^3) concentrations compared with the other three modes of transportation, while subway exposed people to the lowest median $PM_{2.5}$ level (92.3 $\mu g/m^3$), and riding a bus was the least polluted modes in terms of BC concentration (median of 7575.0 ng/m^3). Riding a car and a subway still had the lowest (64.3 dBA) and highest (75.5 dBA) mean noise levels, respectively, in the winter time.

Estimates from multivariable linear mixed models adjusted for weekends and workdays and hours of the day are summarized in Table 7. Trips in the winter exposed travelers to higher $PM_{2.5}$ and BC concentrations and lower noise levels. Controlling for season and neighborhood, riding a car resulted in lower $PM_{2.5}$ exposures (-34.4 $\mu g/m^3$; 95% CI: -47.5, -21.3), lower BC exposures (-2016.4 ng/m^3; 95% CI: -3383.8, -648.6), and also decreased noise exposures (-9.3 dBA; 95% CI: -10.5, -8.0) compared to biking. Riding a subway exposed commuters to increased BC (2349.6 ng/m^3; 95% CI: 987.1, 3722.1) and noise levels (3.0 dBA; 95% CI: 1.7, 4.3) compared to biking. Taking a bus also exposed travelers to higher noise levels (1.8 dBA; 95% CI: 0.5, 3.0) than biking. Compared to traveling in the suburban area, commuting in the Urban Core increased $PM_{2.5}$ and BC levels ($PM_{2.5}$: 18.8 μg/m^3; 95% CI: 6,5, 31.1; BC: 1939.4 ng/m^3; 95% CI: 650.8, 3219.3). Differences in noise levels were not statistically significant between neighborhoods.

Estimates from multivariable linear mixed models with interactions between modes and neighborhoods are summarized in Figure 6 and Table A3 in the appendix. The left half of Figure 6 shows the contrast of pollutant levels between modes in each neighborhood and the right half of the figure shows the contrast of pollutant levels between neighborhoods for each mode. The interaction term was only statistically significant for noise ($p = 0.0007$). After adding the interaction term into linear mixed models, the direction of main effects did not change compared to results from the mixed effect model without an interaction term between modes and neighborhoods. In the selected Suburb, riding a car had the lowest $PM_{2.5}$ concentrations compared to biking, taking the subway, or a bus. In the Urban Core, taking a bus exposed individuals to 25.4 μg/m^3 (95% CI: 3.3, 47.5) higher $PM_{2.5}$ than riding a car. In the Developing Neighborhood, biking exposed travelers to higher $PM_{2.5}$ concentrations than people using a car or the subway. Between neighborhoods, biking in the Urban Core had higher $PM_{2.5}$ concentration than in the Developing Neighborhood, while riding a car had higher $PM_{2.5}$ levels in the Suburb than in the Urban Core. For BC exposures, biking exposed commuters to higher BC levels in the Suburb and Developing Neighborhood. Traveling in the Urban core had similar BC levels for the four modes of transportation; also, taking a bus or the subway expose travelers to similar BC concentrations across different areas of the city. Noise levels of different modes of transportation have similar patterns in the three measured areas, riding a bus or a bike had the highest noise levels, while riding a car exposed commuters to the lowest noise levels. Biking, riding the subway, and riding a bus did not vary significantly between areas in the city; however, riding a car in the Developing Neighborhood was noisier than in the Urban Core and the Suburb.

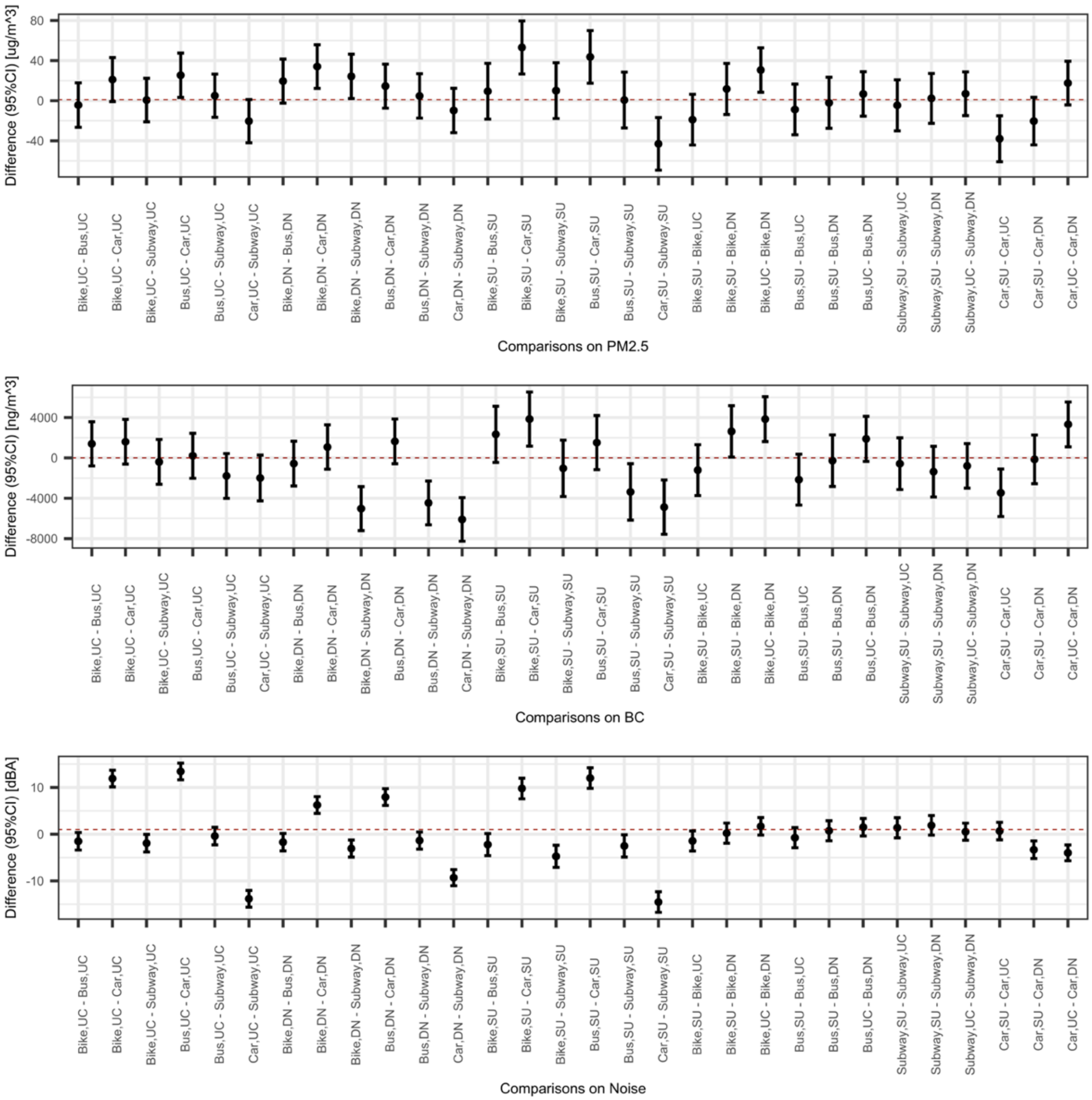

Figure 6. Pairwise comparisons for PM2.5, BC, and noise exposure during trips in mixed effect models with interaction terms between modes and neighborhoods.

Abbreviations: UC represents Urban Core, DN represents Developing Neighborhood, SU represent suburb. Models were adjusted for season, days of the week (weekend/workdays). and hours of the day; The pairwise comparison is the contrast between groups, in which case, comparisons were computed between modes of transportation and neighborhoods. The x axis shows the specified comparison groups, the y axis is the difference between comparison groups. The point in the figure is the estimated difference in pollutant levels between groups, while the bar shows the 95% CI of the point estimate.

2.5 Discussion

The choice of daily commuting can have important consequences on an individual's exposure to traffic-related pollution. Personal exposure to $PM_{2.5}$, BC, and noise in four transportation modes (biking, car, subway, and bus) were examined in summer and winter 2017 in Chengdu, China. A total of 120 trips were assessed to characterize traffic-related pollution in the megacity. Linear mixed models showed $PM_{2.5}$ and BC levels in transportation were much higher in the winter time than the summer months, while noise levels were lower in the winter months. $PM_{2.5}$ and BC concentrations varied spatially, and the Urban Core had the higher air pollution levels compared to other areas. All the pollutants varied between transportation modes. Commuters using a car were exposed to lower $PM_{2.5}$ and BC levels, while riding a subway had higher BC concentrations than other modes. Riding a car also exposed commuters to lower noise levels. However, $PM_{2.5}$, BC, and noise exposures were not affected by neighborhood during bus and subway trips in Chengdu city.

$PM_{2.5}$ and BC concentrations in different microenvironments showed large seasonal variation. Both of the two air pollutants levels were more than three times higher in the winter time than in the summer. Previous ambient air studies reported large seasonal variation of ambient air pollution levels in Chengdu. Wang et al. used 47-mm Teflon filters to collect $PM_{2.5}$ samples, and observed the highest monthly mean $PM_{2.5}$ concentrations in winter (113.5 ± 47.8 μg/m^3) and the lowest in summer (45.1 ± 15.2 μg/m^3) [108]. Shi et al. used medium-volume air samplers to measure $PM_{2.5}$ and their components from January 2009 to March 2013, and found the concentration peak of $PM_{2.5}$ and elemental carbon (or BC) was in winter (especially in January and December) [109]. Unfavorable meteorological conditions, such as low wind speeds, low mixing heights, and relatively low precipitation amount in Sichuan Basin, were common in the winter time in Chengdu [108]. The lower atmospheric boundary layer and large number of days with stagnant atmospheric conditions impair the transport and dispersion capacity of ambient air pollutants [110]. Compared to other provincial capitals, Chengdu has a relatively high fractional contribution to $PM_{2.5}$ concentration from transportation (7.4%); however, the maximum daily fractional contributions from transportation did not present significant seasonal variations [111]. Thus, peaks of air pollution levels in traffic found in the winter time may be due to the higher ambient air pollution concentrations during those months.

Measured $PM_{2.5}$ and BC concentrations also presented spatial variations. The urban core neighborhood had the highest $PM_{2.5}$ and BC concentrations. The Urban Core is not only the economic center, but also a transportation center of the megacity. Similar to the ring-like urban planning in Beijing, Chengdu consists of five ring roads. All of the arterial roads meet in the urban core. Also, as the economic center, the Urban Core is filled with office buildings and a large number of commercial complexes. Thus, this area suffers from heavy traffic, especially during rush hours. The current study also showed that $PM_{2.5}$ and BC concentrations were highly correlated ($\rho = 0.84$) in the Urban Core, which suggests that the source of the air particles in that area is likely traffic. Therefore, the large amount of vehicle exhaust emission in the Urban Core due to the urban planning in Chengdu may explain the high air pollution levels in this area.

Unlike what is seen in the Urban Core, the Suburb is where many factories are located. Because of this, and the regulation in Chengdu that prohibits trucks from entering the city during the day (except for a very limited number of specific vehicles), the Suburb tends to have much more truck traffic than other neighborhoods. In China, most passenger cars use gasoline or compressed natural gas as fuel, while trucks typically use diesel as fuel, which results in higher emissions of PM. The current study found a strong correlation between $PM_{2.5}$ and BC in the Suburb (ρ = 0.86), which supports the idea that higher truck traffic in that area contributes to the higher air pollution levels measured there. The Developing Neighborhood is still transitioning from an industrial to a residential area and has a lot of construction taking place. Since a very limited number of trucks are allowed to enter the city in the day, there is comparatively less traffic in the daytime. In light of this, the weaker (ρ = 0.55) correlation observed between $PM_{2.5}$ and BC concentrations in the Developing Neighborhood is not surprising.

The linear mixed model results indicate that car passengers were exposed to lower air pollution levels. The observed low exposures in car is supported by previous studies. Huang et al. sampled $PM_{2.5}$ for three commuting modes (taxi, bus, and bicycle) for 18 weekdays between December 2010 and February 2011 in Beijing. Using a portable aerosol spectrometer to measure real-time

$PM_{2.5}$ concentration in both heavy and light traffic, Huang et al. suggested that riding a taxi had the lowest average $PM_{2.5}$ concentrations (31.6 μg/m^3) compared to cycling (49.1 μg/m^3) or riding a bus (42.4 μg/m^3) [47]. Similarly, a study in Santiago, Chile, where a handheld optical particle counter was used to measure $PM_{2.5}$ concentrations during travel on buses, bicycles, cars, and subways in both summer and winter, found that being in a car had the least impact on personal $PM_{2.5}$ exposure [112]. One likely reason for the lowest $PM_{2.5}$ levels found in cars is that most cars in China (as well as the car used in the sampling campaign) are newer designs, and the ventilation system of the car may make the in-cabin microenvironment cleaner.

Published studies have shown inconsistent results for air pollution associated with traveling by subway. A panel study in Taipei sampled $PM_{2.5}$ on 120 young adults during 1-hour morning commutes between January and March in 2012–2014 for same three modes of transportation as the current Chengdu study (electrically powered subway system, gas-powered buses, gasoline-powered cars) and walking. Results of the Taipei study indicated that subjects were exposed to the lowest $PM_{2.5}$ concentrations when using a subway (22.3 ± 6.9 μg/m^3) compared to riding a car (29.2 ± 11.3 μg/m^3), taking a bus (32.2 ± 12.4 μg/m^3), or walking (42.1 ± 18.2 μg/m^3) [113]. However, other studies found riding a subway had higher air pollution concentrations than other modes of transportation in Shanghai and New York [34,114]. Although all of the subway trains are newly designed (implemented in 2010), electrically powered, and the ventilation system is kept running inside both the subway station and the coach of the train, our study suggest highest

BC concentrations during riding a subway than other modes. The source of pollution in subways may come from rails, wheels, catenaries, brake pads, pantographs [115], and brakes [116]. Also, the depth of the subway station and number of trains passing through the station could also help explain the differences seen in air pollution concentration in subways [114]. Additionally, magnetite and hematite resulting from the friction of the metal-to-metal contact between the car wheels and the rail can interfere with the measurement by the Aethalometer in the metro system [117]. This may help explain the higher level of air pollution measured in the Chengdu Metro system.

Based on the mixed effect model for $PM_{2.5}$ exposure, cycling in the urban core in winter months exposed people to the highest air pollution levels. Previously, it has been suggested that modes that come into close proximity to traffic would lead those travelers to experience higher exposures [118]. Huang et al. found in Shanghai that cycling had the highest average $PM_{2.5}$ concentrations (49.1 $\mu g/m^3$) compared to riding a bus (42.4 $\mu g/m^3$) or a taxi (31.6 $\mu g/m^3$) [47]. A panel study in Taipei also showed subjects who walked were exposed to the highest air pollution concentration ($PM_{2.5}$: 42.1 ± 18.2 $\mu g/m^3$) in the winter sampling campaign [113]. Chaney et al. examined personal $PM_{2.5}$ exposures in the summer on a single 2.7 km arterial urban route in Salt Lake City during rush hour. They found that higher $PM_{2.5}$ exposures occurred while biking, walking, and taking a bus compared to riding a window-closed car or the light rail [41]. Biking in the winter exposes people directly to the high ambient air pollution levels and vehicle exhaust emissions, while the ventilation and filtration system of the vehicles reduce the penetration of air pollutants from the outside. Aside from the possibility of direct exposure to high air pollution levels during cycling, people tend to have higher inhalation rate when biking and would intake increased amount of air pollutants. This study presents air pollution concentrations by mode, instead of exposure or inhaled dose experienced during commuting. The differences in concentrations observed in this study between car trips and biking would be magnified by the increased inhalation rate (minute ventilation) and longer traveling time to cover the prescribed route associated with biking. Thus, biking during highly polluted days or in polluted areas could increase personal intake of air pollutants compared to vehicle transportation and may have the highest potential to affect health in the city. Therefore, more research is needed to determine the tradeoffs between cardiovascular health benefits from cycling versus the harm from pollution exposure in Chengdu.

Riding a car was found to result in lower noise exposures than the other transportation modes. Car travel is an almost-closed microenvironment compared to the other three modes of transportation, and newly designed cars generally incorporate sound insulation. Thus, riding a car may be less noisy than the other commuting modes. The current study's measurements showed subway and bus trips were noisier, which is inconsistent with some previous studies. Studies in Taipei and Europe indicated that walking and biking to be the noisiest mode of transportation. [38,113]. The inconsistency between our study and previous ones may be due to the differences in rail and wheel design, as well as sound insulation design of the bus and Metro system. Additionally, the subway and bus in Chengdu were usually at full passenger capacity when noise measurements were taken. Higher passenger exchange rate during commuting, as well as the larger number of passengers in the microenvironment observed in the Chengdu study, may explain the difference between our study and others. Our study also found slightly higher noise levels in the summer compared to the winter. Chengdu is humid in summer and many insects can be found in the city, such as cicadas. Cicadas are a major source of ambient noise aside from traffic during the summer time monitoring campaign by field staff. Both acute and chronic noise exposure have been associated with adverse health outcomes, including hearing loss, annoyance, sleep disturbance, cardiovascular diseases, and cognitive impairment (mainly in children) [119]. Other investigators have found increased noise exposure is associated with arousals of the autonomic nervous system and endocrine system, increased systolic and diastolic blood pressure, changes of heart rate, and causes the release of stress hormones [120,121]. Meta-analyses have determined associations between transportation noise and cardiovascular diseases, with observed thresholds for the exposure–response link of different diseases ranging from 40 to 60 dBA [122,123]. The average noise levels found in this current study for different modes of transportation all exceeded 60 dBA. As a known risk factor, noise levels should be monitored to evaluate the health effect in commuter studies, and also in health effect analysis of traffic-related air pollution to tease out potential confounding effects of noise.

It is noteworthy that published exposure studies on traffic-related air pollution have various inconsistencies. Aside from modes of transport, other factors potentially influencing the assessment of personal exposure in traffic include measurement factors (e.g., pollutants measured, position of the measurements in relation to the breathing zone), personal or individual factors (e.g., breathing rate, personal behavior or choices, and personal sources), traffic factors (e.g., traffic count and type, traffic flow, junction layout, link length, etc.), and meteorological factors (e.g., wind speed, wind direction, etc.) [118]. Additionally, personal exposure in different modes of transportation may also be related to the energy source of the vehicle, passenger population in the microenvironment, and ventilation and filtration systems that are in place in the vehicles. Differences in any of the above-mentioned factors may lead to inconsistent results between studies.

The world's population is estimated to reach 10 billion people by 2050, with 75% of this population living in cities [124]. At that time, 90% of the 2.5 billion more people expected to be in urban areas will be found in Asia and Africa [2]. Intra-city commuting potentially affects human health by choices in transportation modes, route, time through various air pollution, physical activity, climate factors, as well as interactions between these variables. The current study further analyzed the interaction between modes of transportation and commuting neighborhoods in mixed effect models. Statistical results showed different modes of transportation had similar BC concentrations in the urban core. Biking as an active mode of transportation has been recommended, but there is concern about the high air pollution concentrations present during biking. However, the current study's findings suggest that in certain areas, different modes of transportation had similar pollution levels. This may potentially impact urban planning and policy decision-making to support active and public modes of travel in Chengdu. As mentioned previously, the developing neighborhoods are still under construction. Designing bike-friendly communities in this area would be suggested to promote physical activity and population health. The Urban Core has been confronted with traffic congestion for a long time. Promoting the use of public transportation in the urban core area would help reduce traffic emissions and solve traffic congestion issues being experienced there. Additionally, personal intake of air pollutants is also related to time of exposure and inhalation rate. This current study found lower air pollutant levels when riding a subway or a car. However, the time spent on the same route is generally shorter when traveling by subway than the other modes. This is especially true when traveling in urban areas during peak hours. In contrast, although, riding a car exposes a commuter to the lowest $PM_{2.5}$, BC, and noise levels, it is not unusual to spend more time on the road because of traffic jam, particularly in the urban core. Thus, further studies are needed to fully consider pollutant exposure and transportation time to better recommend commuting choices to citizens.

Every study has limitations, and the current one is no exception. The main limitation of this study was the use of a limited number of scripted trips and neighborhoods. Thus, the generalizability of the study may be limited. Air concentrations were collected in the summer and winter of 2017 only, so no between-year variations could be examined. Aside from pollutants levels were only measured in the daytime, while no measurements were taken at night. Also, measurements were collected by research staff and we relied on scripted measurements for three specific routes, rather than taking samples from actual, unscripted routes used by real commuters. Nevertheless, the monitoring mimicked personal monitoring with repeated measurements, which captured several important characteristics of pollution during different modes of transportation. Additionally, the successive measured data points in scripted trips were not truly independent. The estimates of confidence interval and statistical significance may be influenced by the autocorrelation between measurements.

Although this study measured pollution levels under different situations, it did not address the cumulative exposure for each pollutant. The cumulative exposure, which accounts for total time of exposure, would be more relevant to understanding the health effects of exposures during intra-city commuting. Thus, further studies are needed to generalize personal air pollution exposure models in transportation by mode choice, commuting route and time, and meteorological factors, and to assess the potential health effects on urban populations.

2.6 CONCLUSIONS

The current study investigated personal exposures to $PM_{2.5}$, BC, and noise experienced during trips in cars, buses, and subways, as well as during bicycling in Chengdu, China. All transportation modes utilized scripted and repeated routes in three different neighborhoods. The total of 120 trips was conducted across summer and winter seasons, and covered the mornings and afternoons of weekdays and weekends. The monitoring campaign showed personal $PM_{2.5}$, BC, and noise exposures in traffic microenvironments varied by season, neighborhood, and modes of transportation. Air pollution levels in traffic were significantly higher in the winter than in the summer. Traveling in the urban core area of Chengdu resulted in higher air pollution levels. Riding a car resulted in lower $PM_{2.5}$ concentrations. Taking a bus or the subway resulted in higher noise levels, while car trips had lower noise levels. However, in certain areas, $PM_{2.5}$ and BC levels were not affected by trip mode, or had lower concentrations during active and public transportation. Riding a bike in the Urban Core during the winter months may have the highest potential to affect individual health in this city. In the future, exposure models that account for environmental, meteorological, and behavioral factors, as well as duration of commuting, are needed in health studies of urban traffic microenvironments.

Chapter 3. ACUTE CARDIORESPIRATORY HEALTH EFFECTS OF AIR POLLUTION EXPOSURES DURING DIFFERENT TRANSPORTATION MODES

3.1 ABSTRACT

Background: The exposure characteristics of traffic-related air pollution (TRAP) may differ between transportation modes (*e.g.*, walking, taking a bus/subway and riding a car). This study aims to investigate the association between TRAP exposures during different transportation modes and cardiorespiratory function in Chengdu, China.

Methods: This analysis was part of a randomized double-blind crossover intervention trial, intended to investigate the effect of using a respirator to reduce exposure to TRAP. Each of the 21 recruited healthy adults completed a total of 8 trips on a scripted route between November and December 2019 in Chengdu, China. Subjects repeated each of the four tested modes (*i.e.*, walking, riding a bus, riding a subway and riding a car) under two experimental conditions; one trip using an effective respirator and the other using a sham respirator. Each trip lasted for two hours and the order of sham vs. effective filters was randomized. Ultrafine particles (UFP), size resolved particulate matter (PM_1, $PM_{2.5}$, PM_{10}), black carbon (BC), noise and physical activity levels were monitored over all experimental conditions. Changes in blood pressure, fractional exhaled nitric oxide (FeNO), spirometry, and perceived stress were measured through pre/post measurements taken immediately before and after each trip. Linear mixed effects models were used to explore the association between TRAP exposure and cardiorespiratory functions.

Results: Mean age of the 21 subjects was 27.4 years; 15 were female and 6 were male. Subjects inhaled the highest dose of TRAP when walking and the lowest dose during car trips. Traveling by bus, subway or walking was associated with increased heart rate and decreased lung function as compared to riding a car over these two-hour scenarios. After adjusting for potential confounders, each 1 μg/m^3 increase in the average concentration of BC during the 2-hour trip was estimated to lead to 1.39 ppb (95% CI: 0.07, 2.71) increased FeNO; each 10 μg/m^3 increase in the mean concentration of PM_1 was associated with 0.04 L/sec (95% CI: 0.00, 0.08) decrease in FEV1 and 0.79% (95% CI: 0.07, 1.5) increase in airway obstruction (ΔFEV1/FVC). No independent effect of short-term TRAP exposure was found on blood pressure or heart rate.

Conclusion: Results from this study suggested that increased short-term TRAP exposure was associated with elevated airway inflammation and large airway obstruction among healthy young adults. The short-term adverse health effects of high levels of air pollution exposure could outweigh the benefit of physical activity during active transportation for healthy commuters in Chengdu, China.

Keywords: traffic related air pollution; personal monitoring; exposure metrics; airway inflammation; lung function

3.2 INTRODUCTION

Traffic is the largest source of air pollution in urban areas globally [5], yet despite an increasing number of epidemiologic studies on the health effects of traffic related air pollution (TRAP), there are contradictory findings that suggest the need for methodological improvements. Epidemiological studies provide cumulative evidence for the association between traffic-related air pollution exposure and adverse health outcomes (*e.g.*, exacerbation of asthma symptoms, all-cause and cardiorespiratory mortality, lung function, birth outcomes) [29]. Cohort studies estimate long-term health effects of TRAP using surrogate indicators of air pollution from traffic, including distance of the home address to major roads [125-127] and modelled ambient air pollution concentrations (*e.g.*, NO_2, black carbon [BC], and $PM_{2.5}$) [65,128,129]. Recent studies have utilized portable air pollution monitors to measure personal TRAP exposures in-vehicle or on-road, which may reduce measurement errors in assessing the acute health effect of TRAP. Existing panel and crossover studies have estimated the association of TRAP exposure on road to lung function measured by spirometry [68,71,73,74], airway inflammation [69,71-74,77,78], heart rate [68,81], and blood pressure [68,74,82]. However, inconsistent conclusions were reported, which may be due to a lack of control on potential confounders. For instance, the effect of noise and psychological stress has not been well examined in the association between TRAP exposure and health outcomes. In addition, most of these studies did not consider the impact of physical activity on both TRAP exposure and health outcomes. Physical activity benefits cardiovascular health [130], increased physical activity levels also lead to increased tidal volume and increased total dose of air pollution which could adversely impact health. Thus, it is important to understand the role of physical activity during transportation, especially with today's world-wide promotion of active transportation.

China, as one of the most polluted regions in the world, suffers from severe haze events nationally. The rapid development and urban sprawl in China has led to higher car dependency and larger share of traffic emissions on ambient air pollution. A systematic review of source apportionment studies from 1987 to 2017 in China showed that the contribution of transportation on ambient $PM_{2.5}$ increased since 2000 [131]. However, very little evidence is available for the association between TRAP exposure and acute cardiorespiratory health in China. Two panel studies of college students were conducted in northern China to explore the acute health effect of TRAP exposure [77,81]. Instead of exploring the exposure-response relationship, both of these two studies employed interventions (*i.e.*, wearing respirators) in traffic to compare health outcomes with and without TRAP particle exposure. Thus, limited evidence is available for the exposure-response function between TRAP exposure and health outcomes, especially in southern China.

This study aims to examine the acute health effect of TRAP exposure in different transportation modes on cardiorespiratory functions in Chengdu, China. Chengdu, is a megacity with more than

15 million residents located in Sichuan basin in southwest China [105]. As a typical rapidly developing city in China, the number of motor vehicles in the city is over 5 million, second only to Beijing [132]. The unique topography, adverse meteorological conditions (*e.g.*, low wind speed, high relative humidity, and frequent temperature inversions), and high pollution emissions make the city one of the most polluted regions in China [133,134]. This study assessed the impact of healthy adults taking different transportation modes on measures of acute cardiorespiratory functions, and estimated the exposure-response function between acute TRAP exposure and several measures of cardiovascular and respiratory function. In particular, this study employed a randomized cross-over design and various portable and wearable sensors to better control for the potential confounders, including physical activity, noise, psychological stress, and meteorological conditions.

3.3 METHODS

3.3.1 Subjects

The study protocols were approved by the Human Subjects Division of the University of Washington and the Sichuan Center for Diseases Control and Prevention (CDC). All the subjects were recruited from the Sichuan CDC (located in Chengdu, China). CDC trainees and employees were invited to participate in the study at the end of a lecture in Sichuan CDC about the health impact of TRAP. Potential participants were asked to complete a baseline questionnaire used for eligibility screening. The inclusion criteria were: a) never smoked, b) disease free, including but not limited to asthma, chronic bronchitis, chronic obstructive pulmonary disease, pneumonia, cirrhosis, hypertension, stroke, myocardial infarction, diabetes, and pulmonary hypertension, c) non-pregnant, and d) age between 20-60 years old. After the screening, eligible volunteers were contacted to participate in an information session where they were presented with the aims and detailed procedures of the study. Informed consent was obtained from each recruited subject at the end of the information session.

3.3.2 Study Design

The study employed a randomized double-blind crossover intervention design. Each recruited subject completed a total of eight trips on a script route between November and December in 2019 in Chengdu, China. Four commonly used commuting modes were tested in the study, including walking, riding in a compressed natural gas (CNG) powered bus, riding in an electric powered subway, and riding in a gasoline powered car. Subjects travelled twice using each of the four transportation modes, where they were provided an effective respirator in one trip, and a sham respirator in the other. The condition of the respirator was double-blind to researchers and subjects. The orders of the eight trips for each subject was randomized and each trip was separated by at least 24 hours. All the trips were on a scripted route. All tested modes were available for the selected route to make the exposure measures comparable between modes and not due to spatial differences. The route followed the central part of an arterial road (Renmin South Rd 3rd and 4th section) crossing Chengdu city. Each trip departed from the Chengdu CDC office, reached the Tongzilin subway station and returned to the starting point (Figure 7). Each subject traveled repeatedly between the two points until two hours.

To avoid potential interference with health measurements (e.g., blood pressure and FeNO), subjects were asked to refrain from consuming lettuce, radish, alcohol, coffee, tea, and drinking lots of water for at least one hour before each trip. The respirator used in the study (Mini Lung Pro, Broadair, China) is based on a powered air purifying respirator (PAPR) design, and relies on a blower instead of lung power to draw air through the filter. The respirator draws air through a high efficiency particulate air (HEPA) filter, which was removed in the experimental sham condition.

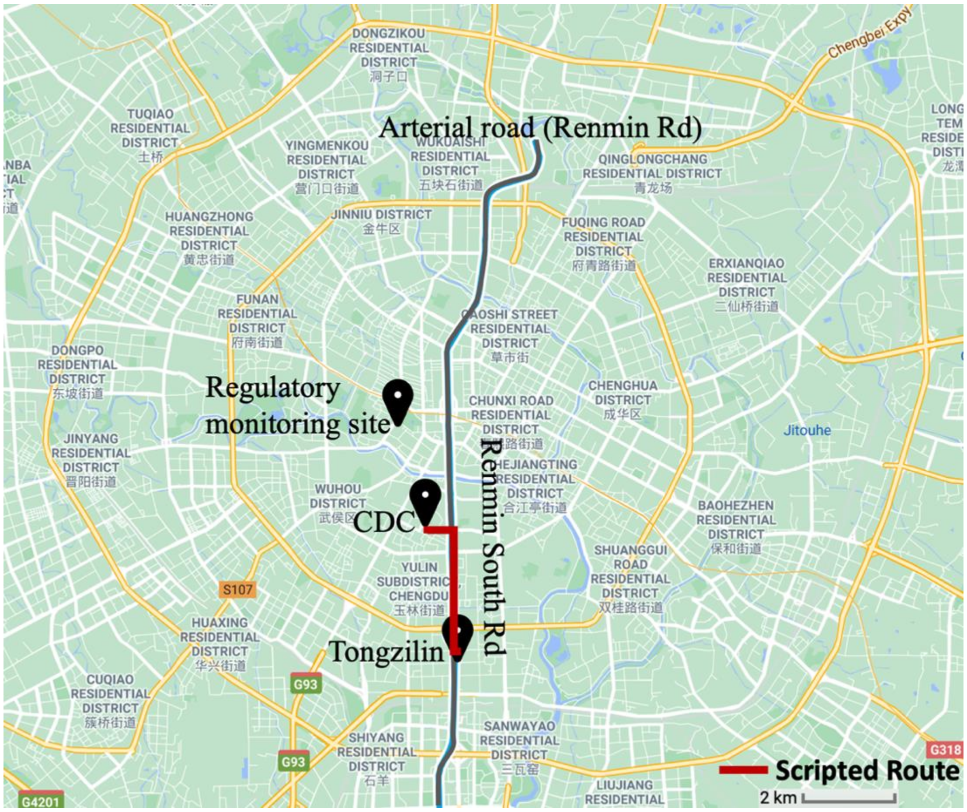

Figure 7. Map of the scripted route and the nearest regulatory monitoring site

3.3.3 Exposure Measurement

Continuous ambient exposures to air pollution and other covariates were monitored using portable direct-reading instruments during all the trips. During each trip, two researchers carrying different instruments traveled alongside subjects to monitor ambient exposures. Size-fractioned concentrations of PM with aerodynamic diameter less than 1.0 µm (PM_1), $PM_{2.5}$, PM with aerodynamic diameter less than 10.0 µm (PM_{10}), temperature and relative humidity were measured using a calibrated Portable University of Washington Particle (PUWP) monitor (University of Washington, Seattle, WA, USA) with a time interval of 5 seconds. The PUWP monitor has been characterized in previous studies and verified for data quality [135,136]. BC concentrations were monitored using a microAeth AE51 (AethLabs, San Francisco, CA, USA) with a flow rate of 100 ml/min and sampling time of 30 seconds. The UFP number concentration, average size and lung deposit surface area (LDSA) was recorded by a Discmini (Testo, West Chester, PA, USA) at a 1-second interval. Noise levels were collected using the NoisePro DLX Dosimeter (3M, St. Paul, MN, USA) with 1-second measurements. Additionally, subjects wore the ActiGraph (ActiGraph, Pensacola, FL, USA) activity monitor on the left wrist to record their physical activity levels (3-axis accelerations) continuously. Because only four sets of ActiGraph activity monitor were available in the study, when more than four subjects travelled together in a trip, two males and two females were selected randomly to wear the activity monitor in the trip. Before each trip, clocks in all of the instruments were synchronized, and the noise dosimeter was calibrated to a 114 dB calibrator. After each trip, the noise dosimeter was re-calibrated, and all the exposure measurements were immediately downloaded from all instruments and safely archived as separate files for later data analyses. After the data extraction, all the data checks were performed to identify any potential instrument failure.

Apart from measuring spatiotemporal ambient particle pollution (*i.e.*, UFP, PM_1, $PM_{2.5}$, PM_{10}, and BC) during each trip, regional gaseous pollutant concentrations were collected from the nearest regulatory monitoring site (approximately 2 km from the scripted route, Figure 7). The average concentration of SO_2, NO_2, CO and O_3 were calculated for each 2-hour trip.

3.3.4 Health Measurement

Immediately before and after the 2-hour trips, subjects were measured for selected cardiorespiratory functions, including lung function, fractional exhaled NO (FeNO), blood pressure, and heart rate (HR). All the health measurements were taken in a quiet office room by trained technicians according to standard operating procedures. In both pre and post trip health measurement, blood pressure and HR were collected, followed by FeNO, and then lung function. The subjects were asked to use the restroom before the health assessment.

An oscillometric wrist blood pressure monitor (HEM-8611, Omron, Kyoto, Japan) was used for the blood pressure and HR measurement. Subject was guided to sit with feet flat on the floor, back supported, arm at heart level on a table surface without talking for 5 minutes before blood pressure readings and for the duration of all measurements. Each participant was measured three times for systolic blood pressure (SBP), diastolic blood pressure (DBP) and HR. The latter two measurements were averaged to represent the subject’s blood pressure and HR at that timepoint.

An electrochemical instrument (NIOX VERO, Circassia Limited, Morrisville, NC, USA) was used to measure FeNO non-invasively. An elevated FeNO after a commute indicates acute airway inflammation. Daily quality control (QC) measurement was performed by a qualified QC tester (> 18 years, no ongoing cold or known airway disease, no allergies or asthma, non-smoker, expected stable FeNO values between 5 and 40 ppb).The FeNO measurements followed the American Thoracic Society (ATS) and the European Respiratory Society (ERS) guideline [137]. In brief, subjects were seated and guided to exhale slowly and steadily during the FeNO test until an acceptable measurement was obtained. Mobile phones were kept away from the instrument due to possible interference.

Lung function was assessed using a portable spirometer (Micro Direct MicroLoop Spirometer, Medical Device Depot, Inc., Ellicott City, MD, USA). The spirometry testing followed the guidance of Occupational Safety and health Administration (OSHA) [138]. In brief, before the test, the age, race, height and weight were recorded for subjects. Subjects were asked to loosen tight clothing and applied nose clips. During the test, subjects stood in front of a steady chair, and were instructed to inhale maximally, blow air out as hard and as fast as possible and continue to exhale until the breath is fully recorded by a trained research staff. After subjects completing three valid tests according to the ATS/ERS quality criterion [139], the best values of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, peak expiratory flow (PEF), mean forced expiratory flow at 25%, 50% and 75% of forced vital capacity (FEF25, FEF50, FEF75) and FET (forced expiratory time) were recorded.

Aside from the health measurements, subjects also completed a questionnaire after each trip, which incorporated the 4-item version of Cohen's Perceived Stress Scale (PSS4) [140] and a question asking for their perception of the respirator: if he/she thinks the respirator was a sham one, or an effective one, or do not know.

3.3.5 Statistical Analysis

3.3.5.1 Descriptive Analysis

Recorded data for BC, PM, UFP, noise, temperature, and relative humidity for each trip were extracted from the raw data files. A series of quality control measures were used to ensure an acceptable level of data quality. First, an optimized noise-reduction algorithm (ONA) was used to reduce noise in real-time BC data obtained, which accounted for changes in sensitivity of the measurement related to changes in filter attenuation [107]. The ONA BC data were used in subsequent analyses. Second, observations with missing values were removed (9 missing data points for $PM_{2.5}$, 14 missing data for BC, and no missing data for UPF and noise measurements). Then, $PM_{2.5}$ measurements with corresponding $PM_{0.3}$ counts equal to 0 were considered unreliable and were removed (111 data points). Finally, all the measurements were checked for outliers (no outlier identified).

The raw physical activity data (3-axis acceleration) were processed in the ActiLife data analysis platform (ActiGraph, Pensacola, FL, USA) to calculate the average METs and time in different activity levels (sedentary, light, moderate, vigorous) during each trip based on the Crouter Adult

Algorithm [141]. Then, the mean METs and time in different activity levels was summarized for male and female subjects separately to represent their activity levels during each trip.

After the quality control processes, characteristics of UFP, PM_1, $PM_{2.5}$, PM_{10}, BC, noise, temperature, and relative humidity were summarized by commuting modes. The inhaled dose of TRAP (*i.e.*, UFP, PM_1, $PM_{2.5}$, PM_{10}, and BC) was calculated using the following equation:

$$D = \sum_{i=0}^{t} C_i \times IR_i \qquad (eq\ 1)$$

where D was the total inhalation dose (*e.g.*, μg for $PM_{2.5}$) of air pollutants in a trip, C_i was the real-time TRAP concentrations (*e.g.*, μg/m^3 for $PM_{2.5}$) recorded by portable monitors at time i, t was the total traveling time (min) at an activity level of a trip, and IR_i was the average inhalation rate (m^3/min) at the given time i in the trip which was determined by the inhalation rates from *Highlights of the Chinese exposure factors handbook* [142] at different activity levels (sedentary, light, moderate and vigorous) measured by the ActiGraph activity monitor [47,143,144]. The inhaled dose was calculated for male and female subjects separately. This inhaled dose was used in the sensitivity analysis described in Section 3.2.5.5 below.

3.3.5.2 Health Effects of Transportation Modes

To understand the combined effect of TRAP exposure and physical activity levels on selected cardiorespiratory functions during different transportation modes, exposures and health outcomes measured for trips with sham respirators were analyzed. With repeated health measurements from each subject, the linear mixed effects model was employed to estimate associations between transportation modes and cardiorespiratory outcomes:

$$y_{ij} = b_0 + b_1 x_{ij} + v_i + e_{ij} \qquad (eq\ 2)$$

where y_{ij} was the difference of health response before and after j-th trip of i-th subject, b_0 was the fixed intercept for the regression model, b_1 was the fixed slope for the regression model, x_{ij} was the main exposure of interest (*i.e.*, different transportation modes) and other covariates for *j*-th trip of *i*-th subject, $v_i \sim N(0, \sigma v)$ was the random intercept for the i-th subject, and $e_{ij} \sim N(0, \sigma e)$ was a Gaussian error term.

A reduced model was built to include only the categorical variable of transportation mode as the exposure of interest; a full model was developed to further account for potential confounding effects of noise, temperature, relative humidity and perceived stress of each subject during the trips.

3.3.5.3 Health Effects of Air Pollution Exposures

In the case of trips with sham respirators, subjects were exposed to real-world varying TRAP concentrations, allowing for assessment of exposure-response relationships for cardiorespiratory functions.

The *eq 2* linear mixed effects model was built for each pair of measured particle pollution and health outcome (single-pollutant models, model 1). The average concentration of measured air pollutants during each 2-hour trip was the main effect of interest. Other covariates examined included perceived stress of subjects, physical activity levels measured as METs by the ActiGraph monitor, noise, temperature and relative humidity during the trip. Two-pollutant models (model 2) were developed to adjust for the impact of regional gaseous pollutant exposures (*i.e.*, SO_2, NO_2, CO, and O_3). Each of the four gaseous pollutants was added to the single-pollutant model. Models with the lowest Bayesian Information Criterion (BIC) were chosen as the final two-pollutant model to be presented in the manuscript.

3.3.5.4 Adjusting for Exposure Characteristics of Transportation Modes

While the mean concentration of air pollutant might capture overall differences in exposure between transportation modes, travel modes could also differ in other characteristics of exposure, which might be better represented by other statistical summary measures (*e.g.*, standard deviation [SD], range, or time of pollutant levels above a certain threshold). To further adjust for residual confounders of TRAP exposure in transportation modes, a few dimension-reduced summary variables of different characteristics of air pollutants were included in the mixed effects model.

First, various exposure metrics of particle pollution exposure during each trip were characterized by a. median, b. SD, c. interquartile range (IQR), d. coefficient of variation (COV), e. minimum (min), f. maximum (max), g. range, and h. the proportion of high-risk levels (high), which corresponded to the proportion of time that pollutant concentrations were above the 3rd quartile of recorded levels across all trips. As UFP with smaller sizes was hypothesized to be more toxic to human health, the proportion of high-risk levels for UFP size was calculated as the proportion of time that UFP size were below the 1st quartile.

To reduce dimension and overcome the multicollinearity of these exposure metrics, a Partial Least Square Discriminant Analysis (PLS-DA) was employed to explore the relationships between air pollution exposures and transportation modes. PLS-DA is a partial least squares (PLS) regression with a categorical response variable, which is a latent regression method that maximizes the correlation of independent variables to the response variable. The PLSDA model was trained based on 5-fold repeated cross-validation. Finally, two latent variables of the PLS-DA model were included as covariates in the traditional mean concentration mixed effect models to adjust for residual confounding effects of other exposure metrics in different transportation modes. Both single pollutant model (model 3) and two-pollutant model (model 4) with the latent variables were developed.

3.3.5.5 Sensitivity Analysis

The inhalation dose of air pollution might be more strongly associated with health outcomes as compared to ambient exposure metrics because it represents the internal exposure of environmental hazards. The association between air pollution exposure and cardiovascular health was explored using the inhalation dose of TRAP. The inhaled dose of measured particle pollutants was calculated using the *eq1* for each trip with sham respirators. Then, single-pollutant and two-pollutant models were examined for each pair of particle pollutant and health outcome. In single-pollutant models, the main effect of interest was the inhalation dose of particle pollutants. Because the inhaled dose of air pollutant already accounted for the different physical activity levels in the trips, other covariates modeled as fixed effects included perceived stress of subjects, noise, temperature and relative humidity in each trip. Regional gaseous pollutants were also examined, and the model with the lowest BIC was chosen as the final two-pollutant model to be present in the manuscript.

All statistical analyses were conducted in R 4.0.3 (http://www.R-project.org/) (R Foundation for Statistical Computing, Vienna, Austria) and RStudio® (Version 1.1.456). The seed value was set to 101 in R in every random number generation (*i.e.*, in PLSDA model fitting) to make the data analysis reproducible.

3.4 RESULTS

3.4.1 Study Subjects

A total of 21 CDC trainees or staff were recruited into the study, of which 19 subjects completed all the eight trips and 2 subjects completed only a portion of the trips because of time conflicts (one subject completed the walking, bus and subway trips, while the other subject only completed the car trips). The study subjects were mostly female, young, and educated (with at least a bachelor's degree), which were in accordance with the characteristics of CDC employees in China [145]. All the health measurements (both pre and post trip measurements) taken during the study were within the normal range (Table 8).

Table 8. Characteristics of the study subjects.

Subjects information*	**Female**	**Male**
N	15	6
Age (year)	26.9 (2.0)	28.7 (4.1)
Body Mass Index (BMI, kg/m^2)	20.6 (1.8)	22.7 (3.2)
Education		
College	12	5
Graduate school	3	1
Income (RMB/year)		
≤ 50,000	2	0
51,000 – 100,000	7	4
100,001 – 150,000	5	1
150,001 – 200,000	1	1
Second-hand smoking		
No	11	6
Yes	4	0
Alcohol drinking frequency		
No	13	5
1/month	0	1
3-5/month	1	0
Exercise frequency		
No	5	3
1/week	4	2
2-3/week	4	1
4-5/week	2	0
SBP (mmHg)#	100.6 (8.9)	111.3 (8.6)
DBP (mmHg) #	65.5 (8.2)	75.2 (9.4)
HR (bpm) #	78.1 (9.6)	83.1 (16.8)
FeNO (ppb) #	20.6 (8.8)	24.6 (11.1)
FEV1 (L) #	2.7 (0.3)	3.6 (0.7)
FVC (L) #	3.0 (0.4)	4.1 (0.8)
FEV1/FVC (%)#	91.0 (4.9)	90.5 (6.8)
PEF (L/sec) #	6.9 (0.9)	9.2 (1.0)
FEF25 (L/sec) #	5.9 (1.0)	7.9 (0.9)
FEF50 (L/sec) #	4.1 (1.0)	4.9 (1.3)
FEF75 (L/sec) #	1.9 (0.6)	2.4 (1.0)
FET (sec) #	2.4 (0.6)	2.4 (0.9)

*Continuous variables were summarized as mean (SD), counts were presented for categorical variables.

Summaries of health measurements were based on all the pre- and post-trip measurements.

3.4.2 TRAP Characteristics by Mode

The recorded BC and PM (*i.e.*, PM_1, $PM_{2.5}$ and PM_{10}) concentrations during each trip were strongly correlated with each other, moderately correlated with the LDSA of UFP, and weakly correlated with the number concentration and average size of UFP (Figure A2). The TRAP concentrations, noise levels and meteorological conditions varied by transportation modes (Table A4). In general, bus trips tended to expose subjects to the highest particle pollution concentrations (*i.e.*, mass concentrations of PM_1, $PM_{2.5}$, PM_{10} and BC, number concentration of UFP, and LDSA), noise and relative humidity levels. The average diameter of UFP in bus trips seemed to be the smallest, while the diameter during walking trips tended to be the largest compared to other modes. Car trips tended to have the lowest particle pollution, noise, and relative humidity levels.

Taking variations of minute ventilation during different transportation modes into account, subjects were estimated to inhale the highest dose of PM (*i.e.*, PM_1, $PM_{2.5}$ and PM_{10}) and BC during walking trips. UFP dose tended to be the highest during walking trips when measured by surface area (LDSA) but highest during bus trips when described as particle number concentration. Car trips seemed to produce the lowest inhalation dose for all measured particle pollutants (Table 9).

Table 9. Inhaled doses of TRAP during the 2-hr trips by transportation modes.

Inhalation Dose		Car	Bus	Subway	Walk
PM (μg)	**PM_1**				
	mean (SD)	28.8 (11.4)	42.1 (15.7)	33.5 (11.7)	57.3 (11.5)
	median (IQR)	24.1 (20.7)	39.0 (5.1)	34.0 (9.2)	55.8 (18.2)
	$PM_{2.5}$				
	mean (SD)	50.3 (22.6)	71.8 (35.1)	57.6 (22.2)	92.0 (19.6)
	median (IQR)	39.0 (41.9)	65.6 (11.9)	59.0 (18.0)	88.1 (29.3)
	PM_{10}				
	mean (SD)	56.2 (22.8)	86.0 (36.1)	68.8 (23.9)	115.0 (20.9)
	median (IQR)	47.7 (42.9)	81.8 (16.6)	71.9 (22.4)	106.2 (38.7)
UFP	**number (pt)**				
	mean (SD)	1.4×10^{10} (2.6×10^{9})	7.6×10^{10} (1.8×10^{10})	2.4×10^{10} (3.9×10^{10})	3.6×10^{10} (6.9×10^{9})
	median (IQR)	1.4×10^{10} (4.510^{9})	7.5×10^{10} (2.2×10^{10})	2.6×10^{10} (5.7×10^{9})	3.5×10^{10} (1.2×10^{10})
	LDSA (μm²)				
	mean (SD)	3.8×10^{7} (6.2×10^{6})	7.8×10^{7} (3.9×10^{7})	5.6×10^{7} (1.1×10^{7})	9.8×10^{7} (2.1×10^{7})
	median (IQR)	3.9×10^{7} (1.0×10^{7})	7.8×10^{7} (2.4×10^{7})	5.3×10^{7} (4.4×10^{6})	9.9×10^{7} (3.1×10^{7})
BC (ng)	mean (SD)	3550 (1300)	4730(2220)	5380 (1610)	7400 (1210)
	median (IQR)	3260 (2440)	4030 (229)	5940 (2150)	6590 (2630)

3.4.3 Health Effects of Transportation Modes

The associations between transportation modes and changes in cardiorespiratory functions during the 2-hour trips were estimated, which reflected the combined effect of measured ambient particle exposure and physical activity in each transportation modes. Compared to riding a car, a 2-hour walking trip was associated with higher HR (13.48 bpm, 95% CI: 5.08, 21.89) and lower FEV1 (-0.22 L, 95% CI: -0.34, -0.09), FVC (-0.23 L, 95% CI: -0.39, -0.06), FEF25 (-1.08 L/sec, 95% CI: -1.71, -0.45), FEF75 (-0.47 L/sec, 95% CI: -0.89, -0.05) and PEF (-0.82 L/sec, 95% CI: -1.36, -0.28) after adjusting for perceived stress, noise exposures, temperature and relative humidity levels (full model). Similar patterns were found for bus and subway trips: compared to car trips, traveling on subways led to higher HR and lower FEV1, FEF25, and PEF; and bus trips were associated with lower FEV1, FVC, and FEF25 (Figure 8 and Table A5).

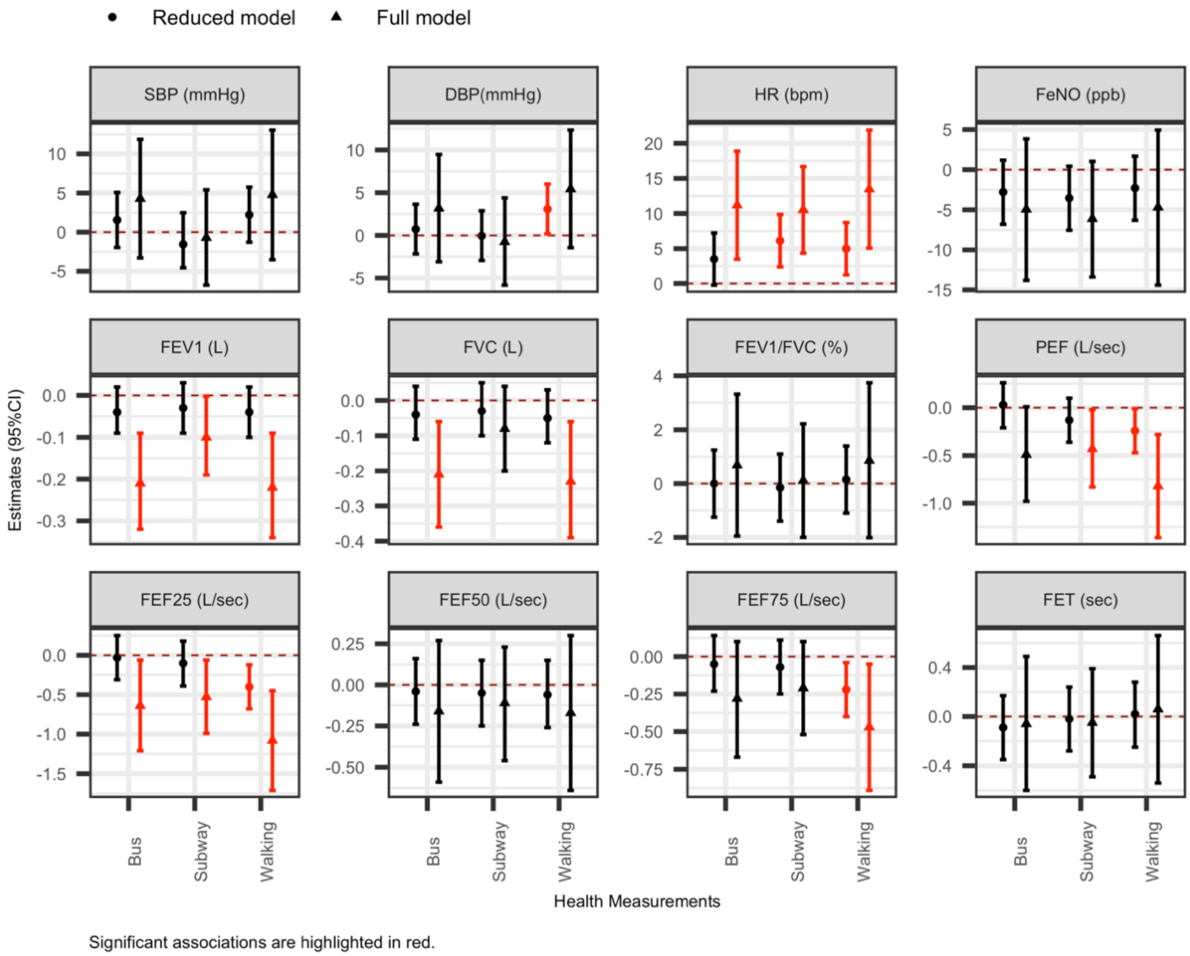

Figure 8. The health impact of different transportation modes on cardiorespiratory functions as compared to car trips.

3.4.4 Health Effects of TRAP Exposures

The associations between each pair of measured particle pollution concentrations and cardiorespiratory functions are shown in Figure 9. The single-pollutant model had the measured particle as main effect of interest with covariates of perceived stress, noise exposure, physical activity levels, temperature and relative humidity. Each of the four regional gaseous pollutants (SO_2, NO_2, O_3 and CO) were additionally included with particle pollutant exposures of interest in the two-pollutant model. The final two-pollutant model results presented in Figure 9 was from models with the smallest BIC. For most of the health outcomes, adding the concentration of regional CO had the smallest BIC; for HR, PEF, and FEF25, two-pollutant models with regional SO_2 concentrations had the least BIC.

Based on the two-pollutant model (model 2) estimates, per 10 nm increase in the averaged UFP diameter during the 2-hour trip, DBP increased 0.94 mmHg (95% CI: 0.07, 1.83). Each 1 $\mu g/m^3$ increase in the average BC concentration was estimated to lead to 1.39 ppb (95% CI: 0.07, 2.71) increase in FeNO immediately after the 2-hour trip. Each 10 $\mu g/m^3$ increase in PM_1 mass concentration during the trips was associated with 0.03 L (95% CI: 0.00, 0.06) lower FEV1. Also, increased PM_1, $PM_{2.5}$, PM_{10} and LDSA levels during the 2-hour trip were associated with longer FET (Table A6).

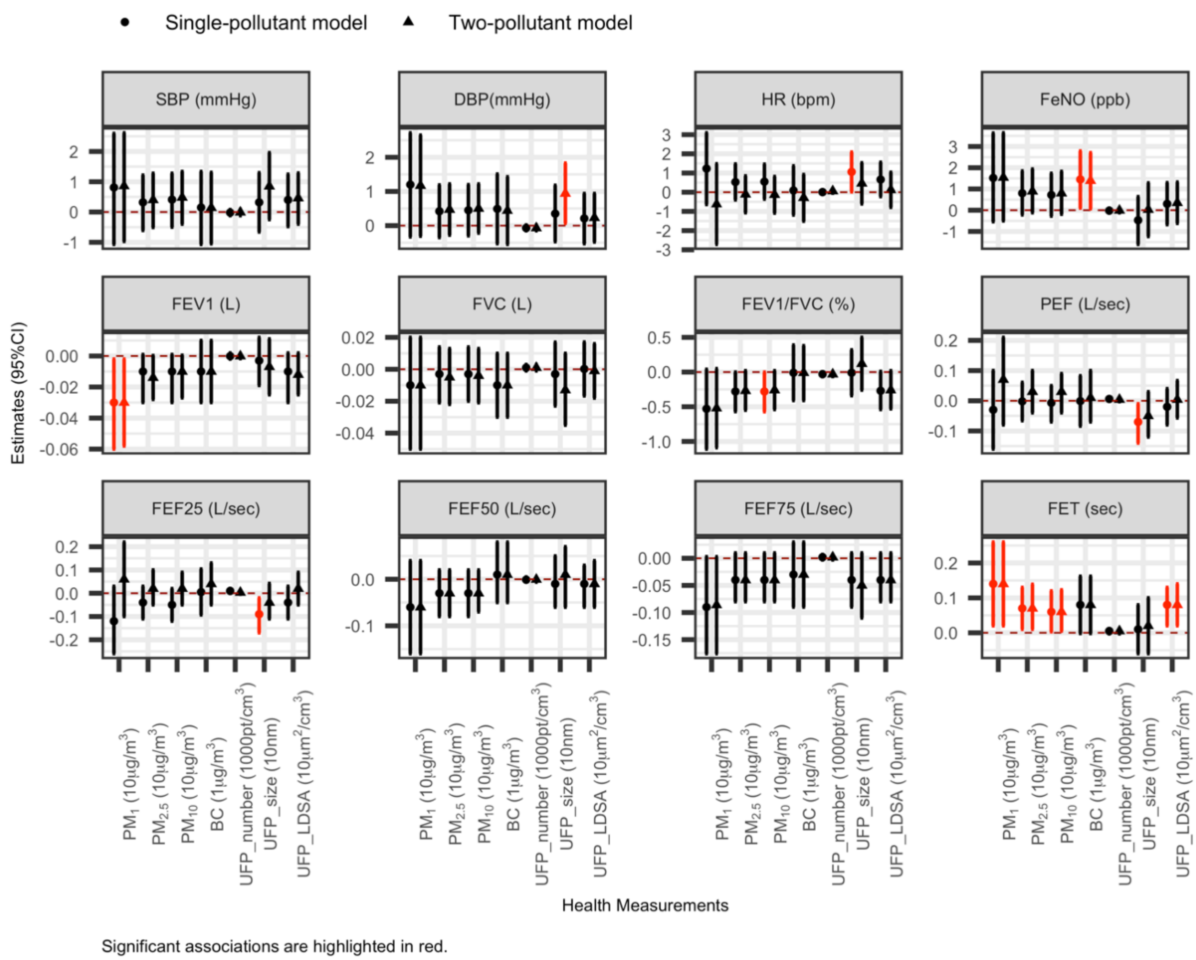

Figure 9. The health impact of different TRAP exposure (concentrations) on cardiorespiratory functions.

3.4.5 Adjusting for Exposure Characteristics of TRAP in Transportation Modes

Two latent variables from the PLS-DA model for TRAP exposure metrics in different transportation modes were added into the linear mixed effects model. Adding the latent variables aimed to adjust for additional confounder in different transportation modes. The PLS-DA model with two latent variables performed well, that the classification accuracy was greater than 90%. Based on the variable importance of the PLS-DA model, the model captured mainly the variation of TRAP exposure during different transportation modes (Figure A3). Similar to the above average concentration model, the two-pollutant model (model 4) with the concentration of regional CO had the smallest BIC, except for FEF25 model, which had the lowest BIC when adding the regional SO_2 concentrations.

Adding latent variables in the linear mixed effects model did not change the health effect estimates prominently. In the two-pollutant models (model 4), no association was found between TRAP exposure and cardiovascular health. The associations of BC to FeNO and PM_1 to FEV1 remained. Negative associations between PM and FEV1/FVC were identified after adding the latent variables. Per 10 $\mu g/m^3$ increase in PM_1, $PM_{2.5}$, and PM_{10}, the ratio between FEV1 and FVC decreased 0.79% (95% CI: 0.07, 1.50), 0.35% (95% CI: 0.02, 0.68), and 0.38% (95% CI: 0.05, 0.71), respectively. Each 10 nm increase in the average size of UFP was associated with 0.19 L/sec (95% CI: 0.03, 0.35) decrement in PEF. Also, all the measured TRAP exposure, except for the average size of UFP, were positively associated with FET (Table A6).

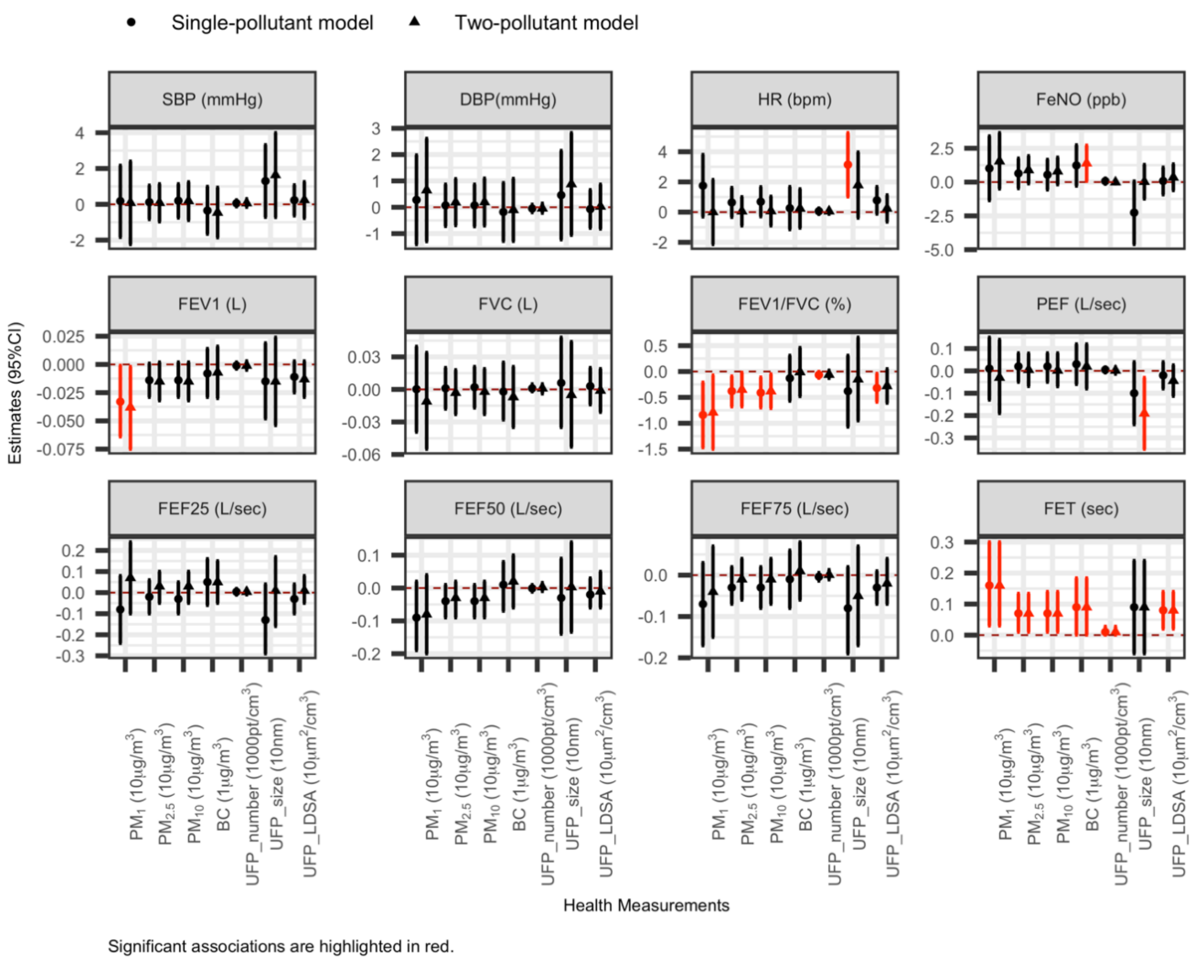

Figure 10. The health impact of different TRAP exposure (concentrations) on cardiorespiratory functions after adjusting for residual confounders related to other exposure metrics in transportation modes.

3.4.6 Sensitivity Analysis

The sensitivity analysis estimated the associations between inhaled dose of TRAP and cardiorespiratory functions. The two-pollutant model with regional CO concentrations had the smallest BIC, except for FEV1 and FEF25 model, which had the lowest BIC when adding the regional SO_2 concentrations. The two-pollutant model showed that each 10 μg increase in inhaled PM_1 during the 2-hour trip led to 0.92 mmHg (95% CI: 0.08, 1.76) increase in DBP and 0.94 bpm (95% CI: 0.06, 1.95) increase in HR. The UFP number concentration was positively associated with FEF25, but the effect was minimal (Table A7).

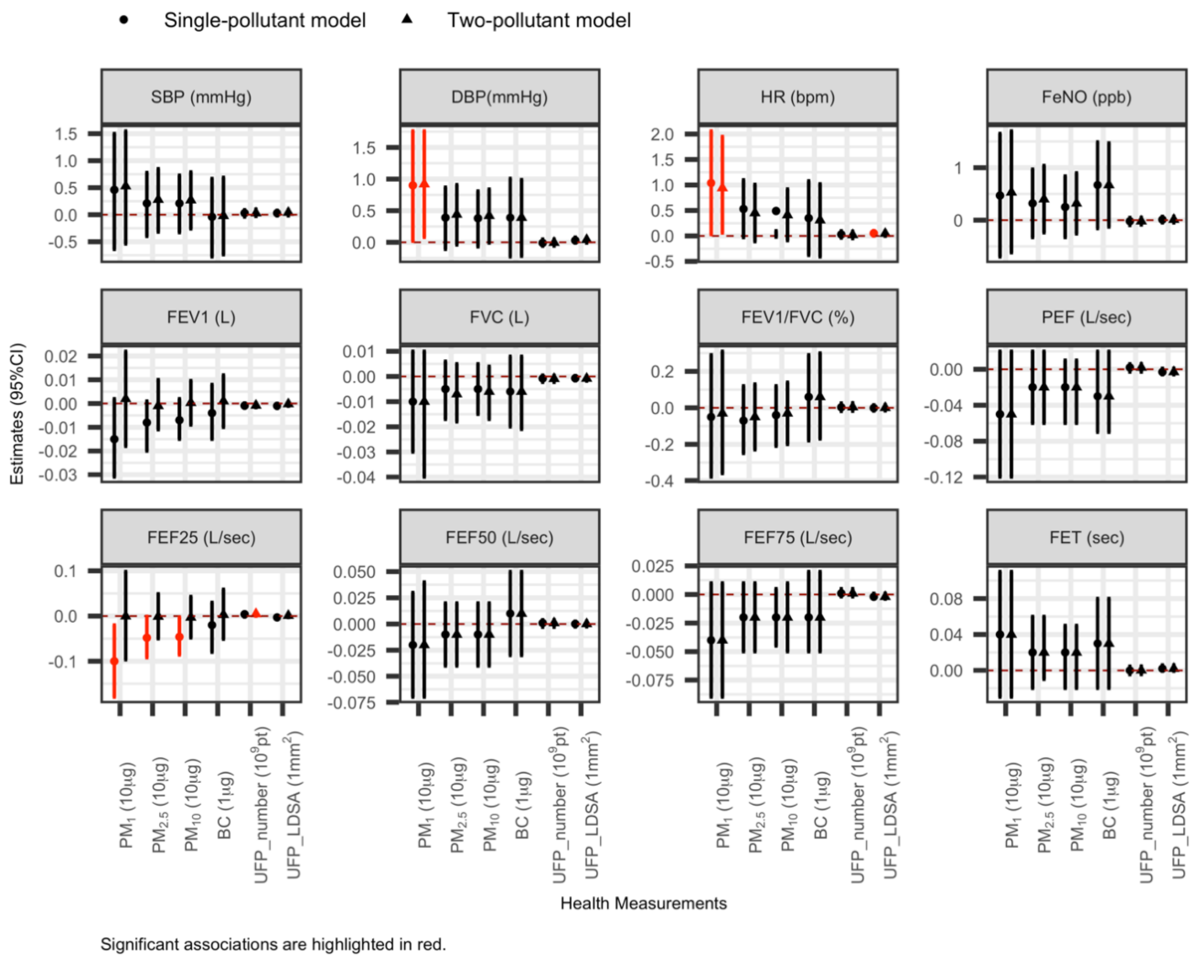

Figure 11. Associated between inhaled dose of TRAP and cardiorespiratory functions.

3.5 Discussion

This study adds to the emerging evidence about the dose-response relationship between TRAP exposure in different transportation modes and cardiorespiratory functions in China. This study employed a randomized double-blind cross-over design with spatiotemporal measures of TRAP exposure and repeated health outcomes to explore the acute health impact of TRAP exposure on cardiorespiratory functions in different transportation modes. Walking, taking a bus and taking a subway for two hours was associated with increased HR and increased airway obstruction (lower FEV1, FVC, PEF, FEF25, and FEF75) compared to riding a car, after adjusting for perceived stress, noise, temperature and relative humidity levels. After accounting for potential impacts of other exposure metrics related with different transportation modes, regional gaseous pollutant exposure, perceived stress, physical activity levels, noise, and meteorological conditions, the increased average BC concentration of TRAP during a 2-hour trip was associated with increased airway inflammation (FeNO) and increased PM_1 exposure was associated with decreased lung function (FEV1, FEV1/FVC, PEF, and FET).

A cross-over design was employed in this study such that all estimates were based on intra-subject comparisons, increasing the power of the study to identify health changes. That is, subjects served as their own controls and individual differences (*e.g.*, age, gender, genotype) were controlled in the study by design. The study also collected information on various potential confounders to disentangle the cardiorespiratory health effect of TRAP exposure during different transportation modes. Publications provide cumulative evidence for the association of gaseous pollutants, noise, meteorological conditions, and psychological stress with cardiorespiratory health [119,146-151], though, very few studies measured and adjusted for these confounders. The current study measured physical activity, noise, temperature, and relative humidity levels using portable and wearable instruments during each trip, collected information on psychological stress using the Cohen's Perceived Stress Scale (PSS4) which had been validated for the Chinese population [152], and leveraged gaseous pollutant concentrations from a nearby regulatory monitoring site to estimate the independent cardiorespiratory effects of TRAP from road traffic.

Active transportation has been promoted globally as a way to increase physical activity levels. Epidemiological studies have estimated the trade-off between the benefit of physical activity and the adverse health effect of air pollution exposure [71,76,153]. However, the complex link between physical activity and air pollution exposures has not been well studied in regions with extremely high air pollution exposures (*e.g.*, China, India) or highly polluted microenvironments (*e.g.*, in traffic) [154]. The combined effect of TRAP exposure and physical activity were explored in this study during different transportation modes and showed increased HR and decreased lung function (FEV1) after walking, taking a bus or a subway for two hours as compared to riding in a car. The results suggested that, at least for short-term exposure and acute cardiorespiratory functions, the adverse health impact of TRAP exposure might outweigh the benefit of physical activity involved in active transportation in highly polluted regions, although the cumulative longer term trade-offs between air pollution exposure and physical activity are not obvious from this current study. A London study investigated the impact of TRAP exposure and physical activity by having study subjects walking for 2 hours along a busy road and in a park [68]. Although walking along a busy road for 2 hours still benefited the cardiorespiratory health, the study found that short-term TRAP exposure attenuated the benefits of walking in both healthy subjects and patients with cardiorespiratory diseases. This study in Chengdu, however, showed that the acute adverse effect of TRAP exposure on cardiorespiratory function might outweigh the beneficial cardiorespiratory effect of physical activity during 2-hour walking. This may be due to the higher air pollution concentrations in Chengdu as compared to levels in London.

Physical activity levels directly impact the minute ventilation and inhaled dose of air pollution in traffic. Previous studies have estimated the inhaled dose of air pollution in different transportation modes [31,34,39,155,156]. However, the variation of ventilation is often ignored in epidemiological studies [157]. This study explored the exposure-response relationship for inhaled dose of TRAP and cardiorespiratory funcitons. The inhaled dose of TRAP was estimated based on the population average of minute ventilation for the Chinese population at different physical activity levels [142]. After adjusting for the regional gaseous pollution exposure, perceived stress, noise, and meteorological conditions, model results suggested significant associations of increased PM_1 inhalation dose with increased DBP and HR, and the adverse effects of increase inhaled UFP numbers on small airway obstruction (decreased FEF25). While only significant associations were found between TRAP exposure and respiratory health when using the mean concentration as the exposure metrics, using inhalation dose of TRAP as the exposure metrics in the linear mixed effects models found cardiovascular health effects of TRAP but no impact on respiratory health. Because very few epidemiological studies used inhalation dose as the exposure metric, future studies are needed to confirm finding from this current study. In addition, the minute ventilation was not measured during the study. Instead, the inhaled dose of TRAP was estimated based on the measured physical activity levels of each trip. It's possible that errors exist in the estimated inhalation does of TRAP, and therefore, bias in the exposure-response relationships. Future studies could employ wearable sensors, for example, the Hexoskin (Carre Technologies Inc, Montréal, Canada) biometric vest to estimate measure minute ventilation more directly using dual channel respiratory inductance plethysmography sensors [158,159].

This is perhaps the first study that has considered the impact of different TRAP exposure metrics in a transportation health effects study. Mean air pollution concentrations are used in almost all previous epidemiological studies to estimate the exposure-response relationship between air pollution exposure and health outcomes. While the average might explain most differences in TRAP levels between different trips, as a measure of central tendency, the mean does not capture the variation in the exposure distribution which may be relevant for short-term acute exposure-health relationships. Therefore, the study also considered using two latent variables to characterize other exposure metrics (*e.g.*, median, SD, COV, proportion of time that pollutant concentrations were above the 3rd quartile of recorded levels across all trips) related to transportation modes in the linear mixed effect model. This analysis aimed to further account for potential confounding effects of other characteristics of air pollution distribution in the traditional mean concentration model. After adding latent variables of other exposure metrics of

TRAP, the associations of the mean TRAP concentration with FeNO, FEV1 and FET remained, whereas, no association was found between the mean concentration of TRAP and cardiovascular health. Additionally, significant associations were found between increased mean concentration of PM exposure and decreased FEV1/FVC after adjusting for other characteristics of TRAP exposure in different transportation modes.

The study found no association between mean TRAP exposure and blood pressure and HR among healthy adults after adjusting for potential confounders. This is consistent with results from previous crossover studies [54,56,68]. However, a crossover study measured blood pressure during commutes and reported positive associations between TRAP exposure and SBP [74]. The study used continuous ambulatory blood pressure, which was a different assessment of blood pressure from this current study. The positive associations identified may be biased due to uncontrolled individual differences. An experimental study in London investigated the associations between TRAP exposure and blood pressure among healthy adults and patients with cardiorespiratory diseases [68]. The London study found increased SBP at 26 hours after 2-hour walking along a busy road as compared to walking in a park among patients with ischemic heart disease. While various exposures (*e.g.*, indoor air pollution, dietary exposure, and psychological factors) during the 26-hour lag time may impact blood pressure, it might be hard to attribute the increased SBP to the 2-hour walking along a busy road.

This study found consistent associations between increased average concentration of BC and elevated FeNO in different mixed effect models, that each 1 $\mu g/m^3$ increment in mean BC concentrations during commutes was associated with 1.39 ppb (95% CI: 0.07, 2.71) FeNO. FeNO is a sensitive biomarker of airway inflammation, which is a key mechanism of asthma exacerbation [160]. This result was consistent with previous studies. A study among asthmatic children in New Jersey reported that each 1.8 $\mu g/m^3$ increase in the average BC concentrations in prior 6 hours was associated with 14% (95% CI: 3%, 26%) increment in FeNO (mean measured FeNO: 30.6 ppb) [161]. Another study found that each 6.3 $\mu g/m^3$ BC exposure in previous hour was associated with 82.2% (95% CI: 63.5, 100.8) increment in FeNO for prediabetic individuals living in Beijing [162]. A crossover study in Seattle showed that each 1 $\mu g/m^3$ increment in 24-hour average BC was associated with 1.2 ppb (95% CI: 0,17, 2.22) increment in FeNO among the elderly with chronic respiratory diseases. However, a study among healthy adults in Barcelona found no association between the mean concentration of BC exposed and FeNO [71]. While the Barcelona study measured FeNO at 30 minutes, 3 hours and 6 hours after the 2-hour TRAP exposure, the mean of post-exposure FeNO measurements were assessed in their analyses. While this study in Chengdu found increased BC immediately after 2-hour commuting, it is possible that the impact of BC on FeNO was transient and last less than 3 hours among healthy adults. This identified association between BC exposure and increased airway inflammation supports the most prominent hypothesized biological mechanism for adverse health impact of air pollution, that certain inhaled air pollutants induce oxidative stress and provoke local and systemic inflammation [163]. While the level of FeNO has been used to assess asthma control [164,165], future efforts are needed to understand the clinical implications of TRAP exposure induced elevated FeNO in healthy adults.

The association between TRAP exposure and lung function has been explored in many previous crossover studies. After adjusting for regional gaseous pollutant exposure, different exposure metrics in transportation modes, stress, physical activity, noise and meteorological conditions, this study found negative associations between PM_1 and FEV1, PM (*i.e.*, PM_1, $PM_{2.5}$ and PM_{10}) and FEV1/FVC, UFP number concentration and PEF, and positive associations of PM, BC, UFP number concentration, UFP LDSA to FET. However, it should be noted that the lung function measurements in this study might not be robust because of short expiratory time (FET) measured among this population. Previous crossover studies reported inconsistent relationships between TRAP exposure and lung function. Some studies showed that increased TRAP exposure (PM_1, $PM_{2.5}$, UFP number concentration) was related with decreased FEV1, FVC, and PEF among healthy adults and asthma, IHD and COPD patients [67,68,73,75]. Whereas, other studies found no statistically significant changes of lung function after short-term exposure to TRAP among healthy adults and patients with asthma or coronary heart disease [48,54,69,70]. The inconsistent results from previous crossover studies may be due to the lack of control for the confounding impact of physical activity on respiratory health in most of these studies. While many studies analyzed spirometry measures related to large airway function (*e.g.*, FEV1, FVC, PEF), the association between TRAP exposure and indicators for small airway resistance has not been well studied. An Austrian study measured lung function among 24 healthy and non-smoking students after 1-hour walking, and found increased PM_1 exposure was related with decreased mid-expiratory flow at 25% lung volume [74]. Another study in Canada had 42 healthy adults cycling along different roads, and found UFP exposure was positively associated with decreased forced expiratory flow at 25%-75% of vital capacity 1-hour after cycling [72]. This current study found the most consistent associations between TRAP exposure FET in different linear mixed effect models. However, because of the relatively large within subject variability of FET compared to other spirometry measures, there has been controversy about using FET as a reliable tool to determine small airway obstruction [166-168]. Therefore, further evidence is needed to assess the health impact of TRAP on small airway function.

Although the cross-over design, personal exposure measurements, real-life exposure conditions, consideration of different potential confounders, and exploration of associations between inhaled dose of TRAP and health outcomes are important strengths of this study, several potential limitations should be discussed. First, health measurements were only taken right before and after each 2-hour trip. The study was not able to examine the delayed effect of TRAP exposure on cardiorespiratory functions, and may miss some meaningful associations between TRAP exposure and cardiorespiratory functions if lag effects exist for certain health outcomes. Second, all the particle pollutants of interests were measured using portable instruments at the individual level, but the gaseous pollutant exposure was determined based on gas concentrations recorded by a nearby regulatory monitoring site. Although the central monitoring site was only 2 km from the scripted route used in the study, gas concentrations at the central site might not reflect the on-road exposure conditions for the study subjects. In addition, associations between inhaled dose of air pollutant and cardiorespiratory functions were assessed in the sensitivity analysis. However, the inhalation dose of each subject was estimated by using the average inhalation rate for Chinese adults according to the exposure factors handbook, instead of measured minute ventilations. Between-subject variations are not considered in the exposure modeling, which may induce exposure measurement error in the inhalation dose analyses. Also, as an exploratory study, multiple comparisons was not adjusted in the study. While no perfect correction methods have been suggested from previous studies and adjusting for multiple comparison might be unreasonable to apply to exploratory studies, the study reported all effect sizes and CIs as recommended by biostatisticians, and focused more on the consistency of the associations [169,170].

3.6 Conclusions

This is the first exploratory study that examined the exposure-response relationships between TRAP exposure in commonly used transportation modes and cardiorespiratory functions in Chengdu, China. With the cross-over design, repeated personal exposure measurement and controls for potential confounders (*e.g.*, perceived stress, noise exposure, physical activity levels), the study found increased HR and decreased lung function among healthy adults after walking, riding a bus or riding a subway for two hours compared to riding a car. The mean concentration of BC exposure was independently associated with elevated airway inflammation (FeNO) and increased PM_1 exposure was associated with reduced large airway resistance (decreased FEV1, FEV1/FVC, and PEF). The results indicated that short-term TRAP exposure in Chengdu, China during different transportation modes adversely impact the acute respiratory function of healthy adults. At least for short-term exposure and acute cardiorespiratory functions, the adverse health impact of TRAP exposure might outweigh the benefit of physical activity on cardiorespiratory function in Chengdu, China, although the more important longer term trade-offs between air pollution exposure and physical activity are not obvious from this current study.

Chapter 4. THE EFFECTIVENESS OF USING POSITIVE PRESSURE RESPIRATORS TO PREVENT ADVERSE CARDIORESPIRATORY HEALTH IMPACTS OF TRAFFIC-RELATED AIR POLLUTION EXPOSURES DURING URBAN COMMUTING

4.1 Abstract

Background: Air pollution exposures are pervasive, but modifiable. Respirator face masks have cultural acceptance in China, and have been used as an intervention to avoid air pollution exposures. This study aims to test the effectiveness of using positive pressure respirators to reduce air pollution exposure and related adverse cardiorespiratory health in Chengdu, China.

Methods: The study employed a randomized double-blind crossover intervention design. A total of 21 healthy young adults travelled 2 hours on a scripted route for 8 times in winter, 2019. Subjects completed two trips using each of the four tested modes (*i.e.*, walking, taking a bus, taking a subway, and riding a car). Subjects used effective positive pressure respirators in one trip, and they wore sham respirators in another one. The respirator condition was blinded to researcher and subject, and the order of the eight trips was randomized. Continuous time-resolved ultrafine particles, particulate matter of different size (PM_1, $PM_{2.5}$, PM_{10}), black carbon, noise, physical activity levels and meteorological conditions were monitored for each trip. Blood pressure, fractional exhaled nitric oxide (FeNO), and lung function were measured right before and after each trip. Additionally, perceived psychological stress and subjects' perception of the respirator were assessed after each trip. Mixed effect models were used to explore the association between wearing positive pressure respirators and cardiorespiratory functions.

Results: When the blower of a positive pressure respirator was set at the lowest level, the respirator could provide sufficient flow for a Chinese adult in moderate-intensity activity and had an average overall fit factor ranging from 10 to 15. No significant differences were found for cardiorespiratory health between subjects wearing effective respirators and those using sham respirators for two hours in traffic. However, the perceived exposure of subjects modified the association between using positive pressure respirators and cardiorespiratory functions. Subjects who were uncertain about the respirator condition tended to have 0.93% lower FEV1/FVC (95% CI: 0.13, 1.72) and 0.22 L/sec lower FEF25 (95% CI: 0.03, 0.41) when they used effective respirators (exposed to filtered air) compared to when they wore sham respirators (exposed to air pollution) in traffic.

Conclusion: Results from this study suggested that wearing positive pressure respirators for two hours in traffic might not impact cardiorespiratory functions among healthy adults in Chengdu, China.

Keywords: traffic related air pollution; intervention; respirator; randomized double-blind crossover design

4.2 INTRODUCTION

Ambient air pollution is the fourth largest risk factor for attributable deaths, responsible for more than six million estimated deaths globally in 2019 [171], motivating efforts to reduce exposures. Air pollution exposures are pervasive, but modifiable. Governmental agencies, industrial companies, and academic institutes make great efforts to mitigate air pollution exposure. For example, the US Environmental Protection Agency (EPA) has developed a map of air quality to provide real-time $PM_{2.5}$ data [172] and to inform public behaviors [173]; different companies have developed various air purifiers to help reduce air pollution indoors [174]; and academia has conducted an increasing number of studies assessing the benefit of using air purifiers to reduce personal exposure to air pollution [175-177].

China is one of the most polluted countries, and has strived to implement mitigation strategies to reduce air pollution levels. The Air Pollution Prevention and Control Action Plan [178] was issued in 2013 to specify measures and goals for air pollution control. Since then, the ambient air pollution concentrations in China decreased continuously [179,180]. However, air pollution is still a severe issue in China, where 1.24 million deaths were attributable to air pollution in 2017 [181].

Personal protective equipment (PPE), such as the respirator face mask (*e.g.*, N95, N99 respirators) has cultural acceptance in China, and has been used as an intervention to avoid traffic-related air pollution exposure during transportation. However, the effectiveness of wearing respirators to reduce air pollution exposure and to improve health has not been well studied [182]. Theoretically, N95 and N99 respirators are able to remove at least 95% and 99% of particles that are 0.3 microns in size or larger, respectively. Few real-world studies have linked respirator wearing to improved cardiovascular outcomes for either healthy adults [183] or patients with cardiovascular diseases [184]. However, respirator fitment issues are often a concern [185]. Because respirators do not fit every face shape, fit testing is necessary to ensure the protection from wearing a respirator. Additionally, users need to be trained to wear respirators tightly to avoid inward leaking air. These two reasons might reduce the practicability and effectiveness for the general public to use N95/N99 respirators in daily life.

To solve the fitness issues of previously studied N95 or N99 respirators, this study tests a commercial positive pressure respirator. The positive pressure respirator uses a blower instead of lung power to draw air through the filter, which mimics the occupationally used powered air purifying respirator (PAPR). With positive pressure around the breathing zone, no fitting test is needed before the use. Additionally, compared to the bulky and noisy PAPR [186], the positive pressure respirator is portable, light-weight, and easy to use in daily life without any training.

This study aims to examine the effectiveness of wearing positive pressure respirators to improve cardiorespiratory health during time spent in transportation for healthy adults in Chengdu, China.

This study employed a randomized double-blind crossover design, comparing the cardiorespiratory functions of healthy adults with effective or sham positive pressure respirators after two-hour commutes on a scripted route.

4.3 METHODS

4.3.1 Study Design

The study is part of a randomized double-blind crossover intervention experiment described in Chapter 3. In brief, a total of 21 never smoked, non-pregnant and healthy trainees or employees of Sichuan Center for Diseases Control and Prevention (Sichuan CDC, located in Chengdu, China) were enrolled in the study. Each recruited subject completed two trips using each of the four commonly used commuting modes (*i.e.*, walking, riding a compressed natural gas powered bus, riding an electric powered subway, and riding a gasoline powered car) on a scripted route between November and December in 2019 in Chengdu, China. Subjects travelled with effective respirators in one trip and used sham respirators in another one. The scripted route was on a major road across the city center, with the origin and destination both at the Sichuan CDC office. Each trip lasted for two hours and the order of the eight trips was randomized.

The concentration of particulate matter (PM, *i.e.*, PM_1, $PM_{2.5}$ and PM_{10}), black carbon (BC), and ultrafine particle (UFP) were monitored using a calibrated Portable University of Washington Particle (PUWP) monitor (University of Washington, Seattle, WA, USA), microAeth AE51

(AethLabs, San Francisco, CA, USA), and Discmini (Testo, West Chester, PA, USA), respectively. The temperature and relative humidity were recorded along with the PM by the PUWP monitor, and noise levels were recorded using a NoisePro DLX Dosimeter (3M, St. Paul, MN, USA). In addition, physical activity levels of subjects were monitored continuously by ActiGraph (ActiGraph, Pensacola, FL, USA) activity monitors on their left wrist. Before and after each trip, the noise dosimeter was calibrated with a 114dB calibrator. Apart from the individual level exposure measurements during each trip, the average concentration of SO_2, NO_2, CO and O_3 during each trip were collected from the nearest regulatory monitoring site (approximately 2km from the script route).

Immediately before and after the 2-hour trips, the cardiorespiratory functions of each subject were measured by trained technicians following standard operating procedures described in Chapter 3. During each health examination, three measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) and heart rate (HR) were taken by an oscillometric wrist blood pressure monitor (HEM-8611, Omron, Kyoto, Japan), where the latter two measurements were averaged to represent the subject's cardiovascular health. Then, subjects were measured for airway inflammation by fractional exhaled NO (FeNO) using an electrochemical instrument (NIOX VERO, Circassia Limited, Morrisville, NC, USA). Finally, the lung function of subjects was tested by spirometry, including measures of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, peak expiratory flow (PEF), mean forced expiratory flow at 25%, 50% and 75% of forced vital capacity (FEF25, FEF50, FEF75) and FET (forced expiratory time). Subjects also completed a questionnaire after each trip, which measured their perceived stress with the 4-item version of Cohen's Perceived Stress Scale (PSS4) [140] and their perception of the respirator used (if they thought the respirator was sham, or effective, or they did not know).

4.3.2 Positive Pressure Respirators

The study used the BROAD AirPro FB2 rechargeable Air Purifying Respirator (BROAD Clean Air Technology, Changsha, China) as the intervention. The positive pressure respirator is marketed as using a high-efficiency particulate absorbing (HEPA) filter to remove 99.9 % of ambient particles, and a blower to provide air flows at three levels (low, medium and high) with low noise levels (27, 30 and 33 dBA respectively). Compared to the occupationally used PAPR, this positive pressure respirator is easy to use, light weight (200 g), quiet when using, and low-cost (approximately $30 USD). For the study, we defined the "effective" respirator as having the manufacturer's supplied HEPA filter and active carbon filter inserted in the case. We also defined the "sham" filter as having only active carbon filter installed in the unit (Figure 12). The air flow was set at $4m^3/h$ during walking, bus and subway trips, and was set at $3m^3/h$ during car trips for each subject. The condition of the positive pressure respirator was double-blinded to researchers and subjects.

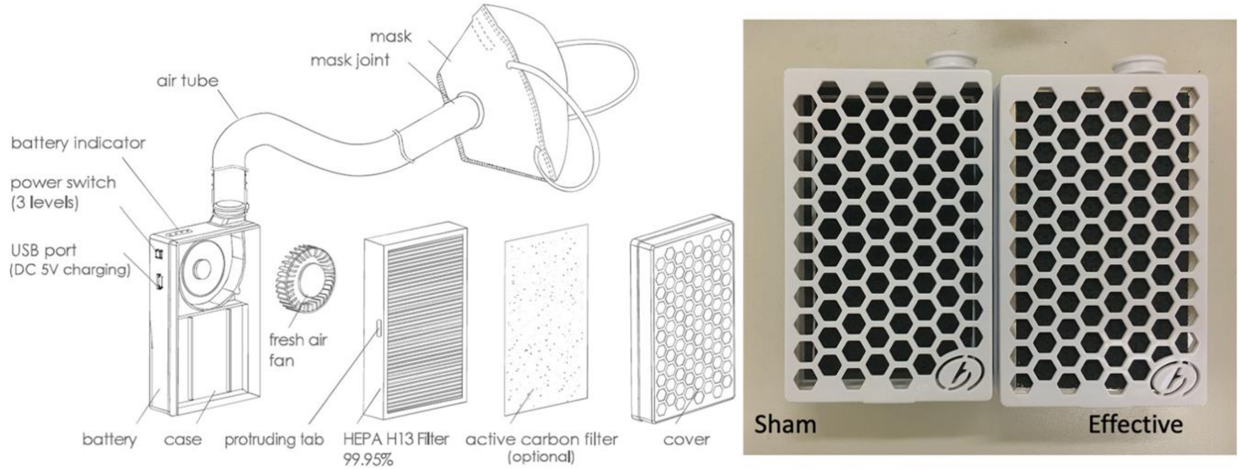

Figure 12. The structure of the positive pressure respirator.

Before using the positive pressure respirator in the study, three respirators were randomly selected to be tested for their flow rates, particle removal rates and fit factors. Only when the flow rate was larger than the minute ventilation of users, the positive pressure within the facepiece could be maintained, with air flowing outward rather than inward though any face seal leakage. The air velocity was measured at the three flow settings in laboratory settings using the TSI VelociCalc 9535A Air velocity meter (TSI Incorporated, Shoreview, MN, USA) in a lab (Figure 13). The testing probe was placed at the center of the air tube. The air velocity was measured when the air tube was straight and had a 90 degree angle. Then the flow rate was calculated as:

$$Flow\ rate = air\ velocity \times section\ area \qquad (eq\ 3)$$

where the section area (cross section of the air tube) was a circle with a diameter of 13mm.

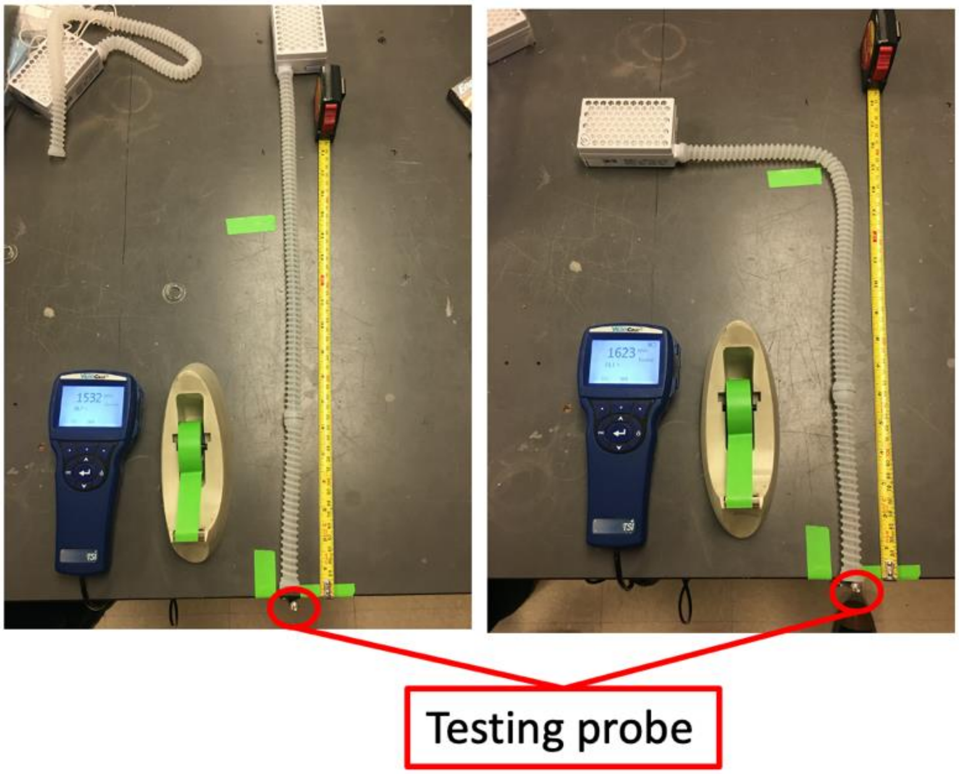

Figure 13. Settings for the flow test of the positive pressure respirator.

The particle removal rates of the three positive pressure respirators were measured outdoors by a roadside using the TSI 3330 particle counter (TSI Incorporated, Shoreview, MN, USA). The air tube and facepiece were removed from the HEPA filter case during testing. The particle number concentration was recorded at the ambient level and at the outlet of the HEPA filter case for 10 minutes at each of the three flow settings. The particle removal rates were calculated as:

$$Particle\ removal\ rate = \frac{C_{ambient} - C_{HEPA}}{C_{ambient}} \qquad (eq\ 4)$$

where $C_{ambient}$ was the ambient PM levels, C_{HEPA} was the number concentration measured at the outlet after the HEPA filtration.

Finally, the three respirators were tested for fit factor in a lab using the TSI Portacount pro 8038 (TSI Incorporated, Shoreview, MN, USA). The fit test followed the standard test cycle, starting with normal breathing, then deep breathing, head side to side, head up and down, talking, bending over and finally backed to normal breathing. The particle concentrations were measured outside and inside the masks, and the fit factor was calculated as:

$$FF_i = \frac{C_B + C_A}{2C_R} \qquad (eq\ 5)$$

$$Overall\ FF = \frac{n}{\frac{1}{FF_1} + \frac{1}{FF_2} + \frac{1}{FF_2} + \cdots + \frac{1}{FF_n}} \qquad (eq\ 6)$$

where the FF_i was the fit factor for each test cycle, C_B was the particle concentration in the ambient sample before the respirator sample, C_A was the particle concentration in the ambient sample after the respirator sample, and C_R was the particle concentration in the respirator sample, the n was the number of test cycles, and FF_x was the fit factor for each test cycle.

4.3.3 Statistical Analysis

4.3.3.1 Effectiveness of wearing respirators

The average of flow rate, particle removal rate and fit factor were summarized for the three randomly selected positive pressure respirators. The measurements for noise, temperature, relative humidity and physical activity levels (metabolic equivalent of task, MET) for each trip were extracted from the raw data files. Missing values (9 missing data points for meteorological conditions, no missing data point for noise and MET) and outliers (no outliers identified) were removed. After the quality control processes the average levels of noise, meteorological conditions and MET was summarized for each trip.

With repeated health measurements for each subject, the effectiveness of wearing respirators was estimated using a linear mixed effects model to compare the health outcomes with effective and sham respirators:

$$y_{ij} = b_0 + b_1 x_{ij} + v_i + e_{ij} \qquad (eq\ 7)$$

where y_{ij} was the difference of health response before and after *j*-th trip of *i*-th subject, b_0 was the fixed intercept for the regression model, b_1 was the fixed slope for the regression model, x_{ij} was the main exposure of interest and other covariates for *j*-th trip of *i*-th subject, $v_i \sim N(0, \sigma v)$ was the random intercept for the *i*-th subject, and $e_{ij} \sim N(0, \sigma e)$ was a Gaussian error term.

A reduced model was built for each health outcome to include the categorical variable of intervention (*i.e.*, effective vs. sham) with covariates included for noise, temperature and relative humidity. The full model further adjusted for other covariates: perceived stress, physical activity, and the regional gaseous pollutant concentrations. The four gaseous pollutants were each added to the model separately and the model with the lowest Bayesian information criterion (BIC) was selected as the final full model. While the ratio between FEV1 and FVC were commonly used in epidemiological studies as an indicator for large airway obstruction, using a single ratio as the dependent variable in regression models might lead to incorrect inferences (*a.k.a.*, spurious correlation) [187]. Therefore, aside from using FEV1/FVC as the dependent variable, the study also built reduced and full models for FEV1 but adjusted for FVC as a covariate.

4.3.3.2 Sensitivity Analysis

While the intervention conditions were double-blinded to researchers and study subjects, the study further examined the modification effect of subjects' perception of the intervention (perceived exposure) on the association between respirator conditions (true exposure) and cardiorespiratory functions. A linear mixed effect model was developed based on the *eq 7* with an interaction term for subjects' perception (*i.e.*, not know, sham, or effective) and the respirator condition (*i.e.*, sham or effective). Other covariates included the average physical activity level (*i.e.*, METs), perceived psychological stress, noise, temperature, relative humidity and one regional gaseous pollutant concentration during each 2-hour trip. Four gaseous pollutants were tested in the model and the one with the smallest BIC was selected for the final model to be presented in the results.

All statistical analyses were conducted in R 4.0.3 (http://www.R-project.org/) (R Foundation for Statistical Computing, Vienna, Austria) and RStudio® (Version 1.1.456).

4.4 RESULTS

4.4.1 Characteristics of Positive Pressure Respirators

Testing of the positive pressure respirators indicated that the flows were greater than average minute ventilations and that filtration was adequate to reduce particle exposures. When the blower was set at the lowest level and the air tube had a 90 degree angle, the average flow rate reached 41.6LPM (Table 10), which was twice of the average minute ventilation of the Chinese population during moderate-intensity activity (male: 24.8 LPM, female: 20.2LPM) [142]. The HEPA filter inside all three respirators all performed well (Table 11). On average, the HEPA filter used in the respirator was able to remove more than 98% of ambient particles. The fit test showed that the respirator had average overall fit factors of 10-15, 18-28 and 27-69 when the flow was at low, medium and high settings, respectively (Table 12). The facepiece alone could remove approximately 70% of the ambient particles (overall fit factor = 3.3). However, the fit factor decreased during movements involving deep breathing.

Table 10. The flow rate of three randomly selected positive pressure respirators at the three flow settings.

	Flow (LPM)					
	Low setting		Medium setting		High setting	
	Straight	90 degree	Straight	90 degree	Straight	90 degree
Respirator 1	44.94	40.35	57.72	51.9	75.43	65.48
Respirator 2	50.18	43.85	62	54.78	78.05	67.18
Respirator 3	46.17	40.48	56.84	52.01	71.3	65.67
Average	47.1	41.56	58.86	52.90	74.93	66.11

Table 11. The removal rate of three randomly selected positive pressure respirators.

PM	Ambient (pt/cm^3)	Respirator 1 (pt/cm^3)	Respirator 2 (pt/cm^3)	Respirator 3 (pt/cm^3)	Average removal rate (%)
$PM_{0.3}$	79149.0	1803.4	1754.7	379.4	98.22%
$PM_{2.5}$	130538.7	2679.8	2755.7	622.7	98.33%
PM_{10}	130580.1	2680.0	2756.1	612.9	98.33%

Table 12. The fit factor of three randomly selected positive pressure respirators.

Fit factors										
Maneuver	Blower turned off	Respirator 1			Respirator 2			Respirator 3		
	(facepiece only)	low	medium	high	low	medium	high	low	medium	high
Normal breathing	3.6	15	32	29	48	45	46	31	70	200+
Deep breathing	4.5	4.4	9	25	7.3	8.1	17	5.3	11	36
Head side to side	3.1	31	33	27	40	51	50	24	72	200+
Head up and down	2.5	11	24	25	27	15	18	22	51	200+
Talking	6.1	21	23	25	21	29	28	25	31	40
Bending over	4.1	6.3	13	30	7.3	18	31	13	18	35
Normal breathing	2	11	31	28	20	16	43	20	42	200+
Overall	3.3	10	19	27	15	18	28	15	28	69

4.4.2 The Effectiveness of Wearing Positive Pressure Respirator

The air pollution concentration, meteorological conditions, noise levels, gaseous pollutant concentrations, physical activity levels and perceived stress score for the 21 study participants were similar for the trips with sham and effective respirators (Table 13).

Table 13. Exposures during the 2-hour trips by intervention condition.

Measurements	Sham respirator (mean ± SD)	Effective respirator (mean ± SD)
LEQ (dBA)	71.42±5.00	71.19±5.36
BC (ng/cm^3)	4090±1270	3990±1270
PM_1 (μg/m^3)	31.59±10.41	30.81±10.66
$PM_{2.5}$ (μg/m^3)	53.49±20.87	52.01±21.40
PM_{10} (μg/m^3)	63.53±21.37	61.94±22.11
UFP_number (pt/cm^3)	28600±18700	28700±18600
UFP_size (nm)	48.40±14.73	47.70±14.72
LDSA (μm^2/cm^3)	51.18±17.58	50.89±17.60
RH (%)	37.54±7.52	37.62±7.34
Temperature (℃)	23.30±4.23	22.95±3.85
SO_2 (μg/m^3)	8.82±3.07	8.72±3.03
NO_2 (μg/m^3)	54.28±15.10	52.89±15.33
O_3 (μg/m^3)	27.54±17.75	27.25±17.51
CO (mg/m^3)	0.79±0.17	0.78±0.20
METs	3.26±0.71	3.26±0.71
Stress scores	4.26±2.84	4.33±2.73

On average, without consideration of potential covariates, the blood pressure (SBP and DBP) seemed to increase after spending two hours in traffic with both sham and effective respirators, while the HR and FeNO tended to decrease after the trip (Table 14). Most spirometry measurements seemed to decrease after traveling with sham respirators, but increase after traveling with effective respirators.

Table 14. Changes of cardiorespiratory functions before and after the 2-hour trips by intervention condition

Measurements	Sham respirator (mean ± SD)	Effective respirator (mean ± SD)
SBP (mmHg)	0.56 ± 6.15	1.99 ± 6.45
DBP (mmHg)	1.18 ± 5.66	1.34 ± 7.11
HR (bpm)	-5.10 ± 6.42	-4.20 ± 6.87
FeNO (ppb)	-2.60 ± 7.11	-2.23 ± 4.33
FEV1 (L)	-0.01 ± 0.10	-0.01 ± 0.09
FVC (L)	-0.03 ± 0.12	0.06 ± 0.59
FEV1/FVC (%)	0.50 ± 2.01	-0.25 ± 2.08
PEF (L/sec)	-0.10 ± 0.42	-0.04 ± 0.33
FEF25 (L/sec)	-0.04 ± 0.49	-0.12 ± 0.50
FEF50 (L/sec)	-0.01 ± 0.33	0.01 ± 0.46
FEF75 (L/sec)	-0.02 ± 0.31	0.03 ± 0.35
FET (sec)	-0.09 ± 0.42	0.16 ± 0.79

Considering personal differences and the impact of other potential confounders, the effectiveness of wearing positive pressure respirators to improve cardiorespiratory health was estimated using the linear mixed effects models (Figure 14). Compared to the reduced model (adjusted for noise, temperature and relative humidity during trips), the full model further adjusted for the impact of perceived stress, physical activity levels, and gas pollutant exposure, and had the lower BIC when adding CO concentrations as compared to models with the concentration of SO_2, NO_2 or O_3. The full model had similar estimates but slightly narrower 95% CIs compared to the reduced model. No statistically significant association was found between wearing positive pressure respirators and cardiovascular health (*i.e.*, blood pressure and HR). However, subjects wearing effective respirators tended to have higher SBP, DBP and HR as compared to subjects using sham respirators. For changes in respiratory health, subjects wearing effective respirators for 2 hours in traffic had longer FET compared to travelling with sham respirators. Additionally, wearing effective respirators in traffic was associated with lower FEV1/FVC compared to wearing sham respirators; however, when having FEV1 as the dependent variable but adjusted for the FVC, the lung function after traveling with effective respirators did not significantly differ from trips with sham respirators (Table A8). Though insignificant associations were found, subjects wearing effective respirators in traffic tended to have increased FeNO, FVC, PEF, FEF50, and FEF75.

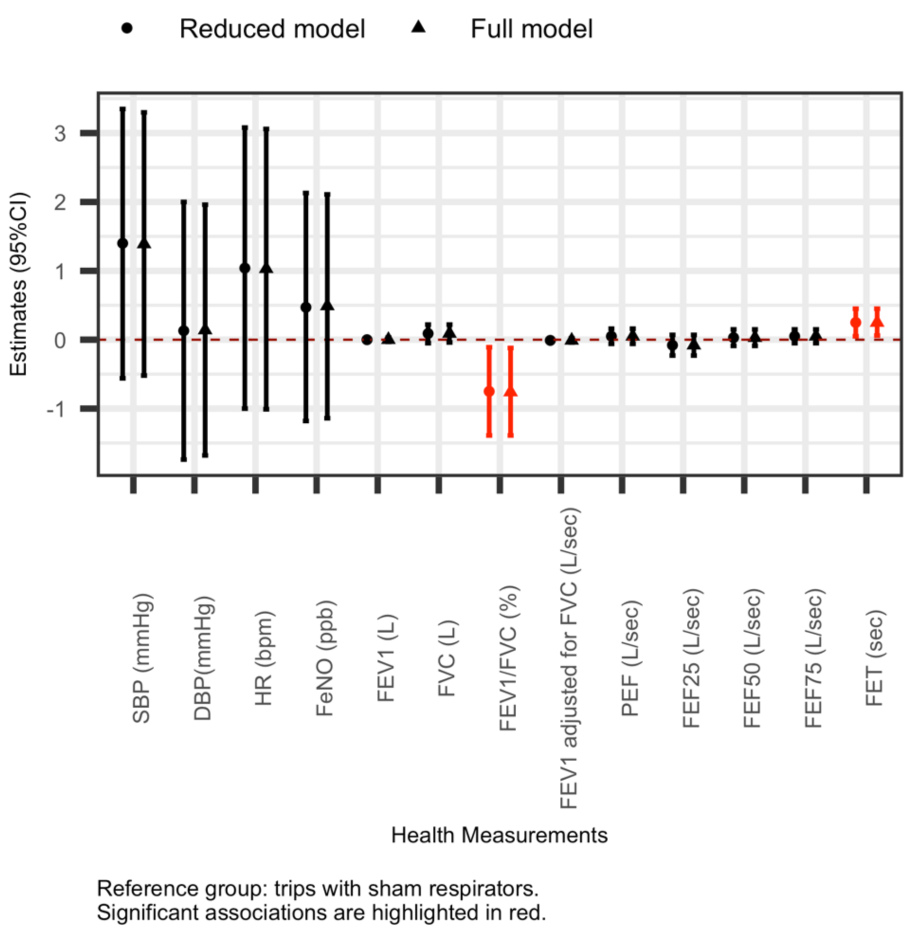

Figure 14. Changes of cardiorespiratory functions during 2-hour trips with effective positive pressure respirators compared to travelling with sham respirators.

4.4.3 Sensitivity Analysis

The study subjects guessed 25% of the filtration conditions correctly. The sensitivity analysis estimated the interaction between subjects' perception on the intervention (perceived exposure) and the respirator condition (true exposure). Models had the smallest BIC when adding the regional CO concentrations. Figure 15 shows the health effect as a function of intervention conditions (*i.e.*, effective vs. sham respirators), where y axis shows the within-subject differences in health measurements before and after trips among them wearing effective respirators vs. sham respirator, and x axis shows the health effects by perceptions (perceived exposure). Subjects' perceived exposure significantly modified with the association of respirator conditions to SBP, FEV1/FVC, FEF25, and FEF75 (Figure 15). Subjects who thought they wore sham respirators had lower SBP (-8.85 mmHg, 95% CI: -2.35, -15.32), higher FEV1/FVC (2.46%, 95% CI: 0.26, 4.68), and larger FEF75 (0.51 L/sec, 95% CI: 0.17, 0.86) after exposure to filtered air (*i.e.*, travelled with effective respirators) compared to exposure to traffic-related air pollution (*i.e.*, travelled with sham respirators). In contrast, subjects who were not certain about the respirator condition tended to have lower FEV1/FVC (-0.93%, 95% CI: -0.13, -1.72) and lower FEF25 (-0.22 L/sec, 95% CI: -0.03, -0.41) even wearing effect respirators (exposed to filtered air) compared to sham respirators (exposed to air pollution) in traffic (Table A9).

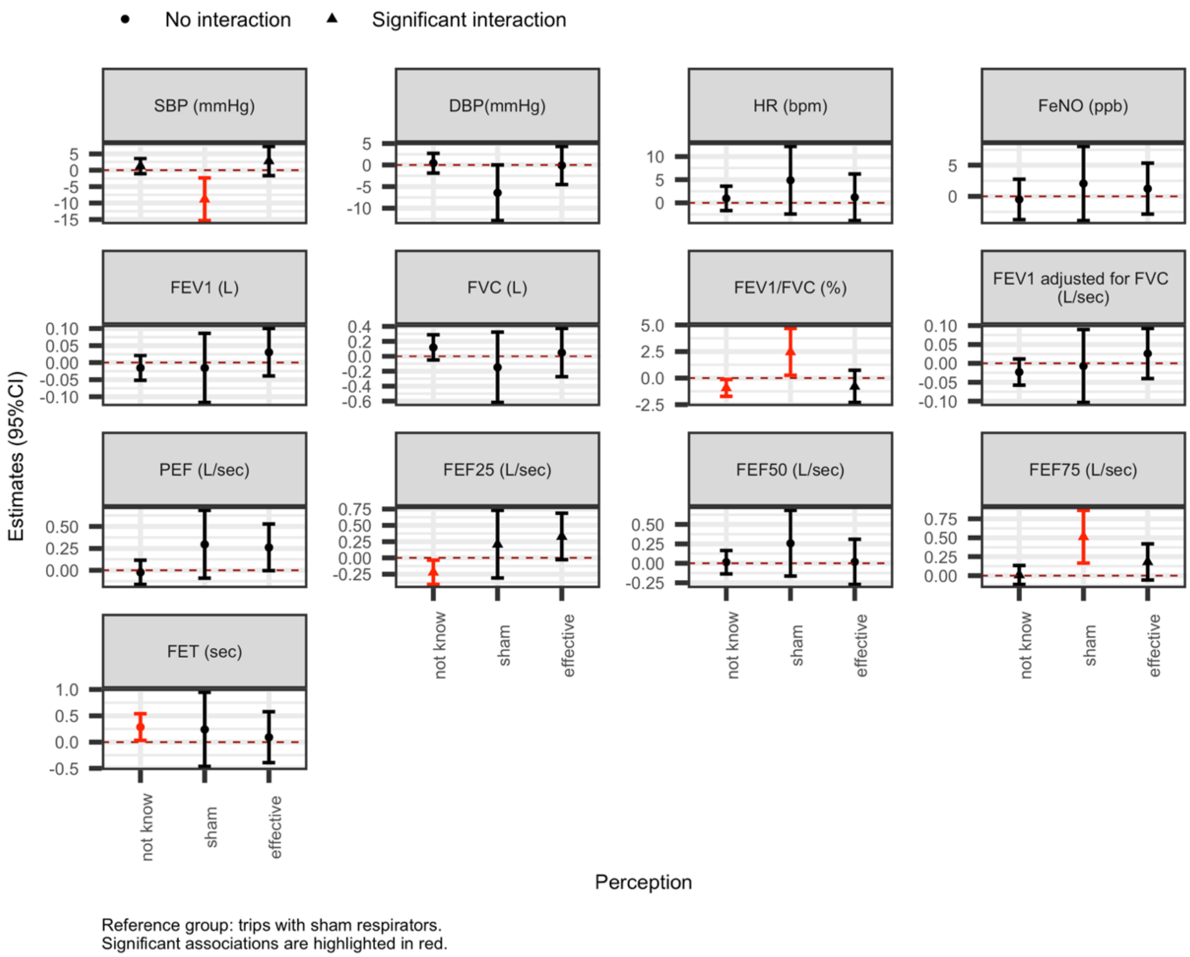

Figure 15. The modification effect of perceived exposure on the associations between true exposure (effective vs. sham respirators) and cardiorespiratory functions.

4.5 DISCUSSION

This study adds to the limited evidence about the effectiveness of wearing positive pressure respirators in traffic on improving cardiorespiratory health for healthy adults in China. This study tested the positive pressure respirators in both laboratory settings and real-world situations. The laboratory tests indicated that the positive pressure respirators would effectively remove at least 90% of ambient particles greater than 0.3 μm in diameter (fit factor:10-15) even when the blower was set at the lowest level. When testing the respirator in real-world travel, wearing the effective respirators was not associated with improved cardiorespiratory health after accounting for potential impacts of regional gaseous pollutant exposure, perceived stress, physical activity levels, noise, and meteorological conditions. In addition, perceived exposure of subjects significantly modified the association of wearing respirators in traffic to SBP and lung function (*i.e.*, FEV1/FVC, FEF25 and FEF75).

This study tested the ratio between FEV1 and FVC as an outcome of interest because FEV1/FVC has been commonly examined in epidemiological study as an airway obstruction and restriction indicator. The study found a counterintuitive association, that subjects had 0.79% lower FEV1/FVC (95% CI: 0.15, 1.43) after they were exposed to filtered air (wearing effective positive pressure respirators) as compared to subjects exposed to air pollution (wearing sham positive pressure respirators) after 2 hours in traffic. However, using ratios as dependent variables in linear models might be problematic. Others have found spurious correlation when having a ratio as the only dependent variable in linear regression models [187]. In the case of this study, the coefficient of a model for FEV1/FVC measured the joint effect of varying intervention (effective vs. sham respirator) and FVC. Because the main purpose of the denominator of a ratio is to adjust for it, previous research suggests using the denominator (FVC) as a covariate in regression models [187]. Therefore, in the current study, additional linear mixed effect models considered the association between intervention and FEV1 after adjusting for FVC. Models of the FEV1 with adjustment for FVC led to a different conclusion that no association was found between wearing positive pressure respirators and changes in lung function.

This study also found a counter intuitive association between using respirator and FET, that subjects using effective positive pressure respirator tended to have longer FET compared to those using sham respirators in traffic. However, FET is a less preferred indicator for airway obstruction as compared to other spirometry measurements, mainly because of its large intrasubject variation [166]. Thus, no robust associations were found in the study between wearing positive pressure respirator and improved cardiorespiratory health for healthy adults in Chengdu, China.

The laboratory test showed that the positive pressure respirator provided sufficient flow of air for Chinese adults and performed well for particle removal, though the field experiment did not find a benefit of wearing positive pressure respirators in traffic on cardiorespiratory functions. It is possible that the flow rate test overestimates the effectiveness of the respiratory, because the maximal inhalation velocity during movement can be much higher than the average velocity. In contrary to results of this study, a few previous studies suggested association between respirator wearing and improved cardiorespiratory health. A randomized crossover study in Shanghai China recruited 24 healthy young adults to wear N95 respirators for 48 hours. In that study, the Bitter test was performed to qualitatively test the fitment of respirators for each subject. The study found improved autonomic nervous function (increased frequency and time domain of heart rate variability) and decreased SBP [183]. Similar studies in Beijing found improved cardiovascular health among both healthy young adults (reduced SBP) after wearing N95 respirators for 2 hours [188] and patients with coronary heart disease (reduced symptoms, maximal ST segment depression, mean arterial pressure and increased hear rate variability) after wearing N95 respirators for 24 hours [184]. However, subjects in these studies wore/not wore respirators, and thus were not blinded. These findings may be biased due to demand characteristics or the placebo effect.

This study also examined if the perceived exposure of subjects modified the effectiveness of wearing positive pressure respirators to improve cardiorespiratory health. Significant interactions between the respirator condition and perceived exposure were found for multiple health measurements (*i.e.*, SBP, FEV1/FVC, FEF25, FEF75). In general, wearing positive pressure respirators in traffic might adversely impact the respiratory health of healthy adults if they were uncertain about the condition of the respirator they wore. Two previous randomized double-blind crossover studies examined the modification and confounding effect of perceived exposure on the association between true exposure and health, neither of which found significant impact of subjects' perception [60,61]. While risk perception may have both physical and psychological effects on human health [189,190], further studies are needed to confirm the modification effect of risk perception on the association between intervention and human health.

This study has several important strengths, including using the low-cost portable positive pressure respirators to solve the fit issue of N95/N99 respirators and to achieve a double-blind design in a real-life trial, and measuring and controlling for potential confounding effect of perceived psychological stress, physical activity level and gaseous pollutant concentration.

The study also has several limitations. First, the study recruited healthy and young adults instead of susceptible individuals (*e.g.*, children, pregnant women, the elderly or patients with underlying diseases). It is possible that the study may underestimate the benefit of wearing positive pressure respirators for the vulnerable population. However, healthy and young adults may be the group that spend the most time in traffic compared to other population groups. It is still important to understand the impact of using respirators on cardiorespiratory health for the healthy and young population. Second, the study had subjects traveling on a scripted route for two hours during each trip, which might be insufficient exposure time to detect the benefit of using positive pressure respirators. The two-hour period is a realistic commuting time for residents living in cities. While no acute impact was found for wearing positive pressure respirators on cardiorespiratory health, future studies may look into the long-term benefit of using respirator in traffic. Additionally, the study measured health effects immediately after exposure. Because health effects may be subject to temporal lags [68,77], maybe insufficient time had elapsed to observe differences in health effects between trips with sham and effective respirators. Future studies of the PAPR design may consider alternative or repeated time-lagged health assessments. Lastly, the study estimates were based on 8 repeated health measurements from 21 subjects. Larger studies are needed to confirm the robustness of associations found in this study.

4.6 CONCLUSION

The study tested the effectiveness of a commercial positive pressure respirator to reduce air pollution exposure and to improve cardiorespiratory functions in both laboratory tests and a real-world randomized double-blind crossover intervention trial. The positive pressure respirator performed well for particle removal. However, no robust association was found between wearing respirators for two hours in traffic and changes in cardiorespiratory functions. The study also suggested a modification effect of perceived exposure on the association between using respirator using and cardiorespiratory functions. Further studies are warranted to confirm the long-term benefit of using respirators in traffic.

Chapter 5. THE IMPACT OF THE BUILT ENVIRONMENT ON MULTI-MODAL COMMUTING AND POPULATION HEALTH IN CHENGDU, CHINA

5.1 ABSTRACT

Background: Urban residents use combinations of transportation modes in daily commute (multi-modal commuting). With changes of the commuting patterns and ongoing planning policies to promote sustainable development, more studies are needed to assess the health impacts of commuting. This study investigates the non-linear relationship between built environment variables and time spent in multi-modal transportation in Chengdu, China, and estimates the health impact of potential built environment changes on cardiovascular health attributable to air pollution and physical activity during multi-modal commuting.

Methods: A commute survey was designed to collect individual information and daily multi-modal commuting (mode used and time spent in each mode) among a convenience sample of adult working populations from selected workplaces in Chengdu, China. Built environment factors were extracted from OpenStreetMap and the Atlas of Urban Expansion with Geographic Information System (GIS) for both residential and work locations of respondents. Random forest models were developed to explore non-linear relationships between individual factors, built environment variables and multi-modal commuting. G-computation was employed to estimate the marginal effect of built environment factors important for urban planning policies in Chengdu, such as garden city and transit oriented development (TOD, easier access to public transit) on time spent in different transportation modes. Finally, as an example of using the modeling results to guide planning policies, a health impact assessment was performed to evaluate the impact of multi-modal commuting under potential built environment changes on cardiovascular diseases (CVD) mortality for employed urban residents in Chengdu.

Results: A total of 216 respondents completing the commute survey were included in the analyses. More than half of the respondents used multi-modal commuting during their daily home-work travels. Random forest models suggested that the body mass index was the most important individual factor associated with time spent in different transportation modes. Home-work distance was identified consistently as an important factor related to commuting time in all transportation mode models. The G-computation results indicated that potential changes in built environment variables related with garden city development might increase the time commuters spend in cycling and subway trips, while potential changes in built environment variables related with TOD might increase the time walking and cycling. Thresholds existed in all the associations between built environment factors and time in multi-modal commute. The health impact assessment showed that generally, garden city and TOD policies would be beneficial to cardiovascular health for residents' commuting. However, a longer home-work distance would lead to excess CVD mortality due to increased air pollution exposure and reduced physical activity in commutes.

Conclusion: Garden city and TOD planning policies have the potential to benefit population health for employed urban residents in Chengdu. However, these policies need to consider the job-housing mismatch in Chinese cities to reduce the commuting distance to avoid air pollution exposure and physically inactive travel modes.

Key words: random forest; G-computation; health impact assessment; multi-modal commuting; air pollution; physical activity

5.2 INTRODUCTION

Commuting patterns have been changing globally with the increasing number of mobility options in metropolitan areas. The emerging shared mobility services and app-based ridesplitting programs provide residents easy access to various commuting modes, like free-floating bikes and Uber/Lyft hailing services, for micro-mobility to medium- or long-distance travels. Compared to years ago, residents in modern cities are no longer constrained to a single commuting mode; instead, daily intra-urban trips may involve combinations of transportation modes (multi-modal commuting), including car, bus, subway, cycling, and walking. For example, it is not unusual to see people who get off a bus head to a nearby subway station on a shared bike.

With these emerging transportation modes, it is important to understand residents' behaviors with respect to their daily commuting modes. The link between the built environment and mode choices is not a new topic. Ewing and Cervero described the concept of "5 Ds", measuring the built environment that impact travel behaviors, including Density, Diversity, Design, Destination accessibility, and Distance to transit [191]. They found that generally, associations between automobile usage (vehicle miles traveled) and accessibility to destinations was the strongest, while public transportation (bus and train) had the strongest relationship with proximity to transit and street network design; non-motorized travel modes (walking and cycling) were mostly related to land-use diversity [191]. However, variations exist between regions, that the west coast of USA differs from the east coast regions and Asian cities differ from western cities. Recently, researchers have examined the non-linear relationship between built environment and travel behaviors. For example, studies have found the number of bus and metro stations were important factors to people's selection of public transportation [192,193]; population and employment density was the strongest predictor of the shared bike using [194]; ridesplitting ratios was mostly impacted by the distance to city center [195]. All these studies have found thresholds for the impact of built environment factors on travel behavior. For example, the metro ridership increased dramatically when the population density increased from 10 to 15 persons/acre, but the impact vanished when the population density was above 35 persons/acre in Washington Metropolitan Area [193].

However, none of these studies have explored the relationship between the built environment and multi-modal commuting. As treating all trips as single-mode ones, studies might misclassify the mode of a trip if it involves multiple transportation modes. Other studies might treat each mode-based component of trip as a stand-alone trip when they investigated how the 5 Ds might affect what's available as options for choices in different areas. Then, individuals chain together these choices in each trip section in a way that works best for them. Such studies might overlook important associations between different components of a trip. If treating components with different transportation modes between origins and destinations as a whole (*e.g.*, a multi-modal commuting between residential and work location which involves a bus trip, a subway trip and some walking), the time spent in one mode could potentially affect the time people spend in another mode. Therefore, it is valuable to investigate the relationship between the built environment and multi-modal commuting to avoid misclassification and missing important impacts between transportation modes.

Aside from the many emerging transportation mode choices, how to travel healthily is another topic intensely discussed in recent years. Developing cities that are healthy and sustainable are common goals shared by urban planners, environment scientists and public health professionals [89]. Policy makers are trying to guide individual travel behavior and in turn combat traffic congestion, lower air pollution levels, and mitigate adverse health impacts by modifying the built environment [196]. For example, active transportation and public transit has been promoted globally to increased people's physical activity and to reduce air pollution and greenhouse emissions from private motor vehicles. Also, choices among mobility options can potentially alter health determinants and outcomes by changing exposures to air pollution, noise, and other environmental stressors. While people increase their physical activity through walking and cycling, they may also be exposed to elevated air pollution concentrations, especially in highly polluted regions. Therefore, it is important to understand the trade-offs between the benefits of physical activity and the risks of air pollution exposure in transportation and to take health impacts into account in local transportation and urban planning policies.

This study aims to understand how the built environment and individual factors influence residents' multi-modal commuting, and the population health impact related to air pollution exposure and physical activity in daily commutes in a major Chinese city, Chengdu, in Sichuan Province. This study hypothesizes that the home-work distance, individual factors and built environment features surrounding residential and work locations impact the mode choices of commuters and the duration of the trip. Additionally, the duration of a mode-based component of the trip is dependent on the time spent in other mode-based components of the trip. While air pollution concentrations and physical activity levels vary by transportation modes, different durations by mode would result in variations of air pollution exposures and physical activity levels during daily commuting, which potentially impact the cardiovascular health. This study uses a random forest algorithm and mediation analysis to examine the non-linear associations of built environment and socio-demographic factors on time spent in different modes of transportations. The study also performs a health impact assessment to estimate the population potential health impacts related to air pollution exposure and physical activity during commuting for urban planning policies that alter different built environmental factors. This study adds to the limited evidence for the non-linear associations between the built environment and multi-modal commuting in China and guidance for healthy city development.

5.3 METHODS

5.3.1 Study Area

Chengdu is the economic and transportation center of southwest China. The city has implemented urban-rural equalized development (URED) since 2003 to mitigate the economic and life differences between urban and rural areas. After this urbanization, the built-up area of Chengdu doubled between 2010 and 2017 [105]. Along with this rapid growth in size, the population in the city increased more than 30% from 11.2 million in 2008 to 14.8 million in 2018 [105], and the car ownership in Chengdu increased considerably (car ownership rates of nearly 30 cars per 100 residents [105]) and is now second only to Beijing, China. To combat traffic congestion and achieve sustainable development, more recently, the city launched urban planning strategies, including transit-oriented development (TOD) and garden city development to further promote active and public transportation [197,198]. The garden city policy in Chengdu aims to build parks and the largest non-motorized transport system to connect with parks. The TOD aims to provide resident easy access to public transit and to reduce reliance on the private automobile. Currently, the city has a mature public transportation system with low ticket prices (1 RMB [around 0.14 USD] for 2 hours on bus regardless of transfers). In 2017, the bus route network was more than 10 times larger in size than in 2000, with more than 1.6 billion passenger trips taken. Additionally, a subway system started operating in 2010, and around 800 million passenger trips were taken in 2017 on the 179 km of subway routes [105]. Recently, shared bike programs have increased in popularity with more than 1.3 million shared bikes available in the city. Additionally, it is noteworthy that the city introduced a driving restriction policy in 2013 with the goal of reducing 20% of private automobile usage on roads every weekday. Private cars are divided into 5 groups by the last digit number of the license plate (1 and 6, 2 and 7, 3 and 8, 4 and 9, 5 and 0), and each group is forbidden on a designated weekday. With various modes of transportation available, the restricted car usage policy and on-going planning policies of TOD and garden city in Chengdu, residents have begun to use a mixture of transportation modes during their daily commutes. Buses, subways along with cars (including private cars, taxis and Didi [Chinese version of Uber]) are used in medium- and long-distance transportation, while biking and walking modes are used in micro-mobility to connect home/workplaces and bus/subway stations (access mode) [199,200].

5.3.2 Commute Survey and Sampling

A self-administered commute survey was developed to collect relevant information from respondents. The main question asked was transportation modes used and time spent in each mode during daily commutes. Respondents were allowed to input different combinations of modes for morning and afternoon commutes and were asked to provide all combinations used in their routine commutes. Other information collected including a) respondents’ home and workplace addresses, b) demographic information (birth date, gender, education, household income), c) self-reported height and weight, d) cigarette smoke exposures (first- and second-hand smoking), e) reasons for using those modes (open-ended questioning), f) mask wearing during commuting (never used, only when they feel sick, sometimes on polluted days, always on polluted days or always while commuting), and g) health status (including common chronic diseases, *e.g.*, chronic rhinitis, hypertension, diabetes).

Convenience sampling was employed at five different work locations to recruit volunteers between December 2018 and February 2019. The aims of the survey were first fully explained to the managers at different workplaces and a sample of the survey was provided for review. With consent from managers, a total of five workplaces were recruited into the study, including two local Center for Diseases Control and Prevention (CDC) offices (one in the city center and another one in a suburban area), a government department (public institute), a state-owned enterprise, and a private enterprise. Then, the questionnaires were distributed to employees at different work locations by the managers. This survey was designed as self-administered with detailed explanation for each question and was conducted anonymously. Volunteers who participated in the study were free to skip any of the questions when completing the survey. Completed surveys were collected two days later at the workplace by researchers. The protocol for the survey was approved by the Human Subjects Division of the University of Washington as well as the Sichuan Center for Diseases Control and Prevention. Informed consent was obtained from each volunteer who agreed to complete the survey.

5.3.3 Variables Extraction

The individual-level socio-demographic information was extracted from the completed commute surveys while the built environment variables related to the “5Ds” were obtained from OpenStreetMap (OSM) and the Atlas of Urban Expansion [201]. Variables extracted from OSM included traffic information (the number of bus and metro stations), road types (the length of cycleway, living street [street prioritized for pedestrians], pedestrian road [street for pedestrians only], motorway [a restricted access major divided highway], trunk road [the most important roads in a country's system second to motorways], and primary road [the next most important roads, often linking large towns]), and land-use information (the area of parks). All of these OSM variables were extracted using ArcGIS in buffers of 200 m, 500 m, 800 m, 1000 m and 2000 m around each respondent's home address and workplace. The Atlas of Urban Expansion classifies the land of cities based on images from Landsat satellites. All the pixels (30-by-30 meter resolution) of a city are classified in the atlas by human-assisted algorithms into urban built-up, suburban built-up, rural built-up, fringe open space, captured open space, rural open space, and water, where the fringe open space and captured open space make up the urbanized open space. The area of each type of land was calculated within 2000 m around a respondent's home and work location. Additionally, the "as the crow flies" spatial distance between home addresses and work locations was calculated for respondents.

5.3.4 Statistical Methods

5.3.4.1 Random Forest Modeling

To explore the relationship of built environment and individual factors on commuting duration for specific mode, a multivariate analysis modeling approach was employed. The modeling utilized the random forest method— a supervised learning algorithm based on bootstrapping and random feature selection. Random forest has the advantage of being robust to outliers and noise, skewness of data and not overfit (because of the Law of Large Numbers) [202]. Previous studies have successfully employed the random forest method to explore the non-linear relationship between built environment and travel mode choices [192,203] and found the modeling performance of random forest was among the best as compared to other machine learning algorithms [204].

Specifically, to explore the relationship of built environment and individual factors on multi-modal commuting, a total of five random forest models were built for the five modes of transportation (*i.e.*, walking, cycling, bus, subway and car trips). The response (*i.e.*, outcome or dependent) variable of each model was the time spent in a specific mode, with time spent in other modes, home-work distance, socio-demographics (*i.e.*, age, gender, education, household income), body mass index (BMI), and all of the extracted built environment factors as the independent variables. Out-of-bag (OOB) validation was used to measure the prediction error and to quantify the performance of random forest models (root mean square error [RMSE] and R^2). Iteration was used to tune the hyperparameters (number of trees grown, number of predictors sampled for splitting at each node, and the maximum number of nodes a tree can have) in random forest models and to identify models with the smallest OOB errors. Finally, the variable importance was extracted from the random forest models based on the percentage increase in mean square error (MSE) for excluding each of the variables.

5.3.4.2 G-computation

As a "black-box" model, it can be difficult to explain results of random forest models. G-computation was employed in this study to better understand the impact of the associations of different variables and time spent in each transportation mode. G-computation was introduced in 1986 to estimate causal effects of time-varying exposures [205]. Epidemiological studies have been using G-computation as a causal inference technique in the field of public health [206-209]. In this study, G-computation was used to estimate the marginal effects of important variables in random forest models on multi-modal commuting. G-computation answers the "what if" question; that is, if one variable was at level *x* for the population while all other conditions of the individuals were kept the same, how much time might people spend in a commuting mode? For example, if there were 3 bus stations within 500 m of all respondents' home addresses and all other conditions (*e.g.,* home-work distances, major road length around home addresses, and household income levels) of respondents were kept the same, how much time would respondents spend on buses during their daily commute? Using G-computation to estimate the counterfactual conditions is based upon following assumptions: 1) counterfactual consistency (a person's potential outcome under a hypothetical condition is precisely the outcome experienced by that person), 2) positivity (there is nonzero possibility for an individual to receive all values of the exposure variable), and 3) exchangeability (potential outcomes under exposures are independent of actual exposures). Important variables in the random forest model, including socio-demographics, BMI and built environment factors related to the ongoing planning policies of garden city and TOD in Chengdu were analyzed.

This study implemented G-computation following a three-step method after the random forest modelling [210,211]:

1. Two identical copies of the dataset were created, where one dataset was the control and the other one was the intervention (the simulation group to create "what if" scenarios). For the control group, important variables identified in random forest models were set to the lowest observed values (as the baseline scenario); while the important variables in the intervention group were assigned different values in the range of observation (hypothetical intervention values to create "what if" scenarios). The baseline and hypothetical intervention dataset would be

used to compare the counterfactual scenarios that if all individuals in the sampled cohort were assigned to the baseline, or all individuals were assigned the intervention

2. The trained random forest model was used to predict outcomes for both the control dataset and the intervention dataset with different assigned values to predict the time spent in a commuting mode under the control (baseline) and each "what if" scenario. To obtain the estimates and corresponding 95% confidence intervals (95% CIs), 100 pairs from the control and intervention dataset were sampled at random in a total of 300 bootstraps. The mean of the 300 point estimates was the robust estimate of the time spent in a mode under each scenario, and the 2.5^{th} and 97.5^{th} percentiles of the estimates approximate the 95% CI on the estimate.

3. Then the marginal effect of the intervention (changes in built environment or socio-demographic factors) was estimated by the difference on time spent in a mode between the paired outcomes (i.e., the difference in time spent in a mode for the i^{th} individual with or without the intervention).

5.3.5 Health Impact Assessment

While the results produced by the G-computation approach provided direct estimate of changes in time spent in physically active travel modes (*e.g.*, walking and cycling), which have health implications, further health impacts can be imputed. A demonstration study of applying the G-computation results to guide healthy and sustainable city development, the study estimated the population health impact of these intervention scenarios (changes in built environment) among the employed urban population living in the city of Chengdu under the assumptions that the sampled population might be representative of the larger working population of the city, and also that the surveyed behaviors might be indicative of long-term commuter behaviors. Health impact assessment was performed for exposures to particulate matter with a diameter of 2.5μm or less ($PM_{2.5}$) and physical activity in multi-modal transportation under these potential intervention scenarios (changes in built environment). This method had been used in previous studies to estimate the health impact of switching from car trips to active transport in Europe [212-214]. The changes in cardiovascular diseases (CVD) mortality attributable to long-term $PM_{2.5}$ exposure and physical activity levels in multi-modal commute under different built environment were calculated following the following equations:

$$AF = 1 - e^{-\beta\Delta c} \qquad eq\ 8$$

$$\Delta Y = AF \times Y_0 \times Pop \qquad eq\ 9$$

where AF was the attributable fraction, β was the cause-specific coefficient of the concentration-response functions (CRF) for $PM_{2.5}$ or physical activity, Δc was the changes in annual $PM_{2.5}$ exposure or physical activity in multi-modal commuting under intervention scenarios, ΔY was the estimated health impact of $PM_{2.5}$ or physical activity levels under intervention scenarios, Y_0 was the baseline CVD mortality, and Pop is the exposed population (employed urban population in Chengdu).

The coefficient of CRF for long-term $PM_{2.5}$ exposure and CVD mortality was adopted from the most recent and largest cohort study in China [215]. This cohort study estimated the $PM_{2.5}$ concentrations from 1990-2005 in China, and estimated the associations between long-term $PM_{2.5}$ exposure and cause-specific mortality among men 40 years old or older. With exposure from 2000-2005, it was estimated that each 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentrations contributed to an 8% (95% CI: 7%, 9%) increase in CVD mortality. This estimate was comparable to estimates from cohort studies in other regions, and had been used in previous health impact assessments [216,217]. The coefficient of CRF for physical activity was based on another cohort study which reported national dose-response association between self-reported physical activity and CVD deaths in China. The study indicated that each 4 elevated metabolic equivalent of task hours per day (MET-h/d, approximately cycling or brisk walking 1 hour/day) was associated with 12% (95% CI: 10%, 14%) decreased CVD mortality [130].

Table 15. Parameters used in health impact assessment.

Parameters		values
$PM_{2.5}$ levels (μg/m^3) [218]	walking & cycling	51.7
	bus	43.6
	subway	39.8
	car	17.3
β	$PM_{2.5}$ (per μg/m^3) [215]	8% (95% CI: 7, 9)
	physical activity (per 4 MET-h/d) [130]	12% (95% CI: 10, 14)
CVD mortality rate (death/100,000 persons) [105]		227.91
Exposed population (person) [105]		5,935,521

The change in $PM_{2.5}$ exposure during daily multi-modal commuting between the intervention and control scenario was calculated as:

$$\Delta C_d = \frac{\sum_{i=0}^{\Delta t} C_{ij}}{24\ hours} \qquad eq\ 10$$

$$\Delta C = \frac{\Delta C_d \times 260 \times 2}{365} \qquad eq\ 11$$

where ΔC_d was the changes in daily $PM_{2.5}$ exposure during multi-modal commuting, C was the average $PM_{2.5}$ concentrations during transportation mode j at time i, Δt was the changes in traveling time spent in mode j in an intervention scenario compared to the control (baseline) scenario, $\Delta C$was the changes in annual $PM_{2.5}$. The average $PM_{2.5}$ concentration during different transportation modes were from a previously published empirical study in Chengdu

[218], with the assumption that air pollution exposures during walking was similar to the exposure levels in cycling. After the calculation of daily $PM_{2.5}$ exposure changes, the changes in annual $PM_{2.5}$ exposure during daily commute was calculated with the assumption that residents commuted twice a day and five days a week.

The changes in daily physical activity levels between the intervention and control scenario was calculated in MET-h/d based on changes in time spent in walking and cycling. Then. the *eq* 11 was used to calculate the changes in annual physical activity levels during daily commute.

The baseline CVD mortality and exposed population (the employed urban population in this assessment) were from Sichuan Health Statistical Yearbook (2020) [105].

All statistical analyses were conducted in R 4.0.3 (http://www.R-project.org/) (R Foundation for Statistical Computing, Vienna, Austria) and RStudio® (Version 1.1.456). The seed value was set to 101 in R in every random number generation (*i.e.*, in Random forest modeling and G-computation) to make the data analysis reproducible.

5.4 RESULTS

5.4.1 Descriptive analysis

A total of 218 respondents completed the commute survey. Two respondents whose home addresses were outside of the Chengdu metropolitan area were excluded in the analysis. The map of Chengdu city, home addresses and work locations of the 216 respondents included in the study are shown in Figure 16. Most of the respondents lived in the central city of Chengdu, and all of the respondents lived in areas classed as urbanized built-up areas based on the Atlas of Urban Expansion.

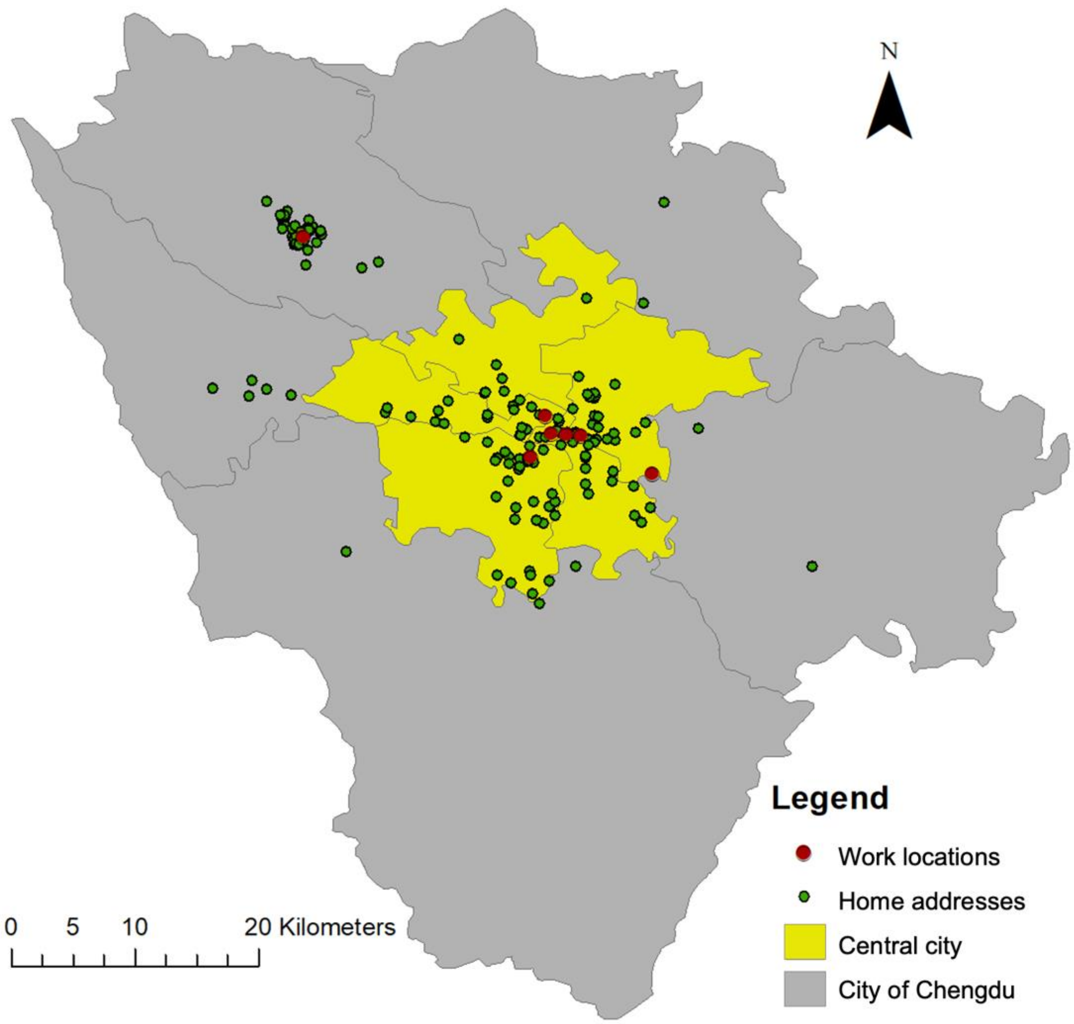

Figure 16. Respondent home addresses and work locations.

Basic information for the 216 respondents is summarized by daily commute mode in Table 16. The commuting modes were not mutually exclusive with each other, as respondents using multi-modal commuting were grouped into all mode groups according to the transportation modes they used. Walking was the most common commuting mode among the respondents in this study.

More than 60% of the respondents walked in their daily commute, and they tended to live closer to their workplaces compared to others. Of the 34 respondents in the car mode group, 15 used shared car services (Didi [n = 4] and taxis [n = 11]). Respondents riding subways was the smallest group (less than 15% of the study population), and on average, they lived farther from their workplaces. More than half of the trips were multi-modal commuting, especially for trips involving buses and subways. Walking with riding buses or subways was the most common combination in multi-modal commuting, while respondents using cars were least involved in multi-modal commuting.

Compared to the male/female ratio of the study population, fewer male respondents walked or used the subway in their daily commutes. Most respondents had annual household incomes between 51,000 and 100,000 RMB, which was slightly higher than the average household income for urban residents in Chengdu (45,181 RMB in 2017) [105]. The distribution of education levels was similar among different commuting groups, with more than half of the respondents in each mode group holding at least undergraduate degrees.

Table 16. Summary of the total 216 subjects recruited.

	Walking	Cycling	Bus	Subway	Car	Total
N	135 (62.5)	43 (19.9)	75 (34.7)	32 (14.8)	37 (17.1)	216 (100.0)
Age (yr) *	36.9 (10.2)	36.8 (10.2)	40.4 (10.4)	36.6 (8.9)	41.5 (9.2)	38.6 (10.3)
Home-work distance (km) *#	3.2 (4.1)	5.2 (6.5)	6.5 (5.7)	11.1 (6.0)	5.8 (4.4)	4.4 (5.3)
BMI (kg/m^2) *	21.7 (3.1)	22.3 (2.9)	22.8 (3.1)	21.6 (2.8)	22.3 (2.6)	22.0 (3.0)
Gender						
Male	43 (31.9)	17 (39.5)	31 (41.3)	9 (28.1)	15 (40.5)	78 (36.1)
Female	92 (68.1)	26 (60.5)	44 (58.7)	23 (71.9)	22 (59.5)	138 (63.9)
Annual household income (RMB)						
< 50k (level 1)	26 (19.3)	7 (16.3)	14 (18.7)	9 (28.1)	4 (10.8)	43 (19.9)
51k - 100k (level 2)	54 (40.0)	22 (51.2)	37 (49.3)	11 (34.4)	15 (40.5)	88 (40.7)
101k - 150k (level 3)	23 (17.0)	8 (18.6)	11 (14.7)	6 (18.8)	7 (18.9)	35 (16.2)
151k - 200k (level 4)	15 (11.1)	5 (11.6)	8 (10.7)	2 (6.3)	4 (10.8)	24 (11.1)
201k - 300k (level 5)	7 (5.2)	0 (0.0)	1 (1.3)	2 (6.3)	3 (8.1)	9 (4.2)
> 300k (level 6)	4 (3.0)	0 (0.0)	0 (0.0)	2 (6.3)	3 (8.1)	5 (2.3)
NA	6 (4.4)	1 (2.3)	4 (5.3)	0 (0.0)	1 (2.7)	12 (5.6)
Education						
High-school degree or below	9 (6.7)	1 (2.3)	7 (9.3)	0 (0.0)	2 (5.4)	16 (7.4)
College degree	36 (26.7)	12 (27.9)	20 (26.7)	10 (31.3)	13 (35.1)	69 (31.9)
Undergraduate degree	57 (42.2)	18 (41.9)	28 (37.3)	13 (40.6)	11 (29.7)	84 (38.9)
Graduate degree or above	33 (24.4)	12 (27.9)	20 (26.7)	9 (28.1)	11 (29.7)	47 (21.8)
Other modes used						
walking	NA	13 (30.2)	32 (42.7)	13 (40.6)	4 (10.8)	NA
cycling	13 (9.6)	NA	4 (5.3)	3 (9.4)	1 (2.7)	NA
bus	32 (23.7)	4 (9.3)	NA	5 (15.6)	0	NA
subway	13 (9.6)	3 (7.0)	5 (6.7)	NA	1 (2.7)	NA
car	4 (3.0)	1 (2.3)	0 (0.0)	1 (3.1)	NA	NA

* Continuous variables are summarized as mean (standard deviation); categorical variables are summarized as count (percentage).
# Distance is "as the crow flies" distance between workplaces and home addresses.

5.4.2 Random Forest Results

While some of the respondents used different combinations of commuting modes in morning and afternoon commutes or on different days of a week, a total of 317 trips with different combinations of commuting modes from the respondents were analyzed using the random forest models. The hyperparameters and performance of the five random forest models for each transportation mode are summarized in Table17. All the models had moderate to good prediction performance, with R^2 ranging from 0.52 (model for time spent in subway trips) to 0.90 (model for time spent in car trips).

Table 17. The hyperparameters and performance of random forest models.

Model	number of trees	number of predictors sampled for splitting at each node	maximum number of nodes	RMSE	R^2
Walking	500	255	253	5.66	0.73
Cycling	500	296	285	4.09	0.78
Bus	500	217	235	8.94	0.84
Subway	500	271	269	6.35	0.52
Car	500	114	269	4.71	0.90

The 20 most important variables are summarized in Figure 17 for each random forest model. The variables at the top of each figure panel were the most important ones as their inclusion in the random forest models reduced the prediction errors the most. The distance between a respondent home address and the workplace, BMI, and age were important variables related to commuting duration in all the models. Built environment factors around work locations were not identified as important variables for predicting multi-modal commuting in the random forest models. The only one built environment factor around the workplace (the trunk road length within 2000 m around work locations) that was ranked within the top 20 most important was useful in predicting time spent in bus trips. Additionally, most of the top ranked important variables were built environment characteristics with large buffer sizes (1000 m and 2000 m) around the residential location.

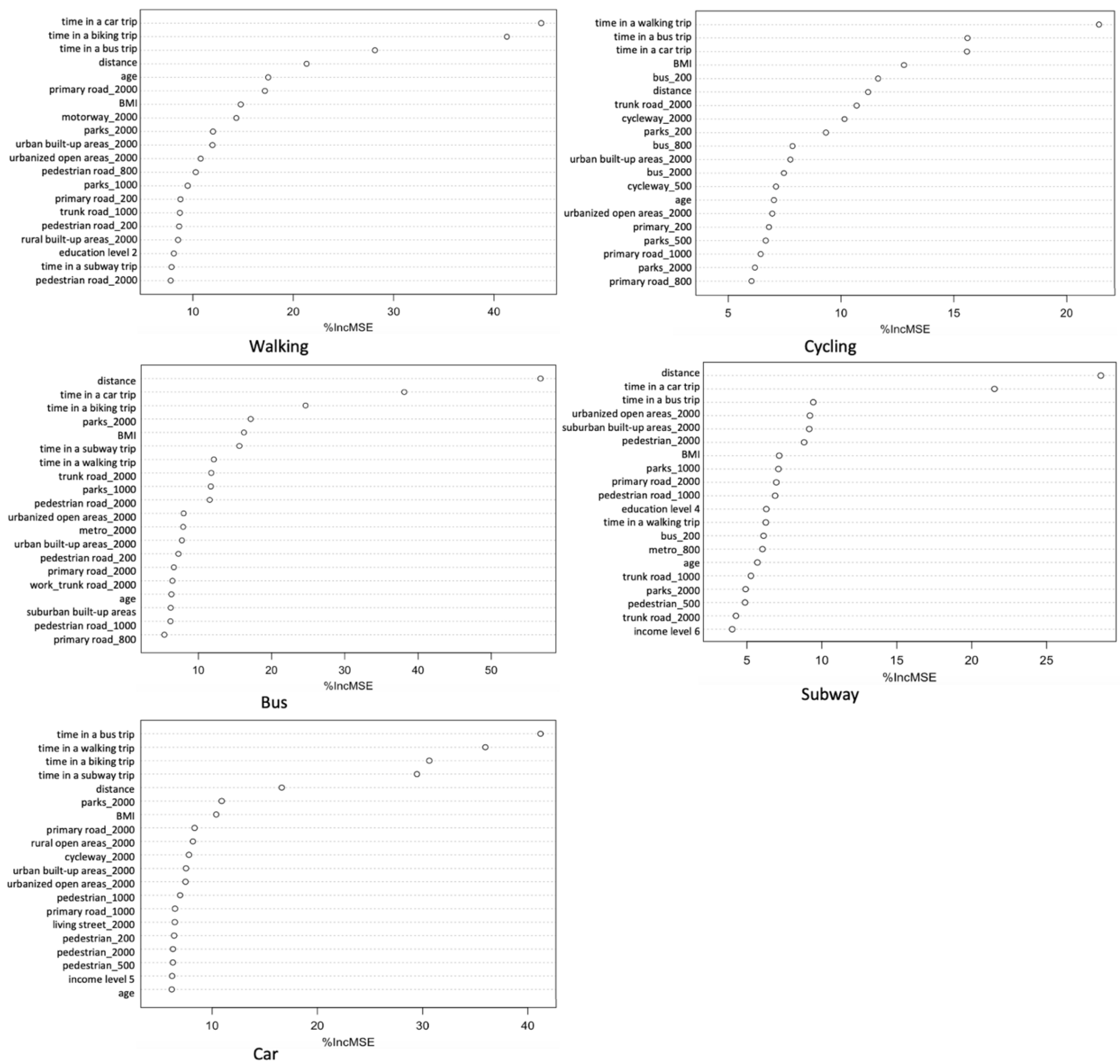

Figure 17. Variable importance in random forest models to predict commuting duration in a mode. The x-axis is the percentage increase in mean square error (MSE) for excluding each of the variables. The labels for built environment variables include the buffer size in meters in their name, and those based on workplace location buffers are preceded by the word "work" in the variables name.

5.4.3 G-computation Results

The G-computation was conducted for selected important variables in the random forest models, including the two most important individual factors (i.e., BMI and age), distance, and top ranked built environmental factors that were related with the ongoing planning policies of garden city and TOD in Chengdu. It was theorized that garden city development would potentially shift values of some variables found to be important in thee commuting models, including urbanized open areas (publicly accessible open places from human activity and enjoyment) within 2000 m, pedestrian road length within 2000 m, and cycleway length within 2000 m around respondents' home. Similarly, TOD theoretically might shift values for the number of metro stations within 800 m and the number of bus stations within 200 m around respondents' home. The marginal effects of these selected variables on time spent in each transportation mode is plotted in Figure 18, where the X-axis shows the "what if" conditions (*i.e.*, varying values of the variable of interest) while the Y-axis is the time spent in different commuting modes.

In general, respondents with larger BMI tended to spend more time in active transport (*i.e.*, walking and cycling) and bus trips, and less time in car trips. However, there appeared to be thresholds and non-linear relationships for these effects. For example, BMI showed negative association with time in car trips when respondents' BMIs were less than 20kg/m^2; the impact of BMI on time in cycling only existed when BMI were larger than 20kg/m^2. Age and time spent in active transport showed "U" shape relationships, such that respondents in their 20s and aged between 55-60 years tended to spend more time walking and cycling during daily commute.

Respondents living farther from where they worked tended to spend more time in inactive transportation modes, especially in bus trips. However, the time spent in subway trips did not change with the distance when respondents lived within 5 km around work locations. Time spent in walking decreased as the home-work distance increased, but stabilized when the distance was larger than 5 km. Distance also did not impact the time respondents spent in cycling.

Generally, the garden city related built environment factors were positively associated with time spent in cycling and subway trips. The urbanized open areas within 2000 m around respondents' residential locations impacted the time commuters spent in subway trips most, but the impact was obvious only when the open area was above 4,000,000 m^2. The cycleway length was positively associated with time spent in cycling and car trips when the cycleway length was less than 1000 m and 3000 m, respectively. G-computation results suggested that longer pedestrian roads within 2 km around the home led to more time in cycling and bus trips, but less time in subway trips. However, the time in bus trips no longer increased when the length of the pedestrian road was larger than 30,000 m, and the time in subway trips did not decrease when the pedestrian road was longer than 10,000 m within 2 km around home.

The TOD related built environment factors were associated with time spent in active transport, but not other transportation modes. When the number of metro stations within 800 around home was larger than 2, people tended to walk more as the number of metro stations increased. The number of bus stations within 200 m around home was associated with more time in cycling, and the impact was stronger when the bus station number was larger than 3.

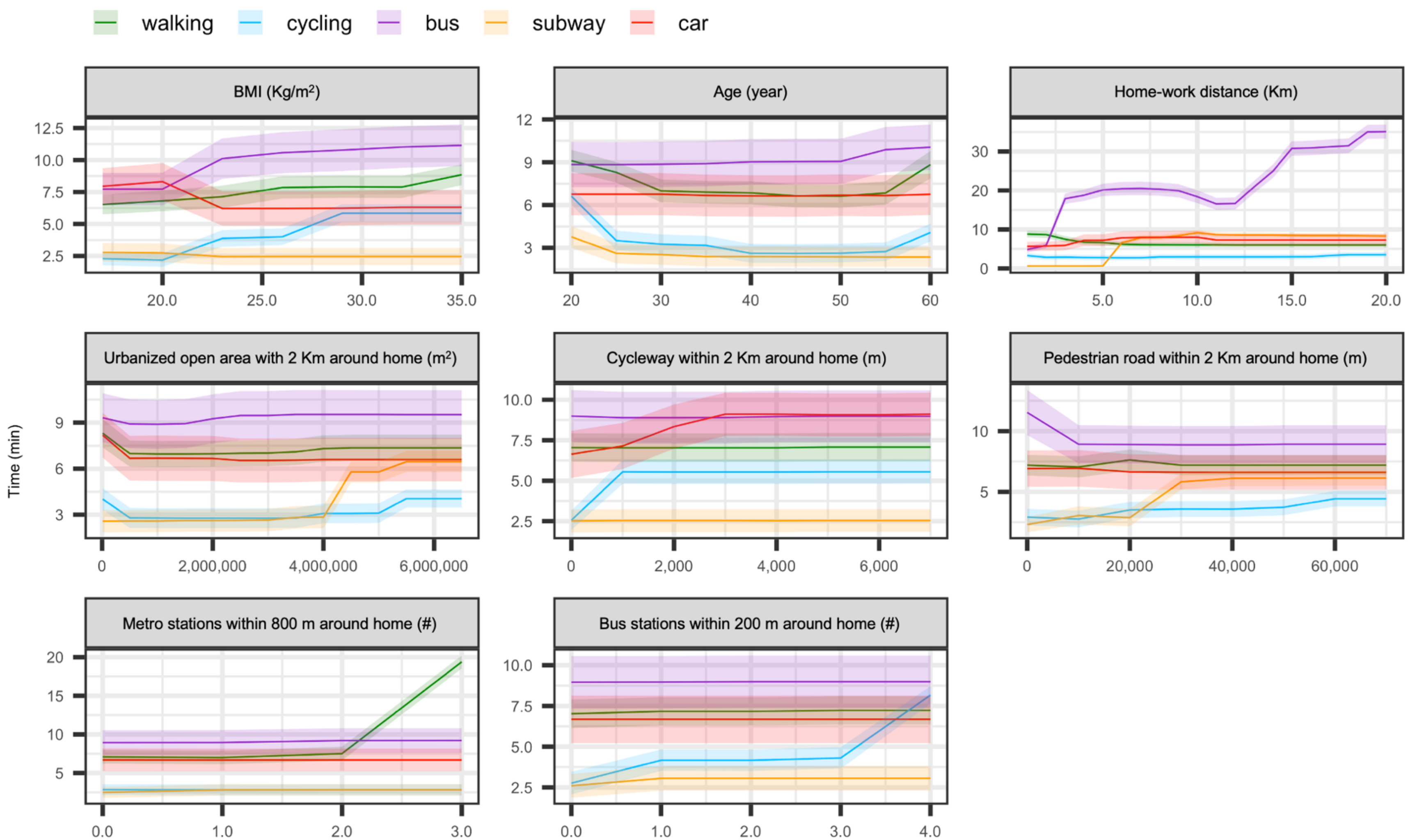

Figure 18. Time spent in different transportation modes with changes in variables of interest. Shaded areas correspond to 95% confidence intervals.

5.4.4 Health impact assessment

The changes of CVD mortality attributable to long-term $PM_{2.5}$ exposure and physical activity levels during daily commute for the 5,935,521 employed urban residents living in Chengdu are shown in Figure 19. The red line shows the increased CVD mortality attributable to $PM_{2.5}$ exposure during daily commute— the red line above the red dashed line ($y = 0$) means increased CVD mortality due to increased exposure to $PM_{2.5}$, and the red line below $y=0$ means decreased CVD mortality attributable to reduced exposure to $PM_{2.5}$ in commutes. The green line shows the reduced CVD mortality attributable to physical activity during daily commute—the green line above the red dashed line ($y = 0$) means reduced CVD mortality attributable to increased physical activity, and the green line below $y=0$ means increased CVD mortality due to decreased physical activity in commutes. Therefore, scenarios with higher green line and lower red line are better for population health.

In general, the home-work distance had the strongest impact on population health as compared to other factors. Increased commuting distance would lead to increased air pollution exposures and reduced physical activity levels during daily commutes. The joint adverse impact of these two factors increased more intensively when the home-work distance was larger than 12 km.

For built environment factors related to the planning policy of garden city, increasing CVD mortality was attributable to decreased physical activity levels during daily commute when the urbanized open area around residents' homes increased. However, the benefit of physical activity outweighed the adverse impact of air pollution exposure during transportation when the length of cycleway around people's home increased, especially when the length of cycleway was above 1 km around home. Similarly, longer pedestrian roads around the home would be beneficial to cardiovascular health, but this advantage was more obvious when the pedestrian road length was shorter than 30 km.

With respect to TOD planning policies, having more metro stations and bus stations around home would both benefit the cardiovascular health of residents during commuting. The benefit of increased bus stations was observed across the entire range considered (0 to 4 stations within 200 m of the home). However, the benefit of an increased number of metro stations only existed when more than 2 metro stations were within 800 m around people's residential locations.

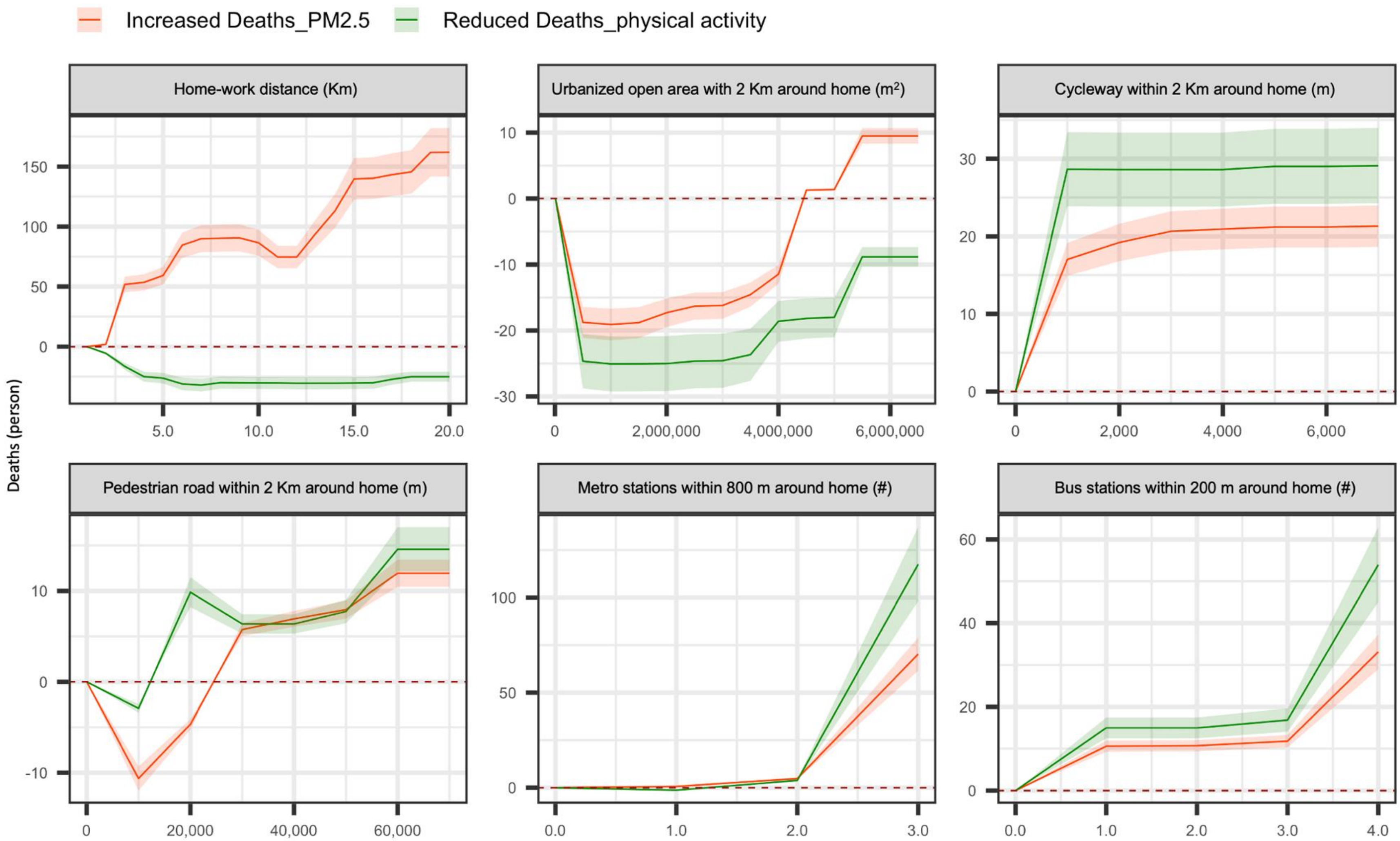

Figure 19. Changes in CVD mortality attributable to PM2.5 and physical activity during daily commute along changes in built environment factors for the employed urban residents living in Chengdu.

5.5 DISCUSSION

With emerging commute choices in the urban area, residents in China increasingly use combinations of transportation modes during daily commute. This study explored the non-linear association of different individual factors, home-work distance, and built environment factors on multi-modal commuting based on a self-administered commute survey in Chengdu, China. Random forest modeling and G-computation were employed to identify key factors that impact multi-modal commuting by estimating the marginal effect of selected built environment factors on time spent in different transportation modes. Age and BMI were important individual-level factors that impacted multi-modal commuting. Other important factors identified included home-work distance and many built environment factors directly related to the ongoing planning policies in Chengdu (*i.e.*, garden city and TOD). The study also performed health impact assessment to estimate the impact of identified important built environment factors on CVD mortality that were attributable to different $PM_{2.5}$ and physical activity levels during multi-modal commuting. Generally, longer home-work distance was found to contribute to increased CVD mortality, and changes in some variables related to planning policy of garden city and TOD might be beneficial to the cardiovascular health of residents in Chengdu.

This study found more than half of the commuting trips of the study population were multi-modal trips. Although the relationship between the built environment and commuting mode choice is not a new topic, limited evidence is available for multi-modal transportation, especially for Chengdu. The current study explored different built-environment factors around both origins and destination to investigate their impacts on multi-modal commuting. The built environment around commuters' homes was identified as more important for influencing multi-modal commuting than the built environment around work locations. Although studies in developed countries generally found built environment at the work locations were more influential than built environment characteristics around home locations, this results is consistent with findings from a previous study in Shanghai [219]. This might be explained by two reasons. First, the residential location choice in Chinese cities might highly correlated with built environment characteristics, as that transportation facilities at residential locations are important factors for residents to select their home addresses [219]. Second, as most sampled workplaces in this study are located close to the city center with various mobility options, it is possible that the commuting choices are limited by options available at home locations instead of options at workplaces. Additionally, while less attention was given to geographic scale selection by transportation research and few studies examining scale variation [220], this study investigated the impact of built environment with sliding geographic scales. This study found most of the top ranked important variables were built environment characteristics with large buffer sizes (*e.g.*, 1000 m and 2000 m) around commuters' homes. This indicated that the multi-modal commuting of residents in Chengdu might be impacted more by the built environment in a relatively large spatial extents (e.g., neighborhood level and bikeable distances) around their home than micro-scale characteristics (e.g., street block level and short walking distances). This result is consistent with previous studies showing positive relationships of land use diversity on walking and bicycling when calculated at larger spatial extents [221] and significant associations between walking/cycling and population density at large buffer sizes (1250 m) [222,223]. Sliding geographic scales improves the fixed scaled delineations of the neighborhood concept because areal buffers helps explain the built environment aspects most likely to affect travel decisions, and place an individual at the center of a neighborhood, which avoids statistical biases linked to placement near another spatial unit [220].

The impact of several individual factors, including age, gender, education level, household income and BMI were explored in the study. Many studies investigated the relationship between age and travel behavior, and concluded that older adults drove more than younger adults because older people tended to own more cars [224,225]. However, this study found that the time spent in car trips was insensitive to age. While Chengdu has very high car ownership, it is possible that there is no significant difference on car ownership between age groups. The BMI was identified as the most important individual factor to impact the time commuters spent in transportation modes. Commuters with larger BMI tended to spend more time in walking, cycling, and bus trips, but spent less time in car trips when the BMI was above 20 kg/m^2. While previous studies found negative associations between the frequency of using active transport and BMI [226,227], this study reported positive associations between the time spent in active transport and BMI. It is possible that respondents of this study (many CDC employees) are health-conscious commuters, so that respondents with larger BMI intend to travel healthier by walking and cycling and driving less in daily commute.

The distance between home and workplace was identified as a consistently important variable that impacts the time spent in different modes. Based on the G-computation, more time was spent in bus or subway trips as the home-work distance increased, but the impact of distance on subway trips only existed when the home-work distance was between 5 km and 7 km. This suggests that the subway may be mainly used for medium-distance travel: commuters rarely took subways when they live very close to work locations (< 5 km), and they used buses instead of subway as the main mode of transportation when they live farther away from the work locations (> 10 km). This may due to the lack of accessibility to subway stations when commuters live far away, as well as the much higher price of taking subways than taking buses for long-distance tips in Chengdu (2-10 RMB of a subway ticket depending on distance vs. 1 RMB of a bus ticket for 2 hours traveling regardless of transfers). In addition, this study found commuters riding cars, walking or cycling were less sensitive to changes in home-work distance. However, previous studies in Japan and western countries found that people living closer to workplaces or schools were more likely to walk or bike compared to individuals who lived further away [94,228]. This study found walking and cycling were mostly used along with bus and subway trips, suggesting that walking and cycling might be used mainly as access modes in Chengdu. That is, commuters walked or cycled to connect different stops along the way between home and workplace, instead of using walking and cycling as the single sole mode to connect home and workplace. Thus, distance might not be a strong determinant for time spent in walking and cycling trips in Chengdu.

The impact of a selection of important built environment factors related with the ongoing planning policy of garden city and TOD in Chengdu on time in multi-modal commuting were estimated, including the urbanized open area, cycleway length and pedestrian road length within 2 km around home, and the number of metro station within 800 m and bus station within 200 m around home. Thresholds existed for all these associations, which were consistent with other studies examining non-linear impacts of the built environment on travel behaviors [193-195,204]. For example, commuters living in areas with no urbanized open area or with more than

5,000,000m^2 of urbanized open area within 2 km around home tended to spend more time cycling compared to commuters living in other areas. Areas with no urbanized open area might represent the old central city of Chengdu where the workplaces, bus stations or subway stations are in close proximity, which encourages cycling among residents living there [229]. For home locations with many urbanized open areas around, the green infrastructure (*e.g.*, bike path, trial) in these open area might make cycling more safe and attractive, and contribute to longer cycling trips in daily commutes [230]. The study also suggested that commuters tended to spend more time cycling if they lived at locations with cycleways and pedestrian roads around. This finding is consistent with results from previous studies [231,232]. However, longer cycleway length within 2 km around home was estimated to increase time spent in car trips. It is possible that increased length of cycleways around home may lead to detour and longer commuting time when driving. Similarly, thresholds presented between the number of metro stations or bus stations and time spent in active transportation. These positive associations became stronger when having more metro and bus stations around home.

Planning policies that encourage active and public transportation have been promoted globally to increase the physical activity levels of residents. Many studies have reported higher air pollution exposure during active transportation than other modes [37,38,40]. For example, Chapter 2 of this dissertation found cycling trips had the highest $PM_{2.5}$ concentrations (51.7 μg/m^3) as compared to other modes in Chengdu; instead, car trips were the cleanest mode (17.3 μg/m^3, Table 15). However, the risk of air pollution exposure during transportation are usually overlooked in urban and transportation planning. Thus, it is important to consider the joint effects of air pollution and physical activity during transportation. As an example, this study performed a health impact assessment on changes in CVD mortality attributable to both air pollution exposures and physical activity during transportation with potential built environment changes in Chengdu. Results indicated that longer commute and increased urbanized open areas within 2 km around home would lead to increased CVD mortality among employed urban residents in Chengdu, while increased cycleway and pedestrian roads within 2 km around home, and increased metro stations with 800 m and bus stations within 200 m around home would contribute to decreased CVD deaths. Similarly, thresholds existed in the health impact assessment. While increased home-work distance would consistently lead to increased CVD mortality, the adverse joint effects of air pollution exposure and physical activity would be more intense when the distance was above 12 km. Chinese cities used to be bonded to jobs located together within socialist *danwei* (work unit) compounds. However, along with the relocation of industries out of central cities, the urban transportation network expansion, and the development of new residential compounds on the outskirt of cities, the job-housing relationship has transformed from the "spatial bond" to "spatial mismatch" since 2000 [233,234]. Such spatial mismatch has led to increased commuting distance and the need for motorized travel. Therefore, future planning policies in China, such as the "new *danwei*" framework for spatial mismatch rectification and multifunctional spatial development [235], may be needed to address the job-housing imbalance, to reduce travel demand, and to promote healthy development.

While this study estimated increased cycleway, pedestrian roads, metro and bus stations would contribute to decreased CVD mortality, more urbanized open areas within 2 km around home was estimated to increase CVD mortality. The estimated impact of urbanized open areas on CVD mortality was relatively small as compared to the impact of other built environment factors.

Importantly, the health impact assessment assumed unchanged ambient air pollution concentrations with the change of built environment. While residents were estimated to spend more time in active and public transportation under the garden city and TOD planning policies, the ambient air pollution levels might decrease under these scenarios due to reduced air pollution emission from private auto vehicles. Therefore, the health impact assessment might have overestimated the adverse effect of air pollution exposures in scenarios of garden city and TOD (*e.g.*, increasing urbanized open areas around residents' home). Additionally, the study only assessed the impact of physical activity in transportation to work but not activity related to recreational or non-work travels. Different from work related travel, which might be driven heavily by time and cost, non-work travel might be more influenced by factors including getting exercise, seeing nature, and visiting built environment amenities (*e.g.*, restaurants, grocery stores). While urban open space has been related with increased recreational physical activity [236-238], the benefit of increased physical activity might be underestimated in the health impact assessment, especially for the scenario of increasing urbanized open areas around residents' residential locations.

This study is the first to examine the non-linear relationship between built environment factors and multi-modal commuting, and the estimated changes in CVD mortality attributable to potential built environment changes on commuting behavior in Chengdu. The study contains several limitations. First, the analysis was based on a total of 317 trips from only 216 respondents of a commute survey in Chengdu. Although these respondents were from different employment sectors, it is possible that selection bias existed, which limits the generalizability of this study to the larger population in Chengdu, China. Future studies with larger sample size are needed to provide empirical evidence about the impact of built environment on mobility behavior and population health. Second, the analyses did not consider the hierarchical structure of the associations between built environment factors and commuting mode choices. For example, it may be the home-work distance determines the primary mode of the commute and the surrounding built environment features impact the choice of access mode. Further studies are needed to better understand the structure of the associations. Third, without evidence on the dose-response relationship between $PM_{2.5}$, physical activity and CVD mortality for the employed urban residents in Chengdu specifically, this study employed CRFs for the general population across China in the health impact assessment. It is possible that the sample population in this study differs from the population of the CRF (*e.g.*, the CRF for $PM_{2.5}$ was based on males in China only). However, using general CRFs are likely appropriate since they are based on evidence from studies with larger groups of population, which would reduce the uncertainty in the estimates. Fourth, the Atlas of Urban Expansion used in the study was based on satellite images in 2009 that the land use information in the study might be outdated. However, all the respondents lived in the urban built-up areas classified by the Atlas of Urban Expansion in 2009. As the urbanization process is irreversible, using the Atlas of Urban Expansion would be acceptable. Lastly, OSM was used to extract most built environment variables in the study. Because OSM is crowd-sourced data, the map might be incomplete for certain information. However, randomly selected locations from the OSM layers were compared to another data source, Baidu map street views. Highly accurate features with agreement larger than 98% were included while incomplete variables (*e.g.*, crossing, parking lot) were excluded in the analysis.

5.6 CONCLUSION

This study found that home-work distance was the most important predictor for time spent in multi-modal commuting in general for Chengdu. However, time spent in walking or cycling were insensitive to commuting distance, which may because active transport is mainly used as the access mode in multi-modal commuting in the city. The health impact assessment suggested the policies of garden city and TOD would be beneficial to the cardiovascular health of employed urban resident in Chengdu, as the benefit of physical activity outweighed the adverse effects of air pollution exposures in transportation. However, these policies need to consider the job-housing mismatch in Chinese cities to reduce the commuting distance to avoid air pollution exposure and physically inactive travel modes.

Chapter 6. CONCLUSIONS

This dissertation employed various exposure assessment and environment epidemiology methods and approaches, including randomized double-blind crossover intervention study design, survey design, use of portable sensors and GIS analysis to investigate the interaction between human and the urban environment. Specifically, the dissertation quantified individual exposures and health after travelling in different transportation modes in a rapidly developing city of a low and middle-income country (LMIC), which is confronting a confluence of issues related to growing urban populations, poor environmental quality, and challenges of sustainable transportation.

Chapter 1 reviewed the existing literature on TRAP exposures in different travel modes and crossover studies investigating the health effects of TRAP exposures. Generally, little evidence was available in China, which is one of the most polluted regions globally. While most studies characterized the variation of air pollution in different travel modes, noise exposures in traffic were not well studied. Also, previous studies reported inconsistent results, which may be due to a lack of consideration about TRAP variations by neighborhood and season. A total of 32 crossover studies investigating the health impacts of TRAP exposure were reviewed following the PRISMA guidelines. These studies reported very different results. Some main gaps found from previous studies included: 1) the role of physical activity during traveling were not well studied, 2) studies inadequately accounted for potential confounding factors (*e.g.*, psychological stress, noise and meteorological factors), 3) most studies with the intervention design were not able to blind subjects, which may lead to biased estimates due to the placebo effect, and 4) most studies measured PM exposures only and overlooked the impact of gaseous pollutants.

Chapter 2 tested the hypothesis that TRAP exposures varied by transportation mode. The goal of this chapter was to characterize variations in personal TRAP and noise exposure experienced in different transportation modes, neighborhoods, and seasons in Chengdu. Findings from Chapter 2 showed exposure disparities between transportation modes, with car commutes being associated with lower $PM_{2.5}$, BC, and noise levels compared to other modes. However, in certain areas, $PM_{2.5}$ and BC levels were not affected by trip mode, or had lower concentrations during active and public transportation. Chapter 2 suggested that exposure models accounting for environmental, meteorological, and behavioral factors, as well as duration of commuting, are needed in health studies of urban traffic microenvironments.

Chapter 3 tested the hypothesis that TRAP exposures experienced in different travel modes were associated with short-term cardiorespiratory health effects. This chapter employed portable sensors to record environmental exposures during two-hour trips using different transportation modes and changes in cardiorespiratory health before and after each trip. Findings from Chapter 3 showed that traveling by bus, subway or walking was associated with increased heart rate and decreased lung function as compared to riding a car. Additionally, increase BC exposures during the trip was related with airway inflammation, while PM_1 exposure was negatively associated with lung functions. Chapter 3 suggested that the adverse health effects of high levels of air pollution exposure could outweigh the benefit of physical activity during active transportation for healthy commuters in Chengdu, China. The promotion of active transport might not be appropriate for highly polluted regions.

Chapter 4 tested the hypothesis that using personal protective respirators could reduce acute adverse effects of TRAP exposure. The aim of this chapter was to evaluate the efficiency of a portable positive pressure respirator to reduce PM exposure in a laboratory setting and to mitigate related adverse cardiorespiratory health in a real-world experiment. Findings from Chapter 4 showed that even when the blower of the positive pressure respirator was set at the lowest level, the respirator could provide sufficient flow for a Chinese adult in moderate-intensity activity and had an average fit factor ranging from 10 to 15. However, no significant differences were found in cardiorespiratory functions measured between subjects wearing effective respirators and those using sham respirators for two-hour trips in traffic. Chapter 4 suggested that wearing the novel positive pressure respirator for two hours in traffic might not improve the cardiorespiratory health among healthy adults in Chengdu, China.

Chapter 5 tested the hypothesis that built environment factors affect employees' commute behavior as well as population health. The goal of this chapter was to explore the non-linear relationship between the built environment and time spent in multi-modal commuting, and to estimate the cardiovascular health impact of changing built environment factors considering $PM_{2.5}$ exposure and physical activities involved in multi-modal commuting. Findings of Chapter 5 showed that the home-work distance was an important predictor for time spent in different transportation modes. Changes in built environment factors related to garden city urban planning would increase the time commuters spent in cycling and subway trips, while potential changes in built environment related with TOD would increase the time in walking and cycling. The health impact assessment showed that generally, the policy of garden city and TOD would be beneficial to cardiovascular health for residents during commuting, but a longer home-work distance would lead to excess CVD mortality. Chapter 5 suggested that the planning policy of garden city and TOD would benefit population health for employed urban residents in Chengdu. However, these policies need to consider the job-housing mismatch in Chinese cities to reduce the commuting distance to avoid air pollution exposure and physically inactive travel modes.

Overall, this dissertation quantified environmental exposures for commuters in different travel modes, assessed associations between TRAP exposure and health outcomes for scripted commute trips, and how built environment factors impact time spent in different transportation modes. Lessons from this dissertation provides evidence for the health impacts of different transportation modes and informs healthy commute by guiding personal behavior and modifying the built environment. Future studies should investigate the health impacts of repeated short-term exposure during daily commuting. Previous studies found the impact of TRAP exposure in a 2-hour travelling could last for more than 24 hours [68]. It is important to assess the long-term health effect of repeated exposure during daily commute, especially for susceptible populations (e.g., children, pregnant women, the elders, and people with underlying health conditions), who might be more vulnerable to TRAP exposures.

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APPENDIX

Table A1. Summary of exposures during trips by workday/weekend and hour of the day.

Hour of the day	$PM_{2.5}$ (ug/m³)			BC (ng/m³)			Noise (dBA)		
	N[1]	median (mean)[2]	IQR (SD)[3]	N[1]	median (mean)[2]	IQR (SD)[3]	N[1]	median (mean)[2]	IQR (SD)[3]
Workdays									
9:00am-10:59am	73	97	92.4	186	8280	3540	6538	67.3	7.7
11:00am-12:59pm	520	43.7	125	1180	6140	8760	36532	72.6	6.8
13:00pm-14:59pm	389	33	34.9	812	2450	5470	24634	73.5	5.8
15:00pm-16:59pm	84	68.8	22.9	321	3720	3160	9596	71.6	6.0
17:00pm-18:59pm	11	147	7.5	62	10400	6260	1832	72.1	6.7
Weekends									
9:00am-10:59am	58	169	98.2	116	12900	5870	3501	66.5	8.6
11:00am-12:59pm	183	213	50.2	370	16700	6350	11251	74.4	5.0
13:00pm-14:59pm	173	52.2	74.3	323	6440	7770	10347	73.9	6.3
15:00pm-16:59pm	155	96	17.5	306	5270	4470	9269	72.9	6.9
17:00pm-18:59pm	24	84.5	13.2	47	7690	9960	1442	77.9	5.0

1. N is the number of measurements for each pollutant
2. For $PM_{2.5}$ and BC, the median was recorded; for noise, the mean was recorded
3. For $PM_{2.5}$ and BC, the interquartile rang (IQR) was recorded; for noise, the mean was recorded

Table A2. Summary of pollutants levels in four modes of transportation.

Modes	PM$_{2.5}$ (ug/m^3)					BC (ng/m^3)					Noise (dBA)				
	N	mean	SD	median	IQR	N	mean	SD	median	IQR	N	mean	SD	median	IQR
Summer															
Bike	239	31.6	14.6	36.6	29.6	463	2640	4540	1670	2370	14333	72.1	4.7	71.7	5.6
Bus	281	30.7	14.6	32.4	20.3	523	1840	2760	1670	2090	16822	75.2	5.4	75.7	6.7
Car	117	13.8	13.2	8.4	22.4	178	436	1770	212	716	6829	62.3	6.8	62.1	8.5
Subway	189	39.4	11.5	43.1	16.1	365	7810	4530	7620	5730	11227	76.1	4.7	75.6	6.3
Winter															
Bike	239	172	54.8	179	103	662	11300	6440	11000	9360	19645	72.8	5.3	72.5	6.8
Bus	310	142	54.4	118	108	789	8880	6010	7580	6190	23796	73.3	6	73	7.7
Car	111	140	41.5	130	58	285	10200	3820	9440	6130	8482	64.3	5.9	64.2	7.2
Subway	184	106	39.5	92.3	53.3	458	9570	5730	9600	8260	13808	75.5	5.4	75	7.6

Table A3. Pairwise comparison for three pollutants in mixed effect models with interaction between modes and neighborhoods

	Comparison	$PM_{2.5}$ ($p_{interaction}$ = 0.908)			BC ($p_{interaction}$ = 0.408)			Noise ($p_{interaction}$ = 0.0007)		
		Estimate	SE	p.value	Estimate	SE	p.value	Estimate	SE	p.value
Urban Core	Bike - Bus	-4.4	11.3	0.7003	1392	1117	0.2126	-1.52	0.96	0.1123
	Bike - Car	21	11.2	0.0645	1600	1132	0.1578	11.91	0.91	<.0001*
	Bike - Subway	0.6	11.1	0.9545	-395	1134	0.7276	-1.92	0.96	0.0444*
	Bus - Car	25.4	11.3	0.0267*	208	1139	0.8553	13.43	0.91	<.0001*
	Bus - Subway	5	11	0.6503	-1787	1134	0.1151	-0.41	0.96	0.6713
	Car - Subway	-20.4	11	0.0663	-1995	1155	0.0842	-13.83	0.91	<.0001*
Developing Neighborhood	Bike - Bus	19.5	11.2	0.0858	-565	1131	0.6174	-1.71	0.96	0.0745
	Bike - Car	34	11.1	0.0031*	1075	1124	0.3391	6.24	0.91	<.0001*
	Bike - Subway	24.3	11.3	0.0347*	-5028	1114	<.0001*	-3.07	0.93	0.001*
	Bus - Car	14.5	11.2	0.1975	1640	1131	0.147	7.94	0.91	<.0001*
	Bus - Subway	4.8	11.3	0.6737	-4463	1106	0.0001*	-1.36	0.93	0.1432
	Car - Subway	-9.7	11.3	0.3902	-6103	1104	<.0001*	-9.31	0.89	<.0001*
Suburb	Bike - Bus	9.4	14.2	0.5099	2336	1420	0.0999	-2.22	1.21	0.0663
	Bike - Car	53.1	13.5	0.0002*	3848	1368	0.0049*	9.79	1.13	<.0001*
	Bike - Subway	10	14.2	0.4832	-1036	1427	0.4681	-4.74	1.21	0.0001*
	Bus - Car	43.7	13.4	0.0017*	1512	1370	0.2697	12.01	1.13	<.0001*
	Bus - Subway	0.6	14.2	0.9645	-3371	1429	0.0183*	-2.52	1.21	0.0375*
	Car - Subway	-43.1	13.4	0.002*	-4883	1371	0.0004*	-14.53	1.13	<.0001*
Bike	SU - UC	-18.9	12.9	0.1468	-1215	1287	0.3449	-1.45	1.1	0.1861
	SU - DN	11.7	13	0.3695	2625	1300	0.0435*	0.22	1.1	0.842
	UC - DN	30.6	11.3	0.0084*	3841	1136	0.0007*	1.67	0.96	0.081
Bus	SU - UC	-8.8	12.9	0.4974	-2159	1288	0.0936	-0.75	1.1	0.4954
	SU - DN	-2.1	13	0.8734	-276	1303	0.8323	0.73	1.1	0.5043

	UC - DN	6.7	11.3	0.5549	1883	1139	0.0983	1.48	0.96	0.1217
Subway	SU - UC	-4.6	13	0.722	-575	1308	0.6605	1.36	1.1	0.215
	SU - DN	2.3	12.7	0.857	-1367	1282	0.2862	1.89	1.07	0.0786
	UC -DN	6.9	11.1	0.5339	-793	1125	0.4813	0.53	0.93	0.573
Car	SU - UC	-38	11.7	0.0017*	-3463	1202	0.004*	0.67	0.95	0.4827
	SU - DN	-20.4	12.1	0.0946	-148	1232	0.9046	-3.33	0.96	0.0005*
	UC - DN	17.6	11.1	0.1176	3316	1134	0.0035*	-4	0.86	<.0001*

Abbreviations: UC represents Urban Core, DN represents Developing Neighborhood, SU represent suburb;
Models were adjusted for days of the week (weekend/workdays) and hours of the day;
$p_{interaction}$ represents the p value for the interaction term in mixed effect models.
* represents $p < 0.05$

Table A4. Summary of measured TRAP concentrations, noise levels, and meteorological condition by transportation modes.

Exposure	Statistics	Car	Bus	Subway	Walk
	N	682	464	461	365
	PM_1				
	mean (SD)	31.4 (13.1)	45.4 (19.6)	35.6 (18.2)	40.6 (10.3)
	median (IQR)	25.5 (18.0)	32.0 (36.5)	33.0 (17.5)	37.5 (15.5)
PM ($\mu g/m^3$)	$PM_{2.5}$				
	mean (SD)	54.3 (25.9)	84.7 (43.5)	62.9 (34.5)	70.8 (24.7)
	median (IQR)	41.5 (37.5)	54.0 (83.0)	56.0 (35.5)	59.0 (39.0)
	PM_{10}				
	mean (SD)	61.7 (25.9)	95.7 (44.4)	72.2 (35.5)	82.6 (22.0)
	median (IQR)	51.0 (35.4)	67.5 (83.0)	70.0 (32.5)	72.0 (28.5)
	N	4019	2761	2904	2153
	Number (pt/cm^3)				
	mean (SD)	17005 (6586)	64124(135255)	19925 (47551)	20676 (26146)
	median (IQR)	15486 (6806)	26456 (43340)	11687 (9257)	15286 (6633)
	Size (nm)				
UFP	mean (SD)	49.8 (9.8)	34.2 (19.6)	59.8 (11.7)	60.1 (13.7)
	median (IQR)	48.0 (14.1)	40.6 (29.1)	60.6 (13.5)	59.3 (15.7)
	LDSA (mm^2/cm^3)				
	mean (SD)	44.2 (11.0)	88.4 (103.2)	51.6 (39.5)	57.8 (27.7)
	median (IQR)	42.7 (13.2)	68.7 (76.0)	42.4 (27.8)	52.5 (15.5)
	N	1156	783	879	649
BC (ng/m^3)	mean (SD)	3871.3 (3163.7)	5397.8 (4078.9)	5142.1 (4545.8)	4631.2 (2517.2)
	median (IQR)	3379.9 (2394.2)	4641.5 (5189.8)	4505.7 (3835.5)	4341.0 (1776.8)
Noise (dBA)	N	40636	27904	36605	21894
	mean (SD)	64.0 (6.8)	73.1 (6.1)	72.2 (5.8)	72.9 (7.2)
	N	682	464	461	365
Meteorological condition	Relative humidity (%)				
	mean (SD)	32.9 (5.9)	43.4 (6.2)	35.2 (8.4)	41.4 (5.2)
	Temperature (℃)				

		mean (SD)	26.7 (4.0)	21.1 (2.5)	24.4 (3.5)	19.3 (2.9)
METs	Male	mean (SD)	1.8 (0.7)	3.6 (0.6)	2.9 (0.9)	4.1 (2.0)
	Female	mean (SD)	2.4 (0.7)	4.2 (0.6)	3.2 (1.1)	3.5 (2.2)

Table A5. Associations between different transportation modes on cardiorespiratory health (car trips as the reference).

Health outcome	Reduced Model			Full Model		
	Bus	**Subway**	**Walking**	**Bus**	**Subway**	**Walking**
SBP (mmHg)	1.55 (-1.96, 5.08)	-1.55 (-4.56, 2.48)	2.22 (-1.29, 5.75)	4.29 (-3.30, 11.86)	-0.71 (-6.80, 5.41)	4.77 (-3.53, 13.05)
DBP (mmHg)	0.73 (-2.17, 3.65)	-0.05 (-2.94, 2.88)	3.08 (0.18, 6.00)	3.17 (-3.09, 9.47)	-0.74 (-5.84, 4.40)	5.43 (-1.43, 12.33)
HR (bpm)	3.5 (-0.23, 7.23)	6.13 (2.39, 9.86)	4.98 (1.24, 8.71)	11.19 (3.48, 18.89)	10.52 (4.35, 16.68)	13.48 (5.08, 21.89)
FeNO (ppb)	-2.79 (-6.80, 1.18)	-3.54 (-7.55, 0.43)	-2.29 (-6.30, 1.68)	-4.94 (-13.82, 3.84)	-6.11 (-13.39, 1.03)	-4.68 (-14.41, 4.94)
FEV1 (L/sec)	-0.04 (-0.09, 0.02)	-0.03 (-0.09, 0.03)	-0.04 (-0.10, 0.02)	-0.21 (-0.32, -0.09)	-0.1 (-0.19, 0.00)	-0.22 (-0.34, -0.09)
FVC (L/sec)	-0.04 (-0.11, 0.04)	-0.03 (-0.10, 0.05)	-0.05 (-0.12, 0.03)	-0.21 (-0.36, -0.06)	-0.08 (-0.20, 0.04)	-0.23 (-0.39, -0.06)
FEV1/FVC (%)	0.00 (-1.25, 1.25)	-0.15 (-1.40, 1.10)	0.15 (-1.10, 1.40)	0.69 (-1.95, 3.32)	0.11 (-2.00 2.22)	0.86 (-2.01, 3.74)
FEF25 (L/sec)	-0.03 (-0.31, 0.25)	-0.1 (-0.39, 0.18)	-0.4 (-0.68, -0.12)	-0.64 (-1.21, -0.06)	-0.53 (-0.99, -0.06)	-1.08 (-1.71, -0.45)
FEF50 (L/sec)	-0.04 (-0.24, 0.16)	-0.05 (-0.25, 0.15)	-0.06 (-0.26, 0.15)	-0.16 (-0.59, 0.27)	-0.11 (-0.46, 0.23)	-0.17 (-0.64, 0.30)
FEF75 (L/sec)	-0.05 (-0.23, 0.14)	-0.07 (-0.25, 0.11)	-0.22 (-0.40, -0.04)	-0.28 (-0.67, 0.10)	-0.21 (-0.52, 0.10)	-0.47 (-0.89, -0.05)
PEF (L/sec)	0.03 (-0.21, 0.26)	-0.13 (-0.36, 0.10)	-0.24 (-0.47, -0.01)	-0.49 (-0.98, 0.01)	-0.43 (-0.83, -0.02)	-0.82 (-1.36, -0.28)
FET (sec)	-0.09 (-0.35, 0.17)	-0.02 (-0.28, 0.24)	0.02 (-0.25, 0.28)	-0.06 (-0.60, 0.49)	-0.05 (-0.49, 0.39)	0.06 (-0.54, 0.66)

Table A6. Associations between TRAP exposure (the mean concentration during each trip) and cardiorespiratory health.

Health outcome	**PM_1 (10 μg/m^3)**	**$PM_{2.5}$ (10 μg/m^3)**	**PM_{10} (10 μg/m^3)**	**BC (1 μg/m^3)**	**UFP_number (1000pt/m^3)**	**UFP_size (10nm)**	**UFP_LDSA (10 μm^2/cm^3)**
SBP (mmHg)							
Model 1	0.81 (-1.07, 2.60)	0.32 (-0.61, 1.22)	0.41 (-0.50, 1.28)	0.15 (-1.07, 1.34)	-0.02 (-0.12, 0.08)	0.32 (-0.66, 1.30)	0.4 (-0.48, 1.25)
Model 2	0.86 (-0.97, 2.62)	0.4 (-0.51, 1.28)	0.48 (-0.40, 1.34)	0.14 (-1.05, 1.31)	-0.01 (-0.12, 0.09)	0.85 (-0.25, 1.96)	0.46 (-0.40, 1.29)
Model 3	0.18 (-1.84, 2.17)	0.12 (-0.84, 1.06)	0.2 (-0.76, 1.14)	-0.35 (-1.66, 0.99)	0.06 (-0.13, 0.24)	1.3 (-0.72, 3.32)	0.23 (-0.64, 1.08)
Model 4	0.09 (-2.24, 2.40)	0.09 (-0.97, 1.14)	0.19 (-0.89, 1.25)	-0.46 (-1.86, 0.94)	0.07 (-0.16, 0.30)	1.64 (-0.73, 4.00)	0.25 (-0.78, 1.26)
DBP (mmHg)							
Model 1	1.20 (-0.33, 2.72)	0.42 (-0.35, 1.19)	0.45 (-0.30, 1.20)	0.49 (-0.53, 1.51)	-0.07 (-0.15, 0.02)	0.35 (-0.47, 1.18)	0.21 (-0.53, 0.94)
Model 2	1.17 (-0.31, 2.65)	0.47 (-0.28, 1.22)	0.50 (-0.22, 1.22)	0.44 (-0.55, 1.43)	-0.07 (-0.15, 0.02)	0.94 (0.07, 1.83)	0.23 (-0.48, 0.94)
Model 3	0.28 (-1.41, 1.98)	0.07 (-0.72, 0.87)	0.07 (-0.73, 0.87)	-0.18 (-1.29, 0.93)	-0.05 (-0.20, 0.11)	0.46 (-1.23, 2.15)	-0.07 (-0.79, 0.66)
Model 4	0.65 (-1.30, 2.61)	0.19 (-0.69, 1.08)	0.20 (-0.70, 1.10)	-0.10 (-1.29, 1.09)	-0.04 (-0.22, 0.15)	0.88 (-1.06, 2.83)	0.03 (-0.82, 0.87)
HR (bpm)							
Model 1	1.23 (-0.64, 3.10)	0.53 (-0.40, 1.47)	0.55 (-0.36, 1.46)	0.09 (-1.19, 1.37)	0.01 (-0.11, 0.12)	1.06 (0.02, 2.09)	0.66 (-0.23, 1.56)
Model 2	-0.62 (-2.72, 1.48)	-0.11 (-1.07, 0.85)	-0.13 (-1.09, 0.82)	-0.29 (-1.51, 0.92)	0.06 (-0.05, 0.17)	0.46 (-0.61, 1.53)	0.12 (-0.79, 1.04)
Model 3	1.75 (-0.31, 3.81)	0.64 (-0.34, 1.62)	0.69 (-0.30, 1.67)	0.26 (-1.15, 1.68)	0.06 (-0.14, 0.26)	3.14 (1.02, 5.26)	0.78 (-0.12, 1.68)
Model 4	0.01 (-2.14, 2.15)	0.06 (-0.90, 1.01)	0.07 (-0.90. 1.04)	0.24 (-1.05, 1.53)	0.06 (-0.13, 0.24)	1.79 (-0.39, 3.97)	0.24 (-0.65, 1.13)
FeNO (ppb)							
Model 1	1.52	0.8	0.72	1.45	-0.02	-0.47	0.3

	(-0.54, 3.64)	(-0.22, 1.85)	(-0.28, 1.74)	(0.10, 2.79)	(-0.13, 0.10)	(-1.61, 0.64)	(-0.68, 1.30)
Model 2	1.54 (-0.50, 3.65)	0.89 (-0.12, 1.94)	0.80 (-0.19, 1.83)	1.39 (0.07, 2.71)	-0.01 (-0.12, 0.10)	0.03 (-1.24, 1.29)	0.35 (-0.62, 1.33)
Model 3	1.01 (-1.36, 3.40)	0.64 (-0.47, 1.76)	0.54 (-0.57, 1.67)	1.23 (-0.29, 2.74)	0.07 (-0.15, 0.28)	-2.26 (-4.61, 0.07)	0.08 (-0.93, 1.09)
Model 4	1.54 (-0.50, 3.65)	0.89 (-0.12, 1.94)	0.8 (-0.19, 1.83)	1.39 (0.07, 2.71)	-0.01 (-0.12, 0.10)	0.03 (-1.24, 1.29)	0.35 (-0.62, 1.33)
FEV1 (L/sec)							
Model 1	-0.03 (-0.06, 0.00)	-0.01 (-0.03, 0.00)	-0.01 (-0.03, 0.00)	-0.01 (-0.03, 0.01)	0.00 (0.00, 0.00)	0.00 (-0.02, 0.01)	-0.01 (-0.03, 0.00)
Model 2	-0.03 (-0.06, 0.00)	-0.01 (-0.03, 0.00)	-0.01 (-0.03, 0.00)	-0.01 (-0.03, 0.01)	0.00 (0.00, 0.00)	-0.01 (-0.03, 0.01)	-0.01 (-0.03, 0.00)
Model 3	-0.03 (-0.06, 0.00)	-0.01 (-0.03, 0.00)	-0.01 (-0.03, 0.00)	-0.01 (-0.03, 0.01)	0.00 (0.00, 0.00)	-0.02 (-0.05, 0.02)	-0.01 (-0.03, 0.00)
Model 4	-0.04 (-0.08, 0.00)	-0.02 (-0.03, 0.00)	-0.02 (-0.03, 0.00)	-0.01 (-0.03, 0.02)	0.00 (-0.01, 0.00)	-0.02 (-0.05, 0.02)	-0.01 (-0.03, 0.00)
FVC (L/sec)							
Model 1	-0.01 (-0.05, 0.02)	0.00 (-0.02, 0.01)	0.00 (-0.02, 0.01)	-0.01 (-0.03, 0.01)	0.00 (0.00, 0.00)	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)
Model 2	-0.01 (-0.05, 0.02)	0.00 (-0.02, 0.01)	0.00 (-0.02, 0.01)	-0.01 (-0.03, 0.01)	0.00 (0.00, 0.00)	-0.01 (-0.04, 0.01)	0.00 (-0.02, 0.02)
Model 3	0.00 (-0.04, 0.04)	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)	0.00 (-0.03, 0.03)	0.00 (0.00, 0.01)	0.01 (-0.04, 0.05)	0.00 (-0.01, 0.02)
Model 4	-0.01 (-0.06, 0.03)	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)	-0.01 (-0.04, 0.02)	0.00 (0.00, 0.01)	-0.01 (-0.05, 0.04)	0.00 (-0.02, 0.02)
FEV1/FVC (%)							
Model 1	-0.53 (-1.11, 0.04)	-0.28 (-0.57, 0.00)	-0.28 (-0.57, 0.00)	-0.01 (-0.41, 0.39)	-0.03 (-0.07, 0.00)	-0.01 (-0.34, 0.32)	-0.27 (-0.54, 0.01)
Model 2	-0.52 (-1.09, 0.05)	-0.27 (-0.55, 0.02)	-0.26 (-0.54, 0.02)	-0.01 (-0.41, 0.38)	-0.03 (-0.06, 0.00)	0.12 (-0.26, 0.50)	-0.26 (-0.53, 0.02)
Model 3	-0.84 (-1.47, -0.21)	-0.38 (-0.68, -0.09)	-0.41 (-0.70, -0.11)	-0.13 (-0.57, 0.31)	-0.07 (-0.13, 0.00)	-0.38 (-1.07, 0.31)	-0.32 (-0.59, -0.04)
Model 4	-0.79	-0.35	-0.38	-0.01	-0.06	-0.15	-0.28

	(-1.50, -0.07)	(-0.68, -0.02)	(-0.71, -0.05)	(-0.48, 0.46)	(-0.13, 0.02)	(-0.95, 0.66)	(-0.61, 0.05)
PEF (L/sec)							
Model 1	-0.03 (-0.16, 0.10)	0.00 (-0.07, 0.06)	-0.01 (-0.07, 0.05)	0.00 (-0.08, 0.08)	0.01 (0.00, 0.01)	-0.07 (-0.14, -0.01)	-0.02 (-0.08, 0.04)
Model 2	0.07 (-0.08, 0.21)	0.03 (-0.04, 0.10)	0.03 (-0.04, 0.09)	0.01 (-0.07, 0.10)	0.00 (0.00, 0.01)	-0.05 (-0.12, 0.03)	0.00 (-0.06, 0.07)
Model 3	0.01 (-0.13, 0.15)	0.02 (-0.05, 0.08)	0.02 (-0.05, 0.08)	0.03 (-0.06, 0.12)	0.01 (-0.01, 0.02)	-0.10 (-0.24, 0.04)	-0.02 (-0.08, 0.04)
Model 4	-0.03 (-0.19, 0.14)	0.01 (-0.07, 0.08)	0.00 (-0.07, 0.08)	0.02 (-0.08, 0.12)	0.00 (-0.01, 0.02)	-0.19 (-0.35, -0.03)	-0.04 (-0.11, 0.03)
FEF25 (L/sec)							
Model 1	-0.12 (-0.26, 0.03)	-0.04 (-0.11, 0.03)	-0.05 (-0.12, 0.02)	0.01 (-0.09, 0.10)	0.01 (0.00, 0.02)	-0.09 (-0.17, -0.02)	-0.04 (-0.11, 0.03)
Model 2	0.06 (-0.10, 0.22)	0.02 (-0.05, 0.10)	0.02 (-0.05, 0.09)	0.04 (-0.05, 0.13)	0.00 (0.00, 0.01)	-0.04 (-0.11, 0.04)	0.02 (-0.05, 0.09)
Model 3	-0.08 (-0.24, 0.08)	-0.02 (-0.10, 0.06)	-0.03 (-0.10, 0.05)	0.05 (-0.06, 0.16)	0.00 (-0.01, 0.02)	-0.13 (-0.29, 0.04)	-0.03 (-0.10, 0.04)
Model 4	0.07 (-0.10, 0.24)	0.03 (-0.05, 0.10)	0.03 (-0.05, 0.10)	0.05 (-0.05, 0.15)	0 (-0.01, 0.02)	0.01 (-0.16, 0.17)	0.01 (-0.05, 0.08)
FEF50 (L/sec)							
Model 1	-0.06 (-0.16, 0.04)	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)	0.01 (-0.05, 0.08)	0.00 (-0.01, 0.01)	-0.01 (-0.06, 0.05)	-0.01 (-0.06, 0.03)
Model 2	-0.06 (-0.16, 0.04)	-0.03 (-0.08, 0.02)	-0.03 (-0.07, 0.02)	0.01 (-0.05, 0.08)	0.00 (-0.01, 0.01)	0.01 (-0.06, 0.07)	-0.01 (-0.06, 0.04)
Model 3	-0.09 (-0.19, 0.02)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)	0.01 (-0.07, 0.08)	0.00 (-0.01, 0.01)	-0.03 (-0.14, 0.09)	-0.02 (-0.06, 0.03)
Model 4	-0.08 (-0.20, 0.04)	-0.03 (-0.09, 0.02)	-0.03 (-0.09, 0.02)	0.02 (-0.06, 0.10)	0.00 (-0.01, 0.02)	0.00 (-0.13, 0.14)	-0.01 (-0.06, 0.05)
FEF75 (L/sec)							
Model 1	-0.09 (-0.18, 0.00)	-0.04 (-0.08, 0.01)	-0.04 (-0.08, 0.01)	-0.03 (-0.09, 0.03)	0.00 (0.00, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.08, 0.01)
Model 2	-0.09 (-0.12, 0.00)	-0.04 (-0.08, 0.01)	-0.04 (-0.08, 0.01)	-0.03 (-0.09, 0.03)	0.00 (0.00, 0.01)	-0.05 (-0.11, 0.01)	-0.04 (-0.08, 0.01)

Model 3	-0.07 (-0.17, 0.03)	-0.03 (-0.07, 0.02)	-0.03 (-0.08, 0.02)	-0.01 (-0.08, 0.06)	0.00 (0.01, 0.01)	-0.08 (-0.19, 0.02)	-0.03 (-0.07, 0.01)
Model 4	-0.04 (-0.15, 0.07)	-0.01 (-0.06, 0.04)	-0.01 (-0.07, 0.04)	0.01 (-0.06, 0.08)	0.00 (0.01, 0.01)	-0.05 (-0.17, 0.07)	-0.02 (-0.07, 0.04)
FET (sec)							
Model 1	0.14 (0.02, 0.26)	0.07 (0.01, 0.13)	0.06 (0.00, 0.12)	0.08 (-0.00, 0.16)	0.01 (0.00, 0.01)	0.01 (-0.06, 0.08)	0.08 (0.02, 0.13)
Model 2	0.14 (0.02, 0.26)	0.07 (0.01, 0.139)	0.06 (0.01, 0.123)	0.08 (0.00, 0.16)	0.01 (0.00, 0.01)	0.02 (-0.06, 0.10)	0.08 (0.02, 0.14)
Model 3	0.16 (0.03, 0.30)	0.07 (0.01, 0.134)	0.07 (0.01, 0.14)	0.09 (0.00, 0.18)	0.01 (0.00, 0.03)	0.09 (-0.06, 0.24)	0.08 (0.02, 0.14)
Model 4	0.16 (0.03, 0.30)	0.07 (0.01, 0.134)	0.07 (0.01, 0.14)	0.09 (0.00, 0.18)	0.01 (0.00, 0.03)	0.09 (-0.06, 0.24)	0.08 (0.02, 0.14)

Model 1 was adjusted for perceived stress, physical activity levels, noise, temperature and relative humidity.
Model 2 included all the covariates in Model 1 and one regional gaseous pollution.
Model 3 included all the covariate in Model 1 and two latent variables from the PLSDA model.
Model 4 included all the covariate in Model 2 and two latent variables from the PLSDA model.

Table A7. Associations between TRAP exposure (the inhalation does during each 2-hour trip) and cardiorespiratory health.

Health outcome	**PM_1 (10 μg)**	**$PM_{2.5}$ (10 μg)**	**PM_{10} (10 μg)**	**BC (1 μg)**	**UFP_number (10^9 pt)**	**UFP_LDSA (1 mm^2)**
SBP (mmHg)						
Single-pollutant model	0.46 (-0.64, 1.50)	0.21 (-0.40, 0.78)	0.21 (-0.33, 0.73)	-0.04 (-0.78, 0.67)	0.03 (-0.04, 0.09)	0.03 (-0.02, 0.08)
Two-pollutant mode	0.53 (-0.54, 1.55)	0.28 (-0.32, 0.85)	0.27 (-0.26, 0.79)	-0.02 (-0.74, 0.69)	0.03 (-0.03, 0.10)	0.04 (-0.02, 0.09)
DBP (mmHg)						
Single-pollutant model	0.9 (0.02, 1.76)	0.39 (-0.11, 0.87)	0.38 (-0.07, 0.81)	0.39 (-0.23, 1.01)	-0.01 (-0.06, 0.05)	0.03 (-0.01, 0.08)
Two-pollutant mode	0.92 (0.08, 1.76)	0.44 (-0.04, 0.91)	0.42 (-0.01, 0.84)	0.39 (-0.22, 0.99)	-0.01 (-0.06, 0.05)	0.04 (-0.01, 0.08)
HR (bpm)						
Single-pollutant model	1.04 (0.03, 2.06)	0.53 (-0.03, 1.10)	0.49 (-0.02, 0.10)	0.35 (-0.38, 1.08)	0.03 (-0.04, 0.10)	0.05 (0.00, 0.10)
Two-pollutant mode	0.94 (0.06, 1.95)	0.45 (-0.11, 1.01)	0.41 (-0.09, 0.92)	0.31 (-0.41, 1.02)	0.02 (-0.05, 0.09)	0.05 (0.00, 0.10)
FeNO (ppb)						
Single-pollutant model	0.47 (-0.70, 1.65)	0.32 (-0.33, 0.97)	0.25 (-0.33, 0.84)	0.67 (-0.16, 1.49)	-0.02 (-0.10, 0.05)	0.01 (-0.05, 0.07)
Two-pollutant mode	0.53 (-0.62, 1.70)	0.4 (-0.24, 1.04)	0.32 (-0.26, 0.90)	0.67 (-0.13, 1.47)	-0.02 (-0.09, 0.05)	0.01 (-0.05, 0.07)
FEV1 (L/sec)						
Single-pollutant model	-0.02 (-0.03, 0.00)	-0.01 (-0.02 0.00)	-0.01 (-0.02, 0.00)	0.00 (-0.02, 0.01)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Two-pollutant mode	0.00 (-0.0w, 0.02)	0.00 (-0.01, 0.01)	0.00 (-0.01, 0.01)	0.00 (-0.01, 0.01)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
FVC (L/sec)						
Single-pollutant model	-0.01 (-0.03, 0.01)	-0.01 (-0.02, 0.01)	-0.01 (-0.02, 0.01)	-0.01 (-0.02, 0.01)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)

Two-pollutant mode	-0.01 (-0.04, 0.01)	-0.01 (-0.02, 0.01)	-0.01 (-0.02, 0.00)	-0.01 (-0.02, 0.01)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
FEV1/FVC (L/sec)						
Single-pollutant model	-0.05 (-0.38, 0.29)	-0.07 (-0.25, 0.12)	-0.04 (-0.21, 0.12)	0.06 (-0.18, 0.29)	0.00 (-0.02, 0.03)	0.00 (-0.02, 0.02)
Two-pollutant mode	-0.03 (-0.36, 0.31)	-0.05 (-0.23, 0.13)	-0.03 (-0.20, 0.14)	0.06 (-0.17, 0.30)	0.00 (-0.02, 0.03)	0.00 (-0.02, 0.02)
PEF (L/sec)						
Single-pollutant model	-0.05 (-0.12, 0.02)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.01)	-0.03 (-0.07, 0.02)	0.00 (0.00, 0.01)	0.00 (-0.01, 0.00)
Two-pollutant mode	-0.05 (-0.12, 0.02)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.01)	-0.03 (-0.07, 0.02)	0.00 (0.00, 0.01)	0.00 (-0.01, 0.00)
FEF25 (L/sec)						
Single-pollutant model	-0.10 (-0.18, -0.02)	-0.05 (-0.09, 0.00)	-0.05 (-0.09, 0.00)	-0.02 (-0.08, 0.03)	0.00 (0.00, 0.01)	0.00 (-0.01, 0.00)
Two-pollutant mode	0.00 (-0.10, 0.10)	0.00 (-0.05, 0.05)	0.00 (-0.05, 0.04)	0.00 (-0.05, 0.06)	0.00 (0.00, 0.01)	0.00 (0.00, 0.01)
FEF50 (L/sec)						
Single-pollutant model	-0.02 (-0.07, 0.03)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.02)	0.01 (-0.03, 0.05)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Two-pollutant mode	-0.02 (-0.07, 0.04)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.02)	0.01 (-0.03, 0.05)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
FEF75 (L/sec)						
Single-pollutant model	-0.04 (-0.09, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.02)	0.00 (0.00, 0.01)	0.00 (0.00, 0.00)
Two-pollutant mode	-0.04 (-0.09, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.01)	-0.02 (-0.05, 0.02)	0.00 (0.00, 0.01)	0.00 (0.00, 0.00)
FET (sec)						
Single-pollutant model	0.04 (-0.03, 0.11)	0.02 (-0.02, 0.06)	0.02 (-0.02, 0.05)	0.03 (-0.02, 0.08)	0.00 (0.00, 0.00)	0.00 (0.00, 0.01)
Two-pollutant mode	0.04 (-0.03, 0.11)	0.02 (-0.01, 0.06)	0.02 (-0.02, 0.05)	0.03 (-0.02, 0.08)	0.00 (0.00, 0.00)	0.00 (0.00, 0.01)

Table A8. Changes of cardiorespiratory health during 2-hour trips with effective positive pressure respirators compared to trips with sham respirators.

Health outcome	Reduced model	Full model
SBP (mmHg)	1.40 (-0.56, 3.35)	1.39 (-0.52, 3.30)
DBP (mmHg)	0.13 (-1.74, 2.00)	0.14 (-1.68, 1.96)
HR (bpm)	1.04 (-1.00, 3.08)	1.03 (-1.01, 3.06)
FeNO (ppb)	0.47 (-1.18, 2.13)	0.49 (-1.14, 2.11)
FEV1 (L/sec)	-0.004 (-0.032, 0.025)	0.00 (-0.03, 0.03)
FVC (L/sec)	0.09 (-0.05, 0.22)	0.09 (-0.04, 0.22)
FEV1/FVC (%)	-0.75 (-1.39, -0.11)	-0.76 (-1.39, -0.12)
FEV1 (adjusted for FVC) (L/sec)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.02)
PEF (L/sec)	0.05 (-0.06, 0.16)	0.05 (-0.06, 0.16)
FEF25 (L/sec)	-0.08 (-0.23, 0.07)	-0.08 (-0.23, 0.07)
FEF50 (L/sec)	0.03 (-0.09, 0.15)	0.03 (-0.09, 0.15)
FEF75 (L/sec)	0.05 (-0.05, 0.15)	0.05 (-0.05, 0.15)
FET (sec)	0.25 (0.05, 0.45)	0.25 (0.06, 0.45)

Reference group: trips with sham respirator.
Reduced model was adjusted for noise, temperature and relative humidity.
Full model included all the covariates in reduced model and perceived stress, MET and CO levels.

Table A9. Associations between different transportation modes on cardiorespiratory health (car trips as the reference).

Health outcome	$p_{interaction}$	Perception		
		Not know	**Effective**	**Sham**
SBP (mmHg)	0.009	1.25 (-1.07, 3.57)	2.80 (-1.65, 7.27)	-8.85 (-15.32, -2.35)
DBP (mmHg)	0.134	0.41 (-1.88, 2.72)	-0.11 (-4.52, 4.32)	-6.44 (-12.85, 0.00)
HR (bpm)	0.584	0.96 (-1.67, 3.60)	1.20 (-3.80, 6.22)	4.87 (-2.40, 12.18)
FeNO (ppb)	0.828	-0.50 (-3.73, 2.75)	1.23 (-2.85, 5.33)	2.06 (-3.88, 8.03)
FEV1 (L/sec)	0.488	-0.02 (-0.05, 0.02)	0.03 (-0.04, 0.10)	-0.02 (-0.12, 0.09)
FVC (L/sec)	0.539	0.12 (-0.05, 0.29)	0.05 (-0.27, 0.37)	-0.15 (-0.62, 0.32)
FEV1/FVC (%)	0.013	-0.93 (-1.72, -0.13)	-0.79 (-2.3, 0.73)	2.46 (0.26, 4.68)
FEV1 (adjusted for FVC) (L/sec)	0.408	-0.02 (-0.06, 0.01)	0.03 (-0.04, 0.09)	-0.01 (-0.10, 0.09)
PEF (L/sec)	0.072	-0.02 (-0.16, 0.11)	0.26 (0.00, 0.53)	0.30 (-0.09, 0.68)
FEF25 (L/sec)	0.012	-0.22 (-0.41, -0.03)	0.33 (-0.03, 0.69)	0.21 (-0.31, 0.73)
FEF50 (L/sec)	0.548	0.01 (-0.14, 0.17)	0.02 (-0.27, 0.31)	0.26 (-0.16, 0.68)
FEF75 (L/sec)	0.016	0.01 (-0.12, 0.13)	0.18 (-0.06, 0.42)	0.51 (0.17, 0.86)
FET (sec)	0.768	0.29 (0.03, 0.54)	0.09 (-0.39, 0.58)	0.24 (-0.46, 0.95)

Reference group: trips with sham respirator.
Models were adjusted for noise, temperature and relative humidity, perceived stress, MET and CO levels.

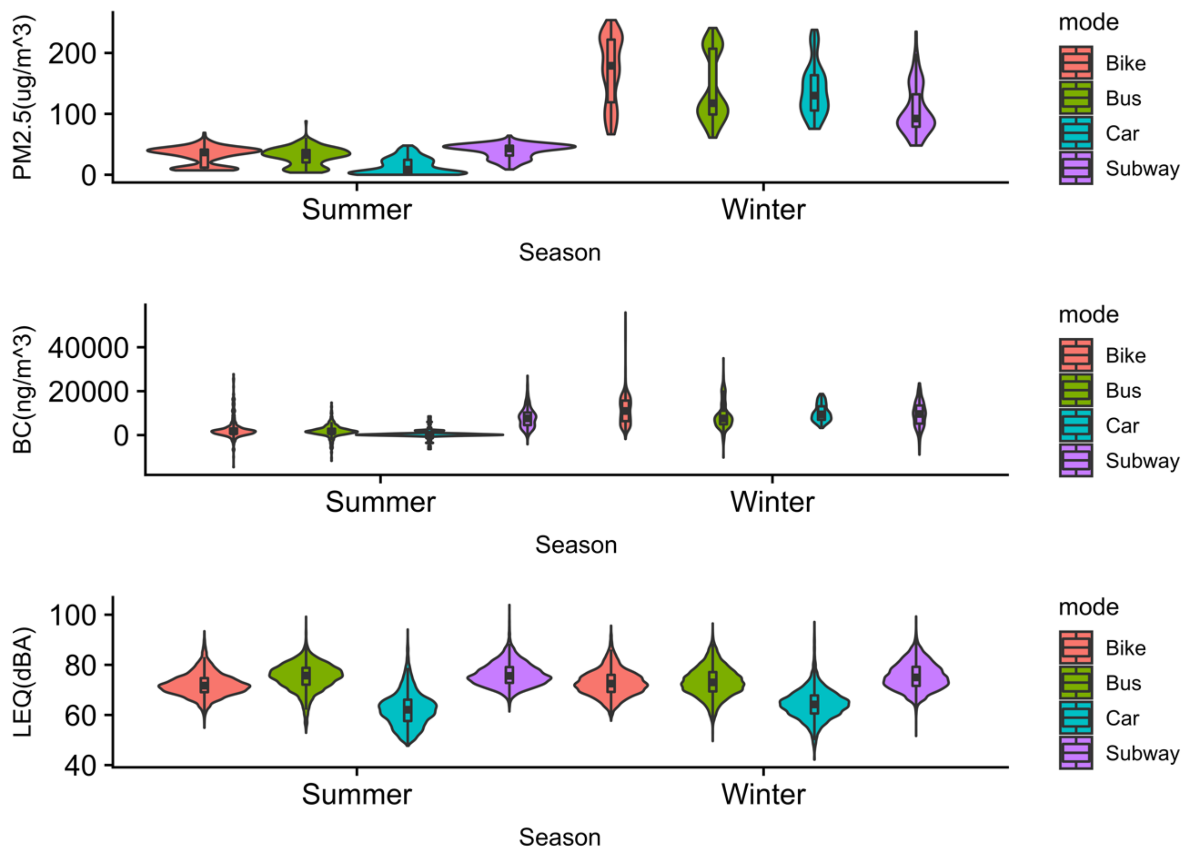

Figure A1. Violin plot for three-pollutant levels in the four modes of transportation

The violin plot includes all the sample points, with the width proportionate to the density of the data at different values. The box plot is also plotted upon the violin plot showing the median and interquartile range.

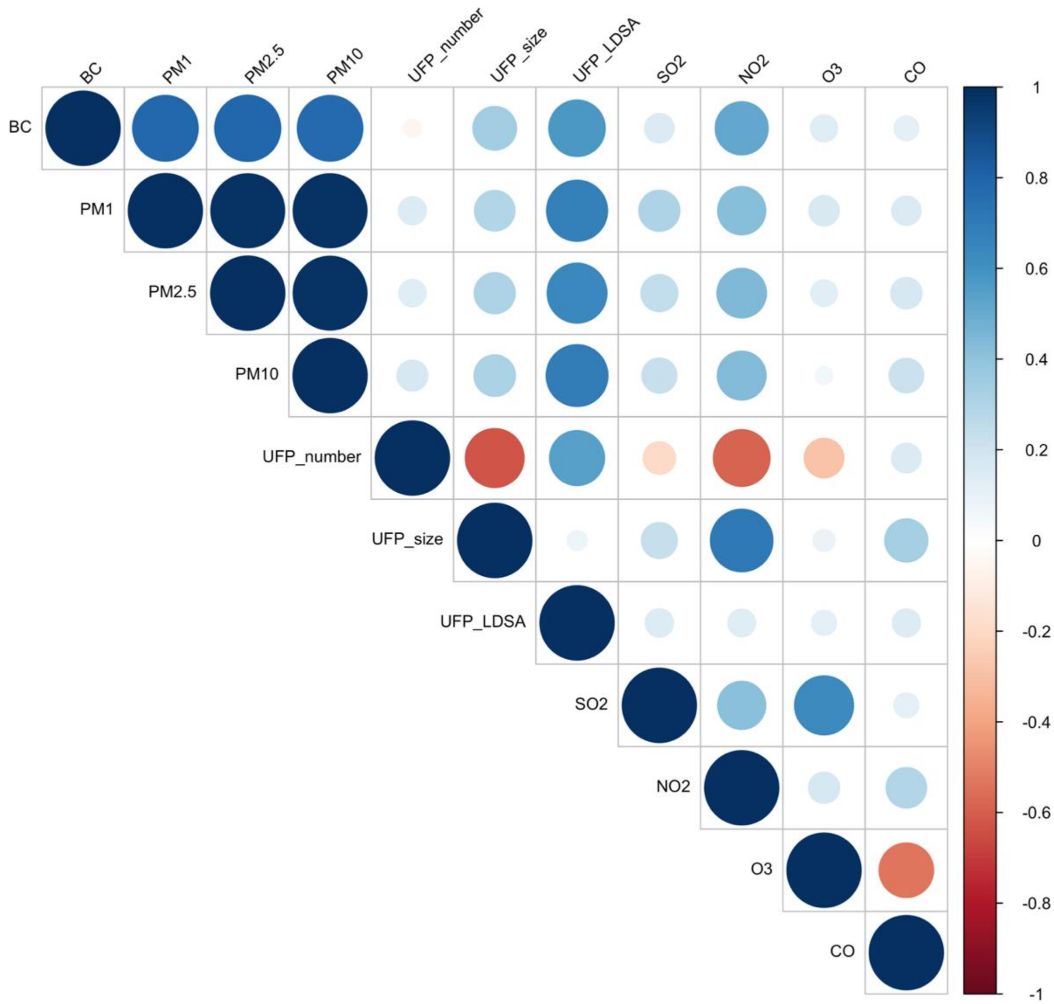

Figure A2. Correlations between measure particle pollutants and regional gaseous pollutants.

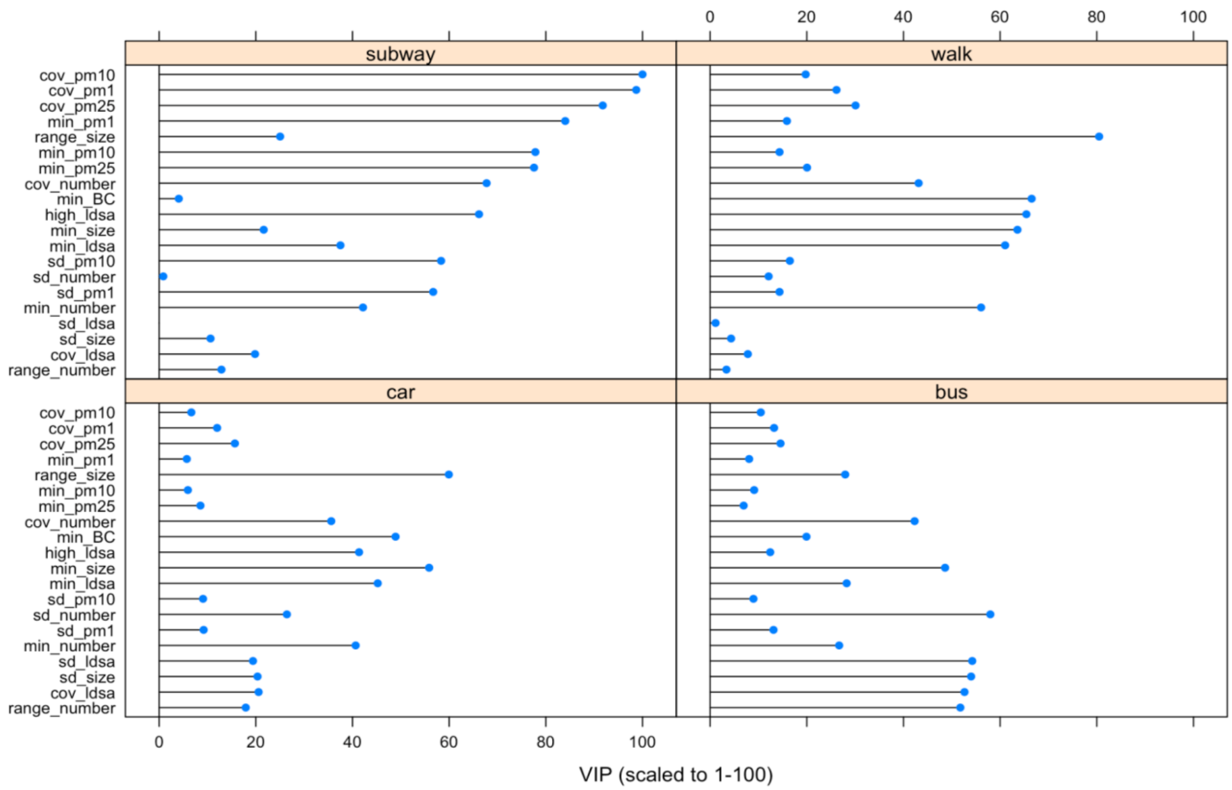

Figure A3. Variable importance of different exposure metrics on transportation modes in the PLSDA model.