UNIVERSITY OF CALIFORNIA

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Assessing and Reducing Worker Exposure to Exhaled E-cigarette

Aerosols in Vape Shops

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Environmental Health Sciences

by

Charlene Minh Chau Nguyen

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ABSTRACT OF THE DISSERTATION

Assessing and Reducing Worker Exposure to
Exhaled E-cigarette Aerosols in Vape Shops

by

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Doctor of Philosophy in Environmental Health Sciences
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Professor Yifang Zhu, Chair

The electronic cigarette (e-cig) has become a popular alternative nicotine delivery device that continues to grow in use and revenues. E-cigs are largely sold in vape shops, retail establishments dedicated to selling vape products. Customer sampling of e-liquids and social vaping permitted in vape shops make them sites of secondhand exposure to e-cig aerosols, which may pose potential occupational risk to vape shop workers. Pollutants emitted from e-cig use include ultrafine particles, nicotine, metals, and aldehydes, which have been previously found to induce oxidative stress responses, cause cytotoxicity in humans and animals, and increase risk of cardiovascular events. Although there is growing literature studying the health effects of

mainstream e-cig aerosol inhalation, studies about health risks from secondhand exposure, particularly in workplaces, are limited. This study assessed exhaled e-cig aerosols as a potential occupational exposure among vape shop workers, and tested potential air mitigation strategies to reduce vape shop worker exposure to exhaled e-cig aerosols. First, sixty-seven vape shops were randomly surveyed and fine and ultrafine particles measured in six representative shops. Simultaneous measurements were also taken at increasing distances away from a vaping area to assess the mixing and spatial profiles of particle levels inside the shops. During vaping activity, real-time indoor particle number concentration (PNC) and gravimetric-corrected $PM_{2.5}$ mass concentration across the six vape shops varied from 1.3×10^4 to 4.8×10^5 particles/cm^3 and from 15.5 to 37,500 μg/m^3, respectively, and could rise up to 10,000 times above background for $PM_{2.5}$ and 100 times above background for PNC. Exhaled e-cig particles persisted in the air, traveling and mixing in the shops. $PM_{2.5}$ decayed faster than PNC over distances greater than 1.5 m from a vaping source.

To explore employee exposure to e-cig aerosols in vape shops and potential associated effects as a result of exposure, urinary cotinine as a metabolic marker for nicotine exposure and select urinary oxidative stress, systemic inflammation, and metal exposure response markers were measured in thirty vape shop workers, fifteen vaping and fifteen non-vaping, at the start and end of a work shift on two days, which were either the first and last days of a consecutive workday period or two separate days if a subject had a nonconsecutive workday schedule. Elevated oxidative stress, inflammation, and metal toxicity/reactive oxygen species response markers observed within a work shift were much stronger among vaping workers, whose e-cig aerosol dosage is compounded with their own e-cig use during a work shift. However, increasing cotinine, and a corresponding upward trend in a lipid peroxidation marker (8-isoprostane)

between the first and last work shifts were observed in non-vaping workers with a consecutive workday schedule, indicating that these increases in nicotine exposure and oxidative stress effect may be attributable to workplace exposure to exhaled e-cig aerosols. This is further suggested with the significant association observed between cotinine and 8-isoprostane in the non-vaping group varied by vape shop, suggesting that worksite characteristics, which could include vaping activity during the shift, may induce oxidative stress.

With workplace exposure to nicotine, likely from exhaled e-cig aerosols in the vape shop, a possible contributor to oxidative stress in non-vaping workers, air mitigation strategies may then be needed to reduce exposure. Effectiveness of two air mitigation strategies (enhanced ventilation at the ASHRAE-recommended ventilation rate for beauty and nail salons and high-rate portable filtration) were tested in six vape shops for particle and nicotine air concentration reduction over business hours. From baseline, mean PNC levels were reduced by an average 40% after enhanced ventilation and 61% after portable filtration across the studied shops, and mean $PM_{2.5}$ levels reduced by 47% and 26%, respectively. During high vaping density in the shop, average PNC and $PM_{2.5}$ concentrations were lower by 36% and 19%, respectively, during enhanced ventilation than during baseline. During portable filtration, average PNC and $PM_{2.5}$ levels stayed low at varying vaping densities compared to baseline and enhanced ventilation, suggesting filtration to have a different mechanism (i.e. removal of particles) of indoor pollutant control than dilution or exhausting indoor air. From baseline, mean time-weighted average air nicotine concentrations were reduced by an average 46% after enhanced ventilation and 9% after portable filtration, suggesting enhanced ventilation may be more effective in reducing gas-phase nicotine.

The dissertation of Charlene Minh Chau Nguyen is approved.

Shane Que Hee

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2022

You keep him in perfect peace whose mind is stayed on you, because he trusts in you.

Isaiah 26:3

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VITA

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1. Cetintas, E., Luo, Y., **Nguyen, C.**, Guo, Y., Li, L., Zhu, Y., Ozcan, A. (2021). Characterization of exhaled e-cigarette aerosols in a vape shop using a field-portable holographic on-chip microscope. *Physics*, https://arxiv.org/abs/2109.10865

2. Li, L., **Nguyen, C.**, Lin, Y., Fadel, A.N., Zhu, Y. (2021). Impacts of electronic cigarettes usage on air quality of vape shops and their nearby areas. *Sci Total Environ,* 760, 143423.

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5. Zhao, T., **Nguyen, C.**, Lin, C-H., Middlekauff, H.R., et al. (2017). Characteristics of secondhand electronic cigarette aerosols from active human use. *Aerosol Sci Technol*, 51, 1368–1376.

Selected Presentations

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1. Personal Safety Division Occupational Health and Safety Scholarship, 3M (May 2018)

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3. University Regent Fellowship, UCLA Graduate Division (July 2016)

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1. OVERVIEW

Vaping, defined as the inhalation and exhalation of aerosolized e-liquid produced by e-cigs, is a popular nicotine delivery alternative to tobacco smoking. The e-cig is a nicotine delivery device whereby a mixture of propylene glycol (PG), vegetable glycerin (VG), water, nicotine, and flavor additives in a reservoir (i.e. cartridge, "tank," or "pod"), is heated and aerosolized by a battery-powered heating coil. In 2021, the global e-cig market was worth more than $18 billion, with North America holding 40% of the market share, and is expected to grow to over $182 billion by 2030 (Grand View Research, 2022). Contributing to this market are vape shops, stores that exclusively sell vape products and also function as a lounge where customers can bring their own e-cig devices for repair, sample e-liquids, and vape.

Figure 1.1. A vape shop in Southern California

Regulation addressing e-cigs and e-cig use has progressed in the last several years as concerns about e-cig use safety and health risks and youth vaping have been increasing. On

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August 8, 2016, the Food and Drug Administration (FDA) began to regulate e-cigs as tobacco products (Mendes, 2017). In September 2018, the FDA declared teen vaping an "epidemic," and issued new guidelines in March 2019 restricting the sale of most flavored tobacco products including e-cigs, at convenience stores, gas stations, and pharmacies (FDA, 2018). San Francisco, CA became the first U.S. city to ban the sale of e-cig products (Cerullo, 2019). Many cities and several states have banned vaping in public areas and workplaces as well as included vaping prohibitions in venues with existing smoke-free provisions (ANRF, 2022). However, vaping is still permitted in vape shops, largely due to the exclusive exemption of these businesses from the vaping prohibitions (ANRF, 2022).

Studies have shown that mainstream e-cig aerosols contain substantial amounts of nicotine and particulate matter (PM) in the FP (aerodynamic diameter ≤ 2.5 μm) and UFP (diameter ≤ 100 nm) size range (McAuley et al., 2012; Czogala et al., 2014; Fromme and Schober, 2015; Zhao et al., 2016). Furthermore, carbonyl compounds possibly formed from the thermal dehydration of glycols and glycerin in the e-liquid, volatile organic compounds, and heavy metals have also been detected in mainstream e-cig aerosol (McAuley et al., 2012; Ohta et al., 2011; Williams et al., 2013; Mikheev et al., 2016). These types of pollutants have also been measured in exhaled e-cig aerosols. Several animal and toxicological studies have demonstrated that e-cig aerosol causes oxidative stress and impairs respiratory function (Canistro et al., 2017; Atkins and Drescher, 2015; Lee et al., 2018; Hureaux et al., 2014; Vardavas et al., 2014). However, the risks of inhalation toxicity from exhaled e-cig aerosols in humans are still unclear. There is strong need for intensive studies assessing short- and long-term human health risks of mainstream and secondhand exposure to e-cig emissions. An essential component of these risk assessments is the measurement and quantification of real-world exposures to these emissions.

Vape shops are small businesses that have less than 20 employees and employ workers who are young, who are of a diverse racial makeup, and at minimum wage. In June 2019, there were approximately 3,139 vape shops in Southern California (Yelp.com, 2019). This number has gone down, due to several possible explanations including stricter regulations on vape products, the outbreak of vaping-associated lung injury in April 2019 – February 2020, the COVID-19 pandemic (March 2020 – present), and business-specific features such as shops not having a bar-like atmosphere, employee knowledge of products, and product diversity (Galimov et al., 2020; Darmiento, 2019). Still, there are over 800 active vape/smoke shops in Southern California (Yelp.com, 2022). With a conservative estimate of two full-time employees working in one shop, at least approximately 1,600 vape shop workers are occupationally exposed to e-cig-related air contaminants in Southern California. Vape shop retailers perceive e-cigs as safe, but evidence has emerged of e-cig aerosol's potential health impacts, which raises concern about exposure levels among workers where vaping occurs. As small businesses, they most likely have little access to health and safety specialists and may have little information on protecting their workers from occupational air contaminant exposure. Before regulatory measures can be considered, knowledge about the pollutant levels from exhaled e-cig aerosols inside these shops, the level of exposure experienced by workers, and influencing factors are needed. To address these knowledge gaps, this study was conducted to characterize the indoor air quality of vape shops, investigate exhaled e-cig aerosols as a potential occupational hazard, and identify potential controls for effectively reducing the exhaled e-cig aerosol levels in the vape shop and improving the associated indoor air quality.

In Chapter 2, indoor air quality surveys of representative vape shops in the Greater LA area were conducted to examine vape shops as potential high-exposure workplaces, measuring

fine and ultrafine particles attributed to exhaled e-cig aerosols. An exploratory study, Chapter 3 evaluates exhaled e-cig aerosols as an occupational exposure in vape shops by using nicotine as a tracer. E-cig-using workers can be exposed to mainstream and exhaled e-cig aerosols and non-e-cig-using workers can be exposed to just exhaled e-cig aerosols. Measurement and comparison of urinary cotinine (a primary metabolite of nicotine) levels between e-cig- and non-e-cig-using workers may help weight the relative contribution of exhaled e-cig aerosols to the total e-cig aerosol exposure experienced by a vape shop worker during work. Furthermore, Chapter 3 investigates the potential health impact from exhaled e-cig aerosol exposure by measuring select urinary markers of oxidative stress, systemic inflammation, and metal toxicity/antioxidant activity and assessing their association with cotinine. Chapter 4 prescribes options for effective mitigation of workplace exposure to pollutants from exhaled e-cig aerosols by testing ventilation and portable filtration strategies in vape shops.

Overall, this study assesses exhaled e-cig aerosols as an occupational exposure in Southern California vape shops and reduces this exposure using air mitigation strategies. Results of this study would inform employers and policymakers on the need for implementing controls to reduce occupational e-cig aerosol exposure.

2. FINE AND ULTRAFINE PARTICLES CONCENTRATIONS IN VAPE SHOPS

2.1. Abstract

Vape shops are widespread due to the popularity of electronic cigarettes (e-cigs) as an alternative to tobacco cigarettes. In this study, sixty-seven Southern California vape shops were randomly surveyed for building characteristics, ventilation, and business patterns. Based on the survey results, six representative shops were recruited for real-time measurements of indoor and outdoor fine and ultrafine particles concentrations on a busy and less busy day. Occupancy, vaping frequency, and opening and closing of doors were recorded, and shop air exchange rate was determined. Indoor CO_2, relative humidity, and temperature were also recorded. In addition, simultaneous measurements were taken at increasing distances away from a vaping area to assess the mixing and spatial profiles of particle levels inside the shops. During active vaping, real-time indoor particle number concentration and gravimetric-corrected $PM_{2.5}$ mass concentration across the six vape shops varied from 1.3×10^4 to 4.8×10^5 particles/cm^3 and from 15.5 to 37,500 μg/m^3, respectively. The spatial profiles of particle number and mass were more uniformly mixed than expected in an indoor environment. Total vaping frequency was the main predictor of particle concentrations inside the vape shops when indoor-outdoor particle mass transfer is minimal (doors closed).

2.2. Introduction

Vaping, the inhalation and exhalation of aerosolized e-liquid produced by electronic cigarettes (e-cigs), is a popular nicotine delivery alternative to tobacco smoking. By 2025, the global e-cig market is expected to grow over $86 billion, of which $16 billion will be in the

United States (BIS Research, 2018). Contributing to this market are vape shops, stores that exclusively sell vape products and also function as a lounge where customers can bring their own e-cig devices for repair, sample e-liquids, and vape. Retail outlets, which include vape shops and convenience stores, generate more than 60% of the revenue and remain the primary form of distribution for e-cig products (BIS Research, 2018). A March 2019 search on Yelp.com showed that there were 3,344 vape shops in Southern California alone. Many cities have banned vaping in public areas (ANRF, 2019), but the vape shop is one of few public spaces where unlimited vaping is permitted.

Studies have shown that mainstream e-cig aerosols contain substantial amounts of nicotine and particulate matter (PM) in the fine (aerodynamic diameter $\leq$ 2.5 μm) and ultrafine (diameter $\leq$ 100 nm) size range (McAuley et al., 2012; Czogala et al., 2014; Fromme and Schober, 2015; Zhao et al., 2016). Furthermore, carbonyl compounds possibly formed from the thermal dehydration of glycols and glycerin in the e-liquid, other volatile organic compounds, and heavy metals have also been detected in mainstream e-cig aerosol (McAuley et al., 2012; Ohta et al., 2011; Williams et al., 2013; Mikheev et al., 2016). PM concentrations and size distribution reported for exhaled e-cig aerosols differ from these measurements reported for mainstream e-cig aerosols. A study by Schripp et al. (2013) showed that exhaled e-cig aerosols from a single e-cig user have a real-time bimodal particle size distribution at 30 and 100 nm, compared to a bimodal particle size distribution that varied at 11 – 25 and 96 – 175 nm for mainstream e-cig particles (Mikheev et al., 2016). Particle number concentrations (PNCs) ranging from 7.7×10^7 to 8.4×10^9 particles/cm^3 in undiluted mainstream e-cig aerosols have been reported (Zhao et al., 2016; Mikheev et al., 2016; Schripp et al., 2013; Fuoco et al., 2014; Ingebrethsen et al., 2012). However, in a study conducted by Czogala et al. (2014) in which an e-

cig user vaped in a large room, the highest PNC observed was approximately 1.0×10^5 particles/cm^3, almost four orders of magnitude less than the PNCs observed in mainstream e-cig aerosol. Exposure chamber experiments, generally consisting of a cigarette-like or pen-style e-cig puffed by a machine on a controlled puff regimen, have reported mean PM$_{2.5}$ mass concentrations of 43 – 184 µg/m^3 in mainstream e-cig emissions (Czogala et al., 2014; Pellegrino et al., 2012; Lee et al., 2017). Experiments where e-cig aerosols were exhaled by a single user vaping a similar e-cig freely or with a consistent puff pattern have reported mean PM$_{2.5}$ mass concentrations up to 375 µg/m^3 (Czogala et al., 2014; Zhao et al., 2017). PM concentrations measured in tank-style e-cig emissions and associated exhaled aerosols were generally higher (Melstrom et al., 2017). These quantitative differences between mainstream and exhaled e-cig particles prompted desire to study the air quality impact of e-cigs in real indoor environments.

Zhao et al. (2017) was the first study to characterize the temporal and spatial profiles of exhaled e-cig particles produced by an e-cig user in a small patient room. They recorded PNC and PM$_{2.5}$ concentrations as high as 10^5 particles/cm^3 and 3,000 µg/m^3, respectively. However, the particle concentrations and size distributions measured were a result of the e-cig user following a uniform puffing schedule in a reserved indoor setting. An accurate understanding of the characteristics of e-cig-related air contaminants is still lacking for everyday public, commercial settings where vaping is not controlled.

No building surveys or indoor air quality studies of vape shops have been published. Before regulatory measures can be considered, knowledge about the contaminant levels from exhaled e-cig aerosols inside these shops and influencing factors are needed. In this study, sixty-seven vape shops were surveyed for their physical and business characteristics such as shop size and days of high and low customer traffic. Real-time indoor measurements of PNC, PM$_{2.5}$, and

CO_2 as well as particle size distribution were measured at six shops that possessed the characteristics of interest as gathered from the survey. These data were also used to assess the spatial distribution with respect to proximity to vaping activity and potential predictors of particle levels inside vape shops.

2.3. Material and Methods

2.3.1. Vape Shop Survey and Sampling Site Selection

Vape shops in the Greater Los Angeles area were identified from a Yelp.com search (2016) using the keywords "vape shop." From these identified vape shops, walk-in surveys were conducted at sixty-seven randomly selected shops. The surveys were conducted from May 2016 to February 2017. During the walk-ins, information on the shop volume (m^3), use of central ventilation, and building location were collected in order to identify representative shops for follow-up studies and possible predictors of e-cig-related particle exposure. Furthermore, vape shop owners and/or managers received informational brochures about the study and were asked if they were interested in having their shop be a potential location for indoor air sampling. Owners or managers that expressed interest were asked to provide consent to participating in the study by signing an agreement letter. Due to survey results showing binary trends for the categories of information collected (e.g., large- or small-sized shop, with or without central ventilation, shop location is storefront or inside a plaza), representative shops would possess at least one characteristic observed in each category (i.e., a small shop located in a shopping plaza and uses central ventilation or a large storefront shop that does not use central ventilation). Out of the sixty-seven surveyed shops, seventeen agreed to participate in an indoor air study, and six were chosen for indoor air sampling. The shops that did not agree cited fear of regulation, distraction to customers, and risk of losing business.

2.3.2. Sampling Protocol

At least two indoor air sampling sessions were conducted at each of the six vape shops (shop IDs A – F): one on a busy day (high customer traffic, typically Thursday through Saturday) and another on a less busy day (low customer traffic, typically Sunday through Wednesday), as informed by vape shop personnel during the surveys. Most sampling sessions were 8 – 10 hours, spanning from opening to closing of business, with the exception of shops D and E, where sampling sessions were four hours. Number and duration of sampling sessions were dependent on the discretion of the shop. Temporal profiles of PNC and $PM_{2.5}$ mass concentrations were investigated in all six shops. Mixing and spatial profiles of these concentrations were investigated in shops A, B, C and E. Particle size distributions were measured in shop C. Throughout the sampling session, additional potential PM concentration predictors were visually observed and recorded by a research team member, beginning from the closest top or bottom of the hour: (1) tally of vaping occupants per 30-minute period; (2) tally of e-cig puffs by vaping occupants per 30-minute period (total vaping frequency, TVF); (3) opening and closing of doors; and (4) any other particle emission source or activity.

2.3.2.1 Measurement of Particle Number, $PM_{2.5}$, and CO_2 Concentrations

Condensation Particle Counter (CPC) Model 3007 (TSI Inc., Shoreview, MN, USA) and DustTrak II Aerosol Monitor 8532 (TSI Inc., Shoreview, MN, USA) were used to measure real-time PNC and $PM_{2.5}$ mass concentrations, respectively, at 1-second (s) intervals. A set of instruments was placed at heights ranging from 0.79 to 1.07 m from the floor and within 1.2 m away from the vaping bar, where vaping activity was most prevalent in the shop. Distances between the sample intake and customers at the bar ranged from 1.1 to 6.1 m. To compare indoor and outdoor particle concentrations, another set of instruments was placed outside of the shop to

measure the outdoor particle concentrations simultaneously. To investigate indoor mixing and the spatiality of exhaled e-cig particles, simultaneous measurements were taken where one set of instruments was placed within the personal space of a vaping source while another set was placed as far as the public space of a vaping source (see Section 2.4.4 for details on definition of personal and public spaces). Placement of instruments for temporal and spatial profile measurements in the shop was made with considerations to instruments not blocking customer or employee traffic and availability of nearby electric outlets. For data reduction and analysis, all particle concentration readings were averaged to 1-minute data points. Indoor carbon dioxide (CO_2) concentration, temperature, and relative humidity (RH) were measured at 1-minute intervals using Q-Trak Plus Model 8554 (TSI Inc., Shoreview, MN, USA) placed with the instruments in the high-activity area. Room air exchange rate (AER) was calculated by the CO_2 tracer gas decay method (ASTM, 1995). Section S1 in the Appendix – Supplemental Information details the AER calculation method.

2.3.2.2 Measurement of Particle Size Distribution

In addition to the instruments previously described, particle size distributions were measured by a Scanning Mobility Particle Sizer (SMPS) 3080 (TSI Inc., Shoreview, MN, USA) (0.6 L/minute sampling flow rate; 100-second up scan, 20-second down scan) and an Aerodynamic Particle Sizer (APS) 3321 (TSI Inc., Shoreview, MN, USA) in vape shop C with the sample inlets collocated with the real-time particle monitors. The particle size ranges measured by the SMPS and APS were 7 – 289 nm and 0.5 – 19.8 μm, respectively. Using the TSI Data Merge Software Module (TSI Inc., Shoreview, MN), which converts electronic mobility diameter measured by the SMPS to aerodynamic diameter, SMPS data were merged

with APS data and fit into two- or three mode-distributions, resulting in composite size distributions.

<u>*2.3.2.3 Quality Control/Quality Assurance for Data Collection and Analysis*</u>

To ensure that data from multiple units of the CPC and DustTrak II were analogous, 30-minute collocation tests were conducted before and after the sampling campaign. The sample inlets or sensors of two units of the same instrument were put together in one location, and the units recorded concentrations at 1-s intervals simultaneously. Regression results from the collocation tests were used to correct all particle data in this study (Tables S1 – S2 in Appendix – Supplemental Information). Before each sampling session, the instruments were zero-checked, and units of the same instrument were collocated for three minutes to check that there were no major discrepancies in concentration readings compared to those of the collocation tests.

Gravimetric calibration of DustTrak II $PM_{2.5}$ measurements in chamber-puffed e-cig aerosols were conducted in a previous study, which found the calibration factor to be 0.27 (Zhao et al., 2017). Following the same protocol, gravimetric calibration of the DustTrak II readings were performed inside selected vape shops during weekend business hours. The field calibration factor was determined to be 0.25 ± 0.01 ($R^2 = 0.95$) with a 95% confidence interval (CI) of 0.22 – 0.28. This calibration factor is similar to the previously determined factor and was used to correct all indoor DustTrak II data. The rescaled $PM_{2.5}$ concentrations reflect the expected gravimetrically measured levels after sampling and post-conditioning of filters. They are likely to underestimate the actual environmental concentrations due to the evaporation losses during filter sampling, which currently cannot be resolved. Future studies examining possible correction methods that account for evaporation losses during sampling would be useful. A calibration factor of 0.48 ± 0.03 ($R^2 = 0.98$) with 95% CI of 0.41 – 0.55, determined from gravimetric

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analysis of outdoor $PM_{2.5}$, was used to correct all outdoor DustTrak II data. Field calibration methods and results are provided in Section S2 and Fig. S1 of Appendix – Supplemental Information.

Synced SMPS- and APS-measured particle size distributions were merged and composited using the TSI Data Merge Software Module. Then, the composite total PNCs and mass concentrations up to 2.5 μm were cross-checked with the collocated CPC data (lower limit at 0.01 μm particle size) and gravimetric-corrected DustTrak II data, respectively. Composite total PNCs were comparable (factor of 1.00 with 95% CI of 0.97 – 1.03) to the collocated CPC data (R^2 = 0.82). Composite $PM_{2.5}$ mass concentrations were lower than the (gravimetric-corrected) collocated DustTrak II data by a factor of 4.15 (R^2 = 0.62) with 95% CI of 3.82 – 4.48. A summary of the particle size distribution cross-checks is provided in Fig. S2 of Appendix – Supplemental Information.

2.3.3. Data and Statistical Analysis

The datasets for particle and CO_2 concentrations failed the Kolmogorov-Smirnov and Shapiro-Wilk tests for normality ($p < 0.05$), respectively, so the Kruskal-Wallis ANOVA on Ranks was used to compare indoor pollutant concentrations grouped by categories such as ventilation type characterizing the vape shops. Statistical significance was taken at $p < 0.05$. Linear regression analysis was used to determine correlation between background-subtracted particle concentrations and average occupancy and TVF data from all vape shops sampled. To assess indoor mixing and effects of proximity to vaping on particle concentrations, the 1-minute averaged concentrations at the two sampling distances were corrected for background. Computation of the summary statistics for particle concentration and indoor air quality data,

normality and significance tests, and linear regression were performed using R 3.2.2. All figures were generated with Sigmaplot 12.5 (Systat Software Inc., San Jose, CA).

2.4. Results and Discussion

2.4.1. Vape Shop Building and Business Characteristics

Fig. 2.1 presents the results of the vape shop survey. Of the sixty-seven shops surveyed, majority were located in a plaza and were of small size ($\leq$250 m^3). Eighty percent of the shops claimed to have central ventilation installed, of which only 32% were working during the walk-in survey. Twenty percent did not have central ventilation installed in the shop and instead had a commercial A/C unit or fan that just circulates the indoor air. A common reason for the lack of working ventilation was that stagnant indoor air conditions allowed for shops to get cloudy with e-cig aerosol and gave an optimal environment for doing vape tricks (e.g. blowing clouds or smoke rings). More than 90% of the shops surveyed were open daily, 7 days a week, for at least 10 hours a day.

Vape shops located in multi-unit commercial buildings, as is typical in plazas, tend to have larger air handling systems that are connected to neighboring shops, putting these adjacent businesses at possible risk of exposure to e-cig-related air contaminants. All vape shops surveyed were adjacent to at least one other business (e.g. retail shops, office spaces, beauty salons, restaurants, and tutoring centers). After the survey, six of the surveyed shops were recruited for indoor air sampling. Table 2.1 presents the summary of the shops' characteristics, including AER, average TVF, and ventilation type used.

a)

Building Location
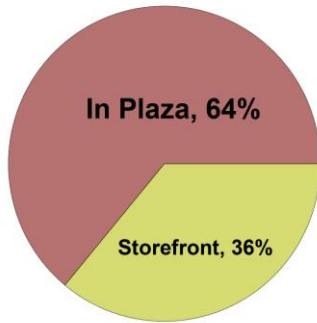
b)

Shop Size
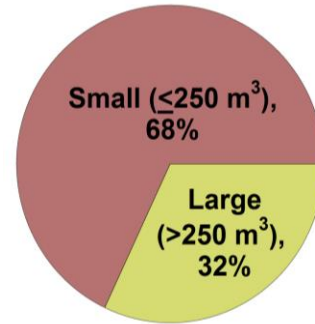
c)

Central Ventilation
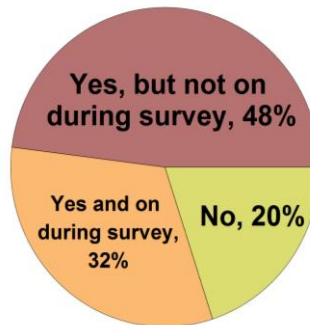
Figure 2.1. Southern California vape shop survey results (n = 67). Observations of (a) where the shop was located (e.g. in a plaza or storefront), (b) shop volume (m³), and (c) whether or not the shop had central ventilation were recorded.

Table 2.1. Characteristics of the six studied vape shops

Vape Shop	Location	Shop Size (m³)	Ventilation Type	AER (h⁻¹)	Avg TVF (#/30 min)
A	Storefront	318	A/C	0.2 ± 0.03	88 ± 96
B	Storefront	262	Central ventilation	4.8 ± 0.49	19 ± 16
C	In plaza	244	Natural ventilation[b]	1.7 ± 0.07	16 ± 15
D	Storefront	323	Natural ventilation[b]	NA[a]	9 ± 5
E	In plaza	168	No ventilation	0.2 ± 0.08	91 ± 25
F	Storefront	175	A/C	0.1 ± 0.02	13 ± 3

[a] Due to technical malfunction of the Q-Trak Plus, CO_2 decay could not be measured to calculate AER.
[b] Doors open during business hours

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2.4.2. Particle Emissions in Vape Shops from Vaping

Vaping is the primary indoor source for particle emissions in the vape shops studied. As seen in Fig. 2.2, the temporal profiles of real-time indoor concentrations of particle number and $PM_{2.5}$ were dynamic inside the vape shop. The sharp peaks in the figure indicate particle emissions during active vaping. For instance, in Fig. 2.2a beginning at the 15:27:00 mark, the indoor background PNC (9.2×10^3 particles/cm^3) spiked up by 11 times (1.0×10^5 particles/cm^3) in two minutes after active vaping, and then fell to background level after four minutes. Likewise, in Fig. 2.2b beginning at the 15:02:00 mark, the indoor background $PM_{2.5}$ mass concentration (23.4 µg/m^3) spiked up by 22 times (515 µg/m^3) in two minutes, and then fell to background level after three minutes. Since the shop door was open, the decay of exhaled e-cig particles was quick due to dilution from outdoor air, coupled with particle surface deposition, coagulation, and evaporation as a result of the high vapor pressures of the e-liquid mixture containing propylene glycol (Ingebrethsen et al., 2012; Zhao et al., 2017). The background particle concentration increase from the moment of no active vaping to after an e-cig puff indicates that there may be residual exhaled e-cig particles that were less volatile, possibly glycerin-based as its vapor pressure (0.01 Pa 25 ºC) is much lower than that of propylene glycol (20 Pa at 25 ºC). However, when the shop door was closed, the PNC and $PM_{2.5}$ decayed and remained at levels as high as 2.8×10^4 particles/cm^3 and 370 µg/m^3 after active vaping. By keeping the door closed, the dilution of exhaled e-cig particles from outdoor air was reduced, allowing for these particles to persist in the shop after continuous vaping and background particle levels to increase. Combined with the increased partial pressure of gas-phase e-cig aerosol in the indoor air and slight increased indoor RH (29.1% when the door was open to 35.6% after the door was closed), the evaporation rate of exhaled e-cig particles was likely decreased (Zhao et al., 2017; Hinds, 1999; Lee et al., 2017).

a)

b)
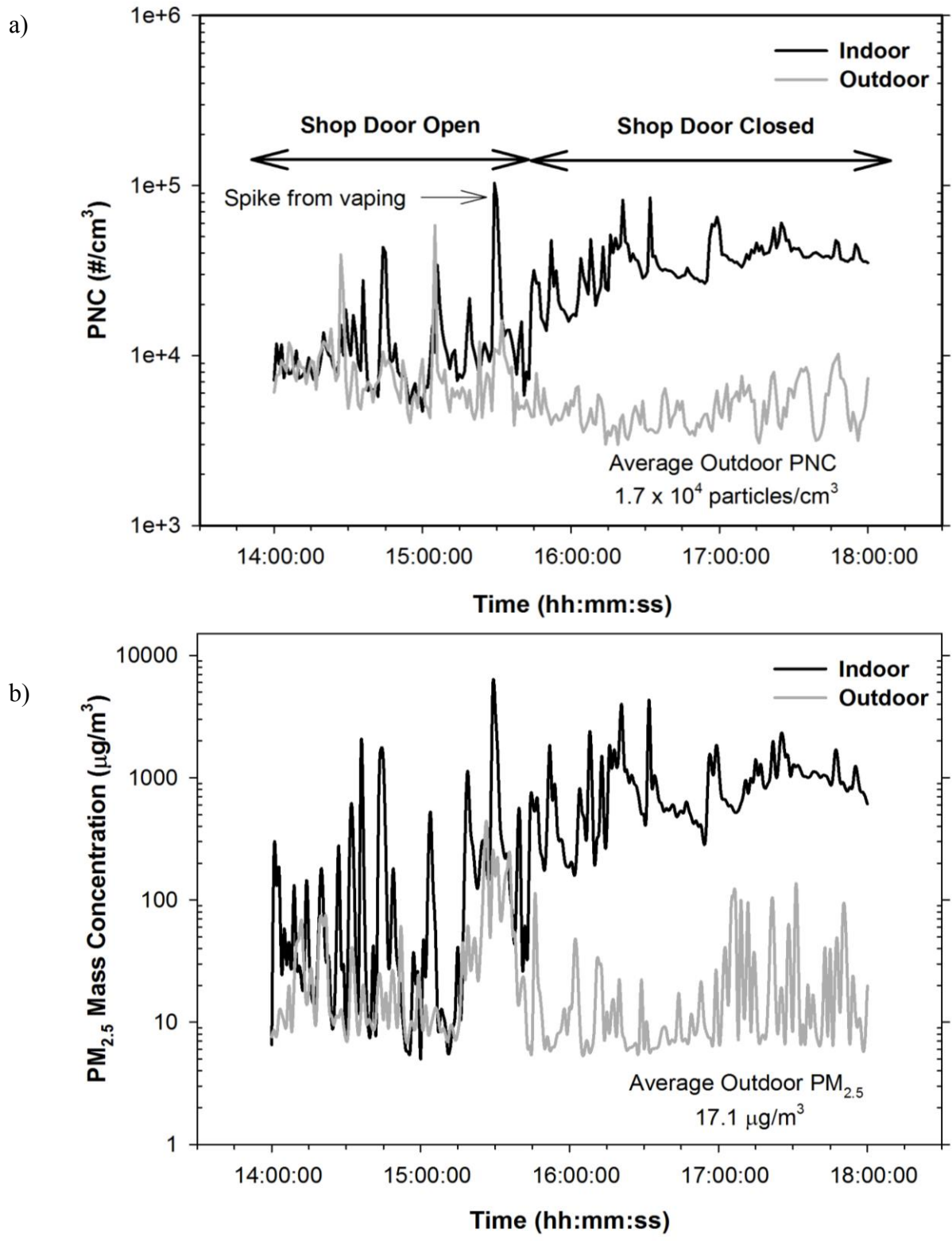
Figure 2.2. Temporal profiles of (a) PNC and (b) PM$_{2.5}$ mass concentration, measured simultaneously, in vape shop F on a Monday. Indoor and outdoor concentrations are shown in black and gray, respectively.

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Composition of the vaped e-liquid, i.e. ratio of propylene glycol to glycerin, may also be an influential factor in the evaporation of exhaled e-cig particles. Systematic approaches to determine how e-liquid composition affects exhaled e-cig particle decay are needed in future studies.

2.4.3. Particle Concentrations in Vape Shops and their Predictors

Table S3 in the Appendix – Supplemental Information presents the summary statistics for indoor and outdoor particle and CO_2 concentrations plus additional indoor air quality parameters measured for each vape shop on a busy day and on a less busy day. While there was no vaping, indoor PNCs ranged from 5.5×10^3 to 3.3×10^4 particles/cm^3 and indoor $PM_{2.5}$ concentrations ranged from 3.2 to 39 μg/m^3 among the six studied vape shops. During active vaping, indoor PNCs ranged from 1.3×10^4 to 4.8×10^5 particles/cm^3 and indoor $PM_{2.5}$ concentrations ranged from 15.5 to 37,500 μg/m^3 among the studied shops. Indoor particle concentrations during the sampling sessions were, on average, 1.5 and 22 times higher than the outdoor concentrations for PNC and $PM_{2.5}$, respectively. When shop doors were closed, the average outdoor PNC and $PM_{2.5}$ mass concentrations varied from 8.5×10^3 to 5.6×10^4 particles/cm^3 and 7.5 to 72 μg/m^3, respectively. Outdoor concentrations exceeding the background and tracking with indoor concentrations occurred while the shop doors were open, showing that exhaled e-cig aerosols coming from indoors affected the outdoor readings. Further, while shop doors were closed, there were instances of a spike in outdoor PNC shortly after a spike in indoor PNC. These were most likely a result of indoor particles venturing outside due to an indoor-to-outdoor pressure differential when a customer opens the door. During these periods altogether, the range of average outdoor PNCs did not increase (1.1×10^3 to 3.1×10^4 particles/cm^3), but the range of average outdoor $PM_{2.5}$ mass concentrations increased up to 271 μg/m^3 (corrected with 0.25

calibration factor). With this transport of exhaled e-cig particles to an outdoor environment, passersby and neighboring business patrons may also be at risk of exposure.

Fig. 2.3 presents the distributions of PNC and $PM_{2.5}$ data collected across the studied vape shops. There is currently no standard for UF particles or particle number, but PNCs measured in the vape shops were comparable to those previously reported in smoking bars and rooms. Overall, the mean PNC measured in the shops during the busy day, 6.9×10^4 particles/cm^3 (geometric mean 5.4×10^4 particles/cm^3), was slightly higher than the mean reported in 14 smoking bars in Rome, Italy (6.1×10^4 particles/cm^3 (geometric mean 4.9×10^4 particles/cm^3)) (Valente et al., 2007), but 39% lower than the mean PNC reported in 59 Viennese smoking venues (1.1×10^5 particles/cm^3) (Neuberger et al., 2013) (Fig. 2.3a). The overall mean PNC measured on the less busy days was only 3.9×10^4 particles/cm^3 (geometric mean 2.6×10^4 particles/cm^3). As for $PM_{2.5}$, the mean concentrations measured during the busy and less busy days in the studied vape shops were 846 μg/m^3 (geometric mean 577 μg/m^3) and 302 μg/m^3 (geometric mean 155 μg/m^3), respectively, which were 24 (16) and 9 (4) times greater than the outdoor U.S. Environmental Protection Agency 24-hour standard for $PM_{2.5}$ (35 μg/m^3) (U.S. EPA, 2016), respectively (Fig. 2.3b). At these average indoor levels, the visibility was quite low, equivalent to a visual range of less than 1 km (Lipsett et al., 2008). The mean $PM_{2.5}$ concentration measured in the vape shops over all sampling days (836 μg/m^3 (geometric mean 385 μg/m^3)) exceeded most mean $PM_{2.5}$ levels reported in various bars and hookah lounges by at least 2.2 times (Ott et al., 1996; Repace, 2004; Repace et al., 2006; Waring and Siegel, 2007; Bohac et al., 2010; Fiala et al., 2012; Cobb et al., 2013). One study conducted at eight New York City hookah bars, however, reported an overall mean $PM_{2.5}$ concentration that was 41% higher than the mean $PM_{2.5}$ concentration among the studied vape shops (Zhou et al., 2015) (Fig. 2.3b).

a)

b)
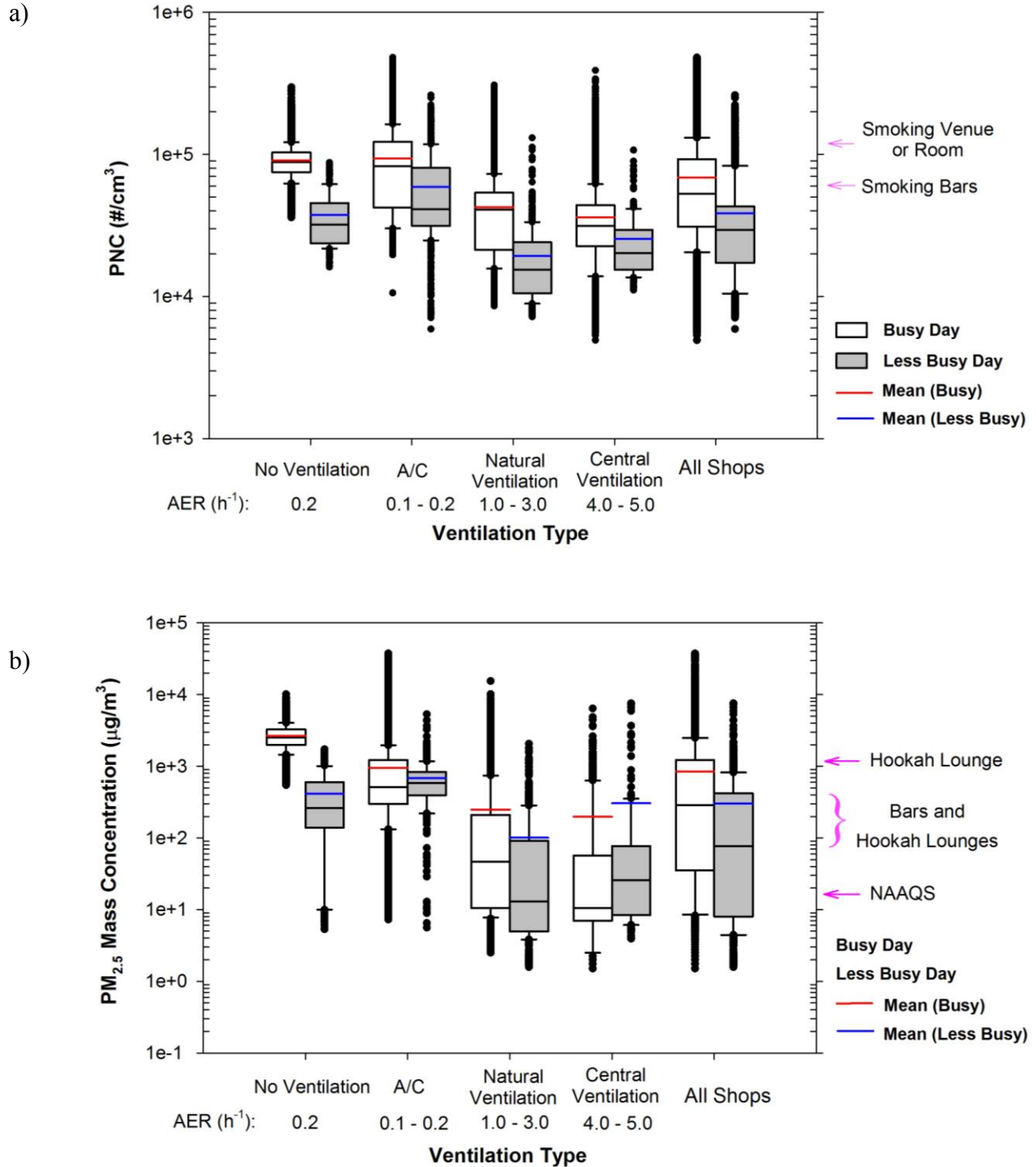
Figure 2.3. Box plots summarizing (a) PNC and (b) PM$_{2.5}$ mass concentrations measured during a busy day and less busy day for all six shops and categorized by ventilation type. Shop AERs correspond to ventilation type. The pink arrows point at mean particle concentrations reported in literature for comparable indoor smoking environments.

Only one study has measured $PM_{2.5}$ from vaping emissions in a public venue. Soule et al. (2016) measured $PM_{2.5}$ concentrations over six time points during a two-day e-cig event inside a hotel, and reported that the average mean concentration in the main event room was 607 $\mu g/m^3$ (after correction using a calibration factor of 0.32 for cigarette secondhand smoke; using a calibration factor for exhaled e-cig aerosols would yield a lower concentration). Due to the hotel event room being much larger in size (4,023 m^3) than the vape shops (average 248 m^3), the average mean $PM_{2.5}$ concentration reported during the e-cig event would be lower than the average mean among the shops studied (941 $\mu g/m^3$), despite fewer people actively vaping in the shops (1 – 13) than at the hotel event (59 – 86). Along with shop AERs probably being lower than that of the hotel, particulate concentrations from vaping emissions would increase in more intimate indoor settings.

2.4.3.1. Air exchange rate (AER)

The results of the vape shop survey (Section 2.4.1) identified potential predictors of indoor exhaled e-cig particulate concentrations. In Fig. 2.3, indoor PNC and $PM_{2.5}$ measurements collected in the studied vape shops are presented with respect to ventilation type, split by busy day and less busy day and represented by AER. There were four ventilation categories observed: (1) no ventilation (shop E); (2) A/C (window unit in shop A and rooftop unit in shop F); (3) natural ventilation (shops C and D); and (4) central ventilation (shop B). As the AER increases from no ventilation to central ventilation, average busy-day $PM_{2.5}$ concentrations decreased for each step. Significant difference was found among the four groups of busy-day $PM_{2.5}$ measurements (Kruskal-Wallis, $p < 0.05$). For PNCs measured on a busy day, the average concentration in the group with no ventilation was slightly lower than the average of the group with A/C (~2,950 particles/cm^3 more), but the average concentrations decreased for subsequent

groups. The AERs in the shops with A/C were as low as the AER in the shop with no ventilation, indicating that the A/C in those shops did not effectively increase outdoor-to-indoor air exchange. The four groups of busy-day PNC measurements were found to be significantly different (Kruskal-Wallis, $p<0.05$). Average CO_2 levels also followed a similar trend when grouped by ventilation type. Median CO_2 level measured among shops using A/C was significantly higher than the levels measured in shops using natural or central ventilation (Kruskal-Wallis, $p<0.05$).

Due to a small number of sampled vape shops, however, significant linear correlations between real-time CO_2 and PM concentrations could not be observed. Although lower AERs in the shop can increase particle levels, CO_2 may not be a strong predictor for exhaled e-cig particle levels. PNCs measured on a busy day were higher than those measured on a less busy day, indicating elevated particle concentrations presumably because vaping emissions are higher when there is more customer traffic, increasing the number of occupants actively vaping in the shop. This general trend was also observed for $PM_{2.5}$ concentrations, except for the data in the central ventilation category. For vape shop B, there was higher vaping frequency reported on the less busy day than on the busy day, even when the number of customers was less, explaining the higher average $PM_{2.5}$ during the sampling period.

2.4.3.2. Total vaping frequency (TVF)

On a busy day among the vape shops, where the average puff count range was 13 – 191, the range of average PNCs was $1.6×10^4 – 1.3×10^5$ particles/cm^3 and the range of average $PM_{2.5}$ concentrations was 10.6 – 2,676 µg/m^3. On a less busy day among the vape shops, where the average puff count range was 5 – 49, the range of average PNCs was $1.2×10^4 – 6.9×10^4$ particles/cm^3 and the range of average $PM_{2.5}$ concentrations was 8.1 – 687 µg/m^3. Given the

observation that particle concentrations were generally higher on a day with high customer traffic than on a day with low customer traffic, occupancy (# of people vaping per 30 minutes) was initially analyzed as a predictor of particle exposure in the studied vape shops. In Figs. 2.4a-b, linear regression demonstrated that occupancy was a statistically significant but weak predictor of indoor PNC and $PM_{2.5}$ concentrations while shop doors were closed and open ($R^2 = 0.24 – 0.30$, $p<0.001$). Then, total vaping frequency, defined as the total number of puffs within a given period of time, (TVF per 30 minutes) was analyzed as a predictor. As seen in Figs. 2.4c-d, TVF had a stronger positive correlation with indoor PNC and $PM_{2.5}$ concentrations while shop doors were closed ($R^2 = 0.55 – 0.56$, $p<0.001$). While shop doors were open, TVF had a weaker positive correlation with indoor PNC and $PM_{2.5}$ concentrations ($R^2 = 0.15 – 0.16$, $p\leq0.001$).

Present with both occupancy and TVF as predictors of the indoor particle concentrations, the slope of the regression for doors closed was greater than that for doors open, with the difference in slopes being much greater in the TVF plots than in the occupancy plots. Unlike for TVF, the strengths (R^2) of the linear relationship between the indoor concentrations and occupancy during closed door versus open door were similar, further supporting TVF as the better indoor particle concentration predictor. Occupancy being a weaker indoor particle concentration predictor in vape shops aligns with the finding reported in Section 2.4.3.1 that CO_2 levels did not significantly correlate with particle concentrations. As the primary source of CO_2 in the vape shops, occupancy is not necessarily proportional to vaping frequency as not all occupants are actively vaping. CO_2 levels reflect the occupancy at a certain time in the shop rather than the strength of the exhaled e-cig aerosol emissions (i.e. the frequency and magnitude of exhaled puffs). Closing entrances and decreasing the air exchange in a shop can increase the
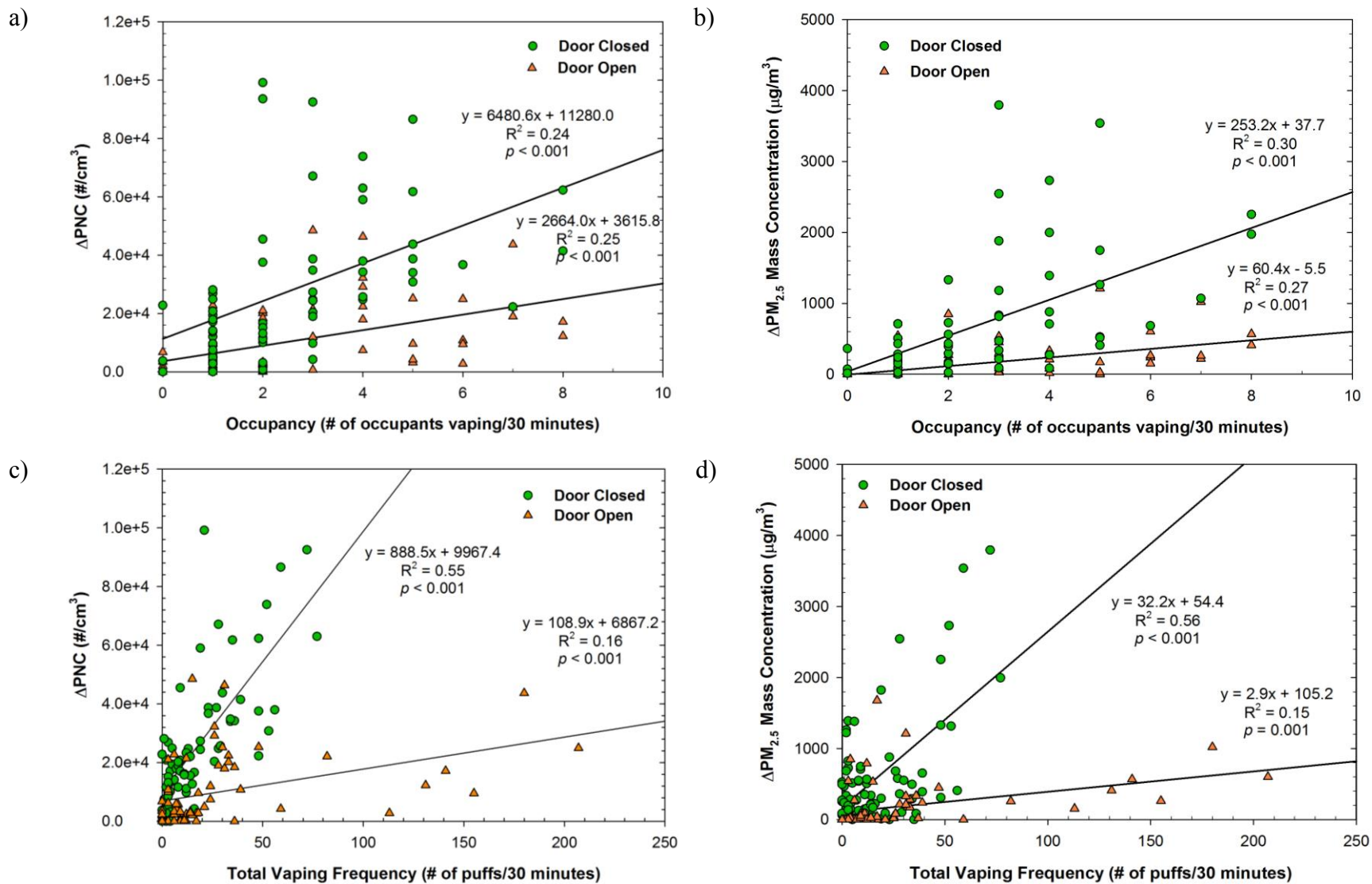
Figure 2.4. Relationships between background-corrected PNC and PM₂.₅ concentrations and (a – b) occupancy, (c – d) total vaping frequency (TVF)

effect of TVF on exhaled e-cig particle levels inside vape shops. On the other hand, opening entrances increases the room air exchange and allows infiltration of outdoor particles into the shop, decreasing particle levels at the same TVF. Under low ventilation conditions with minimal introduction of particles from other indoor and outdoor sources, TVF serves as the primary predictor of indoor particle concentrations due to vaping.

2.4.4. Effects of Proximity to Vaping on Particulate Concentrations

Particulate concentrations at distances closer and farther from a vaping customer were measured in four vape shops. Distances were designated based on the following degrees of proximity from a person: (1) personal space (0.45 to <1.2 m); (2) social space (1.2 to <3.6 m); and (3) public space (3.6 m and beyond) (Hall, 1966). Concentrations were compared at points within the personal space to public space except in shop B, where concentrations were measured within the personal space to social space. Mean PNC and PM$_{2.5}$ concentrations measured in the shops within the personal space of a vaping source were $2.0 - 12.6 \times 10^4$ particles/cm^3 and $102 - 1,858$ µg/m^3, respectively. Simultaneously from the social space over to the public space of the vaping source, mean PNC and PM$_{2.5}$ concentrations were $0.6 - 8.6 \times 10^4$ particles/cm^3 and $34 - 1,375$ µg/m^3, respectively. The observed concentration decrease from the personal space to the social/public space suggests a proximity effect (Furtaw et al., 1996) with exhaled e-cig particle concentrations. Fig. 2.5 plots this study's mean particle number and PM$_{2.5}$ mass concentrations measured over increasing distance from a vaping source.

Previous studies have reported low indoor PM concentrations (less than 3×10^3 particles/cm^3 or under 10 µg/m^3 for PM$_{2.5}$ above background) within the social space of an e-cig user, owing to the rapid volatilization of exhaled e-cig aerosols (Zhao et al., 2017; Fernandez et al., 2015; Ruprecht et al., 2014). However, high concentrations were still measured more than 4

a)

b)
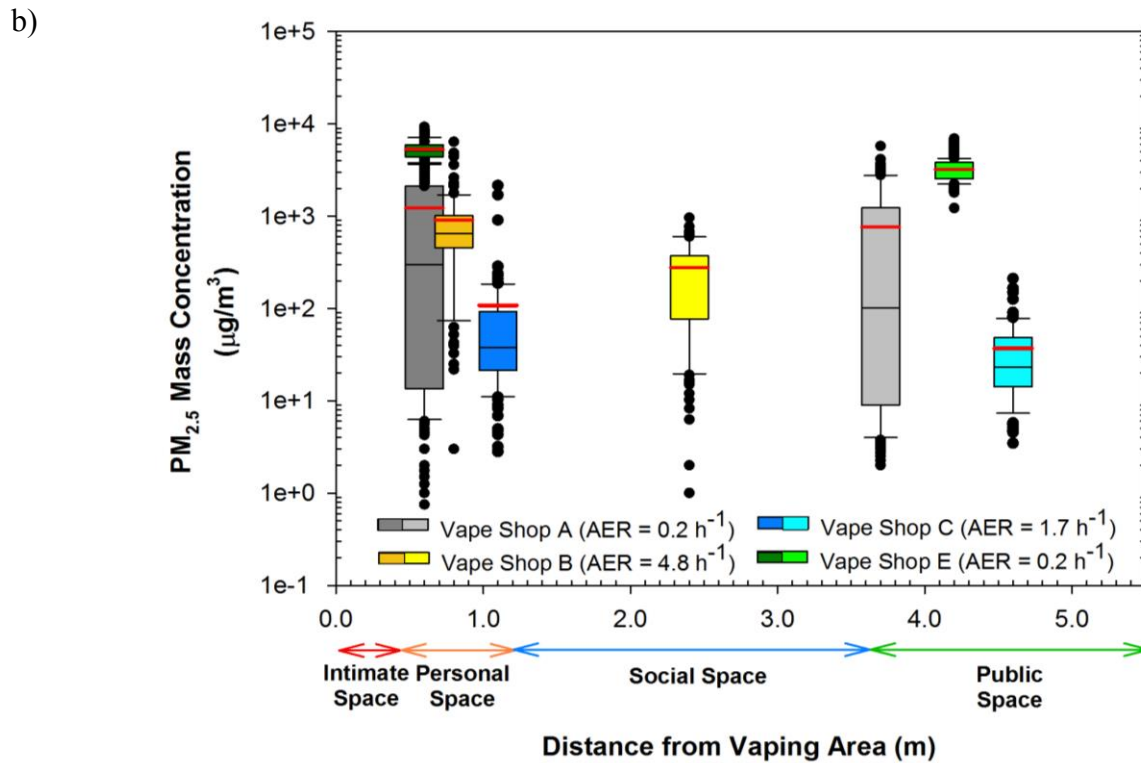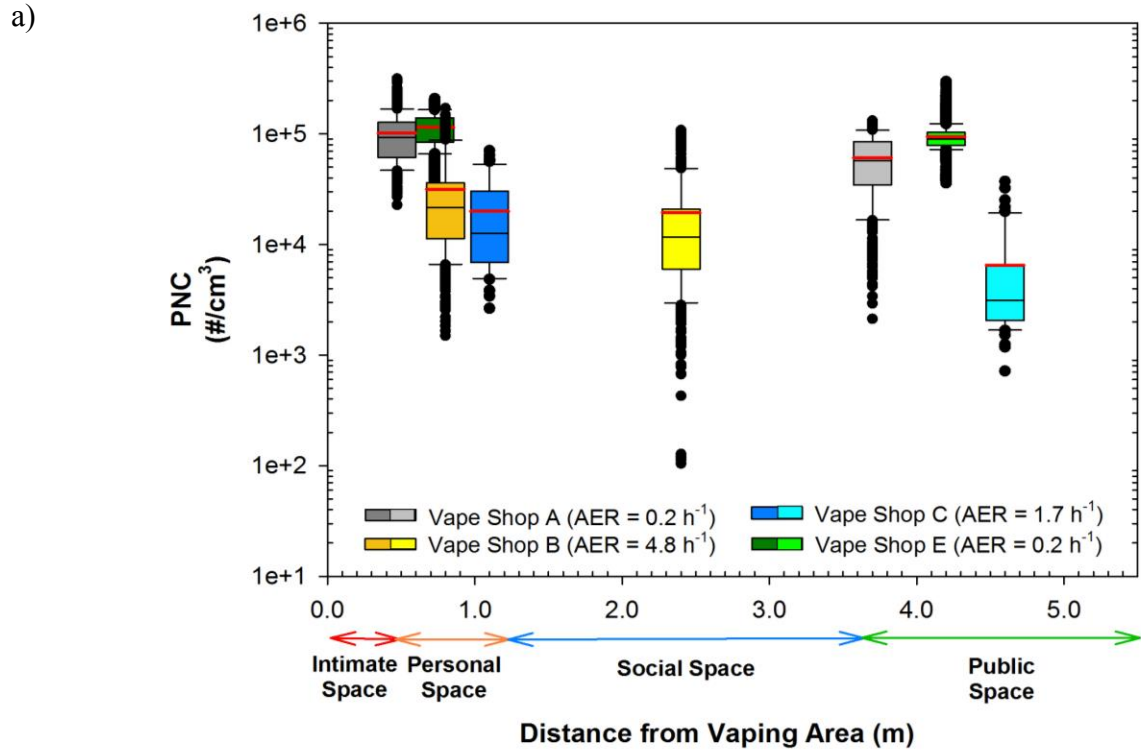
Figure 2.5. Particle number (a) and PM₂.₅ (b) concentrations at personal, social, and public distances away from vaping activity. From vaping activity, concentrations were measured at 0.6 and 3.7 m away in shop A, 0.8 and 2.4 m away in vape shop B, 1.1 and 4.6 m away in vape shop C, and 0.6 and 4.2 m away in vape shop E.

m away from the vaping source, showing that exhaled e-cig aerosols can travel and mix in the room, and even potentially travel to adjacent rooms or businesses. As seen in Fig. 2.5, as high as 77% of PNC and 62% of $PM_{2.5}$ measured within the personal space of a vaping source remained when measured at the public space of the source. This is unlike the PNC and $PM_{2.5}$ monitored in the patient room in Zhao et al.'s study, where only 7% and 1% remained beyond the social space of the e-cig user. In the patient room study, the AER was 4.1 h^{-1} and spatial analysis was conducted after short-term puffing by a single e-cig user. Even among the four vape shops, a greater percentage of PM remaining was observed in shops A and E, where the AERs were lower and average TVFs were higher, than in shop C, where the AER was higher and the average TVF was lower, over a similar distance (~3 m). In shop B, which had the highest AER and similar average TVF to shop C, the decays of PNC and $PM_{2.5}$ concentration over approximately half of the distances studied in the other shops were commensurate with the decay observed in shop C. Factors contributing to the persistence and mixing of exhaled e-cig aerosols in the vape shops could include: 1) lower shop AERs, leading to exhaled e-cig-vapor partial pressure build-up inside the shop and decrease in aerosol evaporation; 2) continuous puffing by multiple e-cig users, extending the proximity effect from aggregate emissions and leading to subsequent microplume transportation caused by turbulence (Ott et al., 2002); 3) more people moving around and doors opening/closing; and 4) more random exhalation of e-cig aerosols.

This study demonstrates that the high-vaping density, low-ventilation environment of vape shops presents conditions that heighten the mixing potential of and sustained exposure to exhaled e-cig aerosols unlike in clinical and residential settings. Additional studies are needed to better understand the mechanisms governing the spatial impacts of vaping emissions and how it can be used for further exposure analysis.

2.4.5. Particle Size Distribution in Vape Shops

Fig. 2.6 presents the particle size distribution data measured in vape shop C on both a busy and less busy day. On the busy day, there were two particle diameter modes around 60 nm and 250 nm when the door was closed, during which TVF was initially high (Fig. 2.6a). These modes were different from those found by Zhao et al. (2017), who measured two modes at 15 nm and 85 nm 0.8 m away from e-cig users. The aerosol shifted from a bimodal size distribution to a relatively smaller, unimodal distribution at 40 nm after the door was open. Opening the shop door increased dilution and allowed for mixing with outdoor air. The resulting size distribution reflects a combination of residual exhaled e-cig aerosol and possible vehicle emissions from the parking lot. Even with a higher TVF, both the particle size mode and PNC decreased after the door was open. TVF was still observed as an important variable related to particle size distribution. On a less busy day, when the TVF was much lower, the particle size distribution in the shop was largely unimodal despite the door being closed (Fig. 2.6b).

Many e-cig aerosol studies using a chamber to simulate vaping conditions have shown that modes of particle size distribution are less than 200 nm. Mikheev et al. (2016) detected a bimodal particle size distribution of 11 – 25 nm and 96 – 175 nm, and Fuoco et al. (2014) measured e-cig aerosol with modes ranging 20–165 nm. Another vaping study using a 30-m^3 chamber showed that particles in the size range of 20 – 300 nm constantly increased during vaping activity (Geiss et al., 2015). The larger bimodal particle size distribution of 60 – 250 nm measured in vape shop C of this study might be attributed to human exhalation creating more humidity in a relatively enclosed space, where hygroscopic growth and increase in coagulation of aerosols due to higher PNC shifted the particle diameter to a larger size (Pichelstorfer et al.,

a)

b)
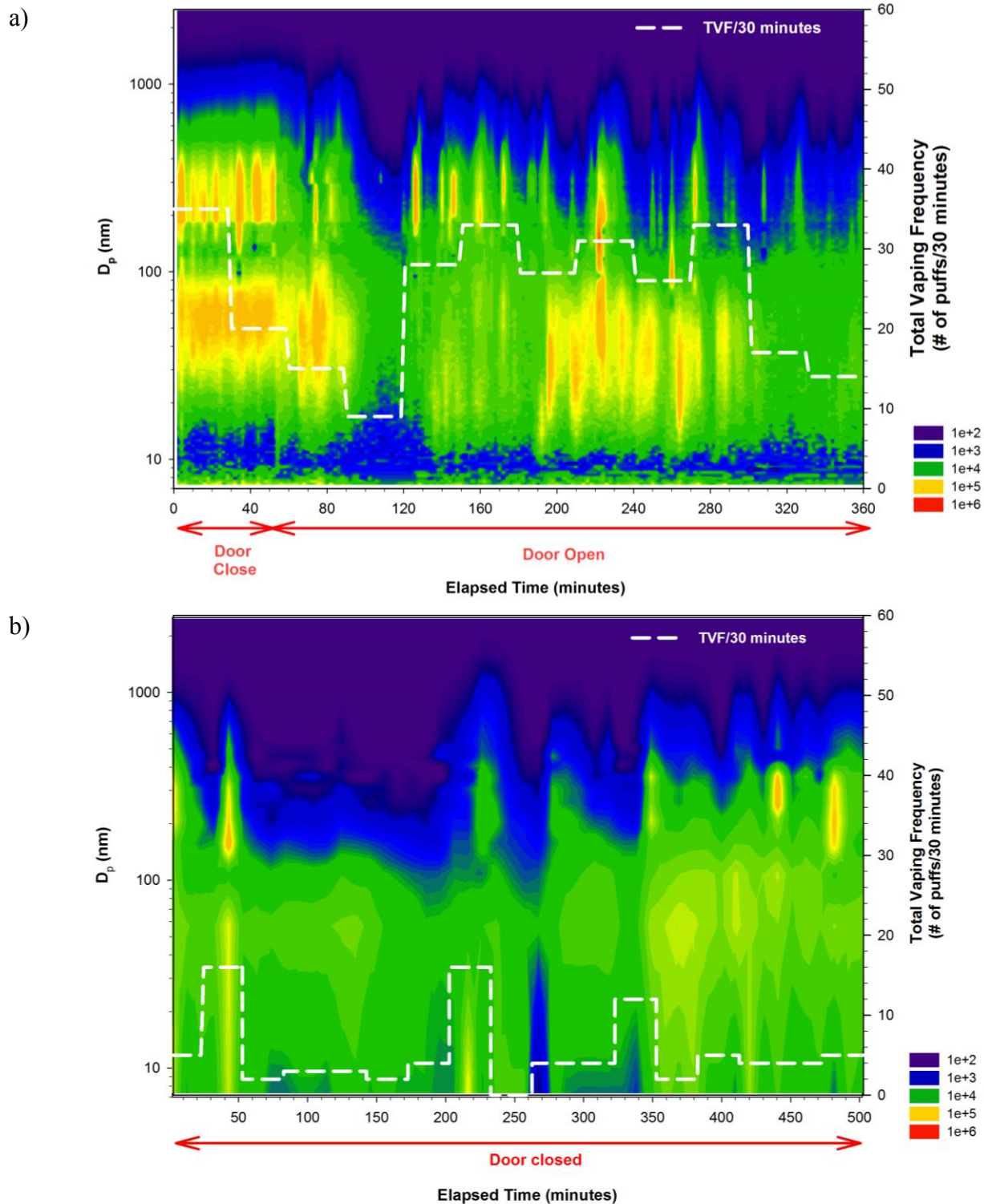
Figure 2.6. Particle size distribution measured in vape shop C during (a) a busy day and (b) a less busy day. The dotted white lines plot TVF. The vertical axes represent particle size on a logarithmic scale, the horizontal axes represent elapsed time in minutes from the start of sampling, and the color scale represents PNC at certain time and diameter.

2016). Pichelstorfer et al. (2016) found that hygroscopic growth rates of e-cig droplets were more significant than those of tobacco cigarette smoke particles, which may explain the noticeable shift to larger particle diameters at the end of vaping. High variability of particle size distribution of e-cig aerosols is reported by other studies. Meng et al. (2017) concluded that the inconsistency of particle size distributions of e-cig aerosols might be due to the impacts of humidity, e-cig device heating power, vaping patterns, and e-liquid components. The high hygroscopicity and volatility of the particles in the e-cig aerosol might yield an even more dynamic particle behavior than tobacco smoke (Ingebrethsen et al., 2012). Further studies are needed to investigate the particle dynamics of e-cig aerosols in the indoor environment and the potential health implications.

2.5. Conclusion

This study showed that emissions of F and UF particles are high and continuous during business hours in vape shops, one of few public indoor spaces where occupants can freely vape. This is the first study that provides information on the temporal and spatial profiles of F and UF particles concentrations and the particle size distribution in vape shops, and establishes total vaping frequency (TVF) as a strong predictor of exhaled e-cig particle levels. During active vaping, indoor PNCs ranged from 1.3×10^4 to 4.8×10^5 particles/cm^3 and indoor PM$_{2.5}$ concentrations ranged from 15.5 to 37,500 μg/m^3. Ventilation inside these shops, as measured by AER, also contributed to lower levels of particles inside. Due to indoor mixing and travel of exhaled e-cig particles, exhaled e-cig particles still persisted in the shops at high levels and at distances farther from vaping. More studies are needed to assess the transport and transformation of exhaled e-cig particles and other contaminants and investigate air mitigation strategies in vape shops and other commercial buildings.

3. SELECT BIOMARKERS OF OXIDATIVE STRESS, SYSTEMIC INFLAMMATION, AND METAL TOXICITY/REACTIVE OXYGEN SPECIES RESPONSE AND ASSOCIATION WITH E-CIGARETTE AEROSOL EXPOSURE IN VAPE SHOP WORKERS

3.1. Abstract

Vape shops are currently exempt from smokefree workplace regulations, which puts vape shop workers at potential occupational risk of repeated exposure to e-cigarette (e-cig) aerosols. To explore vape shop worker exposure to exhaled e-cig aerosols and potential effects of exposure, urine samples were collected from thirty vape shop workers, fifteen vaping and fifteen non-vaping, at the start and end of a shift on two days, which were either the first and last days of a consecutive workday period or two separate days if a subject had a nonconsecutive workday schedule. Cotinine, a marker for nicotine as a tracer for e-cig aerosol, and select markers of oxidative stress (8-OHdG, 8-isoprostane (8-iso)), systemic inflammation (human C-reactive protein (CRP)), and metal toxicity and antioxidant activity (metallothionein (MT)) were quantified. Although cotinine increase was only observed in one of the shifts, cotinine significantly increased between the first and last days for non-vaping workers with a consecutive workday schedule. A corresponding upward trend in 8-iso between the first and last days was also observed. Significant association between cotinine and 8-iso ($p<0.05$), varied by vape shop, was observed in the non-vaping group, suggesting that worksite characteristics, which could include vaping activity during the shift, may increase oxidative stress. Decreases in 8-OHdG, CRP, and MT were observed within both non-vaping worker shifts studied, but changes in these markers among vaping workers were consistent with elevated oxidative stress and inflammatory responses expected from e-cig use during shifts. Significant high associations observed among

cotinine and 8-OHdG, CRP, and MT ($p<0.001$) for vaping workers indicate that mainstream e-cig aerosol is more likely to increase oxidative stress, inflammation, and metal toxicity/reactive oxygen species response than exhaled e-cig aerosol. This study provides preliminary data to support future studies to systematically assess and quantify the relative contribution of exhaled e-cig aerosol exposure to health impacts among vape shop workers.

3.2. Introduction

Retail outlets hold more than 80% of the global e-cig market share in 2021 and remain the primary form of distribution for e-cig products (Grand View Research, 2022). Among these retail outlets are vape shops, which serve a dual function of being a one-stop shop for all vape-related products and a lounge or hangout spot for vape supporters and friends of employees. There are at least 800 vape/smoke shops currently in Southern California (Yelp.com, May 2022). A shop can have one to five employees working at a time, as observed during the vape shop surveys conducted previously (Section 2.4.1). Vape shop retailers perceive e-cigs as safe, but there is growing evidence that e-cig aerosols may have serious health impacts, which raises concern about exposure levels among workers where vaping occurs. Like smoke lounges or bars where secondhand smoke/environmental tobacco smoke (SHS/ETS) is an occupational hazard, exhaled e-cig aerosol may be an occupational hazard in vape shops. Furthermore, vape shop workers may also be e-cig users, presenting another occupational health challenge.

Air contaminants released during e-cig use, including ultrafine particles (UFPs), nicotine, metals, and formaldehyde, have been previously found to induce oxidative stress responses and cytoxicity in animals and humans (Saffari et al., 2014; Olmedo et al., 2018; Cheng, 2014; Sun et al., 2015; Zhang et al., 2014; Zhang et al., 2012; Yildiz, 2004; Li et al., 2003; Araujo et al., 2008; Delfino et al., 2009; Murta et al., 2016; Lima et al., 2015). Flavoring compounds commonly

added to e-liquid, notably butanedione (diacetyl) and 2,3-pentanedione (acetyl propionyl) are known to cause respiratory disease when inhaled (Allen et al., 2016; Leigh et al., 2016). Literature on the potential health impacts of e-cig aerosol is growing. Toxicological and in vitro studies have demonstrated that e-cig aerosol can cause oxidative stress and DNA damage (Canistro et al., 2017; Lee et al., 2018), have pro-inflammatory effects (Scott et al., 2018), impair respiratory function (Atkins et al., 2015; Hureaux et al., 2014; Vardavas et al., 2012; Reinikovaite et al., 2018), impact oral and cardiovascular health (Ji et al., 2016), and induce carcinogenic activity in lung and bladder cells (Lee et al., 2018; Tang et al., 2019). Human health impacts after e-cig aerosol exposure have also been documented. A study by Moheimani et al. (2017) saw increased acute cardiac sympathetic activity (risk factor for future adverse cardiac events) within subjects who had detectable plasma cotinine after use of an e-cig with nicotine compared to use of an e-cig without nicotine. The same authors also saw increased cardiac sympathetic activity and oxidative stress in habitual e-cig users in another study (Moheimani et al., 2017). Other studies observed elevated cellular oxidative stress in immune cells, important in the pathogenesis of many diseases including atherosclerosis, pulmonary endothelial oxidative stress, and inflammation after a single vaping session in otherwise healthy young people with no history of smoking or vaping (Chatterjee et al., 2019; Kelesidis et al., 2021).

Studies have been published about occupational risks faced by workers who are exposed to SHS/ETS, e.g. smoking bar workers, or in smoking-dedicated workplaces e.g. hookah lounges (Bates et al., 2002; Semple et al., 2007; Cobb et al., 2013; Fiala et al., 2012; Zhou et al., 2015; Zhou et al., 2017). Recent studies have been conducted measuring levels of e-cig-related air contaminants in the vape shop environment, but none assess the actual exposure to e-cig aerosols and potential health impacts through biomonitoring of vape shop workers (Attfield et al., 2022;

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Son et al., 2020; Li et al., 2021; Nguyen et al., 2019). Despite there being statewide regulations prohibiting tobacco smoking and vaping in enclosed workplaces and public venues (ANRF, 2022), vape shops and any other retail establishments selling e-cig products are exempt from these regulations (CA Labor Code Section 6404.5), allowing e-cig aerosol exposure to continue to pose a potential occupational health risk. To address the knowledge gap of evaluating vape shop worker exposure to e-cig aerosols, this study explored employee exposure to e-cig aerosols in vape shops and potential associated effects as a result of exposure by measuring urinary cotinine as a marker for e-cig-related nicotine and select urinary oxidative stress, systemic inflammation, and metal exposure response markers in vape shop workers at the start and end of a work shift on two days. By measuring the changes in these biomarker concentrations within a work shift and over multiple work shifts, this study investigated the prospect of exhaled e-cig aerosols as being a occupational hazard and helps to inform designs of future studies assessing health impacts e-cig aerosol exposure in occupational settings.

3.3. Material and Methods

3.3.1. Subjects and Study Design

Thirty vape shop workers (15 vaping workers and 15 non-vaping workers) were directly recruited for urine sampling from randomly selected vape shops located in the Greater Los Angeles area. Since vaping workers are exposed to mainstream and exhaled e-cig aerosols, non-vaping workers were also recruited to serve as a comparison group as they are only exposed to exhaled e-cig aerosols. During direct recruitment, potential subjects were screened for inclusion and exclusion criteria. Exclusion criteria included concurrent use of tobacco cigarettes or using any other tobacco product (i.e. hookah, cigars, smokeless tobacco, nicotine patch); living with a person(s) who smokes tobacco or vape; and working only one day a week at the vape shop. To

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recruit as much study participants as possible, illicit drug use (e.g. marijuana smoking) was not included as an exclusion criterion given the emergence of marijuana vaping and cannabis products being sold in vape shops (Berg et al., 2020). All eligible subjects were given an informed consent form to read and sign prior to participating in the study. From each consenting subject, a urine sample was collected at the start and end of a work shift for two days. The two days of sampling were either the first and last days of a consecutive workday period (i.e. a subject with a Monday-through-Friday work schedule would be studied on Monday and Friday), or two separate days if a subject had a nonconsecutive workday schedule (i.e. a subject with a Monday-and-Thursday work schedule would be studied on Monday and Thursday). The initial day of sampling was scheduled after an off-work period (i.e. a subject with a Monday-through-Friday work schedule would be studied first on Monday because they do not work on Saturday or Sunday) to ensure the first urine sample collected at the start of the shift is used as the subject's own control and to establish a baseline for the biomarkers measured prior to workplace e-cig aerosol exposure. To control activity prior to the start of the shift that may influence the urinary biomarker levels, subjects were asked to observe an 8-hour fasting period before beginning their shift and refrain from vaping or using any nicotine containing products and any exposure to exhaled e-cig aerosols or tobacco smoke. Urine sample collection was conducted from September 2019 to May 2021.

3.3.2. Sampling Protocol

3.3.1.1. Urine

Spot urine samples of the vape shop workers were collected in sterile specimen containers at the start and end of a work shift on two days. Immediately after collection, urine

samples were stored on-site in a refrigerator or in an icebox, then transported after the study visit to the laboratory freezer and stored at -20 ºC for analysis.

3.3.1.2. Air nicotine

For the work shift duration, airborne nicotine was collected using a modified sampling method (Lopez et al. 2013; Chen et al. 2017). The modified sampling method was found to have nicotine recovery rate of 97%. The nicotine sampling device and associated nicotine sample analysis method was adapted from Hammond and Leaderer (1987). The sampler consisted of a 37-mm quartz filter impregnated with sodium bisulfate and assembled in a modified polystyrene sampling cassette, covered with a porous diffusion membrane. The sampler was connected to a pump at a sampling rate of 3 L/min. The active nicotine samplers were placed at the breathing zone height (1.3 – 1.6 m from the floor) and within 1.2 m away from the vaping bar, where workers spend most of their shift and vaping activity is most prevalent in the shop. The 1.2-m distance designates a personal proximity from the vaping source in the shop, so air sampling within this distance would be representative of the nicotine air concentrations workers would be exposed to. To ensure nicotine data quality, an outdoor nicotine air sample was collected and a field blank was used for each shift.

3.3.3. Analysis of Urinary Biomarkers of Exposure and Effect and Air Nicotine

Select biomarkers of exposure and effect were chosen for analysis in the urine samples to evaluate work shift exposure to e-cig aerosols in the vape shop and potential health impacts from exposure. Cotinine, a primary metabolite of nicotine, was measured to evaluate absorption of e-cig aerosols as it has a longer half-life (16 – 19 hr) than nicotine (1 – 4 hr) and could roughly coincide with peak 24-hr excretions observed for 8-OHdG and 8-isoprostane, two oxidative stress markers measured in this study. When nicotine is inhaled through the lungs, it enters the

bloodstream and goes to the liver, where 70 – 80% of nicotine is converted to cotinine by the liver enzyme CYP450 2A6, but only 10 – 15% of the metabolite (may be different if there was previous nicotine exposure) is excreted in the urine while the rest is converted to other metabolites (Benowitz, 1996; Hukkanen et al., 2005). Compared to nicotine, cotinine levels from intermittent exposure from cigarette smoking and environmental tobacco smoke build up throughout the day and remain relatively constant at near steady-state, and is eliminated much slower at an average 45 ml/min. It takes about 4 days for cotinine at smoking levels to go down to nonsmoking levels. By assuming steady-state for cotinine levels, it is reasonable to measure nicotine exposure using cotinine on a daily basis in the workplace. The other nicotine metabolites, (3′R,5′S)-trans-3′-hydroxycotinine (3-HC) and (3′R,5′S)-trans-3′-hydroxycotinine glucuronide (3-HC-Gluc), have shorter elimination half-lives (3.9 – 9.4 hr), which may make these two metabolites better nicotine tracer candidates than cotinine, but their peak excretions were shown to occur the morning after exposure (up to 24 hrs) (Benowitz and Jacob, 2001; Benowitz et al., 2009). Since this study sampled end-of-shift urine to avoid capturing effects from non-work-shift-related activities, cotinine was still the most reasonable nicotine tracer to ensure the most representative measurable change after a work shift as possible.

Urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG), a DNA oxidation marker, and 8-isoprostane (8-iso), a lipid peroxidation marker, were measured to evaluate oxidative stress. Urinary 8-OHdG is advantageous in its long stability in urine and sensitivity as an oxidative DNA damage marker. A lipid peroxidation marker was also used to measure oxidative stress as lipids in biological membranes and lipoproteins are major peroxidation targets (Graille et al., 2020). Despite malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE) being major lipid

peroxidation products, the half-life of MDA may be too long (>20 days) (Siciarz et al., 2001) and the half-life of 4-HNE may be too short (~2 mins) (Breitzig et al., 2016). Urinary 8-iso has a half-life commensurate with 8-OHdG and could coincide with cotinine excretion from intermittent nicotine exposure with respect to its peak excretion at 24 hrs. Human C-reactive protein (CRP), a systemic inflammation marker, was measured to evaluate potential cardiovascular disease risk (Danesh et al., 1998; Ridker et al., 1997; Ridker et al., 1998). Metallothionein (MT), a marker for metal exposure, was measured to evaluate oxidative stress and heavy metal toxicity from metal exposure (Ruttkay-Nedecky et al., 2013; Klaassen et al., 2009). CRP has a kinetics profile similar to cotinine, making this marker potentially ideal for measuring within-day and multiple-day differences (Markanday, 2015), whereas MT can be detected in urine after three days from heavy metal exposure (Lloyd, 1989). MT measurement may be more indicative of body burden for metal exposure and antioxidant activity. The effect biomarkers selected for analysis have been measured in past studies with e-cig users (Sakamaki-Ching et al., 2020; Singh et al., 2019) and can be measured using rapid detection techniques like enzyme-linked immunosorbent assay (ELISA). Creatinine concentrations were also measured to account for urine dilution and used to normalize the biomarker concentration data.

Cotinine was analyzed using cotinine ELISA kits (CALBIOTECH, Spring Valley, CA) following a 1:80 dilution for vaping subject urine samples and no dilution for non-vaping subject urine samples. Information about selectivity of cotinine in a mixture was not provided by the kit manufacturer. Following a 1:20 dilution for all urine samples, creatinine, 8-OHdG, and MT were analyzed using creatinine colorimetric assay kits (Cayman Chemical Company, Ann Arbor, MI), DNA Damage (8-OHdG) ELISA kits (StressMarq Biosciences, Victoria, Canada), and Human Metallothionein ELISA kits (Aviva Systems Biology Corporation, San Diego, CA), respectively.

8-iso was analyzed using urinary 8-isoprostane ELISA kits (Detroit R&D, Michigan, USA) following a 1:4 dilution for all urine samples. CRP was analyzed using Human C-Reactive Protein ELISA kits (MilliporeSigma, Burlington, MA). In all kit analyses, biomarkers were measured in triplicate wells for each urine sample.

For air nicotine analysis, the sodium bisulfate impregnated filter was extracted in dichloromethane (DCM) with an internal standard (quinoline), the DCM concentrated using the nitrogen blowing method, and analyzed using gas chromatography-mass spectrometry (GC-MS). Airborne nicotine concentrations were calculated by dividing the amount of nicotine collected by each filter (µg), corrected using the 97% nicotine recovery for the sampler, by the volume of air sampled (m^3). The limit of quantification of the GC-MS was 0.05 µg per filter, equivalent to 0.04 µg/m^3 air nicotine concentration over an 8-hour period. The accuracy, which was also used to correct the nicotine concentration, and precision is $9.2 \pm 6.5\%$ error and 7.2% CV, respectively.

3.3.4. Shift Observations and Subject Questionnaires

To identify potential e-cig aerosol exposure predictors, the following field observations were manually recorded real-time during the duration of each subject's studied work shift: 1) e-cig puffs, identified by subject, non-subject vape shop worker, or customer; 2) opening/closing of doors/windows; and 3) any outdoor tobacco cigarette smoking event. Furthermore, room air exchange rate (AER) was measured using the method described in Section 2.3.2.1. Subjects were also administered a general questionnaire that collected information on demographic factors (e.g. sex, age, race/ethnicity), previous smoking history (e.g. never, former), regular marijuana use (yes/no), and diet to check for exposure to barbecued or grilled meats. Then, more detailed questionnaires focusing on pre-shift activity and within-shift activity were administered on each sampling day. These questionnaires gathered the following information: 1) 24-hour dietary

intake going back from end-of-shift; 2) amount of e-liquid(s) vaped in mL by the vaping subject during past 4 days and their nicotine, VG/PG ratio, and flavoring compositions; 3) secondhand nicotine exposure in past 4 days (yes/no); and 4) amount of e-liquid(s) vaped in mL by the vaping subject during the work shift and their nicotine, VG/PG ratio, and flavoring compositions.

3.3.5. Data Analysis

Urinary biomarker concentrations were log-transformed for normalization and checked for normality using the Kolmogorov-Smirnov test. Urinary biomarker concentrations were analyzed for changes at each sampling point following the start of the first work shift (Start Day 1) using repeated measures ANCOVA with post-hoc pairwise comparisons using Tukey's HSD (Honest Significant Difference) test with simultaneous confidence intervals. With inclusion of Sampling Point by Vaping Status interaction variable in the repeated measures analysis, the following was calculated for vaping and non-vaping subjects: 1) unadjusted (arithmetic and geometric) and adjusted (geometric) concentration means at each sampling point; 2) concentration ratios between end and start of the work shift for the two sampling days; and 3) concentration ratios between each subsequent sampling point and Start Day 1. For covariate adjustments, only statistically significant differences were applied from the following variables: sex (Male or Female), age (21 – 25, 26 – 35, 36 – 45), body mass index (BMI), regular marijuana user (yes/no), workweek schedule (consecutive or nonconsecutive day), and time of day urine sample was taken (morning = 8 a.m. – 12 p.m., afternoon = 12 p.m. – 4 p.m., evening = 4 p.m. – 8 p.m., night = 8 p.m. – 12 a.m.). Within-shift concentration ratios (change from start to end of work shift) of measured urinary biomarkers were also calculated and compared between vaping and non-vaping subjects and analyzed for change from a ratio of 1.0 using Mann-Whitney Ranked Sum Tests and One-Sample Signed Rank Tests, respectively.

A simple linear regression model and three linear mixed-effects models were used to investigate associations between: 1) urinary cotinine and urinary 8-OHdG, 8-isoprostane, CRP, and MT concentrations; 2) urinary cotinine and urinary 8-OHdG, 8-isoprostane, CRP, and MT within-shift concentration ratios; and 3) urinary biomarker within-shift concentration ratios and potential predictor variables recorded during field observation. In the linear mixed-effects models, subject, vape shop, and both subject and vape shop were each considered as random effect and sex, age, BMI, and marijuana use (individual characteristics found to be significant factors ($p<0.05$)) were included as fixed effects. Shift length (hr), air nicotine concentration ($\mu g/m^3$), vaping density (number of puffs per hour over 100 m^3 shop volume), AER (hr^{-1}), subject-only vaping (puff) frequency, and subject nicotine intake (mg) during the work shift and past four days were potential predictor variables assessed.

All statistical analyses were conducted in SPSS version 28.0 (IBM, Armonk, NY). All figures were generated with Sigmaplot 12.5 (Systat Software Inc., San Jose, CA).

3.4. Results and Discussion

3.4.1. Description of the Studied Subjects, Vape Shop Worksites, and Work Shift Characteristics

All 30 subjects in this study were healthy vape shop workers recruited from 12 vape shops. Most of the vape shops (10 out of 12) from where the studied subjects were recruited were small sized (≤ 250 m^3). Vaping subjects were primarily male, while non-vaping subjects were distributed almost evenly between male and female. At the time of sampling, subject age was mostly within the 21 – 35 range and subject BMI ranged widely from 18.6 to 48.7 kg/m^2. Close to half of the vaping subjects and 33% of the non-vaping subjects indicated they were marijuana users. Majority of the subjects worked a consecutive-day work schedule, which averaged about

four days during the week, with shifts averaging 6.5 hours. Table 3.1 presents the description of

the studied subjects and characteristics of the subjects' work shifts.

Table 3.1. Characteristics of the studied vape shop workers and their work shifts

	Vaping	Non-vaping
Number of workers	15	15
Sex		
Male	14	8
Female	1	7
Age, yrs		
21-25	9	7
26-35	5	7
36-45	1	1
BMI, kg/m^2 (mean ± SD)	27.4 ± 8.2	25.5 ± 3.4
Race		
White/Non-Latino	6	5
Latino	4	2
Black	1	0
Asian/Pacific Islander	1	5
Multiple/Mixed	3	3
Marijuana User		
Yes	7	5
No	8	10
Work schedule		
Consecutive days	9	10
Nonconsecutive days	6	5
Shift length, hrs (mean ± SD)	6.9 ± 2.8	6.4 ± 1.7
Shift span		
Morning to Afternoon	5	8
Morning to Evening	3	3
Morning to Night	2	0
Afternoon to Evening	3	1
Afternoon to Night	1	2
Evening to Night	1	1
Shift TWA air nicotine concentration (mean µg/m^3 ± SD)	0.41 ± 0.24	0.16 ± 0.11
Vaping density during shift[a] (mean #puffs/hr/100 m^3 ± SD)	10.6 ± 6.2	3.4 ± 4.9

[a] From all occupants (customer and worker)

All the vape shops in this study had low AERs, ranging from 0.09 to 1.65 hr-1, during

business hours. When comparing to 24-hr time-weighted (TWA) nicotine air concentrations

(0.65 – 3.99 µg/m3) previously measured in Southern California vape shops (Li et al., 2021), the air nicotine concentrations measured during the shifts were on the lower end of the concentration range and were more comparable to nicotine levels measured in the businesses neighboring the sampled Southern California vape shops (0.06 – 0.42 µg/m3) and e-cig users' home (average 0.13 µg/m3) (Ballbe et al., 2014). This finding is likely due to the fact that: 1) previous air sampling in Southern California vape shops was conducted in 2017 – 2019, when use of larger cloud-producing tank-style/mod e-cig devices were still popular compared to the smaller cloud-producing pod/disposable e-cig devices that currently dominate the e-cig market; and 2) part of the data collection in this study took place while COVID-19 restrictions/guidelines (e.g. reduced indoor occupancy, mask-wearing, discontinued sampling of e-liquids) were in effect. Shift TWA air nicotine concentrations and vaping densities measured during the work shifts of vaping subjects were higher on average than non-vaping subjects, highlighting the additional contribution of vaping activity from the vaping subjects themselves, as opposed to vaping activity from just customers if the non-vaping workers were alone on their shift. Based on the vaping frequencies recorded in this study, about 40% of the vaping density during the vaping worker's shift is from the vaping subject and about half of the vaping density during the non-vaping worker's shift is from vaping coworkers.

3.4.2. Concentrations of Select Urinary Biomarkers of Exposure and Effect

Table 3.2 summarizes the unadjusted and adjusted means for each biomarker among vaping and non-vaping subjects resulting from the repeated measures ANCOVA. Figure 3.1 shows the distribution of urinary concentrations of cotinine, 8-OHdG, 8-iso, CRP, and MT measured at each of the four sampling points among vaping and non-vaping subjects.

Table 3.2. Summary of select urinary biomarkers of exposure and effect measured at each sample point in vaping and non-vaping subjects

| | | Vaping (n = 15) | | | | | Non-vaping (n = 15) | | | | |
| | | Unadjusted | | | Adjusted[a] | | Unadjusted | | | Adjusted[a] | |
Biomarker	Sample Point	Arith. Mean (Median; Range)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value[b])	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)	Arith. Mean (Median; Range)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)
Cotinine (ng/mg creat.)	Start Day 1	4087.5 (3890.5; 436.5-10471.3)	3119.1 (1967.9-4624.9)	1.00 (Ref.)	4623.9 (1996.2-10700.0)	1.00 (Ref.)	6.95 (1.13; 0.29-50.9)	2.20 (0.95-5.79)	1.00 (Ref.)	1.49 (0.64-3.44)	1.00 (Ref.)
	End Day 1	3659.8 (3548.1; 631.0-6456.5)	3190.7 (2281.8-4255.2)	1.02 (0.75-1.40; 0.88)	4989.0 (2273.3-11047.9)	1.08 (0.72-1.62; 0.70)	3.86 (1.54; 0.21-30.27)	2.27 (0.95-5.83)	1.03 (0.75-1.41; 0.85)	1.45 (0.66-3.22)	0.98 (0.65-1.47; 0.91)
	Start Day 2	3174.8 (3090.3; 812.8-6025.6)	2875.6 (2236.8-3580.7)	1.00 (Ref.)	3090.2 (1448.1-6601.2)	1.00 (Ref.)	5.94 (2.63; 0.20-30.0)	2.96 (1.20-7.57)	1.00 (Ref.)	2.76 (1.29-5.88)	1.00 (Ref.)
	End Day 2	4811.5 (3801.9; 977.2-18197.0)	3689.7 (2619.4-5255.9)	1.28 (0.88-1.87; 0.19)	3334.2 (1394.1-7974.5)	1.08 (0.64-1.81; 0.76)	8.72 (1.75; 0.85-35.5)	3.27 (1.27-8.84)	1.10 (0.76-1.61; 0.60)	3.61 (1.51-8.65)	1.31 (0.78-2.20; 0.29)
8-OHdG (ng/mg creat.)	Start Day 1	149.6 (119.3; 40.7-331.1)	130.3 (99.5-167.7)	1.00 (Ref.)	123.6 (76.6-199.7)	1.00 (Ref.)	174.1 (168.0; 15.8-380.5)	136.6 (90.3-195.6)	1.00 (Ref.)	144.0 (89.2-232.5)	1.00 (Ref.)
	End Day 1	132.11 (100.1; 33.9-389.0)	103.8 (72.6-150.2)	0.80 (0.53-1.11; 0.16)	113.1 (64.1-199.5)	0.91 (0.58-1.29; 0.46)	149.6 (119.1; 15.8-378.5)	105.1 (64.8-165.3)	0.77 (0.55-1.15; 0.22)	96.4 (54.7-170.0)	0.67 (0.40-1.12; 0.12)
	Start Day 2	146.0 (98.3; 22.9-478.6)	114.1 (80.7-166.0)	1.00 (Ref.)	97.7 (60.06-158.9)	1.00 (Ref.)	156.9 (157.5; 41.6-313.2)	137.5 (101.6-184.9)	1.00 (Ref.)	160.5 (98.7-261.1)	1.00 (Ref.)
	End Day 2	179.4 (122.9; 45.7-537.0)	145.0 (107.2-203.3)	1.27 (0.50-1.30; 0.36)	160.8 (96.4-268.3)	1.65 (0.92-2.94; 0.09)	150.0 (127.4; 32.7-512.2)	110.5 (74.0-167.2)	0.80 (0.78-2.06; 0.32)	99.7 (59.7-166.3)	0.62 (0.35-1.11; 0.10)

Biomarker	Sample Point	Vaping (n = 15)					Non-vaping (n = 15)				
		Unadjusted			Adjusted[a]		Unadjusted			Adjusted[a]	
		Arith. Mean (Median; Range)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value[b])	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)	Arith. Mean (Median; Range)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)
8-iso (pg/mg creat.)	Start Day 1	834.1 (635.5; 166.0-2630.3)	635.2 (415.7-949.4)	1.00 (Ref.)	555.6 (322.8-957.2)	1.00 (Ref.)	1286.2 (426.6; 153.5-7732.7)	600.6 (339.7-1055.7)	1.00 (Ref.)	686.8 (398.6-1182.0)	1.00 (Ref.)
	End Day 1	523.2 (403.2; 93.3-1071.5)	423.8 (300.9-606.2)	0.67 (0.53-0.84; 0.001)	380.7 (231.6-625.2)	0.69 (0.53-1.04; 0.03)	1065.5 (380.3; 200.7-5266.0)	610.3 (375.2-1002.9)	1.02 (0.81-1.28; 0.89)	679.9 (413.6-1116.6)	0.99 (0.66-1.28; 0.60)
	Start Day 2	696.9 (321.7; 177.8-3715.4)	456.7 (316.5-696.4)	1.00 (Ref.)	387.6 (214.7-699.2)	1.00 (Ref.)	1744.9 (484.2; 144.5-14545.4)	684.0 (392.8-1246.4)	1.00 (Ref.)	805.9 (446.8-1455.4)	1.00 (Ref.)
	End Day 2	962.8 (578.0; 112.2-3311.3)	659.4 (403.4-1038.3)	1.44 (0.47-1.02; 0.06)	600.6 (341.7-1054.7)	1.55 (0.93-2.83; 0.08)	1631.5 (654.9; 187.1-14076.5)	728.3 (449.4-1199.1)	1.06 (0.72-1.57; 0.75)	799.5 (455.3-1405.3)	0.99 (0.54-1.65; 0.84)
CRP (pg/mg creat.)	Start Day 1	2051.4 (470.2; 3.5-11749.0)	310.0 (94.5-1096.6)	1.00 (Ref.)	459.9 (94.0-2253.0)	1.00 (Ref.)	2020.4 (344.4; 18.6-12324.3)	425.8 (163.0-1199.8)	1.00 (Ref.)	286.9 (58.6-1405.3)	1.00 (Ref.)
	End Day 1	993.1 (139.7; 8.9-7244.4)	177.0 (63.7-549.7)	0.57 (0.20-1.65; 0.29)	159.5 (35.6-714.1)	0.35 (0.082-1.47; 0.14)	403.1 (144.8; 14.8-3037.0)	146.7 (71.6-328.5)	0.34 (0.12-1.00; 0.05)	162.9 (36.4-729.2)	0.57 (0.13-2.41; 0.43)
	Start Day 2	381.8 (40.9; 8.7-10964.8)	97.9 (35.7-346.4)	1.00 (Ref.)	183.5 (36.5-922.4)	1.00 (Ref.)	2119.3 (467.1; 3.69-13837.8)	481.7 (153.0-1350.2)	1.00 (Ref.)	257.0 (51.2-1290.8)	1.00 (Ref.)
	End Day 2	871.2 (121.5; 11.2-4491.8)	151.4 (58.6-435.5)	1.55 (0.42-5.70; 0.50)	221.2 (44.9-1089.0)	1.21 (0.86-6.28; 0.82)	600.8 (218.9; 7.35-2780.4)	186.3 (73.4-475.3)	0.39 (0.10-1.42; 0.15)	127.6 (25.9-628.9)	0.50 (0.10-2.59; 0.39)

| Biomarker | Sample Point | Vaping (n = 15) | | | | | Non-vaping (n = 15) | | | | |
| | | Unadjusted | | | Adjusted[a] | | Unadjusted | | | Adjusted[a] | |
		Arith. Mean (Median; Range)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value[b])	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)	Arith. Mean (Median; Range)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)	Geom. Mean (95% CI)	End/Start of Shift Ratio[c] (95% CI; p-value)
MT (pg/mg creat.)	Start Day 1	541.5 (95.5; 26.3- 5495.4)	125.5 (61.5-265.2)	1.00 (Ref.)	387.6 (33.4-4500.8)	1.00 (Ref.)	686.7 (139.5; 16.8-6005.7)	189.3 (94.4-402.9)	1.00 (Ref.)	61.3 (5.28-711.9)	1.00 (Ref.)
	End Day 1	684.8 (128.8; 4.0-4466.8)	123.8 (47.8-308.4)	0.99 (0.53-1.84; 0.97)	1526.9 (60.1-38793.2)	3.94 (0.50-30.8; 0.18)	614.9 (103.2; 2.30-3835.1)	136.2 (45.4-353.5)	0.72 (0.39-1.34; 0.29)	11.0 (0.43-280.6)	0.18 (0.02-1.41; 0.10)
	Start Day 2	208.0 (112.2; 1.6-4466.8)	78.9 (33.5-168.0)	1.00 (Ref.)	386.1 (31.5-4731.5)	1.00 (Ref.)	587.2 (223.3; 9.64-2017.0)	226.6 (104.9-487.8)	1.00 (Ref.)	46.3 (3.78-566.8)	1.00 (Ref.)
	End Day 2	1338.3 (93.3; 1.7-14125.4)	127.2 (42.1-398.3)	1.61 (0.75-3.47; 0.21)	488.8 (14.1-16983.5)	1.27 (0.07-21.9; 0.86)	436.9 (94.9; 16.3-3334.9)	120.5 (60.1-263.6)	0.53 (0.25-1.14; 0.10)	31.4 (0.90-1089.0)	0.68 (0.04-11.7; 0.78)

[a] Adjusted for sex, age, BMI, and marijuana use.
[b] All p-values reported from post-hoc Tukey's HSD tests.
[c] Ratios calculated with geometric means.
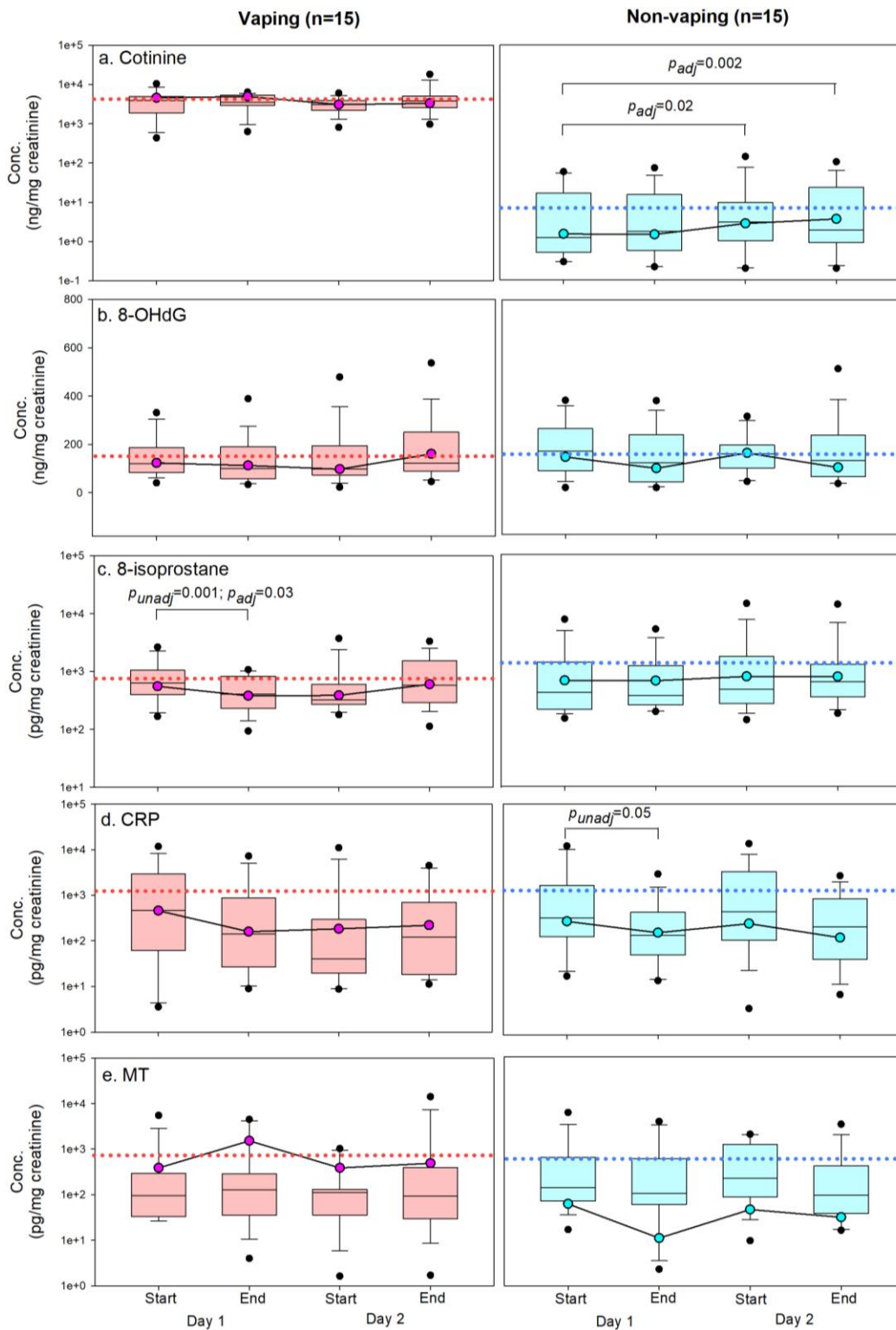
Figure 3.1. Urinary concentrations of (a) cotinine and select biomarkers of effect (b-e) in vaping and non-vaping subjects at each sampling point. Dotted red and blue lines represent overall concentration arithmetic mean (unadjusted). Plotted pink and blue points represent geometric means adjusted by age, sex, BMI, and marijuana use. Noted *p*-values indicate statistical significance (<0.05) from post-hoc Tukey's HSD tests.

3.4.2.1. Nicotine exposure marker cotinine

As expected with inhalation of mainstream nicotine from e-cig use, the unadjusted cotinine levels of vaping subjects (3,925 ± 2,733 ng/mg) were markedly higher by more than 2.5 orders of magnitude than the non-vaping subjects (6.8 ± 11.1 ng/mg) (Figure 3.1). The average urinary cotinine levels measured in the non-vaping subjects are indicative of passive exposure to nicotine and are greater than the average urinary cotinine levels measured in: 1) nonsmoking residents of e-cig-using homes regularly exposed to exhaled e-cig aerosols (2.64 ng/mg) (Ballbe et al., 2014); 2) nonsmoking/non-e-cig-using attendees immediately after a 6-hour visit to an indoor e-cig event (0.28 – 1.08 ng/mg) (Johnson et al., 2019); and 3) nonsmokers after exposure to hookah tobacco smoke at hookah lounges (1.0 ng/mg) (Kassem et al., 2018). Since living with a tobacco smoker or e-cig user was used as a study exclusion criterion plus subjects were asked to refrain from passive exposure to SHS/exhaled e-cig aerosols prior to the work shift, it is likely that workplace exposure to exhaled e-cig aerosols is contributing to cotinine levels in vape shop workers. Compared to nonsmoking employees studied from workplaces where SHS/ETS is an occupational hazard (e.g. casinos, bars and restaurants), the average urinary cotinine concentration measured in the non-vaping vape shop workers was about 1.4 to 4 times less (6.8 ng/mg or 10.3 ng/mL vs. 9.5 ng/mg or 38.2 ng/mL) (Ellingsen et al., 2006; Jensen et al., 2010; Wilson et al., 2011; Achutan et al., 2011), suggesting that exhaled e-cig aerosol may be less of an occupational hazard as SHS/ETS.

It should be noted that the maximum urinary cotinine concentration measured among the non-vaping workers (50.9 ng/mg) was much larger than the maximum urinary cotinine concentrations reported in the passive nicotine exposure studies previously mentioned (4.04 ng/mg). This could be explained by the subject's possible exposure to exhaled e-cig aerosol or

SHS/ETS outside of work prior to the time of sampling (e.g. going to a party or meeting with e-cig-using/smoking friends the day before or after work), which may contribute to cotinine levels in addition to work shift exposure. Activities conducted outside of the work shift where exposure to nicotine is possible should be accounted for in future studies.

3.4.2.2. Oxidative stress (8-OHdG and 8-isoprostane) and systemic inflammation (human c-reactive protein) markers

In contrast with cotinine levels between the vaping and non-vaping subjects, mean unadjusted urinary concentrations of 8-OHdG (151.5 ± 104.4 ng/mg in vaping vs. 158.7 ± 106.9 ng/mg in non-vaping) and human c-reactive protein (CRP) (1249 ± 2491 ng/mg in vaping vs. 1286.9 ± 2688.8 ng/mg in non-vaping) among the two subject groups were similar with less than 5% and 3% difference, respectively (Figure 3.1). The observation of similar urinary 8-OHdG and CRP levels among vaping and non-vaping subjects differs from previous studies that showed urinary 8-OHdG and serum high-sensitivity (hs) CRP being significantly higher in e-cig users than in non-e-cig users/nonsmokers (Sakamaki-Ching et al., 2020; Singh et al., 2019; Moon et al., 2020). On the other hand, one study of nationally representative population of adults found no difference in inflammatory (hsCRP) and oxidative stress markers between exclusive e-cig and non-e-cig users (Stokes et al., 2021), which it attributed to nicotine and toxicant exposure from e-cigs being less than tobacco cigarettes (Goniewicz et al., 2018). Another study saw no significant difference in plasma CRP between normal and e-cig users (Singh et al., 2019). After covariate adjustment, geometric mean 8-OHdG levels in vaping subjects (123.8 ng/mg) did not change relative to non-vaping subjects (125.2 ng/mg), but geometric mean CRP levels were elevated in the vaping subjects by about 25% compared to non-vaping subjects (Table 3.2).

Interestingly, the unadjusted mean urinary 8-OHdG levels in the vaping worker group were about 32% less than the levels measured among nonsmokers (221.6 ng/mg) in the study that found elevated 8-OHdG among e-cig users compared to nonsmokers. Some studies reported that 8-OHdG in secondhand smokers was not significantly higher than in never smokers (Mahrous et al., 2019; Pilger et al., 2001; Lodovici et al., 2005). These findings suggest that inhalation of mainstream e-cig aerosols with nicotine might have an inhibitory effect on oxidative stress. A study where mice exposed to aerosolized propylene glycol/vegetable glycerin (PG/VG) e-liquid showed suppressed levels of plasma 8-oxodG (the tautomer of 8-OHdG) at increasing nicotine levels in the e-liquid compared to PG/VG alone supports this notion (Sun et al., 2021). However, mean CRP levels being higher in vaping than non-vaping subjects is consistent with studies showing pro-inflammatory effects of chronic mainstream e-cig aerosol inhalation (Alexander et al., 2018; Masso-Silva et al., 2021), which suggests that any possible inflammatory effects from repeated exposure to exhaled e-cig aerosol exposure is transient or not significant. Urine levels of 8-OHdG and CRP in healthy (nonsmoking, no disease) populations that have been published in literature (geom. mean 2 – 61 ng/mg creat. for 8-OHdG and <0.15 mg/L for CRP) are 2 to 63 times less and are orders of magnitude higher than the mean levels found for 8-OHdG and CRP, respectively, in this study (Graille et al., 2020; Chuang et al., 2010). The inconsistent ranges of urinary 8-OHdG and CRP levels within control-type groups across different studies point at potential analytical measurement method or sampling population (e.g. geography, race) differences, making the need for establishing a control group (e.g. workers in nearby businesses) important for future vape shop worker studies.

Meanwhile, unadjusted mean urinary concentrations of 8-isoprostane (8-iso) were about 1.9 times higher among non-vaping (1433.0 ± 2738.5 pg/mg) than vaping subjects (755 ± 737.7

pg/mg) (Figure 3.1). In agreement with past findings, levels of 8-iso were elevated among female subjects and subjects of older age (35 – 45 years) (Sakamaki-Ching et al., 2020). Furthermore, potential oxidative stress from toxic combustion products generated from heating or burning cannabis could have contributed to elevated 8-iso levels among non-vaping subjects who reported being a marijuana user (Sarafian et al., 1999; Lorenz et al., 2021; Wolff et al., 2015). After adjusting for these factors, geometric mean 8-iso among non-vaping subjects was still 1.3 times higher than vaping (Table 3.2). This finding contrasts with previous studies that saw elevated urinary 8-iso levels in e-cig users compared to non-e-cig users/nonsmokers (Sakamaki-Ching et al., 2020; Singh et al., 2019). However, these studies did not assess for possible marijuana use, which could have contributed to the elevated 8-iso in e-cig users in the studies. Urine levels of 8-iso in healthy (nonsmoking, no disease) populations that have been published in literature (geom. mean 180 – 400 pg/mg creat.) encompass some of the geom. mean levels calculated for the vaping group in this study (Graille et al., 2020), suggesting that external exposures may be causing the elevated 8-iso levels observed in this study's non-vaping subjects. On the other hand, there was one study that found no significant difference in urinary 8-iso between exclusive e-cig users and non-e-cig users (Stokes et al., 2021), which it also attributed to nicotine and toxicant exposure from e-cigs being less than tobacco cigarettes (Goniewicz et al., 2018). Considering after covariate adjustment geometric mean 8-iso levels remained elevated among non-vaping subjects, there may be factors outside of e-cig aerosol exposure that may be contributing to the elevated oxidative stress level (e.g. lifestyle, diet (sans barbecue/grilling), stress) in this group. Since these non-vaping workers are exposed to exhaled e-cig aerosol on a regular basis through workplace exposure, exhaled e-cig aerosol playing a role in oxidative stress is still a possibility.

3.4.2.3. Heavy metal and reactive oxygen species exposure response marker (metallothionein)

Urinary metallothionein (MT) was shown to be significantly elevated in e-cig users when compared to nonsmokers by more than three times in a study by Sakamaki-Ching et al. (2020). In this study, unadjusted mean urinary metallothionein (MT) concentration measured in vaping subjects (694.7 ± 2070.0 pg/mg) was only about 1.2 times higher than non-vaping subjects (582.5 ± 1085.4 pg/mg) (Figure 3.1). Evaluation of this study's raw MT concentration data among the non-vaping group showed that female levels were significantly higher than male levels, there was an inverse linear relationship between MT concentration and BMI, and MT was highest among 21 – 25 year old subjects. After adjusting for these factors, the geometric mean urinary MT level rose significantly in vaping subjects and lowered significantly in non-vaping subjects, resulting in mean vaping MT levels being 18.6 times higher than non-vaping. Considering that the vaping group had only one female subject versus the non-vaping group which had seven female subjects, the stark increase in mean MT level among the vaping group after adjustment is reasonable and further supports the finding that e-cig aerosol inhalation increases exposure to metals and free radicals contained in the aerosol that can cause oxidative damage and/or metal toxicity (Williams et al., 2013; Williams et al., 2017; Goel et al., 2015), but suggests that either the exposure to metals or free radicals in exhaled e-cig aerosol or levels of these constituents in exhaled e-cig aerosol may not be high enough to produce an oxidative damage response.

3.4.3. Changes in Urinary Biomarker Concentrations Within-Shift and Across Multiple Consecutive Work Shifts

Initial concentration ratios (prior to adjustment) corresponding to change in concentration between end and start of the work shift, pooled among Days 1 and 2, and to change in concentration between each subsequent sampling point and baseline (start of shift on Day 1),

were calculated to assess if changes alone were significant and to identify any trend in changes from baseline among subjects who work a consecutive workday schedule. Figure 3.2 presents the concentration ratios between end and start of shift pooled among all sampled work shifts, stratified by vaping and non-vaping workers. One vaping subject who had a BMI greater than 40 kg/m^2 (morbidly obese) was excluded from the initial ratios calculated for CRP and MT due to having very high urinary CRP concentrations at the start of their sampled shifts, indicating a low-grade chronic systemic inflammatory condition related to obesity (Visser et al., 1999; Hakeam et al., 2009), and low urinary MT concentrations across all sampling points, indicating a micronutrient deficiency (i.e. low zinc levels) associated with obesity (Ernst et al., 2009; Garcia
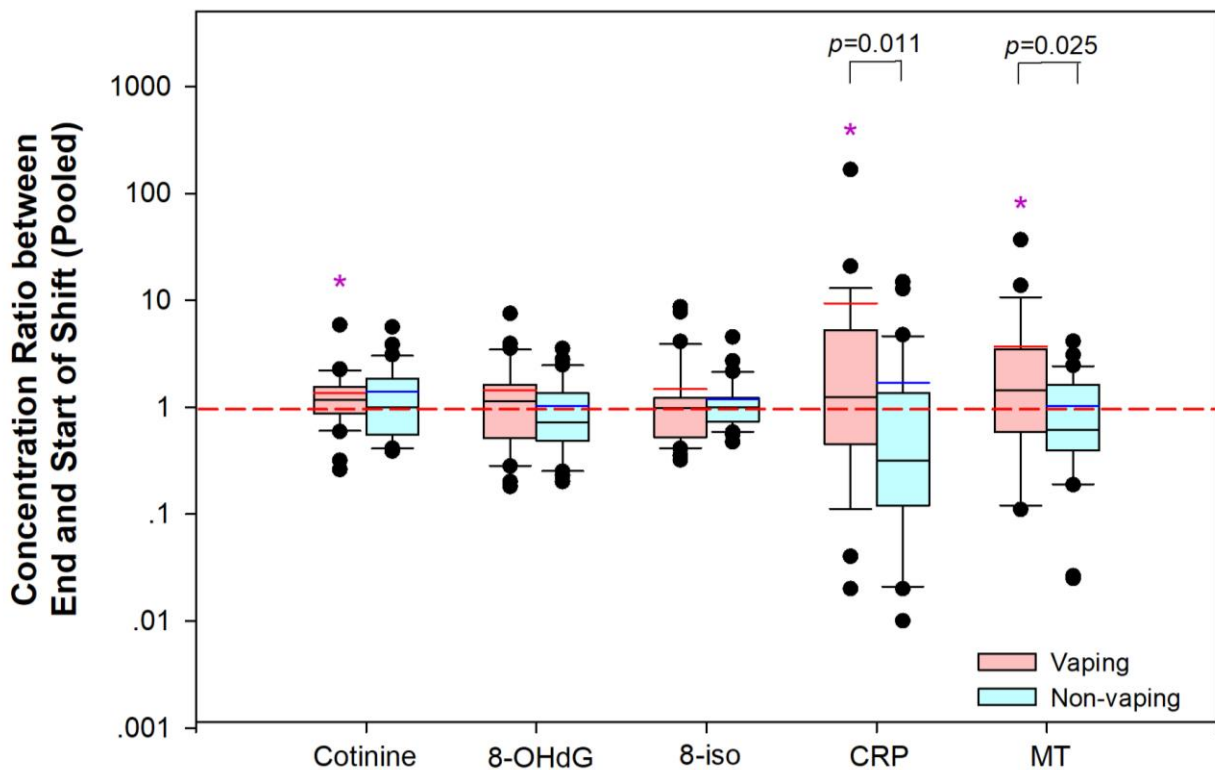
Figure 3.2. Concentration ratios of end of shift over start of shift for urinary cotinine and select biomarkers of effect. Ratios represent change of concentration from start to end of work shift. Red dashed line marks a ratio of 1.0, meaning no change. Purple asterisks (*) above the boxplot indicates significant change over a 1.0 ratio. Significant *p*-values were determined with One-Sample Signed Rank Tests and Mann-Whitney Rank Sum Tests.

et al., 2009). Median (mean ± SD) concentration ratios for urinary cotinine among vaping and non-vaping subjects were 1.17 (1.35 ± 0.98) and 0.99 (1.40 ± 1.18), respectively. Median concentration ratios for urinary 8-OHdG and 8-iso were 1.14 (1.45 ± 1.46) and 0.98 (1.48 ± 1.96) among vaping subjects, and 0.72 (1.03 ± 0.82) and 0.99 (1.19 ± 0.80) among non-vaping subjects, respectively. Median concentration ratios for urinary CRP and MT were 1.25 (9.37 ± 31.3) and 1.23 (3.48 ± 7.01) in vaping, and 0.32 (1.66 ± 3.43) and 0.61 (1.02 ± 0.99) among non-vaping subjects, respectively. One-Sample Signed Rank Tests showed that the change above a 1.0 ratio, which represents no change in urinary marker concentration from the start to end of a work shift, was significant for urinary cotinine for the vaping group (p=0.032) but not for the non-vaping group (p=0.47), denoting that e-cig use during a work shift significantly increases cotinine immediately after a work shift due to much higher nicotine intake than passive e-cig aerosol exposure. Change above 1.0 ratio was not significant (p>0.05) for 8-OHdG and 8-iso in the vaping and non-vaping groups, but was higher among the vaping group, denoting that mainstream e-cig aerosol inhalation induces a greater oxidative stress response than just exhaled e-cig aerosol inhalation. Lastly, change above 1.0 ratio was statistically significant for CRP (p=0.044) and MT (p=0.042) in the vaping group but not in the non-vaping group, indicating that mainstream inhalation of e-cig aerosols produces significant acute systemic inflammation, heavy metal toxicity, and oxidative damage responses, but not so immediately after a work shift when just exposed to exhaled e-cig aerosol. Compared to the non-vaping workers, the pooled within-shift CRP and MT concentration ratios calculated for vaping subjects were significantly higher.

Table 3.2 shows the differences in the unadjusted and adjusted mean urinary concentrations of cotinine, 8-OHdG, 8-iso, CRP, and MT measured at the start and end of each work shift. Results of the post-hoc pairwise comparisons between the start and end-of-shift

concentrations measured on each sampling day are also provided in Table 3.2. Repeated measures ANCOVA only detected statistically significant change across the sampling points for 8-iso in the vaping group ($p<0.05$). With a small sample size, for exploratory purposes post-hoc comparisons with Tukey's HSD tests were conducted for all biomarkers to identify any notable within-shift and across multiple work shift changes. Figure 3.3 plots the unadjusted and adjusted concentration ratios between each subsequent sample point and baseline (start of shift on Day 1) among subjects that had a consecutive workday schedule. After adjusting for sex, age, BMI, and marijuana use, most notably cotinine increased across multiple consecutive work shifts for non-vaping subjects, significantly higher by 86% on start of Day 2 shift compared to baseline ($p=0.02$) and additionally 31% higher from start to end of shift on Day 2.

3.4.3.1. Urinary cotinine and workplace exposure to exhaled e-cig aerosols

Among vaping subjects, adjusted geometric mean urinary cotinine levels slightly increased (<10%) from start to end of shift (within-shift) on Days 1 and 2 (Figure 3.1 and Table 3.2). The stability of the cotinine levels from start to end of shift was expected given that cotinine levels from intermittent exposure (e.g. cigarette smoking) build up throughout the day and remain relatively constant at near steady-state, and is eliminated much slower at an average 45 ml/min[61]. There was a downward trend from start of shift on Day 1 to end of shift on Day 2, though not significant. Based on worker questionnaires completed, nicotine intake (mg) workers estimated for 4 days prior to the work shift on Day 1 (205.2 ± 373.4) was higher than Day 2 (136.4 ± 193.3). It is clear that urinary cotinine trends within-shift and across the two sampling days among the vaping group is caused by their own e-cig use while working.
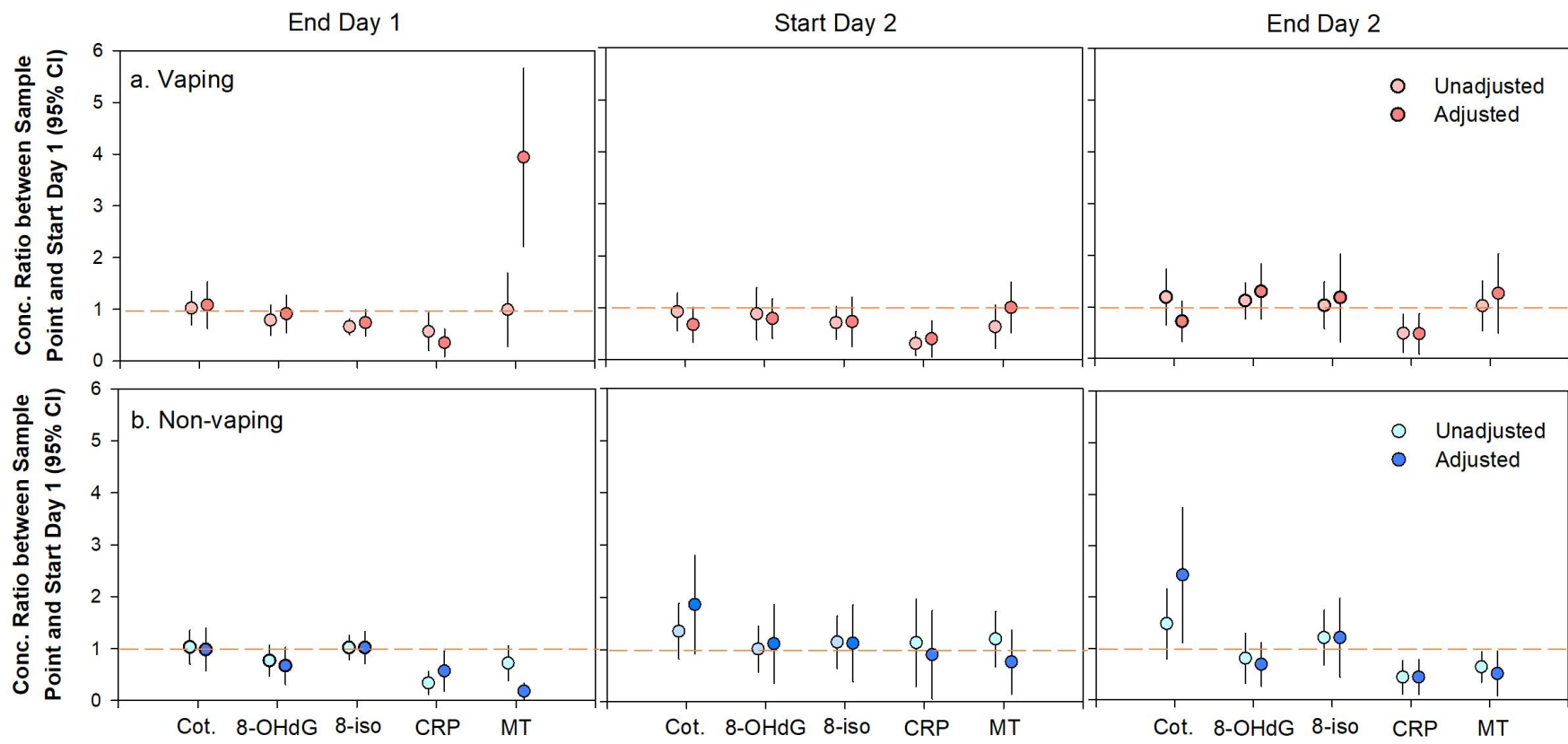
Figure 3.3. Concentration ratios of subsequent sample point over baseline (start of Day 1 shift) for urinary cotinine and select biomarkers of effect. Ratios represent change of concentration from start to end of consecutive workday schedule based on geometric means. Red dashed line marks a ratio of 1.0, meaning no change. Ratios adjusted for age, sex, BMI, and marijuana use.

Among non-vaping subjects, within-shift changes in mean urinary cotinine levels (adjusted and unadjusted) on Day 1 were negligible, but on Day 2 were notably larger (31%). The stark contrast in the magnitude of within-shift change suggests either the shifts on Day 2 were all coincidentally busier vaping days compared to Day 1 among the studied non-vaping subjects, or inhaled nicotine (partially or entirely) from exhaled e-cig aerosol exposure while working in the vape shop accumulates over a consecutive workday period, falls slowly during periods of non-exposure, then is excreted at peak four to six hours from the last exposure[59]. Since vaping density and TWA air nicotine concentration on the Day 1 and Day 2 shifts were similar, it is likely that the latter reason in the previous statement is the explanation, signifying that exhaled e-cig aerosol in the workplace is contributing to increased urinary cotinine levels. As seen in Fig. 3.1a in the non-vaping panel, there was a significant increase from the shift start on Day 1 to the shift start on Day 2 by 1.9 times and to the shift end on Day 2 by almost 2.5 times for adjusted cotinine geometric means ($p=0.02$ and $p=0.002$, respectively).

To assess the average increase observed in urinary cotinine levels among the non-vaping workers after a work shift (pooled over Days 1 and 2) and after each sampling point from baseline (start of shift on Day 1) among the non-vaping subjects with consecutive workday schedule relative to similar studies where workers or subjects are passively exposed to nicotine, effect sizes (Hedges's g) were calculated using the adjusted geometric means and data provided in the studies (see Figure 3.4). On a within-shift basis, the effect size among the non-vaping subjects was very small ($g=0.07$) relative to effect sizes estimated from studies of: 1) nonsmoking residents of e-cig-using homes regularly exposed to exhaled e-cig aerosols compared to control (nonsmoking) homes ($g=0.46$) (Ballbe et al., 2014); 2) nonsmoking/non-e-cig-using attendees immediately after a 6-hr visit to an indoor e-cig event ($g=1.87$) (Johnson et

56

al., 2019); 3) nonsmoking casino workers after an 8-hr work shift (g=1.88) (Achutan et al., 2011); and 4) smoking bar patrons after a 6-hr visit (g=2.38) (Repace et al., 2006). However, effect sizes calculated between mean urinary cotinine levels at each subsequent sampling point relative to baseline became larger up to g=0.50 for end of shift on Day 2 relative to baseline. This effect size is comparable to the mean difference measured between nonsmoking residents of e-cig-using homes regularly exposed to exhaled e-cig aerosols and residents of nonsmoking/non-e-cig-using homes. It should be noted that the effect size determined after passive exposure to e-cig aerosol at an e-cig event was quite large. In that study, the e-cig events attended took place in 2016-2017, prior to when pod-based devices became popular, and the number range of attendees was 150-1500. These parameters are not representative of an everyday exposure event, and thus, should be considered an atypical circumstance.

Figure 3.4. Effect sizes (95% CI) calculated from cotinine increases observed in prior studies after secondhand nicotine exposure compared to non-vaping workers in this study. Within-Shift (Pooled), Start Day 1 – End Day 1, Start Day 1 – Start Day 2, and Start Day 1 – End Day 2 refer to this study.

Among the vaping subjects, within-shift increase in mean urinary 8-OHdG, 8-iso, and CRP levels (unadjusted and adjusted) was observed, even trending toward significant for 8-OHdG and 8-iso, on the Day 2 shift (Figure 3.1 and Table 3.2). Conversely, significant decreases in the mean levels of these biomarkers were observed on Day 1. The aligned trends of these three biomarkers makes sense due to the mediating effect of reactive oxygen species on pro-inflammation and CRP is associated with increasing reactive oxygen species production and inducing DNA damage (Lugrin et al., 2014; Hooten et al., 2012). The contrasting within-shift changes in Day 1 versus Day 2 is an interesting observation that would need to be explored further as past studies have only shown e-cig use to induce acute oxidative stress and inflammatory responses for first-time or abstinent-enforced users and elevated levels of oxidative stress and systemic inflammation markers in cross-sectional studies among e-cig users (Benowitz et al., 2020; Canistro et al., 2017; Sakamaki-Ching et al., 2020; Singh et al., 2019; Moon et al., 2020; Chatterjee et al., 2019; Kelesidis et al., 2020). When looking at subject vaping frequency during the study days, Day 2 shifts had a higher subject vaping frequency average (48.3 ± 1.8) than Day 1 (35.0 ± 2.3), which could be a possible indicator for why an increase within-shift was not seen until Day 2. If active e-cig use, like active smoking, is speculated to induce chronic oxidative stress, albeit to a lesser degree given the reduction in toxicants generated compared to tobacco (Dai et al., 2022; Liu et al., 2021; Round et al., 2019; Goniewicz et al., 2018), a steady-state urinary excretion of any 8-OHdG and 8-iso being generated would be observed. Taking into account these markers in vaping subjects are on par and even less than in non-vaping subjects (Section 3.4.2) and a significant decrease was observed within-shift on Day 1 but an increase within-shift on Day 2 was observed, there may be a threshold in dosage of e-cig aerosol

inhalation where oxidative stress markers begin to form. Longitudinal trends of oxidative stress and inflammation markers need to be further studied within regular e-cig users.

Among non-vaping subjects, there was a decrease in mean urinary 8-OHdG and CRP levels (adjusted and unadjusted) within-shift on both sample days (Figure 3.1 and Table 3.2). Mean 8-OHdG and CRP returned to levels measured on the start of the shift on Day 1, on start of the shift on Day 2. This is indicative that exposure to exhaled e-cig aerosols during work shift did not lead to acute oxidative DNA damage or systemic inflammation. Increase in urinary CRP should be observed from Day 1 sample points to Day 2 as the half-life of urinary CRP is approximately 19 hours, begins to rise after 12-24 hours, and peaks 2-3 days (Markanday, 2015). Increase in oxidative DNA damage should be observed after a work shift as the half-life of urinary 8-OHdG is 6-7 hours (Takeuchi et al., 1997). However, peak excretion of urinary 8-OHdG can occur up to 24 hours after exposure (Jongeneelen et al., 1987). Seen in Figure 3.1 and Table 3.2, mean 8-OHdG was elevated on the start of shift on Day 2 compared to the start of shift on Day 1. This could signify a potential delayed oxidative stress effect, but since a sharp decrease is observed after the shift on Day 2, it is uncertain if the increase from Day 1 to Day 2 is due to prior shift exposure to exhaled e-cig aerosol.

On the other hand, no significant changes were observed within-shift for mean urinary 8-iso levels (adjusted and unadjusted), but an upward trend was apparent from Day 1 to Day 2 sample points, though not significant. These observations suggest that exposure to exhaled e-cig aerosols during the work shift may not have an acute lipid peroxidation effect, which should be observed after a work shift as the half-life of urinary 8-iso is within a minutes-to-hours timeframe (Basu, 1998). The increase observed across Start Day 1 to End Day 2, however, could be indicative of slow lipid peroxidation, as urinary 8-iso also has peak excretion up to 24 hours

after exposure (Nuernberg et al., 2008) as well as a slower production of 8-isoprostane (Morrow et al., 1992). Since the exposure level of e-cig-related air contaminants during the Days 1 and 2 shifts for non-vaping workers is less in comparison to vaping workers, which inhale a higher dosage of e-cig-related contaminants from mainstream inhalation, it is probable that increase in 8-iso would occur hours later and the peak detected the next day.

To assess the average increase observed in urinary 8-iso levels among the non-vaping workers after a work shift (pooled over Days 1 and 2) and after each sampling point from baseline (start of shift on Day 1) among the non-vaping subjects with consecutive workday schedule relative to similar studies where workers or subjects are exposed to contaminants that may increase 8-iso, effect sizes (Hedges's g) were calculated using the adjusted geometric means
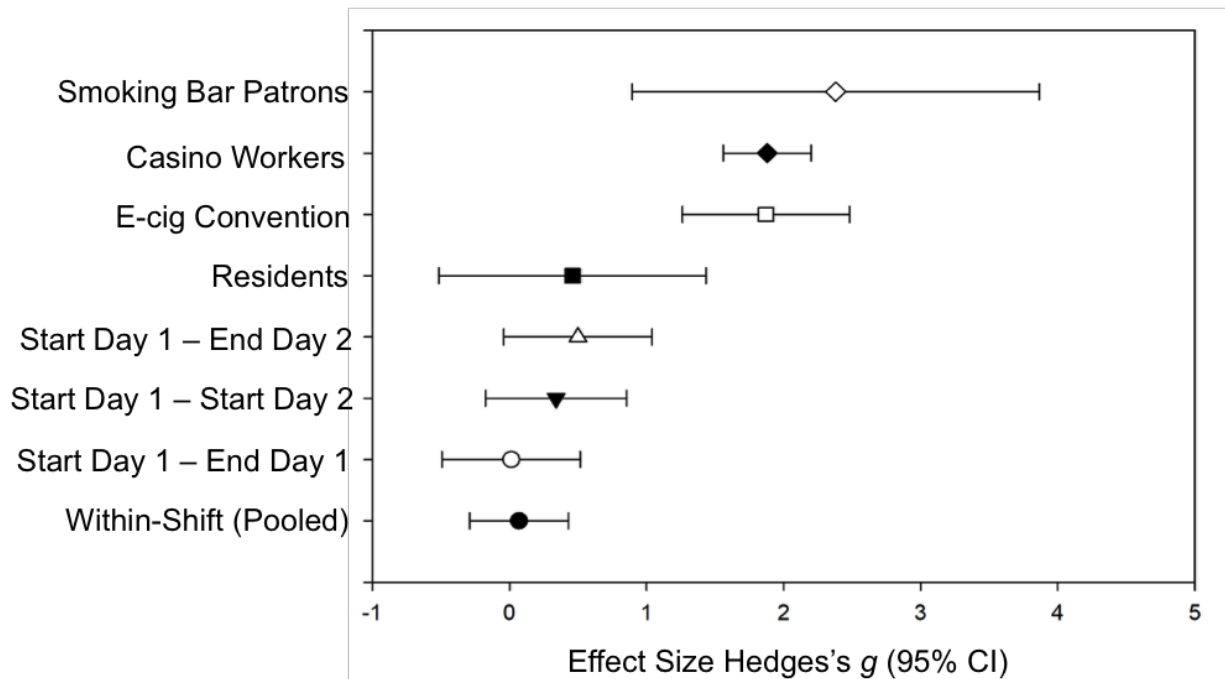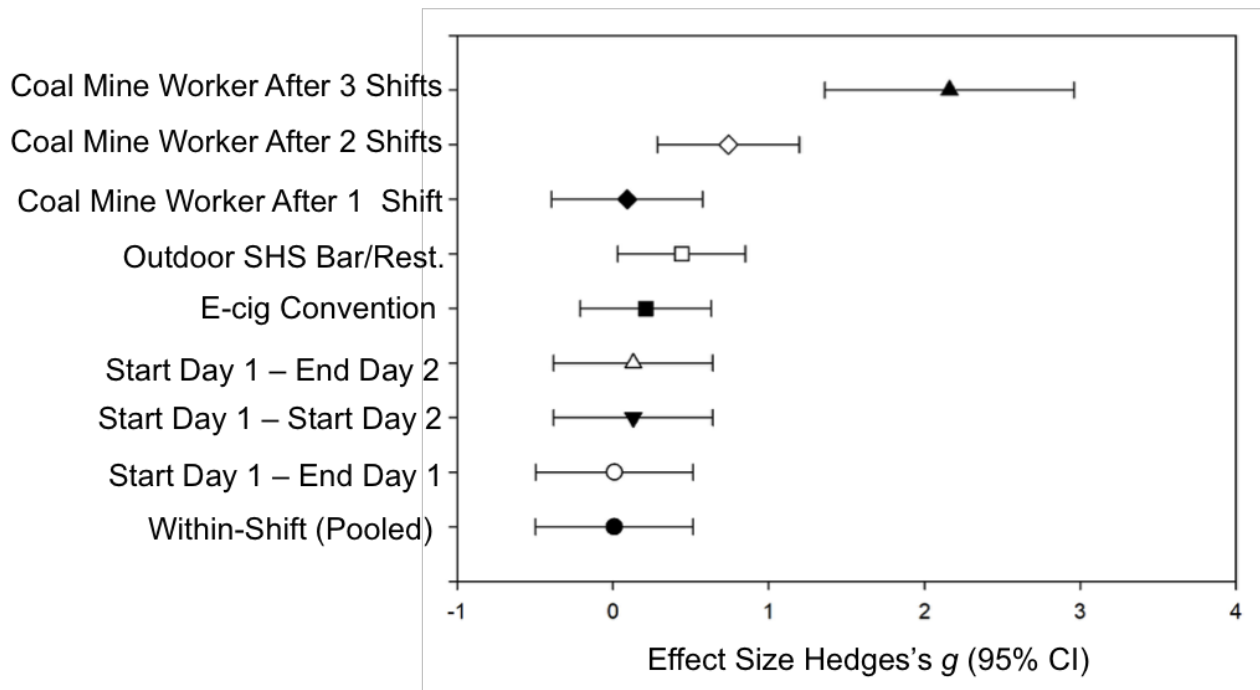

Figure 3.5. Effect sizes (95% CI) calculated from 8-isoprostane increases observed in prior studies after secondhand nicotine exposure compared to non-vaping workers in this study. Within-Shift (Pooled), Start Day 1 – End Day 1, Start Day 1 – Start Day 2, and Start Day 1 – End Day 2 refer to this study.

and data provided in the studies (see Figure 3.5). On a within-shift basis, the effect size among the non-vaping subjects was very small (g=0.008) relative to effect sizes estimated from studies of: 1) nonsmoking/non-e-cig-using attendees immediately after a 6-hr visit to an indoor e-cig event (g=0.21) (Johnson et al., 2019); 2) healthy nonsmokers exposed to outdoor SHS at a bar/restaurant for 3 hrs (g=0.44) (Morris, 2012); and 3) coal mine workers after one, two, and three 6-hr shifts on sequential workdays (g=0.09, 0.74, and 2.16) (Zimet et al., 2016). Effect sizes calculated between mean urinary cotinine levels at each subsequent sampling point relative to baseline became larger up to g=0.13 for end of shift on Day 2 relative to baseline. This effect size is larger than the size determined with coal mine workers after one 6-hr shift, and is close to the mean difference measured among nonsmoking/non-e-cig-using attendees immediately after a 6-hr visit to an indoor e-cig event. From this analysis, gradual effect of oxidative stress, marked by increase in urinary 8-iso levels over consecutive workdays, is occurring in non-vaping vape shop workers which could be attributable to workplace exhaled e-cig aerosol.

3.4.3.3. Urinary MT levels after workplace exposure to exhaled e-cig aerosol exposure

Among non-vaping subjects, there was decrease in mean MT levels (adjusted and unadjusted) within-shift on Days 1 and 2. This indicates that the metal content and free radicals in exhaled e-cig aerosols that the subject is exposed to during the work shift may not have induced formation of MT. Several studies show lower metal concentrations from exhaled e-cig aerosol than mainstream (Palazzolo et al., 2017; Attfield et al., 2022; Zwack et al., 2017). Among vaping subjects, after adjustment, within-shift increase in geometric mean MT levels was observed on both days, with Day 1 being markedly higher than Day 2. In relation to the decreased urinary 8-OHdG, 8-iso, and CRP levels after the Day 1 shift, the large elevation in adjusted geometric mean MT level could be an indicator of MT's role as a heavy metal-binding

protein and scavenger for oxygen free radicals, which may have caused the oxidative stress and inflammation markers to decrease correspondingly. It is reported that transcription of MT is up-regulated in response to reactive oxygen species or chemicals that induce oxidative stress to protect against oxidative damage (Cobb et al., 2018; Bauman et al., 1991). One study demonstrated suppression of 8-OHdG after heavy metal exposure (Min et al., 2005). In contrast, the mean MT increase within Day 2 shifts in the vaping subjects is commensurate to the Day 2 shift increases in mean 8-OHdG, 8-iso, and CRP levels. More studies to examine the dynamics between MT generation with heavy metal exposure and response to oxidative stress-inducing species with respect to e-cig aerosols are warranted.

3.4.4. Potential Predictors of Exposure and Effect from Exhaled E-cig Aerosol Exposure

3.4.4.1. Association between Urinary Cotinine and Biomarkers of Effect

Initial investigation of potential associations between urinary cotinine and the studied biomarkers of effect was conducted using simple linear regressions. Figure 3.6 presents the linear regressions of urinary cotinine concentration on 8-OHdG, 8-iso, CRP, and MT concentrations, stratified by vaping and non-vaping subjects. Within vaping subjects, urinary CRP and MT were significantly correlated with urinary cotinine concentrations ($p<0.05$). 8-OHdG correlated with cotinine concentrations, but it did not rise to statistical significance, suggesting there are potential interfering factors. Correlations between cotinine and 8-OHdG and MT urinary concentrations are consistent with a prior study that found the same correlations among its sampled e-cig user population (Sakamaki-Ching et al., 2020). The correlation between cotinine and CRP urinary concentrations among the vaping group further supports the pro-inflammatory response documented after e-cig aerosol inhalation. These correlation findings confirm that mainstream e-cig aerosol inhalation, as demonstrated by cotinine levels as a marker
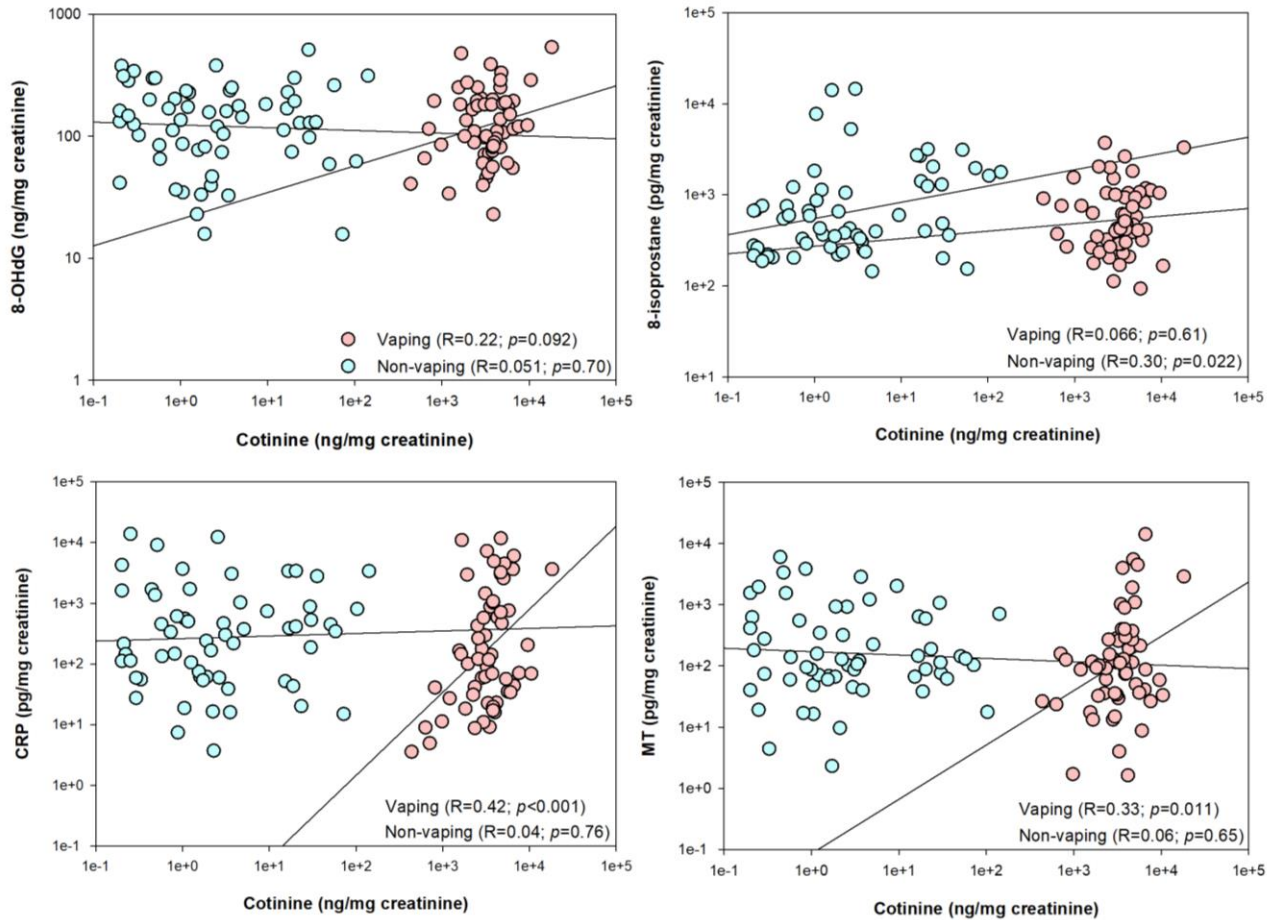
Figure 3.6. Correlations between urinary cotinine and select biomarkers of effect

for e-cig-related nicotine, increase oxidative damage activity and systemic inflammation. Among non-vaping subjects, urinary 8-iso concentrations were significantly correlated with cotinine concentrations ($p<0.05$), possibly suggesting that increased nicotine and/or other e-cig-related contaminant exposure, contributed partially or entirely from exhaled e-cig aerosol during work shifts, can increase lipid peroxidation-related oxidative stress.

Figure 3.7 presents the results of the simple linear regression model and three linear mixed-effect models to investigate if subject or the vape shop worksite were varying factors in the association between urinary cotinine as a marker of e-cig aerosol exposure and the studied biomarkers of effect. As seen in Fig. 3.7a, urinary cotinine was significantly associated with CRP
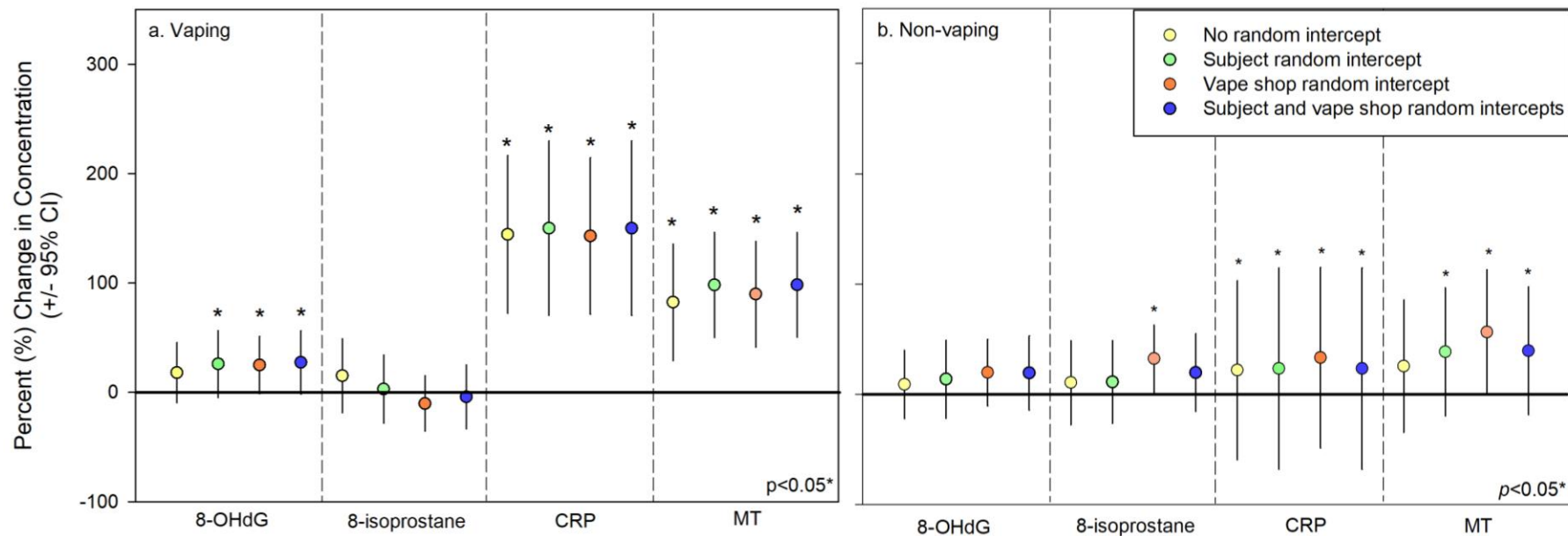
Figure 3.7. Associations between urinary cotinine and select biomarkers of effect. Associations interpreted as percent (%) change in effect biomarker concentration with one-fold (100%) increase of cotinine concentration. Fixed effects included in linear mixed models were age, sex, BMI, and marijuana use.

and MT concentrations in all models tested among the studied vaping group. Cotinine levels were significantly associated with 8-OHdG levels after subject and vape shop effects were included as random intercepts in the model, indicating that contribution of mainstream e-cig aerosol exposure to oxidative DNA damage is not constant among individuals or vape shop worksite. This suggests that individual differences (e.g. biological mechanisms regulating 8-OHdG expression) and other factors inherent to the worksite (e.g. work stress, local air pollution, diet) may be affecting 8-OHdG levels in the vaping workers. The finding that urinary 8-OHdG was associated with cotinine levels in the vaping group, when accounting for individual differences, demonstrates urinary 8-OHdG as an acceptable marker of longitudinal oxidative stress from mainstream e-cig aerosol exposure on a subject-basis, despite the levels of this marker being not much different between the vaping and non-vaping subjects (Section 3.4.2.2).

Although Figs. 3.6 and 3.6a show that mainstream e-cig aerosol exposure is associated with oxidative stress using 8-OHdG as a marker, no significant association was observed for 8-iso, which is also a marker for oxidative stress. As discussed previously in Section 3.4.2.2, the overall urinary 8-iso levels in the vaping group was less than in the non-vaping group, suggesting that nicotine and toxicant levels in e-cig aerosol are not to the level to produce sustained oxidative stress effect through lipid peroxidation as has been demonstrated from tobacco smoking. Alternatively, the increased oxidative DNA damage in response to increasing cotinine levels may be attributable to the increasing inflammatory activity via CRP formation, which increases the amount of reactive oxygen species and induces the DNA base lesion (8-OHdG formation), rather than as a direct response to mainstream e-cig inhalation (Hooten et al., 2012).

As seen in Fig. 3.7b, among the studied non-vaping group urinary cotinine was significantly associated with 8-iso concentrations in the model with vape shop as the random

intercept compared with the simple model and model with subject as a random intercept. This indicates that the association of urinary cotinine and 8-iso varied among the different vape shop work sites, suggesting that the indoor environment characterized by e-cig-related air contaminants in from vaping activity (exhaled e-cig aerosol) and possibly, other factors inherent to the worksite (e.g. work stress, local air pollution, diet), may be inducing oxidative stress by lipid peroxidation. Furthermore, urinary cotinine was also significantly associated with CRP concentrations in all models tested and MT concentrations when subject and vape shop random effects were included among the non-vaping group. These results indicate that passive nicotine exposure, contributed by workplace exposure to exhaled e-cig aerosol, can induce oxidative stress (about 32% increase in 8-iso levels after one-fold increase in cotinine level) and systemic inflammation, with MT activity more likely linked to the increase in free radicals denoted by the increase in lipid peroxidation (8-iso). Understandably, the percent increases in systemic inflammation (CRP) and oxidative damage response (MT) in this group after nicotine exposure were much less than the vaping group (Fig. 3.7a), given that this group is exposed to higher dose of metals, nicotine, and other toxicants from mainstream e-cig aerosol. Considering that airborne metal, VOC, aldehyde, and other respiratory toxicant concentrations from exhaled e-cig aerosol in vape shops are low relative to mainstream e-cig aerosol (Attfield et al., 2022; Zwack et al., 2017), it is possible that nicotine is playing the main role of promoting inflammation and producing oxidative stress (Benowitz et al., 2016; Mao et al., 2012).

3.4.4.2 Potential Work Shift-Characterizing Predictors of Urinary Cotinine and Biomarkers of Effect

Field observations and work shift characteristics recorded during study visits were assessed for potential to be predictors of exposure to exhaled e-cig aerosol and exposure-related effects while working in a vape shop. Figure 3.8 presents the results of the mixed-effect
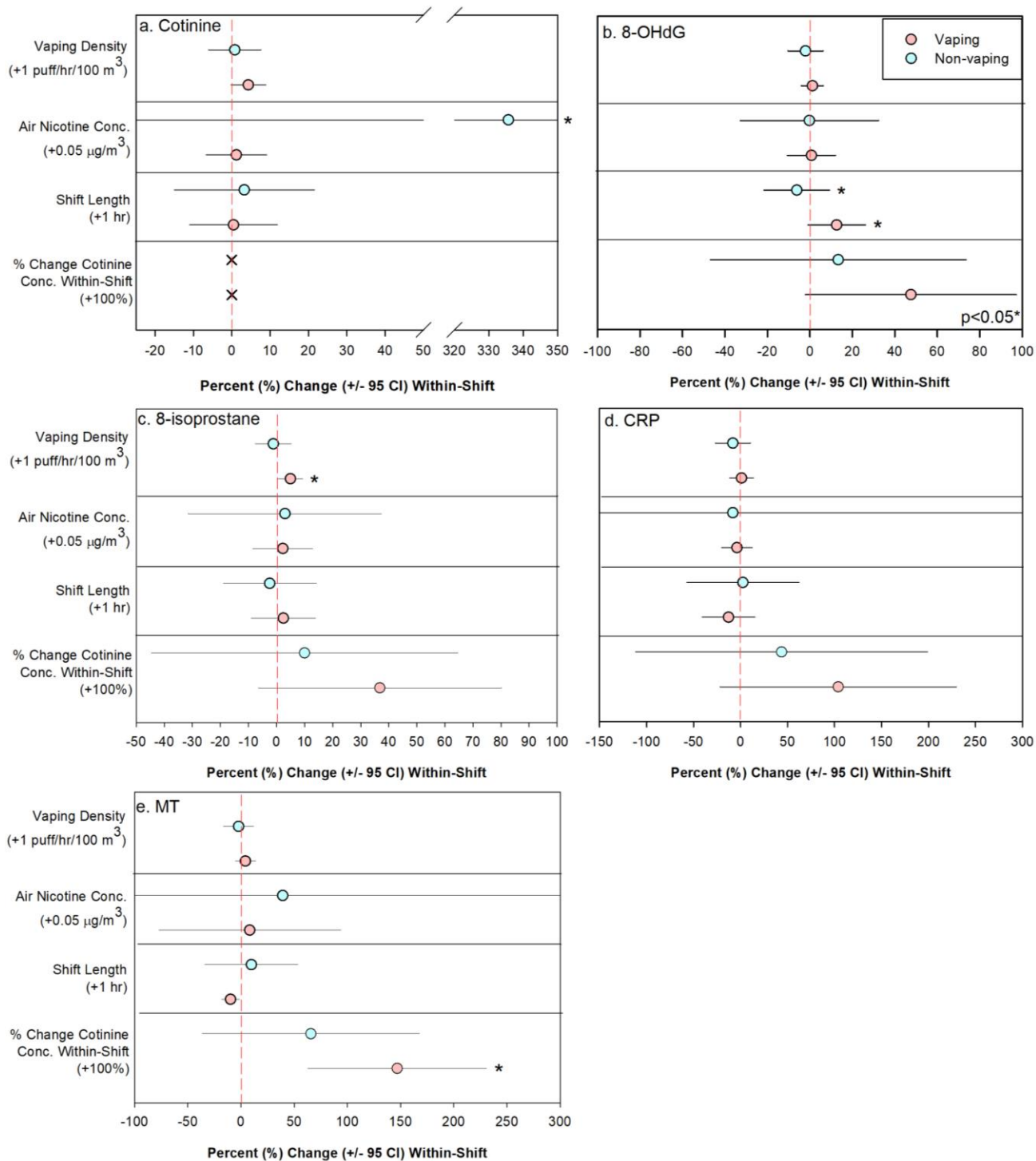
Figure 3.8. Associations between work shift-characterizing exposure predictors and studied biomarkers. Associations interpreted as percent (%) change in effect biomarker concentration with specified unit increase in exposure predictor. Fixed effects included in linear mixed models were age, sex, BMI, and marijuana use.

model ran with each predictor variable that was observed or measured during the work shift. As seen in Fig. 3.8a, for percent change in urinary cotinine as a marker of e-cig aerosol exposure after a work shift, air nicotine concentration was a significant predictor for cotinine levels in non-vaping subjects, strongly indicating that non-vaping workers are exposed to airborne nicotine from exhaled e-cig aerosol as a result of working at a vape shop. On the other hand, airborne nicotine from exhaled e-cig aerosol during work shift probably accounts for negligible cotinine increase in vaping subjects.

Change in urinary cotinine concentration within-shift, as a result of exposure to e-cig aerosol (i.e. mainstream and exhaled for vaping subjects and exhaled for non-vaping subjects), was a main predictor tested for increase in each of the studied biomarkers of effect within-shift. As seen in Figure 3.8b-e, results of the linear mixed-effect model (includes subject and vape shop as random effects) saw significant positive associations between within-shift changes in urinary cotinine and MT concentrations among vaping subjects ($p<0.05$). Potential positive associations were also detected between urinary cotinine and 8-OHdG, 8-iso, and CRP for vaping subjects ($p<0.10$). These associations, particularly with 8-iso, signify that nicotine exposure, largely from e-cig use during the work shift, produces an acute increase in oxidative stress and inflammatory markers. For non-vaping subjects, no significant associations were detected, signifying that any oxidative stress or pro-inflammatory effects from exposure to exhaled e-cig aerosol is most likely a result of cumulative exposure from working multiple consecutive shifts rather than an acute response after working just one shift.

To lesser degree (smaller % change within-shift), the mixed-effect model showed shift length to be a predictor for urinary 8-OHdG levels, with a positive association (~13%) among vaping subjects but a negative association (~-6%) among non-vaping subjects, and vaping

density to be a predictor for urinary 8-iso levels among vaping subjects. These findings are reflective of the recurring e-cig use, and the vaping activity probably highly weighted by the subject's own e-cig use, by vaping subjects during a work shift contributing to an acute increase in 8-OHdG. On the other hand, it is possible spending more time at work may be shielding the non-vaping subjects from stronger oxidative stressors outside of work by spending more time at work, further supporting that exposure to exhaled e-cig aerosol does not induce acute oxidative stress after a work shift. Interestingly, though not significant ($p>0.01$), shift length and air nicotine concentration showed higher positive associations for cotinine and MT within non-vaping than vaping subjects. This identifies shift exposure to exhaled e-cig aerosols, defined by how long the subject is in the vape shop environment (exposure duration to e-cig-related indoor air contaminants) and/or how high the time-weighted air nicotine concentration is during a work shift (dose of e-cig-related indoor air contaminants being inhaled in the vape shop environment), as a possible occupational hazard. Other shift or vape shop related observations that were measured or recorded (i.e. AER, subject vaping frequency, and nicotine intake estimated from e-liquid consumption) showed no significant association with any of the biomarker levels.

3.4.5. Comparing Biomarker Level Changes in Vape Shop Workers with Tobacco Smokers

Centers for Disease Control and Prevention (CDC) have deemed e-cig aerosols less harmful than tobacco smoke due to findings of fewer harmful chemicals than tobacco smoke, but do not consider e-cigs as safe (CDC, 2022). Results of this study support this determination. Lipid peroxidation marker 8-isoprostane among the vaping vape shop workers were shown to markedly increase from the start to end of a work shift (Day 2), which can be estimated as a 7-hr e-cig use period. Comparing the effect size (Hedge's *g;* 95% CI) calculated for this parameter (*g* = 0.21; -0.29 – 0.74) with one study that measured acute changes in breath condensate 8-iso in

healthy smokers at 15 minutes and 5 hours after smoking two tobacco cigarettes (Montuschi et al., 2000), the effect sizes calculated in the smoker study ($g = 4.58$; $2.81 - 7.03$ and $g = 2.46$; $1.37 - 3.89$, respectively) were larger and do not overlap with this study's effect size calculation, indicating that e-cig aerosols produce less acute lipid peroxidation effect than tobacco smoke. Furthermore, comparison of the association between urinary cotinine and 8-OHdG among the vaping workers in this study and smoking office workers in another study showed that 8-OHdG increases by approximately 63% after a one-fold increase in cotinine in the smoking office workers (Lu et al., 2014), but only $25 - 27\%$ in the vaping workers, indicating that e-cig-related nicotine contributes less than half of the increase to oxidative DNA damage than tobacco-related nicotine.

As described in Section 3.4.3.1, the increases in urinary cotinine observed among the non-vaping vape shop workers were smaller in effect size and below the ranges calculated from studies with casino workers and smoking bar patrons exposed to SHS/ETS during their work shifts. On the other hand, as described in Section 3.4.3.2, the increases in urinary 8-iso observed among the non-vaping subjects were within the 95% CI of nonsmokers exposed to outdoor SHS at a bar/restaurant for 3 hours. For these markers, these comparisons indicate that exposure time and setting are influential factors in determining the safety of e-cig aerosol or tobacco smoke as a secondhand exposure. For instance, casino and smoking bar patrons are exposed to SHS/ETS in indoor environments, where AERs can be low and amounts of smoking activity can be large, leading to more potent exposures to nicotine than in vape shops where vaping activity or indoor nicotine air concentrations may be less. The non-vaping workers had exposure times averaging about 6.5 hours based on their observed shift length in the vape shop, while exposure to SHS/ETS in the other study was shorter at 3 hours and the subjects were outdoors, where

nicotine concentrations were most likely diluted. These factors could explain the 95% CI of the effect size calculated for these subjects overlapping with this study's non-vaping worker calculated effect sizes for 8-iso changes. Still, the effect size calculated for the outdoor SHS/ETS exposure study is higher than those calculated for this study, indicating that tobacco smoke is most likely more harmful as a secondhand exposure than e-cig aerosol.

3.5. Conclusion

This study is the first to longitudinally assess exposure and effect biomarkers of workplace-related exhaled e-cig aerosol in vape shop workers. Furthermore, it is also the first to investigate longitudinal trends of oxidative stress, systemic inflammation, and metal toxicity/reactive oxygen species response markers among exclusive e-cig users and non-e-cig users passively exposed to e-cig aerosol. Elevated oxidative stress, inflammation, and metal toxicity/reactive oxygen species response markers observed within a work shift were much stronger among vaping workers, whose e-cig aerosol dosage is compounded with their own e-cig use during a work shift. However, increasing cotinine, and a corresponding upward trend in 8-iso, between the first and last work shifts was observed in non-vaping workers with a consecutive workday schedule, indicating that these increases in nicotine exposure and oxidative stress may be attributable to workplace exposure to exhaled e-cig aerosols. This is further suggested with the significant association observed between cotinine and 8-iso in the non-vaping group varied by vape shop, suggesting that worksite characteristics, which could include vaping activity during the shift, may increase oxidative stress. Largely exploratory, this chapter provides preliminary evidence showing the potential impact workplace exposure to exhaled e-cig aerosol can have on regularly exposed workers, and can inform future studies needed to quantify the

contribution of workplace exhaled e-cig aerosol on oxidative stress, inflammation, and other health impacts.

4. ENHANCED VENTILATION AND PORTABLE FILTRATION AS AIR MITIGATION STRATEGIES TO REDUCE EXPOSURE TO E-CIGARETTE AEROSOLS IN VAPE SHOPS

4.1 Abstract

E-cig use inside the vape shop can increase indoor e-cig-related air contaminant levels, posing a potential occupational hazard to vape shop workers. Air mitigation strategies may be needed to reduce potential exposure. Effectiveness of two air mitigation strategies, enhanced ventilation at ASHRAE-recommended ventilation rate for beauty and nail salons and high-rate portable filtration, were tested in six vape shops for indoor fine and ultrafine particle and nicotine air concentration reduction. Simultaneous measurements were also taken at increasing distances away from the vaping area to assess the effect of air mitigation on the mixing and spatial profiles of particle levels inside the shops. From baseline, mean PNC levels reduced by an average 40% after enhanced ventilation and 61% after portable filtration across the studied shops, indicating that ultrafine particles are more sensitive to filtration. Mean $PM_{2.5}$ levels reduced by 47% after enhanced ventilation and 26% after portable filtration, indicating that fine particles are more sensitive to dilution effects from increasing the AER. During high vaping density in the shop, average PNC and $PM_{2.5}$ concentrations were lower during enhanced ventilation than during baseline. During portable filtration, average PNC and $PM_{2.5}$ levels stayed low at varying vaping densities compared to baseline and enhanced ventilation, suggesting filtration to have a different mechanism (i.e. removal of particles) of indoor pollutant control than dilution or exhausting indoor air. From baseline, mean time-weighted average air nicotine concentrations were reduced

by an average 46% after enhanced ventilation and 9% after portable filtration, suggesting enhanced ventilation may be more effective in reducing gas-phase nicotine.

4.2 Introduction

Exhaled e-cig aerosols present similar public health concerns as SHS/ETS as non-users can be exposed to e-cig-related air contaminants by being in close proximity to an e-cig user or the contaminants can transport to adjacent spaces and other rooms through cracks or vents in multiunit buildings (Li et al., 2021; Khachatoorian et al., 2018). In a ventilated room, particulate matter, volatile organic compounds, polycyclic aromatic hydrocarbons, carbonyls, and metals were found to significantly increase after e-cig use (Schober et al., 2014). Secondhand exposure to exhaled e-cig aerosols was also demonstrated by the absorption of e-cig-related nicotine by non-smokers in e-cig-using homes (Ballbe et al. 2014) and nonsmoking attendees at large e-cig events (Johnson et al., 2019). Successful reduction of exposure to indoor air pollutants and inhalation risks through air mitigation strategies such as ventilation and filtration has been well documented in various indoor environments including residences, workplaces, and hospitals (Chan et al., 2017; Barn et al., 2008; Howard-Reed et al., 2002; Miller and Nazaroff, 2001; Sextro et al., 1986; Jacobs and Gids, 2005; Gids and Opperhuizen, 2013; Polidori et al., 2013; Sharma and Balasubramanian, 2019; Miller-Leiden et al., 1996). Since exhaled e-cig aerosols are highly evaporative and will be subject to the air conditions in the indoor environment, it is important to see how different air mitigation strategies will affect indoor air concentrations of e-cig-related contaminants especially when there are real workplaces or indoor spaces that allow vaping.

In residential settings, opening windows during smoking episodes where rooms were occupied by an active smoker or operating a filtration device during waking hours in rooms

where smoking was allowed decreased the 24-hour average nonsmoker SHS particle exposure concentrations by 54 – 73% (Klepeis and Nazaroff, 2006). In the hospitality industry, reductions of 50 – 90% and of 98% to the exposure concentration of ETS by increased dilution ventilation and displacement ventilation, respectively, could be achieved (Chan et al., 2017; Jacobs and Gids, 2005). In a multi-zone test environment, uses of a portable air filtration unit and enhanced ventilation in the smoking room yielded about 65 – 90% and 30 – 75% reduction, respectively, in predicted lung deposition of ETS particle mass in a nonsmoker located in an adjacent room (Miller and Nazaroff, 2001). Although many cities and states have banned vaping in public areas and workplaces as well as included vaping prohibitions in venues with existing smoke-free provisions (ANRF, 2022), vaping is still permitted in vape shops (CA Labor Code Section 6404.5). With vape shops known to purposely keep the ventilation off to allow for stagnant indoor air conditions optimal for doing vape tricks (e.g. blowing clouds or smoke rings), testing and prescription of effective air mitigation strategies are warranted for this type of workplace. Enhanced ventilation, portable filtration, and segregation of vaping activity were strategies demonstrated to decrease particle concentrations in a controlled multiunit setting during an active vaping session (Zhang et al., 2020).

This study tests and measures the effectiveness of standard air mitigation strategies in representative vape shops, where permitted e-cig use poses potential occupational hazards through impacts on indoor air quality and secondhand exposure. Reductions in area concentrations of FPs, UFPs, and nicotine were evaluated after increasing the air exchange rate via the shop's ventilation system and introducing air cleaning using a portable air filtration device during business hours.

4.3 Material and Methods

4.3.1. Air Mitigation Tests

Effectiveness of two air mitigation strategies, enhanced ventilation and portable filtration, were tested in six vape shops. Representative of the survey results presented in Chapter 2 Section 2.4.1, the vape shops tested were small-sized shops (≤ 250 m^3) and had their own mechanical ventilation system that was not shared with adjacent businesses and not normally turned on or in full operation during business hours (low air exchange rate). Real-time PNC and PM$_{2.5}$ concentrations as well as time-weighted air nicotine concentrations were measured during business hours over two to four consecutive days at baseline (typical ventilation setting of vape shop with no filtration) and for each of the two mitigation strategies to assess the changes in pollutant levels after mitigation. Pollutant concentrations were measured within 1.2 m of the vaping bar, also described as within the personal space from the vaping source, in all six shops. The same measurements were also conducted outdoors simultaneously. To investigate the effect of the mitigation strategy on indoor mixing and spatiality of exhaled e-cig aerosols, a second set of monitoring instruments was operated in shops #3, #5, and #6 and placed at distances which are considered the social space and public space from the vaping bar. Section 4.4.2 details the definitions of personal, social, and public spaces in proximity to a person. In one shop (#5), particle size distribution was also measured within 1.2 m of the vaping bar during the air mitigation tests. Placement of instruments for temporal and spatial profile measurements in the shop was made with considerations to instruments not blocking customer or employee traffic and availability of nearby electric outlets. To maintain consistency of vaping activities and customer traffic across each mitigation strategy as best as possible, air mitigation tests were conducted on the same set of days each week.

Measurements of CO_2, temperature, and relative humidity (RH) levels; air exchange rate (AER) calculation; and field observations were also conducted on the mitigation test days. Materials and methods for all measurements conducted for this study are described previously in Chapter 2 Section 2.3.2 and Chapter 3 Section 3.3.3 for airborne nicotine. Table 4.1 summarizes the characteristics of the studied vape shops and the mitigation conditions.

Table 4.1. Characteristics of the six studied vape shops and mitigation conditions

Vape Shop	Shop Size (m^3)	Ventilation during Baseline	Minimum AER (hr^{-1}) to Meet Target ASHRAE Standard	AER (hr^{-1})			Average (SD) Vaping Density* (puffs/hr/100 m^3)
				Baseline	Enhanced Ventilation	Portable Filtration	
1	184	None	NA	0.1	NA	0.1	1.0 ± 2.6
2	208	Natural Ventilation (Door Open)	1.2	0.9	1.7	NA	1.7 ± 1.6
3	99	None	1.3	0.1	1.7	0.1	3.8 ± 2.5
4	204	Natural Ventilation (Door Open)	2.0	0.5	2.1	0.2	5.1 ± 3.3
5	205	A/C	1.5	0.1	2.8	0.2	5.6 ± 4.2
6	114	None	2.4	0.2	2.9	0.2	11.4 ± 12.5

* Averaged over all study days

4.3.1.1. Enhanced ventilation

Each vape shop's ventilation system was operated with the exhaust and/or supply fans on and doors closed to increase the AER inside the shop to meet the ASHRAE ventilation standard of 20 cubic feet per minute (cfm) per person for acceptable indoor air quality in beauty and nail salons (ASHRAE, 2016). The ASHRAE ventilation standard for beauty and nail salons was chosen as the minimum instead of retail sales as both vape shop and beauty/nail salon spaces are highly impacted by indoor emission sources. Shop AER was calculated using the CO_2 tracer gas

method discussed in Chapter 2 Section 2.3.2 while the ventilation system was operating, then compared with the AER converted from the ASHRAE ventilation standard for beauty and nail salons to verify that the ventilation system was operating at the desired level. Equation 4.1 was used to convert the ASHRAE standard to the corresponding AER for each vape shop:

$$\text{AER} = (20\ \text{cfm/ft}^2 \times \text{shop occupancy} \times 60\ \text{min})/\text{volume of shop in ft}^3 \qquad (4.1)$$

The minimum AER to meet the ASHRAE ventilation standard was calculated for each shop using the maximum shop occupancy recorded during all study visits at the shop. All AERs calculated during testing of the enhanced ventilation strategy met or exceeded the AERs corresponding to the beauty/nail salon ASHRAE ventilation standard for each vape shop.

4.3.1.2. Portable filtration

The Blueair Classic 605 Air Purifier (Blueair, Inc., Chicago, IL) was placed on the floor of the shop and operated in a location as close to the vaping bar as possible where the unit can be safely plugged to an electrical outlet, was at least 2 feet away from any obstacles or corners, and was not blocking customer or employee traffic. Locations of the air purifier in the shops were approximately 1 to 5 m away from the vaping bar. The Blueair Classic 605 model is an Association of Home Appliance Manufacturers (AHAM) certified portable air cleaner, equipped with high efficiency particulate air (HEPA) and activated carbon filters and an ionizer, rated at a clean air delivery rate (CADR) of 500 cfm for smoke; the CADR range for smoke typically goes up to 450 cfm (Harriman et al., 2019). CADR refers to the air cleaner's delivery of relatively clean air, expressed in cfm, and is a product of the fractional removal efficiency for a particular pollutant and the air flow rate through the air cleaner (U.S. EPA, 2018). Ventilation conditions in the vape shop were maintained at the baseline level while the air purifier was in operation.

4.3.2. Data Analysis and Mitigation Effectiveness Evaluation

Decay rates of select real-time concentrations were calculated from representative temporal profiles of PNC and $PM_{2.5}$ using the following equation:

$$\ln(C_t/C_{t=0}) = -k \times t \tag{4.2}$$

where k is the particle decay rate, t is the elapsed time, C_t and $C_{t=0}$ are the particle concentrations measured at times t and $t=0$, respectively, during the decay period. The particle decay rate (k) was calculated by fitting a line to the plot of $\ln(C_t/C_{t=0})$ versus time.

Mitigation effectiveness was assessed as relative percent reduction in pollutant concentrations, defined as $100\% \times (C_{TWA,base} - C_{TWA,exp})/C_{TWA,base}$ for each mitigation strategy. For C_{TWA} (time-weighted averaged concentration) used in the mitigation effectiveness calculation for particulates, real-time 1-minute PNCs and $PM_{2.5}$ concentrations measured during each sampling day were averaged over each hour and corrected for background. The hour TWA pollutant concentrations were then divided by the corresponding vaping density (e-cig puffs per hour, corrected for dilution using shop volume) and averaged among all the sampling days for the designated mitigation strategy. The PNC and $PM_{2.5}$ TWA concentrations failed the Kolmogorov-Smirnov tests for normality ($p<0.05$), respectively, so Kruskal-Wallis ANOVA on Ranks was used to compare the particle concentrations between vape shops. Statistical significance was taken at $p<0.05$. C_{TWA} for airborne nicotine, integrated over business hours when the mitigation was in effect, was corrected for vaping density averaged over the sampling day. For the spatial profile analysis of pollutant concentrations during baseline and mitigation, C_{TWA} for each pollutant was calculated as described above for the set of measurements at the vaping bar (personal space) and at the location farther away (social or public space).

Linear regression was used to assess the impact of the mitigation strategy on the correlation between background-subtracted particle concentrations and vaping density, which was shown to be a strong predictor for indoor particle levels (Li et al., 2021), from all vape shops sampled. Computation of the summary statistics for pollutant concentrations, normality and significance tests, and linear regression were performed using Sigmaplot 12.5 (Systat Software Inc., San Jose, CA). All figures were generated with Sigmaplot 12.5.

4.4 Results and Discussion

4.4.1. Effects of Mitigation on Particle Emissions and E-cig-related Air Pollutant Concentrations from Vaping

4.4.1.1. Particle emissions

Compared to baseline settings, temporal profiles of real-time indoor concentrations of particle number and $PM_{2.5}$ were still dynamic inside the studied vape shops during both mitigation strategies. As seen in Fig. 4.1, the sharp peaks indicate particle emissions during active vaping and were not much different among the three mitigation settings. However, the indoor background PNC and $PM_{2.5}$ concentration decreased after mitigation was introduced. For instance, in Fig. 4a beginning at the 15:13:00 mark, the indoor background PNC (3.7×10^4 particles/cm^3) spiked up by about 5 times (1.7×10^5 particles/cm^3) after active vaping, and then fell to background level after 5 min. In Fig. 4b while enhanced ventilation was in effect, beginning at the 15:10:00 mark, the indoor background PNC was almost 4 times lower (1.0×10^4 particles/cm^3) before spiking after active vaping, and then fell to background level after 4 min. In Fig. 4c while portable filtration was in effect, beginning at the 15:51:00 mark, the indoor background PNC was almost 25 times lower (1.5×10^3 particles/cm^3) than the baseline indoor background PNC before spiking after active vaping, and then fell to background level after 4 min. Likewise, in Fig. 4d beginning at the 15:13:00 mark, the indoor background $PM_{2.5}$ (685

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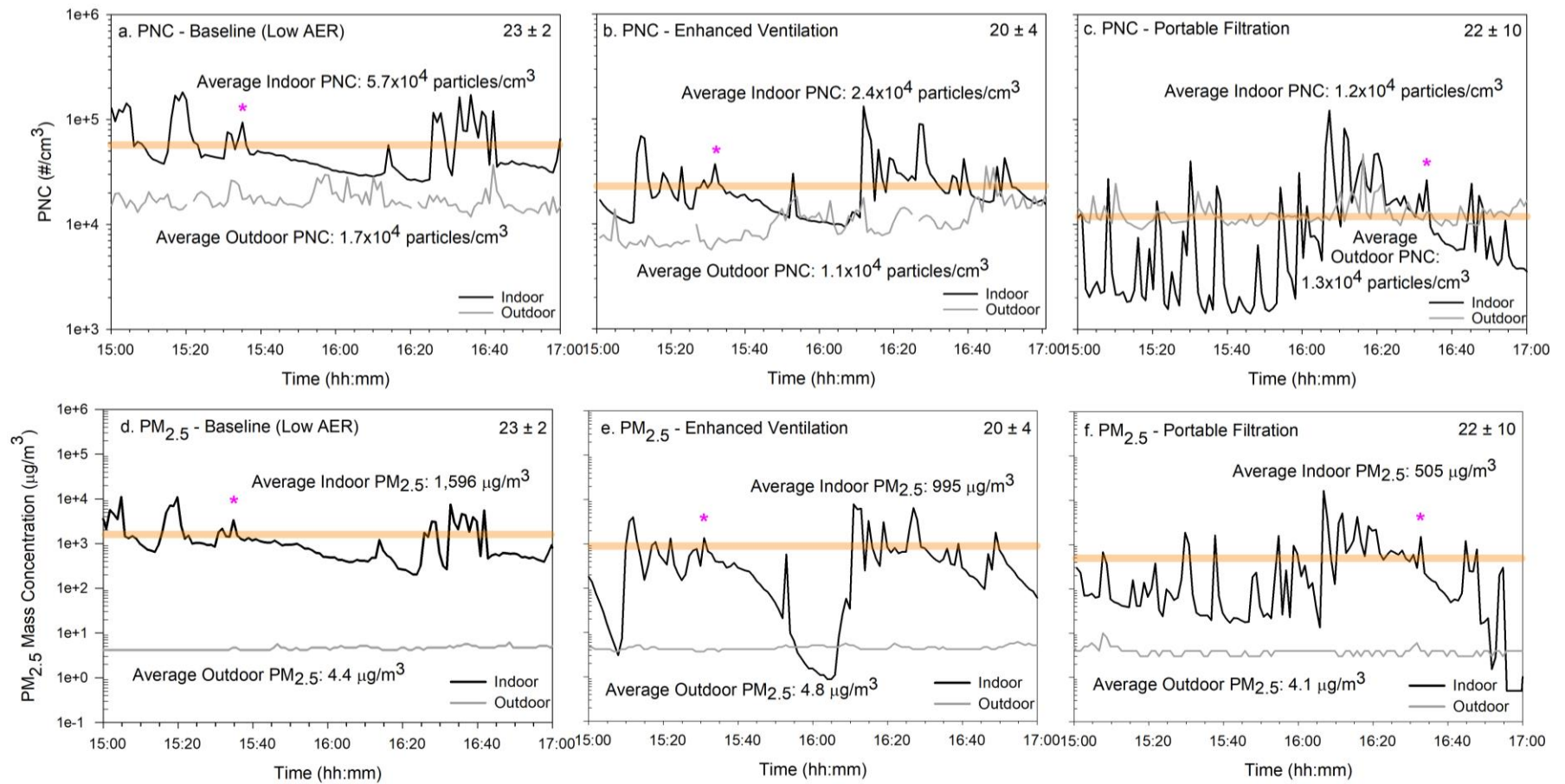
Figure 4.1. Temporal profiles of PNC (a-c) and PM$_{2.5}$ mass concentration (d-f), measured simultaneously per mitigation strategy and baseline, in vape shop #6. Indoor and outdoor concentrations are show in black and gray, respectively. The pink asterisk (*) denotes an exhalation of e-cig aerosol followed by a period of no vaping. The orange line represents the average indoor concentration during the sampling period. Average vaping density (puffs/hr/100 m^3) during the sampling period was provided in the top right corner of each panel.

$\mu g/m^3$) spiked up by about 16 times (11,000 $\mu g/m^3$), then fell to background level after 2 min. In Fig. 4b while enhanced ventilation was in effect, beginning at the 15:10:00 mark, the indoor background $PM_{2.5}$ was 4 times lower (155 $\mu g/m^3$) before spiking after active vaping, then fell to background level after 3 min. In Fig. 4c while portable filtration was in effect, beginning at the 15:46:00 mark, the indoor background $PM_{2.5}$ was 38 times lower (18 $\mu g/m^3$) than the baseline indoor background $PM_{2.5}$ before spiking after active vaping, then fell to background level after 2 min.

In addition to decreasing indoor background particle levels, the rate of particle concentration decrease to background level after active vaping was also higher during mitigation compared to baseline. For periods in Figure 4.1 when there were indoor particle concentration decays while no vaping was occurring, the decay rates averaged to be 2.8 – 4.7 hr^{-1} during baseline, 5.2 – 15.5 hr^{-1} during enhanced ventilation, and 10.0 – 12.0 hr^{-1} during portable filtration. During default low AER condition, it is expected that background indoor particle concentrations in vape shops increase from the moment of no active vaping to after an e-cig puff due to residual exhaled e-cig particles that are less volatile persisting in the shop after continuous vaping and reduced dilution of exhaled e-cig particles from outdoor air entering the shop, all decreasing the evaporation rate of exhaled e-cig particles (Nguyen et al., 2019). By increasing the AER in the shop, enhanced ventilation increases the particle decay by removing and diluting the exhaled e-cig particles with fresh air, while by introducing a particle removal mechanism, portable filtration increases the particle decay by pulling in air within the shop, filtering the particles, and returning particle-removed air to the shop. The decay rate of $PM_{2.5}$ (15.5 hr^{-1}) was higher than PNC (5.2 hr^{-1}) during enhanced ventilation (Fig. 4b and 4e), but the decay rate of PNC was higher (12.0 hr^{-1}) than $PM_{2.5}$ (10.0 hr^{-1}) during portable filtration (Fig. 4c and 4f). This

is likely due to a higher AER environment promoting particle evaporation as a previous chamber study showed higher loss rates of $PM_{2.5}$ (i.e. 4.4-7.0 hr^{-1}) compared to ultrafine particles (i.e. 0.6-1.2 hr^{-1}) (Li et al., 2020). Furthermore, air purifiers using HEPA filters or ionization have been shown to have higher control efficiency with smaller particles (i.e. 0.1μm or less), most likely because small-sized particles travel farther and faster due to less inertia and are more likely to deposit via diffusion onto the fiber of the filter (Shiue et al., 2011; Dubey et al., 2021; Wallace, 2008; Chuanfang, 2012). In comparison to a previous study testing mitigation strategies on exhaled e-cig aerosols in a test indoor environment, the particle number decay rate during enhanced ventilation (5.8 hr^{-1}) was slightly higher than during increased filtration (5.0 hr^{-1}) (Zhang et al., 2020). The air purifier used in this study had a higher CADR, or particle removal rate, than the air purifier used by the previous study. Since particle decay in a room when filtration is applied is due to a balanced mix of AER and aerosol dynamics (Zhang et al., 2020), the application of a high CADR air purifier in the vape shops increases the aerosol dynamic contribution to particle decay.

When comparing the average indoor concentrations during baseline and the two mitigation strategies within the sampling periods in Fig. 4.1, among similar vaping densities, the mean PNC and $PM_{2.5}$ mass concentration decreased from baseline to enhanced ventilation, to portable filtration. Alternately, the indoor-to-outdoor (I/O) ratios of the average PNC and $PM_{2.5}$ concentration decreased in the same order (i.e. 3.4 > 2.2 > 0.9 for PNC and 363 > 207 > 123). This highlights the effectiveness of enhanced ventilation and portable filtration as mitigation strategies for exhaled e-cig aerosols in vape shops. Filtration showing the most reduction in average particle concentration and I/O ratio in this study can be attributed to the strength of the air purifier used in this study to pull in a high volume of air, trap particles with combined

electrostatic and mechanical filtration, and release cleaned air, versus just increased AER (i.e. exhaust of indoor air and dilution with make-up air).

4.4.1.2. Particle concentrations

Table S4 in Appendix – Supplemental Information presents the summary statistics for indoor and outdoor particle concentrations measured for each vape shop during baseline and the mitigation test days. During no vaping activity, indoor PNCs ranged from 4.8×10^3 to 2.4×10^4 particles/cm^3 during baseline settings, 7.4×10^3 to 2.3×10^4 particles/cm^3 during enhanced ventilation, and 1.8×10^2 to 7.5×10^3 particles/cm^3 during portable filtration among the six vape shops. Meanwhile, indoor PM$_{2.5}$ concentrations ranged from 3 to 72 µg/m^3 during baseline, 0.6 to 16 µg/m^3 during enhanced ventilation, and 1 to 64 µg/m^3 during portable filtration. During active vaping, indoor PNCs ranged from 2.4×10^4 to 5.2×10^5 particles/cm^3 during baseline settings, 5.3×10^3 to 4.8×10^5 particles/cm^3 during enhanced ventilation, and 2.3×10^3 to 7.5×10^5 particles/cm^3 during portable filtration among the studied shops. Meanwhile, indoor PM$_{2.5}$ concentrations ranged from 13 to 20,900 µg/m^3 during baseline, 3 to 12,800 µg/m^3 during enhanced ventilation, and 3 to 19,300 µg/m^3 during portable filtration. Although PNCs and PM$_{2.5}$ concentrations reached high levels during mitigation to the magnitude observed in baseline during active vaping, the range of PNCs was lower than baseline during portable filtration and the range of PM$_{2.5}$ concentrations was lower than baseline during both enhanced ventilation and portable filtration while there was no vaping. These results indicate that mitigation strategies reduce build-up and sustained elevation of particle concentrations expected during low AER/low filtration shop conditions. Enhanced ventilation was also shown to lower background particle mass concentrations more than portable filtration, while filtration lowered background particle number concentrations more than ventilation. Previewed in the previous section, indoor particle

concentrations during sampling sessions were, on average, were higher than outdoor concentrations by only 1.8 and 1.1 times for enhanced ventilation and portable filtration, respectively, compared to 2.4 times during baseline for PNC, and 15 and 12 times, respectively, compared to 31 times during baseline for $PM_{2.5}$. These I/O ratios highlight the ability of the tested mitigation strategies to lower positive indoor-to-outdoor particle concentration differentials while shop doors are closed.

Figure 4.2 presents the distributions of PNC and $PM_{2.5}$ data collected across the studied vape shops during each mitigation test condition. Though mean PNC concentrations across the three test conditions were still high for shops with ≥ 1 puffs/hr/100 m^3, portable filtration was able to reduce the mean levels to or below PNCs in low indoor emission workplaces (e.g. 9,100 particles/cm^3 in offices) (Wu et al., 2012) (Fig. 4.2a). There is currently no standard for ultrafine particles or particle number. Mean $PM_{2.5}$ concentrations were markedly higher among shops #5 and #6 than the rest of the shops, exceeding the U.S. Environmental Protection Agency 24-hr National Ambient Air Quality Standard (NAAQS) for $PM_{2.5}$ (35 $\mu g/m^3$) (U.S. EPA, 2016) by 20 – 29 times among baseline measurements (Fig. 4.2b). Though the mean levels were still above the 24-hr $PM_{2.5}$ NAAQS by a significant amount, enhanced ventilation and portable filtration were able to reduce the median $PM_{2.5}$ levels below the standard. These median levels (3 – 26 $\mu g/m^3$) are representative of background indoor levels while these mitigation strategies were being applied in the shops, and thus, the elevated mean $PM_{2.5}$ are influenced by the high vaping frequency. For shops #2 and #3 where mean $PM_{2.5}$ concentrations were above the 24-hr $PM_{2.5}$ NAAQS, increased ventilation and filtration reduced the average concentrations to or below the standard.
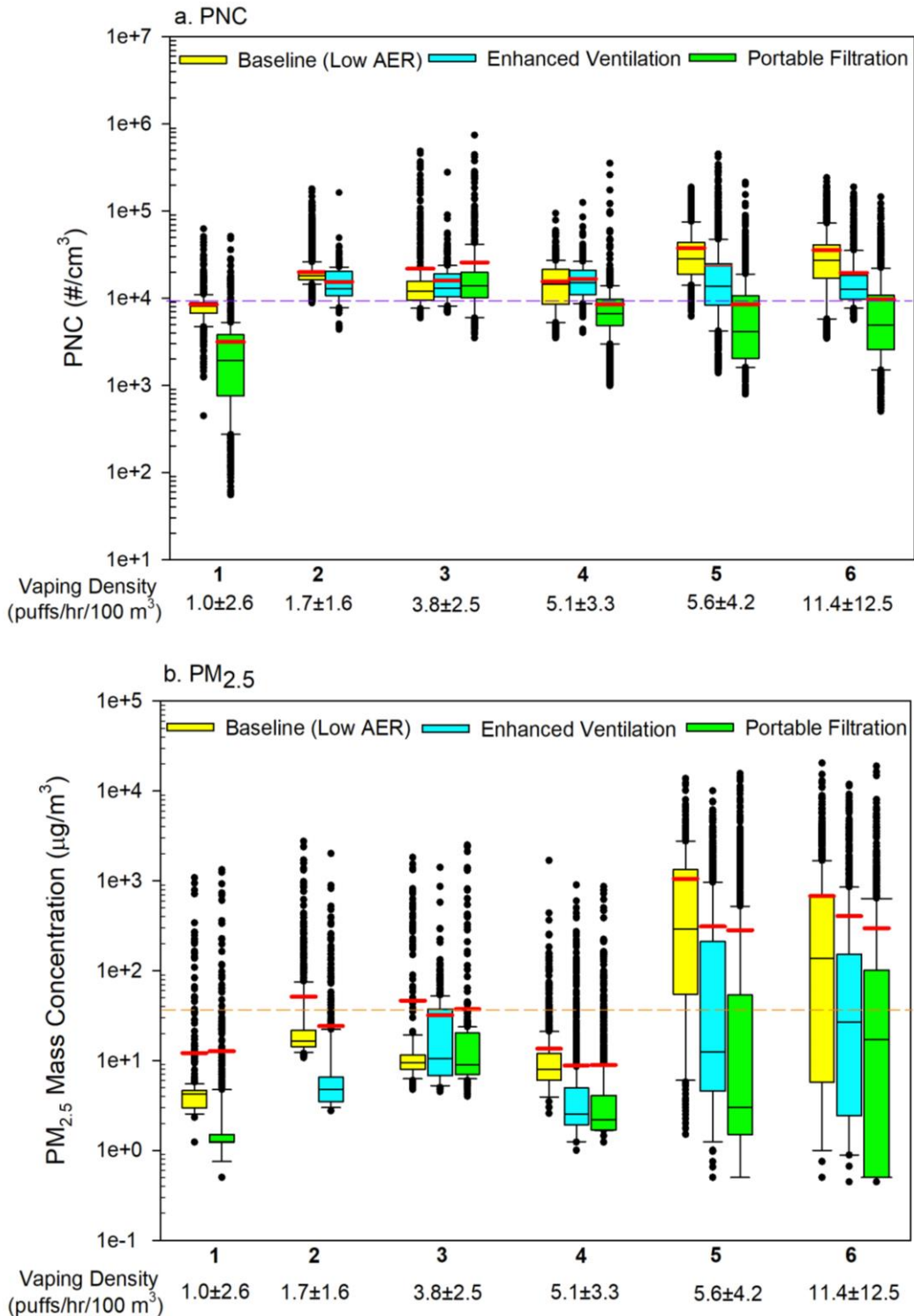
Figure 4.2. Boxplots summarizing (a) PNC and (b) PM2.5 mass concentrations measured during each mitigation test conditions for all six shops and ordered by increasing average vaping density. The dashed purple line marks the mean PNC measured in offices (Wu et al., 2012). The dashed orange line marks the U.S. EPA 24-hr PM2.5 NAAQS (U.S. EPA, 2016). Red lines on the boxes represent the mean and black lines on the boxes represent the median.

Table 4.2. Time-weighted corrected particle number concentration and mitigation effectiveness calculations

Vape Shop	Business Hours (Length of Sampling)	C_{TWA}* ± SD PNC (#/cm³)		
		Baseline	Enhanced Ventilation (Eff.)	Portable Filtration (Eff.)
1	5.5	6,400 ± 6,700	NA	2,000 ± 2,700 (69%)
2	6	7,100 ± 4,400	2,300 ± 700 (68%)	NA
3	4	1,900 ± 900	1,300 ± 700 (31%)	1,000 ± 1,200 (46%)
4	12	3,700 ± 8,000	3,000 ± 2,100 (18%)	1,100 ± 1,000 (70%)
5	8	4,600 ± 2,000	2,900 ± 2,000 (38%)	1,700 ± 1,200 (64%)
6	6.5	2,100 ± 3,300	1,200 ± 900 (43%)	900 ± 1,100 (56%)

*Background corrected and vaping density normalized

Using background-corrected and vaping density-normalized C_{TWA} for PNC and PM$_{2.5}$, mitigation effectiveness was calculated for each shop among all sampling days. Table 4.2 presents the average C_{TWA} and mitigation effectiveness calculations for PNC per shop. From baseline, enhanced ventilation reduced C_{TWA} PNC levels by 18 – 68% and portable filtration reduced these levels by 46 – 70%. The high percent PNC reductions achieved within the studied shops using these mitigation strategies exceeded the percent PNC reductions measured by Zhang et al. (2020) after applying air mitigation strategies, which resulted in mean PNC decrease of 42% in an enhanced ventilated room and 17% in an increased filtered room following vaping activity. The reduction in vape shop PNCs achieved through enhanced ventilation is consistent with increasing PNC reduction from increased ventilation in a room with vaping activity (Oldham et al., 2021). Portable filtration showed higher PNC mitigation effectiveness than enhanced ventilation in shops where both strategies were tested, suggesting that filtration may be

more effective in controlling ultrafine particles. This is consistent with prior studies reporting that HEPA filters or ionization can control smaller particles (i.e. 0.1 µm or less) at a higher efficiency due to small-sized particles being more likely to deposit via diffusion onto the fiber of the filter than larger particles that move slower due to more inertia (Shiue et al., 2011; Dubey et al., 2021; Wallace, 2008; Chuanfang, 2012; Singer et al., 2016).

Table 4.3 presents the average C_{TWA} and mitigation effectiveness calculations for PM$_{2.5}$ per shop. From baseline, enhanced ventilation reduced C_{TWA} PM$_{2.5}$ levels by 29 – 68% and portable filtration reduced these levels by 0.8 – 49%. The higher percent PM$_{2.5}$ reductions achieved within the studied shops using these mitigation strategies exceeded the percent PM$_{2.5}$ reductions measured by Zhang et al. (2020) after applying air mitigation strategies, which resulted in mean PM$_{2.5}$ decrease of less than 13% in an enhanced ventilated room an increased filtered room following vaping activity. Enhanced ventilation showed higher PM$_{2.5}$ mitigation effectiveness than portable filtration in shops where both strategies were tested, suggesting that increasing the AER may be more effective in controlling particle mass due to its higher evaporation rate than particle number, which persists longer in the air (Li et al., 2020; Nguyen et al., 2019).

Fig. 4.2 organizes the particle concentration distributions in order of increasing average vaping density measured across all sampling days per shop. As vaping density increased, average baseline PNCs relatively increased each step with median PNC measured in vape shop #6 with the highest vaping density being significantly higher than the levels measured among shops with lesser vaping density (Kruskal-Wallis, $p<0.001$). Average baseline PM$_{2.5}$ concentrations among the shops with the two highest vaping densities were significantly higher than the levels measured among the rest of the four shops (Kruskal-Wallis, $p<0.001$). For shops with lower

Table 4.3. Time-weighted corrected PM₂.₅ mass concentrations and mitigation effectiveness calculations

Vape Shop	Business Hours (Length of Sampling)	C_{TWA}* ± SD PM$_{2.5}$ (μg/m³)		
		Baseline	Enhanced Ventilation (Eff.)	Portable Filtration (Eff.)
1	5.5	7.2 ± 5.4	NA	7.1 ± 8.1 (0.8%)
2	6	28 ± 64	9 ± 7 (68%)	NA
3	4	4.6 ± 3.1	1.8 ± 1.4 (62%)	2.4 ± 3.4 (49%)
4	12	2.5 ± 1.8	1.8 ± 1.5 (29%)	1.5 ± 1.4 (38%)
5	8	92 ± 52	51 ± 34 (44%)	69 ± 68 (25%)
6	6.5	42 ± 36	29 ± 29 (31%)	34 ± 36 (18%)

*Background corrected and vaping density normalized

average vaping densities (i.e. ≤5 puffs/hr/100 m³), the average and/or interquartile range (IQR) PM$_{2.5}$ were at or below the 24-hr PM$_{2.5}$ NAAQS. Average and IQR PNC in shop #1 with minimal vaping density was below the 9,000 particles/cm³ level. These observations denote that indoor vaping ban or e-cig user segregation/isolation strategies could be more effective than engineering controls in reducing indoor exhaled e-cig aerosol levels. Zhang et al. (2020) found that segregation of e-cig users in a closed, separate room adjacent to a room with no vaping activity was the most effective, reducing e-cig-related particle transport to the non-vaping room by 94%. This level of effectiveness is also observed with isolation or segregation strategies applied to indoor smoking (Klepeis and Nazaroff, 2006; Miller and Nazaroff, 2001). Smoking bans implemented in hospitality venues, bars, and public places can reduce indoor FP and UFP levels up to 99% from pre-ban levels (Waring and Siegel, 2007; Valente et al., 2007; Repace et al., 2006; Ott et al., 1996).

Table S4 in Appendix – Supplemental Information presents the summary statistics for indoor and outdoor vapor-phase nicotine concentrations measured for each vape shop during baseline and mitigation test days. Table 4.4 presents the average vaping density-normalized TWA air concentrations and mitigation effectiveness calculations for nicotine per shop. From baseline, enhanced ventilation reduced nicotine concentrations by 47 – 75% and portable filtration reduced these concentrations by 11 – 52%. The negative percent reductions observed (i.e. increase in average concentration during the mitigation strategy compared to baseline) were in shops where the normalized baseline nicotine concentration was within 30% of the method quantification limit, signifying that the mitigation strategy did not have an effect. The high percent nicotine reductions achieved within the studied shops using enhanced ventilation is consistent with significant air nicotine reduction from increased ventilation in a room with vaping activity (Oldham et al., 2021).

Table 4.4. Time-weighted normalized nicotine (vapor-phase) air concentrations

Vape Shop	Business Hours (Length of Sampling)	TWA* Nicotine ($\mu g/m^3$) ± SD		
		Baseline	Enhanced Ventilation (Eff.)	Portable Filtration (Eff.)
1	5.5	0.24 ± 0.08	NA	0.19 ± 0.23 (20%)
2	6	0.18 ± 0.16	0.10 ± 0.09 (47%)	NA
3	4	0.05 ± 0.03	0.02 ± 0.01 (58%)	0.07 ± 0.04 (-42%)
4	12	0.06 ± 0.03	0.07 ± 0.03 (-11%)	0.06 ± 0.01 (11%)
5	8	0.25 ± 0.19	0.09 ± 0.01 (62%)	0.10 ± 0.06 (58%)
6	6.5	0.07 ± 0.06	0.02 ± 0.01 (75%)	0.08 ± 0.03 (-4%)

*Vaping density normalized

4.4.2. Effects of Mitigation on E-cig-related Air Pollutant Concentrations in Proximity to Vaping

Particle and nicotine concentrations at distances closer and farther from the vaping bar were measured in three vape shops during each mitigation test condition. Distances were designated based on the following proximities to a vaping person or area: 1) personal space (0.45 to <1.2 m); 2) social space (1.2 to <3.6 m); and 3) public space (3.6 m and beyond) (Hall, 1966). Background-subtracted and vaping density-normalized C_{TWA} for PNC and PM$_{2.5}$ were compared at points within the personal space to social space in vape shop #3 (#1 in Figure 4.3 and Table 4.5) and within the personal space to public space in vape shops #5 and #6 (#2 and #3 in Figure 4.3 and Table 4.5). As seen in Fig. 4.3 and Table 4.5, baseline PNC and PM$_{2.5}$ concentrations decreased from the personal space to the social/public space in all three shops, confirming the proximity effect observed in vape shops with exhaled e-cig aerosols (Nguyen et al., 2019). However, the percentage of remaining particle concentrations was lower due to the background and vaping density corrections of the concentrations used for this analysis, highlighting the low dilution effect in the shop during high vaping frequency.

In shop #1, where there were low C_{TWA} for PNC and PM$_{2.5}$ due to high vaping density correction as a result of a smaller shop volume, PM$_{2.5}$ was reduced in the personal space during enhanced ventilation and portable filtration compared to baseline by 92% and 63%, respectively. PNC was reduced in the personal space during enhanced ventilation and portable filtration compared to baseline by 35% and 5%, respectively. However, at the social distance, the PM$_{2.5}$ level was similar during both mitigation strategies as baseline and were representative of background levels, which suggests that in this particular shop, neither mitigation strategies changed the decay of PM$_{2.5}$. Since there was less of the dilution factor in shop #1 than in shops #2 and #3, which had higher shop volumes, the mitigation acted most on reducing concentrations
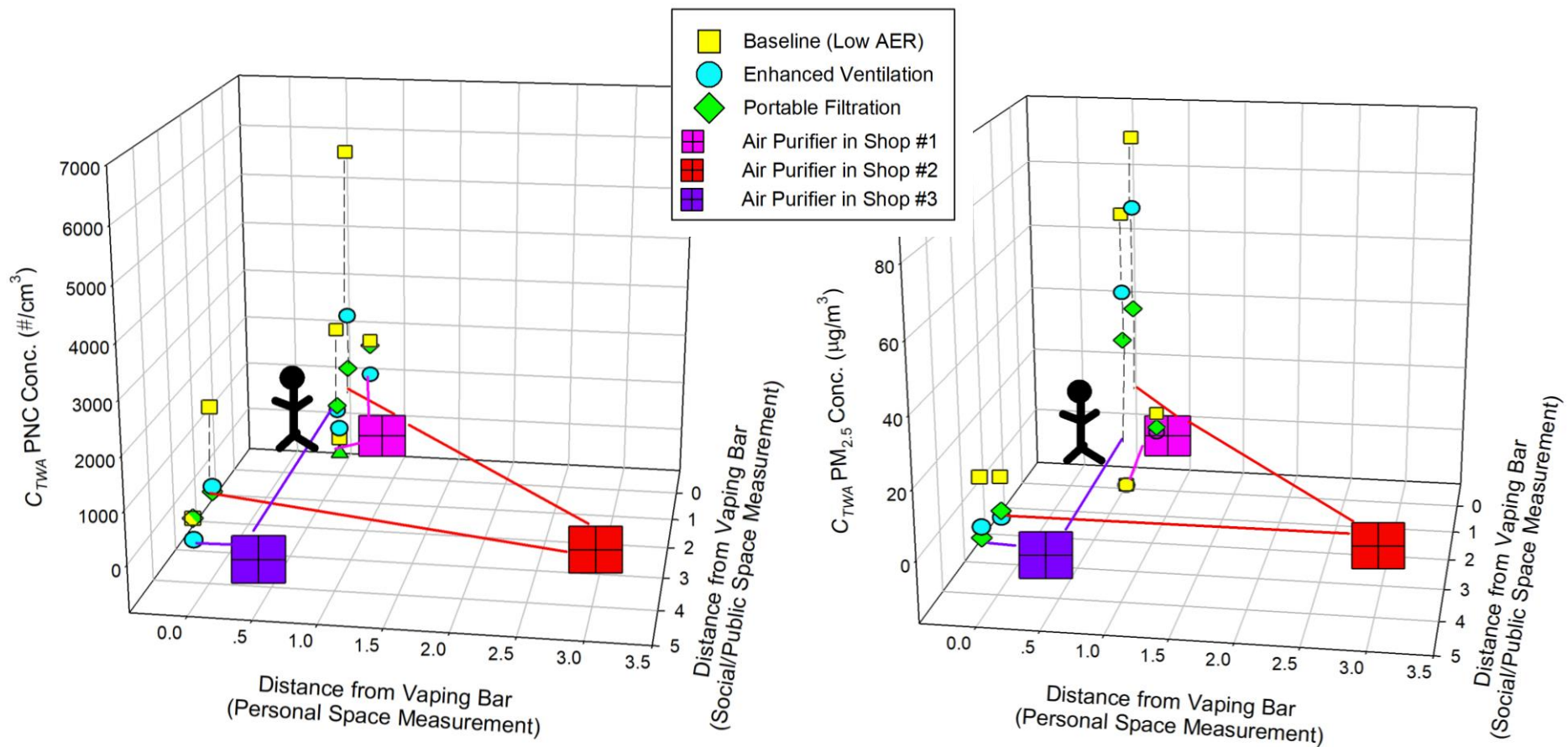
Figure 4.3. Particle number (left) and PM₂.₅ (right) concentrations at personal, social, and public distances away from vaping activity. From vaping activity, concentrations were measured at 0.8 and 2.1 m away in shop #1, 0.6 and 4.7 m away in shop #2, and 0.5 and 4.6 m away in shop #3. The drawn figure represents an e-cig user at the vaping bar.

Table 4.5. Particle number and PM$_{2.5}$ concentrations corresponding to Figure 4.3

Vape Shop	Mitigation	PM$_{2.5}$ C_{TWA} (SD) @ Personal Distance* (µg/m^3)	PM$_{2.5}$ C_{TWA} (SD) @ Social or Public Distance$^+$ (µg/m^3)	% Remain	PNC C_{TWA} (SD) @ Personal Distance* (#/cm^3)	PNC C_{TWA} (SD) @ Social or Public Distance$^+$ (#/cm^3)	% Remain
		0.8m	**2.1m**		**0.8m**	**2.1m**	
1	Baseline	7.1 (32)	0.5 (0.3)	8%	2,000 (7,000)	700 (300)	33%
	Enh. Vent.	1.1 (4.4)	0.4 (0.2)	37%	1,300 (1,100)	1,200 (900)	99%
	Port. Filt.	2.6 (13)	0.5 (0.1)	20%	1,900 (5,600)	1,000 (500)	54%
		0.6m	**3.7m**		**0.6m**	**3.7m**	
2	Baseline	92 (194)	14 (29)	15%	5,800 (4,900)	2,300 (1,500)	40%
	Enh. Vent.	71 (131)	2.2 (10)	3%	2,500 (3,600)	800 (500)	32%
	Port. Filt.	40 (180)	4.1 (8.5)	10%	1,400 (3,800)	700 (600)	50%
		0.5m	**4.6m**		**0.6m**	**4.6m**	
3	Baseline	69 (102)	21 (16)	31%	2,200 (1,800)	700 (300)	33%
	Enh. Vent.	45 (91)	7.0 (10)	15%	500 (1,000)	300 (300)	62%
	Port. Filt.	30 (115)	3.9 (9.3)	13%	600 (1,000)	700 (800)	112%

* 0.45 to <1.25 m

$^+$ Social distance: 1.2 to <3.6 m; Public distance: 3.6 m and beyond

nearest the vaping source. As seen in Fig. 4.3, the air purifier in shop #1 was placed next to the vaping source. Interestingly, the air purifier only reduced PNC in the personal space by 5% from baseline. It is possible that the movement of the e-cig-related particles from the vaping source to the air purifier was contributing to the PNC readings by the condensation particle counter, which was also located in the same location next to the vaping source. This may also explain why enhanced ventilation, for which make-up air vents were centrally located above in the room, was

shown to have the most particle number and mass concentration reduction, bringing levels down to near-background levels, compared to baseline in the personal space. Similar to $PM_{2.5}$, the PNC levels at the social space across the mitigation test conditions were representative of background levels, also suggesting that the absence of the dilution factor with the shop volume focuses the mitigation on reducing concentrations nearest the vaping source.

In shops #2 and #3, where there were higher C_{TWA} for PNC and $PM_{2.5}$ as expected due to lower vaping density correction as a result of larger shop volumes, $PM_{2.5}$ was reduced in the personal space during enhanced ventilation and portable filtration compared to baseline by 23 – 35 – 57%, respectively. PNC was reduced in the personal space during enhanced ventilation and portable filtration compared to baseline by 57 – 77% and 73 – 76%, respectively. Unlike the observations at the social space in shop #1, at the public distance in these two shops, the $PM_{2.5}$ level was lower by 67 – 84% and 71 – 81% during enhanced ventilation and portable filtration than baseline, suggesting that the mitigation strategies increase the $PM_{2.5}$ decay at greater distances in the vape shop. PNC level in shop #2 was also lower by substantial percent reductions during both mitigation strategies than baseline at the public distance, but the percentages remaining when compared to the personal space concentrations were higher than $PM_{2.5}$ due to the personal space concentrations approaching background levels as a result of mitigation. In shop #3, due to the PNC levels in the personal space being at background levels during both mitigation strategies, the percent reductions compared to baseline at the public distance as well as the percentages remaining when compared to the personal space concentrations during these strategies, are arbitrary. Spatial analyses of shops #2 and #3 suggest that the reduced exhaled e-cig aerosol levels measured at distances farther away from the vaping source in larger shops are attributed to the effectiveness of the mitigation strategies in reducing

exhaled e-cig aerosol levels at or near the source, and thus, reducing the level of pollutants that can potentially mix in the shop.

Table 4.6 summarizes the C_{TWA} calculated for airborne nicotine at the personal space and the social/public spaces across the three shops. Nicotine concentration reduced by 50% and 25% during enhanced ventilation and portable filtration compared to baseline, respectively, showing the potential effectiveness, with ventilation being higher, of the mitigation strategies in reducing gas-phase nicotine levels. However, at the social/public distance, the nicotine concentrations were similar during both mitigation strategies as baseline and were below the limit of quantification, suggesting that the mitigation strategies did not change the proximity effect or diffusion coefficient in air for vapor-phase nicotine from the personal to the social/public distances with respect to the vaping source. This is further highlighted by the percent remaining figures being similar across the three test mitigation conditions.

Table 4.6. Air nicotine concentrations measured close to the vaping bar and farther from the vaping bar during each mitigation test

Mitigation	Nicotine		
	C_{TWA} (SD) @ Personal Distance* (μg/m³)	C_{TWA} (SD) @ Social or Public Distance[+] (μg/m³)	% Remain
	0.5 – 0.8m	2.1 – 4.6m	
Baseline	0.09 (0.05)	0.02 (0.02)	25%
Enh. Vent.	0.05 (0.03)	0.01 (0.01)	25%
Port. Filt.	0.07 (0.03)	0.02 (0.02)	33%

* 0.45 to <1.25 m
[+] Social distance: 1.2 to <3.6 m; Public distance: 3.6 m and beyond

4.4.3. Effects of Mitigation on Vaping Density as a Predictor of E-cig-related Air Pollutant Concentrations

With vaping frequency or density having been established as a strong predictor of indoor particle concentrations in vape shops (Nguyen et al., 2019; Li et al., 2021), the linear relationship between vaping density and background-subtracted indoor particle concentrations was analyzed under the effect of the mitigation strategies. In Figure 4.4b for PNC and $PM_{2.5}$, linear regression demonstrated strong positive correlations with indoor average concentrations and vaping density during enhanced ventilation (R=0.70, p=0.003 and R=0.94, p<0.001, respectively), but with lower slopes compared to baseline. The slopes for PNC and $PM_{2.5}$ under enhanced ventilation were 0.64 and 0.81 times the slope at baseline, demonstrating that at the same vaping density, indoor particle concentrations can be lowered by approximately 36% and 19% for PNC and $PM_{2.5}$, respectively, from the concentrations that would be expected at baseline by increasing the AER. The stronger correlation between $PM_{2.5}$ and vaping density supports the susceptibility of particle mass to higher loss from increased AER. In Figure 4.4c for PNC and $PM_{2.5}$, linear regression demonstrated a weak to no correlation with indoor average concentrations and vaping density during portable filtration (R=0.08, p=0.76 and R=0.34, p=0.19, respectively). This indicates that filtration disrupts the linear relationship between vaping density and indoor particle concentrations by implementing a direct particle removal mechanism in the room, resulting in low particle concentrations independent of vaping density. The weaker correlation between PNC and vaping density demonstrates again that particle number may be more susceptible to mechanical and/or electrostatic/ionizing filtration strategies than particle mass.

For nicotine, linear regression demonstrated moderate but nonsignificant correlations between TWA concentrations and vaping density for baseline and enhanced ventilation, which may indicate that vaping density might not be an appropriate predictor for vapor-phase nicotine
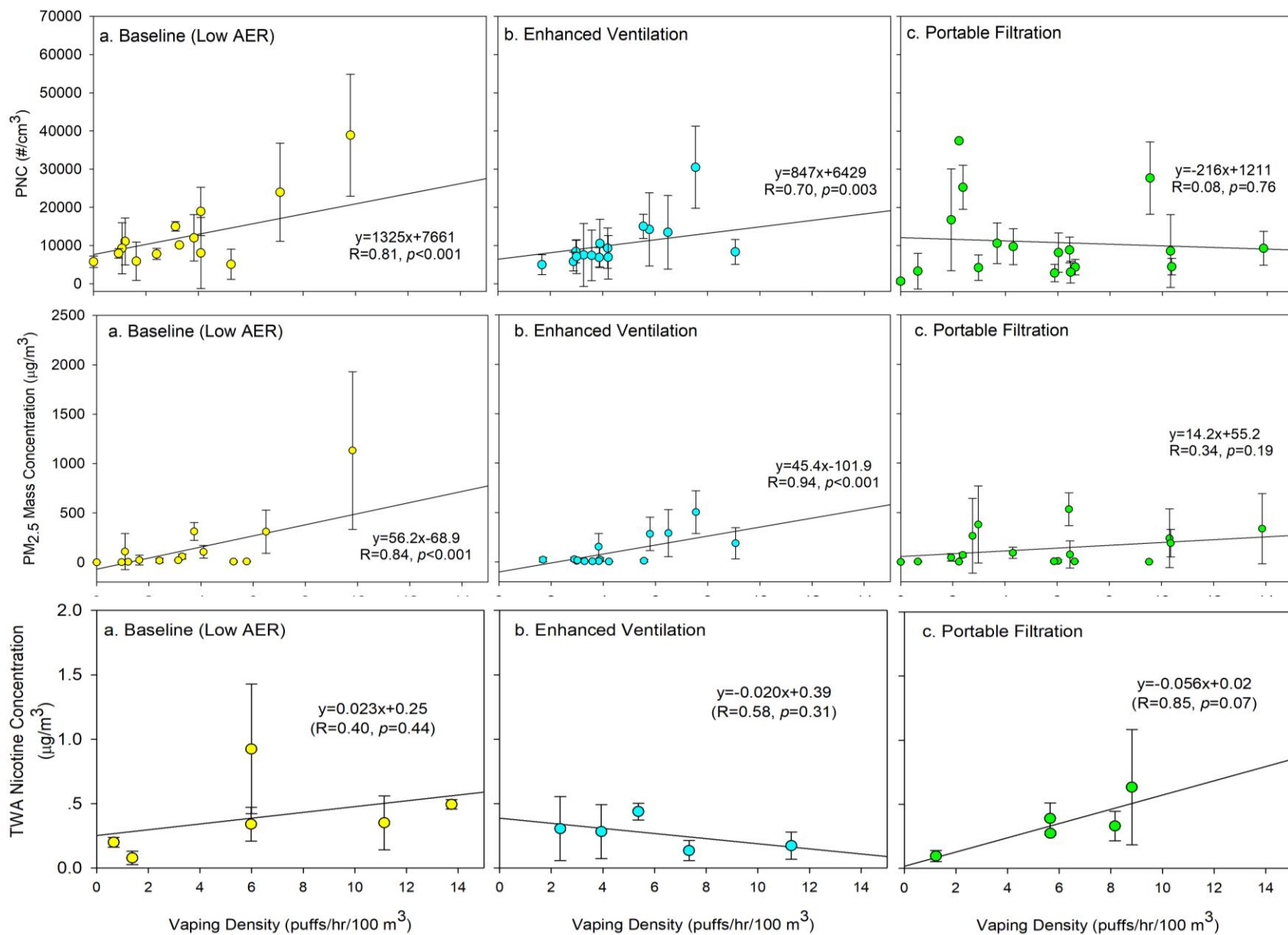
Figure 4.4. Relationships between background-subtracted PNC, PM₂.₅, and nicotine concentrations (top to bottom panel rows) and vaping density during (a) baseline, (b) enhanced ventilation, and (c) portable filtration. Vaping density and particle pollutant concentrations were averaged over the sampling day at each shop. Vaping density and nicotine TWA concentrations were averaged over all designated sampling days for a test conditions per shop.

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given that nicotine in cigarette smoke and e-cig aerosol undergo gas/particle partitioning (Pankow et al., 2018; Pankow, 2001). In fact, a prior study found that the aerosol droplet particle phase of the total nicotine mass emitted by an e-cig was 60% for low power and 95% for high power (Lalo et al., 2020). Another study measured gas and particle phase nicotine concentrations during indoor vaping, and observed higher difference in particle-phase nicotine concentrations between vaping and non-vaping days than with gas-phase nicotine concentrations (van Drooge et al., 2019). These studies suggest that vapor-phase nicotine is not representative of the total airborne nicotine mass inside the vape shop, and thus, additional measurement of particle-phase nicotine is needed to adequately assess air mitigation effectiveness related to vaping density. Nonetheless, the downward slope observed between vaping density and TWA nicotine concentrations in Fig. 4.4b coincides with the finding that increasing AER can lower indoor gas-phase nicotine concentrations even during high vaping activity (Li et al., 2021). Linear regression demonstrated a strong positive correlation between nicotine and vaping density during portable filtration at a higher slope than observed during baseline. This finding suggests that not all filtration devices may be effective in reducing gaseous e-cig-related pollutants, despite the air purifier used in this study having an activated carbon filter. Some potential events could be occurring within the filter to explain the persistence of nicotine in the shop air (Branton and Bradley, 2010): 1) the high flow rate of air collection by the air purifier may be decreasing the contact time between carbon and vapors, decreasing the adsorption of the nicotine onto the carbon filter; and 2) carbon loading of the filter may be high, decreasing the yield of vapor constituents on the filter from the air.

4.4.4. Effects of Mitigation on Particle Size Distribution in Vape Shops

Figure 4.5 presents the particle size distribution data measured in vape shop #5 during baseline and the two mitigation settings under similar vaping frequencies. During baseline (Fig. 4.5a), the particle size distribution was unimodal at 100 nm, with the PNC at this mode strongest during spikes in puffing frequency. It should be noted that the unimodal size distribution contrasts with the bimodal distribution (i.e. 60 and 250 nm) measured previously in vape shops on a busy or high-vaping activity day (Nguyen et al., 2019; Li et al., 2021) and in chamber and clinical e-cig studies (Mikheev et al., 2016; Zhao et al., 2017; Fuoco et al., 2014). This is likely due to the vaping frequency (and relatedly occupancy) being lower in vape shop #5 (max 20 puffs/30 min) at the time of study than the prior studied vape shops (max 35 puffs/30 min), making a less humid and particle-concentrated indoor environment that promotes increase of particle size. Increased human exhalation from high vaping activity may create more humidity in an enclosed space, where hygroscopic growth and increase in coagulation of aerosols due to higher PNC can shift the particle diameter to a larger size (Pichelstorfer et al., 2016). Zhang et al. (2020) also observed a unimodal distribution at a baseline condition in a test indoor environment where one e-cig user was vaping continuously at 120 puffs/hr, but the mode particle diameter measured was much smaller at 15 nm. Since the AER (2.3 hr^{-1}) was higher in this test environment, indoor conditions to promote particle growth were diminished despite high vaping frequency, pointing at increasing AER as a possible effective mitigation measure for exposure to both ultrafine and submicron-sized particles in exhaled e-cig aerosols. In vape shop #5, vaping frequency was commensurate with the PNC at a single mode diameter, but the low AER setting allowed the particles to grow to 100 nm. Though not to the severity that was observed in prior
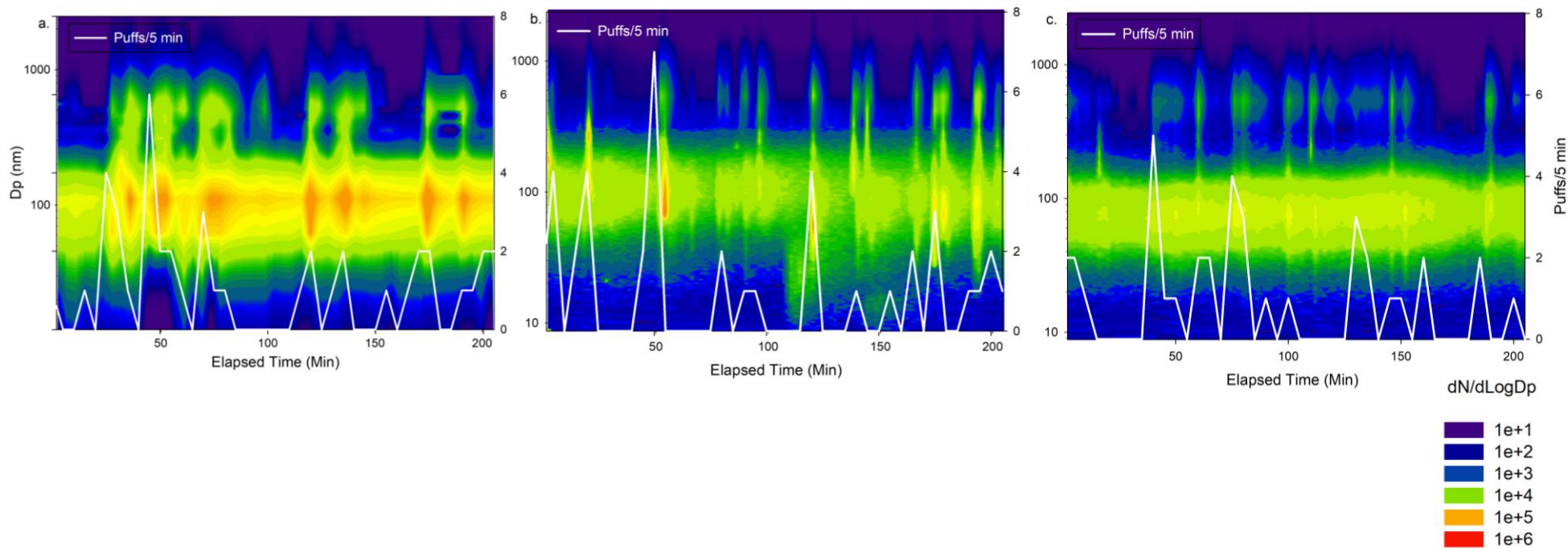
Figure 4.5. Particle size distribution measured in vape shop #5 during baseline (a), enhanced ventilation (b), and portable filtration (c). The color intensity indicates the normalized particle number concentration (dN/dLogDp) for a given particle size at a given time. The white line notes the number of e-cig puffs every 5 minutes over the sampling period.

studies, the baseline particle size distribution observed in this study still calls for mitigation measures.

During enhanced ventilation (Fig. 4.5b), the particle size distribution was also unimodal but the mode diameter was slightly above 100 nm for the first ~100 min of sampling then shifted back to 100 nm for the rest of the sampling period, with slight mode shifts ranging from 50 nm to just below 300 nm at puff frequency spikes throughout the sampling period. Compared to baseline, PNCs decreased by at least one order of magnitude. The mode shift to the larger particle size marked by a transient increase in PNCs that quickly decayed, was most likely attributed to high puff frequency within 5 minutes (e.g. 7 puffs/5 min at 50 min mark in Fig. 4.5b) or possibly a change in vaping device or e-liquid vaped during that point. The mode shifts to the smaller size as well as appearance of smaller particles (<50 nm) around the 110 min-mark may be due to a mixture of outdoor particles entering the shop through the ventilation system, which could explain the introduction of the smaller particles as traffic exhaust particles are <50 nm, and decreased coagulation and hygroscopic growth. The unimodal size distribution, decreased PNCs, and quick decay of peak exhaled e-cig aerosol concentration was consistent with Zhang et al.'s (2020) study, which found that enhanced ventilation (i.e. increase in room AER from baseline) made the e-cig aerosols decay faster and peak concentration decrease. With indoor conditions created with enhanced ventilation as discussed in the previous paragraph, increasing the AER leads to faster evaporation of the exhaled e-cig particles. As for the slightly larger mode diameter at the beginning of sampling, it has been reported that higher ventilation rates increase the I/O ratio of particles larger than 90 nm and that I/O ratios of particles in the accumulation mode (<100 nm) are strongly dependent on ventilation rate (Olstrup et al., 2021; Wang et al., 2010; Koponen et al., 2001). With coagulation of residual exhaled e-cig aerosols

and less deposition, enhanced ventilation may allow larger size e-cig particles to persist in the air.

During portable filtration (Fig. 4.5c), PNC continued to be low (~10,000 particles/cm^3), even during spikes in puffing frequency, at a unimodal distribution, but the mode diameter was slightly smaller than 100 nm throughout the sampling period. This decrease in particle mode diameter could be due to the decrease in accumulation mode particles, which no longer linger in the shop as filtration actively removes airborne e-cig particles, minimizing coagulation and other smaller particle sinks (e.g. deposition). In Zhang et al.'s (2020) study, size distribution of exhaled e-cig aerosols during increased filtration in the test room was similar to baseline, noting that when the air purifier was on in the room, particle decay due to AER decreased about 50% and suggested that AER is the primary contributor to the decay rate of exhaled e-cig aerosols. This suggestion contrasts with this study finding portable filtration, governed primarily by aerosol dynamics, to be most effective in keeping PNC at low indoor levels at a single smaller particle diameter. This discrepancy might be due to this study's air purifier having a higher CADR than the one used in the other study and shop AERs during the portable filtration tests were low in this study, making aerosol dynamics the primary contributor to particle decay. Overall, both enhanced ventilation and portable filtration reduced PNCs to background indoor levels and the unimodal size distribution was maintained. Further field studies are needed to investigate the impact of these air mitigation strategies on the particle dynamics of e-cig aerosols during high vaping activity.

4.5 Conclusion

This study showed that enhanced ventilation and portable filtration are effective air mitigation strategies to reduce exhaled e-cig aerosol levels in vape shops. This is the first study

that provides information on the temporal and spatial profiles of fine and ultrafine particle concentrations, gas-phase nicotine concentrations, and particle size distribution in vape shops while applying air mitigation strategies and demonstrates the potential reversal or elimination of the effect of vaping frequency or density, which was previously established to be a strong predictor of indoor exhaled e-cig particle levels. Compared to baseline conditions, increasing the AER through enhanced ventilation can reduce fine and ultrafine particles up to 68%, while portable filtration can reduce fine particles up to 49% and ultrafine particles up to 70%. Up to 75% reduction in gas-phase nicotine concentration compared to baseline can be achieved through enhanced ventilation. Reducing e-cig-related pollutant concentrations, as demonstrated with measurements nearest the vaping source (i.e. vaping bar), can subsequently reduce these pollutant concentrations measured at farther distances from the vaping source. More studies are needed to assess the effects of these air mitigation strategies on the transport and transformation of exhaled e-cig particles and other pollutants to businesses neighboring vape shops and the effects of mitigation strategies on workplace exposure to exhaled e-cig aerosols and related biological effects.

5. CONCLUSIONS

Understanding of the potential health effects and indoor air quality impacts from vaping has grown in recent years as more studies are being conducted in reaction to the growing e-cig industry. Although regulatory actions are beginning to catch up with this evolving product, e-cig use and e-cig aerosol exposure continues to be a serious health concern. This research fills the knowledge gap of exhaled e-cig aerosol as an occupational hazard by assessing and reducing vape shop worker exposure to exhaled e-cig aerosols.

To investigate exhaled e-cig aerosols as an indoor air quality issue, sixty-seven vape shops were surveyed and six selected for indoor fine and ultrafine particle sampling. Fine and ultrafine particles were high and continuous during business hours, which were attributed to vaping activity. During vaping, $PM_{2.5}$ and PNC were as high as four and two magnitudes above background, respectively. Exhaled e-cig particles persisted in the air, traveling and mixing in the shops. $PM_{2.5}$ decayed faster than PNC over distances greater than 1.5 m from the vaping bar. This study was the first to provide information on the temporal and spatial profiles of fine and ultrafine particles concentrations and the particle size distribution in vape shops. High particle emissions found in vape shops from vaping activity shed light on the potential occupation hazard of exhaled e-cig aerosols for vape shop workers.

To assess workplace exposure to exhaled e-cig aerosols among vape shop workers, fifteen vaping and fifteen non-vaping workers were sampled for urinary cotinine, a metabolic marker for nicotine as a tracer for e-cig aerosol exposure, and select urinary oxidative stress (8-OHdG and 8-isoprostane (8-iso)), systemic inflammation (human c-reactive protein (CRP)), and metal toxicity and antioxidant activity (metallothionein (MT)) markers at the start and end of a work shift on two days. Non-vaping workers with a consecutive workday schedule showed

significant increase in cotinine from the start to the end of their work schedule, with a corresponding upward trend in 8-iso. Urinary cotinine was significantly associated with urinary 8-iso among non-vaping workers when accounting for vape shop differences, suggesting worksite characteristics, which could include vaping activity during the shift, may contribute to increased oxidative stress. Elevated oxidative stress and inflammatory responses were stronger among vaping workers. Significant high associations were observed between cotinine and 8-OHdG, CRP, and MT for vaping workers. These results indicate that mainstream e-cig aerosol inhalation produces stronger oxidative stress, inflammation, and metal toxicity/reactive oxygen species responses, but exhaled e-cig aerosol could be a potential contributor to oxidative stress in non-vaping workers. This study provides initial data to support future studies to systematically assess and quantify the relative contribution of exhaled e-cig aerosol exposure to health impacts among other types of workers and populations exposed to e-cig aerosols.

Now that exhalation of e-cig aerosols has been established as an indoor air quality issue and potential workplace hazard in vape shops, strategies to reduce e-cig-related pollutant levels and worker exposure are needed. Short of banning or isolating e-cig use, two air mitigation strategies, enhanced ventilation and portable filtration, were tested in six vape shops to assess reductions to fine and ultrafine particles and nicotine as a result of these strategies. Enhanced ventilation and portable filtration were both effective air mitigation strategies for e-cig-related indoor pollution. Portable filtration may be more effective in reducing e-cig-related ultrafine particles, while enhanced ventilation may be more effective for reducing e-cig-related fine particles and gaseous compounds (e.g. nicotine). These findings provide important policy implications in terms of reducing e-cig-related air pollutant exposure among non-vaping

workers, neighboring business workers, and other occupants and bystanders around vape shops, where indoor vaping is still permitted.

In summary, vape shops are sites of high exposure to fine and ultrafine particles and nicotine due to unregulated vaping activity by customers and workers. Although e-cig-using vape shop workers are more susceptible to increased oxidative stress, systemic inflammation, and heavy metal toxicity due to higher dosage of e-cig-related pollutants and toxic compounds formed from direct inhalation of aerosolized e-liquids, increase in nicotine absorption and related oxidative stress was observed in non-e-cig-using vape shop workers, indicating that secondhand exposure to e-cig aerosol may be a workplace health issue. This research can inform future studies to assess exposure and effects of exhaled e-cig aerosol on a larger scale at other worksites or indoor environments where e-cig use is permitted (e.g. casinos, homes) and support policy efforts to reduce exposures to e-cig aerosols in indoor environments.

APPENDIX

S1. AER Calculation using CO_2 Tracer Gas Decay Method

In vape shops where the average CO_2 levels were below 500 ppm, CO_2 gas was injected into the shop after business hours where there were no customers in the shop until the indoor concentration reached ~1500 ppm under well-mixed conditions. Then, the Q-Trak Plus measured the CO_2 decay to background level (~350 ppm). In shops where the average CO_2 levels were above 800 ppm, the Q-Trak Plus measured the decay of CO2 concentration after business hours when there were no occupants in the shop. The ventilation setting of the shop during business hours remained the same during the CO_2 decay measurement. Another Q-Trak Plus unit measured the outdoor CO_2 for that sampling day, and the average was used in calculating AER. Average outdoor CO_2 ranged from 325 to 360 ppm for the studied shops. The following equation was used to calculate AER (λ):

$$\ln(C_{(t)} - C_{out}) = \ln(C_0 - C_{out}) - \lambda t \tag{1}$$

where $C_{(t)}$ = CO_2 concentration as a function of time; C_{out} = outdoor CO_2 concentration; C_0 = initial CO_2 concentration; λ = AER (h^{-1}); and t = time (hr). The difference between log linear regression R^2 values for AER determination with and without CO_2 gas injection was not statistically significant (95% confidence interval -0.004 to 0.05).

Table S1. Results from Condensation Particle Counter (CPC) collocation tests before and after sampling campaign

Dataset	Vape Shop Location	R^2	Intercept [95% CI]	Slope [95% CI]	Intercept p-Value	Slope p-Value
Before	Inside A	0.94	299 [-90.0 – 688]	1.08 [1.04 – 1.12]	0.134	<0.001
After	Inside A	0.57	5,618 [4,631 – 6,605]	0.70 [0.61 – 0.79]	<0.001	<0.001
Before	Inside B	0.91	-506 [-1,190 – 178]	1.18 [1.13 – 1.23]	0.149	<0.001
After	Inside B	0.97	-33.7 [-275 – 208]	1.09 [1.06 – 1.12]	<0.001	<0.001
Before	Inside C	0.97	19.0 [-157 – 195]	1.06 [1.03 – 1.09]	<0.001	<0.001
After	Inside C	0.99	152 [11.7 – 292]	1.07 [1.05 – 1.09]	0.035	<0.001
Before	Inside D	0.96	836 [573 – 1,099]	0.99 [0.96 – 1.02]	<0.001	<0.001
After	Inside D	0.97	784 [565 – 1,003]	0.96 [0.93 – 0.99]	<0.001	<0.001
Before	Inside E	0.95	-56.1 [-353 – 241]	1.08 [1.04 – 1.12]	<0.001	<0.001
After	Inside E	0.95	259 [-13.5 – 532]	1.03 [0.99 – 1.07]	0.064	<0.001
Before	Inside F	0.99	114 [21.1 – 207]	1.01 [1.00 – 1.02]	0.017	<0.001
After	Inside F	0.97	-70.7 [-244 – 102]	1.03 [1.01 – 1.05]	<0.001	<0.001

Table S2. Results from DustTrak II collocation tests before and after sampling campaign

Dataset	Vape Shop Location	R^2	Intercept [95% CI]	Slope [95% CI]	Intercept p-Value	Slope p-Value
Before	Inside A	0.96	-1.69 [-2.77 – -0.61]	1.30 [1.26 – 1.34]	0.003	<0.001
After	Inside A	0.96	-0.17 [-0.59 – 0.25]	1.08 [1.04 – 1.12]	0.418	<0.001
Before	Inside B	0.99	0.03 [0.029 – 0.031]	1.08 [1.077 – 1.083]	<0.001	<0.001
After	Inside B	0.84	0.64 [0.36 – 0.92]	1.29 [1.26 – 1.32]	<0.001	<0.001
Before	Inside C	0.96	0.01 [0.0096 – 0.0104]	1.12 [1.11 – 1.13]	<0.001	<0.001
After	Inside C	0.83	1.58 [1.27 – 1.89]	1.13 [1.11 – 1.15]	<0.001	<0.001
Before	Inside D	0.93	7.32 [6.30 – 8.34]	1.33 [1.31 – 1.35]	<0.001	<0.001
After	Inside D	0.99	-0.01 [-0.011 – -0.009]	1.31 [1.306 – 1.314]	<0.001	<0.001
Before	Inside E	0.96	-0.01 [-0.0105 – -0.0095]	1.97 [1.95 – 1.99]	<0.001	<0.001
After	Inside E	0.98	0.00 [-0.0005 – 0.0005]	1.44 [1.43 – 1.45]	0.020	<0.001
Before	Inside F	0.91	0.00 [-0.001 – 0.001]	1.00 [0.99 – 1.01]	<0.001	<0.001
After	Inside F	0.73	0.01 [0.009 – 0.011]	1.01 [0.98 – 1.04]	<0.001	<0.001

S2. Field Calibration of DustTrak II for PM$_{2.5}$ Mass Concentrations

A reference DustTrak II instrument and one personal cascade impactor (Sioutas Cascade Impactor, SKC Inc., Eighty Four, PA, USA) were operated simultaneously in the vape shop during business hours and outdoors in separate trials. The impactor was loaded with 25-mm PTFE stage filters (Pall Corporation, Port Washington, NY, USA) and a 37-mm PTFE after-filter (SKC Inc.) and connected to an air sampling pump (SP-280, Air Diagnostics and Engineering Inc., Harrison, ME, USA) to collect particles below the 2.5 μm cut-size. The impactor was taped to the DustTrak II so that the sample inlets were as close to each other as possible at heights ranging from 0.8 to 1.2 m from the floor and within 1.2 m away from the end of the vaping bar. The sampling flow rate of the impactor was 9.09 ± 0.21 L/min and was calibrated by a TSI 4146 Primary Flow Calibrator (TSI Inc., Shoreview, MN, USA). Pre- and post-sampling conditioning of filters was done for 48 hr each in an environmental chamber controlled at 23°C temperature and 50% RH. A second personal cascade impactor was used to collect a field blank. The sampling duration for an experiment was 4 – 8 hr, and the experiments were completed on a weekend (Friday – Sunday). Figure S1 shows the field calibration results.

a)

b)
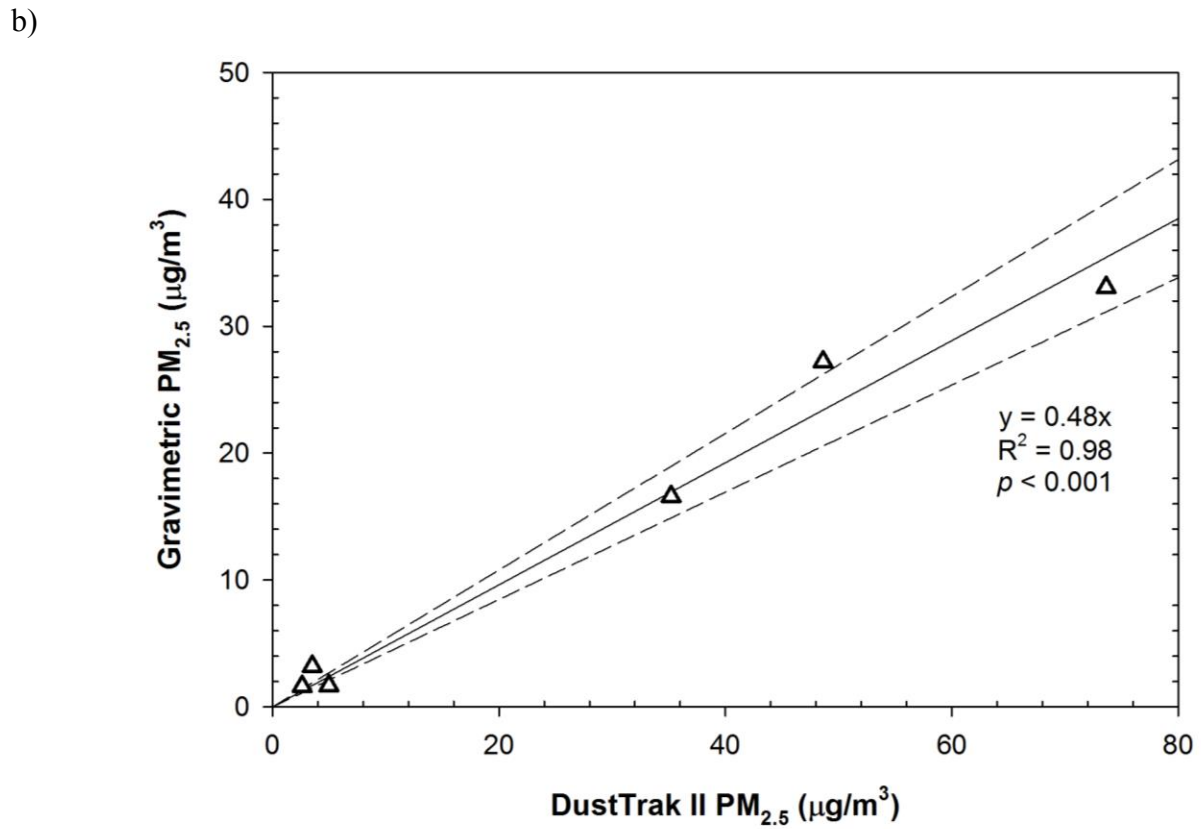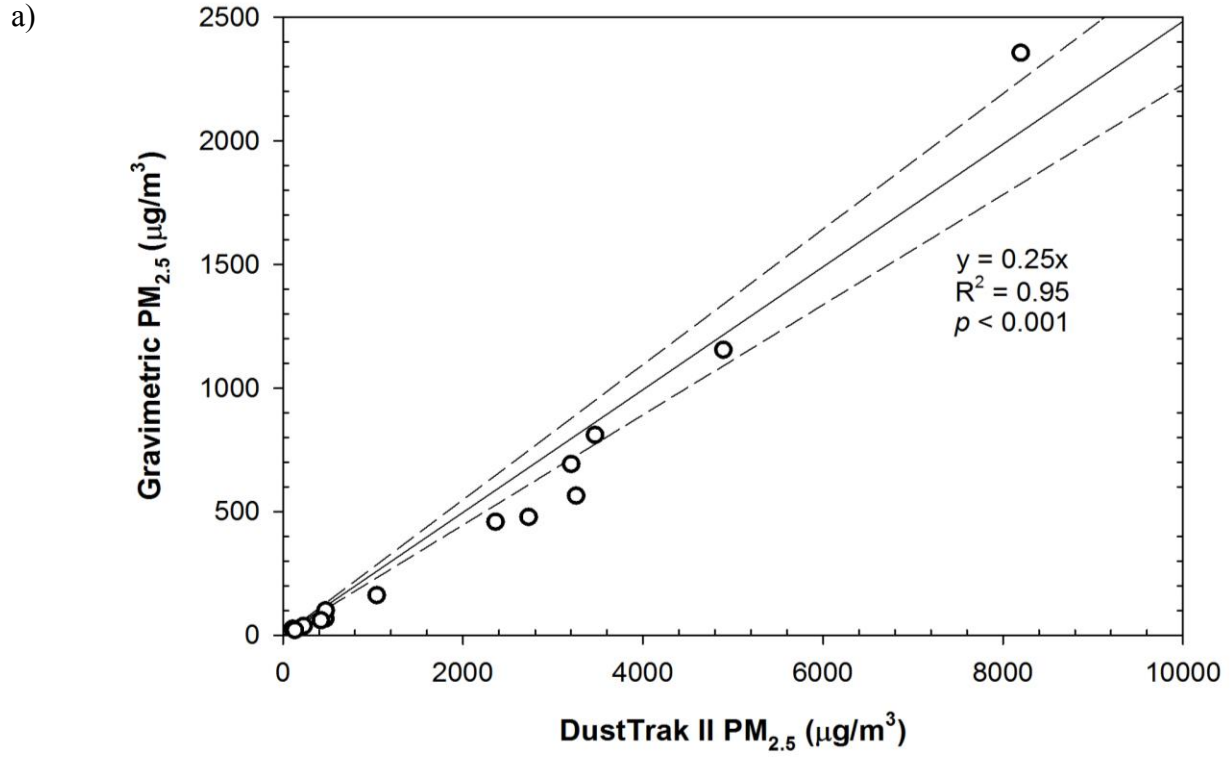
Figure S1. Field calibration of DustTrak II for PM$_{2.5}$ mass concentrations (a) inside vape shops (n = 14) and (b) outdoors (n = 6). Dotted lines represent 95% confidence intervals.

(a)

$$y = 1.00x$$
$$R^2 = 0.82$$
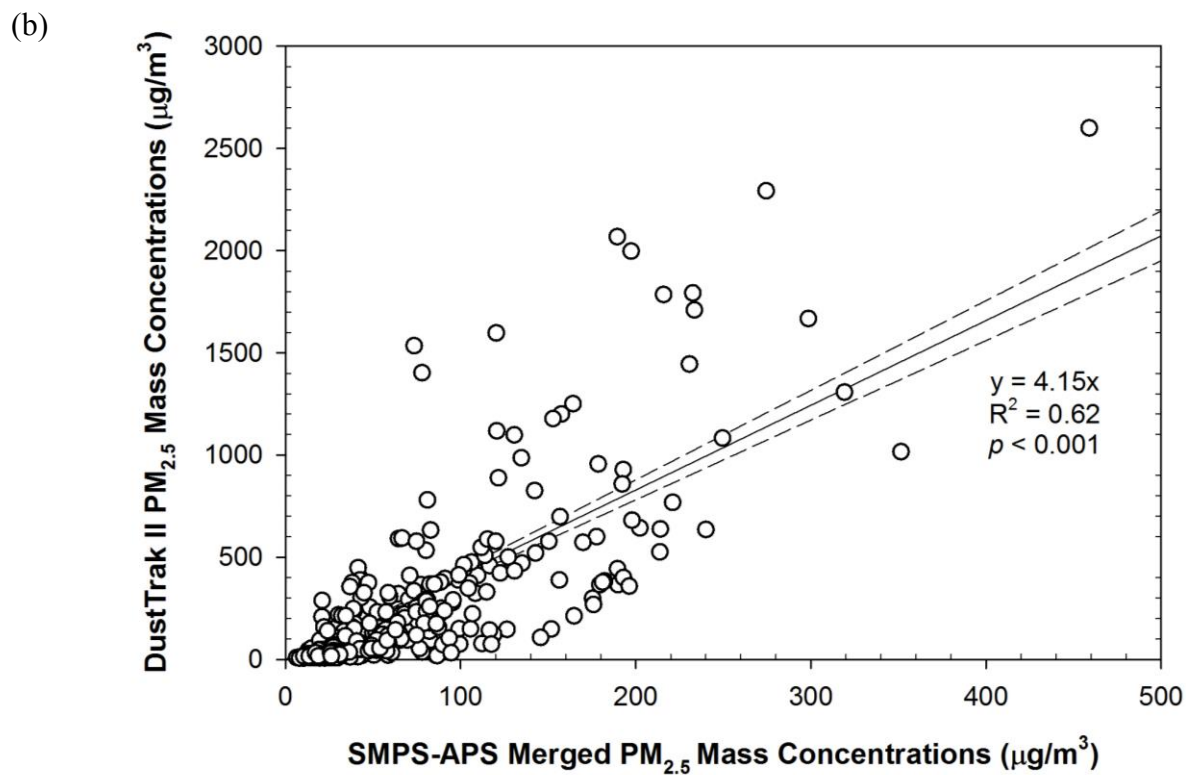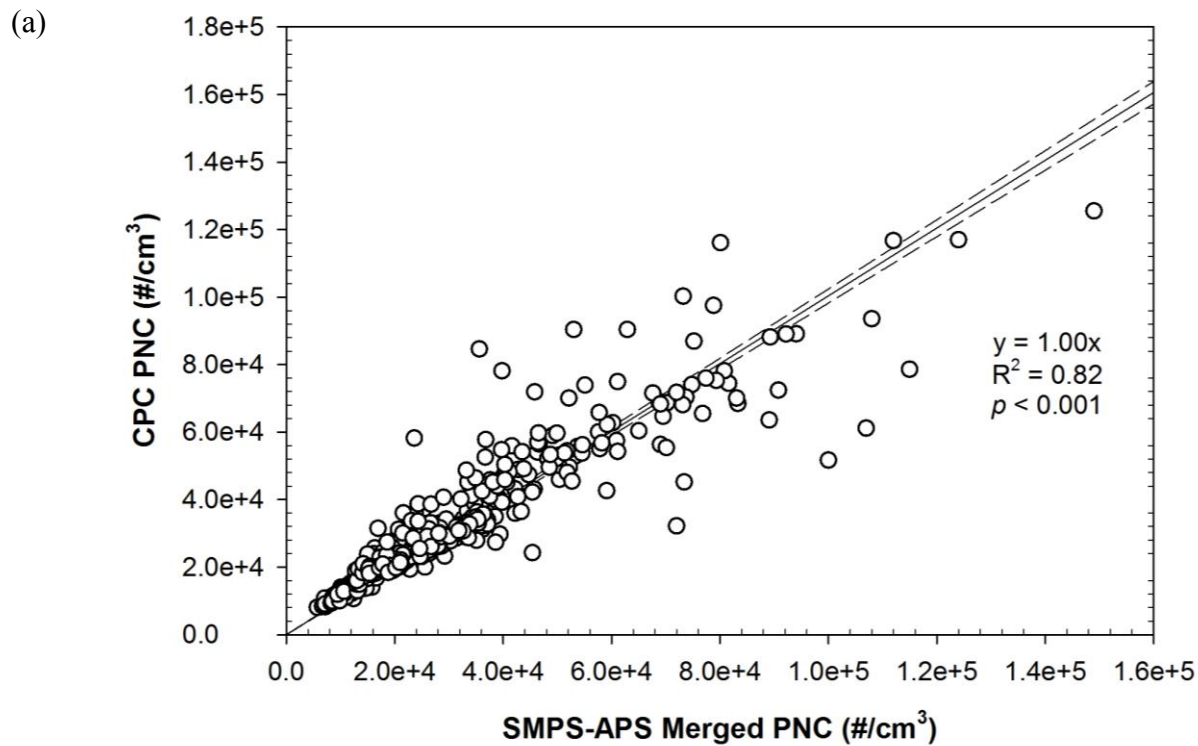$$p < 0.001$$

(b)

$$y = 4.15x$$
$$R^2 = 0.62$$
$$p < 0.001$$

Figure S2. Calibration of SMPS-APS Merged (a) PNC with CPC PNC and (b) PM2.5 with gravimetric-corrected DustTrak II PM2.5. Dotted lines represent 95% confidence intervals.

Table S3. Summary statistics of indoor air parameters measured in the studied vape shops.

Vape Shop	Particle Number (PNC) ($\#\times10^3/cm^3$)		PM$_{2.5}$ ($\mu g/m^3$)		Indoor CO$_2$ (ppm)	Indoor Temp (°C)	Indoor RH (%)
	Indoor	Outdoor	Indoor	Outdoor			
A							
Busy Day							
Arith. Mean (SD)	8.4 (1.2)	NA[a]	1,574 (3,259)	45.5 (25.7)	1,510 (230)	24.8 (0.97)	42.9 (1.72)
Median	7.0 (1.5)	NA[b]	515	52.9	1,561	24.6	43.2
Geom. Mean (SD)	10.7 (5.0)	8.7 (1.5)	297 (2.40)	29.0 (1.37)	1,488 (1.07)	24.8 (1.02)	42.9 (1.02)
Less Busy Day							
Arith. Mean (SD)	68.7 (45.1)	25.3 (7.92)	NA[b]	NA[b]	651 (406)	22.8 (1.56)	47.2 (6.43)
Median	56.6	23.9	NA[b]	NA[b]	455	23.1	48.6
Geom. Mean (SD)	57.4 (0.001)	24.4 (0.001)	NA[b]	NA[b]	549 (1.28)	22.8 (1.01)	46.7 (1.06)
B							
Busy Day							
Arith. Mean (SD)	36.2 (22.4)	25.6 (13.4)	198 (564)	51.8 (192)	498 (94.2)	23.0 (1.96)	26.7 (2.14)
Median	31.5	23.4	10.5	10.8	489	22.7	25.8
Geom. Mean (SD)	30.9 (0.001)	23.5 (0.001)	23.3 (2.13)	16.9 (1.46)	494 (1.05)	22.9 (1.04)	26.6 (1.03)
Less Busy Day							
Arith. Mean (SD)	25.4 (15.4)	24.4 (6.41)	306 (1,074)	24.6 (48.5)	490 (31.9)	23.3 (1.74)	40.0 (3.33)
Median	20.3	23.3	25.9	9.81	485	23.0	40.2
Geom. Mean (SD)	22.5 (0.001)	23.7 (0.001)	35.7 (1.96)	13.0 (1.41)	489 (1.03)	23.2 (1.03)	39.8 (1.04)
C							
Busy Day							
Arith. Mean (SD)	42.7 (25.8)	31.5 (29.7)	250 (547)	17.2 (7.17)	393 (36.8)	19.0 (2.54)	28.6 (0.76)
Median	41.1	21.2	47.8	15.7	391	19.4	28.5
Geom. Mean (SD)	36.2 (0.001)	24.6 (0.001)	125 (1.96)	16.1 (1.07)	391 (1.04)	19.0 (1.02)	28.6 (1.01)
Less Busy Day							
Arith. Mean (SD)	23.7 (13.6)	15.9 (17.2)	111 (209)	2.90 (6.31)	289 (45.0)	20.8 (20.9)	38.7 (6.60)
Median	20.3	12.7	34.1	2.42	299	1.18	35.5
Geom. Mean (SD)	21.0 (0.001)	11.8 (0.001)	29.7 (1.99)	2.39 (1.16)	285 (1.08)	20.8 (1.01)	38.2 (1.07)
D							
Busy Day							
Arith. Mean (SD)	15.7 (2.80)	17.0 (4.20)	10.6 (2.90)	20.8 (8.33)	NA[d]	NA[d]	NA[d]
Median	14.9	16.0	10.7	20.6	NA[d]	NA[d]	NA[d]
Geom. Mean (SD)	15.5 (0.001)	16.5 (0.001)	10.1 (1.06)	19.7 (1.07)	NA[d]	NA[d]	NA[d]

Vape Shop	Particle Number (PNC) ($\#\times10^3$/cm^3)		PM$_{2.5}$ (μg/m^3)		Indoor CO$_2$ (ppm)	Indoor Temp (ºC)	Indoor RH (%)
	Indoor	Outdoor	Indoor	Outdoor			
Less Busy Day							
Arith. Mean (SD)	11.8 (9.70)	13.4 (3.52)	8.17 (7.81)	19.8 (25.2)	NA[d]	NA[d]	NA[d]
Median	10.4	12.7	5.50	11.6	NA[d]	NA[d]	NA[d]
Geom. Mean (SD)	10.9 (0.001)	13.0 (0.001)	6.67 (1.18)	14.9 (1.21)	NA[d]	NA[d]	NA[d]
E							
Busy Day							
Arith. Mean (SD)	90.6 (24.4)	NA[c]	2,676 (1,056)	NA[c]	NA[d]	NA[d]	NA[d]
Median	88.3	NA[c]	2,528	NA[c]	NA[d]	NA[d]	NA[d]
Geom. Mean (SD)	87.4 (0.001)	NA[c]	2,463 (1.11)	NA[c]	NA[d]	NA[d]	NA[d]
Less Busy Day							
Arith. Mean (SD)	37.6 (16.5)	25.3 (5.63)	413 (412)	8.90 (7.60)	NA[d]	NA[d]	NA[d]
Median	32.1	23.9	260	7.69	NA[d]	NA[d]	NA[d]
Geom. Mean (SD)	34.5 (0.001)	24.7 (0.001)	196 (1.82)	8.19 (1.06)	NA[d]	NA[d]	NA[d]
F							
Busy Day							
Arith. Mean (SD)	42.0 (21.1)	17.6 (5.96)	935 (1,722)	4.60 (45.6)	1,902 (363)	23.0 (0.75)	29.1 (2.54)
Median	35.2	16.4	515	1.36	1,987	23.0	29.0
Geom. Mean (SD)	39.0 (0.001)	17.0 (0.001)	542 (1.45)	1.64 (1.27)	1,864 (1.09)	23.0 (1.01)	29.0 (1.04)
Less Busy Day							
Arith. Mean (SD)	25.4 (17.2)	8.54 (7.22)	687 (561)	11.6 (27.7)	844 (407)	22.8 (1.60)	33.7 (1.64)
Median	28.7	5.54	584	5.57	739	23.4	34.0
Geom. Mean (SD)	20.0 (0.001)	7.56 (0.001)	504 (1.41)	7.15 (1.26)	746 (1.24)	22.7 (1.03)	33.7 (1.02)

[a] Concentrations reported were during periods where there was minimal SHV particle detection (no vaping or shop doors closed).

[b] Due to scheduling conflicts, PM$_{2.5}$ measurement could not be conducted.

[c] Due to unforeseen rain, outdoor measurements could not be conducted.

[d] Due to a technical malfunction, CO$_2$, temperature, and RH measurements could not be reported.

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Table S4. Summary statistics of indoor air parameters measured in the vape shops studied for mitigation.

Vape Shop	Mean (SD) Particle Number (PNC) ($\#\times10^3/cm^3$)		Mean (SD) PM$_{2.5}$ ($\mu g/m^3$)		TWA Nicotine ($\mu g/m^3$)	
	Indoor	Outdoor	Indoor	Outdoor	Indoor	Outdoor
1						
Baseline						
Day 1	8.4 (1.2)	NA[a]	3.5 (1.2)	NA[a]	0.19	<LOD
Day 2	7.0 (1.5)	NA[b]	4.0 (0.4)	NA[b]	0.17	<LOD
Day 3	10.7 (5.0)	8.7 (1.5)	27.0 (49.3)	2.0 (3.7)	0.24	<LOD
Port. Filtration						
Day 1	6.0 (4.7)	7.2 (1.2)	5.0 (7.2)	13.0 (5.4)	0.14	<LOD
Day 2	0.8 (0.6)	7.3 (1.9)	1.3 (0.2)	7.5 (3.5)	0.06	<LOD
Day 3	3.5 (2.8)	5.9 (1.3)	75.5 (137.1)	7.5 (0.01)	0.09	<LOD
2						
Baseline						
Day 1	16.8 (1.2)	12.8 (6.2)	26.6 (19.7)	27.4 (6.2)	0.09	<LOD
Day 2	21.1 (5.5)	15.2 (14.1)	19.9 (1.7)	45.1 (17.8)	0.58	<LOD
Day 3	21.8 (5.8)	19.0 (13.0)	110.2 (159.4)	39.8 (15.8)	0.24	<LOD
Enh. Ventilation						
Day 1	10.7 (2.4)	10.2 (3.7)	24.7 (21.5)	47.5 (0.04)	0.03	<LOD
Day 2	22.6 (2.6)	22.6 (10.2)	24.9 (22.7)	125.2 (0.11)	0.06	<LOD
Day 3	15.6 (4.4)	16.8 (3.7)	20.9 (16.6)	0.10 (0.30)	0.14	<LOD
3						
Baseline						
Day 1	26.7 (12.9)	9.1 (10.9)	52.3 (31.9)	24.5 (6.2)	0.11	<LOD
Day 2	19.6 (0.5)	NA[b]	67.7 (25.9)	NA[b]	0.52	<LOD
Day 3	20.9 (1.2)	15.3 (14.7)	26.7 (1.4)	13.0 (5.3)	0.42	<LOQ
Enh. Ventilation						
Day 1	15.3 (3.0)	NA[b]	48.4 (6.0)	NA[b]	0.14	<LOD
Day 2	16.8 (2.5)	NA[b]	33.1 (18.9)	NA[b]	0.24	0.11
Day 3	15.3 (8.2)	11.5 (7.5)	11.8 (5.9)	13.4 (3.8)	0.08	<LOQ
Port. Filtration						
Day 1	21.2 (13.3)	NA[b]	63.2 (38.8)	NA[b]	0.34	<LOD
Day 2	34.0 (5.8)	11.6 (3.4)	74.3 (21.5)	17.3 (8.2)	0.42	<LOD
Day 3	31.2 (9.5)	7.5 (4.5)	7.4 (0.2)	17.3 (5.8)	0.16	<LOD
Day 4	16.1 (2.4)	NA[b]	8.8 (1.6)	NA[b]	0.40	<LOD

Vape Shop	Mean (SD) Particle Number (PNC) ($\#\times10^3/cm^3$)		Mean (SD) $PM_{2.5}$ ($\mu g/m^3$)		TWA Nicotine ($\mu g/m^3$)	
	Indoor	Outdoor	Indoor	Outdoor	Indoor	Outdoor
4						
Baseline						
Day 1	17.1 (6.1)	20.7 (0.7)	12.3 (5.6)	1.0 (7.2)	0.19	<LOQ
Day 2	24.0 (7.2)	NA[b]	19.9 (12.9)	NA[b]	0.37	<LOD
Day 3	9.3 (4.4)	20.4 (4.6)	11.0 (7.7)	6.7 (21.1)	0.45	<LOD
Enh. Ventilation						
Day 1	19.8 (7.1)	14.1 (4.7)	9.0 (8.2)	6.7 (2.0)	0.09	<LOQ
Day 2	10.4 (3.0)	26.1 (5.4)	12.0 (12.4)	1.9 (8.2)	0.51	<LOD
Day 3	13.9 (6.4)	18.1 (14.4)	6.1 (4.2)	2.4 (0.5)	0.25	<LOQ
Port. Filtration						
Day 1	9.9 (5.4)	12.7 (3.0)	10.5 (12.5)	1.9 (11.0)	0.26	<LOD
Day 2	4.1 (2.3)	5.8 (2.2)	8.1 (7.8)	1.0 (2.4)	0.29	<LOD
Day 3	8.2 (3.4)	14.5 (9.5)	6.9 (6.0)	9.1 (6.7)	0.27	<LOQ
5						
Baseline						
Day 1	50.9 (15.3)	43.7 (26.5)	976.5 (766.0)	7.5 (4.7)	1.09	<LOD
Day 2	35.8 (20.7)	15.6 (11.9)	457.1 (574.5)	9.1 (0.6)	0.36	<LOD
Day 3	30.9 (6.3)	NA[b]	346.0 (227.3)	NA[b]	1.33	<LOD
Enh. Ventilation						
Day 1	15.7 (6.3)	6.1 (3.3)	175.3 (133.3)	8.2 (8.9)	0.27	<LOD
Day 2	18.0 (9.2)	NA[b]	299.1 (227.0)	NA[b]	0.49	<LOD
Day 3	52.1 (12.2)	NA[b]	479.3 (176.8)	NA[b]	0.49	<LOD
Day 4	13.6 (9.9)	12.9 (23.6)	292.0 (225.5)	6.5 (1.9)	0.39	0.04
Port. Filtration						
Day 1	5.2 (3.2)	5.3 (8.7)	392.4 (402.1)	21.1 (20.6)	0.46	0.06
Day 2	10.6 (2.9)	NA[b]	500.5 (162.7)	NA[b]	0.46	<LOD
Day 3	11.6 (4.5)	NA[b]	79.1 (61.7)	NA[b]	0.43	<LOD
Day 4	9.4 (9.5)	9.0 (15.7)	239.2 (297.7)	7.7 (1.0)	0.21	0.07
6						
Baseline						
Day 1	22.6 (9.3)	18.8 (2.6)	106.6 (64.8)	8.6 (5.8)	0.50	0.11
Day 2	25.5 (18.0)	21.4 (9.0)	355.3 (386.3)	2.9 (2.4)	0.45	<LOD
Day 3	60.4 (13.6)	17.4 (7.6)	1622 (427.1)	1.0 (3.4)	0.53	<LOD

Vape Shop	Mean (SD) Particle Number (PNC) ($\#\times10^3/cm^3$)		Mean (SD) PM$_{2.5}$ ($\mu g/m^3$)		TWA Nicotine ($\mu g/m^3$)	
	Indoor	Outdoor	Indoor	Outdoor	Indoor	Outdoor
Enh. Ventilation						
Day 1	14.9 (3.3)	19.7 (0.3)	204.7 (157.2)	2.0 (2.0)	0.06	<LOD
Day 2	12.6 (5.7)	14.1 (7.9)	4.5 (4.1)	1.5 (2.0)	0.27	<LOD
Day 3	29.9 (17.9)	12.4 (7.6)	946.4 (709.0)	1.4 (2.9)	0.19	<LOD
Port. Filtration						
Day 1	13.3 (4.9)	12.9 (6.8)	515.9 (541.6)	1.9 (2.4)	0.84	0.04
Day 2	4.8 (2.5)	22.1 (7.8)	160.7 (144.9)	3.8 (3.4)	0.94	<LOD
Day 3	9.4 (6.4)	10.5 (4.5)	264.6 (378.6)	7.7 (1.9)	0.12	<LOD

[a] Due to unforeseen rain or [b] available instruments being used for spatial profile analyses, outdoor measurements could not be conducted.

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