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Firefighters' urinary concentrations of VOC metabolites after controlled-residential and training fire responses

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Abstract

Introduction: Firefighters are exposed to volatile organic compounds (VOCs) during structural fire responses and training fires, several of which (e.g., benzene, acrolein, styrene) are known or probable carcinogens. Exposure studies have found that firefighters can absorb chemicals like benzene even when self-contained breathing apparatus (SCBA) are worn, suggesting that dermal absorption contributes to potentially harmful exposures. However, few studies have characterized VOC metabolites in urine from firefighters.

Objectives: We quantified VOC metabolites in firefighters' urine following live firefighting activity across two field studies.

Methods: In two separate controlled field studies, spot urine was collected before and 3 hours after firefighters and firefighter students responded to simulated residential and training fires. Urine was also collected from instructors from the training fire study before the first and 3 hours after the last training scenario for each day (instructors led three training scenarios per day). Samples were analyzed for metabolites of VOCs to which firefighters may be exposed.

Results: In the residential fire study, urinary metabolites of xylenes (2MHA), toluene (BzMA), and styrene (MADA) increased significantly (at 0.05 level) from pre- to post-fire. In the training fire study, MADA concentrations increased significantly from pre- to post-fire for both firefighter students and instructors. Urinary concentrations of benzene metabolites (MUCA and PhMA) increased significantly from pre- to post-fire for instructors, while metabolites of xylenes

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(3MHA+4MHA) and acrolein (3HPMA) increased significantly for firefighter students. The two highest MUCA concentrations measured post-shift from instructors exceeded the BEI of 500 μg/g creatinine.

Conclusions: Some of the metabolites that were significantly elevated post-fire are known or probable human carcinogens (benzene, styrene, acrolein); thus, exposure to these compounds should be eliminated or reduced as much as possible through the hierarchy of controls. Given stringent use of SCBA, it appears that dermal exposure contributes in part to the levels measured here.

Keywords

Benzene; styrene; acrolein; urine; biomarker; fire

1. Introduction

Firefighters, firefighter students, and instructors may be exposed to volatile organic compounds (VOCs) during a variety of combustion events, including structure, vehicle, dumpster, vegetation, and training fires. The types of VOCs previously reported in personal air sampling on the exterior of gear of firefighters, firefighter students, and instructors responding to fires include benzene, toluene, ethylbenzene, xylenes, styrene (BTEX+S), formaldehyde, acrolein, 1,3-butadiene, and naphthalene along with many other organic compounds (Jankovic et al. 1991, Austin et al. 2001a, Austin et al. 2001b, Fent et al. 2018, Fent et al. 2019a). While the composition and magnitude of VOCs will vary depending on the type of materials being burned, VOCs will always be present in smoke and several of the most common constituents have been classified as known (e.g., benzene, formaldehyde, 1,3-butadiene) and probable (e.g., acrolein, styrene) carcinogens by the International Agency for Research on Cancer (IARC) (IARC 2012a, IARC 2012b, IARC 2019, IARC 2021).

In 2010, IARC evaluated the occupation of firefighting and based on evidence at that time, classified it as “possibly carcinogenic to humans” (IARC 2010). In 2019, IARC listed the occupation of firefighting as a high priority for re-evaluation as new evidence has become available, including several epidemiologic studies that have found increased risk of certain types of cancer (Daniels et al. 2014, Pukkala et al. 2014, Tsai et al. 2015, Glass et al. 2016, Muegge et al. 2018, Jalilian et al. 2019, Soteriades et al. 2019, Casjens et al. 2020, Lee et al. 2020, Pinkerton et al. 2020) as well as biomarker studies that have shown genetic and epigenetic changes in firefighters (Andersen et al. 2017,Zhou et al. 2019, Jung et al. 2021).

A number of exposure studies have also characterized the biological uptake of combustion byproducts for firefighters, firefighter students, and instructors, including polycyclic aromatic hydrocarbons (PAHs) and benzene (Feunekes et al. 1997, Caux et al. 2002, Laitinen et al. 2010, Laitinen et al. 2012, Oliveira et al. 2016, Keir et al. 2017, Fent et al. 2019b, Fent et al. 2020). Some of these studies were also able to confirm that self-contained breathing apparatus (SCBA) was worn consistently throughout the fire event, suggesting that dermal absorption contributed to the PAH metabolites measured in urine and benzene measured in exhaled breath of the firefighters, firefighter students, and instructors (Fent et al. 2019b, Fent et al. 2020). Mayer et al. (Mayer et al. 2020) employed stationary mannequins in a smoke exposure chamber to show that benzene can come through or around turnout jackets. It is plausible, then, that benzene vapor is contacting firefighters' skin during live-fire events and a small percentage is being absorbed through skin, as has been shown in animal studies (Franz 1984, Wester et al. 1993, Thrall et al. 2000, Wester and Maibach 2000).

Compounds with lower vapor pressure that contact skin should have an increased propensity for being dermally absorbed; although, the specific properties of the compounds, such as octanol/water coefficient, also play an important role (Frasch 2002, Rauma et al. 2013). It's also possible that turnout gear could off-gas VOCs after SCBA has been removed, contributing to firefighters' exposure through inhalation and dermal absorption (Fent et al. 2015). Regardless, given the overall abundance of VOCs in the fire environment, an understanding of the extent to which those VOCs may be absorbed by firefighters is crucial. However, few studies have attempted to quantify VOC metabolites in firefighters after live-fire events. Of the studies that have measured VOC biological burden in firefighters, most have collected exhaled breath (Fent et al. 2019b, Fent et al. 2020) or only measured urinary metabolites of benzene (Caux et al. 2002, Laitinen et al. 2010, Rosting and Olsen 2020).

We conducted two field studies: one involving controlled residential fires (firefighters) and a second involving three types of training environments (firefighter students and instructors), each with different fuel packages and structures. These two studies allowed us to investigate the biological uptake of PAHs (urine) and VOCs including benzene (exhaled breath) and compare these values to airborne measurements as well as dermal exposure monitoring results for PAHs (Fent et al. 2017, Fent et al. 2018, Fent et al. 2019a, Fent et al. 2019b, Fent et al. 2020). The purpose of this paper is to quantify and compare specific VOC metabolites in urine across the two studies and collection time points. Specifically, firefighters and firefighter students responded to a single fire scenario and a spot urine sample was collected before and 3 hours after the fire responses. Urine was also collected from instructors each day before they led three training scenarios and 3 hours after the training scenarios.

2. Methods

2.1 Study design

This paper reports biomonitoring results from two separate live-fire exposure studies: 1) residential fire study and 2) training fire study, both of which took place at the Illinois Fire Service Institute. The residential fire study was approved by the Institutional Review Boards (IRBs) at the University of Illinois and the National Institute for Occupational Safety and Health (NIOSH). The training fire study was also approved by the University of Illinois IRB, with reliance out by NIOSH IRB. The methodology used to recruit and consent participants has been described previously (Fent et al. 2017, Fent et al. 2019a). Firefighters with any known cardiovascular disease, who used tobacco products, were younger than 18 or older than 55 years of age, or pregnant were excluded from participating in the studies. Details about each study design, including the fire structures and fuels, are provided in Table 1.

For the residential fire study, participating firefighters included in this analysis were assigned to either fire attack, where they advanced the hoseline and suppressed all active fires, or search and rescue, where they conducted forcible entry and then searched for and rescued two simulated victims (75 kg manikins). Of the 36 firefighters included in the analysis (median age=36), 32 were male and 4 were female.

For the training fire study, two instructors acted as stokers to light the fires and control ventilation for fire and smoke development, two instructors were assigned as company officers and supervised the attack team, and the remaining instructor was the officer in charge of the search and rescue team. Meanwhile, firefighter students undergoing the training performed either fire attack or search and rescue and performed very similar activities as the firefighters in the residential fire study, including hose advance and suppression and rescuing two simulated victims. Twenty-four firefighter students (median age= 40; 22 male and 2 female) and 10 instructors (median age 35; 9 male and 1 female) participated in this study.

All participants (firefighters, firefighter students, and instructors) wore National Fire Protection Association (NFPA) 1971-compliant protective ensembles (NFPA 2018), and NFPA 1981-compliant self-contained breathing apparatus (SCBA). The participants were required to wear SCBA (mask-up) before entering any of the fire structures. The SCBA masks were not removed until the fire was suppressed, and participants were upwind of the fire structures. The participants removed their turnout gear before reporting to the climate-controlled data collection areas. In the residential fire study, the attack and search firefighters continued to breath from their SCBA until they reached the data collection area, thus further minimizing the potential to inhale any airborne contaminants from the fires or off-gassing from their gear. In the training fire study, the participants removed their turnout gear before reporting to the climate-controlled data collection areas.

Participants cleaned their skin using commercial skin-cleansing wipes soon after entering the data collection area. All participants other than the instructors then subsequently (within about 30 min) showered and put on clean station gear. Instructors waited until the end of their shift (after the third fire of the day) to shower, which is common practice. After showering, all participants reported to a climate-controlled area of the research facility to await additional biological sample collection. Personal and area air sampling for VOCs was also conducted for both studies and reported previously (Fent et al. 2018; Fent et al. 2019a).

2.2. Urine sampling and analysis

Participants provided spot urine samples pre-firefighting. All participants other than the instructors also provided spot urine samples 3-hr post firefighting. For the instructors, urine samples were collected 3-hr after the last fire of the day (end-of-shift).

Specific gravity was measured in the field by using a manual handheld specific gravity refractometer (Atago USA., Inc, Bellevue, WA). The manual refractometer was calibrated by placing 2 drops deionized room temperature (RT) distilled water on the faceplate and holding the refractometer to light and setting the indicator line to 0.000 on the specific gravity or UG scale. The specific gravity of urine (RT) was determined by reading the indicator line on the UG scale after similarly placing 2 drops of urine on the faceplate and holding the refractometer to light. Calibration was rechecked throughout and after reading urine samples.

The urine samples were then aliquoted into labeled tubes and stored on dry ice while in the field. Samples pending creatinine and cotinine analyses were then stored at −80 °C and those pending VOC metabolite analyses at −20 °C. Creatinine and cotinine analyses took place within a few months of the sample collections. The residential fire and training fire urine samples were stored for approximately 3 years and 2 years, respectively, before VOC metabolite analyses.

Creatinine was measured using a Vitros Autoanalyzer (Johnson & Johnson, New Brunswick, NJ) with a Vitros CREA slide. Cotinine, a metabolite of nicotine, was measured using Diagnostic Products Corporation (Siemens Corporation, Washington, DC) Immulite® 2000 analytical platform. Cotinine concentrations were used to confirm current non-tobacco use status of the participants and to quantify possible exposure to environmental tobacco smoke (ETS), which can be a source of VOC exposure (Jain 2015). The vast majority of urine samples (92% and 96% in the residential and training fire, respectively) had cotinine levels consistent with non-tobacco use status and no ETS exposure (<10 ng/mL).

The urine samples were analyzed for VOC metabolites using ultraperformance liquid chromatography-tandem mass spectrometry. Benzene metabolites (MUCA and PhMA) were measured using the analytical method by Bhandari et al. (2019). 2MHA, 3MHA+4MHA, MADA, 4HBeMA, 3HPMA, and BzMA were measured using a different method published by Alwis et al. (2012). Table 2 provides a list of the VOC metabolites that were measured and the associated parent compounds.

Urinary VOC metabolite concentrations (ng/mL) were corrected by creatinine (by unit conversion and division, resulting in units of μg/g creatinine in mg/dL urine) and by specific gravity using the following equation (described in Sauve et al. 2015):

$$C_{corr} = \frac{C_i(SG_{ref} - 1)}{(SG - 1)}$$

C_{corr} = Corrected concentration (μg/L urine)

C_i = Measured concentration of the biological indicator (μg/L urine)

SG_{ref} = Reference specific gravity value, here we used 1.016

SG = Specific gravity of the urine analyzed

2.3. Data analysis

Summary statistics were presented as mean, median, and range for VOC metabolite creatinine-adjusted concentrations, stratified by collection period (pre and 3-hr post-fire) and, for the training fire study, firefighter type (student and instructor). Median and 95th percentile urinary concentrations of VOC metabolites were calculated from the National

Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the U.S. general population, from 2013–2014 for individuals aged 18 to 55 years and stratified by smoking status. In calculating the descriptive statistics, non-detectable VOC metabolite concentrations below the limits of detection (LOD) were assigned values using the β-substitution method (Ganser and Hewett 2010) that adjusts each non-detectable value based on the uncensored data. Box and whisker plots with minimum, 25th percentile, median, 75th percentile, and maximum were performed for the detailed stratifications with respect to position (attack and search) or fuel type (Alpha OSB, Bravo OSB, and pallet and straw).

A mixed model that accounted for left censoring was fit using maximum likelihood estimation with individual firefighter as a random effect was utilized to account for the statistical correlation among repeated measures from the same firefighter and to examine whether the change in urinary VOC metabolites between pre-firefighting and 3-hr post firefighting was significantly different from zero in the residential fire study and by firefighter type in the training fire study (Jin et al. 2011). A median regression model for skewed exposure data with repeated measures and non-detects, incorporating an exchangeable working correlation structure, was used to investigate whether the median in post-fire urinary VOC metabolites among firefighter types was significantly different from zero (Chen et al. 2021). All tests were two-sided at the 0.05 significance level. Statistical analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Urinary VOC metabolites for firefighters participating in the residential fire study

Table 3 summarizes creatinine-adjusted VOC metabolite concentrations for 24 firefighters participating in the residential fire study assigned to fire attack and search and rescue. The VOC metabolites that increased significantly from pre- to post-fire are summarized in Figure 1 and include 2-Methylhippuric acid (2MHA), N-Acetyl-S-(benzyl)-L-cysteine (BzMA), and mandelic acid (MADA) (p-values 0.005, <0.001, and <0.001, respectively). Benzene metabolites trans, trans-Muconic acid (MUCA) and N-Acetyl-S-(phenyl)-L-cysteine (PhMA) did increase from pre- to post-fire, but that increase was not significant.

Compared to the general population (Table 3), median post-fire BzMA levels (7.23 μg/g creatinine) were higher than median concentrations for general population smokers (6.06 μg/g creatinine) and non-smokers (6.32 μg/g creatinine). Pre-fire MADA median concentrations (122 μg/g creatinine) were similar to median non-smoker general population concentrations (116 μg/g creatinine), while median post-fire MADA concentrations (177 μg/g creatinine) were elevated to near median levels reported in general population smokers (182 μg/g creatinine).

VOC metabolite concentrations adjusted for specific gravity for the same firefighters are provided in Supplemental Materials (Table S1). Overall, specific gravity-adjusted VOC metabolite concentrations were similar to the creatinine-adjusted results, as 2MHA, BzMA, and MADA increased significantly from pre- to post-fire.

3.2. Urinary VOC metabolites for firefighter students and instructors participating in the training fire study

Creatinine-adjusted VOC metabolite concentrations for training fire participants stratified by participant type (firefighter students vs. instructors) are summarized in Table 4. MADA concentrations increased significantly from pre- to post-fire for both firefighter students and instructors (p-values <0.001 and <0.0001, respectively). Concentrations of benzene metabolites including MUCA and PhMA also increased significantly from pre- to post-fire for instructors (p-values 0.038 and 0.016, respectively), while 3-methylhippuric acid + 4-methylhippuric acid (3MHA+4MHA) and N-acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA) increased significantly for firefighter students (p-values 0.011). On the other hand, 4HBeMA and MUCA results significantly decreased for firefighter students (p-values 0.008 and 0.015, respectively).

Figure 2 shows creatinine-adjusted results for metabolites that increased significantly from pre- to post-fire, stratified by fuel type. Post-fire MUCA concentrations were significantly elevated for instructors responding to Alpha OSB scenarios. 3HPMA and MADA concentrations, on the other hand, were elevated for firefighter students and instructors responding to Bravo OSB scenarios. Post-fire PhMA concentrations were elevated for both Alpha and Bravo OSB scenarios.

Median post-fire MADA concentrations for both firefighter students (227 µg/g creatinine) and instructors (356 µg/g creatinine) were higher than the median smoker (182 µg/g creatinine) and non-smoker (116 µg/g creatinine) general population concentrations (Table 4). In fact, median post-fire MADA concentrations for instructors were higher than the 95th percentile of the non-smoking general population (299 µg/g creatinine). Median post-fire BzMA concentrations for firefighter students (8.65 µg/g creatinine) and instructors (9.31 µg/g creatinine) were also above median smoker (6.06 µg/g creatinine) and non-smoker (6.32 µg/g creatinine) general population levels. Median post-fire 3HPMA concentrations for firefighter students (211 µg/g creatinine) and instructors (322 µg/g creatinine) were well above median concentrations for the non-smoking general population (174 µg/g creatinine) but below levels found in smokers (508 µg/g creatinine). The two highest post-shift concentrations of MUCA measured from instructors (750 and 631 µg/g) exceeded the American Conference of Governmental Industrial Hygienists (ACGIH) biological exposure indices (BEI) of 500 µg/g creatinine (ACGIH, 2021). It's important to note that instructors completed three fire exercises each day while firefighter students completed one.

VOC metabolite concentrations adjusted for specific gravity for the firefighter students and instructors are in Supplemental Materials (Table S2). Like the results from the residential fire study, the specific gravity-adjusted VOC metabolite concentrations for firefighter students and instructors were similar to the creatinine-adjusted results. Specifically, MADA concentrations increased significantly from pre- to post-fire for both firefighter students and instructors (p-values <0.001 and 0.011). 3MHA+4MHA and 3HPMA increased significantly for firefighter students (p-values 0.039 and 0.022), while MUCA and PhMA concentrations increased significantly from pre- to post-fire for instructors (p-values 0.037 and 0.016).

4. Discussion

Although many studies have documented firefighters' airborne exposures to VOCs, to our knowledge, this is the first study to quantify the biological uptake of numerous types of VOCs measured as metabolites in urine following live fire suppression or training. Exposures to combustion byproducts will vary due to a variety of factors, including the materials in and orientation of products being burned, the duration of the fires, and the ventilation conditions. Nevertheless, the live fires described in this paper represent fire conditions that are likely to be encountered during responses to residential fires that involve household furnishings and during typical types of live-fire training scenarios.

4.1. Urinary VOC metabolites for firefighters participating in the residential fire study

The urinary VOC metabolite results from the residential fire study indicate that firefighters assigned to attack and search absorbed xylenes (2MHA), toluene (or benzyl alcohol) (BzMA), and styrene (MADA) during the live-fire scenarios. The metabolites of these compounds were all significantly elevated in the 3-hr post fire urine samples. The metabolites of benzene (MUCA and PhMA) were not significantly elevated. Benzene is often one of the most abundant combustion byproducts produced during fires (Jankovic et al. 1991, Austin et al. 2001b), which was the case for this study (Fent et al. 2018). Studies have also reported that firefighters can have significant increases of benzene in breath and benzene metabolites in urine post firefighting (Caux et al. 2002, Laitinen et al. 2010, Fent et al. 2020). In fact, firefighters in this study had significant increases of exhaled breath concentrations of benzene after firefighting (Fent et al. 2019b). While the post-fire increase of the benzene metabolites in urine did not meet the level of significance, it does suggest that some biological absorption took place.

Although typically not present in as high of concentrations as benzene, styrene and toluene are also commonly produced during structure fires. For example, when we measured the personal air concentrations of VOCs for attack firefighters during the residential fire study, we found median levels of benzene, styrene, and toluene of 40, 2.7, and 2.4 ppm, respectively. For search firefighters, we found similar median air concentrations (38, 2.6, 2.6 ppm, respectively) (Fent et al. 2018). When we stratified the urinary concentrations by job assignment (Figure 1), we found a larger increase in MADA concentrations for attack firefighters than search firefighters, suggesting absorption of styrene might be higher for those assigned to attack even though personal air concentrations of styrene were similar.

4.2. Urinary VOC metabolites for firefighter students and instructors participating in the training fire study

For the training fire study, we found differences among the urinary VOC metabolites between firefighter students and instructors. This is not unexpected, because the instructors participated in three training exercises per day and their post-fire urines were collected at the end of their shift (~9 hours after first scenario and ~3 hours after last scenario). In comparison, the firefighter students only participated in one training scenario per day and had their post-fire urine samples collected 3-hours after that single scenario. Hence, the timing of specimen collection and duration of the exposures differ between these two groups. Additionally, instructors did not doff their gear and shower until after the third training exercise each day, potentially contributing to their exposure relative to firefighter students. This design is consistent with real-life scenarios where instructors often participate in multiple training exercises in a day. This difference between instructors and students might also help elucidate the differences among the VOC metabolites that were measured.

For the firefighter students, we saw significant increases in metabolites of xylenes (2MHA), acrolein (3HPMA), and styrene (MADA). For the instructors, we saw significant increases in metabolites of benzene (MUCA, PhMA) and styrene (MADA). When comparing the level of increase for the metabolite of styrene (MADA, the only metabolite found to increase significantly in both groups), we found that instructors had a significantly larger post-fire increase than firefighter students (p-value <0.001), most likely due to their repeated exposures. For the metabolites of xylenes and acrolein, the inconsistent findings of significance between firefighter students and instructors may have more to do with lower statistical power for the instructors (i.e., study included three times the number of firefighter students compared to instructors). Figure 2 provides some visual evidence that the firefighter students and instructors had similar trends in the excretion patterns of these metabolites despite different post-fire collection periods. Still, because firefighter students had increased urinary levels of 3MHA+4MHA and 3HPMA after just one fire, we might expect an even bigger increase in these metabolites among instructors after three consecutive fires than what we found.

However, there are numerous factors that may influence the urinary VOC metabolite levels, including different activities and proximity to the fires between instructors and firefighter students (i.e., students were generally closer to the seat of the fires), as well as the rate of metabolism after absorption of the parent compounds and differences among the analyte elimination half-lives. These factors are further complicated by the different routes of exposure (inhalation and dermal).

We previously showed a statistically significant post-fire increase in exhaled breath concentrations of benzene among the participants of both studies, indicating some absorption of benzene (Fent et al. 2019b, Fent et al. 2020). However, for benzene or the other VOCs to be measured in urine after absorption into the bloodstream, they must first be metabolized and then excreted in urine. The elimination half-lives of the mercapturic acid metabolites of acrolein and benzene have been estimated at ~9 hours, the elimination half-life of MUCA has been estimated at ~5 hours, and it is safe to assume that all the VOC metabolites in this study have elimination half-lives of several hours (Van Sittert et al. 1993, Boogaard and Van Sittert 1995, Watzek et al. 2012, St Helen et al. 2020). That post-fire benzene metabolites were not elevated in the firefighter students' urine but were elevated in the instructors' urine may suggest that not enough time had transpired after benzene exposure to show up as metabolites in the students' urine. In fact, the post-shift urine sample collected from the instructors might only be reflecting the peak excretion from exposures encountered during the first scenario that day, even for MUCA that theoretically would be eliminated faster than PhMA.

Another factor that may impact the urinary levels of VOCs is the type and orientation of fuel that was burned and the structure layout that created the training fire environment. For the training fire study, we were able to compare the urinary metabolites measured after training scenarios involving two types of OSB (in a metal container with some fuels on the ceiling) and pallet and straw (in a concrete structure with fuel located in a hopper, slightly elevated off the floor) (Figure 2). Instructors' post-fire levels of MUCA (metabolite of benzene) were most elevated during the Alpha OSB scenario; conversely, 3HPMA (acrolein) and MADA (styrene) were most elevated during the Bravo OSB scenario. The urinary benzene metabolite findings are surprising because personal air concentrations of benzene were far higher during the Bravo OSB scenario (median = 20 ppm) than the Alpha OSB scenario (median = 5.8 ppm) or the pallet and straw scenario (median = 3.9 ppm) (Fent et al. 2019a). Hence, we would have expected instructors overseeing the Bravo OSB scenarios to have the highest post-shift urinary benzene metabolite concentrations. Styrene air concentrations were also higher during the Bravo OSB scenario (median = 2.3 ppm) compared to the Alpha OSB (median = 0.79 ppm) or pallet and straw scenarios (median = 0.39 ppm) (Fent et al. 2019a), which was consistent with the instructors' MADA urinary results reported here. Additionally, area air sampling from this study found acrolein concentrations during Bravo OSB scenarios (median- 60.6 mg/m^3) were significantly higher than Alpha OSB (median= 4.85 mg/m^3) and pallet and straw scenarios (median=5.38 mg/m^3), which is consistent with the 3HPMA results in the current study.

4.3. Comparison of urinary VOC metabolites between residential fire and training fire participants

The burning materials for the residential fire study included a variety of furnishings and synthetic materials (e.g., stuffed chair, innerspring mattress with foam topper, carpet, and padding, etc.). Thus, we might expect more pronounced increases in urinary VOC metabolites for firefighters in that study compared to firefighter students in the training fire study. Post-fire urine was collected 3 hours after the burns in both studies, so comparisons can be made. When we compared the 3-hr post-fire median concentrations between the firefighters and firefighter students for the urinary metabolites that increased significantly in at least one of the study populations (i.e., 2MHA, 3MHA+4MHA, 3HPMA, BZMA, and MADA), we found that firefighters had significantly higher 2MHA, 3MHA+4MHA, and MADA concentrations compared to firefighter students.

Much of the increase in urinary metabolites that were observed in the training fire study can be attributed to the OSB scenarios (Figure 2). We previously published findings that showed significant and more pronounced increases in urinary metabolites of PAHs in firefighter students after the OSB training fires than the pallet and straw fires (Fent et al. 2019b). In fact, the students' median 3-hr post-fire concentration of 1-hydroxypyrene following the Bravo-OSB scenario (0.78 µg /g) was near what we measured 3-hr post fire from firefighters in the residential fire study (median = 0.81 µg /g) (Fent et al. 2019b, Fent et al. 2020). As such, the use of OSB in the upper layer of training fires should be minimized when it is possible to achieve the same training objective with pallet and straw in a more well ventilated configuration.

It appears that some types of training fires can result in VOC exposures that are on par with those experienced during residential fires involving a variety of synthetic materials. This is an especially important finding for instructors who may participate in several training fires per day. The instructors in our study participated in three consecutive training fires each day and had post-shift concentrations of MUCA (metabolite of benzene) that were significantly higher than the students who only participated in one fire. As previously published, the instructors' repeated exposures also resulted in concentrations of 1-hydroxypyrene well above the levels measured from students in the same study or from firefighters in the residential fire study (Fent et al. 2019b, Fent et al. 2020). While we did not (and cannot) measure exposure to all possible combustion byproducts, many of the parent compounds that were quantified as metabolites (e.g., benzene, styrene, acrolein) are known and probable carcinogens (IARC 2012, IARC 2019, IARC 2021), and exposures should be reduced as much as possible.

The firefighters, firefighter students, and instructors in both studies were instructed to wear SCBA throughout the duration of firefighting operations that occurred inside of the structures. Still, some inhalation exposure likely occurred; for example, after responding to the structure prior to donning SCBA or when the firefighters were doffing their contaminated gear, which has been shown to off-gas VOCs for several minutes after firefighting (Fent et al. 2015). It is even possible that instructors who oversaw the Alpha OSB scenarios (compared to the Bravo OSB scenarios) were not as careful about wearing SCBA throughout the entire training exercises and had more inhalation exposure to benzene (hence higher levels of MUCA). Another possibility is that the Alpha OSB instructors unintentionally had looser fitting gear, which could have resulted in more skin exposure to benzene. However, all three groups wore identical PPE that was similarly fit based on participants chest and waist size.

We have previously shown using mannequins that turnout gear provides very little attenuation (< 43%) against the ingress of benzene vapors (Mayer et al. 2020; Mayer et al. 2021 (in Press)). Previous research has also shown that small amounts of benzene vapor (< 1%) can be absorbed dermally, and that skin absorption increases with increasing temperature and humidity (Franz 1984, EPA 1992, Thrall et al. 2000). Dermal absorption, in addition to inhalation, likely contributed to the urinary levels that were measured at least for some of the VOCs. Skin permeation coefficients can be used to estimate the potential for dermal absorption. According to the CDC skin permeation calculator and the Frasch Model (Frasch 2002), xylenes, styrene, and toluene have similar skin permeation coefficients ($6.3E^{-2}$, $5.8E^{-2}$, and $5.6E^{-2}$ cm/hr), followed by benzene ($3.4E^{-2}$ cm/hr) and then acrolein ($4.0E^{-4}$ cm/hr). The ability for acrolein to be absorbed transdermally is estimated to be very low compared to the other compounds (which are not especially high themselves). That urinary 3HPMA (acrolein) was elevated ~3 hour after firefighting for the training firefighter students provides evidence of the inhalation route of absorption. Urinary 3HPMA did not increase in the 3-hr collection for the residential fire study participants. However, in the residential fire study, we instructed the attack and search firefighters to breath from their SCBA until right before breath collection (Fent et al. 2020), which was not required for the training fire participants. The fact that we still found increased urinary metabolites of some VOCs post-firefighting among the residential fire study participants, as well as increased exhaled breath concentrations of benzene (Fent et al. 2020), indicates contribution from the dermal route of absorption. Both routes likely contributed to the biological levels we found, but the inhalation route was probably more predominant in the training fire study. This finding is further evidence of the importance of wearing SCBA throughout the response.

4.4. Comparison of urinary VOC concentrations among participants of the two studies to general U.S. population and BEI concentrations

To put the biological levels (i.e., urinary concentrations) into perspective, we provided comparisons to the general population levels for smokers and non-smokers. Note that, according to the cotinine analysis, nearly all of the firefighters in these two studies were not exposed to tobacco smoke (94%). The majority of the VOC metabolites that were found to be significantly elevated post-fire were measured at levels between the median non-smoking and median smoking general population levels (where the data exist). The exceptions to this were for MADA (styrene) and BzMA (toluene). The post-fire median MADA and BzMA concentrations for firefighter students and instructors who participated in the training fire study (as well as the residential firefighters' post-fire BzMA concentrations) exceeded the smoking general population levels.

Both firefighter students and instructors had median post-fire 3HPMA concentrations that were well above the non-smoking general population levels after having median pre-fire 3HPMA concentrations that were near or below median non-smoking general population levels (Table 4). When we further stratified the training fire study participants by type of fuel, we found that instructors participating in Bravo OSB scenarios had median post-shift urinary 3HPMA (acrolein) concentrations well above smoking general population levels (Figure 2).

NHANES has not yet reported general population levels of MUCA or PhMA measured using the current assay. However, exposure studies have measured urinary MUCA in firefighters and other workers. Laitinen et al. (Laitinen et al. 2010) measured urinary MUCA in fire instructors following three training fires in a day and reported concentrations as molar volume, thereby complicating our comparisons. However, assuming urinary creatinine of 200 mg/dL (middle of the normal range), the mean post-fire urinary levels following training fires involving plywood as fuel was ~100 μg/g creatinine (with pre-exposure ~40 μg/g creatinine). The mean post-fire levels we measured from instructors across all types of live-fire training (186 μg/g creatinine) was greater than this, and for Alpha OSB (558 μg/g creatinine), it was substantially greater. A study of gas station workers in Brazil measured mean post-shift MUCA concentrations of 204 μg/g creatine (Geraldino et al. 2020), which is within the range of post-shift concentrations we measured for instructors across all types of training and substantially lower than what we found for instructors following the Alpha OSB training.

Comparisons were also made to any applicable ACGIH BEIs. Although median urinary VOC metabolite concentrations were below all applicable BEIs, two post-shift urine samples collected from fire instructors had concentrations of MUCA that exceeded the BEI. This suggests that the amount of benzene absorbed for a few of the participants were above the levels ACGIH considers to be acceptable for safe working conditions. What is most striking about this finding is that the actual exposure or fire periods were relatively short (most fire responses were 10–15 minutes in duration), and participants were generally very good about wearing their SCBA inside and even outside the structure. This warrants further investigation into firefighters' VOC metabolite concentrations after longer duration emergency fires where SCBA usage may not be as tightly monitored.

Often biomarker exposure studies correct for hydration status by using creatinine (hence the comparisons made in this paper). However, specific gravity of urine can also be used and has even been suggested by some researchers to be the preferred approach because creatinine may be more affected by physiological differences in the study population (Suwazono et al. 2005, Sauve et al. 2015). We have provided specific gravity corrected urinary metabolite concentrations in the supplemental materials. In general, the results did not differ in that significant pre- to post-fire differences observed using creatinine correction were also observed using specific gravity correction. It is important to note that the participants in both the residential fire and training fire studies were strongly encouraged to hydrate both before and after the fires. As a result, most of the participants were well hydrated, especially at the 3-hr or post-shift urine collections.

The studies in this paper are not without limitations. Other sources of VOCs may have been present at the fire training institute; although, we attempted to control these exposures by keeping participants in a climate-controlled facility following the fire scenarios. By collecting only one post-fire urine sample (3 hours after firefighting) for the firefighters and firefighter students, we may not have captured the peak excretion period for some VOCs. Our urine sampling regimen (3 hours after the last of three fires) may have even underestimated the cumulative exposures for the fire instructors. However, a recent study found that firefighter intstructors' peak PMA and HPMA urinary concentrations occured 3 hours after the training exercise (Rossbach et al. 2022). The possibility also exists that non-occupational factors like diet (e.g., sorbic acid in food) and application of beauty of products (e.g., benzyl alcohol in cosmetics) could impact the urinary concentrations reported here (e.g., MUCA and BzMA, respectively). However, participants were provided the same breakfast and lunch during study days and thus differences in urinary concentrations of MUCA by job title were unlikely due to ingestion of sorbic acid.

Another potential limitation is that the residential and training fire urine samples were stored for 3 years and 2 years, respectively, prior to the VOC metabolite analysis. However, because the samples were kept at a temperature well below freezing (−20°C), we do not expect the extended storage time to greatly impact the results reported here. Additionally, we did not analyze urine for metabolites of some other hazardous compounds (e.g., acetaldehyde, formaldehyde, isocyanates) that were measured in area air samples taken during the training fires (Fent et al.2019a). Future exposure studies of firefighters are warranted, including quantifying urinary metabolite concentrations of hazardous combustion products not analyzed here while also validating the findings from this study.

5. Conclusions

We have reported and compared the urinary VOC metabolite concentrations among firefighter participants from two separate studies focusing on residential fire environments and training fire environments. The participants in both studies were instructed to wear SCBA throughout the response and to not remove their SCBA until the fire was suppressed and they were upwind of the fires. Some participants (i.e., attack and search firefighters in the residential fire study) continued to breathe from their SCBA until they reached the climate-controlled biological collection area. It is unlikely that firefighters would maintain such stringent SCBA protocols under normal circumstances. Still, we found post-fire urine metabolite levels of a variety of VOCs increased from pre-fire levels. In some cases, the post-fire VOC metabolite concentrations were above smoking general population levels. Because many of the VOC metabolites have elimination half-lives of several hours, it is likely that we did not capture the peak excretion levels. Some of the compounds that were significantly elevated post-firefighting are metabolites of known or probable carcinogens (benzene, styrene, acrolein) and exposure to them should be eliminated or reduced as much as possible through the hierarchy of controls (NIOSH, 2016). Further research is needed to better understand the exposure pathways for these compounds (dermal vs. inhalation) and interventions that can be implemented to reduce biological uptake. These results suggest firefighters should wear SCBA on scene, especially in the presence of smoke or combustion products, and remove contaminated gear and clean skin as soon as possible post-fire to further reduce their exposures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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7. References

Alwis K, Blount B, Britt A, Patel D, and Ashley D (2012). "Simultaneous analysis of 28 urinary VOC metabolites using ultra high performance liquid chromatography coupled with electrospray ionization tandem mass spectrometry (UPLC-ESI/MSMS)". Analytic Chimica Acta. 750: 152–160.

American Conference of Governmental Industrial Hygienists (ACGIH) (2021). "2021 TLVs and BEIs with 9th Edition Documentation". Cincinnati, OH: ACGIH.

Andersen MHG, Saber AT, Clausen PA, Pedersen JE, Lohr M, Kermanizadeh A, Loft S, Ebbehoj N, Hansen AM, Pedersen PB, Koponen IK, Norskov EC, Moller P and Vogel U (2017). "Association between polycyclic aromatic hydrocarbon exposure and peripheral blood mononuclear cell DNA damage in human volunteers during fire extinction exercises." Mutagenesis.

Austin CC, Wang D, Ecobichon DJ and Dussault G (2001a). "Characterization of volatile organic compounds in smoke at experimental fires." J Toxicol Environ Health A 63(3): 191–206. [PubMed: 11405415]

Austin CC, Wang D, Ecobichon DJ and Dussault G (2001b). “Characterization of volatile organic compounds in smoke at municipal structural fires.” J Toxicol Environ Health A 63(6): 437–458. [PubMed: 11482799]

Bhandari D, McCarthy D, Biren C, Movassaghi C, Blount B, et al. (2019). “Development of a UPLC-ESI-MS/MS method to measure urinary metabolites of selected VOCs: Benzene, cyanide, furfural, furfuryl alcohol, 5-hydroxymethylfurfural, and N-methyl-2-pyrrolidone” Journal of Chromatography B 1126.

Bolstad-Johnson DM, Burgess JL, Crutchfield CD, Storment S, Gerkin R and Wilson JR (2000). “Characterization of firefighter exposures during fire overhaul.” AIHAJ 61(5): 636–641. [PubMed: 11071414]

Boogard PJ, van Sittert NJ (1995). “Biological monitoring of exposure to benzene: a comparison between S-phenylmercapturic acid, trans,trans-muconic acid, and phenol.” Occup Environ Med 52:611–620. [PubMed: 7550802]

Casjens S, Bruning T and Taeger D (2020). “Cancer risks of firefighters: a systematic review and meta-analysis of secular trends and region-specific differences.” Int Arch Occup Environ Health 93(7): 839–852. [PubMed: 32306177]

Caux C, O’Brien C and Viau C (2002). “Determination of firefighter exposure to polycyclic aromatic hydrocarbons and benzene during fire fighting using measurement of biological indicators.” Appl Occup Environ Hyg 17(5): 379–386. [PubMed: 12018402]

Chen IC, Bertke SJ, Curwin BD (2021). “ Quantile regression for exposure data with repeated measures in the presence of non-detects.” J Expo Sci Environ Epidemiol 31: 1057–1066. [PubMed: 34108633]

Daniels RD, Kubale TL, Yiin JH, Dahm MM, Hales TR, Baris D, Zahm SH, Beaumont JJ, Waters KM and Pinkerton LE (2014). “Mortality and cancer incidence in a pooled cohort of US firefighters from San Francisco, Chicago and Philadelphia (1950–2009).” Occup Environ Med 71(6): 388–397. [PubMed: 24142974]

EPA (1992). Dermal Exposure Assessment: Principles and Applications. Washington, DC, Exposure Assessment Group, Office of Health and Environmental Assessment, U.S. Environmental Protection Agency (EPA)

Fent KW, Alexander B, Roberts J, Robertson S, Toennis C, Sammons D, Bertke S, Kerber S, Smith D and Horn G (2017). “Contamination of firefighter personal protective equipment and skin and the effectiveness of decontamination procedures.” J Occup Environ Hyg 14(10): 801–814. [PubMed: 28636458]

Fent KW, Evans DE, Babik K, Striley C, Bertke S, Kerber S, Smith D and Horn GP (2018). “Airborne contaminants during controlled residential fires.” J Occup Environ Hyg 15(5): 399–412. [PubMed: 29494297]

Fent KW, Evans DE, Booher D, Pleil JD, Stiegel MA, Horn GP and Dalton J (2015). “Volatile Organic Compounds Off-gassing from Firefighters’ Personal Protective Equipment Ensembles after Use.” J Occup Environ Hyg 12(6): 404–414. [PubMed: 25751596]

Fent KW, Mayer A, Bertke S, Kerber S, Smith D and Horn GP (2019a). “Understanding airborne contaminants produced by different fuel packages during training fires.” J Occup Environ Hyg 16(8): 532–543. [PubMed: 31169466]

Fent KW, Toennis C, Sammons D, Robertson S, Bertke S, Calafat AM, Pleil JD, Geer Wallace MA, Kerber S, Smith DL and Horn GP (2019b). “Firefighters’ and instructors’ absorption of PAHs and benzene during training exercises.” Int J Hyg Environ Health 222(7): 991–1000. [PubMed: 31272797]

Fent KW, Toennis C, Sammons D, Robertson S, Bertke S, Calafat AM, Pleil JD, Wallace MAG, Kerber S, Smith D and Horn GP (2020). “Firefighters’ absorption of PAHs and VOCs during controlled residential fires by job assignment and fire attack tactic.” J Expo Sci Environ Epidemiol 30(2): 338–349. [PubMed: 31175324]

Feunekes FD, Jongeneelen FJ, vd Laan H and Schoonhof FH (1997). “Uptake of polycyclic aromatic hydrocarbons among trainers in a fire-fighting training facility.” American Industrial Hygiene Association Journal 58(1): 23–28. [PubMed: 9018833]

Franz TJ (1984). Percutaneous absorption of benzene. Advances in Modern Environmental Toxicology. Vol. 6, Applied Toxicology of Petroleum Hydrocarbons. McFarland HN Princeton, NJ, Scientific Publishers: 61–70.

Frasch HF (2002). “A random walk model of skin permeation.” Risk Anal 22(2): 265–276. [PubMed: 12022675]

Ganser GH and Hewett P (2010). “An accurate substitution method for analyzing censored data.” J Occup Environ Hyg 7(4): 233–244. [PubMed: 20169489]

Geraldino BR, Nunes RFN, Gomes JB, Giardini I, da Silva PVB, Campos E, da Poca KS, Hassan R, Otero UB and Sarpa M (2020). “Analysis of Benzene Exposure in Gas Station Workers Using Trans,Trans-Muconic Acid.” Int J Environ Res Public Health 17(15).

Glass DC, Del Monaco A, Pircher S, Vander Hoorn S and Sim MR (2016). “Mortality and cancer incidence at a fire training college.” Occup Med (Lond) 66(7): 536–542. [PubMed: 27371948]

IARC (2010). Painting, Firefighting, and Shiftwork. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol. 98. Lyon, France, World Health Organization.

IARC (2012a). Chemical agents and related occupations, Volume 100F: A review of human carcinogens, IARC monographs on the evaluation of carcinogenic risks to humans. Lyon, France, World Health Organization, International Agency for Research on Cancer.

IARC (2012b). Monographs on the evaluation of the carcinogenic risks to humans: vol. 29, sup. 7, 100F benzene. Lyon, France, World Health Organization, International Agency for Research on Cancer.

IARC (2019). Styrene, styrene-8,8-oxide, and quinoline, Volume 121, IARC monographs on the identification of carcinogenic hazards to humans. Lyon, France, World Health Organization, International Agency for Research on Cancer.

IARC (2021). Acrolein, crotonaldehyde, and arecoline, Volume 128, IARC monographs on the identification of carcinogenic hazards to humans. Lyon, France, World Health Organization, International Agency for Research on Cancer.

Jain (2015). “Levels of selected urinary metabolites of volatile organic compounds among children aged 6–11 years.” Environ Res 142: 461–470. [PubMed: 26257031]

Jalilian H, Ziaei M, Weiderpass E, Rueegg CS, Khosravi Y and Kjaerheim K (2019). “Cancer incidence and mortality among firefighters.” Int J Cancer 145(10): 2639–2646. [PubMed: 30737784]

Jankovic J, Jones W, Burkhart J and Noonan G (1991). “Environmental study of firefighters.” Ann Occup Hyg 35(6): 581–602. [PubMed: 1768008]

Jin Y, Hein MJ, Deddens JA and Hines CJ (2011). “Analysis of lognormally distributed exposure data with repeated measures and values below the limit of detection using SAS.” Ann Occup Hyg 55(1): 97–112. [PubMed: 21177260]

Jung AM, Zhou J, Beitel SC, Littau SR, Gulotta JJ, Wallentine DD, Moore PK and Burgess JL (2021). “Longitudinal evaluation of whole blood miRNA expression in firefighters.” J Expo Sci Environ Epidemiol.

Keir JLA, Akhtar US, Matschke DMJ, Kirkham TL, Chan HM, Ayotte P, White PA and Blais JM (2017). “Elevated Exposures to Polycyclic Aromatic Hydrocarbons and Other Organic Mutagens in Ottawa Firefighters Participating in Emergency, On-Shift Fire Suppression.” Environ Sci Technol 51(21): 12745–12755. [PubMed: 29043785]

Laitinen J, Makela M, Mikkola J and Huttu I (2010). “Fire fighting trainers’ exposure to carcinogenic agents in smoke diving simulators.” Toxicol Lett 192(1): 61–65. [PubMed: 19576276]

Laitinen J, Makela M, Mikkola J and Huttu I (2012). “Firefighters’ multiple exposure assessments in practice.” Toxicology Letters 213(1): 129–133. [PubMed: 22710199]

Lee DJ, Koru-Sengul T, Hernandez MN, Caban-Martinez AJ, McClure LA, Mackinnon JA and Kobetz EN (2020). “Cancer risk among career male and female Florida firefighters: Evidence from the Florida Firefighter Cancer Registry (1981–2014).” Am J Ind Med 63(4): 285–299. [PubMed: 31930542]

Mayer AC, Horn GP, Fent KW, Bertke SJ, Kerber S, Kesler RM, Newman H and Smith DL (2020). “Impact of select PPE design elements and repeated laundering in firefighter protection from smoke exposure.” J Occup Environ Hyg 17(11–12): 505–514. [PubMed: 32990508]

Mayer AC, Fent KW, Wilkinson A, Chen I, Kerber S, Smith DL, Kesler RM, and Horn GP " Characterizing exposure to benzene, toluene, and naphthalene in firefighters wearing different types of new or laundered PPE." Int J Hyg Environ Health (In Press)

Muegge CM, Zollinger TW, Song Y, Wessel J, Monahan PO and Moffatt SM (2018). "Excess mortality among Indiana firefighters, 1985–2013." Am J Ind Med 61(12): 961–967. [PubMed: 30421827]

NIOSH. Current intelligence bulletin 68: NIOSH chemical carcinogen policy. (2016) By Whittaker C, Rice F, McKernan L, Dankovic D, Lentz TJ, MacMahon K, Kuempel E, Zumwalde R, Schulte P, on behalf of the NIOSH Carcinogen and RELs Policy Update Committee. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2017–100.

NFPA (2018). NFPA 1971 standard on protective ensembles for structural fire fighting and proximity fire fighting. 2018 ed. Quincy, MA, National Fire Protection Association.

Oliveira M, Slezakova K, Alves MJ, Fernandes A, Teixeira JP, Delerue-Matos C, Pereira MDC and Morais S (2016). "Firefighters' exposure biomonitoring: Impact of firefighting activities on levels of urinary monohydroxyl metabolites." Int J Hyg Environ Health 219(8): 857–866. [PubMed: 27449739]

Pinkerton L, Bertke SJ, Yiin J, Dahm M, Kubale T, Hales T, Purdue M, Beaumont JJ and Daniels R (2020). "Mortality in a cohort of US firefighters from San Francisco, Chicago and Philadelphia: an update." Occup Environ Med 77(2): 84–93. [PubMed: 31896615]

Pukkala E, Martinsen JI, Weiderpass E, Kjaerheim K, Lynge E, Tryggvadottir L, Sparen P and Demers PA (2014). "Cancer incidence among firefighters: 45 years of follow-up in five Nordic countries." Occup Environ Med 71(6): 398–404. [PubMed: 24510539]

Rauma M, Boman A and Johanson G (2013). "Predicting the absorption of chemical vapours." Adv Drug Deliv Rev 65(2): 306–314. [PubMed: 22465561]

Rossbach B, Roehm-Irle I, Backer S, Jager T, Bader M, and Letzel S (2022). "Uptake of benzene and acrolein by firefighting instructors during live fire training" Safety and Health at Work. 13: S241.

Rosting C and Olsen R (2020). "Biomonitoring of the benzene metabolite s-phenylmercapturic acid and the toluene metabolite s-benzylmercapturic acid in urine from firefighters." Toxicol Lett 329: 20–25. [PubMed: 32380125]

Sauve JF, Levesque M, Huard M, Drolet D, Lavoue J, Tardif R and Truchon G (2015). "Creatinine and specific gravity normalization in biological monitoring of occupational exposures." J Occup Environ Hyg 12(2): 123–129. [PubMed: 25192246]

Soteriades ES, Kim J, Christophi CA and Kales SN (2019). "Cancer Incidence and Mortality in Firefighters: A State-of-the-Art Review and Meta-Analysis." Asian Pac J Cancer Prev 20(11): 3221–3231. [PubMed: 31759344]

St Helen G, Liakoni E, Nardone N, Addo N, Jacob P 3rd and Benowitz NL (2020). "Comparison of Systemic Exposure to Toxic and/or Carcinogenic Volatile Organic Compounds (VOC) during Vaping, Smoking, and Abstention." Cancer Prev Res (Phila) 13(2): 153–162. [PubMed: 31554628]

Suwazono Y, Akesson A, Alfven T, Jarup L and Vahter M (2005). "Creatinine versus specific gravity-adjusted urinary cadmium concentrations." Biomarkers 10(2–3): 117–126. [PubMed: 16076727]

Thrall KD, Poet TS, Corley RA, Tanojo H, Edwards JA, Weitz KK, Hui X, Maibach HI and Wester RC (2000). "A real-time in-vivo method for studying the percutaneous absorption of volatile chemicals." International Journal of Occupational and Environmental Health 6(2): 96–103. [PubMed: 10828137]

Treitman RD, Burgess WA and Gold A (1980). "Air contaminants encountered by firefighters." Am Ind Hyg Assoc J 41(11): 796–802. [PubMed: 7457369]

Tsai RJ, Luckhaupt SE, Schumacher P, Cress RD, Deapen DM and Calvert GM (2015). "Risk of cancer among firefighters in California, 1988–2007." Am J Ind Med 58(7): 715–729. [PubMed: 25943908]

van Sittert NJ, Boogaard PJ and Beulink GD (1993). "Application of the urinary S-phenylmercapturic acid test as a biomarker for low levels of exposure to benzene in industry." Br J Ind Med 50(5): 460–469. [PubMed: 8507599]

Watzek N, Scherbl D, Feld J, Berger F, Doroshyenko O, Fuhr U, Tomalik-Scharte D, Baum M, Eisenbrand G and Richling E (2012). "Profiling of mercapturic acids of acrolein and acrylamide in human urine after consumption of potato crisps." Mol Nutr Food Res 56(12): 1825–1837. [PubMed: 23109489]

Wester R, Maibach H, and C GL J. (1993). Bioavailability of benzene through inhalation and skin absorption. Sampling Analysis of Airborne Pollutants. Winegar E and Keith L Boca Raton, FL, Lewis Publishers: 339–351.

Wester RC and Maibach HI (2000). "Benzene percutaneous absorption: dermal exposure relative to other benzene sources." International Journal of Occupational and Environmental Health 6(2): 122–126. [PubMed: 10828141]

Zhou J, Jenkins TG, Jung AM, Jeong KS, Zhai J, Jacobs ET, Griffin SC, Dearmon-Moore D, Littau SR, Peate WF, Ellis NA, Lance P, Chen Y and Burgess JL (2019). "DNA methylation among firefighters." PLoS One 14(3): e0214282. [PubMed: 30913233]

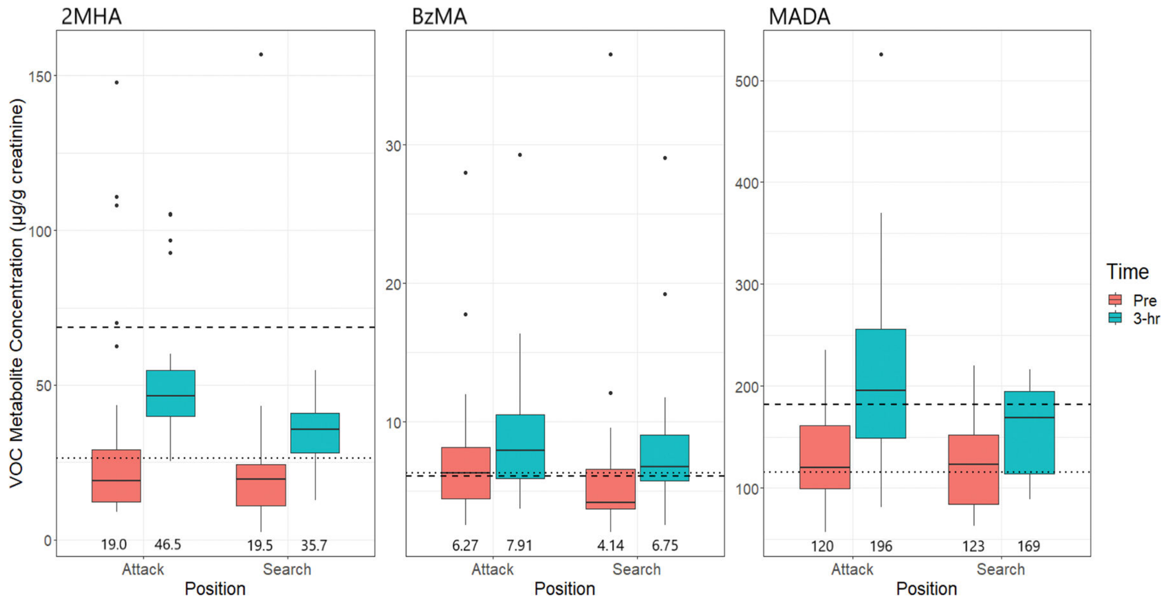

Figure 1.

Summary of urinary VOC metabolites (µg/g creatinine) with medians included at the bottom of each plot for the residential fire study participants stratified by position for analytes that increase significantly post-fire. The number of firefighters in each position (attack and search) is 24. Dashed and dotted lines represent VOC medians of smoking and non-smoking general population, respectively.

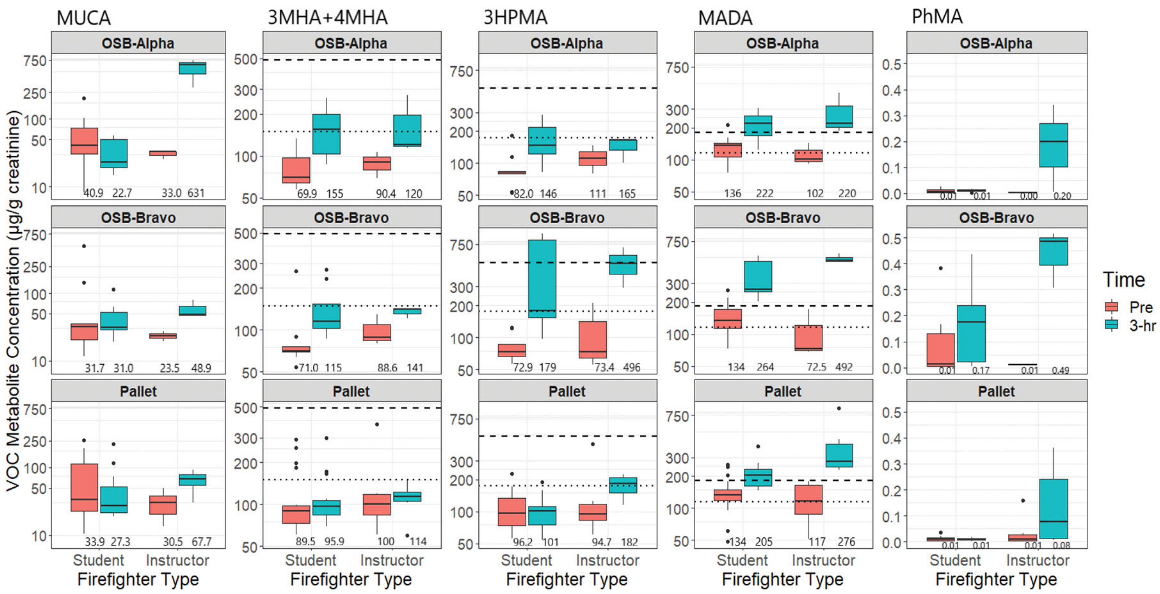

Figure 2.

Summary of urinary VOC metabolites (μg/g creatinine) with medians included at bottom of each plot for the training fire participants stratified by participant type and fuel type for the analytes that increase significantly post-fire. The number of firefighter students for OSB-Alpha, OSB-Bravo, and Pallet are 9, 9, and 18, respectively, and the number of instructors is 3, 3, and 6. Dashed and dotted lines represent VOC medians of smoking and non-smoking general population, respectively.

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Table 1.

Summary of the two studies where urine samples were collected before and after live-fire training and subsequently analyzed for VOC metabolites

	Residential fire study	Training fire study
Design	Repeated measures	Repeated measures
Fire structure and fuels	Fires ignited in two rooms of a 111 m^2 wood frame residential structure containing residential furnishings, including double bed with polyurethane foam topper, stuffed chair, wood side table and dresser, lamp, flat screen TV, and polyester carpet with recycled polyurethane foam padding oriented as in a residential bedroom common in the 21st century United States.	Training fires involved obscuring visibility by 1) Burning of **pallet and straw** in a ground-based rack inside single story concrete training building, 2) Burning of oriented strand board (**OSB**) attached to the training structure ceiling, along with pallet and straw in a ground-based rack in each of two rooms of a T-shaped metal shipping container. Two types of OSB were used denoted as Alpha and Bravo (see supplemental files for more details), 3) Generation of simulated smoke and electronic flame inside series of metal shipping containers.
Participants	12 firefighters per response team, 3 response teams, each team fought 4 fires (1 per day), firefighters assigned to new positions after two fires. Positions included: attack (2), search (2), outside vent (2), overhaul (4), incident command and pump operator (2). There were 41 total participants as five firefighters did not complete all 4 fires and were replaced.	24 firefighter students total. Six crews of 4 firefighter students. Each crew fought 1 training fire per day over 3 non-consecutive days. 10 instructors total (two groups of 5 instructors) who oversaw 3 training fires per day over 3 non-consecutive days.
Sampling	Spot urine collected pre-fire and 3-hr post fire.	For the firefighter students, spot urine collected pre-fire and 3-hr post fire. For the instructors, spot urine collected pre-fire and 3-hr post third fire (end of shift).
Total number of samples	Only urine samples collected from firefighters assigned to interior firefighting ("Attack" and "Search") were analyzed for VOC metabolites. 24 pre and 24 3-hr post fire urine samples were analyzed from both the attack and search firefighters.	Only urine samples collected during OSB and pallet and straw scenarios were analyzed for VOC metabolites. For students, 36 pre and 36 3-hr post fire urine samples were analyzed. For instructors,12 pre and 12 end-of-shift urine samples were analyzed.

Table 2.

VOC metabolites and associated parent compounds

Acronym	Analyte	Detection Limit, in µg/L	Parent Compound
3HPMA	N-Acetyl-S-(3-hydroxypropyl)-L-cysteine	13	Acrolein
MUCA	trans, trans-Muconic acid	9.81	Benzene
PhMA	N-Acetyl-S-(phenyl)-L-cysteine	0.6	Benzene
MADA	Mandelic acid	12	Styrene
BzMA	N-Acetyl-S-(benzyl)-L-cysteine	0.5	Toluene or benzyl alcohol
3MHA+4MHA	3-Methylhippuric acid + 4-Methylhippuric acid	8	Xylenes
2MHA	2-Methylhippuric acid	5	Xylenes
4HBeMA	N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine	0.6	1,3-Butadiene

Table 3.

VOC metabolite results (μg/g creatinine) for the residential fire participants (attack and search firefighters).

Analyte	Collection Period	N (N of non-detects)	Mean	Median	Min-Max	P-value[A]	General Population (Non-Smoker/ Smoker)[B]		Biological Exposure indices (BEI)[C]
							Median	95th Percentile	
3HPMA	Pre	48 (0)	207	182	68.1 – 739	0.871	175 / 508	835 / 2,579	Not Available
	3 hr	48 (0)	209	196	92.2 – 665				
MUCA	Pre	48 (5)	46.9	27.3	14.1 – 259	0.257	Not Available	Not Available	500
	3 hr	48 (10)	53.4	38.4	20.1 – 266				
PhMA	Pre	48 (39)	0.04	0.01	0.00 – 0.37	0.078	Not Available	Not Available	25
	3 hr	48 (38)	0.07	0.02	0.00 – 0.75				
MADA	Pre	48 (0)	129	122	56.5 – 235	**<0.001**	116 / 182	299 / 600	400,000
	3 hr	48 (0)	184	177	80.9 – 526				
BzMA	Pre	48 (0)	7.07	5.68	2.01 – 36.5	**<0.001**	6.32 / 6.06	38.9 / 33.1	Not Available
	3 hr	48 (0)	8.85	7.23	2.53 – 29.3				
3MHA+4MHA	Pre	48 (0)	145	84.7	23.4 – 1,550	0.498	149 / 488	872 / 2,026	1,500,000
	3 hr	48 (0)	158	134	46.1 – 1,130				
2MHA	Pre	48 (2)	29.1	19.2	2.42 – 157	**0.005**	26.4 / 68.5	141 / 354	1,500,000
	3 hr	48 (1)	44.0	40.4	12.7 – 105				
4HBeMA	Pre	48 (0)	5.41	5.32	1.77 – 10.7	0.136	4.02 / 15.5	14.9 / 87.9	Not Available
	3 hr	48 (3)	4.83	4.64	2.01 – 7.65				

A. Test of significant mean difference between pre and 3-hr post-fire concentrations.

B. National Health and Nutrition Examination Survey (NHANES) (2018). 2013–2014 data documentation, codebook, and frequencies. Volatile Organic Compounds & Metabolites - Urine (UVOC_H). Available at https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/UVOC_H.htm.

C. American Conference of Governmental Industrial Hygienists (ACGIH) (2021). "2021 TLVs and BEIs with 9th Edition Documentation". Cincinnati, OH: ACGIH.

Table 4.

VOC metabolite results (μg/g creatinine) for the training fire participants, stratified by participant type.

Analyte	Firefighter Type	Collection Period	N (N of non-detects)	Mean	Median	Min-Max	P-value	General Population[A] (Non-Smoker/ Smoker) Median	95th Percentile	Biological Exposure indices (BEI)[B]
3HPMA	Firefighter Student	Pre	36 (0)	172	146	92.7 – 403	**0.011** [C]	175 / 508	835 / 2,579	Not Available
		3 hr	36 (0)	342	211	96.3 – 1660				
	Instructor	Pre	12 (0)	231	168	97.7 – 764	0.052			
		3 hr	12 (0)	439	322	179 – 1230				
MUCA	Firefighter Student	Pre	36 (7)	74.0	34.0	8.03 – 499	**0.015** [D]	Not Available	Not Available	500
		3 hr	36 (11)	42.8	28.6	14.9 – 222				
	Instructor	Pre	12 (3)	28.7	27.4	13.6 – 49.9	**0.038** [C]			
		3 hr	12 (1)	186	74.2	29.9 – 750				
PhMA	Firefighter Student	Pre	36 (33)	0.03	0.01	0.00 – 0.38	0.121	Not Available	Not Available	25
		3 hr	36 (31)	0.05	0.01	0.00 – 0.44				
	Instructor	Pre	12 (11)	0.02	0.01	0.00 – 0.16	**0.016** [C]			
		3 hr	12 (4)	0.22	0.24	0.01 – 0.51				
MADA	Firefighter Student	Pre	35 (0)	141	134	48.7 – 259	**<0.001** [C]	116 / 182	299 / 600	400,000
		3 hr	36 (0)	244	227	124 – 549				
	Instructor	Pre	12 (0)	114	97.2	51.2 – 178	**<0.001** [C]			
		3 hr	12 (0)	393	356	188 – 873				
BzMA	Firefighter Student	Pre	36 (1)	9.02	5.85	1.26 – 36.3	0.634	6.32 / 6.06	38.9 / 33.1	Not Available
		3 hr	36 (0)	9.68	8.65	0.77 – 28.7				
	Instructor	Pre	12 (0)	5.47	5.01	2.38 – 10.3	0.080			
		3 hr	12 (0)	20.6	9.31	4.32 – 94.6				
3MHA+ 4MHA	Firefighter Student	Pre	36 (0)	100	77.4	54.0 – 293	**0.002** [C]	149 / 488	872 / 2,026	1,500,000
		3 hr	36 (0)	133	104	69.1 – 298				
	Instructor	Pre	12 (0)	117	89.5	60.7 – 377	0.619			

Analyte	Firefighter Type	Collection Period	N (N of non-detects)	Mean	Median	Min-Max	P-value	General Population[A] (Non-Smoker/ Smoker) Median	95th Percentile	Biological Exposure indices (BEI)[B]
		3 hr	12 (0)	131	121	59.4 – 271				
2MHA	Firefighter Student	Pre	36 (8)	21.2	19.0	5.50 – 69.9	0.106	26.4 / 68.5	141 / 354	1,500,000
		3 hr	36 (8)	26.7	18.9	9.33 – 92.7				
	Instructor	Pre	12 (0)	23.8	15.8	4.43 – 101	0.227			
		3 hr	12 (0)	33.7	31.9	14.7 – 63.5				
4HBeMA	Firefighter Student	Pre	36 (1)	6.65	6.24	1.52 – 13.7	**0.008** [D]	4.02 / 15.5	14.9 / 87.9	Not Available
		3 hr	36 (2)	5.25	4.40	1.61 – 13.5				
	Instructor	Pre	12 (0)	5.22	5.16	2.68 – 7.74	0.292			
		3 hr	12 (0)	4.62	4.66	1.81 – 7.35				

A. National Health and Nutrition Examination Survey (NHANES) (2018). 2013–2014 data documentation, codebook, and frequencies. Volatile Organic Compounds & Metabolites - Urine (UVOC_H). Available at https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/UVOC_H.htm.

B. American Conference of Governmental Industrial Hygienists (ACGIH) (2021). “2021 TLVs and BEIs with 9th Edition Documentation”. Cincinnati, OH: ACGIH.

C. 3-hr post-fire mean concentrations were significantly higher than pre-fire mean concentrations.

D. 3-hr post-fire mean concentrations were significantly lower than pre-fire mean concentrations.