Predictors of blood volatile organic compound levels in Gulf coast residents

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Abstract

To address concerns among Gulf Coast residents about ongoing exposures to volatile organic compounds, including benzene, toluene, ethylbenzene, o-xylene, and m-/p- xylene (BTEX), we characterized current blood levels and identified predictors of BTEX among Gulf state residents.

We collected questionnaire data on recent exposures and measured blood BTEX levels in a convenience sample of 718 Gulf residents. Because BTEX is rapidly cleared from the body, blood levels represent recent exposures in the past 24 hours. We compared participants' levels of blood BTEX to a nationally representative sample. Among nonsmokers we assessed predictors of blood

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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BTEX levels using linear regression, and predicted the risk of elevated BTEX levels using modified Poisson regression.

Blood BTEX levels in Gulf residents were similar to national levels. Among nonsmokers, sex and reporting recent smoky/chemical odors predicted blood BTEX. The change in log benzene was −0.26 (95% CI: −0.47, −0.04) and 0.72 (0.02, 1.42) for women and those who reported odors, respectively. Season, time spent away from home, and self-reported residential proximity to Superfund sites (within a half mile) were statistically associated with benzene only, however mean concentration was nearly an order of magnitude below that of cigarette smokers.

Among these Gulf residents, smoking was the primary contributor to blood BTEX levels, but other factors were also relevant.

Keywords

biomonitoring; volatile organic compounds; personal exposure

INTRODUCTION

The 2010 *Deepwater Horizon* (*DWH*) oil spill raised people's awareness of the potential for health effects associated with spill-related chemicals. In the years following the oil spill, residents of affected communities raised concerns about ongoing chemical exposures, particularly volatile organic compounds (VOCs), including benzene, toluene, ethylbenzene, o-xylene, and m-/p-xylene (BTEX) (1). In response to these concerns, as well as to case reports of elevated blood BTEX levels in individuals residing near the Gulf coast, we conducted a study designed to understand the distribution of these chemicals among Gulf residents. The BTEX chemicals are of concern because they have been associated with a range of adverse neurological, respiratory, and hematological health outcomes including cancer (1). Benzene, the most widely studied of these compounds, is a known human carcinogen (2, 3).

BTEX chemicals are ubiquitous in the environment and sources are both natural and anthropogenic (4). Human populations can be exposed to BTEX through both outdoor and indoor sources (5). In the general population, active and passive cigarette smoke are principal sources of BTEX exposure among smokers and nonsmokers, respectively (6, 7). Primary outdoor sources include industrial emissions (4, 8, 9), refueling of vehicles (6, 10), and exposure to vehicular exhaust (11). The presence of oil and gas development is pervasive in the Gulf region, known as the "energy coast", potentially creating frequent opportunities for continuing exposure to BTEX through industrial emissions, smaller oil spills, and related contamination events. At the same time, indoor air concentrations of BTEX have been reported to be higher than outdoor levels (12), with sources including tobacco smoke (45), off-gassing from attached structures with enclosed vehicles and fuel containers (8, 13), and from building materials, furniture, textiles, cleaning products, and paints (14). Cooking can also contribute to indoor levels of BTEX (14, 15). In the United States, some people may also be exposed to BTEX through drinking water (16). BTEX are found in petroleum products, such as gasoline, diesel, and lubricating and heating oil (17).

Half-lives of BTEX in blood are relatively short and determined by redistribution rates in the lungs (i.e., α-phase) and rates between the blood and tissues (e.g., β-phase). For example, the estimated half-life of benzene is minutes to hours (18) and that of toluene is up to 21 hours (19). Because of the short half-lives, biomonitoring of these chemicals captures only recent exposures. Likewise, BTEX degrades in the environment rapidly. The half-lives of BTEX ranges from three hours to a month in the atmosphere, soil, ground water, and surface water (20–23). These chemicals do no bioaccumulate significantly in aquatic organisms (20–23). Previous studies have described BTEX levels in general populations, but few studies have focused on residents of the Gulf states (6, 24, 25).

The heightened concern among Gulf coast residents about possible ongoing exposure to BTEX and associated health effects was hampering our ability to conduct *DWH*-related epidemiologic research in this community. Media reports described high levels of BTEX chemicals in blood taken from Gulf coast residents, and some potential study participants were reluctant to participate if they would not receive information about their own exposure levels. Therefore, we conducted this study, allowing us to address these persistent community concerns and to characterize current exposures to BTEX in this community. Although it is implausible that the *DWH* oil spill would be contributing to blood BTEX levels years later (because of rapid environmental degradation and metabolism in the body), the petrochemical industry is a potentially important source of continuing background exposure to these VOCs in Gulf coast communities. We compared blood measures of BTEX in Gulf coast residents to U.S. population levels and identified demographic, socioeconomic, behavioral, occupational, and residential factors associated with higher levels of BTEX to better understand exposures to these chemicals. Participants received written reports describing their blood levels relative to the general U.S. population, as well as educational information about interpreting individual VOC levels, and contact information if they had remaining concerns.

METHODS

Study Design and Participants

In combination with ongoing home visits for the Gulf Long-Term Follow-up Study (GuLF STUDY) we enrolled participants in a biomonitoring study to measure current blood VOC chemical levels. The GuLF STUDY is a prospective cohort of adults (ages 21 and older) who participated in oil spill response activities and others who received safety training, but were not hired following the *DWH* disaster. A detailed description of this study is available elsewhere (26). Among those who enrolled in the cohort, 11 193 participants who spoke English or Spanish and who lived in Florida, Alabama, Mississippi, Louisiana, or eastern Texas participated in a home visit exam. Between September 2012 and March 2013 (two to three years after the *DWH* oil spill), a sample of GuLF STUDY participants who had not yet completed a home exam were invited to participate in a biomonitoring study (BTEX Study) to address community concerns about exposure to VOCs. Participation in the BTEX Study involved providing an extra blood sample for measuring BTEX and other compounds and completing a questionnaire about usual and past 24 hour exposures. We initially oversampled nonsmokers and women, but because of timing of the parent study, we

ultimately invited all remaining home visit participants to participate. A total of 1 042 individuals who participated in the BTEX Study provided blood samples of sufficient quantity to measure BTEX levels (27–29); 849 of these individuals had a measurement for the tobacco smoking biomarker 2,5-dimethylfuran (2,5-DMF) as well as self-reported smoking information. These 849 participants were included in analyses comparing blood VOC levels between the BTEX Study and the National Health and Nutrition Examination Survey (NHANES) (30, 31).

For the remaining analyses, we further restricted to participants who had complete covariate information on all modeled predictors (n=718). We excluded participants who were missing measured values for all BTEX (n=1) or data on demographic factors and/or predictors (n=130). We performed sensitivity analyses to evaluate the impact of these restrictions on observed associations. Analytic sample sizes vary slightly across BTEX analyses due to compound-specific exclusions for quality control. A portion of ethylbenzene measurements were excluded due to analytical measurement interference, so the sample size for ethylbenzene analyses is reduced (n=528).

Participants provided written consent, and the Institutional Review Board of the National Institute of Environmental Health Sciences approved this study.

Exposure Monitoring Questionnaire

We collected demographic, socioeconomic, occupational, lifestyle, and health information during the GuLF STUDY enrollment and home visit interviews. BTEX Study participants also answered questions about potential contributors to blood BTEX levels, including residential building characteristics, self-reported proximity to industrial operations and waste sites (participants were asked to indicate whether they lived within a half mile of each of the following: major highways, a boatyard, docks, an oil refinery, a petroleum storage or transfer facility, a gas station, a factory, a power plant, a hazardous waste or Superfund site, and a landfill), personal chemical exposures, perceived air quality, drinking and bathing water source, smoking and tobacco use, and hobbies, including exposure opportunities in the past 24 hours (e.g. refueling vehicles or lawn equipment), using forms adapted from the Center for Disease Control and Prevention (CDC) NHANES 2007–2008 questionnaire (30) and US Environmental Protection Agency Detroit Exposure and Aerosol Research Study (DEARS) survey (32).

Blood collection and blood volatile organic compounds

Blood collection tubes containing potassium oxalate and sodium fluoride anticoagulant were used to collect 10 mL of blood for VOC measurement. Blood samples were collected using tubes and stoppers that had been pre-treated by the CDC laboratory to remove VOCs to minimize pre-collection contamination (33, 34). Samples were centrifuged and aliquoted into cryo-vials upon receipt and then stored at 2–6 °C for up to one week before being shipped in batches to the Division of Laboratory Sciences, National Center for Environmental Health, CDC in Atlanta, Georgia for analysis of VOCs. This laboratory conducts all NHANES VOC analyses. Analysis of VOCs followed the standard CDC procedures for NHANES samples, using equilibrium headspace solid-phase micro-

extraction with benchtop gas chromatography/mass spectrometry (27, 29), reducing potential bias in comparisons between measurements in the BTEX Study and in NHANES. 3 mL of blood was required per analysis and permitted simultaneous analysis of VOCs, including BTEX. If all or any single analyte failed to run or failed the sample and batch QC evaluation, there typically remained enough sample to repeat the analysis once more. In the case where there was no data available or no data that passed sample and batch QC analysis no result could be reported. Missing results and QC failures were on average 5.5 %, however ethylbenzene (27.3 %) was atypically high in this study because of coeluting interference.

We measured 2,5-dimethylfuran (2,5-DMF), a VOC used as a smoking biomarker with comparable sensitivity and specificity to serum cotinine (a well-validated nicotine biomarker) (35). Blood 2,5-DMF concentration of 0.014 ng/mL has been established as a threshold for distinguishing between current daily smokers (0.014 ng/mL) and nonsmokers or less-than-daily smokers (< 0.014 ng/mL) (35, 36), with the latter comprising infrequent smokers whose blood VOC levels have essentially returned to that of nonsmokers. We use this definition to identify smokers and nonsmokers throughout all analyses.

Statistical Analysis

We compared the distributions of blood VOC levels measured in the BTEX Study to those observed in NHANES participants ages 21 and older who had blood VOCs measured during the 2005–2006 and 2007–2008 NHANES cycles (N=4 442). Because all comparisons between NHANES and the BTEX Study were stratified by the 2,5-DMF threshold for smoking status (0.014 ng/mL), we restricted the BTEX Study sample to participants with measured blood 2,5-DMF (N=849). For comparisons to NHANES, we imputed blood VOC concentrations below the limit of detection (LOD) as the LOD divided by the square root of two (37), as is done in NHANES. For all other statistical analyses, we used all measured values, including the actual values below the LOD (38).

We compared the geometric means, 75th and 95th percentiles between BTEX Study and NHANES participants. We also calculated the proportion of BTEX Study participants with blood levels exceeding the NHANES 95th percentile. To account for possible differences between the population structures of the two cohorts, we standardized the NHANES sample to the joint age-sex distribution of the BTEX Study. We presented this standardization approach without applying NHANES sampling weights, but also conducted parallel analyses using NHANES sampling weights to verify that the weighting approach didn't influence results.

Because cigarette smoke is a well-documented major source of blood BTEX exposure in the general population (36), we restricted our analysis of factors that predict BTEX levels to participants with blood 2,5-DMF < 0.014 ng/mL (n=423).

BTEX concentrations were approximately log-normally distributed, so we used natural logarithmically-transformed concentrations in continuous analyses. We selected predictors *a priori* based on previous literature (4, 6, 8, 39–42), considering residential building characteristics, lifestyle and behaviors, recreational and occupational activities, and relevant recent exposures as candidate predictors. We used analysis of variance and t-tests to

prioritize candidates based on the strength and statistical significance of their unadjusted relationship with blood benzene. BTEX are correlated and share exposure sources, so we developed a single predictive model for benzene, and then applied it to toluene, ethylbenzene, and xylenes. We selected benzene because it exhibits the strongest evidence of health effects at environmental levels, as well as being the most widely represented in the exposure literature.

We implemented a predictive modeling approach aimed at maximizing the model adjusted R^2, and retained covariates with p-values < 0.10. We chose this approach because many sources of BTEX exposure were rare in this population. We maintained a statistical significance threshold of α=0.05, and report the change in log-BTEX concentration (β coefficient) attributed to each predictor, and its associated standard error and p-value.

In addition to evaluating predictors among previously reported BTEX associations, we evaluated exposure sources of concern to the community as well as demographic factors in relation to BTEX by adding them to the final hypothesized predictive model. Possible exposure sources of concern expressed by the community included work on the *DWH* oil spill response and cleanup (43–45), seafood consumption (44, 46, 47), and well water consumption (44). Race, income, age, body mass index, and state of residence were also added to the model to account for demographic and socioeconomic differences across communities potentially affected by the spill.

We also used multivariable regression to estimate prevalence ratios (PR) for a blood BTEX measurement in the highest quartile. Due to model convergence problems for the log-binomial model, all analyses were completed using a modified log-binomial approach with a Poisson distribution (48). The same parameters identified in the linear analysis were included in the modified Poisson model, and demographic factors and community concerns were then added to assess their contributions.

To identify a subgroup with no tobacco smoke-related BTEX exposure, we conducted sensitivity analyses restricted to participants with blood 2,5-DMF < 0.014 ng/mL and removing an additional 101 individuals who reported any active or passive tobacco smoke exposure (n=322). For comparison purposes, we also ran regression models among all eligible participants, regardless of smoking status (n=718). To account for exposure to cigarette smoke in these latter models with all participants, the binary indicator of blood 2,5-DMF (0.014 ng/mL vs. < 0.014 ng/mL) was included as a covariate (49). While continuous 2,5-DMF is a more suitable biomarker for adjustment among smokers, we elected to use the binary indicator due to its superior model fit among nonsmokers, our primary population of interest. All analyses were conducted in SAS 9.4 (Cary, NC, USA).

RESULTS

BTEX detection frequencies were consistently higher for smokers than for nonsmokers. The proportion of samples with blood BTEX levels above the limit of detection among nonsmokers ranged from 27% (for benzene) to 99% (for toluene), and among smokers ranged from 88% (for ethylbenzene) to 100% (for benzene, toluene, and m-/p-xylene) (Table

1). Blood BTEX levels for nonsmokers in both the BTEX Study and 2005–2008 NHANES were generally comparable (Table 1). The distributions of BTEX levels for smokers between the two studies were also similar. Results for these comparisons were unchanged in sensitivity analyses in which we applied NHANES sampling weights and other approaches to standardization. The distribution of BTEX levels for participants who were excluded due to missing covariate information (n=130) was similar to that of included participants (data not shown).

Compared to smokers, nonsmokers had a higher median income, were older, and had a higher proportion of white participants (Table 2). Blood BTEX levels were highly correlated between analyte pairs, especially among smokers. In the nonsmokers, Spearman correlation coefficients between benzene and toluene, ethylbenzene, and xylene ranged from 0.31–0.52 (mean=0.42). Participants who were excluded due to analytical interference with their ethylbenzene blood measurement are similar to participants included in the modeled sample, with respect to the demographic characteristics reported in Table 2.

Smoking strongly predicted blood BTEX levels (R^2 range: 0.21–0.65, data not shown). The predictive model for BTEX levels among nonsmokers (Table 3) included sex (women or men), time spent away from home (reporting at least 8 hours away in the past 24 hours), requiring support (reporting receiving financial or material support in the past year), self-reported residential proximity to hazardous waste sites (reporting living within a half mile of any Superfund or hazardous waste sites since 2012), season of blood collection (fall/winter or spring/summer), smoky/chemical smells (smelled smoke or any unusual chemical smells in or around the home in the past 24 hours), and recent home construction (reporting any new construction to the home in the past six months).

Among nonsmokers, sex was the most consistent predictor of BTEX levels in the fourth quartile in both the linear model and in the Poisson model (Tables 3 and 4, respectively), with higher blood BTEX levels among men than women. Similarly, reporting smoky and/or chemical smells around the home in the past 24 hours was consistently associated with increased blood BTEX (Table 3). The effect of season on blood levels was inconsistent. Having blood drawn in fall or winter (compared to spring or summer) was significantly associated with lower levels of benzene only (β, −0.60; 95% CI: −0.91, −0.29). Season effects were non-significant and varied in magnitude and direction for toluene, ethylbenzene, and xylene. Spending time away from home (at least eight hours in the previous 24) was weakly and negatively associated with all BTEX but the association was statistically significant for benzene only (β, −0.33; 95% CI: −0.52, −0.13). Requiring some type of financial or material support was weakly associated with higher blood levels of benzene only (β, 0.21; 95% CI: −0.01, 0.43). Reported home construction in the previous six months was non-significantly associated with higher benzene (β, 0.34; 95% CI: −0.04, 0.72), toluene (β, 0.13; 95% CI: −0.15, 0.42), and xylene (β, 0.04; 95% CI: −0.29, 0.36) levels. Conversely, the association was inverse for ethylbenzene (β, −0.21; 95% CI: −0.68, 0.26).

Self-reported living within a half mile of a Superfund or hazardous waste site since 2012 was the strongest predictor of blood benzene levels among nonsmokers (β, 0.86; 95% CI: 0.05, 1.67), although this association is based on six participants (Table 3). The association

for blood benzene in the top quartile among nonsmokers (n=4) was also significant, with those living near hazardous waste sites being nearly three times as likely to have elevated blood benzene, compared to those who did not report living near hazardous waste sites (Table 4). Furthermore, among *all* participants, including smokers (data not shown), self-reported living near a hazardous waste site was significantly associated with higher blood benzene levels (β=0.56; 95% CI: 0.07, 1.06). These associations are based on limited exposure, with only 6 nonsmokers and 7 smokers who report living within a half mile of a hazardous waste site. Blood BTEX levels varied independently of living within a half mile of petroleum refining operations, petrochemical manufacturing sites, and gas stations (data not shown). Similarly, living in or near US Census Bureau designated urban areas (50) was not associated with blood BTEX levels, nor was reported time spent in motor vehicles.

A number of factors obtained in the linear model (Table 3) were associated with having levels in the highest quartile (Table 4), but fewer results were statistically significant. Specifically, benzene blood levels in the top quartile were associated with required financial or material support (PR=1.4, 95% CI: 1.0, 2.0) and living near a hazardous waste site (PR=2.7, 95% CI: 1.6, 4.6). Blood benzene in the highest quartile was inversely associated with time away from home (PR=0.6, 95% CI: 0.4, 0.9) and fall/winter blood collection (PR=0.4, 95% CI: 0.3, 0.6). Smoky/chemicals smells predicted levels in the highest quartile for each of toluene, ethylbenzene, and xylenes (Table 4). Women were less likely to have blood BTEX levels in the highest quartile, but the association was only significant for toluene (PR=0.6, 95% CI: 0.4, 1.0) and xylenes (o-xylene, PR=0.5, 95% CI: 0.3, 0.9; m-/p-xylene, PR=0.6, 95% CI: 0.4, 0.9).

To examine community concerns about blood BTEX levels and exposure to the 2010 *DWH* disaster, we added seafood consumption, working on oil spill response or cleanup for at least one day, and consuming well water at home, as well as demographic factors, to the linear model. As shown in Table 5, none of these additional covariates were predictive nor did they improve model fit or explain additional variation in blood benzene levels. Results for other chemicals were similar, except for a suggestive inverse association between seafood consumption and toluene, ethylbenzene, and xylenes (Supplemental Table 1). Likewise, these factors were not associated with blood BTEX above the 75th percentile (Supplemental Table 2).

Predictors of blood BTEX levels among participants classified as nonsmokers were not affected by further excluding 101 participants who reported recent active or passive smoke exposure despite having 2,5-DMF below the smoking cutpoint. Results were also similar when we examined the entire study sample (including smokers and nonsmokers), and adjusted for 2,5-DMF blood concentration (data not shown).

When evaluating the impact of excluding participants with incomplete covariate information on associations with BTEX levels, we observed that parameter estimates obtained when these participants were included were not materially different from those presented in the main analyses, although precision was slightly improved with a larger sample (data not shown).

DISCUSSION

This study was conducted to address concerns among some Gulf state residents about potentially higher levels of exposure to BTEX. Newspaper and internet reports at the time suggested that some Gulf state residents had high levels of these chemicals in their blood and attributed these and related health concerns to the *DWH* oil spill. As expected, *DWH*-related exposure sources, including seafood, well water consumption, and prior work on oil spill response, did not predict blood BTEX levels two to three years after the spill, after taking into account current exposures, which is consistent with the short biological and environmental half-lives of BTEX, as well as with the absence of continued exposure to DWH-related chemical exposures.

We did, however, identify other predictors of BTEX exposure. As expected, smoking was highly associated with blood BTEX. Among nonsmokers, sex and smoky/chemical odors were associated with all BTEX, while time away from home, requiring financial support, residential proximity to hazardous waste sites, season of blood collection, and recent home construction were uniquely associated with benzene.

To our knowledge, only one other study has compared blood BTEX levels among Gulf state residents exposed to the *DWH* oil spill with levels in NHANES (51). Sammarco et al. (51) concluded that blood BTEX levels (except for o-xylene) in their study population were significantly higher than NHANES 95th percentiles. However, the study was smaller (69 people), lacked any information on smoking, and measured blood levels closer in time to the oil spill (5–19 months after the well was capped). In contrast, we found little difference in mean blood VOC levels between our sample and a nationally representative US sample.

Our preliminary analyses corroborated previous findings that smoking is the primary source of blood BTEX levels in the general population (49), which can make it difficult to discern other environmental sources (40).

Accurate assignment of tobacco smoke exposure is particularly important in this study given the strong association between smoking and blood BTEX levels (35, 36). Smoking status was determined based on the blood 2,5-DMF concentration. Blood 2,5-DMF has been previously validated against serum cotinine using NHANES data, and performs well as an indicator of daily tobacco smoke exposure (49). Although strongly correlated with self-reported smoke exposure, 2,5-DMF was an imperfect predictor of smoking, with 7.1 percent of self-reported smokers having 2,5-DMF below the cut-point. To adequately account for smoking, we completed sensitivity analyses excluding participants with any apparent cigarette smoke exposure, whether indicated by blood 2,5-DMF level or self-report of current smoking or recent passive exposure. Using this more sensitive definition of exposure to tobacco smoke, we excluded 101 additional participants, but observed comparable results to those generated using the biomarker-only definition of smoking.

Contrary to previous studies that have reported higher blood BTEX levels in women than in men (6), females had lower blood BTEX in our analysis. This difference may be explained by our unique study population of people who volunteered for disaster-related cleanup activities.

Time spent away from home was inversely associated with blood BTEX levels. One plausible explanation is that participants may be spending this time in areas with lower BTEX levels than their homes, such as outdoors (52) or in places of employment with higher air exchange rates or less environmental tobacco smoke.

Participants who reported receiving some type of financial or material support in the past year were more likely to have higher blood benzene levels, suggesting a possible association between economic vulnerability and benzene exposure. This association may reflect increased benzene exposure opportunities due to residential location or housing characteristics (53). It is unlikely that the effect of economic vulnerability is due to occupational or recreational exposures, as we observed no associations with blood BTEX for those exposure opportunities.

We also identified other exposure sources that were predictors of increased blood BTEX levels. Non-smoking individuals who reported living within a half mile of a Superfund or hazardous waste site had statistically higher benzene levels than those that did not, although this association is based on six nonsmokers and should therefore be viewed with caution. This association may be attributed to higher environmental levels of benzene frequently found near hazardous waste sites (54), including Superfund sites (55) and other industrial sources (20). We did not, however, find associations between BTEX and residential proximity (within a half mile) to petroleum refining operations, petrochemical manufacturing sites, or gas stations. All exposure metrics indicating proximity to possible sources of VOCs are based on self-report, and are therefore limited by participants' knowledge and definition of such locations in their communities, as well as their perception of distance surrounding their homes.

Seasonal variation in personal and ambient BTEX levels has been well documented, though patterns vary between regions (21–23, 56–58). We observed lower benzene levels in fall and winter than in spring and summer. The seasonal effect on ambient BTEX levels may be due to climate-driven changes in photochemical reactivity and volatilization by season, which in turn affect emissions rates and outdoor air concentrations (57). Personal BTEX levels likely vary seasonally due to region-specific practices for regulating home temperature, as well as varying home construction materials (56).

Smoky or chemical odors in or around the home in the 24 hours preceding blood collection were strongly associated with increasing blood BTEX levels. This is consistent with a previous study, which found that self-reported odor annoyance predicted ambient air BTEX concentrations (59). Because the associations in our study were based on only twelve participants reporting smoky/chemical smells, they should be interpreted with caution. Nonetheless, the associations with smoky or chemical odors were consistent in magnitude, statistically significant for all BTEX, and robust to all tobacco smoke-related exclusions in sensitivity analyses. Given the available data, we are unable to determine the source(s) of these odors, although limited evidence suggests that recent exposure to smoke from outdoor fires drives at least part of the association.

Off-gassing of home construction materials is a known source of indoor BTEX exposure (14, 60, 61). The observed association between reported home construction in the six months preceding blood collection and increasing blood benzene level is supported by this.

Previous studies have demonstrated modest associations between airborne and blood BTEX concentrations in the general population (6). Among nonsmokers, most BTEX is derived from fuel emissions (7, 62), which are present at higher concentrations in urban areas (63). We did not assess ambient airborne BTEX concentrations. We did, however, assess time spent in motor vehicles, as well as the US Census Bureau urban area designation (50) for the geocoded residence. We did not observe any associations between reported time in motor vehicles, or living in urban areas, and blood BTEX levels. Indoor air concentrations demonstrate stronger correlations with blood BTEX levels than do outdoor air concentrations (64). We did analyze detailed self-reported information characterizing the indoor air environment, including recent ventilation, cooking, use of chemicals and cleaning products, housing characteristics, and perceived indoor air quality. Blood BTEX levels varied independently of these factors.

Although regulatory exposure limits exist for airborne benzene (65, 66), there are no established toxicity levels or regulatory limits for benzene/BTEX measured in blood (20–23). However, Hays et al. report biological equivalence (BE) for benzene in blood from 0.04 to 1.29 µg/L (67) where health (i.e., hematopoietic in the case of benzene) is expected to be negatively impacted. Therefore, we compared blood BTEX levels between the BTEX Study and NHANES, defining elevated blood BTEX levels based on exposure distributions in the general population. Blood BTEX levels in our study sample were similar to those levels found in the general U.S. population.

Repeated measurements may provide a more reliable estimate of usual exposure than the single measurement used in our study, particularly because of the rapid metabolism and excretion of these chemicals. The assessment of recent sources of BTEX exposure is most relevant, given that blood BTEX half-lives reflect the half-lives of the VOC redistributing from the tissues (68, 69). We are only able to interpret the blood measures of an individual if collected within the exposure environment or if the individual is removed from the exposure source with respect to the past 24 hours. On the other hand, our study employed the use of detailed exposure questionnaires that allowed us to capture a variety of recent (24-hour) exposures using a previously validated questionnaire (32), and we were able to address ongoing community concerns and evaluate other potential BTEX chemical sources from the environment.

The primary strength of our study is the examination of predictors of internal burden of blood BTEX in individuals living in the Gulf states where concerns about ongoing oil spill related exposures have been reported. BTEX biomonitoring potentially yields a more relevant metric of personal exposure than estimates obtained through ambient monitoring because it provides an internal dose of the chemicals, capturing exposure from different routes (e.g., inhalation, adsorption, ingestion), and potentially different sources (70).

In addition, our comparison with NHANES BTEX blood levels was strengthened by the fact that the VOCs measured in both studies were analyzed in the same laboratory and using the same laboratory methods, reducing the potential for bias that might be introduced from use of differing methods. Also, the methods used in both populations allow for quantification of blood measures relevant to the typical exposure levels of the general population (27).

Since blood BTEX have limited elimination half-lives, our recent exposure questionnaires were well-suited for capturing the relevant and plausible timing of exposure sources. Additionally, our questionnaires required only a short recall time, minimizing risk of recall bias. Our study further employed the use of a previously validated biomarker for smoking (2,5-DMF) and did not solely rely on self-reported smoking status. Finally, our study was carried out in an understudied population that has been frequently exposed to multiple natural and man-made disasters.

Findings may provide some reassurance for oil spill response workers and community members concerned about lasting exposure to BTEX and related health effects. Although our study does not aim to address exposure levels during the *DWH* oil spill response and cleanup work (because blood measurements were obtained two to three years after the *DWH* oil spill), we demonstrated that current BTEX chemicals levels were generally similar in those living in the Gulf region compared to a nationally representative sample. Our study did not replicate case reports of elevated blood BTEX levels in Gulf communities. Universally, smoking was the strongest predictor of BTEX levels, though other community and personal factors did explain additional variability in BTEX.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Distribution of blood BTEX levels in the BTEX Study (N=848) and NHANES 2005–2008 (N=4 442)

Blood 2,5-dimethylfuran ≥ 0.014 ng/mL[1]

VOC (ng/mL)	BTEX Study (n=350)				NHANES (n=923)			
	N > LOD (%)	GM	P75	P95	N > LOD (%)	GM[2]	P75[2]	P95[2]
Benzene	347 (100)	0.20	0.33	0.61	895 (100)	0.18	0.30	0.56
Toluene	348 (100)	0.50	0.80	1.35	870 (100)	0.45	0.70	1.35
Ethylbenzene	270 (96)	0.09	0.13	0.21	871 (98)	0.08	0.12	0.20
o-Xylene	298 (88)	0.04	0.06	0.10	842 (94)	0.05	0.07	0.14
m-/p-Xylene	348 (100)	0.18	0.26	0.45	907 (100)	0.22	0.32	0.57

Blood 2,5-dimethylfuran < 0.014 ng/mL[1]

VOC (ng/mL)	BTEX Study (n=498)				NHANES (n=3 519)			
	N > LOD (%)	GM	P75	P95	N > LOD (%)	GM[2]	P75[2]	P95[2]
Benzene	133 (27)	—	0.03	0.08	923 (28)	—	0.03	0.06
Toluene	488 (99)	0.09	0.13	0.32	3,087 (95)	0.09	0.13	0.34
Ethylbenzene	131 (38)	—	0.04	0.12	1,565 (47)	—	0.04	0.08
o-Xylene	162 (34)	—	0.03	0.10	1,935 (56)	0.03	0.04	0.09
m-/p-Xylene	359 (72)	0.06	0.08	0.30	3,123 (91)	0.09	0.13	0.27

N > LOD, Number of participants with analyte level above limit of detection; GM, Geometric mean (not reported for analytes with detection rates below 50%); P75, 75th percentile; P95, 95th percentile. Analyte levels expressed as ng/mL.

BTEX Study: Benzene, n=836 (missing 13 samples); Toluene, n=844 (missing 5); Ethylbenzene, n=626 (missing 223); o-Xylene, n=818 (missing 31); m-/p-Xylene, n=846 (missing 3). The lower sample size for ethylbenzene results from a loss of samples due to analytical measurement interference.

Analytic limits of detection (BTEX Study and NHANES): Benzene, 0.024 ng/mL; Toluene, 0.025 ng/mL; Ethylbenzene, 0.024 ng/mL; o-Xylene, 0.024 ng/mL; m-/p-Xylene, 0.034 ng/mL.

[1] Blood 2,5-DMF concentration ≥ 0.014 ng/mL (≥ 14 ng/L) indicates current daily smokers, and blood 2,5-DMF concentration < 0.014 ng/mL (< 14 ng/L) indicates nonsmokers and "less-than-daily smokers"

[2] Standardized to joint age-sex distribution of BTEX Study population.

Table 2

Selected population characteristics of BTEX Study, by blood 2,5-dimethylfuran level (n=718)

Characteristic	Blood 2,5-DMF 14 ng/L (n=295) N (%)	Blood 2,5-DMF < 14 ng/L (n=423) N (%)
DWH response worker		
Yes	260 (88)	353 (83)
No	35 (12)	70 (17)
State		
Florida	65 (22)	112 (26)
Alabama	89 (30)	118 (28)
Mississippi	68 (23)	76 (18)
Louisiana	73 (25)	117 (28)
Age, years		
<30	61 (21)	70 (17)
30–50	160 (54)	205 (48)
>50	74 (25)	148 (35)
BMI, kg/m^2		
<25	99 (34)	80 (19)
25–30	80 (27)	126 (30)
>30	116 (39)	217 (51)
Sex		
Women	67 (23)	118 (28)
Men	228 (77)	305 (72)
Race		
Black	143 (47)	161 (38)
White	133 (45)	227 (54)
Other	19 (6)	35 (8)
Income, USD		
20,000	150 (51)	149 (35)
20,001–50,000	105 (36)	147 (35)
>50,000	40 (14)	127 (30)

2,5-DMF, blood 2,5-Dimethylfuran; *DWH* response worker, participated in at least one day of oil spill response or cleanup work; State, state of residence at time of blood collection; BMI, body mass index; Income, annual household income.

Table 3

Linear predictors of blood BTEX levels among participants classified as nonsmokers with blood 2,5-dimethylfuran < 0.014 ng/mL (n=423)

	Benzene (n=418)		Toluene (n=421)		Ethylbenzene (n=294)		o-Xylene (n=406)		m-/p-Xylene (n=422)	
Adj. R-squared	0.09		0.05		0.05		0.05		0.05	
Predictor	N	β (95% CI)	N	β (95% CI)	N	β (95% CI)	N	β (95% CI)	N	β (95% CI)
Sex										
Women	116	−0.26 (−0.47, −0.04)	118	−0.24 (−0.40, −0.08)	81	−0.32 (−0.58, −0.06)	113	−0.32 (−0.50, −0.14)	118	−0.37 (−0.56, −0.17)
Men	302	Ref	303	Ref	213	Ref	293	Ref	304	Ref
Time away from home										
8 hours	176	−0.33 (−0.52, −0.13)	177	−0.06 (−0.21, 0.08)	117	−0.01 (−0.25, 0.23)	170	−0.05 (−0.21, 0.12)	176	−0.06 (−0.24, 0.12)
< 8 hours	242	Ref	244	Ref	177	Ref	236	Ref	246	Ref
Required support										
Yes	110	0.21 (−0.01, 0.43)	111	−0.01 (−0.17, 0.15)	79	0.01 (−0.25, 0.28)	111	0.02 (−0.17, 0.20)	112	0.05 (−0.15, 0.25)
No	308	Ref	310	Ref	215	Ref	295	Ref	310	Ref
Lived near waste site										
Yes	6	0.86 (0.04, 1.68)	6	0.09 (−0.52, 0.71)	4	0.32 (−0.70, 1.34)	6	−0.13 (−0.82, 0.55)	6	−0.19 (−0.94, 0.56)
No	412	Ref	415	Ref	290	Ref	400	Ref	416	Ref
Season										
Fall/Winter	373	−0.60 (−0.91, −0.29)	374	−0.08 (−0.31, 0.15)	270	−0.29 (−0.72, 0.14)	359	−0.02 (−0.27, 0.24)	375	0.25 (−0.03, 0.53)
Spring/Summer	45	Ref	47	Ref	24	Ref	47	Ref	47	Ref
Smoky/chemical smells										
Yes	8	0.72 (0.02, 1.43)	8	1.16 (0.63, 1.69)	6	1.65 (0.82, 2.48)	8	1.19 (0.60, 1.78)	8	1.10 (0.46, 1.75)
No	410	Ref	413	Ref	288	Ref	398	Ref	414	Ref
Home construction										
Yes	29	0.34 (−0.04, 0.73)	29	0.13 (−0.15, 0.42)	20	−0.21 (−0.68, 0.26)	28	0.04 (−0.29, 0.36)	29	0.05 (−0.30, 0.40)
No	389	Ref	392	Ref	274	Ref	378	Ref	393	Ref

β, regression coefficient associated with change in log BTEX; 95% CI, 95% confidence interval for regression coefficient; units in log ng/mL. Time away from home, hours spent outside the home in the past 24 hours; Required support, reported receiving financial or material support in the past year; Lived near waste site, reported living within ½ mile of Superfund or hazardous waste sites since 2012;

Season, season of blood collection; Smoky/chemical smells, smelled smoke or any unusual chemical smells in or around the home in the past 24 hours; Home construction, reported any new construction to the home in the past six months.

Table 4

Predictors of blood BTEX levels in the highest quartile among participants with blood 2,5-dimethylfuran < 0.014 ng/mL (n=423)

Predictor	Benzene (n=104 in Q4)		Toluene (n=105 in Q4)		Ethylbenzene (n=74 in Q4)		o-Xylene (n=102 in Q4)		m-/p-Xylene (n=105 in Q4)	
	N	PR (95% CI)	N	PR (95% CI)	N	PR (95% CI)	N	PR (95% CI)	N	PR (95% CI)
Women	23	0.7 (0.5, 1.1)	21	0.6 (0.4, 1.0)	17	0.8 (0.5, 1.2)	18	0.5 (0.3, 0.9)	19	0.6 (0.4, 0.9)
8 hours away from home	34	0.6 (0.4, 0.9)	43	0.9 (0.7, 1.3)	30	1.0 (0.7, 1.5)	41	0.9 (0.7, 1.3)	42	0.9 (0.7, 1.3)
Required support	34	1.4 (1.0, 2.0)	30	1.1 (0.8, 1.6)	19	0.9 (0.6, 1.4)	27	1.0 (0.7, 1.4)	29	1.1 (0.7, 1.6)
Lived near waste site	4	2.7 (1.6, 4.6)	2	1.3 (0.4, 4.3)	1	1.2 (0.3, 5.9)	1	0.6 (0.1, 3.9)	2	1.3 (0.4, 4.8)
Fall/Winter blood collection	80	0.4 (0.3, 0.6)	91	0.8 (0.5, 1.3)	67	0.8 (0.4, 1.5)	87	0.7 (0.5, 1.1)	91	0.8 (0.5, 1.3)
Smoky/chemical smells	3	1.7 (0.8, 3.6)	4	2.1 (1.0, 4.3)	4	3.0 (1.5, 6.1)	4	2.1 (1.0, 4.5)	4	2.1 (1.0, 4.4)
Home construction	10	1.3 (0.8, 2.1)	7	0.9 (0.5, 1.8)	2	0.3 (0.1, 1.1)	5	0.6 (0.3, 1.4)	6	0.8 (0.4, 1.6)

Q4, Fourth (highest) quartile; N, number of participants with both the exposure and elevated compound (highest quartile); PR, prevalence ratio; 95% CI, 95% confidence interval.

8 hours away from home, reported time away from home in the past 24 hours; Required support, reported receiving financial or material support in past year; Lived near waste site, reported living within ½ mile of Superfund or hazardous waste sites since 2012; Smoky/chemical smells, smelled smoke or any unusual chemical smells in or around the home in the past 24 hours; Home construction, reported any new construction to the home in the past six months

Table 5

Community concerns and linear predictors of blood benzene level among participants with blood 2,5-dimethylfuran < 0.014 ngm/L (n=418)

Predictor		N	β (95% CI)	p-value
Sex	Women	116	−0.27 (−0.49, −0.05)	0.02
	Men	302	Ref	
Time away from home	8 hours	176	−0.33 (−0.53, −0.13)	0.001
	< 8 hours	242	Ref	
Required support	Yes	110	0.19 (−0.04, 0.42)	0.10
	No	308	Ref	
Lived near waste site	Yes	6	0.75 (−0.09, 1.58)	0.08
	No	412	Ref	
Season	Fall/Winter	373	−0.54 (−0.86, −0.21)	0.001
	Spring/Summer	45	Ref	
Smoky/chemical smells	Yes	8	0.64 (−0.08, 1.35)	0.08
	No	410	Ref	
Home construction	Yes	29	0.39 (0.001, 0.78)	0.05
	No	389	Ref	
DWH response worker	Yes	348	−0.12 (−0.38, 0.15)	0.40
	No	70	Ref	
Seafood	Yes	52	−0.17 (−0.47, 0.13)	0.26
	No	366	Ref	
Well water	Yes	21	−0.09 (−0.55, 0.36)	0.69
	No	397	Ref	
State	Florida	111	Ref	
	Alabama	116	0.10 (−0.18, 0.37)	0.49
	Mississippi	75	−0.01 (−0.31, 0.30)	0.96
	Louisiana	116	0.20 (−0.08, 0.48)	0.15
Age, years	<30	69	Ref	
	30–50	204	0.08 (−0.21, 0.37)	0.59
	>50	145	0.10 (−0.21, 0.42)	0.51
BMI, kg/m^2	<25	79	Ref	
	25–30	123	−0.06 (−0.36, 0.24)	0.70
	>30	216	−0.04 (−0.31, 0.23)	0.77
Race	White	222	Ref	
	Black	161	0.05 (−0.19, 0.30)	0.66
	Other	35	0.34 (−0.03, 0.71)	0.07
Income, USD	20,000	148	0.11 (−0.18, 0.40)	0.47
	20,001–50,000	146	−0.04 (−0.30, 0.22)	0.75
	> 50,000	124	Ref	

Adjusted R-squared=0.08; β, regression coefficient associated with change in log benzene; 95% CI, 95% confidence interval for regression coefficient; units in log ng/mL.

Time away from home, hours spent outside the home in the past 24 hours; Required support, reported receiving financial or material support in the past year; Lived near waste site, reported living within ½ mile of Superfund or hazardous waste sites since 2012; Season, season of blood collection; Smoky/chemical smells, smelled smoke or any unusual chemical smells in or around the home in the past 24 hours; Home construction, reported any new construction to the home in the past six months; DWH response worker, participated in at least one day of oil spill response or cleanup work; Seafood, reported consumption of seafood in the past 24 hours; Well water, consumes well water at home; State, state of residence at time of blood collection; BMI, body mass index; Income, annual household income.