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# Effects of profession on urinary PAH metabolite levels in the US population

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## Abstract

*Purpose* Although exposure to polycyclic aromatic hydrocarbons (PAHs) is common in both environmental and occupational settings, few studies have compared PAH exposure among people with different professions. The purpose of this study was to investigate the variations in recent PAH exposure among different occupational groups over time using national representative samples.

*Method* The study population consisted of 4162 participants from the 2001 to 2008 National Health and Nutrition Examination Survey, who had both urinary PAH metabolites and occupational information. Four corresponding monohydroxy-PAH urine metabolites: naphthalene (NAP), fluorene (FLUO), phenanthrene (PHEN), and pyrene (PYR) among seven broad occupational groups were analyzed using weighted linear regression models, adjusting for creatinine levels, sociodemographic factors, smoking status, and sampling season.

*Results* The overall geometric mean concentrations of NAP, FLUO, PHEN, and PYR were 6927, 477, 335, and 87 ng/L, respectively. All four PAH metabolites were elevated in the "extractive, construction, and repair (ECR)" group, with 21–42 % higher concentrations than those in the reference group of "management." Similar trends were seen in the "operators, fabricators, and laborers (OFL)" group for FLUO, PHEN, and PYR. In addition, both "service" and "support" groups had elevated FLUO. Significant ($p < 0.001$) upward temporal trends were seen in NAP and PYR, with an approximately 6–17 % annual increase, and FLUO and PHEN remained relatively stable. Race and socioeconomic status show independent effects on PAH exposure.

*Conclusions* Heterogeneous distributions of urinary PAH metabolites among people with different job categories exist at the population level. The upward temporal trends in NAP and PYR warrant reduction in PAH exposure, especially among those with OFL and ECR occupations.

**Keywords** PAHs · NHANES · Occupation · Naphthalene · Pyrene

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## Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a complex mixture of compounds formed during incomplete combustion processes and are ubiquitous in the environment (ATSDR 1995). Some PAH compounds, such as benzo[a]pyrene and benz[a]anthracene, have been identified as probable human carcinogens (ATSDR 1995; US EPA 1999) and, in particular, are associated with respiratory tract and bladder cancers (Rota et al. 2014). PAH exposures are also linked to other adverse health effects ranging from cardiovascular diseases (Clark et al. 2012; Xu et al. 2010), birth defects (Langlois et al. 2012), impaired early childhood development (Perera et al. 2006; 2011; 2012), childhood obesity (Jung et al. 2014b; Rundle et al. 2012; Scinicariello and Buser 2014), to asthma and respiratory

symptoms (Jung et al. 2012; Miller et al. 2004; Rosa et al. 2011). In the general environment, major sources of PAHs include tobacco smoking (Scherer et al. 2000), ambient and indoor air pollution generated from traffic, cooking, environmental tobacco smoke (ETS), and space heating (Bostrom et al. 2002; Jung et al. 2010; Naumova et al. 2002), as well as food with high PAH contents such as grilled and smoked meat (Alomirah et al. 2011). The general routes of PAH exposure are through inhalation, ingestion, and dermal contact in multiple environmental media including air, water, food, and soil.

Occupational exposure is a significant contributor to the total PAH exposure in subpopulations (Hansen et al. 2008; Kim et al. 2013; Rota et al. 2014). Inhalation is the main route of occupational exposure to PAHs in most industries; however, some studies have shown that dermal uptake can also be a main exposure route of PAH at workplaces (McClean et al. 2004; Van Rooij et al. 1993). Studies have documented airborne PAH concentrations at the $\mu g/m^3$ levels in certain job sectors, such as aluminum production, coal gasification, coke production, iron and steel foundries, and transport-related industries (Boffetta et al. 1997). Occupational Safety and Health Administration (OSHA) set a permissible exposure limit (PEL) of 0.2 mg/m$^3$ for PAH (as in coal tar pitch volatiles) in workplace. In contrast, typical ambient and residential air concentrations of PAHs are at the ng/m$^3$ levels in the USA (Jung et al. 2014a; Naumova et al. 2002). Occupational exposure to PAHs has been recognized as a high health risk factor, with strong evidence of genotoxicity due to PAH-related exposure associated with coal gasification, coke production, coal tar distillation, paving and roofing, aluminum production, and chimney sweeping occupations (Baan et al. 2009).

Following exposure, PAHs undergo several biotransformation phases inside the human body involving formation of hydroxylated compounds by the hepatic cytochrome P450 monooxygenases (ATSDR 1995). Metabolites of parent PAH compounds smaller than pyrene are usually excreted from urine in the form of monohydroxy-PAHs (OH-PAHs), which give rise to the use of OH-PAHs as effective biomarkers of PAH exposure (Dor et al. 1999; Li et al. 2008). Pyrene is a major constituent of PAHs, and its sole metabolite, 1-hydroxypyrene, has been the most commonly used biomarker of PAH exposure in both environmental and occupational studies (ATSDR 1995; Li et al. 2008). Due to the relatively short half-lives of OH-PAHs, which are on the order of hours to a couple of days (Li et al. 2008, 2012), urinary OH-PAHs are especially useful surrogates for assessing recent PAH exposures.

Multiple factors affect the concentrations of urinary OH-PAHs, including occupations, personal behavior, cooking culture, and demographic profiles (Hansen et al. 2008; Li et al. 2008). Several studies have evaluated multiple

contributors to PAHs in occupational populations and the public (Campo et al. 2014; Scherer et al. 2000). However, previous research was unable to assess the significance of multiple sources in a systematic way, limited by sample size, job information, and demographic factors surveyed. In particular, no study has examined how PAH exposure differs across occupational groups over time. The objective of this study was to investigate the influences of occupation on the national reference PAH exposure over time in the general population. To this end, we investigated the variations in OH-PAHs by occupational groups in a large representative US general population sample from the National Health and Nutrition Examination Survey (NHANES) during the period of 2001–2008.

## Materials and methods

### Data sources

The NHANES is a population-based cross-sectional survey undertaken by the US National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) to assess a variety of health issues and nutritional status of the US civilian population. Briefly, civilians, non-institutionalized persons in the USA aged 2 months or older, were selected through a stratified, multistage, probability-cluster design. The continuous NHANES has a 2-year survey cycle with approximately 5,000 persons enrolled per year since 1999. Participants complete detailed questionnaires, receive physical examinations, and provide biological specimens such as urine and blood. These survey components are administered in homes and in mobile examination centers. The NHANES protocol was developed and reviewed in compliance with the policies for the protection of human research subjects developed by the US Department of Health and Human Services and was described in detail by the CDC (Zipf et al. 2013).

Four cross-sectional cycles (2001–2002, 2003–2004, 2005–2006, 2007–2008) were used and combined using NCHS recommended methods (NCHS 2006, 2013). Of the initial 41,658 participants, those who lacked information on PAH urine metabolite concentrations ($n = 9224$), occupational questionnaire data ($n = 6246$), or both ($n = 22,026$) were excluded. The final population consisted of 4162 participants who had both urinary PAH measurements and occupation information.

### Urinary PAH metabolites

Concentrations of OH-PAH in spot urine samples were used as an indicator of participants' recent PAH exposure. Urine samples were typically collected during the

appointments in the mobile examination centers, which was open 5 days a week and operated on a rotating schedule to accommodate a variety of appointments among participants, who were randomly assigned a morning appointment or an afternoon or evening appointment (Zipf et al. 2013). Laboratory analysis of urine metabolites of PAHs involved enzymatic deconjugation, solid-phase extraction, and derivatization, and quantification using capillary gas chromatography combined with high-resolution mass spectrometry (GC/HRMS) coupled with isotope dilution with $^{13}$C-labeled internal standards (Li et al. 2008; Romanoff et al. 2006). Measurements below the detection limits (DLs) were replaced with $DL/\sqrt{2}$. Urine creatinine was measured by colorimetric determination on a Beckman Synchron CX3 clinical analyzer (Beckman Instruments Inc., Brea, CA).

For this study, we focused on four OH-PAH mixtures grouped according to their parent compounds: metabolites of naphthalene [NAP, sum of 1-hydroxynaphthalene and 2-hydroxynaphthalene], fluorene [FLUO, $\sum$(3-hydroxyfluorene, 2-hydroxyfluorene)], phenanthrene [PHEN, $\sum$(3-hydroxyphenanthrene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene)], and pyrene [PYR, 1-hydroxypyrene]. The eight individual species were the major metabolites with adequate detection limits (DLs between 2.0 and 5.9 ng/L; >95 % above DLs) and were reported in all four survey cycles included in this study. Their parent compounds are small PAHs with 2–4 aromatic rings and are mainly excreted in urine.

## Occupational groups

Information about the participants' current occupation was obtained from the occupational questionnaire, which was administered to participants older than 16 years of age ($n = 206$ for those aged between 16 and 17 years old, ~5 % of the total study population). The current job types were coded by trained interviewers using the US Census Bureau's Census Indexes of Industrial and Occupational Classification Source Codes. The 1999 and 2000 versions of the US Census Bureau occupational data coding systems were used for the 2001–2004 and 2005–2008 survey periods, respectively. The final publically available NHANES occupational variable contains 41 and 22 categories for 2001–2004 and 2005–2008, respectively. While the classifications were different between the two periods, there were also large overlaps, making it possible to combine these occupational categories into one comparable system. We collapsed these categories into seven broad occupation groups (supplementary material, Table S1): operators, fabricators, and labors (OFL); extractive, construction, and repair occupations (ECR); farming, forestry, and fishing (agriculture); service; technical, sales, and administrative

support (support); professional specialty (professional); and management.

## Other covariates

Variations in OH-PAHs were also investigated with regard to the following covariates: sex, age, race/ethnicity, education, poverty income ratio (PIR), body mass index (BMI), smoking status, alcohol use, and sampling season. Race/ethnicity included two categories: non-Hispanic white and others, which include non-Hispanic black, Mexican–American, other Hispanic, as well as other races and multiracial participants. Education was grouped into three categories: less than, equal to, and greater than high school level, where high school was defined as having 12 years of primary and secondary school. PIR in NHANES was calculated by dividing family income by the poverty level issued by the Department of Health and Human Services according to family size, the appropriate year, and state. In this study, PIR was dichotomized by a cutoff of 1. Dichotomized alcohol use was based on positive answers to the question, "Have you had at least 12 alcohol drinks/1 year?" Dichotomized smoking status was based on positive answers to the question, "Have you smoked at least 100 cigarettes in your entire life?" While NHANES also assessed ETS exposure (e.g., secondhand smoke) through household smoker questionnaires, we did not find overlaps between OH-PAHs and ETS exposure data in the study population. Alternatively, serum cotinine, a major metabolite of nicotine and a biomarker for both active and passive smoking, was included, which was available for a subset of the study population ($n = 3009$). Cotinine in serum was measured by an isotope dilution high-performance liquid chromatography/atmospheric pressure chemical ionization tandem mass spectrometry (Bernert et al. 1997). Sampling season is a 2-level variable indicating whether the examination was performed from November 1 through April 30 or from May 1 through October 31.

## Statistical analysis

The main models used to investigate the relationships between OH-PAHs and occupations were ordinary least squares regressions (OLS), with "management" as the reference group. PAH concentrations, urine creatinine, BMI, serum cotinine, and age were treated as continuous variables, and all but age were natural log-transformed due to their skewed-to-right probability distributions. To account for variation in dilution in spot urinary samples, creatinine was treated as an independent predictor in all the regression models as recommended by others (Barr et al. 2005; Ikeda et al. 2003; Scinicariello and Buser 2014). As creatinine was the most intense covariate of urinary PAHs (See

Results), volume-based PAH concentrations (in ng/L) were presented as creatinine-based concentrations (ng/g Creatinine). To account for the complex sampling design, sampling weights were applied according to NHANES guidelines (NCHS 2013). For example, because urinary PAHs were measured in a one-third subsample, special sample weights were used to analyze these data. Weighted summary statistics were generated using *proc surveymeans* and *proc surveyfreq* procedures for continuous (e.g., PAH concentrations) and categorical (e.g., occupational types) variables, respectively. Relationships between occupations and the covariates such as survey cycles, sex, and age were investigated using weighted logistic regressions (*proc surveylogistic*). Relationships between PAHs and occupations with and without adjusting for covariates were investigated using weighted linear regressions (*proc surveyreg*). The fully adjusted model can be simplified as: log(OH-PAH) = *f*(occupational group, sampling period, sex, race, education, PIR, smoking, sampling season, age, log(BMI), log(creatinine)).

In addition, quantile regressions were used to examine the relative influences of occupational groups on OH-PAHs at 10, 25, 50, 75, and 90th quantiles. Quantile regression has the advantage of modeling the occupation–PAH associations without assuming equal effects of occupational groups among different percentiles of OH-PAH levels. The regression coefficients (betas) from the quantile regression were compared with the regression coefficient (beta) from the OLS. While sample weights were used in the quantile regression, the current *proc quantreg* procedure does not take into account the NHANES complex survey designs.

Statistical analyses were performed using SAS software (version 9.3, Cary, NC). Both ordinary least square regression and quantile regression models were adjusted for age, sex, race, education, PIR, smoking, sampling season, BMI, and creatinine in the fully adjusted models. Further adjustment for alcohol (data not shown) did not materially affect the estimates.

## Results

### Study population characteristics

The study population (*n* = 4162) from NHANES 2001–2008 (Table 1) had a mean age of 40.1 years (range = 16–83 years), and 54 % of them were male. Non-Hispanic whites accounted for 71 % of the total study population. A majority (91 %) of the participants had family income level above the poverty threshold (PIR > 1), and 63 % of the participants had above high school educations. Smokers accounted for 46 % of the participants, and their geometric mean serum cotinine level was 5.9 ng/mL with

a 95 % confidence interval (95 % CI) of (3.7, 9.4) ng/mL. Approximately 61 % of the sampling was conducted during the warm season from May 1 through October 31.

The sociodemographic profiles differ considerably across the seven occupations (Table 2). Compared to the reference group of "management" (60 %), males dominated the "OFL" (80 %) and "ECR" (98 %) occupations, while the opposite was true for the "professional specialty" (47 %), "support" (36 %), and "service" (34 %) groups. The percentages of participants with below high school education levels were low in the "professional specialty" (2 %) and "management" groups (5 %), while were higher in the other occupations (ranged = 12–31 %). Compared to the "management" group (84 %), there were fewer whites in the remaining occupation groups (range = 61–78 %). Cotinine levels were similar among the "management," "support," "service," and "agricultural" occupational groups, with the geometrical means ranging from 2.8 to 8.2 ng/mL among smokers and from 0.03 to 0.08 ng/mL among non-smokers. The "professional" smokers group had significantly lower cotinine level (0.6 and 0.04 ng/mL for smokers and non-smokers, respectively) than the "management" group, while significantly higher cotinine concentrations were found in both "OFL" (23.2 and 0.15 ng/mL for smokers and non-smokers, respectively) and "ECR" (16.8 and 0.34 ng/mL for smokers and non-smokers, respectively) regardless of the smoking status. Consistent with the serum cotinine trends, similar patterns were seen in the self-reported smoking status.

### Distributions of urinary PAH metabolite concentrations

The overall geometric mean concentrations (95 % CI) of NAP, FLUO, PHEN, and PYR were 6927 (6396, 7502), 477 (445, 512), 335 (319, 352), and 87 (82, 92) ng/L, respectively (Table S2). If adjusted by creatinine, these concentrations were 6389 (5948, 6863), 441 (415, 469), 309 (297, 322), and 80 (76, 84) ng/g creatinine for NAP, FLUO, PHEN, and PYR, respectively, or 3.32 (3.09, 3.57), 0.23 (0.22, 0.24), 0.16 (0.15, 0.17), and 0.042 (0.040, 0.044) μmol/mol creatinine based on the conversion by Hansen et al. (2008). Concentrations of OH-PAHs varied during the 8 years (Fig. 1). Compared to 2001, the geometric mean concentrations of NAP and PYR in 2008 increased by 60 % from 4784 to 7651 ng/g creatinine (or by 50 % from 5377 to 8075 ng/L) and by 161 %, from 45 to 117 ng/g creatinine (or by 146 % from 51 to 124 ng/L), respectively. There was a statistically significant (*p* < 0.001; data not shown) upward trend for both NAP and PYR from 2001 to 2008, with the regression coefficients ranged from 0.27 to 0.46 and from 0.59 to 0.95 for NAP and PYR, respectively. These changes were equivalent to an average of 11 and 29 % increase per survey cycle, or an average of 6 and

**Table 1** Characteristics of the study population (NHANES 2001–2008)

| Characteristics | Percent (%) | Standard error (SE, %) | | n |
|---|---|---|---|---|
| Sex | | | | |
| M | 54 | 1.0 | | 2228 |
| F | 46 | 1.0 | | 1934 |
| Race/ethnicity | | | | |
| White | 71 | 1.6 | | 1965 |
| Others | 29 | 1.6 | | 2197 |
| Education | | | | |
| <High school (HS) | 13 | 0.8 | | 764 |
| =HS | 24 | 1.2 | | 871 |
| >HS | 63 | 1.4 | | 1997 |
| Poverty income ratio (PIR) | | | | |
| ≤1 | 9 | 0.6 | | 547 |
| >1 | 91 | 0.6 | | 3369 |
| Smoking | | | | |
| Yes | 46 | 1.1 | | 1633 |
| No | 54 | 1.1 | | 1998 |
| Drinking | | | | |
| Yes | 79 | 1.1 | | 2546 |
| No | 21 | 1.1 | | 814 |
| Sampling season | | | | |
| November–April | 39 | 3.0 | | 1926 |
| May–October | 61 | 3.0 | | 2236 |
| | Mean | (95 % CI) | | N |
| Age (years) | 40.1 | (39.7, 40.6) | | 4162 |
| Body mass index (BMI, kg/m$^2$) | 27.5 | (27.3, 27.8) | | 4120 |
| Cotinine (ng/mL)—all | 0.6 | (0.5, 0.8) | | 3009 |
| Cotinine (ng/mL)—smoking: no | 0.08 | (0.06, 0.09) | | 1458 |
| Cotinine (ng/mL)—smoking: yes | 5.9 | (3.7, 9.4) | | 1201 |

17 % annual increase for NAP and PYR, respectively. No significant time trend was found for FLUO and PHEN.

Concentrations of OH-PAHs also varied among the seven occupational groups (Fig. 2). The "ECR" group had the highest geometric mean concentrations for all four OH-PAH mixtures, followed by "OFL." These two occupational groups also had statistically significant ($p < 0.01$; data not shown) higher concentrations than the reference group of "management" for all four OH-PAH mixtures, with regression coefficients ranging from 0.23 to 0.56 for "ECR," and from 0.17 to 0.51 for "OFL." These changes were equivalent to an average of 53 and 43 % increases in the geometric mean concentrations for "ECR" and "OFL," respectively.

Similar temporal and occupational trends were found when both survey periods and occupational groups were simultaneously considered (Fig. 3) and included in the regression model (data not shown). Concentrations of the four PAH metabolites also showed statistically significant differences ($p < 0.05$) between different strata of the covariates while adjusting for creatinine levels (Table S2).

## Associations between occupational types and urinary PAH metabolite concentrations

The influence of occupational types on PAH urine metabolite concentrations was further explored in multiple regressions adjusting for sampling periods and other covariates. In the fully adjusted models (Table 3), "ECR" continued to be the occupation group with elevated concentrations for all four OH-PAH mixtures, with approximately 21–42 % increases in the geometric mean concentrations than the reference group of "management." In addition, "OFL" group had elevated (17–46 % increases) concentrations of FLUO, PHEN, and PYR. Compared to "management," both "service" and "support" groups had approximately 15–16 % increase in FLUO. The remaining occupations had similar PAH levels as those in the reference group.

**Table 2** Characteristics of study population by seven occupational groups

| | Management | Professional | Support | Service | Agriculture | ECR | OFL |
|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | |
| M (%) | 60 | 47 | 36 | 34 | 74[+] | 98 | 80 |
| SE (n) | 3 (222) | 2 (273) | 2 (387) | 2 (325) | 8 (67) | 1 (453) | 2 (501) |
| **Race/ethnicity** | | | | | | | |
| White (%) | 84 | 78 | 70 | 66 | 65 | 72 | 61 |
| SE (n) | 2 (250) | 2 (358) | 2 (497) | 3 (377) | 7 (31) | 3 (222) | 3 (230) |
| **Education** | | | | | | | |
| <HS (%) | 5 | 2 | 12 | 14 | 31 | 22 | 27 |
| SE (n) | 1 (28) | 1 (15) | 1 (162) | 1 (170) | 5 (38) | 2 (133) | 2 (218) |
| =HS (%) | 13 | 6 | 25 | 26 | 18[+] | 38 | 42 |
| SE (n) | 2 (46) | 1 (37) | 2 (221) | 2 (195) | 6 (12) | 3 (153) | 3 (207) |
| **Poverty income ratio** | | | | | | | |
| ≤1 (%) | 2 | 3[+] | 10 | 10 | 20 | 10 | 15 |
| SE (n) | 1 (13) | 1 (25) | 1 (170) | 1 (126) | 5 (20) | 1 (72) | 2 (121) |
| **Smoking** | | | | | | | |
| Yes (%) | 45 | 35 | 42[+] | 47[+] | 50[+] | 63 | 55 |
| SE (N) | 3 (162) | 2 (191) | 2 (358) | 2 (318) | 7 (36) | 3 (274) | 3 (294) |
| **Drinking** | | | | | | | |
| Yes (%) | 88 | 79 | 71 | 74 | 76[+] | 89[+] | 80 |
| SE (n) | 2 (287) | 2 (421) | 2 (544) | 3 (470) | 8 (52) | 2 (353) | 2 (419) |
| **Age (years)** | | | | | | | |
| Mean (n) | 43.9 (375) | 42.0 (598) | 38.7 (1080) | 38.9 (922) | 41.0[+] (82) | 38.2 (466) | 40.3 (639) |
| (95 % CI) | (42.8–45.1) | (40.8–43.2) | (37.7–39.7) | (37.4–40.4) | (37.3–44.7) | (36.8–39.5) | (39.2–41.5) |
| **BMI (kg/m$^2$)** | | | | | | | |
| Mean (n) | 28.0 (369) | 27.1[+] (595) | 27.3[+] (1073) | 27.6[+] (912) | 27.9[+] (80) | 27.5[+] (457) | 28.2[+] (634) |
| (95 % CI) | (27.3–28.7) | (26.6–27.7) | (26.8–27.8) | (27.0–28.2) | (26.3–29.6) | (26.8–28.1) | (27.7–28.7) |
| **Cotinine all (ng/mL)** | | | | | | | |
| Mean (n) | 0.4 (267) | 0.1 (442) | 0.5[+] (758) | 0.6[+] (691) | 0.4[+] (44) | 3.9 (335) | 2.6 (472) |
| (95 % CI) | (0.2–0.7) | (0.1–0.2) | (0.4–0.7) | (0.4–0.8) | (0.1–1.8) | (1.9–7.9) | (1.5–4.4) |
| **Smoking: yes (ng/mL)** | | | | | | | |
| Mean (n) | 2.8 (122) | 0.6 (146) | 6.8[+] (257) | 5.4[+] (238) | 8.2[+] (19) | 16.8 (195) | 23.2 (224) |
| (95 % CI) | (1.1,7.5) | (0.3,1.5) | (3.8, 12.3) | (2.8,10.6) | (1.0, 70.4) | (6.9, 40.8)) | (12.7, 42.4) |
| **Smoking: no (ng/mL)** | | | | | | | |
| Mean (n) | 0.06 (141) | 0.04[+] (281) | 0.07[+] (365) | 0.08[+] (333) | 0.03[+] (16) | 0.34 (122) | 0.15 (200) |
| (95 % CI) | (0.04, 0.09) | (0.03, 0.05) | (0.05, 0.09) | (0.06, 0.11) | (0.02, 0.05) | (0.17, 0.71) | (0.09, 0.25) |

All but those marked with [+] showed $p$ value < 0.05, reference group = management. Weighted percent, weighted means (age) or geometric means (BMI and cotinine), and standard error (SE). HS = High School. BMI = body mass index; Professional = Professional specialty; Support = technical, sales, and administrative support; Agriculture = farming, forestry, and fishing; ECR = extractive, construction, and repair occupations; and OFL = operators, fabricators, and labors

Differences in PAH exposure associated with occupation groups also varied along different quantiles of OH-PAH concentrations. In Fig. 4 (only "ERC" and "OFL" groups are shown), the regression coefficients of NAP, FLUO, and PHEN are generally all above zero and display increasing trends at higher quantiles than lower quantiles. This means that the "OFL" and "ECR" groups had elevated OH-PAH exposures than

the "management" group, and the differences increased at elevated exposure levels. The occupation effect was most pronounced in the middle exposure range (~the 50th quantile) for PYR.

Consistent with the temporal trend in bivariate analyses, significant ($p < 0.001$) temporal variations were only seen for NAP and PYR in the multiple regression models (Table 3). NAP and PYR experienced an approximate 17
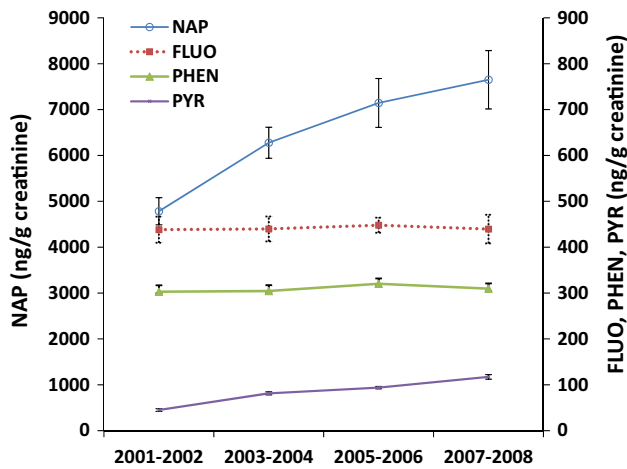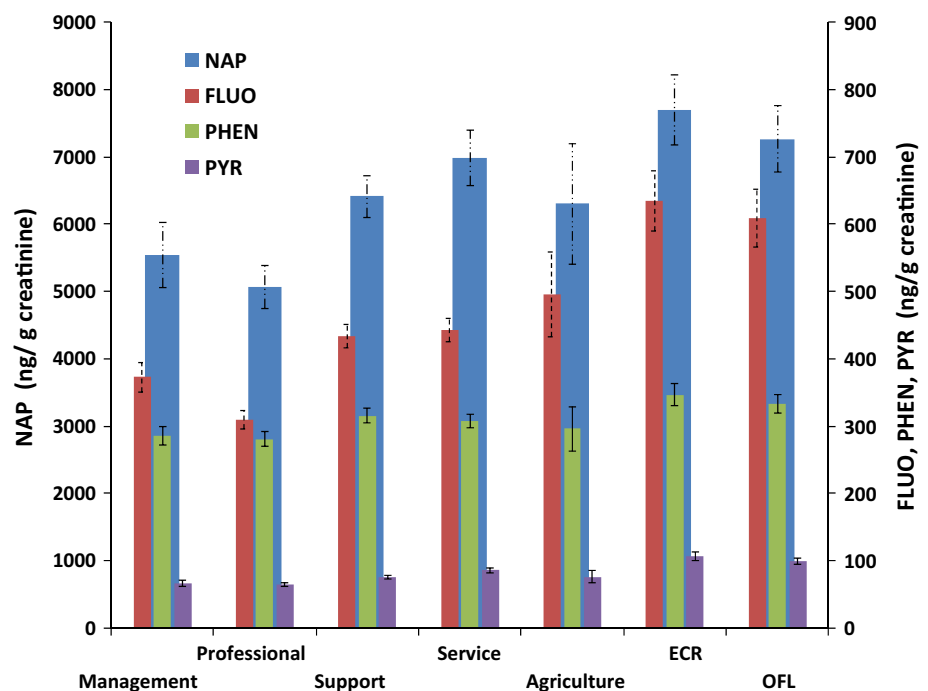
**Fig. 1** Temporal trends of urinary PAH metabolites (weighted geometric mean ± standard error) by survey periods, NHANES 2001–2008

and 35 % increase per survey cycle between 2001 and 2008 (or 2 and 5 % annual increase), respectively.

The fully adjusted models also showed that PAH exposure was disproportionately distributed among a few sociodemographic groups (Table 3). Levels of OH-PAHs decreased with increasing education (not significant for PHEN), and with increasing income levels, though only significant for PYR. In general, nonwhites had lower OH-PAH concentrations than whites, and females tended to have higher OH-PAH concentrations than males. To further understand the influences of socioeconomic status (SES), race/ethnicity, and sex on the exposure, we ran models for

the two high-risk job categories, i.e., "ECR" and "OFL" groups. The results (Table S3) showed that nonwhites continued to have significantly ($p < 0.01$) lower PAH exposure, while differences in PAH levels associated with education levels and sex became nonsignificant. The only significant associations between PIR and PAH were found in PYR, similar to the previous results (Table 3).

With everything else held constant, non-smokers had 39–59 % reduction in the levels of OH-PAHs than smokers (Table 3). The associations between PAH and occupations in stratified analysis based on the smoking status (Table S4) found similar results, which showed "OFL" and "ECR" had generally higher PAH exposures than "management." However, there were also some notable differences. The significantly higher NAP in the "OFL" and "ECR" groups than in "management" was only among smokers. Among smokers, whites had higher NAP than nonwhites, while the opposite was true among non-smokers. Among smokers, the "professional" group had a significantly lower FLUO exposure ($\beta = -0.37$, corresponds to ~31 % reduction, $p = 0.003$) than "management." Non-smokers in the "service" and "support" continued to have significantly higher FLUO exposure than "management," which were not seen among smokers.

## Discussion

While NHANES data are generally regarded as providing a national reference level of biomarkers such as PAHs, we found heterogeneous distributions of PAH urinary
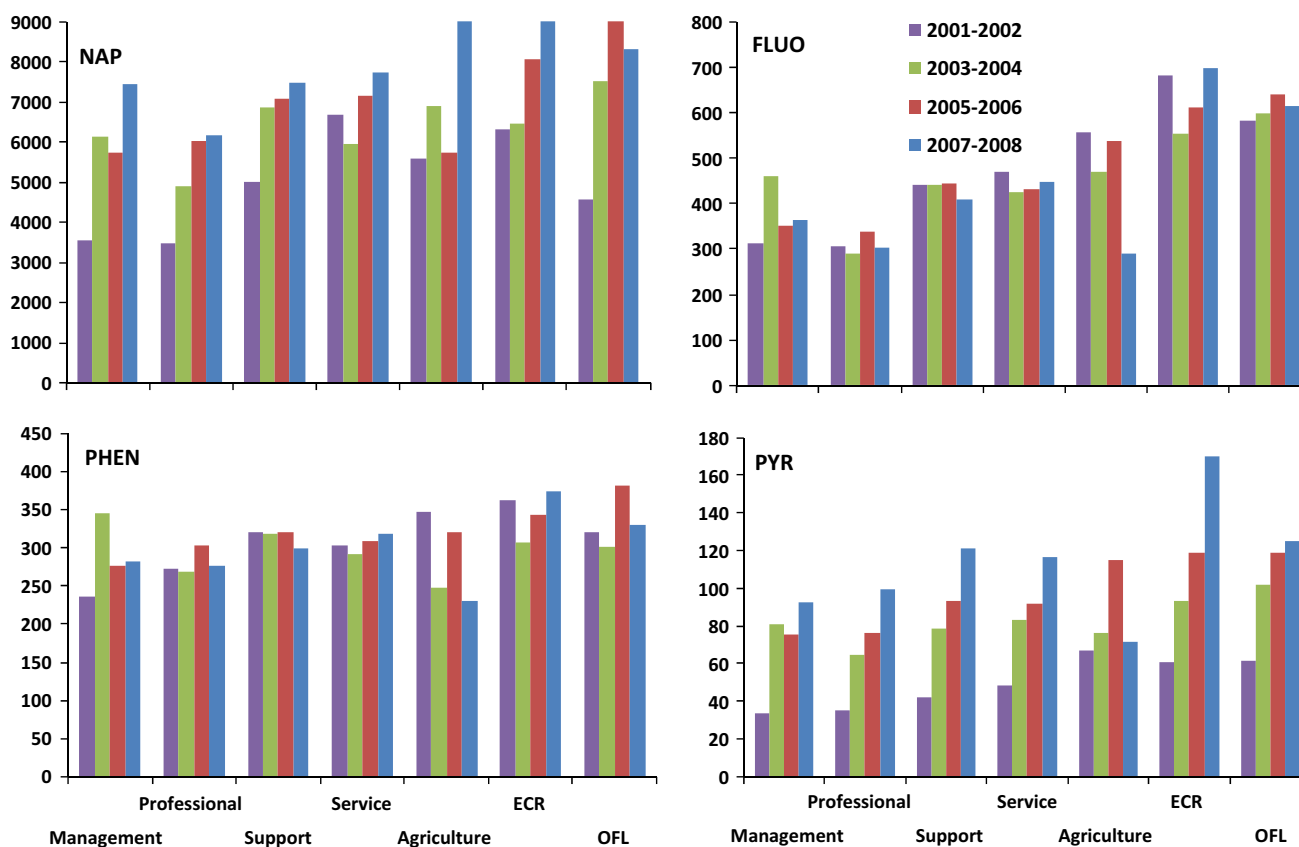


**Fig. 2** Weighted geometric means (±standard error) of urinary PAH metabolites by occupational groups, NHANES 2001–2008

**Fig. 3** Trends of urinary PAH metabolites (ng/g creatinine, weighted geometric means) by occupational groups and survey periods, NHANES 2001–2008

metabolites among people with different job categories. This new finding suggests that occupation is a significant contributor to population-based reference PAH exposures, in addition to the well-known smoking factor. On the other hand, it was not surprising to find elevated levels of OH-PAHs, especially PYR, among people within the "ECR" and "OFL" groups, given that many industrial processes and activities in these two sectors have high PAH sources. A review of PYR studies from different countries by Hansen et al. (2008) found a wide concentration range of PYR among many occupational studies, with a majority of workers from foundries and petrochemical industries ranging from 2 to 145 μmol/mol creatinine. The mean end-of-shift PYR was 2.49 μmol/mol creatinine in a cross-industry occupational hygiene survey in the United Kingdom (Unwin et al. 2006). Among asphalt paving workers, the mean baseline PYR (after a weekend rest) was reported to be 0.4 μg/g or 0.21 μmol/mol creatinine (McClean et al. 2004). In contrast, the geometric mean PYR in the high exposure occupational groups (0.06 and 0.05 μmol/mol creatinine for ECR and OFL groups, respectively) found in this study was generally low and is reflective of reference levels.

The upward temporal trends of NAP and PYR are disconcerting as they suggest that the exposure to PAHs as a whole may be on the rise at the national population level. The increase in the two high OH-PAH occupational groups ("ECR" and "OFL") may be of particular concerns. A recent review of the epidemiological evidence on high exposure to PAHs related to occupations showed an approximately 30 % excess risk for lung cancer in iron and steel foundry industries (Rota et al. 2014). While it remains difficult to assess excess cancer risks associated with increase in PAH at low reference levels in the general environment among the general population, the significant increase in recent PAH exposure found in this study suggests the need to reduce the overall PAH exposure in the general environment and workplaces, especially among those within the "ECR" and "OFL" occupational groups.

In contrast to the overall increase in NAP and PYR, FLUO and PHEN urine metabolites remained stable during the study period (2001–2008). It is unclear what contributes to this discrepancy, which deserves further investigations in future studies. Possible explanations include differences in exposure routes and/or metabolic patterns among these PAH metabolites and their parent compounds in various

**Table 3** Regression coefficients of the associations between urinary PAH metabolites and occupation groups

|  | NAP | FLUO | PHEN | PYR |
|---|---|---|---|---|
| Operators, fabricators, and labors (OFL) | 0.18 | **0.38***** | **0.16**** | **0.27***** |
| Extractive, construction, and repair (ECR) | **0.26**** | **0.35***** | **0.19**** | **0.32***** |
| Farming, forestry, and fishing (Agriculture) | 0.18 | 0.26 | 0.11 | 0.28 |
| Service | 0.13 | **0.14*** | 0.06 | 0.06 |
| Technical, sales, and administrative support (Support) | 0.11 | **0.15*** | 0.09 | 0.06 |
| Professional specialty | −0.04 | −0.10 | 0.003 | −0.04 |
| Management *(Ref)* |  |  |  |  |
| Sampling period | **0.15***** | −0.001 | 0.01 | **0.30***** |
| Sex *(ref: Male)* | **0.22***** | 0.06 | **0.11**** | **0.14**** |
| Race *(ref: White)* | −0.04 | **−0.15**** | **−0.15***** | **−0.06** |
| Education | **−0.12**** | **−0.12***** | −0.04 | **−0.09***** |
| Poverty income ratio *(ref:PIR ≤ 1)* | −0.10 | −0.12 | −0.09 | **−0.14**** |
| Smoking *(ref: Yes)* | **−0.77***** | **−0.89***** | **−0.32***** | **−0.49***** |
| Sampling season *(ref: Nov.–Apr.)* | 0.02 | **0.14*** | **0.15**** | **0.13*** |
| Age | 0.002 | **−0.004*** | 0.002 | **−0.01***** |
| Body mass index (BMI) | **−0.27*** | −0.15 | 0.06 | −0.09 |
| Creatinine | **0.86***** | **0.90***** | **0.88***** | **0.89***** |
| Sample Size | 3372 | 3348 | 3365 | 3335 |

Results from multivariable regression model: log(OH-PAH) = *f*(occupational group, sampling period, sex, race, education, PIR, smoking, sampling season, age, log(BMI), log(creatinine)). Sampling period was coded as a 4-level variable (1: 2001–2002, 2: 2003–2004, 3: 2005-2006, and 4 = 2007–2008). Education was coded as a 3-level variable (1: < high school (HS), 2: = HS, and 3: > HS). Significant associations were indicated in bold and with different *p* values: *, $p < 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$. Ref = Reference level

sources. While PHEN has also been proposed as a biomarker of PAH exposures from all exposure routes (Bostrom et al. 2002), studies have also suggested that PHEN is better suited as a biomarker for the metabolic activation of potentially carcinogenic PAHs rather than detoxification (e.g., excrete from urine) of PAHs (Bostrom et al. 2002; Jacob and Seidel 2002; Kim et al. 2005), thus less representative of the recent overall exposure assessed by urinary metabolites. In addition, different from NAP and PYR, the mass sums of FLUO and PHEN available from the current NHANES data did not include all the urinary OH-PAHs of their corresponding parent compounds.

The influence of smoking on OH-PAHs was mostly reflected in NAP and FLUO. Exposure to naphthalene is primarily through inhalation in the general population (Li et al. 2012), and the two naphthalene urine metabolites are the dominant constituents of the total urinary OH-PAHs. In tobacco smoke, naphthalene is the dominant PAH species in both vapor and particulate phases, and fluorene is the second most abundant species in the vapor phase (Lu and Zhu 2007). In addition, FLUO, in particular 3-FLUO, has been shown to better correlate with their parent airborne compounds than PYR (Nethery et al. 2012). Consistent with these findings, our results showed that the regression coefficients associated with smoking for both NAP and FLUO were larger than those of PHEN

and PYR (Table 3). The significant increase in FLUO in both "service" and "support" groups (Table 3) may in part reflect that these two groups had higher airborne PAH exposure than the "management" group. Further, for these two groups, the exposure is likely related to secondhand tobacco smoke (SHS), as the associations were only significant among the non-smoker group (Table S4). The result on the "service" group was consistent with findings from a recent study (Wei et al. 2014) based on NHANES 1999–2008, which showed that the "service" group had one of the highest serum cotinine levels, indicative of elevated SHS exposure, among the eighteen occupational groups compared.

Our analysis of SES disparities adds new insights into the current environmental justice (EJ) research. A general hypothesis in EJ is that individuals in low SES have greater burdens of environmental toxicants (Bell and Ebisu 2012; Morello-Frosch and Jesdale 2006), which is in agreement with our findings of elevated PAH exposures in individuals with low-education/income levels. However, our results showed nonwhites tend to have lower PAH levels than whites, which was in contrast to numerous EJ studies that tend to show low pollution exposure among whites (e.g., Hajat et al. 2013; Jia et al. 2014). It has been long hypothesized that race and SES should be distinguished in EJ analyses, despite the overrepresentation of minorities in
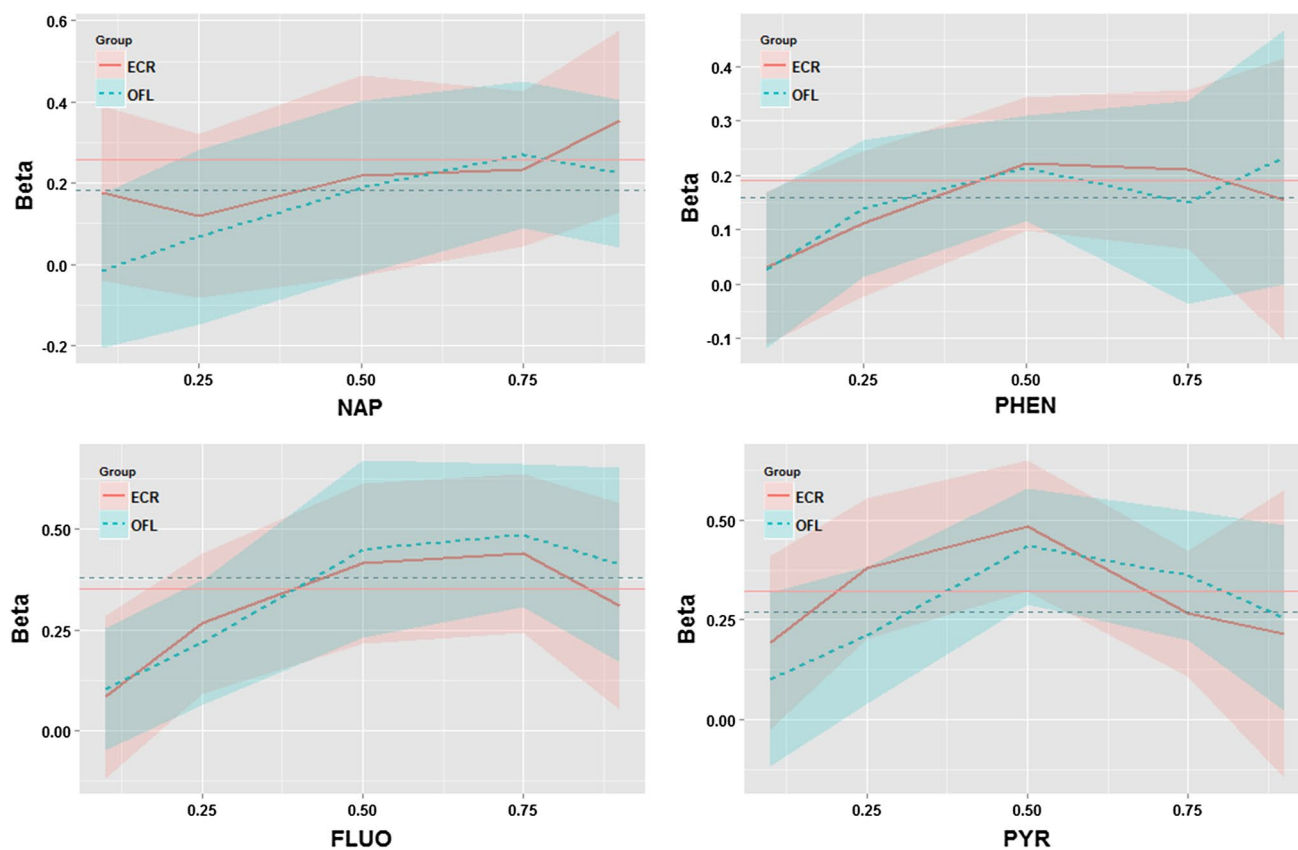
**Fig. 4** Strengths of occupation–PAH associations. The analysis was based on the multivariable model: log(OH-PAH) = f(occupational group, sampling period, sex, race, education, PIR, smoking, sampling season, age, log(BMI), log(creatinine)). Results shown were for two occupational groups: the operators, fabricators, and labors (OFL); extractive, construction, and repair occupations (ECR)), with "man-agement" as the reference. Quantile regression coefficients (betas and the 95 % confidence intervals, *shaded areas*) shown in *curves* are for the 10, 25, 50, 75, and 90th quantiles of OH-PAHs, and betas from ordinary least square regressions (also shown in Table 3) are in straight *horizontal lines*

low-SES subpopulations (O'Neill et al. 2003). Our analyses provided such an example.

This study has several limitations. First, the current study, which is mainly a secondary data analysis, differs from the typical occupational studies in that NHANES sampling was not conducted in typical workplaces but was collected during the appointments in the mobile examination centers, and the exact time interval between urine sample collections and occupational exposure (e.g., directly after occupational exposure, on a vacation day, or after a period of rest since a regular working day) was unknown. Thus, our results should be interpreted with caution. Second, the NHANES occupational data were classified only by broad occupation groups, while PAH exposures may vary among different industry groups or different job task groups within the same occupation classification. Differences in PAH exposures can occur under the same title. Third, misclassification might also have occurred when different occupation groups were summarized into the

seven categories. While detailed occupation classifications may be desirable, insufficient sample size became an issue for such refined analyses. Forth, due to the relatively short half-lives of OH-PAHs (~hours to a couple of days) and the cross-sectional nature of the NHANES data, it is unclear whether the long-term PAH exposure level is also on the rise. Fifth, the urinary PAHs do not reflect exposure to PAHs with more than four rings that mainly exist in particulate phase and detoxified through other routes. Finally, while some of the most important factors of PAH exposure, such as smoking, was accounted for, this study did not adjust other factors, such as diet (Alomirah et al. 2011; Levine et al. 2015), urban/rural residence (Hansen et al. 2005; Levine et al. 2015; Tuntawiroon et al. 2007), or time of the day of urine sample collection (Barr et al. 2005; Han et al. 2008), all of which could also affect our estimated population-based reference levels of OH-PAHs, and the relative influence of occupational types on the variations in PAH concentrations.

## Conclusions

This study provides the first national reference levels of OH-PAHs by occupational groups between 2001 and 2008. The results, based on a large representative sample of the US general population, had meaningful implications, as they help to estimate the reference exposure levels, identify potential risk factors associated with PAH exposures, and provide scientific information for developing policies aimed at reducing PAH exposures in the general environment and workplaces. Our findings suggest that the effects of professional types should be considered in biomonitoring programs due to the heterogeneous distributions of PAH urinary metabolites among different occupation types. Reduction priorities among people within the "ECR" and "OFL" occupational groups are necessary given that they experienced significantly higher PAH exposure over time. In addition, reduction in ETS exposure is also recommended for the "service" occupational group in order to reduce their PAH exposure. Among the four PAH indicators used, both NAP and FLUO appeared to be good indicators of PAH exposure related to ETS. This study also observed independent effects of race and SES on exposure. Finally, this study may inform similar studies to examine occupational differences in exposure to other chemicals measured in NHANES.

## References

Alomirah H, Al-Zenki S, Al-Hooti S, Zaghloul S, Sawaya W, Ahmed N, Kannan K (2011) Concentrations and dietary exposure to polycyclic aromatic hydrocarbons (PAHs) from grilled and smoked foods. Food Control 22(12):2028–2035. doi:10.1016/j.foodcont.2011.05.024

ATSDR (1995) Toxicological profile for polycyclic aromatic hydrocarbons. Atlanta, Georgia: US department of health and human services, agency for toxic substances and disease registry

Baan R, Grosse Y, Straif K, Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L et al (2009) Special report: policy a review of human carcinogens-Part F: chemical agents and related occupations. Lancet Oncol 10(12):1143–1144

Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham LL, Pirkle JL (2005) Urinary creatinine concentrations in the U.S. population: implications for urinary biologic monitoring measurements. Environ Health Perspect 113(2):192–200

Bell ML, Ebisu K (2012) Environmental inequality in exposures to airborne particulate matter components in the United States. Environ Health Perspect 120(12):1699–1704. doi:10.1289/ehp.1205201

Bernert JT Jr, Turner WE, Pirkle JL, Sosnoff CS, Akins JR, Waldrep MK, Ann Q et al (1997) Development and validation of sensitive

method for determination of serum cotinine in smokers and non-smokers by liquid chromatography/atmospheric pressure ionization tandem mass spectrometry. Clin Chem 43(12):2281–2291

Boffetta P, Jourenkova N, Gustavsson P (1997) Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. Cancer Causes Control 8(3):444–472. doi:10.1023/a:1018465507029

Bostrom CE, Gerde P, Hanberg A, Jernstrom B, Johansson C, Kyrklund T, Rannug A et al (2002) Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air. Environ Health Perspect 110(Suppl 3):451–488

Campo L, Fustinoni S, Consonni D, Pavanello S, Kapka L, Siwinska E, Mielzynska D et al (2014) Urinary carcinogenic 4-6 ring polycyclic aromatic hydrocarbons in coke oven workers and in subjects belonging to the general population: role of occupational and environmental exposure. Int J Hyg Environ Health 217(2–3):231–238. doi:10.1016/j.ijheh.2013.06.005

Clark JD 3rd, Serdar B, Lee DJ, Arheart K, Wilkinson JD, Fleming LE (2012) Exposure to polycyclic aromatic hydrocarbons and serum inflammatory markers of cardiovascular disease. Environ Res 117:132–137. doi:10.1016/j.envres.2012.04.012

Dor F, Dab W, Empereur-Bissonnet P, Zmirou D (1999) Validity of biomarkers in environmental health studies: the case of PAHs and benzene. Crit Rev Toxicol 29(2):129–168. doi:10.1080/10408449991349195

Hajat A, Diez-Roux AV, Adar SD, Auchincloss AH, Lovasi GS, O'Neill MS, Sheppard L et al (2013) Air pollution and individual and neighborhood socioeconomic status: evidence from the multi-ethnic study of atherosclerosis (MESA). Environ Health Perspect 121(11–12):1325–1333. doi:10.1289/ehp.1206337

Han IK, Duan X, Zhang L, Yang H, Rhoads GG, Wei F, Zhang J (2008) 1-Hydroxypyrene concentrations in first morning voids and 24-h composite urine: intra- and inter-individual comparisons. J Expo Sci Environ Epidemiol 18(5):477–485. doi:10.1038/sj.jes.7500639

Hansen AM, Raaschou-Nielsen O, Knudsen LE (2005) Urinary 1-hydroxypyrene in children living in city and rural residences in Denmark. Sci Total Environ 347(1–3):98–105. doi:10.1016/j.scitotenv.2004.12.037

Hansen AM, Mathiesen L, Pedersen M, Knudsen LE (2008) Urinary 1-hydroxypyrene (1-HP) in environmental and occupational studies–a review. Int J Hyg Environ Health 211(5–6):471–503. doi:10.1016/j.ijheh.2007.09.012

Ikeda M, Ezaki T, Tsukahara T, Moriguchi J, Furuki K, Fukui Y, Okamoto S et al (2003) Bias induced by the use of creatinine-corrected values in evaluation of beta(2)-microglobulin levels. Toxicol Lett 145(2):197–207. doi:10.1016/S0378-4274(03)00320-5

Jacob J, Seidel A (2002) Biomonitoring of polycyclic aromatic hydrocarbons in human urine. J Chromatogr B Analyt Technol Biomed Life Sci 778(1–2):31–47. doi:10.1016/S0378-4347(01)00467-4

Jia C, James W, Kedia S (2014) Relationship of racial composition and cancer risks from air toxics exposure in Memphis, Tennessee, USA. Int J Environ Res Public Health 11(8):7713–7724. doi:10.3390/ijerph110807713

Jung KH, Patel MM, Moors K, Kinney PL, Chillrud SN, Whyatt R, Hoepner L et al (2010) Effects of Heating season on residential indoor and outdoor polycyclic aromatic hydrocarbons, black carbon, and particulate matter in an Urban Birth Cohort. Atmos Environ (1994) 44(36):4545–4552. doi:10.1016/j.atmosenv.2010.08.024

Jung KH, Hsu S-I, Yan B, Moors K, Chillrud SN, Ross J, Wang S et al (2012) Childhood exposure to fine particulate matter and black carbon and the development of new wheeze between ages 5 and 7 in an urban prospective cohort. Environ Int 45:44–50

Jung KH, Liu B, Lovinsky-Desir S, Yan B, Camann D, Sjodin A, Li Z et al (2014a) Time trends of polycyclic aromatic hydrocarbon

exposure in New York City from 2001 to 2012: assessed by repeat air and urine samples. Environ Res 131:95–103. doi:10.1016/j.envres.2014.02.017

Jung KH, Perzanowski M, Rundle A, Moors K, Yan B, Chillrud SN, Whyatt R et al (2014b) Polycyclic aromatic hydrocarbon exposure, obesity and childhood asthma in an urban cohort. Environ Res 128:35–41. doi:10.1016/j.envres.2013.12.002

Kim JY, Hecht SS, Mukherjee S, Carmella SG, Rodrigues EG, Christiani DC (2005) A urinary metabolite of phenanthrene as a biomarker of polycyclic aromatic hydrocarbon metabolic activation in workers exposed to residual oil fly ash. Cancer Epidemiol Biomarkers Prev 14(3):687–692. doi:10.1158/1055-9965. Epi-04-0428

Kim K-H, Jahan SA, Kabir E, Brown RJC (2013) A review of airborne polycyclic aromatic hydrocarbons (PAHs) and their human health effects. Environ Int 60:71–80. doi:10.1016/j. envint.2013.07.019

Langlois PH, Hoyt AT, Lupo PJ, Lawson CC, Waters MA, Desrosiers TA, Shaw GM et al (2012) Maternal occupational exposure to polycyclic aromatic hydrocarbons and risk of neural tube defect-affected pregnancies. Birth Defects Res Part A-Clin Mol Teratol 94(9):693–700. doi:10.1002/bdra.23045

Levine H, Berman T, Goldsmith R, Goen T, Spungen J, Novack L, Amitai Y et al (2015) Urinary concentrations of polycyclic aromatic hydrocarbons in Israeli adults: demographic and lifestyle predictors. Int J Hyg Environ Health 218(1):123–131. doi:10.1016/j.ijheh.2014.09.004

Li Z, Sandau CD, Romanoff LC, Caudill SP, Sjodin A, Needham LL, Patterson DG (2008) Concentration and profile of 22 urinary polycyclic aromatic hydrocarbon metabolites in the US population. Environ Res 107(3):320–331. doi:10.1016/j. envres.2008.01.013

Li Z, Romanoff L, Bartell S, Pittman EN, Trinidad DA, McClean M, Webster TF et al (2012) Excretion profiles and half-lives of ten urinary polycyclic aromatic hydrocarbon metabolites after dietary exposure. Chem Res Toxicol 25(7):1452–1461. doi:10.1021/ tx300108e

Lu H, Zhu L (2007) Pollution patterns of polycyclic aromatic hydrocarbons in tobacco smoke. J Hazard Mater 139(2):193–198. doi:10.1016/j.jhazmat.2006.06.011

McClean MD, Rinehart RD, Ngo L, Eisen EA, Kelsey KT, Wiencke JK, Herrick RF (2004) Urinary 1-hydroxypyrene and polycyclic aromatic hydrocarbon exposure among asphalt paving workers. Ann Occup Hyg 48(6):565–578. doi:10.1093/annhyg/meh044

Miller RL, Garfinkel R, Horton M, Camann D, Perera FP, Whyatt RM, Kinney PL (2004) Polycyclic aromatic hydrocarbons, environmental tobacco smoke, and respiratory symptoms in an inner-city birth cohort. Chest 126(4):1071–1078. doi:10.1378/ chest.126.4.1071

Morello-Frosch R, Jesdale BM (2006) Separate and unequal: residential segregation and estimated cancer risks associated with ambient air toxics in US metropolitan areas. Environ Health Perspect 114(3):386–393. doi:10.1289/ehp.8500

Naumova YY, Eisenreich SJ, Turpin BJ, Weisel CP, Morandi MT, Colome SD, Totten LA et al (2002) Polycyclic aromatic hydrocarbons in the indoor and outdoor air of three cities in the US. Environ Sci Technol 36(12):2552–2559. doi:10.1021/Es015727h

NCHS (2006) Analytic and Reporting Guidelines. The National Health and Nutrition Examination Survey (NHANES). National Center for Health Statistics. http://www.cdcgov/nchs/data/ nhanes/nhanes_03_04/nhanes_analytic_guidelines_dec_2005pdf Assessed 20 Mar 2014

NCHS (2013) National Center for Health Statistics, Specifying Weighting Parameters. http://www.cdcgov/nchs/tutorials/nhanes/ SurveyDesign/Weighting/introhtm Assessed 20 Mar 2014

Nethery E, Wheeler AJ, Fisher M, Sjodin A, Li Z, Romanoff LC, Foster W et al (2012) Urinary polycyclic aromatic hydrocarbons as a biomarker of exposure to PAHs in air: a pilot study among pregnant women. J Expo Sci Env Epid 22(1):70–81. doi:10.1038/ Jes.2011.32

O'Neill MS, Jerrett M, Kawachi L, Levy JL, Cohen AJ, Gouveia N, Wilkinson P et al (2003) Health, wealth, and air pollution: advancing theory and methods. Environ Health Perspect 111(16):1861–1870. doi:10.1289/ehp.6334

Perera FP, Rauh V, Whyatt RM, Tsai WY, Tang D, Diaz D, Hoepner L et al (2006) Effect of prenatal exposure to airborne polycyclic aromatic hydrocarbons on neurodevelopment in the first 3 years of life among inner-city children. Environ Health Perspect 114(8):1287–1292

Perera FP, Wang S, Vishnevetsky J, Zhang B, Cole KJ, Tang D, Rauh V et al (2011) Polycyclic aromatic hydrocarbons-aromatic DNA adducts in cord blood and behavior scores in New York city children. Environ Health Perspect 119(8):1176–1181. doi:10.1289/ ehp.1002705

Perera FP, Tang D, Wang S, Vishnevetsky J, Zhang B, Diaz D, Camann D et al (2012) Prenatal polycyclic aromatic hydrocarbon (PAH) exposure and child behavior at age 6–7 years. Environ Health Perspect 120(6):921–926. doi:10.1289/ehp.1104315

Romanoff LC, Li Z, Young KJ, Blakely NC, Patterson DG, Sandau CD (2006) Automated solid-phase extraction method for measuring urinary polycyclic aromatic hydrocarbon metabolites in human biomonitoring using isotope-dilution gas chromatography high-resolution mass spectrometry. J Chromatogr B 835(1– 2):47–54. doi:10.1016/j.jchromb.2006.03.004

Rosa MJ, Jung KH, Perzanowski MS, Kelvin EA, Darling KW, Camann DE, Chillrud SN et al (2011) Prenatal exposure to polycyclic aromatic hydrocarbons, environmental tobacco smoke and asthma. Respir Med 105(6):869–876. doi:10.1016/j. rmed.2010.11.022

Rota M, Bosetti C, Boccia S, Boffetta P, La Vecchia C (2014) Occupational exposures to polycyclic aromatic hydrocarbons and respiratory and urinary tract cancers: an updated systematic review and a meta-analysis to 2014. Arch Toxicol 88(8):1479–1490. doi:10.1007/s00204-014-1296-5

Rundle A, Hoepner L, Hassoun A, Oberfield S, Freyer G, Holmes D, Reyes M et al (2012) Association of childhood obesity with maternal exposure to ambient air polycyclic aromatic hydrocarbons during pregnancy. Am J Epidemiol 175(11):1163–1172. doi:10.1093/aje/kwr455

Scherer G, Frank S, Riedel K, Meger-Kossien I, Renner T (2000) Biomonitoring of exposure to polycyclic aromatic hydrocarbons of nonoccupationally exposed persons. Cancer Epidemiol Biomarkers Prev 9(4):373–380

Scinicariello F, Buser MC (2014) Urinary polycyclic aromatic hydrocarbons and childhood obesity: NHANES (2001–2006). Environ Health Perspect 122(3):299–303. doi:10.1289/ehp.1307234

Tuntawiroon J, Mahidol C, Navasumrit P, Autrup H, Ruchirawat M (2007) Increased health risk in Bangkok children exposed to polycyclic aromatic hydrocarbons from traffic-related sources. Carcinogenesis 28(4):816–822. doi:10.1093/carcin/bgl175

Unwin J, Cocker J, Scobbie E, Chambers H (2006) An assessment of occupational exposure to polycyclic aromatic hydrocarbons in the UK. Ann Occup Hyg 50(4):395–403. doi:10.1093/annhyg/ mel010

Us EPA (1999) Integrated Risk Information System (IRIS) on Polycyclic Organic Matter. US Environmental Protection Agency National Center for Environmental Assessment. Office of Research and Development, Washington, DC 1999

Van Rooij JG, Van Lieshout EM, Bodelier-Bade MM, Jongeneelen FJ (1993) Effect of the reduction of skin contamination on the

internal dose of creosote workers exposed to polycyclic aromatic hydrocarbons. Scand J Work Environ Health 19(3):200–207

Wei B, Bernert JT, Blount B, Sosnoff C, Wang L (2014) Occupational exposure to second-hand tobacco smoke in the United States: NHANES 1999–2008. 24th Annual Meeting of The International Society of Exposure Science October 12–16 Cincinnati, Ohio (Abstract # Mo-S-C4-05)

Xu XH, Cook RL, Ilacqua VA, Kan HD, Talbott EO, Kearney G (2010) Studying associations between urinary metabolites of polycyclic aromatic hydrocarbons (PAHs) and cardiovascular diseases in the United States. Sci Total Environ 408(21):4943–4948. doi:10.1016/j.scitotenv.2010.07.034

Zipf G, Chiappa M, Porter KS et al (2013) National health and nutrition examination survey: plan and operations, 1999–2010 National Center for Health Statistics Vital Health Stat 1(56):4–9