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Research article

# Association of urinary metabolites of polycyclic aromatic hydrocarbons with urinary incontinence in adults: A cross-sectional study

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ABSTRACT

This study aims to investigate the association between polycyclic aromatic hydrocarbon (PAH) metabolites and urinary incontinence (UI) in the general adult population. This study analyzed six urinary PAH metabolites in the general adult population from the 2005–2016 National Health and Nutrition Examination Survey (NHANES). UI was distinguished into stress UI (SUI), urgency UI (UUI), mixed UI (MUI), and any UI by self-reported questionnaires. Multiple logistic regression, restricted cubic spline (RCS) regression, and quantile g-computation (QG-C) were applied to assess the association between PAHs (individual and mixture exposure) and the prevalence of UI. A total of 8,136 participants were included in our study. The participants had a median age of 45.9 years, and 48.7 % of individuals were female. Most ln-transformed PAHs were positively and linearly related to the prevalence of SUI and any UI in women ($P < 0.05$). Increasing prevalence of SUI was associated with the highest quantiles of 3-hydroxyfluorene (3-FLU) (OR = 1.72, 95% CI = 1.27–2.33, $P$ for trend = 0.002), 2-hydroxyfluorene (2-FLU) (OR = 1.75, 95%CI = 1.29–2.38, $P$ for trend = 0.008), and 1-hydroxypyrene (1-PYR) (OR = 1.44, 95%CI = 1.05–1.96, $P$ for trend = 0.012) compared with the lowest quantiles in women. The mixture of urinary PAH metabolites was significantly associated with an increased prevalence of SUI (OR = 1.09, 95%CI: 1.01–1.19, $P = 0.038$) in women. Urinary 2-FLU had the greatest positive contribution to the overall effect, while 2-hydroxynapthalene (2-NAP) was the major negative contributor. Our study demonstrated that mixture exposure to PAHs is associated with the prevalence of SUI in adult women, which might be primarily driven by 2-FLU.

## 1. Introduction

Urinary incontinence (UI) is a prevalent health problem worldwide, particularly for women [1]. It can negatively impact quality of life and lead to emotional issues such as anxiety and depression [2]. According to the American Urological Association, UI prevalence ranges from 44 to 57 % in middle-aged and post-menopausal women [3]. Due to most patients being reluctant to seek medical help, the actual prevalence of the condition may be significantly higher than what is currently recognized [4]. UI can be classified into a number of different categories, including stress UI (SUI), urgency UI (UUI), mixed UI (MUI), other UI, and any UI [5]. Many factors can cause UI, including muscle injuries, pregnancy, childbirth, surgeries, and certain medical conditions [6–10]. However, recent research has

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also found that environmental pollutants may affect the incidence of UI [11,12].

Polycyclic Aromatic Hydrocarbons (PAHs) are a type of organic compounds commonly found in both industrial and residential environments [13]. The origin of these compounds is mainly from combustion processes such as burning coal, gasoline, and wood [14]. Exposure to PAHs in humans can happen indirectly through the inhalation of air or ingestion of contaminated food, as well as through skin contact [15]. The effect of PAHs on human health depends on the type and duration of exposure, the amount of PAH concentration, and their relative toxicities [16]. A group of 17 PAHs is identified as highly concerning regarding the potential health impacts on humans and regarded as a category. Additionally, the measurement of hydroxylated PAH metabolites in urine has been used for risk assessment for human exposure to PAHs [17].

Recent findings suggest that PAHs are linked with a variety of acute and chronic ailments, such as lung cancer, colorectal cancer, asthma, and rheumatoid arthritis [18–21]. However, its potential impact on urinary health, particularly UI, remains underexplored. This knowledge gap is significant, given the widespread exposure to PAHs and their established toxicological effects [22]. Importantly, women may be uniquely susceptible to PAH exposure due to biological and hormonal factors [23,24], which can influence the development of conditions like UI. While studies have traditionally focused on individual PAH compounds, environmental exposures typically involve complex mixtures of PAHs, making it essential to evaluate their combined effects.

To address this gap, we conducted a comprehensive analysis of the association between urinary PAH metabolites and UI using data from the 2005–2016 National Health and Nutrition Examination Survey (NHANES). This study examined both individual and mixture exposure to PAHs and their relationship with the prevalence of UI. By employing quantile g-computation (QG-C), we assessed the collective impact of PAH mixtures on UI prevalence. Our findings provide novel epidemiological insights into the role of PAH exposure in UI, offering important implications for public health strategies and preventive interventions.

## 2. Methods

### 2.1. Study population

We utilized data from six cycles (2005–2016) of the NHANES project, which collects diverse information such as demographic, behavioral, clinical, social, dietary, and laboratory data from non-institutionalized individuals [25]. The primary objective of NHANES is to evaluate health and nutrition conditions in American children and adults. Skilled medical personnel conduct physical assessments and collect biospecimens from participants at mobile examination centers (MECs). Informed consent was obtained from all participants before being enrolled, and the Centers for Disease Control and Prevention's Research Ethics Review Board approved the project. This study was conducted in accordance with the STROBE guidelines.

Referring to previous NHANES literature [26,27], participants with missing information were excluded from the analysis. In the 2005–2016 NHANES, 60,936 participants were recruited and analyzed, out of which 45,463 had incomplete data on urinary PAHs and were excluded from the analysis. We excluded participants with age $<20$ years and missing data on UI ($n = 6,320$), those who were pregnant ($n = 184$), and those who had cancer ($n = 833$). A total of 8,136 participants were enrolled for the final analysis (Fig. S1).

### 2.2. Assessment of urinary PAHs

Urine samples were collected by technicians who received professional training and stored under freezing conditions of $-20\ ^{\circ}C$ in accordance with laboratory or medical guidelines until they were sent for analysis [28,29]. Six urinary monohydroxylated metabolites of PAHs (OH-PAHs) including 1-hydroxynapthalene (1-NAP), 2-hydroxynapthalene (2-NAP), 3-hydroxyfluorene (3-FLU), 2-hydroxyfluorene (2-FLU), 1-hydroxyphenanthrene (1-PHE), and 1-hydroxypyrene (1-PYR) were measured using capillary gas chromatography combined with high-resolution mass spectrometry (GC-HRMS) for NHANES 2005–2008 and isotope dilution gas chromatography/-tandem mass spectrometry (GC-MS/MS) for NHANES 2009–2012. In the NHANES 2013–2016, isotope dilution high-performance liquid chromatography-MS/MS (online SPE-HPLC-MS/MS) was used in the detection process. The NHANES website provides details on the test methods (https://wwwn.cdc.gov/nchs/nhanes/Search/DataPage.aspx?Component=Laboratory). All analytic results below the lower limit of detection (LOD) were replaced with the LOD value divided by square root of 2.

### 2.3. Assessment of the UI

The classification of UI for all participants over the age of 20 was determined using specific questionnaires [30]. Those who responded positively to "During the past year, have you leaked or lost even a small amount of urine during physical activities such as coughing, lifting or exercise?" were classified as SUI. UUI was defined as those who answered affirmatively to "During the past year, have you leaked or lost even a small amount of urine when experiencing an urge or pressure to urinate and couldn't make it to the restroom in time?" Individuals who responded positively to both the UUI and SUI questions were diagnosed with MUI [31,32]. For men who did not respond positively to either UUI or SUI questions, a positive response to "During the past year, have you leaked or lost even a small amount of urine during non-physical activities?" was categorized as other UI. Any positive response to a UI question was considered as having UI. Trained interviewers asked the above questions at MECs.

### 2.4. Assessment of covariates

Referring to previous NHANES literature [33,34], information on baseline data was collected through questionnaires and

laboratory tests, including age (years), sex (male or female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, or other race), educational level (below high school, high school, or above high school), and marital status (married/living with partner or living alone). The poverty-income ratio (PIR) is the total family income divided by the poverty threshold for the year of the interview [35]. Participants who reported smoking less than 100 cigarettes over their lifetime were considered never smokers [36,37]. Current smokers were those who had smoked more than 100 cigarettes in their lifetime, while former smokers were individuals who had smoked more than 100 cigarettes but had quit smoking [36]. We categorized drinking status as nondrinker, low-to-moderate drinker (men: less than 2 drinks per day; women: less than 1 drink per day), or heavy drinker (men: 2 or more drinks per day; women: 1 or more drinks per day) [36]. Referring to previous studies [38,39], we assessed the levels of physical activity in NHANES by assessing metabolic equivalents (METs) using a standardized questionnaire, and classified as inactive (no leisure-time physical activity), insufficiently active (moderate activity 1 to 5 times per week with MET 3 to 6 or vigorous activity 1 to 3 times per week with MET greater than 6), and active (individuals who engaged in more moderate or vigorous physical activity than above) [40,41]. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared ($kg/m^2$). Urinary creatinine levels were determined using standard laboratory methods.

### 2.5. Statistical analysis

Normally distributed continuous variables were described as means (standard errors [SEs]). Continuous variables that were not normally distributed were presented as medians (interquartile ranges [IQRs]). Categorical variables were presented as numbers (percentages). To normalize the distributions of urinary PAH metabolites, their concentrations were subjected to ln-transformation. Participants were divided into two groups according to sex. We used Spearman correlation analysis to investigate pairwise correlations between these metabolites. All statistical analyses were conducted using R software (version 4.2.0), and a *P*-value $<0.05$ (two-sided) was considered statistically significant.

**Table 1**
Baseline characteristics of adults with urinary polycyclic aromatic hydrocarbons (PAHs) metabolites in NHANES 1999–2018.

| Characteristics | Total | Men | Women | |
|---|---|---|---|---|
| Participants, N | 8136 | 4177 | 3959 | |
| Age, years | 45.85 (0.29) | 44.74 (0.38) | 46.97 (0.34) | <0.001 |
| Race/ethnicity, % | | | | 0.029 |
| Mexican American | 1339 (16.46) | 691 (9.70) | 648 (8.06) | |
| Other Hispanic | 817 (10.04) | 383 (5.64) | 434 (5.52) | |
| Non-Hispanic White | 3390 (41.67) | 1759 (66.76) | 1631 (66.59) | |
| Non-Hispanic Black | 1758 (21.61) | 913 (10.75) | 845 (12.40) | |
| Other race | 832 (10.23) | 431 (7.14) | 401 (7.43) | |
| Marital status (%) | | | | <0.001 |
| Married or living with partner | 4823 (59.28) | 2701 (67.33) | 2122 (58.51) | |
| Living alone | 3313 (40.72) | 1476 (32.67) | 1837 (41.49) | |
| Education level, % | | | | 0.055 |
| Below high school | 2071 (25.45) | 1097 (18.23) | 974 (15.98) | |
| High school | 1870 (22.98) | 990 (23.21) | 880 (22.58) | |
| Above high school | 4195 (51.56) | 2090 (58.56) | 2105 (61.44) | |
| Smoking status, % | | | | <0.001 |
| Never smoker | 4479 (55.05) | 1954 (49.13) | 2525 (60.17) | |
| Former smoker | 1889 (23.22) | 1187 (27.64) | 702 (20.35) | |
| Current smoker | 1768 (21.73) | 1036 (23.23) | 732 (19.48) | |
| Drinking status, % | | | | <0.001 |
| Nondrinker | 1678 (20.62) | 526 (10.09) | 1152 (22.45) | |
| Low-to-moderate drinker | 5750 (70.67) | 3221 (78.57) | 2529 (68.34) | |
| Heavy drinker | 708 (8.7) | 430 (11.33) | 278 (9.21) | |
| Physical activity, % | | | | <0.001 |
| Inactive | 1798 (22.1) | 753 (13.91) | 1045 (21.56) | |
| Insufficiently active | 3334 (40.98) | 1663 (41.72) | 1671 (44.67) | |
| Active | 3004 (36.92) | 1761 (44.37) | 1243 (33.78) | |
| Body mass index, $kg/m^2$ | 28.91 (0.11) | 28.85 (0.14) | 28.96 (0.16) | 0.578 |
| Family PIR, % | 2.99 (0.04) | 3.04 (0.04) | 2.93 (0.04) | 0.015 |
| Urinary creatinine, mg/dL | 105.00 [56.00,162.00] | 128.00 [76.00,180.00] | 84.00 [43.00,135.00] | <0.001 |
| Self-reported diabetes, % | 971 (11.93) | 522 (9.18) | 449 (8.66) | 0.538 |
| Self-reported SUI, % | 1726 (21.21) | 127 (2.40) | 1599 (42.11) | <0.001 |
| Self-reported UUI, % | 1623 (19.95) | 553 (10.38) | 1070 (25.11) | <0.001 |
| Self-reported MUI, % | 739 (9.08) | 71 (1.10) | 668 (16.34) | <0.001 |
| Self-reported other UI, % | 577 (7.09) | 176 (3.80) | 401 (9.59) | <0.001 |
| Self-reported any UI, % | 2742 (33.7) | 686 (13.68) | 2056 (52.59) | <0.001 |

Abbreviations: PIR, poverty income ratio; UI, urinary incontinence; SUI, stress urinary incontinence; UUI, urgency urinary incontinence; MUI, mixed urinary incontinence. Normally distributed continuous variables are described as means ± SEs, and continuous variables without a normal distribution are presented as medians [interquartile ranges]. Categorical variables are presented as numbers (percentages). N reflect the study sample while percentages reflect the survey-weighted data.

Multiple logistic regression models were utilized to evaluate the connection between different quartiles of urinary PAH metabolites which were ln-transformed, and the prevalence of UI. The upsurge in UI prevalence was reported using Odds ratios (ORs) along with a 95 % confidence interval (CI). All models were adjusted for age, sex, race, marital status, education levels, PIR, smoking status, drinking status, BMI, physical activity, and self-reported diabetes. Additionally, restricted cubic spline (RCS) regression models were employed to explore the dose-response relationship between urinary PAH metabolites and the prevalence of UI. Referring to previous studies, RCS is particularly suitable for analyzing nonlinear dose-response relationships, offering flexibility in capturing variable effects across different intervals [34,42]. In this study, RCS models with three knots positioned at the 10th, 50th, and 90th percentiles of each urinary PAH metabolite were applied to better capture the nonlinear association between PAH exposure and UI prevalence while mitigating the influence of extreme values [43].

Quantile g-computation (QG-C), a statistical method specifically designed for analyzing mixture effects, was used to evaluate the combined impact of urinary PAH metabolites on the prevalence of UI. This method combines the simplicity of weighted quantile sum (WQS) regression with the flexibility of g-computation, allowing for unbiased inference on mixture effects while maintaining appropriate CI coverage [44]. QG-C enables the estimation of the expected change in outcome resulting from a simultaneous increase in all components of the mixture by one quantile. Unlike traditional methods, QG-C does not require directional homogeneity among the chemicals included in the mixture, thus allowing for both positive and negative weight coefficients to reflect the relative contribution of each component. In this study, QG-C was applied to examine the mixture effect of urinary PAH metabolites on UI prevalence, revealing the potential synergistic and antagonistic effects within the PAH mixture.

## 3. Results

### 3.1. Basic characteristics

A total of 8136 participants were included in our study and their baseline characteristics are presented in Table 1. The median age of the participants was 45.9 years, and 48.7 % were female. The prevalence of self-reported SUI, UUI, MUI, and any UI was 21.21 %, 19.95 %, 9.08 %, and 33.7 %, respectively. Significant differences were observed between male and female participants, with female

**Table 2**
Multivariate logistic regression associations of ln-transformed urinary polycyclic aromatic hydrocarbons (PAHs) metabolites with the prevalence of urinary incontinence in adults.

| | Total (n = 8136) | | Men (n = 4177) | | Women (n = 3959) | |
|---|---|---|---|---|---|---|
| | OR (95 % CI) | *P* value | OR (95 % CI) | *P* value | OR (95 % CI) | *P* value |
| SUI | | | | | | |
| 1-NAP | 1.03 (0.97–1.10) | 0.320 | 1.04 (0.86–1.25) | 0.682 | 1.03 (0.97–1.10) | 0.342 |
| 2-NAP | 1.07 (0.97–1.18) | 0.174 | 1.17 (0.86–1.58) | 0.319 | 1.06 (0.95–1.19) | 0.321 |
| 3-FLU | 1.22 (1.12–1.33) | <0.001 | 1.25 (0.95–1.65) | 0.107 | 1.22 (1.10–1.34) | <0.001 |
| 2-FLU | 1.26 (1.14–1.39) | <0.001 | 1.25 (0.92–1.70) | 0.156 | 1.26 (1.13–1.41) | <0.001 |
| 1-PHE | 1.11 (0.98–1.26) | 0.107 | 1.15 (0.77–1.72) | 0.491 | 1.11 (0.97–1.27) | 0.133 |
| 1-PYR | 1.22 (1.09–1.36) | <0.001 | 1.22 (0.93–1.60) | 0.145 | 1.23 (1.08–1.39) | 0.002 |
| UUI | | | | | | |
| 1-NAP | 1.08 (1.02–1.15) | 0.016 | 1.12 (1.00–1.25) | 0.056 | 1.07 (1.00–1.15) | 0.038 |
| 2-NAP | 0.98 (0.90–1.06) | 0.613 | 1.19 (1.04–1.36) | 0.011 | 0.89 (0.79–1.00) | 0.051 |
| 3-FLU | 1.04 (0.94–1.14) | 0.450 | 1.14 (0.98–1.32) | 0.081 | 0.99 (0.88–1.12) | 0.870 |
| 2-FLU | 1.02 (0.92–1.13) | 0.664 | 1.10 (0.93–1.31) | 0.216 | 0.99 (0.87–1.12) | 0.846 |
| 1-PHE | 1.01 (0.90–1.13) | 0.890 | 0.90 (0.76–1.06) | 0.201 | 1.08 (0.93–1.26) | 0.302 |
| 1-PYR | 1.04 (0.97–1.13) | 0.289 | 1.09 (0.96–1.24) | 0.183 | 1.02 (0.91–1.14) | 0.745 |
| MUI | | | | | | |
| 1-NAP | 1.05 (0.97–1.15) | 0.206 | 1.08 (0.89–1.30) | 0.453 | 1.06 (0.97–1.15) | 0.215 |
| 2-NAP | 1.01 (0.88–1.17) | 0.860 | 1.37 (1.06–1.78) | 0.019 | 0.99 (0.85–1.14) | 0.867 |
| 3-FLU | 1.10 (0.96–1.26) | 0.183 | 1.46 (1.05–2.03) | 0.024 | 1.07 (0.92–1.23) | 0.390 |
| 2-FLU | 1.13 (0.97–1.31) | 0.123 | 1.35 (0.88–2.07) | 0.163 | 1.10 (0.94–1.30) | 0.235 |
| 1-PHE | 1.13 (0.96–1.33) | 0.142 | 1.27 (0.83–1.94) | 0.260 | 1.12 (0.94–1.33) | 0.196 |
| 1-PYR | 1.17 (1.02–1.35) | 0.027 | 1.49 (1.16–1.92) | 0.002 | 1.14 (0.98–1.33) | 0.099 |
| Any UI | | | | | | |
| 1-NAP | 1.06 (1.01–1.11) | 0.026 | 1.07 (0.97–1.19) | 0.193 | 1.06 (1.00–1.13) | 0.073 |
| 2-NAP | 0.99 (0.92–1.07) | 0.790 | 1.08 (0.95–1.23) | 0.267 | 0.95 (0.85–1.06) | 0.374 |
| 3-FLU | 1.13 (1.05–1.23) | 0.003 | 1.10 (0.96–1.26) | 0.173 | 1.16 (1.06–1.28) | 0.002 |
| 2-FLU | 1.13 (1.03–1.23) | 0.009 | 1.07 (0.92–1.24) | 0.400 | 1.18 (1.05–1.32) | 0.006 |
| 1-PHE | 1.03 (0.93–1.14) | 0.573 | 0.92 (0.79–1.08) | 0.291 | 1.11 (0.98–1.26) | 0.116 |
| 1-PYR | 1.09 (1.00–1.18) | 0.049 | 1.07 (0.95–1.22) | 0.257 | 1.11 (0.98–1.25) | 0.089 |

Abbreviations: OR, odds ratio; CI, confidence interval; UI, urinary incontinence; SUI, stress urinary incontinence; UUI, urgency urinary incontinence; MUI, mixed urinary incontinence; Models were adjusted for age (continuous), sex (male, or female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, or other race), marital status (married or living with partner, or living alone), education level (below high school, high school, or above high school), family poverty income ratio (continuous), smoking status (never smoker, former smoker, or current smoker), drinking status (nondrinker, low-to-moderate drinker, or heavy drinker), BMI (continuous), physical activity (inactive, insufficiently active, or active), self-reported diabetes (yes, or no).

participants being older, more likely to live alone, nondrinkers, never smokers, and less physically active ($P < 0.001$). They also had lower urinary creatinine levels and a higher prevalence of UI ($P < 0.001$).

### 3.2. Distributions and correlations of urinary PAHs metabolites

The detection limits and distributions of six urinary PAH metabolites are shown in Table S1. 2-NAP and 2-FLU had a detection rate of 100 %, while all other PAHs had a detection rate higher than 89 %. The median concentrations of urinary 1-NAP, 2-NAP, 3-FLU, 2-FLU, 1-PHE, and 1-PYR were 1797 (IQR 730, 6595) ng/L, 4734 (IQR 2052, 10718) ng/L, 84 (IQR 40, 261) ng/L, 229 (IQR 111, 590) ng/L, 124 (IQR 65, 230) ng/L, and 109 (IQR 50, 225) ng/L, respectively. Most urinary PAHs showed strong positive correlations (Spearman's $r > 0.6$), with 2-FLU and 3-FLU demonstrating correlation coefficients above 0.9 (Fig. S2).

### 3.3. Association between urinary PAHs metabolite and the prevalence of UI in the total population

Using a multivariate logistic regression model, Table 2 shows the correlation between the prevalence of UI and the continuous urine PAH metabolites. Urinary 3-FLU (OR = 1.22, 95%CI: 1.12–1.33, $P < 0.001$), 2-FLU (OR = 1.26, 95%CI: 1.14–1.39, $P < 0.001$), and 1-PYR (OR = 1.22, 95%CI: 1.09–1.36, $P < 0.001$) showed significant positive associations with SUI, and 1-NAP (OR = 1.06, 95%CI: 1.01–1.11, $P = 0.026$), 3-FLU (OR = 1.13, 95%CI: 1.05–1.23, $P = 0.003$), 2-FLU (OR = 1.13, 95%CI: 1.03–1.23, $P = 0.009$), and 1-PYR (OR = 1.09, 95%CI: 1.00–1.18, $P = 0.049$) showed significant positive associations with any UI. It's interesting that only women showed these correlations.

### 3.4. Association between urinary PAH metabolites and the prevalence of UI in adult women

Multiple logistic regressions were used to further examine associations between urine PAH metabolites and the occurrence of UI in

**Table 3**
Multivariate logistic regression associations of quartiles of urinary polycyclic aromatic hydrocarbons (PAHs) metabolites with the prevalence of urinary incontinence in women.

| | Quartiles of urinary PAHs metabolites | | | | $P_{trend}$ |
|---|---|---|---|---|---|
| | OR | OR (95 % CI) | OR (95 % CI) | OR (95 % CI) | |
| SUI | | | | | |
| 1-NAP | 1.00 [Reference] | 1.09 (0.85–1.39) | 1.13 (0.86–1.48) | 1.14 (0.85–1.52) | 0.336 |
| 2-NAP | 1.00 [Reference] | 1.11 (0.85–1.46) | 1.00 (0.77–1.30) | 1.16 (0.85–1.58) | 0.492 |
| 3-FLU | 1.00 [Reference] | 1.45 (1.13–1.87) | 1.22 (0.98–1.53) | 1.72 (1.27–2.33) | 0.002 |
| 2-FLU | 1.00 [Reference] | 1.19 (0.93–1.52) | 1.07 (0.83–1.38) | 1.75 (1.29–2.38) | 0.008 |
| 1-PHE | 1.00 [Reference] | 0.96 (0.75–1.23) | 1.10 (0.83–1.46) | 1.13 (0.86–1.50) | 0.242 |
| 1-PYR | 1.00 [Reference] | 1.19 (0.90–1.58) | 1.37 (1.03–1.82) | 1.44 (1.05–1.96) | 0.012 |
| UUI | | | | | |
| 1-NAP | 1.00 [Reference] | 1.08 (0.81–1.45) | 1.27 (0.93–1.73) | 1.30 (0.93–1.81) | 0.081 |
| 2-NAP | 1.00 [Reference] | 0.83 (0.63–1.09) | 0.79 (0.60–1.05) | 0.76 (0.56–1.04) | 0.063 |
| 3-FLU | 1.00 [Reference] | 0.99 (0.75–1.30) | 1.20 (0.93–1.55) | 1.06 (0.75–1.50) | 0.299 |
| 2-FLU | 1.00 [Reference] | 1.02 (0.79–1.32) | 1.20 (0.91–1.59) | 1.09 (0.79–1.51) | 0.259 |
| 1-PHE | 1.00 [Reference] | 1.19 (0.90–1.57) | 1.32 (1.01–1.73) | 1.26 (0.92–1.71) | 0.120 |
| 1-PYR | 1.00 [Reference] | 1.26 (0.97–1.64) | 1.10 (0.87–1.39) | 1.21 (0.92–1.59) | 0.283 |
| MUI | | | | | |
| 1-NAP | 1.00 [Reference] | 1.09 (0.77–1.56) | 1.20 (0.80–1.78) | 1.10 (0.74–1.64) | 0.519 |
| 2-NAP | 1.00 [Reference] | 0.91 (0.66–1.26) | 0.93 (0.65–1.33) | 0.99 (0.68–1.43) | 0.898 |
| 3-FLU | 1.00 [Reference] | 1.15 (0.81–1.62) | 1.32 (0.97–1.79) | 1.24 (0.83–1.86) | 0.120 |
| 2-FLU | 1.00 [Reference] | 0.96 (0.69–1.34) | 1.16 (0.83–1.64) | 1.32 (0.91–1.93) | 0.129 |
| 1-PHE | 1.00 [Reference] | 1.24 (0.86–1.78) | 1.35 (0.94–1.95) | 1.33 (0.93–1.91) | 0.112 |
| 1-PYR | 1.00 [Reference] | 1.52 (1.12–2.06) | 1.25 (0.89–1.76) | 1.50 (1.04–2.15) | 0.076 |
| Any UI | | | | | |
| 1-NAP | 1.00 [Reference] | 1.10 (0.88–1.39) | 1.26 (0.97–1.65) | 1.31 (1.00–1.72) | 0.033 |
| 2-NAP | 1.00 [Reference] | 0.95 (0.71–1.26) | 0.83 (0.64–1.06) | 0.87 (0.64–1.19) | 0.242 |
| 3-FLU | 1.00 [Reference] | 1.34 (1.04–1.72) | 1.24 (0.97–1.59) | 1.58 (1.17–2.15) | 0.005 |
| 2-FLU | 1.00 [Reference] | 1.25 (0.98–1.59) | 1.16 (0.89–1.52) | 1.65 (1.20–2.25) | 0.004 |
| 1-PHE | 1.00 [Reference] | 0.99 (0.78–1.26) | 1.17 (0.87–1.57) | 1.17 (0.89–1.54) | 0.137 |
| 1-PYR | 1.00 [Reference] | 1.07 (0.82–1.39) | 1.25 (0.99–1.59) | 1.23 (0.90–1.67) | 0.097 |

Abbreviations: OR, odds ratio; CI, confidence interval; UI, urinary incontinence; SUI, stress urinary incontinence; UUI, urgency urinary incontinence; MUI, mixed urinary incontinence; Models were adjusted for age (continuous), sex (male, or female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, or other race), marital status (married or living with partner, or living alone), education level (below high school, high school, or above high school), family poverty income ratio (continuous), smoking status (never smoker, former smoker, or current smoker), drinking status (nondrinker, low-to-moderate drinker, or heavy drinker), BMI (continuous), physical activity (inactive, insufficiently active, or active), self-reported diabetes (yes, or no).

adult women (Table 3). In contrast to the lowest quantiles in women, higher quantiles of 3-FLU, 2-FLU, and 1-PYR were linked with increasing prevalence of SUI (OR = 1.72, 95%CI = 1.27–2.33, *P* for trend = 0.002), 2-FLU, (OR = 1.75, 95%CI = 1.29–2.38, *P* for trend = 0.008), and 1-PYR, (OR = 1.44, 95%CI = 1.05–1.96, *P* for trend = 0.012). Women exposed to greater levels of 1-NAP (OR = 1.31, 95%CI = 1.00–1.72, *P* for trend = 0.033), 3-FLU (OR = 1.58, 95%CI = 1.17–2.15, *P* for trend = 0.005), and 2-FLU (OR = 1.65, 95%CI = 1.20–2.25, *P* for trend = 0.004) showed an increase in the prevalence of any UI. Fig. 1 shows that the prevalence of SUI in women was positively and linearly associated to the ln-transformed 3-FLU, 2-FLU, and 1-PYR in RCS models (*P* for nonlinearity>0.05). This relationship also existed between 1-NAP, 3-FLU, and 2-FLU and the prevalence of any UI in women (*P* for nonlinearity>0.05).

### 3.5. Association between mixtures of PAHs and the prevalence of UI in adult women

Six urinary PAHs were evaluated for their combined effects on adult females using the QG-C model (Table 4). The mixed presence of urinary PAHs was substantially linked to a higher prevalence of SUI (OR = 1.09, 95%CI: 1.01–1.19, *P* = 0.038). Urinary 2-FLU made the biggest positive impact, whereas 2-NAP made the biggest negative contribution to the overall effect (Fig. 2). However, in adult women, there was no statistically significant correlation between the mixture of PAHs and the prevalence of the other three UIs.

## 4. Discussion

In this study, we examined the relationship between exposure to PAHs and UI in the general adult population. Using multiple logistic regression models, urinary 3-FLU, 2-FLU, and 1-PYR were found to be positively associated with SUI. Additionally, 1-NAP, 3-FLU, and 2-FLU showed significant positive associations with any UI. Interestingly, these associations were found only in women. Furthermore, there were positive linear relationships between urinary PAH concentrations and the prevalence of SUI and any UI in adult women. When examining the joint effect using the QG-C model, the mixture of six PAHs was associated with a significantly increased prevalence of SUI. Moreover, we emphasized 2-FLU as the strongest risk factor for SUI in women.

Our study findings on the potential association between PAHs and UI are consistent with previous research indicating the diverse health effects of PAH exposure on various bodily systems, including the urinary system. Bosetti et al. found that the risk of bladder cancer is increased in people with occupations associated with PAHs, highlighting the adverse impact of PAHs on bladder health [45].

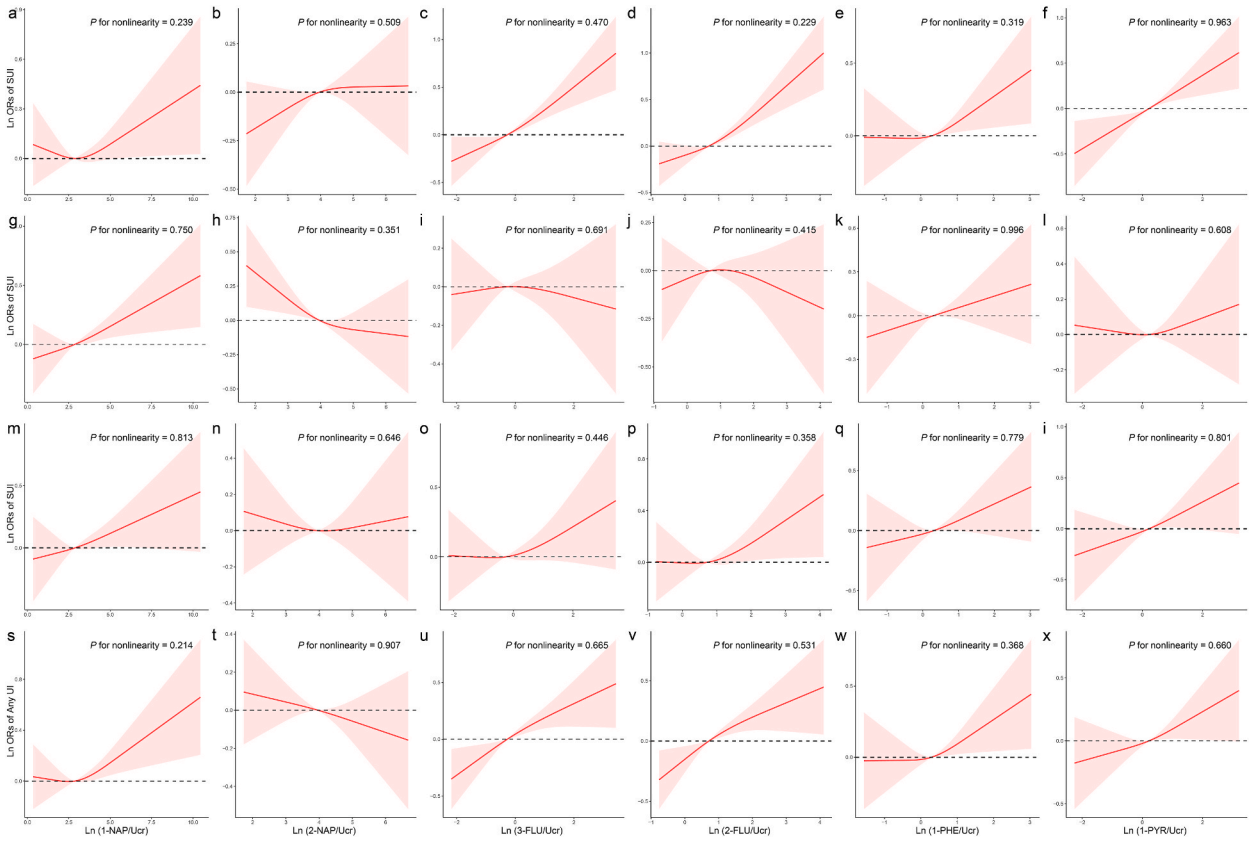


**Fig. 1.** Restricted cubic spline (RCS) regression analysis of the associations of ln-transformed urinary polycyclic aromatic hydrocarbons (PAHs) metabolites with the prevalence of urinary incontinence (UI) in women. Adjusted for age, sex, race, marital status, education levels, PIR, smoking status, drinking status, BMI, physical activity, and self-reported diabetes.

**Table 4**
Quantile g-computation model to assess the association of the mixture of urinary polycyclic aromatic hydrocarbons (PAHs) metabolites with urinary incontinence in women.

| Outcomes | OR (95 % CI) | *P* value | Sum of positive coefficients | Sum of negative coefficients |
|---|---|---|---|---|
| SUI | 1.09 (1.01–1.19) | 0.038 | 0.153 | −0.066 |
| UUI | 1.06 (0.97–1.16) | 0.201 | 0.191 | −0.131 |
| MUI | 1.07 (0.98–1.16) | 0.125 | 0.162 | −0.098 |
| Any UI | 1.09 (0.98–1.22) | 0.174 | 0.164 | −0.077 |

Abbreviations: OR, odds ratio; CI, confidence interval; UI, urinary incontinence; SUI, stress urinary incontinence; UUI, urgency urinary incontinence; MUI, mixed urinary incontinence; Models were adjusted for age (continuous), sex (male, or female), race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, or other race), marital status (married or living with partner, or living alone), education level (below high school, high school, or above high school), family poverty income ratio (continuous), smoking status (never smoker, former smoker, or current smoker), drinking status (nondrinker, low-to-moderate drinker, or heavy drinker), BMI (continuous), physical activity (inactive, insufficiently active, or active), self-reported diabetes (yes, or no).

Farzan et al. suggested that PAHs may contribute to kidney dysfunction in adolescents [46]. They discovered statistically significant relationships between the levels of serum uric acid and the estimated glomerular filtration rate (eGFR), as well as PAH metabolites. Li et al. provided evidence that PAH exposure might potentially be related to albuminuria, indicating potential renal impairment associated with PAH exposure [47]. Rahman et al. looked into the relationship between seven urine PAH concentrations in the US adult population, including 1-NAP, 2-NAP, 3-FLU, 2-FLU, 1-PHE, 2-PHE, and 3-PHE [48]. They discovered that only 2-NAP in the urine is significantly linked to an elevated risk of developing chronic kidney disease (CKD), as opposed to the other six types of urinary PAHs. These findings underscore the relevance of specific PAH metabolites, such as 2-NAP, in contributing to urinary system dysfunction, consistent with our study's observations. According to Shiue et al., kidney stones are substantially correlated with urinary 2-FLU, 3-FLU, 1-PHE, 1-PYR, and 2-NAP levels [49]. Our study adds to this body of evidence by establishing, to the best of our knowledge, the first association between PAH exposure and the prevalence of UI in the general adult population. By demonstrating a significant correlation between PAH metabolites and UI prevalence, our findings underscore the importance of considering environmental PAH exposure as a potential risk factor for urinary health outcomes.

It's interesting to note that our research indicated that women may have a higher risk of UI than men when exposed to PAHs. In the correlation of PAHs with other disorders, this gender disparity also surfaced. Zhou et al. observed that the presence of kidney stones is significantly positively correlated with 2-NAP and 9-FLU in multivariable logistic regression studies [50]. More significantly connected with kidney stones among female individuals was PAH exposure (high 2-NAP, 1-PHE, and 2-PHE). The endocrine-disrupting properties of PHAs may play a role in this connection [51]. The equilibrium of the hypothalamic-pituitary-gonadal axis can be upset, according to earlier research [52]. Low-dose PAH combinations have been shown by Peng et al. to affect rats' levels of steroid hormones [53]. According to another study, PAHs may affect the leytid cells in the testis and lower serum testosterone levels [54]. According to Zajda et al.'s research, PAHs can decrease the release of estradiol by interfering with granule cell activity via the ESR1 and GPER1 receptors [55]. According to studies, UI and sex hormone insufficiency go hand in hand [56]. In particular, MUI and SUI, Zhao et al. discovered unfavorable interactions between testosterone and UI [57]. Augoulea et al. found that women with SUI have significantly lower serum estradiol levels [58]. According to our findings, the public needs to pay immediate attention to women's PAH exposure.

Additionally, exposure to PAHs is positively correlated with oxidative stress and an inflammatory response, both of which are known to be significant risk factors for the emergence of UI. High-sensitivity C-reactive protein (hs-CRP), 8-hydroxy-2′-deoxyguanosine (8-OHdG), and malondialdehyde (MDA) are a few examples of the inflammatory response and oxidative stress biomarkers that have been linked to PAH exposure [59,60]. Zhang et al. also confirmed the above point [61]. y encouraging the immunological response of T cells and dendritic cells (DCs) through the metabolism of polycyclic aromatic hydrocarbons (PAHs) and cytochrome P450 (CYP), PAHs exacerbate the inflammatory response [62]. Huang et al. suggested that ceRNA hsa_circ_0039929/hsa-miR-15b-3p_R-1/FGF2 played an important role in the inflammation and epithelial-mesenchymal transition (EMT) caused by low molecular weight-PAHs (LMW-PAHs) [63]. SUI may be linked to altered extracellular matrix metabolism, estrogen receptors, oxidative stress, apoptosis, inflammation, neurodegenerative processes, and muscle cell differentiation and contractility, according to the data [64]. Constant oxidative stress may be a major component in encouraging bladder overactivity, according to earlier research [65].

The representative sample size in this study gives us the ability to extrapolate the findings to the non-institutionalized civilian population in the United States, which is one of its strong points. Additionally, sex is a significant factor influencing the prevalence of UI, and as such, we carefully examined the association between PAH exposure and UI prevalence across both male and female participants. However, our analysis revealed that the associations between urinary PAH metabolites and UI were more pronounced and consistent in women, with stronger effect sizes observed. The use of stratified analysis allowed us to identify the adult population most at risk for PAH exposure, particularly highlighting the elevated vulnerability in women. This targeted approach provides valuable insights into gender differences in the health impacts of environmental exposures, which is a critical aspect of our study. Third, to calculate the impacts of PAH combinations on UI, this study used an innovative and complex methodology. A recently created model called QG-C is used to analyze the health consequences of chemical mixtures and pinpoints the elements that are most responsible for the connections that are seen.

There are several limitations to this study that must be considered when interpreting the results. First, as a cross-sectional study, we are unable to establish a causal relationship between urinary PAH metabolites and the prevalence of UI. The observed associations do

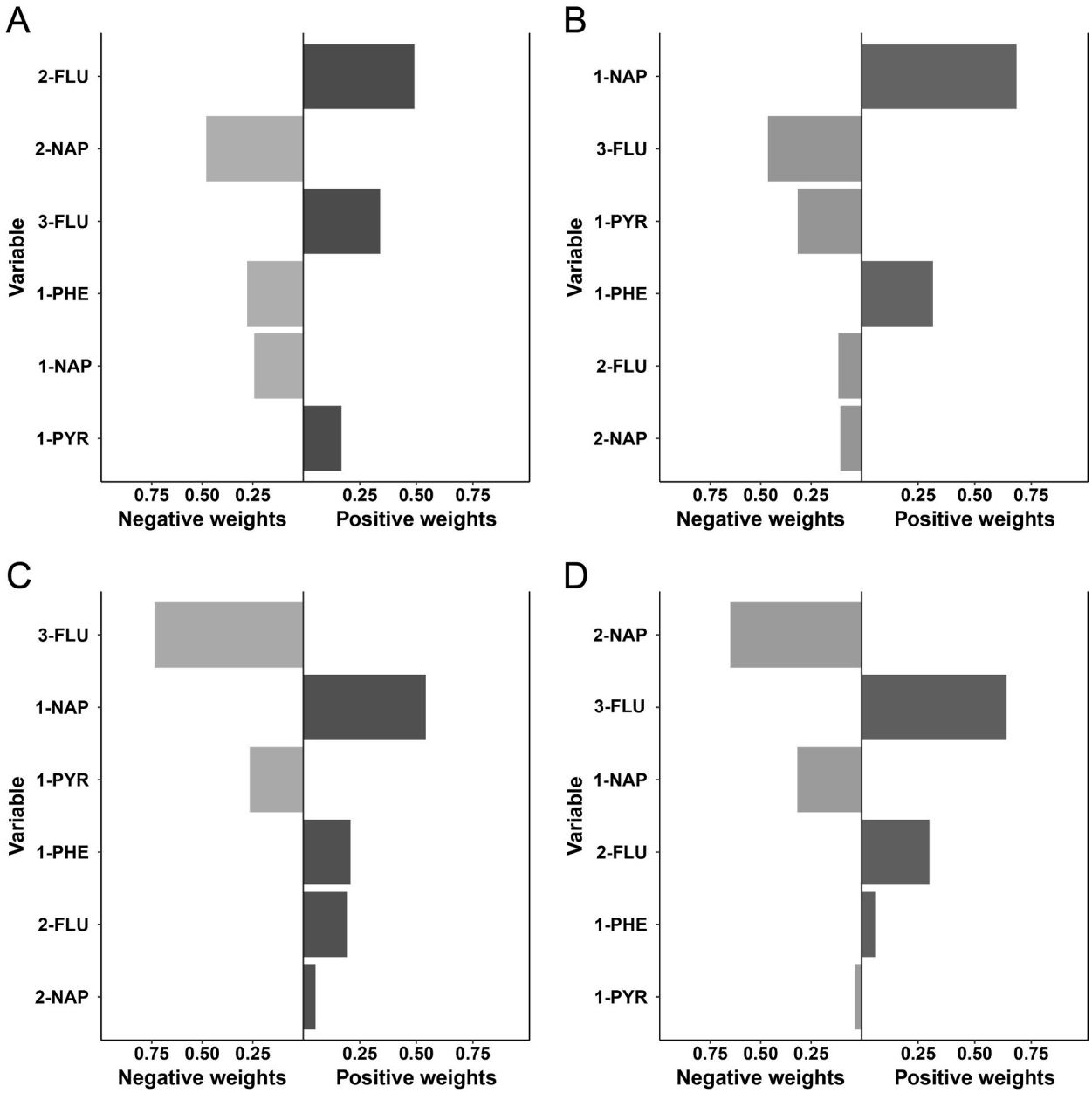


**Fig. 2.** Contribution of each compound to the mixture effect of urinary polycyclic aromatic hydrocarbons (PAHs) metabolites on the prevalence of urinary incontinence (UI) in women. Quantile g-computation model adjusting for age, sex, race, marital status, education levels, PIR, smoking status, drinking status, BMI, physical activity, and self-reported diabetes.

not imply causality, and longitudinal or experimental studies are needed to better understand the directionality of these relationships. Second, the prevalence of UI was determined based on participant self-reported questionnaires, which may introduce recall or reporting biases and may not fully capture the true prevalence of UI. This limitation could lead to an under- or overestimation of UI cases. Third, while we controlled for a range of potential confounders, there may still be unmeasured confounders that are linked to UI but were not included in our analysis. Factors such as underlying medical conditions, medication use, and other environmental exposures could also play a role in the development of UI and remain uncontrolled in our study. Lastly, the urinary PAH concentrations were assessed using single time-point urine samples, which may not accurately reflect participants' long-term exposure to PAHs. Given that PAH exposure can vary over time, relying on a single sample may underestimate or misclassify long-term exposure, potentially limiting the generalizability of the results. Longitudinal studies with repeated measurements of urinary PAHs would provide a more accurate assessment of long-term exposure and its effects on health outcomes.

## 5. Conclusion

Our research showed that being exposed to PAH is linked to the occurrence of SUI in adult women, which may be predominantly caused by 2-FLU. To corroborate the connections and underlying mechanism, more prospective population-based research is necessary.

## CRediT authorship contribution statement

**ChunXiang Bao:** Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jie Luo:** Writing – review & editing, Validation, Data curation. **ShuYing Miao:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition.

## Ethics approval and consent to participant

All participants provided written informed consent and study procedures were approved by the National Center for Health Statistics Research Ethics Review Board (Protocol Number: Protocol #2005-06 and Protocol #2011-17).

## Consent to publication

The manuscript is approved by all authors for publication.

## Data availability

NHANES data described in this manuscript are available at https://wwwn.cdc.gov/nchs/nhanes/.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2025.e42351.

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