Research Square

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Arsenic, Lead, Cadmium, Mercury and Hypertension among Asian Populations in the United States: NHANES 2011-2016

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Abstract

Background:

Asian Americans have been reported having higher arsenic (As), lead (Pb), cadmium (Cd) and mercury (Hg) levels, comparing with non-Asian Americans. Exposure to these metals/metalloids have been associated with risk of hypertension, however, limited studies have explored the associations of As, Pb, Cd and Hg levels with hypertension among general Asian Americans. This study aimed to investigate the associations of As, Pb, Cd and Hg levels with blood pressure and prevalence of hypertension among Asian Americans who participated in the 2011-2016 National Health and Nutrition and Examination Survey (NHANES).

Methods:

The study included participants aged 20 years and older with determinations of As, Pb, Cd and Hg in blood (n=7913) and urine (n=3954). These metals levels were measured by inductively coupled plasma mass spectrometry. Systolic (SBP) and diastolic blood pressure (DBP) levels were examined through a standardized protocol. Censored normal regression model and logistic regression model were employed to explore the associations of As, Pb, Cd and Hg levels with blood pressure levels and hypertension respectively, and potential confounders were also adjusted in these regression models.

Results:

In multivariable-adjusted models, blood Hg levels were associated with increased SBP (tertile 2 *vs.* tertile 1: β=-0.9 mmHg, 95%CI:-6.1, 4.4; tertile 3 *vs.* tertile 1: β=5.6, 95%CI: 0.0, 11.2; *P* trend=0.003), DBP level (tertile 2 *vs.* tertile 1: β=4.1 mmHg, 95% CI: 0.1, 8.1; tertile 3 *vs.* tertile 1: β=5.8 mmHg, 95% CI: 1.9, 9.7; *P* trend=0.003) and prevalence of hypertension (tertile 2 *vs.* tertile 1: OR=1.2, 95% CI: 0.4, 3.4; tertile 3 *vs.* tertile 1: OR=2.8, 95% CI: 1.1, 7.3; *P* trend=0.001) among Asian Americans. The positive associations were also found between blood methyl-Hg level and blood pressure levels and prevalence of hypertension, whereas we did not identify significant associations of As, Pb and Cd levels in blood and urine with blood pressure levels and hypertension among Asian Americans.

Conclusions:

Highly exposed to Hg level among Asian Americans might associated with increased blood pressure levels and prevalence of hypertension. Further prospective studies with larger sample size should be performed to warrant the results.

Introduction

Arsenic (As), lead (Pb), cadmium (Cd) and mercury (Hg) are ubiquitous toxic environmental contaminants, which are on the top priority contaminants list according to the Agency for Toxic Substance and Disease Registry [1]. These toxic metals/metalloids (hereafter simply referred to as metals) have been associated with blood pressure levels and the risk of hypertension. The longitudinal studies have shown that long-term As exposure may increase age-related blood pressure and risk of hypertension [2, 3]. A systematic review pooled 11 cross-sectional studies found that higher As exposure was positively associated with prevalence of hypertension [4]. Low-level Pb exposure was associated with increase blood pressure and risk of hypertension [5, 6]. An updated systematic review and meta-analyses identified a positive association between Cd exposure and blood pressure and/or hypertension [7]. Significant positive associations of Hg with blood pressures levels and hypertension have also been identified in a

meta-analyses [8]. As the leading risk factor globally for attributable deaths, high systolic blood pressure (SBP) accounts for 10.8 million (95% uncertainty interval:9.51–12.1) deaths (19·2% [16.9–21.3] of all deaths in 2019) [9]. In the United States (US), high SBP was also one of leading causes of deaths [10]. Therefore, exposure to these toxic metals is a public health concern, especially for those highly exposed subpopulation groups.

Staring 2011, the National Health and Nutrition and Examination Survey (NHANES) oversampled Asian population in US, and data for Asians were released in a separate race group. Previous studies based on NHANES 2011-2012 reported that levels of As, Pb, Cd and Hg in Asian population were higher than those in other racial/ethnic groups (including whites, blacks and Hispanics) in US [11, 12]. In Asian countries, epidemiological studies have investigated the associations of As, Pb, Cd and Hg with blood pressure levels and risk of hypertension [13-22], but the results were inconsistent across these studies. In addition, the Asian Americans were consisted of Asian Indian (22.4%), Chinese (19.5%) and other Asians (58.2%) (Awata et al. 2017b), which were quite different from the population included in previous studies performed in Asian countries. Levels of As, Pb, Cd and Hg among Asian Americans were less than those among Asian population in Asian countries, but higher than other racial/ethnic population in US [11]. Thus, it is necessary to assess associations of these metals with blood pressure levels and hypertension among Asian Americans.

This study aimed to investigate the associations of exposure to As, Pb, Cd and Hg with blood pressure levels and prevalence of hypertension among Asian Americans and other racial/ethnic groups in a representative sample of US adults who participated in the 2011-2016 NHANES. The exposure assessment includes whole blood Pb, Cd and Hg levels, and urinary As, Pb, Cd and Hg levels. Hg and As species, such as methyl-Hg (MeHg) and dimethylarsinic acid (DMA) were also considered in the present study due its toxicity effect on human health. The outcomes include SBP, diastolic blood pressure (DBP) and hypertension.

Methods

Study population

The population of the current study was derived from the 2011-2016 NHANES. The protocol of NHANES study was described previously [23-25]. Briefly, NHANES employs a complex, multistage probability sampling strategy among the civilian, noninstitutionalized U.S. population to investigate a nationally representative sample. Starting in 2011, a sample design was implemented in NHANES to oversample non-Hispanic Asians (NHA), in addition to the ongoing oversample of Hispanics, non-Hispanic blacks, older adults, and low-income whites/others. All participants completed household surveys conducted by trained study staff, which include questions about demographics and health history. The study protocol also includes standardized medical examinations, collection of a blood sample, and other in-person testing at mobile examination centers. Informed consent was obtained from all NHANES participants.

During 2011-2012, 2013-2014 and 2015-2016 NHANES cycles, 29, 902 participants were investigated. For the present study we included participants (n=16, 513) ≥ 20 years of age, both males and females, and all racial and ethnic groups, except those categorized as “other” (i.e., Pacific Islanders, Native Americans/Alaskan Natives, and multiracial individuals). The “other” race group was excluded because of its small sample size and the heterogeneous nature of the group. Furthermore, we excluded participants with missing blood pressure levels (n=1, 319) and data of covariates (n=1, 037), including sex, education, annual household income, serum cotinine level and alcohol consumption. The associations of metals levels in blood and urine with blood pressure levels and

hypertension were estimated separately. Thus, participants without data of blood Pb, Cd and Hg levels were excluded, which resulted in 7, 913 participants available for analyses based on blood metals (**Figure 1**). NHANES 2011-2016 examined a one-third sample of the study population of urinary As, Pb, Cd and Hg levels, leaving 3, 954 participants eligible for analyses based on urinary metals (**Figure 1**).

Exposure assessment

Whole blood Pb, Cd, total Hg levels were examined at the Environmental Health Sciences Laboratory of the Center for Disease Control and Prevention (CDC) National Center for Environmental Health (NCEH), using inductively coupled plasma mass spectrometry (ICP-MS). The limit of detection (LOD) was 0.25 μg/dL for Pb, 0.16 μg/L for Cd, and 0.16 μg/L for total Hg in NHANES 2011-2012. In NHANES 2013-2016, the LOD values were 0.07 μg/dL for Pb, 0.10 μg/L for Cd and 0.28 μg/L for total Hg. The detection rates of blood metals for participants included were as follow: blood Pb (99.63%), blood Cd (90.53%) and blood Hg (92.01%). In addition, Hg species levels in blood, including inorganic Hg, ethyl Hg and MeHg, are measured using a triple spike isotope dilution method which employs gas chromatography to separate the species followed by introduction into an ICP-MS for detection. The LOD values for inorganic Hg, ethyl Hg and MeHg were 0.27 μg/L, 0.16 μg/L and 0.12 μg/L respectively in these three NHANES cycles. The percentage of study participants with these Hg species levels over LOD was 25.7% for inorganic Hg, 2.3% for ethyl Hg and 87.8% for MeHg. Therefore, only MeHg was considered in final analyses.

Urinary total As, Pb, Cd and Hg levels were also examined using ICP-MS. The LOD was 1.25 μg/L for As, 0.0800 μg/L for Pb, 0.0560μg/L for Cd and 0.05 ng/ml for Hg in NHANES 2011-2012. In NHANES 2013-2016, the LOD for these metals were as follow: As, 0.26 μg/L; Pb, 0.036 μg/L, Cd, 0.030 μg/L; Hg, 0.13 ng/ml. The detection rates were 91.79% for Cd, 98.84% for As, 98.28% for Pb, and 73.19% for Hg among participants included. As species levels in urine, including arsenous acid, arsenic acid, arsenobetaine, arsenocholine, DMA and monomethylarsonic acid, are determined by using high performance liquid chromatography to separate the species coupled to an ICP-MS to detect the As species. The LOD values of As species were 0.48 μg/L for arsenous acid, 0.87 μg/L for arsenic acid, 1.19 μg/L for arsenobetaine, 0.28 μg/L for arsenocholine, 1.8 μg/L for DMA, 0.89 μg/L for monomethylarsonic acid in NHANES 2011-2012. In NHANES 2013-2016, the LOD for these As species were as follow: arsenous acid, 0.12 μg/L; arsenic acid, 0.79 μg/L; arsenobetaine, 1.16 μg/L; arsenocholine, 0.11 μg/L; DMA, 1.91 μg/L; monomethylarsonic acid, 0.20 μg/L; The percentage of study participants with arsenous acid, arsenic acid, arsenobetaine, arsenocholine, DMA and monomethylarsonic acid levels over LOD values was 50.2%, 2.2%, 49.3%, 13.9%, 74.8% and 51.8% respectively. Finally, DMA was included in current study due to low detection rate for other As species. Furthermore, urinary metal concentrations were corrected using the concentration of urinary creatinine concentration to account for the effect of urinary dilution.

For samples with metals levels below LOD, NHANES use “fill values” (LOD divided by the square root of 2). Detailed information about laboratory procedures have been described previously, including sample collection, storing and handling of specimens, quality control, and instrument and equipment used for the chemical analyses [26-34].

Blood pressure and hypertension

The blood pressure was measured consecutively three times after resting quietly in a seated position for 5 minutes. If a blood pressure measurement is interrupted or incomplete, a fourth attempt may be made. Mean SBP and DBP levels were computed discarding the first reading, except when only reading was eligible. Hypertension was defined as a mean SBP ≥ 130 mmHg, or a mean DBP ≥ 80 mmHg, or a self-reported antihypertension medication use currently, according to the 2017 ACC/AHA Guideline for High Blood Pressure in adults [35].

Covariates

Variables including age, sex, race/ethnicity, education, household income, body mass index (BMI), alcohol consumption and smoking (based on the serum cotinine concentration) were considered as potential confounders for the associations of metals levels with blood pressure and hypertension. Age was categorized into ≥20 to ≤39 years, 40 to 59 years and over 60 years. Race/ethnicity was self-reported as non-Hispanic white (NHA), non-Hispanic black (NHB), Mexican American (MA), other Hispanic (OH), non-Hispanic Asian (NHA). Education was classified as < high school, high school graduate/general education development, some college/associate in art degree and ≥ college graduate. Household income was grouped into < $20,000, $20,000 – < $55,000, $55,000 – < $75,000 and ≥ $75,000. Serum cotinine level was ln-transformed due to skew distribution. Alcohol consumption was classified as never drinker, ever drinker and current drinker. BMI was calculated as participant's weight in kilograms divided by the square of the participant's height in meters (kg/m^2). Previous study have demonstrated that fish was the major contributor to dietary Hg and As intake [12]. Omega-3 fatty acids may negatively confound or modify the association of As and Hg with hypertension because these fatty acids are derived from fish consumption and are known to have cardio-protective properties [12, 36]. The omega-3 fatty acid intake data was from two 24-hour recall and calculated as the sum of eicosapentaenoic acid (EPA; 20:5 n-3) and docosahexaenoic acid (DHA; 22:6 n-3). The omega-3 fatty acid data was then categorized into four groups according to quartile values which were determined based on the whole study sample.

Statistical analysis

Demographic characteristics, lifestyle factors, blood pressure and hypertension prevalence were described across racial/ethnic groups. Geometric means (GM) and their confidence intervals of metals concentrations in urine and blood were also described among racial/ethnic categories. Metals levels in urine and blood were categorized into 3 groups for analyses according to the tertile cutoff values which were based on weighted distribution in the whole study sample.

To explore the associations of metals exposure and blood pressure and prevalence of hypertension among NHA, we categorized racial/ethnic groups into other racial/ethnic groups (including NHW, NHB, MA and OH; hereafter these groups simply referred to non-Asian American or non-NHA) and Asian American, due to concentrations of As, Pb, Cd and Hg either in urine or blood in Asian American higher than those in non-Asian American. To account for the influence of antihypertensive medications on blood pressure, the censored normal regression model was employed to analysis the association of metals levels in blood or urine with SBP and DBP levels [37]. The relationship between metal levels in urine or blood and prevalence of hypertension were also explored using multivariable logistic regression model to estimate odds ratio (OR) and confidence interval (CI). All models were adjusted for age, gender, education, annual household income, serum cotinine level, alcohol consumption and BMI. For Hg, MeHg, As and DMA, omega-3 fatty acid intake was adjusted additionally. The dose-response trend of *p* value was calculated by using the median values in each tertile of metal level as continuous variables.

Since the NHANES study was performed with a complex survey design, all the statistical analyses accounted for the sampling weight, clusters and strata. All statistical analyses were used SAS version 9.4 (SAS Institute, Cary, NC), except for the associations of metals levels and blood pressure levels using the command of "*cnreg*" of Stata 13.0 (STATA Corp, College Station, Texas, USA). All the statistical analyses were two tailed, and the *p* values < 0.05 were considered statistically significant.

Results

The characteristics of the study population were presented in Table 1. The distributions of the selected characteristics were similar between participants with urinary metals levels and those with blood metals levels. The proportion of participants over 60 years was higher among NHW (31.6%). The weighted percentages of female were higher than male across racial/ethnic groups, except MA. A higher education status and household income were evident among NHA and NHW, compared with other racial/ethnic groups. More than 50% Asians have a college degree or higher. More than 40% Asians and Whites reported their annual household income ≥ $75,000. The serum cotinine level, alcohol consumption, and BMI variations were fairly large across Asian Americans and other racial/ethnic groups. The highest serum cotinine level was observed in NHB (GM, 0.77 μg/L), followed by NHW (GM, 0.24 μg/L), OH (GM, 0.14μg/L), MA (GM, 0.12μg/L) and NHA (GM, 0.07 μg/L). Approximated thirty percent of Asians were never drinker. Approximated 13.0% of Asians was obese. The proportion of omega-3 fatty acid at quartile 4 was over 40% among Asian Americans, which was higher than other racial/ethnic groups. The highest average SBP level was observed among the blacks (126 ± 0.7 mmHg), whereas the average DBP levels were close among these racial/ethnic groups. The weighted prevalence of hypertension above 40% was observed among whites, blacks and Asians according to the 2017 ACC/AHA Guideline [35].

Table 2 presents the GM and confidence intervals of urinary levels of As, DMA, Pb, Cd and Hg levels and blood levels of Pb, Cd and Hg and MeHg levels across racial/ethnic groups. The average metals levels among NHA were higher than other racial/ethnic groups either in urine or blood. Especially, the concentrations of urinary As (19.5 μg/g creatinine), urinary DMA (8.81 μg/g creatinine), blood Hg (2.06 μg/L) and MeHg (1.63 μg/L) among NHA were over 2 times higher than those across MA (urinary As: 6.92 μg/g creatinine; DMA: 3.67 μg/g creatinine; blood Hg: 0.62 μg/L; MeHg: 0.38 μg/L), OH (urinary As: 8.49 μg/g creatinine; DMA: 4.53 μg/L; blood Hg: 0.92 μg/L; MeHg: 0.64 μg/L), NHW (urinary As: 6.82 μg/g creatinine; DMA: 3.42 μg/L; blood Hg: 0.78 μg/L; MeHg: 0.52 μg/L) and NHB (urinary As: 6.87 μg/g creatinine; DMA: 2.86 μg/L; blood Hg: 0.83 μg/L; MeHg: 6.87 μg/L). Moreover, these metals levels in both urine and blood were approximated close among MA, OH, NHW and NHB. Therefore**,** the study population was divided into NHA and non-NHA groups for the stratified analyses.

For non-NHA, urinary As levels were significantly associated with increased SBP (tertile 2 *vs.* tertile 1: β=1.2, 95%CI: -0.8, 3.2; tertile 3 *vs.* tertile 1: β=2.5, 95%CI: 0.7, 4.4; *P* trend=0.012) (**Table 3**). Similar patterns were observed between urinary DMA levels and SBP levels (tertile 2 *vs.* tertile 1: β=0.2, 95%CI: -1.7, 2.0; tertile 3 *vs.* tertile 1: β=2.5, 95%CI: 0.8, 4.2; *P* trend=0.003) (**Table 3**). However, urinary As and DMA levels were not related to DBP levels and prevalence of hypertension. For NHA, there were no significant associations observed between urinary metals levels and blood pressure levels and hypertension (**Table 3**).

For participants with blood metals levels available, blood Pb levels were positively associated with increased SBP (tertile 2 *vs.* tertile 1: β=1.0, 95%CI: -0.3, 2.4; tertile 3 *vs.*tertile 1: β=3.0, 95%CI: 1.2, 4.8; *P* trend=0.002), DBP levels (tertile 2 *vs.* tertile 1: β=1.5, 95%CI: 0.7, 2.4; tertile 3 *vs.*tertile 1: β=2.0, 95%CI: 0.8, 3.1; *P* trend=0.013) and prevalence of hypertension (tertile 2 *vs.* tertile 1: OR=1.3, 95%CI: 1.1, 1.6; tertile 3 *vs.* tertile 1: OR=1.5, 95%CI: 1.2, 1.9; *P* trend=0.005) among non-NHA. For NHA, blood Hg levels were significantly associated with increased SBP (tertile 2 *vs.* tertile 1: β=-0.9, 95% CI: -6.1, 4.4; tertile 3 *vs.* tertile 1: β=5.6, 95% CI: 0.0, 11.2; *P* trend=0.003) and DBP (tertile 2 *vs.* tertile 1: β=4.1, 95% CI: 0.1, 8.1; tertile 3 *vs.* tertile 1: β=5.8, 95% CI: 1.9, 9.7; *P* trend=0.002) levels and prevalence of hypertension (tertile 2 *vs.* tertile 1: OR=1.2, 95% CI: 0.4, 3.4; tertile 3 *vs.* tertile 1: β=2.8, 95% CI: 1.1, 7.3; *P* trend=0.001) (**Table 4**). Similar patterns were also observed for MeHg (**Table 4**). However, blood Pb and Cd levels were not related to blood pressure levels and hypertension among NHA (**Table 4**).

Discussion

This study combines the NHANES 2011-2012, 2013-2014 and 2015-2016 cycles, and found that the levels of As, Pb, Cd and Hg in NHA aged 20 years and older were higher than those in non-NHA especially for As, DMA, Hg and MeHg levels. The positive associations were observed between blood Hg and MeHg levels and blood pressures levels and prevalence of hypertension among the NHA. In addition, blood Pb levels were positively associated with blood pressure levels and prevalence of hypertension for non-NHA, but not among NHA.

The relationship between As exposure and hypertension risk are extensively studied. Most studies focused on correlation between As levels in drinking water and risk of hypertension. A meta-analysis by Amiri et al. [38] found that odds of the hypertension would increase as 0.08% by increase of each unit in As concentration in drinking water. The studies concentrated on biomarkers of As exposure such as in urine [39-42], blood [43], hair [44] or nail [45] were limited, and the results were inconsistent. Three studies performed in China, including Zhong et al. [42] (urinary As GM: 75.84 μg/g creatinine), Shi et al. [41] (urinary As GM: 33.35 μg/L in non-hypertension subjects, 39.86 μg/L in hypertension subjects) and Li et al. (urinary As GM: 135.59 μg/g creatinine in non-hypertension subjects, 178.33 μg/g creatinine in hypertension subjects), have reported high urinary As levels, which was positively associated with prevalence of hypertension. In present study, the As levels in urine among NHA and non-NHA (GM: 6.92 μg/g creatinine in MA; 8.49 μg/g creatinine in OH; NHW, 6.82 μg/g creatinine in NHW; 6.87 in μg/g creatinine NHB; 19.5 μg/g creatinine in NHA) were lower than the previous studies. There was no significant association between As and DMA levels and prevalence of hypertension among NHA and non-NHA, although positive relationship was observed between As and DMA and SBP level among non-NHA. A study by Spratlen et al. performed in American Indian found no association between urinary As (median, 6.5 μg/L) and DMA levels and hypertension [40]. These studies indicated that low to moderate urinary As levels in NHA and non-NHA might be not associated with prevalence of hypertension.

The Hg and MeHg levels in blood among NHA were over twice higher than non-NHA. Significant positive associations of blood Hg and MeHg levels with blood pressure levels and prevalence of hypertension were observed among NHA, but not among non-NHA. It was indicated that Hg exposure levels may be a factor for this association. However, the association of Hg exposure and hypertension has been inconsistent in previous studies. The discrepancies may be due to differences in study populations and exposure levels, different Hg species and Hg biomarkers used to estimate the exposure, and confounders included [13, 45-50]. A meta-analysis by Hu et al. [8] has transformed the Hg levels in blood, urine and toenail reported by different studies to hair-Hg levels, and found a dose-response relationship between Hg exposure and risk of hypertension, but not for the MeHg, which might due to limited studies explored association of MeHg levels and risk of hypertension. However, Park et al. [47] have found no association of hypertension with blood Hg but a suggestive inverse association with urinary Hg in NHANES 2003-2006, which was inconsistent with present study. The reason may be due to the different survey cycles included, different confounders adjusted and not stratified the population into NHA and non-NHA. Further longitudinal studies should be performed to validate these results. Moreover, highly exposed to Hg among NHA are worth noting.

The Pb levels among NHA were slightly higher than non-NHA. However, the significant associations were observed between blood Pb and blood pressure levels and prevalence of hypertension among non-NHA, but not NHA. The results were consistent with a previous study based on NHANES data, which found significant positive associations between blood Pb levels and blood pressures among non-Hispanic Whites and non-Hispanic Blacks, but not for others (including Asians and other racial/ethnic groups) [51]. Previous studies also reported low-level Pb exposure

was associated with increase blood pressure levels and risk of hypertension [5, 6]. Although significant association of Pb exposure with hypertension among NHA was not observed, the adverse effect of Pb exposure on human health should not be ignored. Cross-sectional design, sample size, adaptation to Pb toxicity and lifestyle habits among NHA might preclude the present study from exploring the association between Pb exposure and risk of hypertension. Further prospective studies with larger sample size should be performed to explore the associations Pb exposure among NHA with risk of hypertension, as well as other health outcomes.

Significant associations between Cd levels in blood and urine and blood pressures and hypertension were not observed among NHA and non-NHA, which were inconsistent with previous study [52]. However, an updated systematic review on the association between Cd exposure, blood pressure and hypertension demonstrated that these association remains uncertain [7].

The findings of our study must be interpreted with caution. Firstly, single blood and urine metals measurements may be limited to fully assess metals exposure and metals internal dose. Secondly, it was difficult to conclude the causal effect with a cross-sectional design in current study. Thirdly, inherent differences across NHA and non-NHA, including lifestyle and social economic status, background prevalence of hypertension, cannot be fully ruled out, although these confounders were adjusted. Finally, the sample size of NHA is small, which may preclude precise estimations of parameters of these associations.

In conclusion, in this cross-sectional study of US general adults, we found positive association between blood Hg (mostly MeHg) and hypertension, and no associations for As, Pb, Cd levels in blood or urine among NHA. Further prospective studies should be performed to validate the association between higher Hg exposure and hypertension among NHA.

Abbreviations

As, arsenic; Pb, lead; Cd, cadmium; Hg, mercury; NHANES, National Health and Nutrition and Examination Survey; SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval; NHA, non-Hispanic Asians; ICP-MS, inductively coupled plasma mass spectrometry; LOD, limit of detection; BMI, body mass index; NHB, non-Hispanic black; MA, Mexican American; OH, other Hispanic; MeHg, methylmercury; DMA, Dimethylarsinic acid; NA, not available; GM, geometric mean.

Declarations

Availability of data and materials

All data generated and analyzed during this study are derived from the National Health and Nutrition and Examination Survey 2011-2016, which are available for the public (https://www.cdc.gov/nchs/nhanes/index.htm).

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors have approved the manuscript for submission.

Conflicts of interest

The authors declare no conflict of interest.

Authors' contributions

Hao Zhao: Conceptualization, Data curation, Methodology, Formal analysis, Writing - Original Draft. **Qinheng Zhu:** Methodology, Software, Validation. **Yang Xu:** Methodology. **Yexinyi Zhou:** Methodology. **Longtao Zhu:** Formal analysis. **Lanfei Jin:** Data Curation. **Jun Tang:** Supervision, Project administration. **Guangdi Chen:** Supervision, Project administration, Writing – Review & Editing, Funding acquisition.

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References

1. **ATSDR's Substance Priority List** [https://. 28 January 2020 2020.
2. Jiang J, Liu M, Parvez F, Wang B, Wu F, Eunus M, Bangalore S, Newman JD, Ahmed A, Islam T, et al. Association between Arsenic Exposure from Drinking Water and Longitudinal Change in Blood Pressure among HEALS Cohort Participants. Environ Health Perspect. 2015;123(8):806–12.
3. Zhang C, Mao G, He S, Yang Z, Yang W, Zhang X, Qiu W, Ta N, Cao L, Yang H, et al. Relationship between long-term exposure to low-level arsenic in drinking water and the prevalence of abnormal blood pressure. J Hazard Mater. 2013;262:1154–8.
4. Abhyankar LN, Jones MR, Guallar E, Navas-Acien A. Arsenic exposure and hypertension: a systematic review. Environ Health Perspect. 2012;120(4):494–500.
5. Gambelunghe A, Sallsten G, Borne Y, Forsgard N, Hedblad B, Nilsson P, Fagerberg B, Engstrom G, Barregard L. Low-level exposure to lead, blood pressure, and hypertension in a population-based cohort. Environ Res. 2016;149:157–63.
6. Hara A, Thijs L, Asayama K, Gu YM, Jacobs L, Zhang ZY, Liu YP, Nawrot TS, Staessen JA. Blood pressure in relation to environmental lead exposure in the national health and nutrition examination survey 2003 to 2010. Hypertension. 2015;65(1):62–9.
7. Martins AC, Almeida Lopes ACB, Urbano MR, Carvalho MdFH, Silva AMR, Tinkov AA, Aschner M, Mesas AE, Silbergeld EK, Paoliello MMB. An updated systematic review on the association between Cd exposure, blood pressure and hypertension. Ecotoxicol Environ Saf. 2021;208:111636.
8. Hu XF, Singh K, Chan HM. Mercury Exposure, Blood Pressure, and Hypertension: A Systematic Review and Dose-response Meta-analysis. Environ Health Perspect. 2018;126(7):076002.
9. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, Abd-Allah F, Abdelalim A, Abdollahi M, Abdollahpour I, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1223–49.
10. The US Burden of Disease Collaborators. The State of US Health, 1990–2016: Burden of Diseases, Injuries, and Risk Factors Among US States. JAMA. 2018;319(14):1444–72.

11. Awata H, Linder S, Mitchell LE, Delclos GL. Biomarker Levels of Toxic Metals among Asian Populations in the United States: NHANES 2011–2012. Environ Health Perspect. 2017;125(3):306–13.
12. Awata H, Linder S, Mitchell LE, Delclos GL. Association of Dietary Intake and Biomarker Levels of Arsenic, Cadmium, Lead, and Mercury among Asian Populations in the United States: NHANES 2011–2012. Environ Health Perspect. 2017;125(3):314–23.
13. Park S, Choi NK. Associations of blood heavy metal levels with intraocular pressure. Ann Epidemiol. 2016;26(8):546–50 e541.
14. Yorifuji T, Tsuda T, Kashima S, Takao S, Harada M. Long-term exposure to methylmercury and its effects on hypertension in Minamata. Environ Res. 2010;110(1):40–6.
15. Kim MG, Kim YW, Ahn YS. Does low lead exposure affect blood pressure and hypertension? J Occup Health. 2020;62(1):e12107.
16. An HC, Sung JH, Lee J, Sim CS, Kim SH, Kim Y. The association between cadmium and lead exposure and blood pressure among workers of a smelting industry: a cross-sectional study. Ann Occup Environ Med. 2017;29:47.
17. Skroder H, Hawkesworth S, Moore SE, Wagatsuma Y, Kippler M, Vahter M. Prenatal lead exposure and childhood blood pressure and kidney function. Environ Res. 2016;151:628–34.
18. Han L, Wang X, Han R, Xu M, Zhao Y, Gao Q, Shen H, Zhang H. Association between blood lead level and blood pressure: An occupational population-based study in Jiangsu province, China. PLoS One. 2018;13(7):e0200289.
19. Lee BK, Ahn J, Kim NS, Lee CB, Park J, Kim Y. Association of Blood Pressure with Exposure to Lead and Cadmium: Analysis of Data from the 2008–2013 Korean National Health and Nutrition Examination Survey. Biol Trace Elem Res. 2016;174(1):40–51.
20. Bulka CM, Scannell Bryan M, Persky VW, Daviglus ML, Durazo-Arvizu RA, Parvez F, Slavkovich V, Graziano JH, Islam T, Baron JA, et al. Changes in blood pressure associated with lead, manganese, and selenium in a Bangladeshi cohort. Environ Pollut. 2019;248:28–35.
21. Ahn J, Kim NS, Lee BK, Park J, Kim Y. Association of Blood Pressure with Blood Lead and Cadmium Levels in Korean Adolescents: Analysis of Data from the 2010–2016 Korean National Health and Nutrition Examination Survey. J Korean Med Sci. 2018;33(44):e278.
22. Lu Y, Liu X, Deng Q, Duan Y, Dai H, Li Y, Xiao T, Ning X, Fan J, Zhou L, et al. Continuous lead exposure increases blood pressure but does not alter kidney function in adults 20–44 years of age in a lead-polluted region of China. Kidney Blood Press Res. 2015;40(3):207–14.
23. **National Health and Nutrition Examination Survey**: **Sample Design**, 2011–**2014**. https://www.cdc.gov/nchs/data/series/sr_02/sr02_162.pdf. March 2014.
24. **National Health**. **and Nutrition Examination Survey**, **2015** – **2018**: **Sample Design and Estimation Procedures**. https://www.cdc.gov/nchs/data/series/sr_02/sr02-184-508.pdf. April 2020.
25. **National Health and Nutrition Examination Survey**: **Estimation procedures**, 2011–**2014**. https://www.cdc.gov/nchs/data/series/sr_02/sr02_177.pdf. March 2014.
26. Antimony. **Arsenic**, **Barium**, **Beryllium**, **Cadmium**, **Cesium**, **Cobalt**, **Lead**, **Manganese**, **Molybdenum**, **Platinum**, **Strontium**, **Thallium**, **Tin**, **Tungsten**, **and Uranium**. https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/labmethods/uhm_g_met_heavy_metals.pdf. October 2013.

27. Urinary. **Iodine** & **Mercury**. https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/labmethods/uiouhg_g_met_iodine_mercury.pdf. October 2013.
28. Cadmium. **Lead**, **Manganese**, **Mercury**, **and Selenium**. https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/labmethods/pbcd_g_met_blood-metals.pdf. September 2013.
29. Cadmium. **Lead**, **Manganese**, **Mercury**, **and Selenium**. https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/labmethods/PbCd_H_MET.pdf. January 2016.
30. **Urinary Metals and Total Arsenic**. [https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/labmethods/UM_UMS_UTAS_UTASS_H_MET.pdf]. January 2016.
31. Iodine. **and Mercury**. https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/labmethods/UHG_UIO_URIO_H_MET.pdf. January 2016.
32. Metals U. https://wwwn.cdc.gov/nchs/data/nhanes/2015-2016/labmethods/UTAS_UTASS_UM_UMS_I_MET.pdf. June 2018.
33. Iodine. **and Mercury**. https://wwwn.cdc.gov/nchs/data/nhanes/2015-2016/labmethods/UIO_UHG_I_MET.pdf. June 2018.
34. Cadmium. **Lead**, **Manganese**, **Mercury**, **and Selenium**. https://wwwn.cdc.gov/nchs/data/nhanes/2015-2016/labmethods/PBCD_I_met.pdf. January 2018.
35. Whelton Paul K, Carey Robert M, Aronow Wilbert S, Casey Donald E, Collins Karen J, Dennison Himmelfarb C, DePalma Sondra M, Gidding S, Jamerson Kenneth A, Jones Daniel W, et al: 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/**ASPC/NMA/PCNA Guideline for the Prevention**, **Detection**, **Evaluation**, **and Management of High Blood Pressure in Adults**. *Journal of the American College of Cardiology* 2018, **71**(19):e127-e248.
36. Guallar E, Sanz-Gallardo MI, van't Veer P, Bode P, Aro A, Gómez-Aracena J, Kark JD, Riemersma RA, Martín-Moreno JM, Kok FJ. Mercury, fish oils, and the risk of myocardial infarction. N Engl J Med. 2002;347(22):1747–54.
37. Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. Stat Med. 2005;24(19):2911–35.
38. Amiri A, Mokhayeri Y, Mohammadi R, Karami MA, Ghaderpoori M, Kamarehie B, Jafari A. Dose-response meta-analysis of arsenic exposure in drinking water and hypertension. Heliyon. 2021;7(3):e06409.
39. Li X, Li B, Xi S, Zheng Q, Wang D, Sun G. Association of urinary monomethylated arsenic concentration and risk of hypertension: a cross-sectional study from arsenic contaminated areas in northwestern China. Environ Health. 2013;12:37.
40. Spratlen MJ, Grau-Perez M, Best LG, Yracheta J, Lazo M, Vaidya D, Balakrishnan P, Gamble MV, Francesconi KA, Goessler W, et al. The Association of Arsenic Exposure and Arsenic Metabolism With the Metabolic Syndrome and Its Individual Components: Prospective Evidence From the Strong Heart Family Study. Am J Epidemiol. 2018;187(8):1598–612.
41. Shi P, Jing H, Xi S. Urinary metal/metalloid levels in relation to hypertension among occupationally exposed workers. Chemosphere. 2019;234:640–7.
42. Zhong Q, Zhang C, Zhang Q, Jiang CX, Qin QR, Chen J, Liang L, Huang F. Arsenic Exposure and Incident Hypertension of Adult Residents Living in Rural Areas Along the Yangtze River, Anhui, China. J Occup Environ Med. 2019;61(4):271–7.

43. Wang H, Li X, Li RJ, Yan J, Lan Z, Chen J, Zhang L. Associations of exposure to metals with the risk of hypertension among an older population aged 40–75 years in rural southwest China. J Appl Toxicol. 2020;40(8):1076–86.
44. Yu Y, Guo Y, Zhang J, Xie J, Zhu Y, Yan J, Wang B, Li Z. A perspective of chronic low exposure of arsenic on non-working women: Risk of hypertension. Sci Total Environ. 2017;580:69–73.
45. Mordukhovich I, Wright RO, Hu H, Amarasiriwardena C, Baccarelli A, Litonjua A, Sparrow D, Vokonas P, Schwartz J. Associations of toenail arsenic, cadmium, mercury, manganese, and lead with blood pressure in the normative aging study. Environ Health Perspect. 2012;120(1):98–104.
46. Mozaffarian D, Shi P, Morris JS, Grandjean P, Siscovick DS, Spiegelman D, Willett WC, Rimm EB, Curhan GC, Forman JP. Mercury exposure and risk of hypertension in US men and women in 2 prospective cohorts. Hypertension. 2012;60(3):645–52.
47. Park SK, Lee S, Basu N, Franzblau A. Associations of blood and urinary mercury with hypertension in U.S. adults: the NHANES 2003–2006. Environ Res. 2013;123:25–32.
48. Vupputuri S, Longnecker MP, Daniels JL, Guo X, Sandler DP. Blood mercury level and blood pressure among US women: results from the National Health and Nutrition Examination Survey 1999–2000. Environ Res. 2005;97(2):195–200.
49. Eom SY, Choi SH, Ahn SJ, Kim DK, Kim DW, Lim JA, Choi BS, Shin HJ, Yun SW, Yoon HJ, et al. Reference levels of blood mercury and association with metabolic syndrome in Korean adults. Int Arch Occup Environ Health. 2014;87(5):501–13.
50. Daneshmand R, Kurl S, Tuomainen TP, Virtanen JK. Associations of serum n-3 and n-6 PUFA and hair mercury with the risk of incident stroke in men: the Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD). Br J Nutr. 2016;115(10):1851–9.
51. Teye SO, Yanosky JD, Cuffee Y, Weng X, Luquis R, Farace E, Wang L. Association between blood lead levels and blood pressure in American adults: results from NHANES 1999–2016. Environ Sci Pollut Res Int. 2020;27(36):45836–43.
52. Tellez-Plaza M, Navas-Acien A, Crainiceanu CM, Guallar E. Cadmium exposure and hypertension in the 1999–2004 National Health and Nutrition Examination Survey (NHANES). Environ Health Perspect. 2008;116(1):51–6.

Tables

Table 1 Distributions of characteristics of participants with weighted percentage, NHANES 2011-2016 across racial/ethnic groups

Variables	Participants with urinary As, DMA, Pb, Cd or Hg levels (n=3, 954)					Participants with Pb, Cd, Hg or MeHg levels (n=7, 913)				
	MA	OH	NHW	NHB	NHA	MA	OH	NHW	NHB	NHA
	546 (8.4)	434 (5.9)	1650 (70.0)	860 (10.7)	464 (4.8)	1003 (8.2)	849 (5.8)	3331 (70.3)	1816 (10.9)	914 (4.8)
Age										
20-39 years	214 (54.0)	135 (47.0)	539 (30.5)	297 (42.0)	188 (43.3)	394 (53.4)	261 (47.6)	1076 (30.8)	597 (41.6)	370 (43.6)
40-59 years	187 (34.1)	142 (34.9)	507 (38.0)	285 (37.6)	164 (35.8)	335 (33.7)	276 (34.9)	1022 (37.4)	627 (37.5)	321 (35.2)
≥ 60 years	145 (11.9)	157 (18.1)	604 (31.6)	278 (20.4)	112 (20.9)	274 (12.9)	312 (17.5)	1233 (31.8)	592 (21.0)	223 (21.2)
Gender										
Male	260 (50.4)	192 (47.6)	845 (49.7)	448 (45.4)	247 (48.4)	496 (51.3)	390 (48.8)	1693 (49.1)	883 (43.8)	462 (47.2)
Female	286 (49.6)	242 (52.4)	805 (50.3)	412 (54.6)	217 (51.6)	507 (48.7)	459 (51.2)	1638 (50.9)	933 (56.2)	452 (52.8)
Education										
< High school (HS)	262 (43.6)	151 (31.4)	219 (8.8)	153 (15.4)	55 (10.8)	477 (43.3)	299 (30.5)	450 (8.9)	353 (16.9)	116 (11.7)
HS graduate/GED	108 (20.3)	100 (24.0)	369 (20.6)	234 (26.0)	50 (10.7)	214 (22.2)	183 (23.5)	751 (20.7)	481 (25.7)	104 (11.1)
Some college/AA	124 (25.1)	117 (27.6)	551 (33.3)	295 (36.1)	108 (23.2)	227 (25.5)	227 (28.1)	1119 (33.7)	632 (36.8)	201 (21.6)
≥ College graduate	52 (11.0)	66 (17.0)	511 (37.3)	178 (22.5)	251 (55.4)	85 (9.1)	140 (17.9)	1011 (36.7)	350 (20.6)	493 (55.6)
Household Income										
< $20,000	124 (20.3)	116 (23.5)	322 (10.8)	223 (25.3)	53 (10.5)	247 (21.8)	232 (23)	704 (10.9)	497 (26.3)	99 (9.8)
$20,000–< $55,000	247 (44.4)	163 (37.5)	622 (32.9)	330 (38.2)	124 (25.1)	460 (45.2)	332 (39.7)	1221 (31.8)	716 (39.9)	265 (26.9)
$55,000–< $75,000	65 (12.5)	53 (14.6)	186 (14.1)	105 (13.2)	59 (13.1)	127 (13.7)	98 (12.0)	360 (13.7)	193 (11.9)	121 (13.7)
≥ $75,000	110 (22.8)	102 (24.5)	520 (42.2)	202 (23.3)	228 (51.3)	169 (19.3)	187 (25.4)	1046 (43.6)	410 (21.9)	429 (49.6)
cotinine level [a], μg/L	0.12 (0.09, 0.16)	0.14 (0.09, 0.2)	0.24 (0.18, 0.31)	0.77 (0.51, 1.15)	0.07 (0.05, 0.09)	0.09 (0.07, 0.11)	0.12 (0.09, 0.17)	0.19 (0.15, 0.25)	0.7 (0.53, 0.91)	0.06 (0.05, 0.08)
Alcohol consumption										
Never drinker	96	75	153	140	135	165	146	317	280	256

	(14.9)	(15.4)	(8.1)	(16.7)	(29.7)	(14.4)	(14.3)	(8.5)	(16.6)	(28.8)
ever drinker	87 (12.7)	82 (17)	285 (14)	134 (12.4)	51 (10.7)	172 (13.8)	150 (15)	596 (14.5)	327 (13.6)	102 (10.8)
Current drinker	363 (72.4)	277 (67.6)	1212 (77.9)	586 (70.9)	278 (59.6)	666 (71.8)	553 (70.7)	2418 (77)	1209 (69.8)	556 (60.4)
BMI										
Normal weight (< 25kg/m^2)	88 (18.3)	109 (26.6)	490 (29.1)	204 (23.8)	267 (57.4)	172 (18.9)	206 (26.0)	974 (28.0)	423 (23.4)	537 (57.4)
Over weight (25-30 kg/m^2)	182 (32.3)	149 (34.1)	579 (35.0)	229 (25.5)	141 (29.6)	340 (33.1)	307 (35.1)	1148 (35.4)	503 (26.6)	274 (30.2)
Obese (≥ 30 kg/m^2)	276 (49.5)	176 (39.4)	581 (35.9)	427 (50.7)	56 (13)	491 (48)	336 (38.9)	1209 (36.6)	890 (50.0)	103 (12.4)
Omega-3 fatty acids (gm/day) [b]										
Q1 (0-0.0087)	122 (22.7)	111 (25.7)	378 (22.9)	142 (17.9)	97 (26.2)	197 (19.2)	181 (21.6)	715 (21.1)	281 (16.0)	159 (22.6)
Q2 (0.0087-0.0189)	100 (19.5)	88 (21.8)	418 (26.4)	174 (20.8)	54 (13.3)	208 (21.9)	180 (22.7)	851 (26.8)	382 (21.9)	110 (13.5)
Q3 (0.0189-0.0491)	131 (25.1)	85 (21.9)	428 (26.9)	209 (27.0)	80 (19.3)	251 (27.0)	197 (25.8)	874 (26.8)	461 (27.5)	156 (19.7)
Q4 (0.0491-6.7650)	166 (32.7)	124 (30.6)	378 (23.9)	294 (34.3)	174 (41.3)	303 (31.9)	236 (29.8)	792 (25.4)	611 (34.6)	370 (44.2)
Blood pressure, mmHg										
Systolic pressure	120 ± 1.0	119 ± 1.0	122 ± 0.5	126 ± 0.7	120 ± 1.0	120 ± 0.5	120 ± 0.8	122 ± 0.4	126 ± 0.5	120 ± 0.7
Diastolic pressure	70 ± 0.7	68 ± 1.1	71 ± 0.5	72 ± 0.6	72 ± 0.6	70 ± 0.5	69 ± 0.8	71 ± 0.4	71 ± 0.5	72 ± 0.4
Hypertension	232 (33.8)	192 (33.9)	822 (48.6)	511 (53.7)	198 (40.8)	430 (35.3)	402 (35.8)	1698 (48.4)	1101 (55.3)	389 (41.6)

Abbreviation: AA, associate in Art degree; As, arsenic; BMI, body mass index; Cd, cadmium; GED, general education development; Hg, mercury; MA, Mexican American; NHA, Non-Hispanic Asian; NHB, Non-Hispanic Black; NHW, Non-Hispanic White; OH, Other Hispanic; Pb, lead. Q, quartile; MeHg, methyl mercury.

[a] Cotinine levels was presented as geometric mean and confidence interval.

[b] Omega-3 fatty acids data, which were divide into 4 groups according to quartile values, were available for 3753 participants with urinary metals levels and 7515 participants with blood metals levels.

Table 2. Weighted geometric means of As, Pb, Cd and Hg levels in urine and blood samples across racial/ethnic groups.

Variables	Urine samples (μg/g creatinine), GM (95%CI)					Blood samples (μg/L), GM (95%CI)				
	MA	OH	NHW	NHB	NHA	MA	OH	NHW	NHB	NHA
As, total	6.92 (6.33, 7.57)	8.49 (7.69, 9.38)	6.82 (6.36, 7.31)	6.87 (6.09, 7.75)	19.5 (17.1, 22.2)	NA	NA	NA	NA	NA
DMA	3.67 (3.47, 3.87)	4.53 (4.18, 4.91)	3.42 (3.28, 3.56)	2.86 (2.62, 3.12)	8.81 (8.04, 9.66)	NA	NA	NA	NA	NA
Pb	0.35 (0.32, 0.38)	0.35 (0.32, 0.39)	0.37 (0.35, 0.39)	0.29 (0.26, 0.31)	0.44 (0.41, 0.48)	0.87 (0.83, 0.92)	0.87 (0.81, 0.95)	0.99 (0.95, 1.04)	0.97 (0.91, 1.04)	1.16 (1.09, 1.22)
Cd	0.16 (0.15, 0.18)	0.18 (0.16, 0.20)	0.19 (0.18, 0.20)	0.18 (0.16, 0.20)	0.31 (0.28, 0.34)	0.26 (0.24, 0.27)	0.27 (0.25, 0.29)	0.30 (0.28, 0.31)	0.35 (0.33, 0.38)	0.41 (0.38, 0.44)
Hg, total	0.25 (0.22, 0.28)	0.32 (0.29, 0.36)	0.30 (0.28, 0.33)	0.22 (0.19, 0.24)	0.45 (0.40, 0.52)	0.62 (0.59, 0.66)	0.92 (0.84, 1.01)	0.78 (0.72, 0.84)	0.83 (0.74, 0.92)	2.06 (1.86, 2.29)
MeHg	NA	NA	NA	NA	NA	0.38 (0.35, 0.43)	0.64 (0.56, 0.73)	0.52 (0.47, 0.58)	0.62 (0.54, 0.72)	1.63 (1.43, 1.85)

Abbreviation: MA, Mexican American; NHA, Non-Hispanic Asian; NHB, Non-Hispanic Black; NHW, Non-Hispanic White; OH, Other Hispanic; As, arsenic; Cd, cadmium; Hg, mercury; GM, geometric mean; CI, confidence interval; DMA, Dimethylarsinic acid; MeHg, methyl mercury; NA, not available.

Table 3. The associations of urinary metals levels with blood pressure and prevalence of hypertension across non-NHA and NHA

Metals [a]	non-NHA			NHA		
	SBP (mmHg) [b, c]	DBP (mmHg) [b, c]	Hypertension [c, d]	SBP (mmHg) [b, c]	DBP (mmHg) [b, c]	Hypertension [c, d]
	β (95%CI)	β (95%CI)	OR (95%CI)	β (95%CI)	β (95%CI)	OR (95%CI)
Urinary As						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	1.2 (-0.8, 3.2)	-0.3 (-1.7, 1.0)	0.9 (0.71, 1.13)	-4.2 (-11.1, 2.6)	-0.1 (-4.1, 3.9)	0.75 (0.27, 2.09)
Tertile 3	**2.5 (0.7, 4.4)**	-0.1 (-1.6, 1.3)	1.15 (0.87, 1.52)	-1.1 (-7.9, 5.6)	1.8 (-2.2, 5.6)	0.58 (0.22, 1.52)
P trend [e]	**0.012**	0.971	0.151	0.228	0.246	0.246
Urinary DMA						
Tertile1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile2	0.2 (-1.7, 2.0)	0.2 (-1.0, 1.3)	0.92 (0.72, 1.17)	-6.9 (-14.2, 0.3)	-1.7 (-5.9, 2.4)	0.44 (0.14, 1.44)
Tertile3	**2.5 (0.8, 4.2)**	0.9 (-0.1, 2.0)	1.15 (0.88, 1.52)	-5.8 (-12.1, 0.4)	-0.4 (-3.9)	0.35 (0.13, 0.98)
P trend	**0.003**	0.075	0.208	0.706	0.455	0.100
Urinary Pb						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	0.2 (-1.4, 1.9)	-0.7 (-1.9, 0.5)	1.01 (0.79, 1.28)	-0.3 (-4.3, 3.8)	0.5 (-3.2, 4.1)	0.60 (0.32, 1.12)
Tertile 3	-0.8 (-3.0, 1.4)	-1.0 (-2.6, 0.5)	0.82 (0.61, 1.1)	-0.8 (-5.4, 3.9)	0.5 (-2.6, 3.6)	0.96 (0.49, 1.87)
P trend [e]	0.394	0.266	0.128	0.726	0.784	0.480
Urinary Cd						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	-2.0 (-3.8, -0.1)	-0.3 (-1.6, 1.0)	0.99 (0.75, 1.3)	2.1 (-1.9, 6.2)	1.6 (-2.9, 6.1)	1.24 (0.45, 3.38)
Tertile 3	-0.7 (-2.8, 1.3)	-0.3 (-2.0, 1.4)	1.11 (0.81, 1.52)	-1.2 (-6.5, 4.0)	-0.4 (-5.0, 4.4)	0.77 (0.23, 2.56)
P trend [e]	0.834	0.859	0.440	0.099	0.231	0.176
Urinary Hg						
Tertile1	Reference	Reference	Reference	Reference	Reference	Reference

tertile2	0.4 (-1.4, 2.3)	-0.8 (-2.0, 0.5)	0.97 (0.73, 1.28)	2.6 (-2.4, 7.5)	0.6 (-4.2, 5.3)	1.11 (0.55, 2.25)
Tertile3	-1.3 (-3.5, 0.9)	-1.3 (-2.9, 0.3)	0.80 (0.59, 1.09)	3.2 (-1.8, 8.2)	2.1 (-2.6, 6.8)	1.19 (0.45, 3.14)
P trend [e]	0.146	0.170	0.123	0.406	0.205	0.746

Abbreviation: As, arsenic; Cd, cadmium; Hg, mercury; Pb, lead; SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidential

Interval; DMA, Dimethylarsinic acid.

[a] Urine metals levels were adjusted by urine creatinine concentration, and then categorized into three groups according to tertile cutoff values based on weighted

distributions in the whole study sample.

[b] To account for the influence of anti-hypertension medication on blood pressure, the censored normal regression model was used to assess the associations of metals

levels and blood pressure levels.

[c] The models were adjusted by age, sex, education, annual household income, cotinine level, alcohol use, BMI. For As, DMA and Hg, omega-3 fatty acids levels were adjusted additionally in the models.

[d] Hypertension was defined as blood pressure at least 130/80 mmHg, or taking antihypertension medication currently.

[e] *P* trend values were calculated by treating the median values of each tertile as continuous variables in regression models. Potential confounders were also adjusted in these models.

Table 4. The associations of blood metals levels with blood pressure levels and prevalence of hypertension across non-NHA and NHA

Metals [a]	Non-NHA			NHA		
	SBP (mmHg) [b, c]	DBP (mmHg) [b, c]	Hypertension [c, d]	SBP (mmHg) [b, c]	DBP (mmHg) [b, c]	Hypertension [c, d]
	β (95%CI)	β (95%CI)	OR (95%CI)	β (95%CI)	β (95%CI)	OR (95%CI)
Blood Pb						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	1.0 (-0.3, 2.4)	**1.5 (0.7, 2.4)**	**1.3 (1.1, 1.6)**	-0.3 (-3.6,3.0)	-1.6 (-4.6, 1.4)	0.7 (0.4, 1.3)
Tertile 3	**3.0 (1.2, 4.8)**	**2.0 (0.8, 3.1)**	**1.5 (1.2, 1.9)**	-1.0 (-5.3, 3.3)	-0.9 (-3.7, 1.9)	0.7 (0.4, 1.2)
P trend [e]	**0.002**	**0.013**	**0.005**	0.627	0.967	0.405
Blood Cd						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	-0.9 (-2.4, 0.7)	-0.4 (-1.6, 0.7)	0.87 (0.69, 1.09)	-3.9 (-9.3, 1.6)	-0.9 (-6.3, 4.4)	0.62 (0.23, 1.7)
Tertile 3	-0.1 (-1.8, 1.5)	-0.8 (-2.0, 0.5)	0.93 (0.74, 1.18)	-2.5 (-8.0, 3.0)	0.2 (-5.1, 5.5)	0.63 (0.22, 1.81)
P trend [e]	0.673	0.240	0.979	0.733	0.398	0.641
Blood Hg						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	0.6 (-1.1, 2.4)	-0.1 (-1.1, 0.8)	1.03 (0.81, 1.3)	-0.9 (-6.1, 4.4)	**4.1 (0.1, 8.1)**	**1.2 (0.4, 3.4)**
Tertile 3	0.1 (-1.6, 1.9)	-0.8 (-1.8, 0.3)	0.9 (0.73, 1.12)	5.6 (0.0, 11.2)	**5.8 (1.9, 9.7)**	**2.8 (1.1, 7.3)**
P trend [e]	0.848	0.095	0.169	**0.003**	**0.002**	**0.001**
Blood MeHg						
Tertile 1	Reference	Reference	Reference	Reference	Reference	Reference
Tertile 2	1.1 (-0.5, 2.7)	0.3 (-0.7, 1.3)	1.1 (0.9, 1.3)	-1.1 (-0.5, 2.7)	3.1 (-1.0, 7.2)	**1.0 (0.4, 2.5)**
Tertile 3	0.5 (-1.0, 2.0)	-0.4 (-1.3, 0.5)	1.0 (0.8, 1.2)	4.2 (-1.6, 10.0)	**5.2 (1.1, 9.2)**	**2.3 (0.9, 6.0)**
P trend [e]	0.966	0.194	0.450	**0.042**	**0.004**	**0.015**

Abbreviation: Cd, cadmium; Hg, mercury; Pb, lead; SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidential Interval;

MeHg, methyl mercury.

[a] Blood metals levels were categorized into three groups according to tertile cutoff values based on weighted distributions in the whole study sample.

[b] To account for the influence of anti-hypertension medication on blood pressure, the censored normal regression model was used to assess the associations of metals

levels and blood pressure levels.

[c] The models were adjusted by age, sex, education, annual household income, cotinine level, alcohol use, BMI. For Hg and MeHg, omega-3 fatty acids levels were adjusted additionally in the models.

[d] Hypertension was defined as blood pressure at least 130/80 mmHg, or taking antihypertension medication currently.

Figures

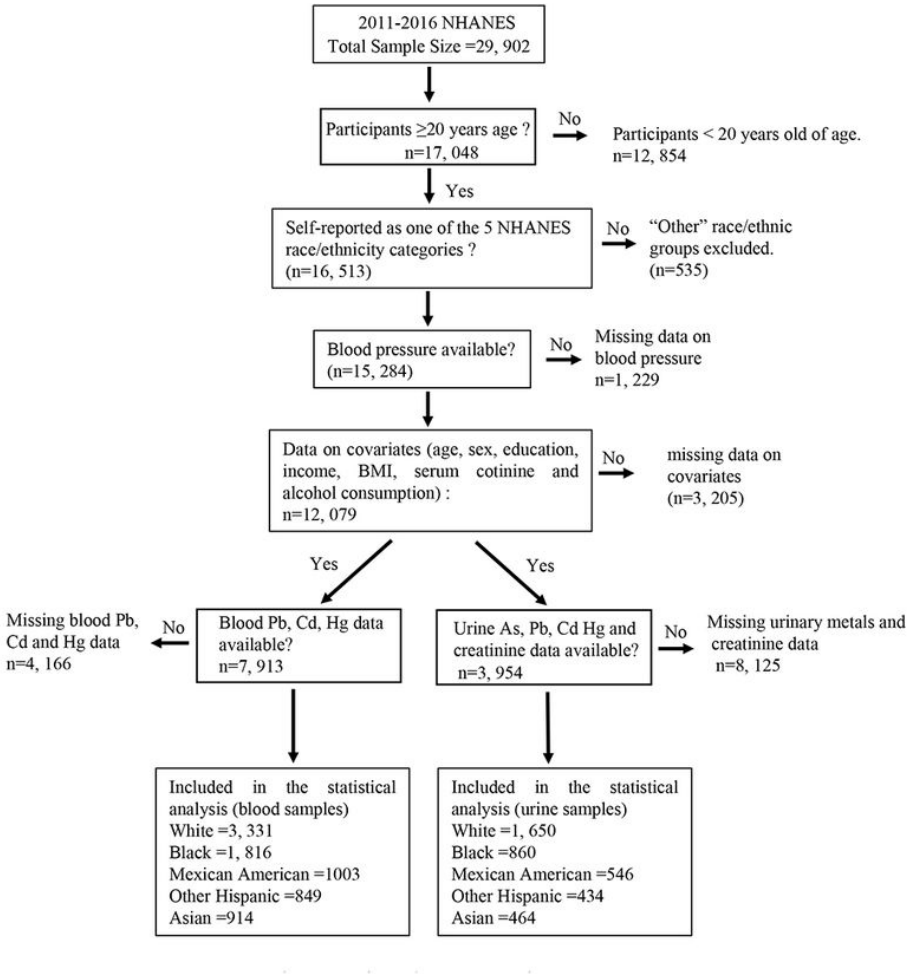

Figure 1

Flow chart of participants selection