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ORIGINAL RESEARCH

Association Between Blood Lead Level and Uncontrolled Hypertension in the US Population (NHANES 1999–2016)

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BACKGROUND: This study aims to explore whether higher blood lead levels (BLL) may be associated with failure to control blood pressure and subsequent uncontrolled hypertension.

METHODS AND RESULTS: We used serial cross-sectional waves of the US National Health and Nutrition Examination Survey (NHANES) from 1999 to 2016. 30 762 subjects aged 20 years and above were included. Uncontrolled hypertension was defined as systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg. We estimated odds ratios (ORs) of quartiles of BLL for any hypertension and uncontrolled hypertension by sex using logistic regression, adjusted for demographics, smoking status, serum cotinine, alcohol intake, body mass index, and menopause status in women. The weighted prevalence of hypertension was 46.7%, of which 80.1% were uncontrolled. Men, younger ages, ethnic minorities, people with lower income, never and current smokers, and people with higher BLL were less likely to have their hypertension controlled. In men, compared with the lowest quartile of BLL (<0.94 μg/dL), the highest 2 quartiles (0.94–1.50 μg/dL, 1.50–2.30 μg/dL) were associated with hypertension (Q2: OR, 1.12; 95% CI, 0.96–1.30; Q3: OR, 1.16; 95% CI, 1.01–1.34; Q4: OR, 1.25; 95% CI, 1.08–1.45), but not in women. In hypertensive men, higher BLL was related to uncontrolled hypertension compared with the lowest quartile (Q2: OR, 1.34; 95% CI, 0.98–1.85; Q3: OR, 1.70; 95% CI, 1.26–2.30; Q4: OR, 1.96; 95% CI, 1.45–2.65). In women, the relationship was similar (Q2: OR, 1.26; 95% CI, 0.95–1.67; Q3: OR, 1.48; 95% CI, 1.10–2.00; Q4: 1.70; 95% CI, 1.26–2.30).

CONCLUSIONS: BLL is associated with higher prevalence of hypertension and uncontrolled hypertension, with more pronounced association in men.

Key Words: cardiovascular disease ■ cardiovascular disease risk factors ■ environmental medicine ■ epidemiology ■ hypertension

Hypertension is one of the most important public health challenges worldwide.[1] Blood pressure (BP) has a dose-response relationship with the risks of cardiovascular diseases, chronic kidney disease, and mortality.[2] In the United States, hypertension was defined as having systolic blood pressure (SBP) ≥140 mm Hg, or diastolic blood pressure (DBP) ≥90 mm Hg, or taking antihypertensive medication.[3] In 2017, the American College of Cardiology/American Heart Association guidelines lowered the diagnostic criteria to SBP/DBP ≥130/80 mm Hg.[4] Previously, the control rate of hypertension in the United States steadily improved from 31.6% in 1999–2000 to 53.1% in 2009–2010, and remained stable through 2015–2016 (48.3%).[5] However, over half of those with hypertension are either untreated or undertreated.[5] The high prevalence of uncontrolled hypertension suggests that a substantial number of cardiovascular events are preventable.[6]

Lead poisoning contributes to cardiac and vascular damage, increasing the risk of hypertension and cardiovascular disease.[7] Potential mechanisms include lead-induced reductions in renal function, enhanced oxidative stress, stimulation of the

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CLINICAL PERSPECTIVE

What Is New?

- Elevated blood lead level is associated with uncontrolled hypertension.
- Men with high blood lead levels are more likely to have uncontrolled hypertension than women.

What Are the Clinical Implications?

- Especially among males, evaluation of blood lead level should be considered in the workup and prevention of uncontrolled hypertension.

Nonstandard Abbreviations and Acronyms

BLL	blood lead level
BMI	body mass index
BP	blood pressure
CCB	calcium channel blocker
DBP	diastolic blood pressure
NHANES	National Health and Nutrition Examination Survey
OR	odds ratio
PIR	income-to-poverty ratio
SBP	systolic blood pressure

renin-angiotensin system, downregulation of nitric oxide, soluble guanylate cyclase, and desensitization of ß-adrenergic receptors.[8,9] An earlier study in National Health and Nutrition Examination Survey (NHANES) II (1976–1980) reported an association of blood lead level (BLL) with BP, with effects predominantly in men,[10] However, that study was at much higher BLLs than prevail currently. BLL in the US population has been substantially declining for decades since the gradual removal of lead from gasoline in 1975.[11] Prior studies in chronological order exploring the association between BLL and hypertension in the low-level-lead exposed population had various findings. A study conducted with NHANES III (1988–1994) data found BLL was significantly associated only with higher SBP in black men and women, higher DBP in black women, and unexpectedly, lower DBP in white men and women. The investigators concluded that there was no consistent relationship between BP and BLL, but some associations may exist based on demographic characteristics.[12] Further studies using 1999–2006 NHANES data and one with NHANES 2003–2010 also found similar patterns of inconsistent relationships based on demographic characteristics, with more pronounced results in lower socioeconomic status.[13,14] However, studies in a community-dwelling cohort of elderly men was able to identify both blood lead and bone lead (marker of cumulative lead exposure) to be associated with hypertension.[9,15] Currently, the association between lead exposure and uncontrolled hypertension in noninstitutionalized general population in the United States has yet to be explored and is an important study question given the possible attributable effect of environmental toxicants on the burden of disease due to BP.

This study aims to examine whether higher BLL is associated with hypertension and uncontrolled hypertension.

METHODS

All data are publicly available and can be accessed at the NHANES website (https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx). Our code is available upon request to the corresponding author.

Study Population

We used data collected in the NHANES, which is conducted by the National Center for Health Statistics, to evaluate the health and nutritional status of a representative sample of the noninstitutionalized, civilian US population.[16] All procedures in the NHANES survey cycles used in this study were approved by the National Center for Health Statistics Research Ethics Review Board, and written informed consent was obtained from all participants.

We examined data from 9 consecutive NHANES survey cycles covering the periods 1999–2016. We included nonpregnant participants aged 20 and above who participated in the laboratory and physical examination. A total of 45 719 subjects were included (1999–2000 [n=4187], 2001–2002 [n=4731], 2003–2004 [n=4523], 2005–2006 [n=4448], 2007–2008 [n=5650], 2009–2010 [n=5991], 2011–2012 [n=5262], 2013–2014 [n=5523], 2015–2016 [n=5404]). We excluded 14 957 subjects whose data on BP, BLL, education, smoking status, serum cotinine, alcohol intake, body mass index (BMI), or family income-to-poverty ratio (PIR) variables were missing. The characteristics of excluded participants tended to have a higher proportion of women and ethnic minorities but did not differ with respect to other characteristics (Table S1). Our final study population consisted of 30 762 participants (15 679 men and 15 083 women).

Outcomes

BP was measured by trained examiners using a standardized protocol. After participants sat quietly for 5 minutes and the maximum inflation level was determined, 3 consecutive measurement of BP were obtained. For those with 3 readings, the first systolic and diastolic readings were discarded, and the mean of the second and third readings was calculated as the average BP; if only 2 readings were available, the second alone was considered to be the average; if only 1 reading was obtained, then it was used as the average BP.[17] Among the 30 762 participants, 28 651 (93.1%) had 3 BP readings, 1264 had 2, and 847 had 1 reading.

Participants were considered to have any hypertension if the average SBP was ≥130 mm Hg, or the average DBP ≥80 mm Hg, or their answer to the question "are you now taking prescribed medicine for high blood pressure" was "yes." Uncontrolled hypertension was identified if the average SBP was ≥130 mm Hg, or the average DBP was ≥80 mm Hg, regardless of medication use (Figure 1).

Blood Lead Measurement

Whole blood specimens were analyzed in the Division of Laboratory Sciences, National Center for Environmental Health, and Centers for Disease Control and Prevention. Whole blood lead was determined on a PerkinElmer Model SIMAA 6000 (PerkinElmer, Norwalk, CT) simultaneous multielement atomic absorption spectrometer with Zeeman background correction in the 1999–2000 and 2001–2002 cycles.[18] In the subsequent waves, BLL was determined using inductively coupled plasma mass spectrometry.[19] To compare possible systematic differences of inductively coupled plasma mass spectrometry and atomic absorption spectrometer methods,[20] we conducted a stratified analysis.

Antihypertensive Medications

Medication usage information was collected during home interviews. The interviewers recorded the names of medications directly from the drug containers if available.[21] We looked at the primary agents listed by the latest guideline, including angiotensin-converting enzyme inhibitors, angiotensin receptor blocker, calcium channel blocker (CCB), and thiazide

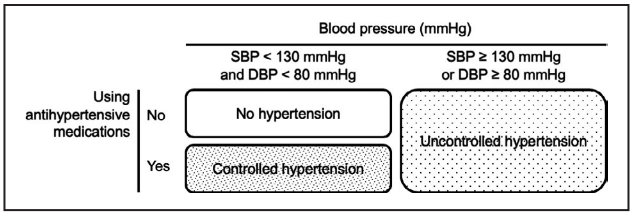

Figure 1. Definition of hypertension, controlled hypertension, and uncontrolled hypertension.
DBP indicates diastolic blood pressure; and SBP, systolic blood pressure.

or thiazide-type diuretics, as well as the secondary agents.[4] The therapeutic classifications of medications were based on the Multum Lexicon Plus drug database (Table S2).[21] In addition, we calculated the number of classes of primary agents taken, from 0 to 4, and the number of classes of both primary and secondary agents, from 0 to 12. We also examined the use of chelating agents for lead, but no participants reported using such medication.

Covariates

We included demographic variables, smoking (never, former, current, and serum cotinine), alcohol intake (never, former, current), BMI (kg/m^2), and menopause status (only for women) as covariates. Demographic variables included sex, age, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), family PIR, and education (less than a high school degree, high school degree or general educational development, college degree or above). Serum cotinine was right skewed and therefore natural log-transformed for analyses. Glomerular filtration rate was estimated from the standardized serum creatinine using the Modification of Diet in Renal Disease 4-variable equation.[22] We also used estimated glomerular filtration rate to indicate the renal function of participants in an additional analysis. Among the covariates, age, family PIR, serum cotinine, and estimated glomerular filtration rate were analyzed as continuous.

Statistical Analysis

We used SAS University Edition for most data analyses and Stata, version 14.0 for the splines. All analyses used newly constructed 18-year NHANES weights adjusting for nonresponse, noncoverage, and unequal probabilities of selection. New weights waves were calculated as two-ninths of WTMEC4YR (a weight variable in NHANES data) for 1999–2000 and 2001–2002 survey cycles, one-ninth of WTMEC2YR for 2003–2004, 2005–2006, 2007–2008, 2009–2010, and 2011–2012 waves, and one-ninth of WTSH2YR (blood metal weight) for 2013–2014 and 2015–2016 survey cycles.[23]

Descriptive statistics used SAS survey procedures (PROC SURVEYFREQ, PROC SURVEYMEANS) because of the complex multistage sampling design. Comparisons between groups used the χ^2 test for categorical variables and *t* test for continuous variables.

The primary analyses included 3 key logistic regression models using PROC SURVEYLOGISTIC. In model I we considered individuals with any hypertension as cases, and those with no hypertension were controls. Model II was limited to participants with hypertension; we took those with uncontrolled hypertension as cases and those with controlled hypertension as controls. In model III, we took those with uncontrolled hypertension as cases again, and those with controlled hypertension or no hypertension were combined as the control group. In all analyses, BLL served as the exposure of interest; it was modeled as a categorical variable defined by quartiles. In addition to the odds ratio (ORs) of each quartile, we also calculated the *P*-trend for an ordinal variable coded 1, 2, 3, 4 for the quartiles of BLL. Moreover, we examined BLL as a continuous linear variable and as a nonlinear variable, modeled with restricted cubic splines with 5 knots. Considering the sex disparity of the BLL and the biology of the incidence of hypertension,[24] we ran the stratified analyses by sex. Both crude and adjusted analyses were conducted. The basic covariates were age, race/ethnicity, family PIR, education, smoking status, serum cotinine (natural log-transformed), alcohol intake, BMI, and menopause status (only for women).

In addition to the primary analyses, we also performed a number of exploratory analyses. To estimate the interaction of various antihypertensive medications and BLL, we conducted stratified analysis by antihypertensive agents in 2 ways. First, we limited the analysis to individuals receiving single agent antihypertensive medications and examined the association between BLL and hypertension in each antihypertensive class. Then, we extended the analyses to individuals receiving any (single or multiagent) antihypertensives. In the second part of the exploratory analyses, we conducted stratified analysis by different BLL measuring methodologies, because the consistency of the recent inductively coupled plasma mass spectrometry methodology and the earlier atomic absorption spectrometer method with Zeeman correction in measuring BLL was unclear. Third, we further adjusted for estimated glomerular filtration rate in the primary models so as to explore the role of renal function in the relationship between BLL and uncontrolled hypertension. Fourth, we ran a series of models further adjusting for the number of primary antihypertensive agents taken or the number of any agents (both primary and secondary), which could better represent the accessibility of medications than income. Fifth, we took stratified analyses, examining people taking or not taking antihypertensives separately. Last, we performed additional analyses with the definition of hypertension in the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report* for comparative purposes. The Joint National Committee 7 Report defined hypertension as the average SBP ≥130 mm Hg, the average DBP ≥80 mm Hg, or taking antihypertensive agents.[25]

RESULTS

Descriptive Analyses

Among a total of 30 762 participants, the weighted prevalence of hypertension was 46.7% (n=15 851). Among those with any hypertension, 80.1% (n=12 711) were uncontrolled hypertension. We found that the tendency of having hypertension varied by most demographic characteristics (Table 1). For example, men were more likely to have hypertension than women; older people tended to have hypertension compared with younger people. Lifestyle factors, menopausal status, BMI, and cotinine levels also differed in hypertensive and nonhypertensive groups. BLL was significantly higher in people with any hypertension than in the nonhypertensive participants for most subgroups. Among people with hypertension, people of various characteristics showed different possibilities of having their BP controlled to satisfactory levels (SBP <130 mm Hg and DBP <80 mm Hg). Men compared with women, and younger people compared with older people tended to have uncontrolled hypertension (P<0.001). Surprisingly, the BMI of participants with uncontrolled hypertension was significantly lower than for those having their BP controlled (29.9 versus 31.4, P<0.001). In most subgroups, people with uncontrolled hypertension had higher BLL than those having hypertension controlled (P<0.05).

Primary Analyses

In the crude analysis, we found that higher BLL had a strong relationship with hypertension in both sexes. However, among people with any hypertension, higher BLL was not associated with uncontrolled hypertension. In model 1, in men, comparing with the first quartile of BLL (<0.94 μg/dL), the ORs (95% CI) of hypertension were 1.335 (1.174–1.517), 1.589 (1.404–1.798), and 1.895 (1.681–2.138) for quartile 2 (Q2: 0.94–1.50 μg/dL), quartile 3 (Q3: 1.50–2.30 μg/dL), and quartile 4 (Q4: >2.30 μg/dL) respectively (P-trend<0.001), comparing with Q1. Among men, each 1 μg/dL increase in BLL was associated with 10% greater odds of hypertension (95% CI, 1.067, 1.135). The ORs (95% CI) of hypertension in women were 1.752 (1.498–2.048), 2.572 (2.186–3.025), 3.778 (3.209–4.448) for quartile 2 (Q2: 0.70–1.08 μg/dL), quartile 3 (Q3: 1.08–1.66 μg/dL), and quartile 4 (Q4: >1.66 μg/dL) respectively (P-trend<0.001), and the OR (95% CI) for per μg/dL increase in BLL was 1.525 (1.416–1.643). In model 2, among men with hypertension, higher BLL was not associated with uncontrolled hypertension; whereas in women, those with BLL >1.66 μg/dL (Q4) had 1.37

Table 1. Participant Characteristics and Geometric Mean of BLL (μg/dL) by Hypertension Status

Characteristics	Overall			Nonhypertension			Hypertension												
							Overall					Controlled			Uncontrolled			*P* Value‡	P Value§
	n	% (SE)	BLL (SE)	n	% (SE)	BLL (SE)	n	% (SE)	*P* Value*	BLL (SE)	*P* Value†	n	% (SE)	BLL (SE)	n	% (SE)	BLL (SE)		
Sex									<0.001										
Male	15 679	49.7 (0.3)	1.50 (0.02)	7141	46.6 (0.5)	1.38 (0.02)	8538	53.3 (0.5)		1.63 (0.02)	<0.001	1515	47.2 (1.1)	1.60 (0.05)	7023	54.8 (0.6)	1.64 (0.02)		0.007
Female	15 083	50.3 (0.3)	1.07 (0.01)	7770	53.4 (0.5	0.94 (0.01)	7313	46.7 (0.5)		1.27 (0.02)	<0.001	1625	52.8 (1.1)	1.22 (0.03)	5688	45.2 (0.6)	1.29 (0.02)		0.005
Age, y									<0.001									<0.001	
20 to 39	10 081	36.5 (0.6)	0.95 (0.01)	7757	52.9 (0.7)	0.92 (0.01)	2324	17.8 (0.5)		1.02 (0.02)	<0.001	149	5.9 (0.7)	0.75 (0.05)	2175	20.8 (0.6)	1.05 (0.02)		<0.001
40 to 59	10 113	38.9 (0.4)	1.38 (0.02)	4860	36.0 (0.6)	1.32 (0.02)	5253	42.2 (0.7)		1.43 (0.02)	<0.001	975	42.1 (1.4)	1.27 (0.03)	4278	42.2 (0.7)	1.48 (0.02)		<0.001
60+	10 568	24.6 (0.5)	1.72 (0.02)	2294	11.1 (0.4)	1.71 (0.03)	8274	40.0 (0.7)		1.72 (0.02)	0.062	2016	52.0 (1.3)	1.59 (0.04)	6258	37.0 (0.8)	1.77 (0.02)		<0.001
Race/ethnicity									<0.001									<0.001	
Non-Hispanic white	15 050	71.5 (1.1)	1.27 (0.02)	7145	70.0 (1.1)	1.12 (0.02)	7905	73.2 (1.1)		1.45 (0.02)	<0.001	1698	78.2 (1.3)	1.39 (0.03)	6207	71.9 (1.2)	1.47 (0.02)		<0.001
Non-Hispanic black	5988	10.1 (0.6)	1.33 (0.03)	2365	8.5 (0.5)	1.12 (0.03)	3623	11.9 (0.7)		1.53 (0.04)	<0.001	730	11.1 (0.8)	1.48 (0.05)	2893	12.1 (0.8)	1.54 (0.04)		0.412
Hispanic	7728	12.6 (0.8)	1.22 (0.03)	4315	15.4 (0.9)	1.15 (0.03)	3413	9.5 (0.7)		1.36 (0.04)	<0.001	573	6.8 (0.8)	1.21 (0.05)	2840	10.2 (0.8)	1.39 (0.04)		<0.001
Other	1996	5.8 (0.3)	1.28 (0.03)	1086	6.1 (0.3)	1.19 (0.03)	910	5.4 (0.3)		1.42 (0.04)	<0.001	139	3.9 (0.5)	1.29 (0.09)	771	5.8 (0.4)	1.44 (0.04)		0.071
Family PIR									<0.001									0.014	
0≤PIR<1	5945	13.2 (0.4)	1.30 (0.03)	3107	14.4 (0.5)	1.16 (0.03)	2838	12.0 (0.5)		1.53 (0.03)	<0.001	498	10.4 (0.7)	1.31 (0.05)	2340	12.4 (0.5)	1.57 (0.04)		<0.001
1≤PIR<2	8152	20.4 (0.5)	1.34 (0.02)	3703	19.5 (0.6)	1.15 (0.03)	4449	21.4 (0.6)		1.56 (0.03)	<0.001	879	20.2 (0.9)	1.53 (0.06)	3570	21.7 (0.7)	1.57 (0.03)		0.201
2≤PIR<3	4817	15.8 (0.4)	1.25 (0.02)	2257	15.7 (0.5)	1.09 (0.03)	2560	15.9 (0.5)		1.47 (0.03)	<0.001	545	16.7 (1.0)	1.44 (0.05)	2015	15.7 (0.5)	1.47 (0.03)		0.176
PIR ≥3	11 848	50.6 (0.9)	1.24 (0.01)	5844	50.4 (1.0)	1.12 (0.01)	6004	50.7 (1.0)		1.38 (0.02)	<0.001	1218	52.7 (1.4)	1.33 (0.04)	4786	50.2 (1.0)	1.40 (0.02)		0.003
Education									<0.001									0.688	
Below high school	8302	16.7 (0.5)	1.62 (0.02)	3552	15.1 (0.6)	1.47 (0.03)	4750	18.6 (0.6)		1.77 (0.03)	<0.001	889	17.9 (1.0)	1.70 (0.05)	3861	18.7 (0.6)	1.78 (0.04)		0.002
High school	7164	23.5 (0.5)	1.35 (0.02)	3242	21.6 (0.5)	1.19 (0.02)	3922	25.7 (0.6)		1.52 (0.03)	<0.001	807	25.6 (1.1)	1.41 (0.05)	3115	25.7 (0.7)	1.55 (0.03)		0.008

(Continued)

Table 1. Continued

Characteristics	Overall			Nonhypertension			Hypertension													
							Overall					Controlled			Uncontrolled			*P* Value‡	P Value§
	n	% (SE)	BLL (SE)	n	% (SE)	BLL (SE)	n	% (SE)	*P* Value*	BLL (SE)	*P* Value†	n	% (SE)	BLL (SE)	n	% (SE)	BLL (SE)		
College or above	15 296	59.8 (0.8)	1.16 (0.01)	8117	63.3 (0.9)	1.04 (0.01)	7179	55.7 (0.9)		1.33 (0.02)	<0.001	1444	56.5 (1.5)	1.28 (0.03)	5735	55.6 (0.9)	1.34 (0.02)		0.002
Smoking									<0.001									<0.001	
Never	16 127	52.8 (0.6)	1.08 (0.01)	8190	54.7 (0.7)	0.96 (0.01)	7937	50.5 (0.7)		1.24 (0.02)	<0.001	1462	46.3 (1.5)	1.19 (0.04)	6475	51.6 (0.7)	1.25 (0.02)		0.025
Former	7927	25.4 (0.5)	1.45 (0.02)	2997	20.7 (0.6)	1.27 (0.02)	4930	30.8 (0.6)		1.61 (0.03)	<0.001	1148	37.0 (1.3)	1.53 (0.04)	3782	29.3 (0.6)	1.63 (0.03)		<0.001
Current	6708	21.8 (0.5)	1.61 (0.02)	3724	24.6 (0.6)	1.46 (0.02)	2984	18.7 (0.5)		1.87 (0.04)	<0.001	530	16.7 (0.9)	1.68 (0.07)	2454	19.1 (0.5)	1.91 (0.04)		<0.001
Alcohol									<0.001									0.175	
Never	4234	11.2 (0.5)	1.10 (0.02)	1856	10.4 (0.6)	0.93 (0.03)	2378	12.0 (0.6)		1.28 (0.03)	<0.001	459	10.9 (0.8)	1.22 (0.05)	1919	12.3 (0.6)	1.30 (0.03)		0.300
Former	4522	12.5 (0.3)	1.21 (0.02)	1966	11.3 (0.3)	1.07 (0.02)	2556	14.0 (0.4)		1.36 (0.03)	<0.001	546	14.9 (0.9)	1.26 (0.06)	2010	13.7 (0.4)	1.39 (0.04)		0.057
Current	22 006	76.3 (0.7)	1.30 (0.01)	11 089	78.3 (0.7)	1.16 (0.01)	10 917	74.0 (0.8)		1.50 (0.02)	<0.001	2135	74.3 (1.3)	1.43 (0.03)	8782	74.0 (0.8)	1.51 (0.02)		<0.001
Menopause‖									<0.001									0.099	
Premenopausal	7803	58.4 (0.7)	0.84 (0.01)	5707	75.0 (0.7)	0.81 (0.01)	2096	36.8 (0.9)		0.94 (0.02)	<0.001	397	34.2 (2.0)	0.94 (0.04)	1699	37.5 (0.9)	0.94 (0.02)		0.817
(Post-) menopausal	7280	41.6 (0.7)	1.50 (0.02)	2063	25.0 (0.7)	1.47 (0.03)	5217	63.2 (0.9)		1.51 (0.02)	0.012	1228	65.8 (2.0)	1.39 (0.04)	3989	62.5 (0.9)	1.55 (0.02)		<0.001
BMI (kg/m^2)¶	30 762	28.7 (0.1)	N/A	14 911	27.3 (1.0)	N/A	15 851	30.2 (0.1)	<0.001	N/A	N/A	3140	31.4 (0.2)	N/A	12 711	29.9 (0.1)	N/A	<0.001	N/A
Cotinine (ng/mL)#	30 762	0.4 (0.0)	N/A	14 911	0.4 (0.0)	N/A	15 851	0.3 (0.0)	<0.001	N/A	N/A	3140	0.2 (0.0)	N/A	12 711	0.3 (0.0)	N/A	0.111	N/A

BLL indicates blood lead level; BMI, body mass index; and family PIR, ratio of family income to poverty.
*P value: to compare the characteristics between nonhypertensive and hypertensive people, using chi-square test for categorical variables and *t* test for continuous variables.
†P value: to compare BLL between nonhypertensive and hypertensive people, using *t* test.
‡P value: to compare the characteristics between participants with controlled and uncontrolled hypertension, using chi-square test for categorical variables and t test for continuous variables.
§P value: to compare BLL between participants with controlled and uncontrolled hypertension, using *t* test.
‖Only for women.
¶Arithmetic mean (SE).
#Geometric mean (SE).

(95% CI, 1.08, 1.73) times the odds of uncontrolled hypertension compared with women with BLL <0.7 μg/dL (Q1). In addition, for hypertensive women, each 1 μg/dL increase in BLL was associated with 7.4% greater odds of uncontrolled hypertension (95% CI, 1.006, 1.147). In model 3, the results were similar to those of Model 1 (Table S3).

Higher BLL was found to be correlated to hypertension in men and uncontrolled hypertension in both sexes, after adjusting for age, sex, race/ethnicity, family PIR, education, smoking status, serum cotinine, alcohol intake, BMI, and menopause status (in female) (Table 2). From Model 1 we observed that Q3 and Q4 of BLL were associated with a greater prevalence of any hypertension compared with Q1 in men (Q3: OR, 1.163; 95% CI, 1.006–1.344; Q4: OR, 1.249; 95% CI, 1.076–1.450; *P*-trend=0.005) but not in women. Each 1 μg/dL increase in BLL showed 1.037 times the odds of any hypertension (95% CI, 1.015–1.060) in men and 1.020 times the odds (95% CI, 0.970–1.074) in women. From Model II, we found that among hypertensive men, those with BLL >1.50 μg/dL (Q3) had a higher prevalence of uncontrolled hypertension compared with men with BLL <0.94 μg/dL (Q1) (Q3: OR, 1.700; 95% CI, 1.258–2.298; Q4: OR, 1.964; 95% CI, 1.453–2.654; *P*-trend<0.001). The result in hypertensive women were similar to that in men (Q3: OR, 1.479; 95% CI, 1.096–1.996; Q4: OR, 1.703; 95% CI, 1.263–2.295; *P*-trend<0.001). The OR (95% CI) for per μg/dL increase in BLL was 1.157 (1.080–1.239) in men and 1.109 (1.020–1.205) in women. In Model III, we found that among all men, Q2–Q4 of BLL were correlated to greater prevalence of uncontrolled hypertension compared with Q1 (Q2: OR, 1.191; 95% CI, 1.032–1.375; Q3: OR, 1.331, 95% CI: 1.169–1.515; Q4: OR, 1.480, 95% CI: 1.280–1.710). However, in women, only Q3 and Q4 of BLL showed this effect (Q3: OR, 1.244; 95% CI, 1.041–1.486; Q4: OR, 1.316; 95% CI, 1.080–1.603). Figure 2 showed restricted cubic splines indicating nonlinear association between BLL and any or uncontrolled hypertension. The splines were based on all the models involved in the primary analysis.

The association of higher BLL with the control of hypertension was found to vary across antihypertension medications. First, we looked at the participants taking primary antihypertensive agents of single category. For men using only CCB, per μg/dL increase in BLL was associated with 22.9% greater odds of uncontrolled hypertension (95% CI: 1.019, 1.481). For women taking only thiazide and thiazide-like diuretics, compared with those with BLL <0.70 μg/dL (Q1), BLL >1.66 μg/dL (Q4) was associated with 3.753 times the odds of uncontrolled hypertension (95% CI, 1.234, 11.410), and the *P*-trend for the quartiles of BLL was 0.043 (Table 3). Then, we observed the participants taking single or multiple primary antihypertensive agents. We estimated the relationship between BLL and uncontrolled hypertension, by groups of people taking certain medications, including angiotensin-converting enzyme inhibitors, CCB and (or) thiazides and thiazide-like diuretics (Table 4). For those taking more than 1 kind of medication, they would appear in 2 or more groups. In the men taking CCB and (or) thiazides and thiazide-like diuretics and the women using thiazides and thiazide-like diuretics, higher BLL was inconsistently associated with greater prevalence of uncontrolled hypertension. In these analyses, the sample size varied by model, and thus the statistical power could be affected to some extent.

To exclude the influence of the different measuring methodology of blood lead, we conducted additional analyses stratified by the BLL assessment methods: atomic absorption spectrometer (1999–2002) and inductively coupled plasma mass spectrometry (2003–2016) (Table S4). However, stratified analysis may reduce statistical predictive power leading to null findings. We did not find any significant association between BLL and any hypertension with either BLL measuring way. Among hypertensive participants, in 1999–2002, women with Q2 and Q4 of BLL were more likely to have uncontrolled hypertension; in 2003–2016, Q3 and Q4 of BLL in men were associated with uncontrolled hypertension. Among men with or without hypertension, Q4 of BLL in 1999–2002 and Q2–Q4 of BLL in 2003–2016 were all associated with uncontrolled hypertension. Moreover, in our analysis further adjusted for estimated glomerular filtration rate (Table S5), the significant association between BLL and any hypertension became weaker, but the effect size for the association between BLL and uncontrolled hypertension was larger.

In the additional analyses involving the types of antihypertensive medications, we had similar findings. First, when we further adjusted for the number of classes of antihypertensive medications taken, we found the association between higher BLL and uncontrolled hypertension was somewhat attenuated after the further adjustment but still significant in both sexes (Table S6). Additionally, in the stratified analyses by whether taking antihypertensive medications, we also found significant association between BLL and uncontrolled hypertension in men and women (Table S7).

In the supplemental analyses based on the Joint National Committee 7 definition of hypertension, the prevalence of any hypertension in US adults was 31.1% (n=11 368), but 47.7% (n=6305) of hypertensive people did not have the BP controlled (Table S8). We also

Table 2. Adjusted ORs (95% CI) of Hypertension and Uncontrolled Hypertension by Quartiles of Blood Lead Level in US Adults

		Model 1 Cases: Any Hypertension Non-Cases: Non-Hypertension			Model 2 Cases: Uncontrolled Hypertension Non-Cases: Controlled Hypertension			Model 3 Cases: Uncontrolled Hypertension Non-Cases: Controlled Hypertension+Non-Hypertension		
Sex	BLL (μg/dL)	Cases	Non-Cases	OR (95% CI)*	Cases	Non-Cases	OR (95% CI)*	Cases	Non-Cases	OR (95% CI)*
Men	Q1 (<0.94)	1205	1633	Reference	1019	186	Reference	1019	1819	Reference
	Q2 (0.94–1.50)	1850	1740	1.116 (0.957–1.301)	1511	339	1.343 (0.975–1.850)	1511	2079	1.191 (1.032–1.375)
	Q3 (1.50–2.30)	2253	1802	1.163 (1.006–1.344)	1816	437	1.700 (1.258–2.298)	1816	2239	1.331 (1.169–1.515)
	Q4 (>2.30)	3230	1966	1.249 (1.076–1.450)	2677	553	1.964 (1.453–2.654)	2677	2519	1.480 (1.280–1.710)
	P-trend †	0.005			<0.001			<0.001		
	Continuous BLL	8538	7141	1.037 (1.015–1.060)	7023	1515	1.157 (1.080–1.239)	7023	8656	1.062 (1.036–1.088)
Women	Q1 (<0.70)	871	2176	Reference	649	222	Reference	649	2398	Reference
	Q2 (0.70–1.08)	1468	2076	1.072 (0.891–1.288)	1113	355	1.257 (0.947–1.668)	1113	2431	1.158 (0.968–1.386)
	Q3 (1.08–1.66)	2115	1859	1.060 (0.870–1.292)	1648	467	1.479 (1.096–1.996)	1648	2326	1.244 (1.041–1.486)
	Q4 (>1.66)	2859	1659	1.059 (0.851–1.317)	2278	581	1.703 (1.263–2.295)	2278	2240	1.316 (1.080–1.603)
	P-trend†	0.684			<0.001			0.005		
	Continuous BLL	7313	7770	1.020 (0.970–1.074)	5688	1625	1.109 (1.020–1.205)	5688	9395	1.056 (1.011–1.102)

BLL indicates blood lead level; and OR, odds ratio.

*All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female).

†*P*-trend: the *P* value for the ordinal variable coded as 1, 2, 3, 4 for the quartiles.

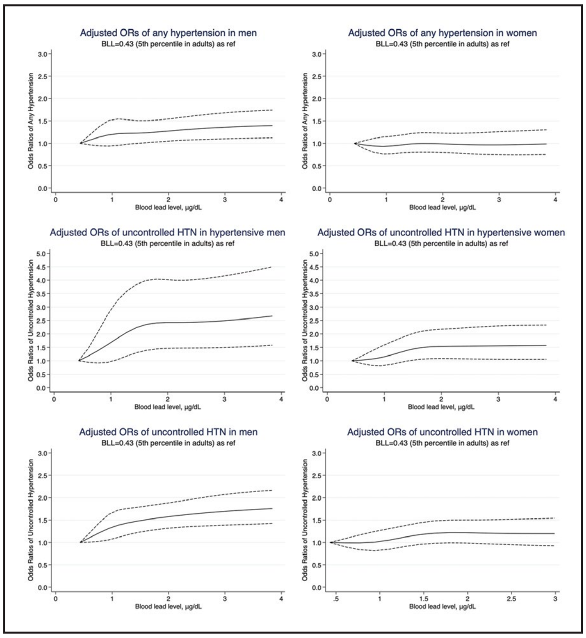

Figure 2. Restricted cubic splines for blood lead level and any hypertension or uncontrolled hypertension.
All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), BMI (kg/m^2), and menopause status (yes/no, only for female). BLL indicates blood lead level; HTN, hypertension; and OR, odds ratio.

conducted the 3 models as in the primary analyses. From both models 2 and 3, we found that Q3 and Q4 of BLL in men and Q4 in women were related to higher prevalence of uncontrolled hypertension, with Q1 as reference (Table S9).

DISCUSSION

The main finding of this study is that BLL is associated with hypertension in men and uncontrolled hypertension in both sexes, and men may be more vulnerable to the negative effect of lead than women. Our results are in alignment with the previous findings, indicating a strong relationship between lead exposure and higher BP.[7] We also found that men have a higher prevalence of hypertension than women in the United States.[2,10] Moreover, the greater effect size between BLL and uncontrolled hypertension in men than women may result from not only the higher general BLL in men but also some potential biological effect modification based on sex. Physiological differences like the ovarian and testicular hormonal milieu and sex chromosomes may contribute to the difference.[24] Health-seeking behavior may play a role, as a cross-sectional study in French adults found that women tended to have a better awareness of hypertension than men and their hypertension was better controlled.[26] Although it is clear that higher BMI is positively correlated with higher SBP and DBP,[27] we found that BMI in the uncontrolled hypertension group was lower than those with controlled hypertension. We did not determine the reasons or etiology for this counterintuitive finding. Although the association between BMI and hypertension was statistically significant, it was not clinically significant. As far as we know, no previous studies focused on the association between blood lead level and uncontrolled hypertension in a cohort representative of the US noninstitutionalized general population.

A number of studies examined the association between blood lead and BP with varying epidemiological methods and target populations. A case-control study with 108 men aged 24 to 59 in Saudi Arabia found significant positive correlations between BLL and SBP as well as DBP (BLL: 1.85±0.132 μg/dL in controls versus 2.21±0.125 μg/dL in hypertensive patients, $P<0.05$).[28] In South Korea, a study suggested that BLL is associated with higher BP and increased risk of hypertension based on a representative sample of 11 979 adults in 2008–2013.[29] Similarly, a population-based study with 948 Brazilian adults aged 40 and above demonstrated that the highest quartile of BLL (>2.76 μg/dL) led to an increased DBP by 0.06 mm Hg ($P<0.001$) compared with the lowest quartile (≤1.32 μg/dL). Participants in the 90th percentile of BLL showed higher OR (OR, 2.77; 95% CI, 1.41–5.46) for hypertension comparing with those in the 10th percentile.[30] In the Normative Aging Study, long-term lead accumulation, indicated by bone lead levels, indicated higher risk of developing of hypertension in adult men.[15] However, a cross-sectional study with 310 male smelting workers in South Korea failed to find a relationship between BLL and BP.[31] A study of 15 431 subjects using NHANES III (1988–1994) did not find consistent association between BLL and BP across all demographic groups.[12] A study with 12 725 participants in NHANES 2003–2010 also found only a small and inconsistent association between BLL and BP.[14]

Although BLL has been declining in the United States,[11] BLL in the US population in recent years still contributes to high blood pressures. The various null and positive findings could result from several reasons as the etiology of high blood pressure is complex and depends on a variety of genetic, lifestyle, and environmental factors. In our analysis, we had a larger sample size of 30 762, which enhanced the ability of detecting small statistical associations. Second, the outcome of the previous study was BP, although our study focused on "having hypertension" or "having uncontrolled hypertension," which

Table 3. ORs (95% CI) of Uncontrolled Hypertension by Quartiles of BLL (μg/dL) in US Adults, Stratified by Use of Single Antihypertensive Medications

Medication Used Only	Cases*	Non-Cases *	Model 1†‡					Model 2‡ ǁ
			Q1	Q2	Q3	Q4	*P*-Trend§	
Male			<0.94	0.94 to 1.50	1.50 to 2.30	>2.30		
ACEI	613	423	Ref.	1.679 (0.897–3.143)	1.695 (0.929–3.092)	1.628 (0.917–2.891)	0.149	1.034 (0.923–1.158)
ARB	209	112	Ref.	0.761 (0.227–2.554)	0.792 (0.263–2.385)	0.634 (0.184–2.183)	0.506	0.998 (0.792–1.256)
CCB	399	172	Ref.	0.758 (0.271–2.117)	0.835 (0.293–2.383)	1.368 (0.489–3.826)	0.266	1.229 (1.019–1.481)
Thiazide and thiazide-like diuretics	140	81	Ref.	4.876 (0.921–25.810)	3.436 (0.524–22.545)	3.415 (0.703–16.592)	0.284	1.150 (0.912–1.450)
Female			<0.70	0.70 to 1.08	1.08 to 1.66	>1.66		
ACEI	528	338	Ref.	1.070 (0.567–2.019)	1.254 (0.642–2.446)	1.256 (0.630–2.502)	0.451	1.122 (0.924–1.364)
ARB	250	175	Ref.	1.118 (0.397–3.148)	1.871 (0.793–4.415)	1.122 (0.472–2.666)	0.607	0.935 (0.732–1.193)
CCB	441	207	Ref.	1.191 (0.448–3.165)	1.527 (0.616–3.786)	1.462 (0.617–3.462)	0.321	1.061 (0.910–1.237)
Thiazide and thiazide-like diuretics	224	113	Ref.	2.446 (0.915–6.539)	2.393 (0.874–6.552)	3.753 (1.234–11.410)	0.043	1.442 (0.939–2.213)

ACEI indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BLL, blood lead level; CCB, calcium channel blocker; OR, odds ratio.

*Cases: people with uncontrolled hypertension; non-cases: those having their hypertension controlled.

†Model 1: estimating odds ratio (95% CI) for quartiles of BLL.

‡All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female).

§*P*-trend: the *P* value for the dummy variable coded 1, 2, 3, 4 for the quartiles.

ǁModel 2: taking the continuous BLL (μg/dL) as the major independent variable and estimating odds ratio (95% CI) for the increase of 1 μg/dL BLL.

specified outcome assessment beyond previous studies. Furthermore, we also conducted analysis based on previous and current guidelines by using the 130/80 mm Hg (SBP/DBP) criteria. Nevertheless, there is a possibility that unknown confounders of hypertension have altered over years, thereby resulting in the different findings of the relationship between BLL and hypertension.

There are some possible factors that may account for the association between uncontrolled hypertension and BLL. First, people with higher BLL may have less access to antihypertensive medications or health care as a whole. Although we adjusted for family income and educational level in the models, the interfering effect of socioeconomic status may still remain. After further adjusting for the number of classes of antihypertensive medications taken and the stratified analysis among people taking and not taking antihypertensive medications, we still found a weaker but significant relationship between higher BLL and uncontrolled hypertension in men, and no significant results presented in women. Therefore, even if taking this variable into consideration, BLL is consistently related to uncontrolled hypertension in men. Poor medication adherence in the low-socioeconomic status group with higher blood lead levels may also be a possible mechanism, but previous evidence on low socioeconomic status and nonadherence to antihypertensive medications did not show a strong relationship.[32] Second, higher BLL possibly inhibit the effect of some types of antihypertensive medications. Among participants taking or only taking angiotensin-converting enzyme inhibitors, CCB, or thiazide and thiazide-like diuretics, higher BLL was related to uncontrolled hypertension, which did not exist in those taking only angiotensin receptor blocker. It indicated that the reduction of renal function is the major cause of lead-induced hypertension,[8] which is consistent with the unsatisfactory effect of diuretics. Lead can also result in hypertension by stimulating the renin-angiotensin system , whereas both angiotensin-converting enzyme inhibitors and angiotensin receptor blocker lower BP by inhibiting the renin-angiotensin system. Toxicology studies have shown that lead induces smooth muscle contraction through release of calcium.[33,34] Further research is needed to better elucidate the relationship between BLL and the effects of specific types of antihypertensive

Table 4. Association Between Uncontrolled Hypertension and BLL (μg/dL) in US Adults, Stratified by Use of Antihypertensive Medications

Medication Used	Cases *	Non-Cases *	Model 1†					Model 2§
			Q1	Q2	Q3	Q4	*P*-Trend‡	
Male			<0.94	0.94 to 1.50	1.50 to 2.30	>2.30		
ACEI	957	628	Ref.	1.472 (0.781–2.774)	1.702 (0.981–2.954)	1.591 (0.926–2.734)	0.070	1.056 (0.962–1.158)
ARB	340	198	Ref.	0.586 (0.268–1.281)	0.624 (0.304–1.278)	0.921 (0.393–2.161)	0.864	1.071 (0.898–1.277)
CCB	780	383	Ref.	1.042 (0.542–2.003)	1.176 (0.601–2.300)	1.811 (0.940–3.490)	0.027	1.187 (1.072–1.314)
Thiazide and thiazide-like diuretics	372	247	Ref.	0.845 (0.297–2.404)	1.172 (0.440–3.125)	1.245 (0.471–3.290)	0.441	1.165 (1.013–1.339)
Female			<0.70	0.70 to 1.08	1.08 to 1.66	>1.66		
ACEI	849	514	Ref.	0.880 (0.521–1.487)	1.064 (0.637–1.775)	1.177 (0.681–2.035)	0.317	1.092 (0.971–1.228)
ARB	423	272	Ref.	1.397 (0.546–3.573)	1.852 (0.820–4.182)	1.235 (0.581–2.624)	0.703	0.953 (0.822–1.104)
CCB	812	374	Ref.	1.305 (0.655–2.601)	1.339 (0.638–2.807)	1.389 (0.750–2.573)	0.360	1.024 (0.922–1.137)
Thiazide and thiazide-like diuretics	485	276	Ref.	1.268 (0.582–2.760)	1.284 (0.641–2.575)	2.018 (1.005–4.053)	0.043	1.199 (0.956–1.505)

ACEI indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; BLL, blood lead level; and CCB, calcium channel blocker.

*Cases: people with uncontrolled hypertension; non-cases: those having their hypertension controlled.

†Model 1: estimating odds ratio (95% CI) for quartiles of BLL.

‡*P*-trend: the *P* value for the dummy variable coded 1, 2, 3, 4 for the quartiles.

§Model 2: taking the continuous BLL (μg/dL) as the major independent variable, and estimating odds ratio (95% CI) for the increase of 1 μg/dL BLL.

‖All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female).

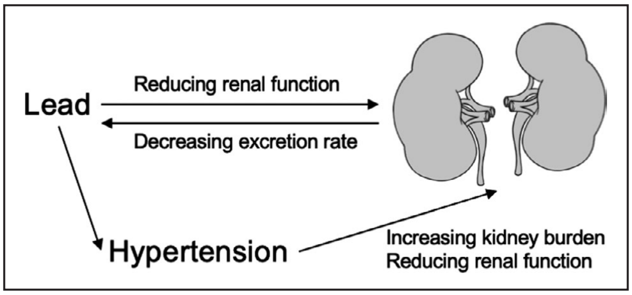

Figure 3. The vicious circle in lead and hypertension.

medication. Whether there is an association between blood lead and indications of types of medication needs to be explored. Third, most of the lead in the body is excreted through kidney.[35] When hypertension begins, it will further increase the kidney burden and may lead to hypertensive renal disease. Thus, the excretion rate of lead will decrease, and lead will be more likely to accumulate in the body, which is a vicious cycle (Figure 3).

Before the publishing of the latest guideline for hypertension in adults in 2017, the definition of hypertension was SBP ≥140 mm Hg or DBP ≥90 mm Hg or currently taking antihypertensive medications, based on the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report.*[25] In this study, we compared the main results based on the 2 definitions of hypertension and found they were quite similar. The consistency of the results enhanced the validity of the conclusion that BLL is associated with uncontrolled hypertension.

Our analysis has several strengths. First, this study combined 9 waves of data, covering over a decade from 1999 to 2016. The nationally representative sample of the US population is also one of our strengths. Additionally, we adjusted for comprehensive covariates in the analyses, including socioeconomic status indicators. Furthermore, this study used the latest definition of hypertension, and thus has greater significance in clinical practice. However, the limitations of this study should also be noted. First, we used serial cross-sectional data, which do not imply a causal relationship of BLL and uncontrolled hypertension. Second, when applying the definitions in the latest guideline in this study, this group of people were sorted as uncontrolled hypertension, which might contribute to a higher estimation of prevalence of uncontrolled hypertension. The supplemental analyses based on the Joint National Committee 7 definition is provided for comparison. Last, type I error inflation may exist in the results because of multiple statistical tests in our exploratory analyses.

In conclusion, considering the negative effect of lead exposure on the control of blood pressure, lead burden should be considered for people with uncontrolled hypertension in clinical settings.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Materials

Tables S1–S9

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Supplemental Material

Table S1. Characteristics of included and excluded participants (unweighted).

	Overall		Included		Excluded	
	n	%	n	%	n	%
Overall	45719	100.0	30762	100.0	14957	100.0
Sex						
Male	22658	49.6	15679	51.0	6979	46.7
Female	23061	50.4	15083	49.0	7978	53.3
Age						
20-39	15019	32.9	10081	32.8	4938	33.0
40-59	14897	32.6	10113	32.9	4784	32.0
60+	15803	34.6	10568	34.4	5235	35.0
Race/ethnicity						
Non-Hispanic white	20594	45.0	15050	48.9	5544	37.1
Non-Hispanic black	9603	21.0	5988	19.5	3615	24.2
Hispanic	11803	25.8	7728	25.1	4075	27.2
Other	3719	8.1	1996	6.5	1723	11.5
Family PIR						
0⩽PIR<1	8676	19.0	5945	19.3	2731	18.3
1⩽PIR<2	11165	24.4	8152	26.5	3013	20.1
2⩽PIR<3	6460	14.1	4817	15.7	1643	11.0
PIR⩾3	15467	33.8	11848	38.5	3619	24.2
Missing	3951	8.6	NA	NA	3951	26.4
Education						
Below high school	12877	28.2	8302	27.0	4575	30.6
High school	10572	23.1	7164	23.3	3408	22.8
College or above	22200	48.6	15296	49.7	6904	46.2
Missing	70	0.2	NA	NA	70	0.5
Smoking						
Never	24460	53.5	16127	52.4	8333	55.7
Former	11368	24.9	7927	25.8	3441	23.0
Current	9840	21.5	6708	21.8	3132	20.9
Missing	51	0.1	NA	NA	51	0.3
Alcohol						
Never	6097	13.3	4234	13.8	1863	12.5

Former	6165	13.5	4522	14.7	1643	11.0
Current	29163	63.8	22006	71.5	7157	47.9
Missing	4294	9.4	NA	NA	4294	28.7
BMI (kg/m^2) *	28.8 (6.7)					
Missing	953	2.1				
Cotinine (ng/mL) *	57.4 (126.5)					
Missing	2845	6.2				
BLL (μg/dL) *	1.9 (1.9)					
Missing	7492	16.4				

family PIR = ratio of family income to poverty, BMI = body mass index, BLL = blood lead level.

* Mean (standard deviation).

Table S2. Classes of antihypertensive medications.

	Drug classes	1st-2nd-3rd Level Category ID	Generic drug code
Primary agents			
1	ACEI	40-42	d00006, d00013, d00242, d00365, d00728, d00730, d00732, d03835, d04008, d04440, h00032
2	ARB	40-56	d03821, d04113, d04222, d04266, d04322, d04364, d04801, d07754
3	CCB	40-48	d00045, d00048, d00051, d00231, d00270, d00315, d00689, d03825
4	Thiazide and thiazide-like diuretics	40-49-156	c00156, d00190, d00192, d00253, d00260, d00299, d00641, d00643, d00645, d00646
Secondary agents			
5	Diuretics—loop	40-49-154	d00070, d00179, d00649, d03189
6	Diuretics—potassium sparing	40-49-155	d00169, d00373, d00396
7	Diuretics—aldosterone antagonists	N/A	d04815, d00373
8	β-blocker	40-47	c00047, d00004, d00016, d00018, d00032, d00128, d00134, d00137, d00139, d00176, d00332, d00371, d00709, d03847, d05265
9	Direct renin inhibitors		d06665
10	Peripheral α-Adrenergic receptor antagonist	40-43	d00131, d00138, d00367, d00386, d00725, d00726, d03151, d04121, d04797, d07354, d07634
11	Central-acting and other antiadrenergic drugs	40-44	d00044, d00130, d00133, d00717
12	Direct Vasodilators	N/A	d00132, d00135

Table S3. Unadjusted ORs (95% CI) of hypertension and uncontrolled hypertension by quartiles of blood lead level in US adults.

Sex	BLL (μg/dL)	Model 1 Cases: Any HTN Non-cases: non-HTN			Model 2 Cases: uncontrolled HTN Non-cases: controlled HTN			Model 3 Cases: uncontrolled HTN Non-cases: controlled HTN + non-HTN		
		Cases	Non-cases	OR (95% CI)	Cases	Non-cases	OR (95% CI)	Cases	Non-cases	OR (95% CI)
Men	Q1 (<0.94)	1205	1633	Reference	1019	186	Reference	1019	1819	Reference
	Q2 (0.94-1.50)	1850	1740	1.335 (1.174 to 1.517)	1511	339	0.966 (0.697 to 1.339)	1511	2079	1.274 (1.109 to 1.462)
	Q3 (1.50-2.30)	2253	1802	1.589 (1.404 to 1.798)	1816	437	1.022 (0.760 to 1.376)	1816	2239	1.501 (1.331 to 1.694)
	Q4 (>2.30)	3230	1966	1.895 (1.681 to 2.138)	2677	553	1.021 (0.772 to 1.352)	2677	2519	1.736 (1.523 to 1.979)
	P-trend *	<0.001			0.752			<0.001		
	Continuous BLL	8538	7141	1.100 (1.067 to 1.135)	7023	1515	1.039 (0.997 to 1.082)	7023	8656	1.089 (1.058 to 1.121)
Women	Q1 (<0.70)	871	2176	Reference	649	222	Reference	649	2398	Reference
	Q2 (0.70-1.08)	1468	2076	1.752 (1.498 to 2.048)	1113	355	1.135 (0.871 to 1.478)	1113	2431	1.718 (1.454 to 2.030)
	Q3 (1.08-1.66)	2115	1859	2.572 (2.186 to 3.025)	1648	467	1.266 (0.971 to 1.651)	1648	2326	2.470 (2.115 to 2.886)
	Q4 (>1.66)	2859	1659	3.778 (3.209 to 4.448)	2278	581	1.368 (1.082 to 1.730)	2278	2240	3.461 (2.954 to 4.056)
	P-trend *	<0.001			0.006			<0.001		
	Continuous BLL	7313	7770	1.525 (1.416 to 1.643)	5688	1625	1.074 (1.006 to 1.147)	5688	9395	1.406 (1.322 to 1.496)

BLL = blood lead level, HTN = hypertension, OR = odds ratio, CI = confidence interval.

* *P*-trend: the *P*-value for the ordinal variable coded as 1, 2, 3, 4 for the quartiles.

Table S4. ORs (95% CI) of hypertension and uncontrolled hypertension by quartiles of blood lead level in US adults, stratified by the blood lead measuring methodology.

Methodology	Sex	BLL (μg/dL)	**Model 1** Cases: Any HTN Non-cases: non-HTN			**Model 2** Cases: uncontrolled HTN Non-cases: controlled HTN			**Model 3** Cases: uncontrolled HTN Non-cases: controlled HTN + non-HTN		
			Cases	Non-cases	OR (95% CI) †	Cases	Non-cases	OR (95% CI) †	Cases	Non-cases	OR (95% CI) †
Atomic absorption spectrometry (1999-2002)	Men	Q1 (<1.4)	285	359	Reference	257	28	Reference	257	387	Reference
		Q2 (1.4-2.0)	403	355	1.025 (0.808 to 1.300)	350	53	0.930 (0.397 to 2.179)	350	408	1.057 (0.853 to 1.311)
		Q3 (2.0-2.9)	493	386	1.010 (0.762 to 1.339)	435	58	1.372 (0.695 to 2.710)	435	444	1.130 (0.874 to 1.461)
		Q4 (>2.9)	727	412	1.358 (0.990 to 1.862)	658	69	1.864 (0.807 to 4.307)	658	481	1.539 (1.099 to 2.156)
		P-trend *		0.087			0.070			0.022	
		Continuous BLL	1908	1512	1.037 (1.005 to 1.070)	1700	208	1.216 (1.044 to 1.415)	1700	1720	1.053 (1.019 to 1.088)
	Women	Q1 (<0.9)	195	407	Reference	164	31	Reference	164	438	Reference
		Q2 (0.9-1.3)	307	381	0.951 (0.661 to 1.369)	269	38	1.901 (1.011 to 3.576)	269	419	1.169 (0.854 to 1.601)
		Q3 (1.3-2.0)	505	447	0.977 (0.731 to 1.306)	429	76	1.410 (0.805 to 2.471)	429	523	1.104 (0.836 to 1.458)
		Q4 (>2.0)	645	359	0.927 (0.640 to 1.341)	573	72	2.889 (1.493 to 5.590)	573	431	1.285 (0.935 to 1.765)
		P-trend *		0.729			0.011			0.168	
		Continuous BLL	1652	1594	1.020 (0.929 to 1.119)	1435	217	1.096 (0.937 to 1.281)	1435	1811	1.037 (0.966 to 1.113)
Inductively coupled plasma–mass spectrometry (2003-2016)	Men	Q1 (<0.88)	925	1267	Reference	777	148	Reference	777	1415	Reference
		Q2 (0.88-1.36)	1421	1368	1.059 (0.907 to 1.235)	1152	269	1.461 (0.998 to 2.138)	1152	1637	1.190 (1.030 to 1.375)
		Q3 (1.36-2.10)	1752	1430	1.121 (0.958 to 1.312)	1380	372	1.639 (1.171 to 2.296)	1380	1802	1.291 (1.120 o 1.488)
		Q4 (>2.10)	2532	1564	1.132 (0.960 to 1.335)	2014	518	1.782 (1.291 to 2.461)	2014	2082	1.335 (1.145 to 1.557)
		P-trend *		0.125			<0.001			<0.001	

	Continuous BLL	6630	5629	1.028 (1.001 to 1.056)	5323	1307	1.105 (1.031 to 1.184)	5323	6936	1.049 (1.017 to 1.081)
Women	Q1 (<0.70)	624	1673	Reference	461	163	Reference	461	1836	Reference
	Q2 (0.70-1.08)	1114	1708	1.060 (0.861 to 1.307)	810	304	1.016 (0.736 to 1.402)	810	2012	1.058 (0.844 to 1.325)
	Q3 (1.08-1.66)	1666	1508	1.000 (0.788 to 1.270)	1265	401	1.300 (0.895 to 1.888)	1265	1909	1.152 (0.919 to 1.444)
	Q4 (>1.66)	2257	1287	1.003 (0.779 to 1.291)	1717	540	1.356 (0.950 to 1.937)	1717	1827	1.179 (0.919 to 1.512)
	P-trend *			0.871			0.028			0.134
	Continuous BLL	5661	6176	1.001 (0.941 to 1.064)	4253	1408	1.069 (0.974 to 1.174)	4253	7584	1.033 (0.979 to 1.090)

BLL = blood lead level, HTN = hypertension, OR = odds ratio, CI = confidence interval.

* *P*-trend: the *P*-value for the ordinal variable coded as 1, 2, 3, 4 for the quartiles.

† All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female).

Table S5. ORs (95% CI) of hypertension and uncontrolled hypertension by quartiles of blood lead level in US adults, further adjusted for estimated glomerular filtration rate (eGFR).

Sex	BLL (μg/dL)	Model 1 Cases: Any HTN Non-cases: non-HTN			Model 2 Cases: uncontrolled HTN Non-cases: controlled HTN			Model 3 Cases: uncontrolled HTN Non-cases: controlled HTN + non-HTN		
		Cases	Non-cases	OR (95% CI) †	Cases	Non-cases	OR (95% CI) †	Cases	Non-cases	OR (95% CI) †
Men	Q1 (<0.94)	1197	1626	Reference	1012	185	Reference	1012	1811	Reference
	Q2 (0.94-1.50)	1841	1738	1.108 (0.949 to 1.292)	1502	339	1.368 (0.997 to 1.878)	1502	2077	1.188 (1.031 to 1.370)
	Q3 (1.50-2.30)	2244	1799	1.154 (0.998 to 1.334)	1808	436	1.736 (1.287 to 2.341)	1808	2235	1.332 (1.171 to 1.515)
	Q4 (>2.30)	3216	1954	1.238 (1.065 to 1.438)	2666	550	2.042 (1.510 to 2.762)	2666	2504	1.486 (1.285 to 1.718)
	P-trend *		0.007			<0.001			<0.001	
	Continuous BLL	8498	7117	1.037 (1.015 to 1.060)	6988	1510	1.167 (1.086 to 1.255)	6988	8627	1.063 (1.038 to 1.089)
Women	Q1 (<0.70)	864	2166	Reference	644	220	Reference	644	2386	Reference
	Q2 (0.70-1.08)	1457	2067	1.060 (0.881 to 1.275)	1106	351	1.291 (0.975 to 1.708)	1106	2418	1.163 (0.973 to 1.392)
	Q3 (1.08-1.66)	2099	1854	1.039 (0.853 to 1.266)	1636	463	1.541 (1.137 to 2.089)	1636	2317	1.245 (1.042 to 1.488)
	Q4 (>1.66)	2845	1650	1.042 (0.836 to 1.298)	2266	579	1.793 (1.324 to 2.427)	2266	2229	1.325 (1.086 to 1.616)
	P-trend *		0.801			<0.001			0.005	
	Continuous BLL	7265	7737	1.018 (0.968 to 1.072)	5652	1613	1.124 (1.033 to 1.225)	5652	9350	1.057 (1.012 to 1.104)

BLL = blood lead level, HTN = hypertension, OR = odds ratio, CI = confidence interval.

* *P*-trend: the *P*-value for the ordinal variable coded as 1, 2, 3, 4 for the quartiles.

† All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), menopause status (yes/no, only for female), and eGFR.

Table S6. ORs (95% CI) of hypertension and uncontrolled hypertension by quartiles of blood lead level (μg/dL) in US adults.

Models †	Cases *	Non-cases *	Q1	Q2	Q3	Q4
Male			**<0.94**	**0.94-1.50**	**1.50-2.30**	**>2.30**
Model 1	7021	1514	Ref.	1.263 (0.914 to 1.746)	1.512 (1.118 to 2.045)	1.697 (1.251 to 2.304)
Model 2	7021	1514	Ref.	1.324 (0.957 to 1.831)	1.610 (1.186 to 2.185)	1.851 (1.370 to 2.500)
Female			**<0.70**	**0.70-1.08**	**1.08-1.66**	**>1.66**
Model 1	5685	1625	Ref.	1.211 (0.914 to 1.606)	1.464 (1.104 to 1.941)	1.636 (1.221 to 2.191)
Model 2	5685	1625	Ref.	1.201 (0.902 to 1.600)	1.401 (1.051 to 1.868)	1.635 (1.221 to 2.191)

* Cases: people with controlled hypertension; non-cases: those having their hypertension controlled.

† All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female). Model 1 was further adjusted for number of primary agents taken, and model 2 was further adjusted for number of primary and secondary agents taken.

Table S7. Association between uncontrolled hypertension and blood lead level (μg/dL), stratified by the use of antihypertensive medications.

Models		**Reported not taking antihypertensive medications** Cases: w/ uncontrolled HTN; Non-cases: w/o HTN		**Reported taking antihypertensive medications** Cases: w/ uncontrolled HTN; Non-cases: w/ controlled HTN	
		Male (M)	Female (F)	Male (M)	Female (F)
Cases		4727	3078	2296	2610
Non-cases		7141	7770	1515	1625
Model 1: ORs (95%CI)	Q1 (M: <0.94; F: <0.70)	Ref.	Ref.	Ref.	Ref.
	Q2 (M: 0.94-1.50; F: 0.70-1.08)	1.183 (1.009 to 1.387)	1.208 (0.992 to 1.472)	1.209 (0.858 to 1.703)	1.085 (0.782 to 1.504)
	Q3 (M: 1.50-2.30; F: 1.08-1.66)	1.351 (1.158 to 1.575)	1.193 (0.965 to 1.477)	1.335 (0.961 to 1.856)	1.378 (1.013 to 1.875)
	Q4 (M: >2.30; F: >1.66)	1.484 (1.253 to 1.758)	1.340 (1.037 to 1.731)	1.542 (1.118 to 2.126)	1.366 (1.005 to 1.856)
	P-trend ‡	<0.001	0.038	0.006	0.018
Model 2	OR (95% CI)	1.058 (1.031 to 1.085)	1.064 (1.006 to 1.126)	1.099 (1.033 to 1.170)	1.053 (0.979 to 1.133)

BLL = blood lead level, HTN = hypertension, OR = odds ratio, CI = confidence interval.
* Model 1: examining ORs (95%CI) of quartiles of BLL.
† P-trend: the p-value for the ordinal variable coded 1,2,3,4 for the quartiles.
‡ Model 2: taking the continuous BLL (μg/dL) as the major independent variable.
§ All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female).

Table S8. Participant characteristics and geometric mean of blood lead level (BLL, μg/dL) by hypertension status. (based on the JNC 7 definition).

Characteristics	Overall			Non-hypertension			Hypertension											P #	P **
							Overall					Controlled			Uncontrolled				
	n	% (SE)	BLL (SE)	n	% (SE)	BLL (SE)	n	% (SE)	P §	BLL (SE)	P ‖	n	% (SE)	BLL (SE)	n	% (SE)	BLL (SE)		
Sex									0.276									0.004	
Male	15679	49.7 (0.3)	1.50 (0.02)	9983	50.0 (0.4)	1.43 (0.02)	5696	49.2 (0.6)		1.69 (0.03)	<0.001	2453	47.1 (1.1)	1.63 (0.04)	3243	51.1 (0.8)	1.74 (0.03)		<0.001
Female	15083	50.3 (0.3)	1.07 (0.01)	9411	50.0 (0.4)	0.97 (0.01)	5672	50.8 (0.6)		1.34 (0.02)	<0.001	2610	52.9 (1.1)	1.23 (0.03)	3062	48.9 (0.8)	1.45 (0.03)		<0.001
Age									<0.001									<0.001	
20-39	10081	36.5 (0.6)	0.95 (0.01)	9225	48.7 (0.6)	0.94 (0.01)	856	9.6 (0.5)		1.01 (0.03)	0.282	246	6.3 (0.6)	0.82 (0.04)	610	12.5 (0.7)	1.11 (0.03)		<0.001
40-59	10113	38.9 (0.4)	1.38 (0.02)	6737	38.7 (0.6)	1.37 (0.02)	3376	39.4 (0.8)		1.40 (0.02)	0.006	1604	42.3 (1.2)	1.30 (0.03)	1772	36.8 (0.9)	1.51 (0.04)		<0.001
60+	10568	24.6 (0.5)	1.72 (0.02)	3432	12.6 (0.4)	1.73 (0.03)	7136	51.0 (0.8)		1.71 (0.02)	0.402	3213	51.4 (1.1)	1.60 (0.03)	3923	50.7 (1.0)	1.81 (0.03)		<0.001
Race/ethnicity									<0.001									<0.001	
Non-Hispanic white	15050	71.5 (1.1)	1.27 (0.02)	9353	70.4 (1.1)	1.17 (0.02)	5697	73.9 (1.2)		1.50 (0.02)	<0.001	2682	77.2 (1.2)	1.41 (0.03)	3015	70.9 (1.4)	1.60 (0.03)		<0.001
Non-Hispanic black	5988	10.1 (0.6)	1.33 (0.03)	3224	8.8 (0.5)	1.17 (0.03)	2764	12.8 (0.8)		1.62 (0.04)	<0.001	1213	11.6 (0.8)	1.51 (0.05)	1551	13.9 (0.9)	1.71 (0.05)		0.002
Hispanic	7728	12.6 (0.8)	1.22 (0.03)	5403	14.6 (0.9)	1.19 (0.02)	2325	8.3 (0.7)		1.35 (0.04)	0.305	921	6.9 (0.7)	1.19 (0.05)	1404	9.6 (0.9)	1.47 (0.05)		<0.001
Other	1996	5.8 (0.3)	1.28 (0.03)	1414	6.2 (0.3)	1.23 (0.03)	582	5.0 (0.4)		1.44 (0.05)	<0.001	247	4.3 (0.4)	1.40 (0.08)	335	5.6 (0.5)	1.47 (0.06)		0.357
Family PIR									<0.001									<0.001	
0≤PIR<1	5945	13.3 (0.4)	1.30 (0.03)	3917	13.9 (0.5)	1.21 (0.03)	2028	11.9 (0.5)		1.59 (0.04)	<0.001	845	10.5 (0.6)	1.40 (0.04)	1183	13.1 (0.7)	1.74 (0.06)		<0.001
1≤PIR<2	8152	20.4 (0.5)	1.34 (0.02)	4824	19.3 (0.5)	1.20 (0.02)	3328	22.7 (0.8)		1.63 (0.03)	<0.001	1387	20.7 (0.9)	1.54 (0.04)	1941	24.6 (1.0)	1.70 (0.04)		0.016
2≤PIR<3	4817	15.8 (0.4)	1.25 (0.02)	2911	15.5 (0.4)	1.14 (0.03)	1906	16.5 (0.5)		1.51 (0.03)	<0.001	867	16.8 (0.8)	1.42 (0.04)	1039	16.1 (0.7)	1.61 (0.05)		0.003
PIR≥3	11848	50.6 (0.9)	1.24 (0.01)	7742	51.3 (0.9)	1.16 (0.01)	4106	48.9 (1.1)		1.42 (0.02)	<0.001	1964	51.9 (1.3)	1.35 (0.03)	2142	46.2 (1.3)	1.50 (0.03)		<0.001
Education									<0.001									0.003	
Below high school	8302	16.7 (0.5)	1.62 (0.02)	4711	15.2 (0.5)	1.51 (0.03)	3591	20.0 (0.7)		1.80 (0.03)	<0.001	1480	18.5 (0.8)	1.73 (0.04)	2111	21.4 (0.8)	1.86 (0.04)		0.002
High school	7164	23.5 (0.5)	1.35 (0.02)	4321	22.3 (0.5)	1.26 (0.02)	2843	26.2 (0.7)		1.53 (0.03)	<0.001	1270	26.0 (0.9)	1.40 (0.04)	1573	26.4 (0.8)	1.66 (0.05)		<0.001

College or above	15296	59.8 (0.8)	1.16 (0.01)	10362	62.5 (0.8)	1.07 (0.01)	4934	53.8 (1.0)		1.39 (0.02)	<0.001	2313	55.6 (1.2)	1.31 (0.03)	2621	52.2 (1.1)	1.46 (0.03)		<0.001
Smoking									<0.001									0.009	
Never	16127	52.8 (0.6)	1.08 (0.01)	10472	54.1 (0.7)	0.99 (0.01)	5655	49.8 (0.8)		1.31 (0.02)	<0.001	2437	48.1 (1.2)	1.22 (0.03)	3218	51.3 (0.9)	1.38 (0.02)		<0.001
Former	7927	25.4 (0.5)	1.45 (0.02)	4127	21.7 (0.5)	1.34 (0.02)	3800	33.7 (0.8)		1.63 (0.03)	<0.001	1813	35.7 (1.1)	1.56 (0.04)	1987	31.8 (0.9)	1.70 (0.04)		0.002
Current	6708	21.8 (0.5)	1.61 (0.02)	4795	24.2 (0.6)	1.52 (0.02)	1913	16.6 (0.5)		1.93 (0.05)	<0.001	813	16.2 (0.8)	1.72 (0.05)	1100	16.9 (0.6)	2.15 (0.07)		<0.001
Alcohol									<0.001									0.001	
Never	4234	11.1 (0.5)	1.10 (0.02)	2394	10.3 (0.6)	0.97 (0.03)	1840	13.0 (0.6)		1.35 (0.03)	<0.001	767	11.5 (0.7)	1.23 (0.04)	1073	14.4 (0.8)	1.44 (0.03)		<0.001
Former	4522	12.5 (0.3)	1.21 (0.02)	2549	11.2 (0.3)	1.11 (0.02)	1973	15.4 (0.5)		1.40 (0.03)	<0.001	873	15.0 (0.7)	1.31 (0.04)	1100	15.8 (0.6)	1.48 (0.05)		0.002
Current	22006	76.3 (0.7)	1.30 (0.01)	14451	78.5 (0.7)	1.21 (0.01)	7555	71.5 (0.9)		1.55 (0.02)	<0.001	3423	73.4 (1.0)	1.45 (0.03)	4132	69.8 (1.0)	1.65 (0.03)		<0.001
Menopause *									<0.001									0.001	
Pre-menopausal	7803	58.4 (0.7)	0.84 (0.01)	6561	71.8 (0.7)	0.82 (0.01)	1242	29.3 (1.0)		1.00 (0.03)	<0.001	613	32.2 (1.4)	0.94 (0.04)	629	26.5 (1.2)	1.08 (0.04)		<0.001
(Post-) menopausal	7280	41.6 (0.7)	1.50 (0.02)	2850	28.2 (0.7)	1.48 (0.02)	4430	70.7 (1.0)		1.51 (0.02)	0.011	1997	67.8 (1.4)	1.41 (0.03)	2433	73.5 (1.2)	1.61 (0.03)		<0.001
BMI (kg/m^2) †	30762	28.7 (0.1)	N/A	19394	27.7 (0.1)	N/A	11368	30.8 (0.1)	<0.001	N/A	N/A	5063	31.5 (0.1)	N/A	6305	30.1 (0.1)	N/A	<0.001	N/A
Cotinine (ng/mL) ‡	30762	0.4 (0.0)	N/A	19394	0.4 (0.0)	N/A	11368	0.2 (0.0)	<0.001	N/A	N/A	5063	0.2 (0.0)	N/A	6305	0.3 (0.0)	N/A	0.325	N/A

: family PIR = ratio of family income to poverty, BMI = body mass index.

* Only for women.

† Arithmetic mean (SE).

‡ Geometric mean (SE).

§ P value: to compare the characteristics between non-hypertensive and hypertensive people, using Chi-square test for categorical variables and t-test for continuous variables.

|| P value: to compare BLL between non-hypertensive and hypertensive people, using t-test.

P value: to compare the characteristics between participants with controlled and uncontrolled hypertension, using Chi-square test for categorical variables and t-test for continuous variables.

** P value: to compare BLL between participants with controlled and uncontrolled hypertension, using t-test.

Table S9. ORs (95% CI) of hypertension and uncontrolled hypertension by quartiles of blood lead level in US adults (based on the JNC 7 definition).

Sex	BLL (μg/dL)	Model 1 Cases: Any HTN Non-cases: non-HTN			Model 2 Cases: uncontrolled HTN Non-cases: controlled HTN			Model 3 Cases: uncontrolled HTN Non-cases: controlled HTN + non-HTN		
		Cases	Non-cases	OR (95% CI) †	Cases	Non-cases	OR (95% CI) †	Cases	Non-cases	OR (95% CI) †
Men	Q1 (<0.94)	669	2169	Reference	368	301	Reference	368	2470	Reference
	Q2 (0.94-1.50)	1211	2379	1.093 (0.891 to 1.340)	671	540	1.344 (0.939 to 1.924)	671	2919	1.264 (1.004 to 1.590)
	Q3 (1.50-2.30)	1545	2510	1.005 (0.825 to 1.225)	830	715	1.430 (1.054 to 1.940)	830	3225	1.231 (1.012 to 1.497)
	Q4 (>2.30)	2271	2925	1.037 (0.855 to 1.259)	1374	897	1.768 (1.252 to 2.497)	1374	3822	1.424 (1.163 to 1.743)
	P-trend *		0.995			<0.001			<0.001	
	Continuous BLL	5696	9983	1.008 (0.983 to 1.033)	3243	2453	1.107 (1.046 to 1.172)	3243	12436	1.042 (1.013 to 1.072)
Women	Q1 (<0.70)	582	2465	Reference	249	333	Reference	249	2798	Reference
	Q2 (0.70-1.08)	1058	2486	0.911 (0.724 to 1.147)	498	560	1.110 (0.828 to 1.487)	498	3046	1.045 (0.806 to 1.356)
	Q3 (1.08-1.66)	1660	2314	0.951 (0.749 to 1.208)	889	771	1.237 (0.915 to 1.672)	889	3085	1.181 (0.922 to 1.513)
	Q4 (>1.66)	2372	2146	0.908 (0.730 to 1.129)	1426	946	1.740 (1.299 to 2.331)	1426	3094	1.431 (1.126 to 1.818)
	P-trend *		0.518			<0.001			<0.001	
	Continuous BLL	5672	9411	1.002 (0.956 to 1.051)	3062	2610	1.129 (1.047 to 1.217)	3062	12021	1.080 (1.033 to 1.129)

BLL = blood lead level, HTN = hypertension, OR = odds ratio, CI = confidence interval.

* *P*-trend: the *P*-value for the ordinal variable coded as 1, 2, 3, 4 for the quartiles.

† All models were adjusted for age, sex, race/ethnicity, ratio of family income to poverty, education (< high school, high school, > high school), smoking status (never, former, current), serum cotinine (natural log-transformed), alcohol intake (never, former, current), body mass index (kg/m^2), and menopause status (yes/no, only for female).