Association of Blood Lead Level and Breast Cancer Risk in US Women: A Cross-Sectional Study(NHANES 2003-2014)

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Research

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Abstract

Background:

Environmental chemical exposures may play a important role in breast cancer etiology.Higher levels of exposure to environmental chemicals, such as heavy metals, may be associated with a high risk of patients with breast cancer, but the evidence is limited and inconsistent. Thus, In the current study, we used National Health and Nutrition Examination Survey (NHANES) data to to assess the influence of blood lead on risk of patients with breast cancer.

Methods: This cross-section study was conducted by extracting data from NHANES database(2003-2014). Logistic regression was applied to explore the association between the blood lead and the incidence of breast cancer. Cox proportional hazards regression models were used to estimate the odds ratio (OR) and 95% confifidence interval (CI) of association between blood lead and the risk of breast cancer adjusted for confounder factors.

Results: A total of 10153 participants were included. Elevated blood levels of lead was associated with higher risks of breast cancer (OR 1.16; 95% CI, 1.09–1.22)in the unadjusted analysis.But after adjustment for established risk factors, we did not observe significant association between blood levels and breast cancer risk (OR 1.00; 95% CI, 0.95–1.15).

Conclusion: We found no significant association between elevated blood lead levels and high risk of breast cancer in our cross-section study.

Background

Breast cancer is the most prevalent women's cancer in United States[1].Higher levels of environmental chemicals, such as metals□air pollution, have became the focus of several studies looking for associations with cancer[2].Also,there is growing concern about the role of environmental chemicals in breast cancer development [3].In 2006, Siddiqui reported in a study that there were statistically significant correlations between lead in normal tumor free breast tissue of benign and malignant cases ($r = 0.41–0.73$; $p < 0.05 – 0.001$)[4].Jacob K Kresovich reported that metallic air pollutants exposure such as lead,cadmium, cobalt were associated with increased odds of developing ER/PR-negative breast cancer[5].These metals including lead (Pb) are ubiquitously present in the environment, leading to widespread exposure in the general population mainly through inhalation of contaminated particles in ambient air and ingestion of contaminated food, water and dust[6]. There several previous studies reported the potential role of exposure to the ubiquitous environmental pollutant lead in breast cancer etiology. White et al[7] evaluated several airborne metals (including lead) and found that women living in areas with higher concentrations of airborne lead were more likely to have dense breast, a risk factor for breast cancer.Ekenga[8] found that Chemical materials exposure in workplace includes lead exposure was found being associated with an increased risk of premenopausal breast cancer among women enrolled in

the Sister Study. But there was few studies investigating the potential relationship between blood lead level and breast cancer.To further explore the relationship between blood lead level and breast cancer, we used the NHANES database. Blood lead levels were measured in a single point of time in the NHANES refecting recent exposure, but they may also represent a long-term exposure, as results of a long biological half-life of these metals[9].Mielke reported that blood lead can be thought of as a steady-state marker of lead exposure[10, 11]. So we assessed the association between blood levels of Pb and prevalent breast cancer among US women who participated in the 2003–2014 NHANES using multivariate logistic regression models adjusting for potential confounder factors.Blood lead levels were determined in the participants with and without breast cancer, as well as in different subgroups of the study participants with varying demographic, behavioral, and reproductive health status.

Materials And Methods

Study design

We examined the data from 6 consecutive NHANES survey cycles covering the periods 2003 to 2014. The NHANES is a cross-sectional survey to assess the health and nutritional status of the US population, which has been continuously conducted and released in 2-year cycles since 1999 by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC)[12] . The survey design, questionnaires, and examination methodology of NHANES are described in details at the CDC website. The survey was approved by the NCHS Research Ethics Review Board and participants provided written informed consents. All analyses used newly constructed 12-year NHANES weights adjusting for nonresponse, noncoverage, and unequal probabilities of selection. New weights waves were calculated as one-sixth of WTMEC2YR for 2003–2004, 2005–2006, 2007–2008, 2009–2010, and 2011–2012 waves, and one-sixth of WTSH2YR (blood metal weight) for 2013–2014 survey cycles[13]. We included female participants aged 20 and above who participated in the laboratory and physical examination. Patients who had been diagnosed with other cancers were excluded.Patients with missing data of blood lead level were also excluded.A total of 10153 women met the inclusion and exclusion criteria including 291 with breast cancer and 9862 without breast cancer(Figure 1).

Assessment of metal exposure

NHANES blood sample collection and processing have been described. Blood lead levels of 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 using inductively coupled plasma dynamic reaction cell mass spectrometer (ELAN® DRC II) (PerkinElmer

Norwalk, CT, USA).The detailed methods of measuring these blood metal levels is described in the laboratory procedure manual [14].Blood lead levels were expressed as μg/L. Values below the the limit of detection (LOD) were assigned the default value of 1/2 LOD.Limit of detection (LOD, see Data Analysis

section) for Survey years 03-04, 05-06, 07-08, 09-10,11-12 and 13-14 are 0.28, 0.25, 0.25, 0.25,0.07and 0.07 respectively[15].

Covariates

We considered the age (20–59 years, 60–74 year, and≥75 years) , race (non-Hispanic white, non-Hispanic black, Hispanic, and other), family income poverty ratio(below poverty <1,above poverty >=1), education(< high school,>=high school, BMI(body mass index) (underweight<18.5 kg/m2, normal weight 18.5 to <25 kg/m2 , overweight 25 to <30 kg/m2,obese ≥30 kg/m2), vigorous physical activity, smoking history, alcohol consumption, marital status and reproductive health status (including menopause status, ever been pregnant and female hormone use) as covariates. Vigorous physical activity was categorized as self-reported moderate or vigorous physical recreational activity versus none. Smoking (never, past or current smokers) and alcohol consumption (yes,no) were categorized based on the questionnaire data. Additional covariates are the questionnaire data on reproductive health, including menopuase status (Had regular periods in past 12 months?), history of pregnancy (yes or no) ,marital status (married or have partner,widowed or divorced□seperated□never married)and female hormone use (such as estrogen and progesterone use, yes or no).Self-reported cancer diagnosis was obtained from the medical conditions questionnaires. Participants were being asked a question “Have you ever been told by a doctor or other health professional that you had cancer or a malignancy of any kind?’. Participants who answered “yes” were subsequently asked “What kind of cancer was it? Only women who reported “no cancer” diagnosis or a “breast cancer” diagnosis were included in our study population. The study population was categorized into with breast cancer and without breast cancer in the analytical models. We selected these confounders on the basis of their associations with the outcomes of interent or a change in effect estimate of more than 10%.Supplmentaray tables [see Additional file 1]shows the associations of each confounder with the outcomes of interest.

Statistical Analysis

We used SAS (version 9.3) and Empowerstats (version 3.0) for all statistical analyses. Descriptive statistics was performed on weighted characteristics of the study population by breast cancer status.Blood metal levels in women with breast cancer were compared with those without breast cancer. A multivariate logistic regression model was constructed to examine the association between blood lead levels and prevalent breast cancer, adjusting for potential covariates. *P*-values less than 0.05 were considered statistically significant.

Results

Table 1 displays weighted characteristics of the study participants by breast cancer status. A different distribution in demographic characteristics was seen between women with breast cancer and without breast cancer. Women with breast cancer were more likely to be older, postmenopausal,non-Hispanic white, and have a higher income and high education status, compared to women without breast cancer.

There were no signifcant diferences in the distribution between women with and without breast cancer regarding the BMI categories, education,alcohol consumption,and marital status.Women with breast cancer were more likely to have pregnant history and smoking history, but less likely to have female hormone use and vogiours physical activiy, than women without breast cancer.

Metal blood lead levels were determined in the total study participants as well as in the subgroups of participants with varying covariates (Table 2).By unltivariate analysis,there were no signifcant differences in blood lead levels between different age groups and different menopause status. Blood lead level were increased with increasing BMI, but blood lead levels were only signifcantly increased in the group of BMI (18.5-24.9kg/m2) as compared with the group of BMI(<18.5kg/m2). Non-Hispanic White group had signifcantly elevated blood levels of lead than Non-Hispanic black and other racial group. Women with higher family income showed signifcantly increased lead levels as compared to women with lower family income. Women with higher education level (≥high school) had signifcantly higher levels of lead compared to women with low school diploma. Women who were not physically active had a signifcantly increased level of lead than with physically active women. Further, women who were widowed□divorced or singal had a signifcantly increased level of lead than married women or women with partner. Among the reproductive health variables,women with pregnant history, but without female hormone use, had signifcantly elevated levels of lead. Women with alcohol comsuption showed signifcantly higher levels of lead. In addition, both past and current smokers had signifcantly elevated lead levels than women who had never smoked.

We then determined blood lead levels in women with and without breast cancer using unltivariate analysis (Table 3). The geometric mean of blood levels of lead in breast cancer women was signifcantly higher than women without breast cancer (p<0.001).

We further examined the association between blood lead levels and prevalent breast cancer using multivariate logistic regression models (Table 4).There was statistically signifcant association between blood lead levels and breast cancer in a dose-dependent manner in the unadjusted model with an odds ratio (OR) of 3.04 in Q2, 3.34 in Q3, and 5.6 in Q4. The p value for trend of increasing risk with increasing blood lead levels was significant.However, a adjusted modelI(adjusted for:age groups,menopause status,race,vogiours activiy) attenuated this association and the trends for increased odds of breast cancer across increasing blood lead levels was not significant.In a multivariable-adjusted modelII(adjusted for age, race, BMI, education,alcohol consumption,marital status,pregnant history,smoking history,female hormone use,vogiours activiy and menopause status) no signifcant associations were seen between blood lead levels and breast cancer.The OR values became smaller compared with the unadjusted model. In reference to Q1, the OR of the association was 1.44 (95% CI 0.89, 2.34) for Q2, 1.03 (95% CI0.63, 1.68) for Q3, and 1.27 (95% CI0.79, 2.03) for Q4. (Table 4)Also,we did not find any statistical differences in the ORs of the main effect when stratifying analyses by menopause status□pregnant history□hormone use history. (Table 5)

Disscussion

Accumulating evidence has suggested a role of chemical exposures in the environment in breast cancer etiology[16]. We used NHANES sample(among US women who participated in the 2003–2014 NHANES) to estimate the potential impact of blood lead level on breast cancer risk.In this study, we did not observe a signifcant association between blood lead levels and prevalent breast cancer after adjusting for potential confounders although blood lead levels were higher in breast cancer women.

In unadjusted models we observed signifcant associations between blood lead levels and breast cancer risk.But after adjusting cofound factors our finding indicates that blood lead level is not signifcantly associated with an increased breast cancer risk. To our knowledge,this is among the first few studies investigating the potential relationship between blood lead level and breast cancer.

Association between airborne metals (including lead) and lead exposure in workplace and an increased risk of breast cancer were found in previous studies. These studies reported the potential role of exposure to the ubiquitous environmental pollutant lead in breast cancer etiology. Bergdahl and Fukui proposed that urine and blood lead levels had good correlation[17, 18].In a population-based case-control study,Jane found that urinary lead levels as determined by specific gravity-adjusted urinary lead concentrations, is not associated with a significant increased risk for breast cancer[19]. But Yudan Wei observed blood lead levels was signifcantly associated with the risk of breast cancer among US women who participated in the 2003–2012 NHANES by adjusting for potential confounders[20].Nevertheless, there are discrepancies with the fndings.The variations of fndings between the studies might be due to the difference in study design, assessment of exposure, and the adjustment of different confounding variables.

Lead could be associated with breast cancer via direct and indirect mechanisms. It had been demonstrated that some of these metals are endocrine-disrupting chemicals (EDC) by experimental studies using in vitro and animal models.They can mimic or interfere with the actions of endogenous hormones particularly endogenous estrogens, and mediate epigenetic alterations leading to mammary carcinogenesis[21].Chang found that lead was positively, although not statistically significantly, associated with estradiol, similar to previous findings in a case-control study of infertility[22]. Pollack also found that increases in mean serum levels of progesterone were observed with increasing blood lead levels in premenopausal women[23]. Further, a high level of lead has been detected in breast tumor tissues as well as in the endometrium[24].

And increased endogenous exposure of lead release from resorbed bone to blood have been linked with menopausal status, pregnancy in women with age[25–29].

There is close interrelationships between reproductive hormone levels(which may influenced by menopuase status、history of pregnancy、female hormone use and so on) and lead level.

Also,lead exposure begins in utero and continues throughout life. It increases in bone lead plateaus at middle age and decreases at higher ages[30].This trend is more pronounced in females.This is consistent with the findings of this study,blood lead level of lead were decreased with increasing age.Taking account

to these potential confounders,we increased more covariates and sample size in our study.Different from some results, we did not observe a signifcant association between blood lead levels and prevalent breast cancer after adjusting for potential confounders(including menopause status□pregnant history□hormone use history) for breast cancer.Although we considered the potential reproductive confounders,we were unable to assess hormonal patterns, especially in association with environmental exposures that may alter hormone levels at certain times[31]. Though,our fndings indicated that different reproductive hormone levels may strongly influenced potentially biologically active blood lead levels. This fnding provides insights on the endocrine-disrupting property of lead and further investigations is warranted to unpick the possible biological mechanisms that might be related to the association between blood lead and endocrine-related breast cancer etiology.Given the ubiquitous exposure of the general population to lead and the potential accessibility of endogenous exposure from bone cycling, the mode of the association between different blood lead level and different hormone level exposure for breast cancer warrants further study.

Despite the limitations of this study,there are a number of strengths. We used a a large and nationally representative sample of US women for a 12-year period of time who participated in the NHANES to explore the association between blood lead level and breast cancer.And we considered a number of potential confounders including demographic, behavioral, and reproductive health factors which may had affection on assessing the association.Due to the nature of a cross-sectional design of the NHANES, our study by analyzing the NHANES data cannot reveal a causal relationship between blood lead and breast cancer.

Conclusions

There is no significant association between elevated blood levels and high risk of breast cancer in our cross-section study.Additional epidemiologic and mechanistic studies would further explore these relation between female breast cancer development and different blood lead level due to different homones level.

Abbreviations

NHANES National Health and Nutrition Examination Survey

OR the odds ratio

CI confifidence interval

NCHS National Center for Health Statistics

CDC Centers for Disease Control and Prevention

LOD the limit of detection

EDC endocrine-disrupting chemicals

Declarations

Ethics approval and consent to participate

No applicable.

Consent for publication

No applicable.

Availability of data and material

No applicable.

Competing interests

The authors have no conflicts of interest to disclose.

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Authors' contributions

Qin Xu carried out the data collation, participated in the Statistical analysis and drafted the manuscript. Shan Gao carried out the Statistical analysis and reviewed the manuscript. Qinchuan Yi conceived of the study, and participated in its design and helped to draft the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Weighted baseline characteristics of the breast cancer participants among

women≥20 years of age in the 2003–2014 NHANES (n=10153)

characteristics	All participants (N=10153)	Patients without breast cancer (N=9863)	Patients with breast cancer (N=291)	*P*-value
Demographic				
Age(years) mean±SD	48.71 ± 18.08	48.14 ± 17.91	68.29 ± 11.79	<0.001
20-59	6883 (67.79%)	6822 (69.17%)	61 (20.96%)	
60-74	2237 (22.03%)	2109 (21.39%)	128 (43.99%)	
≥75	1033 (10.17%)	931 (9.44%)	102 (35.05%)	
BMI(kg/m2), mean±SD	29.24 ± 7.37	29.24 ± 7.37	29.09 ± 7.36	0.796
≤18.5	115 (1.82%)	112 (1.81%)	3 (1.86%)	
18.5-24.9	1902 (30.04%)	1851 (30.00%)	51 (31.68%)	
25-29.9	1838 (29.03%)	1797 (29.12%)	41 (25.47%)	
≥30	2477 (39.12%)	2411 (39.07%)	66 (40.99%)	
Race no.(%)				<0.001
hispanic	2706 (26.65%)	2668 (27.05%)	38 (13.06%)	
non-hispanic white	4600 (45.31%)	4411 (44.73%)	189 (64.95%)	
Non-hispanic black	2179 (21.46%)	2127 (21.57%)	52 (17.87%)	
other race	668 (6.58%)	656 (6.65%)	12 (4.12%)	
Education no.(%)				0.362
< high school	2702 (26.61%)	2615 (26.52%)	87 (29.90%)	
≥high school	7437 (73.25%)	7233 (73.34%)	204 (70.10%)	
NA	14 (0.14%)	14 (0.14%)	0 (0.00%)	

Alcohol comsuption no.(%)				0.350
Yes	6049 (59.58%)	5886 (59.68%)	163 (56.01%)	
No		3969 (40.25%)	128 (43.99%)	
NA	4097 (40.35%)	7 (0.07%)	0 (0.00%)	
	7 (0.07%)			
Marital no.(%)				0.276
Yes or partner	5572 (54.88%)	5423 (54.99%)	149 (51.20%)	
No or other		4436 (44.98%)	142 (48.80%)	
NA	4578 (45.09%)	3 (0.03%)	0 (0.00%)	
	3 (0.03%)			
Income to poverty ratio				0.051
<1.0(below poverty)	2093 (22.20%)	2046 (22.34%)	47 (17.34%)	
≥1.0(above poverty)	7336 (77.80%)	7112 (77.66%)	224 (82.66%)	
Vigorous activity no.(%)				0.040
Yes	1563 (15.39%)	1526 (15.47%)	37 (12.71%)	
No	8292 (81.67%)	8053 (81.66%)	239 (82.13%)	
NA	298 (2.94%)	283 (2.87%)	15 (5.15%)	
Menopause no.(%)				<0.001
No	5079 (50.02%)	5063 (51.34%)	16 (5.50%)	
Yes	5074 (49.98%)	4799 (48.66%)	275 (94.50%)	
Pregnant no.(%)				0.021
Yes	8613 (85.15%)	8349 (84.99%)	264 (90.72%)	
No		1469 (14.95%)	27 (9.28%)	
NA	1496 (14.79%)	6 (0.06%)	0 (0.00%)	
	6 (0.06%)			
Hormone use no.(%)				<0.001

Yes	2024 (19.95%)	1930 (19.58%)	94 (32.30%)	
No	8082 (79.65%)	7891 (80.06%)	191 (65.64%)	
NA	41 (0.40%)	35 (0.35%)	6 (2.06%)	
Smoke no.(%)				<0.001
past or current smoke	8198 (80.74%)	7986 (80.98%)	212 (72.85%)	
Never smoke	1955 (19.26%)	1876 (19.02%)	79 (27.15%)	

Table2 unltivariate analysis of associatiation of blood lead levels and incidence of breast cancer in the total study population as well as by selected variables

characteristics	N=10155	Blood lead(μg/dL)	*P*-value
Age(years) mean±SD			
20-59	6883	1.14 (1.01, 1.29)	0.0672
60-74	2237	1.00 (0.88, 1.14)	0.8312
≥75	1033	0.95 (0.80, 1.13)	0.8817
BMI(kg/m2), mean±SD			
≤18.5	115	0.92 (0.34, 2.50)	0.8754
18.5-24.9	1902	1.24 (1.08, 1.42)[a]	0.0034
25-29.9	1838	1.11 (0.95, 1.29)	0.1671
≥30	2477	1.11 (0.95, 1.28)	0.1821
Race no.(%)			
hispanic	2706	1.06 (0.87, 1.29)	0.5555
non-hispanic white	4600	1.29 (1.18, 1.42)[a]	<0.0001
Non-hispanic black	2179	1.11 (0.98, 1.25)	0.1255
other race	668	1.13 (0.88, 1.46)	0.5855
Education no.(%)			
< high school	2702	1.04 (0.94, 1.17)	0.4857
≥high school	7437	1.28 (1.18, 1.40)[a]	<0.0001
Alcohol comsuption no.(%)			
Yes	6049	1.21 (1.13, 1.30)[a]	<0.0001
No	4097	1.08 (0.97, 1.19)	0.1719
MARITAL no.(%)			
Yes or partner	5572	1.14 (1.06, 1.23)	0.0016
No or other	4578	1.18 (1.08, 1.28)[a]	<0.0001
Income to poverty ratio			
<1.0(below poverty	2093	1.04 (0.87, 1.24)	0.4473
≥1.0(above poverty)	7336	1.19 (1.11, 1.27)[a]	<0.0001

Vigorous activity no.(%)			
Yes	1563	1.22 (1.05, 1.41)	0.0082
No	8292	1.15 (1.07, 1.22)[a]	<0.0001
Menopause no.(%)			
No	5079	1.20 (0.83, 1.74)	0.3327
Yes	5074	1.01 (0.93, 1.10)	0.8292
Pregnant no.(%)			
Yes	8613	1.15 (1.08, 1.22)[a]	<0.0001
No	1496	1.17 (0.99, 1.39)	0.0732
Hormone use no.(%)			
Yes	2024	1.09 (0.97, 1.23)	0.1384
No	8082	1.16 (1.09, 1.24)[a]	<0.0001
Smoke no.(%)			
ex or now smoke	8198	1.16 (1.08, 1.24)[a]	<0.0001
Never smoke	1955	1.14 (1.04, 1.25)	0.0031

Weighted geometric means (95% CI)

[a] Statistically signifcant diference compared to the reference group

Table 3 unltivariate analysis of blood levels of lead among women with and without breast cancer

metal	All participants	Patients without breast cancer	Patients with breast cancer	*P*-value
	N=10153	N=9863	N=291	
Blood lead(μg/dL)	1.16(1.09, 1.22)	1.13 (1.11 1.14)	1.55 (1.46 1.66)[a]	<0.001

[a] Statistically signifcant increase compared to participants without breast cancer

Table 4 association between blood lead levels and prevalent breast cancer using multivariate logistic regression models

Incident	n	Non-adjusted model		Model I		Model II	
		OR (95% CI)	*P for trend*	OR (95% CI)	*P for trend*	OR (95% CI)	*P for trend*
Blood lead(μg/dL)	10153	1.16 (1.09, 1.22)	<0.0001	1.01 (0.98, 1.17)	0.5223	1.00 (0.95, 1.15)	0.3273
Blood lead							
Q1(<0.8)	2969	Ref		Ref		Ref	
Q2(0.8 to <1.2)	2451	3.04 (1.95, 4.74)	<0.0001	1.41 (0.89, 2.23)	0.1445	1.44 (0.89, 2.34)	0.1371
Q3(1.2 to <1.8)	2305	3.34 (2.15, 5.19)	<0.0001	1.00 (0.63, 1.59)	0.9959	1.03 (0.63, 1.68)	0.8971
Q4(≥1.8)	2428	5.60 (3.70, 8.48)	<0.0001	1.27 (0.81, 1.98)	0.2924	1.27 (0.79, 2.03)	0.3245
P value for trend test		<0.0001		0.7084		0.8525	

[a] Statistically signifcant compared to the reference group (Q1)

Model I:adjusted for:age groups,menopause status,race,vogiours activiy;

Model II:adjusted for:age groups, race, BMI, education,alcohol consumption,marital status,pregnant history,smoking history,female hormone use,vogiours activiy. menopause status.

Table 5 Stratification analysis of association between blood lead levels and prevalent breast cancer by menopause status□pregnant history□hormone use history

Incident	Pre-menopause status		Post-menopause status	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Blood lead(μg/dL)	1.16 (1.09, 1.22)	<0.0001	0.98 (0.89, 1.08)	0.7060
Blood lead				
Q1(<0.8)	Ref		Ref	
Q2(0.8 to <1.2)	3.08 (0.73, 13.04)		1.42 (0.86, 2.35)	
Q2(1.2 to <1.8)	3.33 (0.65, 17.05)		1.04 (0.63, 1.72)	
Q3(≥1.8)	6.13 (1.16, 32.34)		1.36 (0.85, 2.19)	

adjusted for:age groups, race, BMI, education,alcohol consumption,marital status,pregnant history,smoking history,female hormone use,vogiours activiy.

Incident	Pregnant history		No Pregnant history	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Blood lead(μg/dL)	1.00 (0.91, 1.10)	0.9354	0.79 (0.50, 1.23)	0.2931
Blood lead				
Q1(<0.8)	Ref		Ref	
Q2(0.8 to <1.2)	1.54 (0.93, 2.57)	0.0944	2.33 (0.54, 10.03)	0.2549
Q2(1.2 to <1.8)	1.10 (0.66, 1.84)	0.7067	2.87 (0.66, 12.43)	0.1587
Q3(≥1.8)	1.59 (0.98, 2.59)	0.0607	1.10 (0.23, 5.25)	0.9017

adjusted for:age groups, race, BMI, education,alcohol consumption,marital status,menopause status,smoking history,female hormone use,vogiours activiy.

Incident	Hormone use history		No Hormone use history	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Blood lead(μg/dL)	0.96 (0.79, 1.16)	0.6748	0.94 (0.82, 1.07)	0.3415
Blood lead				
Q1(<0.8)	Ref		Ref	
Q2(0.8 to <1.2)	1.45 (0.56, 3.79)	0.4442	1.58 (0.89, 2.80)	0.1182
Q2(1.2 to <1.8)	1.14 (0.45, 2.88)	0.7803	1.05 (0.58, 1.90)	0.8845
Q3(≥1.8)	1.29 (0.52, 3.19)	0.5822	1.37 (0.78, 2.41)	0.2762

adjusted for:age groups, race, BMI, education,alcohol consumption,marital status,pregnant history,smoking history,menopause status,vogiours activiy.

Figures

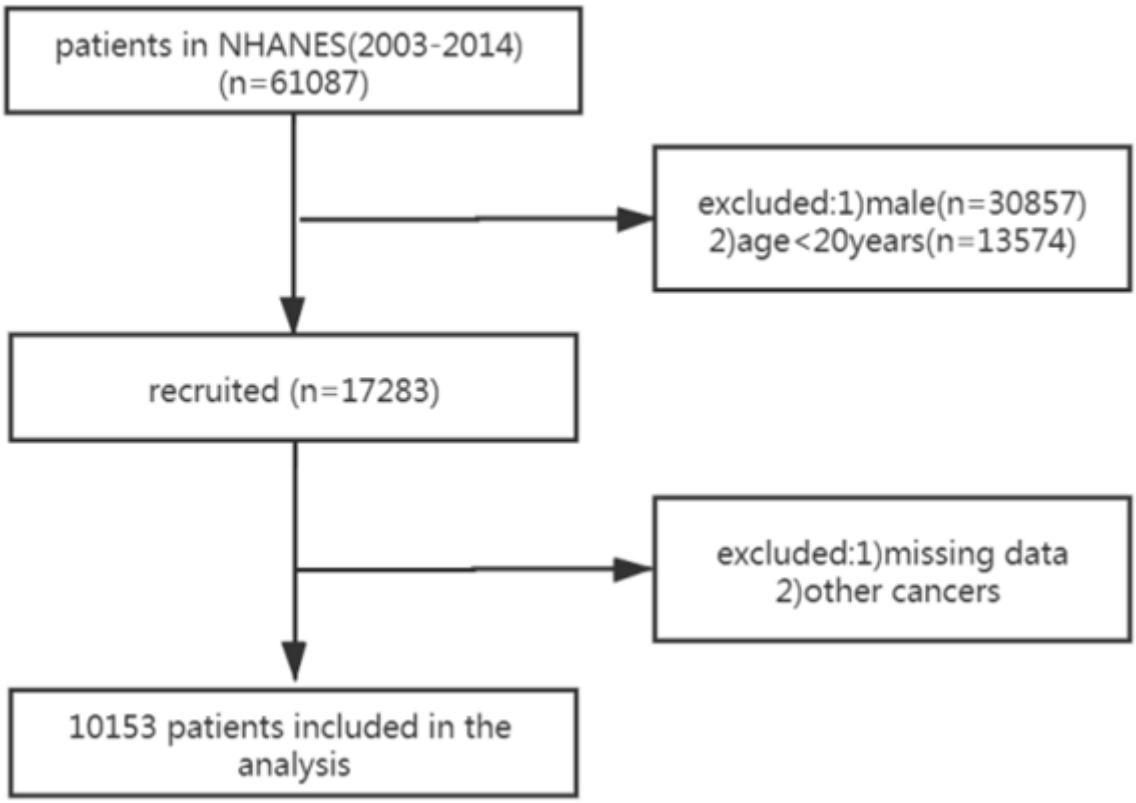

Figure 1

Flowchat of patient selection

Supplementary Files

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- additiontalfile1.doc