Lead Exposure and Metabolic Syndrome in U.S. Population, NHANES 2013-2014

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Lead Exposure and Metabolic Syndrome in U.S. Population, NHANES 2013-2014

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Abstract

Background: Lead is a known endocrine disruptor and can impair regulation of blood glucose, blood pressure, abdominal adiposity, blood lipid levels which are risk factors for metabolic syndrome (MetS).

Objective: To study the association of lead exposure and MetS in United States (U.S.) adults.

Methods: Data from 523 male and 528 female participants aged 20 years and older from the 2013 to 2014 National Health and Nutrition Examination Survey (NHANES) were analyzed. Based on blood lead distribution in males and females, participants were categorized into low and high blood lead groups in both genders. Adjusted logistic regression analysis was used to determine association between lead exposure and MetS; controlling for age, ethnicity, income and smoking status.

Results: The overall median blood lead levels for U.S. adults aged 20 years and older were 1.03 ug/dL; median blood lead levels were higher for males (1.23ug/dL) and lower for females (0.86 ug/dL). Prevalence of MetS in the male and female was 57.55% and 38.60%, respectively. Compared to low blood lead groups, neither men nor women in high blood lead group showed any elevated risk of MetS. The adjusted odds ratio (95% confidence interval) of MetS in males was 0.741 (0.464-1.20), p-value: 0.209, in females it was 0.921 (0.563-1.51), p-value: 0.745.

Conclusion: For adults aged 20 years and older low median blood lead levels in the U.S. were not significantly associated with MetS.

Keywords: metabolic syndrome, NHANES, blood lead levels, public health
Lead Exposure and Metabolic Syndrome in U.S. Population, NHANES 2013-2014

Lead is a blue-gray metal that naturally occurs in all parts of our environment and is found in small quantities in the earth’s crust (Shukla, Shukla, & Tiwari, 2018). Most of the lead exposure seen today comes from human activities. Although the majority of these activities have been either banned or restricted the burning of fossil fuels, mining and manufacturing have been known leading contributors (Obeng-Gyasi, 2018).

Common sources of lead include household paint, petrol, industrial emissions, canning and drinking water (Obeng-Gyasi, 2018). Government regulations has since restricted or limited the usage or emission of lead as a means to curb the environmental and human burden of lead exposure. The fate of inhaled or ingested lead or lead particles depends on several factors. The bloodstream is the primary repository for absorbed lead and distributes lead through the body, allowing for further absorption by other tissues (Centers for Disease Control and Prevention [CDC], 2017). Lead is primarily housed in the blood, mineralized tissue (the bones and teeth) and soft tissue (CDC, 2018). The amount of lead absorbed is dependent upon the route of exposure. Small particles of lead found in dust can result in a higher absorption levels than lead that may be ingested (CDC, 2017).

Lead is found in both organic and inorganic compounds (CDC, 2017). Organic lead compounds, the type of lead found in petrol and used as additives, are metabolized in the liver (Moon, 2013); whereas inorganic lead is not metabolized by the liver. In an adult human the half-life of lead within the blood is estimated to be between 28 to 36 days (CDC, 2018). Exposure to lead is measured using Blood Lead Levels (BLL) (CDC, 2017). It has been estimated that 94% of the total lead body burden of adults is located in the bones and teeth (CDC, 2017). Lead in mineralizing tissues are not distributed equally, lead accumulates in bones
that are undergoing the most calcification at the time of exposure (CDC, 2017). Since lead is stored in the bones symptoms of lead exposure can be present without significant current exposure (CDC, 2018). Most instances of toxic BLL are from a mixture of current and previous lead exposures (CDC, 2017). However, acute high rates of exposure can cause high short term BLL’s and symptoms of lead poisoning (CDC, 2018).

Lead exposure continues to be a public health issue. As a heavy metal and an endocrine disruptor, lead is associated with adverse human cardio metabolic outcomes such as high blood pressure, increased Body Mass Index and high cholesterol (Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004). Metabolic syndrome (MetS) is a clustering of risk factors that predispose the body to the development of cardiovascular disease (CVD) (Huang, 2009). Lead has been linked with higher prevalence of MetS in Korean population (Rhee et al., 2013). The five components that contribute to MetS are high blood pressure, high blood glucose levels, a larger waist circumference, high blood lipid levels and lastly low high-density lipoproteins (HDL). The presence of any three of these five components is considered MetS (Grundy et al., 2004). The prevalence of MetS in the United States (U.S.) is estimated to be 33% (Aguilar, Bhuket, Torres, Liu, & Wong, 2015), while the worldwide prevalence of MetS is estimated to be 25% (Nolan, Carrick-Ranson, Stinear, Readings, & Dalleck, 2017). However, in the U.S. MetS prevalence in regard to lead has not been explored in the general adult population. The present study aimed to examine this question using data from National Health and Nutrition Examination Survey (NHANES) 2013 to 2014.

**Research Question**

What effect does exposure to lead have on the development of MetS among the U.S. population? It has been documented that lead is an endocrine disruptor and that disruption of the
endocrine system has the potential to lead to MetS. Therefore, we hypothesize that there will be a positive association between blood lead levels and MetS.

**Literature Review**

**Lead Exposure**

Lead is a naturally occurring metal in the environment which has been known to have irreversible and toxic effects on the body. Mineral deposits within the Earth’s crust are a primary source of the toxic heavy metal (Shukla et al., 2018). Lead is a persist heavy metal that can linger in the environment, leaving populations to be potentially exposed in areas where lead may have been previously deposited.

Exposure to lead can affect nearly all of the systems within the human body (CDC, 2018). Lead exposure can occur with no obvious signs and symptoms. In fact, lead has two characteristics which are of great concern; it does not have a detectible taste or smell causing it to frequently appear unrecognized until exposure related damage has occurred (Shukla et al., 2018). Before U.S. policy changes primary sources of lead exposure were from petrol, industrial emissions, household paint, food canning processing and drinking water. It was a widely held belief that the lead content in petrol would improve the performance of engines in automobiles (Obeng-Gyasi, 2018). This led to the respiratory absorption of lead from automobile emissions. Once the harmful effects of breathing in lead from automobile emissions was recognized, new government regulations enacted in the 1970’s pushed for the removal of lead from petrol (Perron, Hartt, McCann, McGowan, & Segers, 2018). Also, in this era the government regulated the output of industrial facilities in the hopes of decreasing environmental exposures of lead (Perron et al., 2018). Paints containing lead where banned in 1978, while domestic food processors voluntarily removed lead seals from their cans in the early 1990’s (Shukla et al.,
Drinking water can be another source of lead exposure. Water can be contaminated at its source by the environment or by pipes that are used to transport water, either because they are made of lead or use lead components (Brochin et al., 2011).

There is no safe level of lead exposure, and even low levels can have an effect on one’s health. The World Health Organization recommends that adults should have a blood lead concentration below 10 µg/dL (CDC, 2018). The National Institute for Occupational Safety and Health (NIOSH) also recommends that BLL for adults should be less than 10µg/dL, with adults defined as those age sixteen years and older (CDC, 2018).

**Absorption, Metabolism and Excretion**

Absorption of lead can occur via the gastrointestinal tract by digestion through contaminated foods, food preparation or storage containers or by lead particles on hands. Inhalation of lead particles in dust is a pathway for lead to enter the body through the respiratory system. Once absorbed by the body it can be stored in the soft tissues and bones (Leech, Adams, Weathers, Staten, & Filippelli, 2016). BLL increases once exposure has occurred; however, within one month these levels decrease as the lead is deposited into the bones. More than 90% of the total bodily lead content is housed in the bones of the body where the half-life can be decades long (Leech et al., 2016). Excretion of lead is through the hair, sweat and nails; the primary excretion method however is in the urinary system.

**Lead Health Effects**

Lead exposure primarily affects the nervous system in both adults and in children; however, in adult populations increased BLL is associated with cardiovascular disease, hypertension, decreased renal function, increase in waist-to-hip ratio, and elevated blood lipid
levels (Moon, 2013). The diseases and conditions associated with increased BLL’s are closely tied to the endocrine function of the human body.

**Impact of Lead on Endocrine Function**

Bodily functions are controlled by a network of glands throughout the body, the endocrine system. Two of the most important glands to the endocrine system are the hypothalamus and the pituitary gland. The hypothalamus is responsible for maintaining the stability of the internal environment, homeostasis. It is here that the nervous system and the endocrine system are connected via the pituitary gland. The function of the pituitary gland is to secrete hormones that release or inhibit hormones for bodily function (Brochin et al., 2011). Some of the bodily functions controlled by hormones of the pituitary gland include: regulating metabolism, triggering the release of cortisol (stress hormone), tissues of the liver, protein synthesis, elevation of blood glucose levels, and maintenance of blood pressure (Brochin et al., 2011).

The most detrimental effects of lead exposure are seen in the nervous system, where lead blocks receptors in the brain that would naturally communicate to maintain normal bodily functions (Brochin et al., 2011). The toxicity of lead disrupts the communication of the receptor cells and crosses the blood-brain barrier (Brochin et al., 2011). Maintenance of the fluid environment of the nervous system is one of the very important functions of the blood-brain barrier. Unlike other organs in the body that transport molecules by simple diffusion, the blood-brain barrier only uses certain essential molecules that are water-soluble to be transported by carriers in the plasma membrane (Brochin et al., 2011). Exposure of high levels of lead causes plasma to move into interstitial spaces of the brain causing edema (Brochin et al., 2011).
The central nervous system and hormonal changes govern hunger, satiety, sleep patterns which can impact metabolic functions such as blood glucose levels, blood pressure, and eating habits that lead to increased waist circumference and blood lipid levels. These are all individual components of the endocrine disorder metabolic syndrome (Huang, 2009). Exposure to lead affects these individual components by way of the endocrine system. Increased blood glucose levels have been associated with lead exposure; it is thought that chronic exposure to lead inhibits the metabolism of glucose and lipids (Leff, Stemmer, Tyrrell, & Jog, 2018). In addition, a study that examined exposure of heavy metals on human pancreatic function concluded that an adverse correlation exists between heavy metal exposure and pancreatic function (Leff et al., 2018). This evidence suggests that lead exposure can impact endocrine function of the pancreas (Leff et al., 2018).

**Effects on blood pressure.** As previously discussed lead affect parts of the central nervous system that regulates blood pressure levels. In addition, it has been hypothesized that the damaging effects of lead on renal function is the primary cause of hypertension in those exposed to lead (Gambelunghe et al., 2016). Other studies have concluded that lead inhibits the compliance of vascular smooth muscles to contract and dilate in the cardiovascular system essentially inhibiting the control of blood pressure (Kristal-Boneh, Coller, Froom, Harari, & Ribak, 1999). In either instance the effects of lead exposure on the body’s ability to self-regulate blood pressure have been explored and documented.

**Effects on obesity.** Lead exposure is also associated with obesity. The association of obesity with increased waist circumference has also been well documented. Alterations in the function of the hypothalamic-pituitary hormones have been linked with obesity (Delavari, Forouzanfar, Akikhani, Sharifian, & Kelishadi, 2009). In particular, lead exposure inhibits the
release of growth hormones (Brochin et al., 2011) and increases insulin release, both of which are linked to obesity (Delavari et al., 2009).

**Effects on blood lipid levels.** Lastly, blood lipid levels are another component of metabolic syndrome that is impacted by exposure of lead on the endocrine system. It hypothesized in the Kristal-Boneh, Coller, Froom, Harari, and Ribak (1999) study that the release of enzymes needed to metabolize lipids in the bloodstream are impeded by exposure to lead, thus causing the lipid levels to accumulate and remain within the body. Growth hormone deficiencies are also associated with increased total cholesterol and decreased HDL cholesterol levels; as previous discussed lead is an inhibitor of growth hormones release (Kristal-Boneh et al., 1999).

Evidence suggests that the delicate functioning of the endocrine system can easily be disturbed by the exposure of heavy metals such as lead. The previously discussed metabolic functions are governed by the endocrine system. However, with the disturbed homeostasis of the endocrine system, disorders such as metabolic syndrome can develop.

**Metabolic Syndrome**

MetS is a grouping of risk factors associated with the development of atherosclerotic cardiovascular disease. It is comprised of five components: elevated blood pressure, elevated blood glucose levels, a larger waist circumference, elevated blood lipid levels and low HDL (Huang, 2009). Defining criteria for MetS as developed by the National Cholesterol Education Program (NCEP) Adult Treatment Plan (ATP) III in 2001 for adult populations and is summarized in Table 1 (Akbaraly et al., 2010). Based on the definitions by the American Heart Association and the National Heart, Lung, and Blood Institute diagnosis of MetS is diagnosed when a patient has three of the five conditions noted in Table 1 from NCEP ATP III (Grundy et
al., 2004). Since it is known that the disruption of the endocrine systems has the potential to lead to MetS, we will examine whether lead exposure can be associated with the development of MetS.

Table 1

<table>
<thead>
<tr>
<th>NCEP ATP III Criteria for Metabolic Syndrome*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Factor</td>
</tr>
<tr>
<td>Blood Pressure</td>
</tr>
<tr>
<td>Blood Glucose Level</td>
</tr>
<tr>
<td>Blood Triglycerides Level</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Waist Circumference</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
</tbody>
</table>

*According to the National Cholesterol Education Program (NCEP) Adult Treatment Plan III. Copied verbatim from Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004, p. 3.

Methods

Data Source and Study Design

Data were obtained from the 2013 to 2014 NHANES population-based survey. The survey collects health and nutritional information about noninstitutionalized U.S. individuals every two years. The purpose of the survey is to collect a representative sample of the U.S. population. All consent documents, brochures, and operational manuals for the 2013 to 2014 dataset are available online, at the NHANES website that is part of the CDC.

In the 2013 to 2014 survey cycle a total of 14,332 persons were selected from 30 different survey locations. From those selected 10,175 completed the interview and 9,813 were examined. Participants were examined at a mobile examination center (MEC), where physical assessments, laboratory measurements and examinations were conducted. Testing of serum
samples were conducted by the CDC’s Division of Laboratory Sciences of National Center for Environmental Health (CDC, 2015).

From the 2013 to 2014 dataset, individuals with available blood lead samples and data for the five components of MetS (waist circumference, blood pressure, glucose, triglycerides and HDL) were included in the analysis. The final sample size was $N = 5,215$.

**Cofounders**

Socioeconomic and sociodemographic information (i.e., age, race/ethnicity, gender, smoking status and income) were collected as part of the NHANES Family Questionnaire by the Computer-Assisted Personal interview (CAPI) system. Race/ethnicity was reported as Hispanic, non-Hispanic White, non-Hispanic Black, and other multi-racial; with Hispanic as the referent group. Income was reported as <$25000, $25000-$54999, and >$55000; <$25000 was the referent group. Smoking status was determined by utilizing the serum cotinine levels in blood samples that were obtained at the MEC. Categories for smoking status were broken down into ‘Never’, ‘Ex-smoker’, and ‘Current smoker’. The never smoked category is the referent group.

**Laboratory Procedures and Examination**

All measurements were taken at a MEC (CDC, 2015). Waist circumference, weight and height were measured by trained health professionals. A retractable steel measuring tape was used for waist circumference measurements in centimeters (cm), a digital scale was used for weight in kilograms (kg) and a stadiometer was used for height measurements in meters (m).

Blood pressure measurements (systolic and diastolic) were also taken at a MEC. Three consecutive readings were taken from the right arm of the participant; the left arm was only used if there was a problem with the right arm. If a participant has any issues with both arms (casts,
paralysis, rashes, edema, open sores, any dressings, wounds and/or if the cuff does not fit) the participants were excused from this part of the examination (CDC, 2015).

Fasting glucose, triglycerides and HDL levels were tested on all participants samples, with the blood samples were collected at the MEC and sent to the testing labs (CDC, 2015).

Metabolic Syndrome Determination

Clinical criteria determinations for MetS are listed in Table 1. The criteria are based on the NCEP Adult Treatment Plan (ATP) III (Akbaraly et al., 2010). A diagnosis of MetS is made if a subject has at least three of the five criteria outlined in Table 1 (Grundy et al., 2004). Male and female participants are characterized as having MetS when they met the recommended gender specific criteria in Table 1.

Statistical Analysis

Data analyses were conducted using the Statistical Package for Social Science (SPSS). Descriptive statistics for continuous variables were generated for the overall sample population and at the median value for both genders. This includes measures of centrality and dispersion. Frequency distributions were computed for all categorical variables (smoking, income, race/ethnicity) and MetS criteria (waist circumference, blood pressure, triglycerides, HDL, and blood glucose levels).

To test statistical significance for continuous variable across gender, a 2-tailed t-test at an α=0.05 level of significance was used. The testing of statistical significance for categorical variables across gender utilized a chi-square test. BLL was dichotomized at the median into a low exposure group (<1.23 ug/dL) and high exposure group (≥1.23 ug/dL) for males and a low exposure group (<0.86 ug/dL) and high exposure group (≥0.86 ug/dL) for females.
An unadjusted logistic regression was conducted to assess the odds ratio (OR), 95% confidence interval (CI) and \( p \)-value of MetS with high exposure to BLL. A bivariate adjusted logistic regression model was built-up beginning with first regressing the effect of high BLL on MetS. In the next step, one variable was introduced at a time and the OR, 95% CI and \( p \)-value for the effect on BLL was reported. In the subsequent steps this variable was removed and another one was introduced to test its impact on BLL and MetS.

Finally, a multivariable logistic regression was carried out for MetS, with MetS being the outcome or dependent variable. Covariates included age, income levels, race/ethnicity and smoking status.

**Results**

**Descriptive Statistics**

The sample for this study included 1,061 participants aged 20 and older. Table 2 illustrates the demographic profile of the sample by gender and by amount of lead exposure. The median BLL for adults aged 20 years and older was 1.03 \( \text{ug/dL} \); with males (1.23\( \text{ug/dL} \)) having a higher median BLL than females (0.86 \( \text{ug/dL} \)). The mean ages for males and females are similar; males 49.6 years of age and females 48.8 years of age. Race distribution was predominately non-Hispanic Whites, with 45.30% of males and 46.80% of females identifying as non-Hispanic White. The predominant income was >\$55000 (high income) with 37.50% in males and 37.90% in females. As for smoking 22.20% were current smokers in males. In the female sample 17.60% were current smokers. BMI distribution was comparable, both males and females were within the overweight category, mean values for males were 28.13 and 29.68 for females.
Table 2

*Characteristics of 2013-2014 NHANES Adult Participants and Metabolic Factors by Gender*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male</th>
<th>Female</th>
<th>P-value</th>
<th>Male</th>
<th>Female</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall n=523</td>
<td>Overall n=528</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low Exposure (&lt;1.23 ug/dL)</td>
<td>Low Exposure (&lt;0.86 ug/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>High Exposure (≥1.23 ug/dL)</td>
<td>High Exposure (≥0.86 ug/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Blood lead levels</td>
<td>1.23 ug/dL</td>
<td>0.86 ug/dL</td>
<td>0.001</td>
<td>48.74±16.75</td>
<td>56.31±14.91</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years), mean±SD</td>
<td>49.57±17.12</td>
<td>55.29±16.24</td>
<td>0.001</td>
<td>41.22±15.02</td>
<td>56.31±14.91</td>
<td>0.001</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
<td></td>
<td></td>
<td>0.455</td>
<td></td>
<td></td>
<td>0.291</td>
</tr>
<tr>
<td>NHW and Others</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHW</td>
<td>189 (36.20%)</td>
<td>185 (35.03%)</td>
<td></td>
<td>105 (39.60%)</td>
<td>127 (48.28%)</td>
<td></td>
</tr>
<tr>
<td>NHB</td>
<td>237 (45.30%)</td>
<td>247 (46.80%)</td>
<td></td>
<td>120 (45.30%)</td>
<td>127 (48.28%)</td>
<td></td>
</tr>
<tr>
<td>Annual Income, n(%)</td>
<td></td>
<td></td>
<td>0.523</td>
<td></td>
<td></td>
<td>0.546</td>
</tr>
<tr>
<td>&lt;$25000</td>
<td>138 (26.40%)</td>
<td>158 (29.20%)</td>
<td></td>
<td>67 (25.30%)</td>
<td>91 (34.60%)</td>
<td></td>
</tr>
<tr>
<td>$25000-$549999</td>
<td>152 (29.10%)</td>
<td>158 (29.20%)</td>
<td></td>
<td>87 (32.60%)</td>
<td>71 (27.00%)</td>
<td></td>
</tr>
<tr>
<td>&gt;$550000</td>
<td>196 (37.50%)</td>
<td>200 (37.90%)</td>
<td></td>
<td>105 (39.60%)</td>
<td>95 (36.10%)</td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
<td>0.316</td>
<td></td>
<td></td>
<td>0.160</td>
</tr>
<tr>
<td>Never</td>
<td>240 (45.90%)</td>
<td>343 (65.00%)</td>
<td></td>
<td>191 (72.10%)</td>
<td>152 (57.80%)</td>
<td></td>
</tr>
<tr>
<td>Ex</td>
<td>167 (31.90%)</td>
<td>92 (17.40%)</td>
<td></td>
<td>41 (15.50%)</td>
<td>51 (19.40%)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>116 (22.20%)</td>
<td>93 (17.60%)</td>
<td></td>
<td>33 (12.50%)</td>
<td>60 (22.80%)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m**2), mean±SD</td>
<td>28.13±6.13</td>
<td>29.68±7.91</td>
<td>0.001</td>
<td>30.52±8.23</td>
<td>28.84±7.50</td>
<td>0.001</td>
</tr>
<tr>
<td>MetS Prevalence</td>
<td>301 (57.55%)</td>
<td>204 (38.60%)</td>
<td></td>
<td>116 (43.8%)</td>
<td>88 (33.50%)</td>
<td></td>
</tr>
<tr>
<td>MetS Variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP≥130/≥90mmHg</td>
<td>428 (81.80%)</td>
<td>423 (80.10%)</td>
<td></td>
<td>208 (78.50%)</td>
<td>215 (81.70%)</td>
<td></td>
</tr>
<tr>
<td>TG≥150 mg/dL</td>
<td>152 (29.10%)</td>
<td>112 (21.20%)</td>
<td></td>
<td>51 (19.20%)</td>
<td>61 (23.20%)</td>
<td></td>
</tr>
<tr>
<td>FBG≥100 mg/dL</td>
<td>278 (53.20%)</td>
<td>212 (40.20%)</td>
<td></td>
<td>99 (37.40%)</td>
<td>113 (43.00%)</td>
<td></td>
</tr>
<tr>
<td>WC &gt; 102 cm*</td>
<td>212 (40.50%)</td>
<td>88 (34.10%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WC &gt; 88 cm†</td>
<td>--</td>
<td>362 (68.60%)</td>
<td></td>
<td>367 (69.50%)</td>
<td>192 (73.00%)</td>
<td></td>
</tr>
<tr>
<td>HDL&lt;40 mg/dL*</td>
<td>148 (28.30%)</td>
<td>367 (69.50%)</td>
<td></td>
<td>175 (66.00%)</td>
<td>192 (73.00%)</td>
<td></td>
</tr>
<tr>
<td>HDL&lt;50 mg/dL†</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: NHW, Non-Hispanic White; NHB, Non-Hispanic Black; BMI, Body Mass Index; BP, Blood Pressure; TG, Triglycerides; FBG, Fasting Blood Glucose; WC, Waist Circumference; HDL, High Density Lipoproteins

*Waist circumference and high density lipoproteins cutoff values for males
†Waist circumference and high density lipoproteins cutoff values for females
Amongst the males 57.5% had MetS, while only 38.6% of females had MetS. Furthermore, 78.5% of the females who had low exposure to lead met the MetS criteria for blood pressure, whereas 81.7% of the females who had high exposure met the criteria. In addition, females met the MetS criteria for larger waist circumference and low HDL levels; 68.6% and 69.5% respectively when compared to males.

**Logistic Regression Analysis**

**Bivariate logistic regression results.** As illustrated in Table 3 males with high exposure to BLL did not have a significant association with MetS, neither in the unadjusted nor the bivariate adjusted models. For females, in the unadjusted models high BLL was associated with 55% increased risk of MetS, OR=1.55 (1.08-2.20), \( p = .015 \). However, when adjusted for all other risk, high BLL in females was not associated with MetS.

Table 3

**Bivariate Adjusted Odds Ratio (OR) and 95% Confidence Interval for Blood Lead Levels and Risk Factors of Metabolic Syndrome in Males and Females**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male Adjusted OR (95% CI)</th>
<th>p-Value</th>
<th>Female Adjusted OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Lead</td>
<td>0.815 (0.576-1.15)</td>
<td>0.249</td>
<td>1.55 (1.08-2.20)</td>
<td>0.015</td>
</tr>
<tr>
<td>Age</td>
<td>0.599 (0.409-0.877)</td>
<td>0.008</td>
<td>0.758 (0.498-1.15)</td>
<td>0.196</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>0.593 (0.404-0.869)</td>
<td>0.007</td>
<td>0.742 (0.487-1.13)</td>
<td>0.167</td>
</tr>
<tr>
<td>Annual Income</td>
<td>0.524 (0.349-0.786)</td>
<td>0.002</td>
<td>0.727 (0.472-1.12)</td>
<td>0.148</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>0.537 (0.354-0.825)</td>
<td>0.003</td>
<td>0.672 (0.430-1.05)</td>
<td>0.082</td>
</tr>
<tr>
<td>BMI</td>
<td>0.741 (0.464-1.18)</td>
<td>0.209</td>
<td>0.921 (0.563-1.51)</td>
<td>0.745</td>
</tr>
</tbody>
</table>

*Note:* CI, Confidence Interval; BMI, Body Mass Index

**Multivariable logistic regression results.** After adjusting for all risk factors in the multivariable model illustrated in Table 4, neither men nor women had any increased risk for MetS in the high blood lead group compared to the low blood lead group.
Table 4

Multivariable Adjusted Odds Ratio (OR) for Blood Lead Levels and Risk Factors of Metabolic Syndrome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted OR (95%CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Blood Lead (ug/dL)</td>
<td>0.741 (0.464-1.20)</td>
<td>0.209</td>
</tr>
<tr>
<td>Age in years</td>
<td>1.03 (1.01-1.04)</td>
<td>0.001</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHW vs. Hispanic/others</td>
<td>0.751 (0.466-1.21)</td>
<td>0.239</td>
</tr>
<tr>
<td>NHB vs. Hispanic/others</td>
<td>0.635 (0.343-1.20)</td>
<td>0.166</td>
</tr>
<tr>
<td>Annual Income</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$25000-$54999 vs. &lt;$25000</td>
<td>0.717 (0.420-1.23)</td>
<td>0.246</td>
</tr>
<tr>
<td>&lt;$55000+ vs. &lt;$25000</td>
<td>0.562 (0.331-0.954)</td>
<td>0.035</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex vs. Never</td>
<td>1.422 (0.853-2.40)</td>
<td>0.204</td>
</tr>
<tr>
<td>Current vs. Never</td>
<td>1.345 (0.746-2.243)</td>
<td>0.423</td>
</tr>
<tr>
<td>BMI (kg/m**2)</td>
<td>1.240 (1.174-1.300)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Note: CI, Confidence Interval; NHW, Non-Hispanic White; NHB, Non-Hispanic Black; BMI, Body Mass Index

A one-unit increase in age and BMI was associated with 3% and 24% greater odds of MetS in males and were statistically significant. In race/ethnicity, non-Hispanic Whites and non-Hispanic Blacks when compared to Hispanic/others had a protective factor for MetS although this not statistically significant. For annual income both categories had a protective factor, with high income vs. low income reaching statistical significance.

In females, a one unit increase in age and BMI showed 6% and 16% respectively greater odds of MetS and were statistically significant [OR=1.06, 95% CI=1.04-1.08, p = .001 and OR=1.16, 95% CI=1.12-1.20, p = .001]. Greater odds of MetS were also shown in middle income vs. low income category, as well as the current vs. never smoking category [OR=1.97,
95% CI= 1.13-3.46 and OR=1.95, 95% CI= 1.05-3.62]. Both odds were statistically significant with \( p = .018 \) and \( p = .035 \) respectively.

**Discussion**

In this cross-sectional analysis of the NHANES 2013 to 2014 data, blood lead was not associated with MetS in U.S. adult males and females aged 20 years older in adjusted models. Although in the unadjusted analysis, females had 55% significantly higher risk of MetS within the high mean blood lead groups as compared to the low group, this association was not significant once we adjusted for confounders.

Earlier studies have shown a positive association between lead exposure and hypertension (Gambelunghe et al., 2016), waist circumference (Delavari et al., 2009) and blood lipid levels (Kristal-Boneh et al., 1999). The study on lead exposure by Kristal-Boneh et al., (1999) was based on occupational lead exposure (high exposure) which is not generalizable to the U.S. general population exposure that currently has very low mean blood lead levels (0.76 ug/dL in males). In contrast to our study a Korean study reported significant association between blood lead and MetS, however their blood lead levels were 2.08 ug/dL, which is significantly higher than the blood lead levels reported for the sample in the present study (Moon, 2013).

The prevalence of MetS in our studied population which is representative of the U.S. population was nearly 58%. Based on published reports the prevalence of MetS in the U.S. adult population has been increasing over the years as evidenced by the rising rates of MetS in NHANES datasets 2003 to 2004 (32.9%) compared to 2011 to 2012 (34.7%) (Aguilar et al., 2015). The highest MetS prevalence of 2014 where 38.6% for Hispanics, 37.4% for non-Hispanic Whites, and over 50% in women and Hispanics older than 60 years of age (Aguilar et al., 2015). In other international studies it has been reported that there is an increasing magnitude
of MetS prevalence. The overall MetS prevalence in adults over the age of 45 had a prevalence above 50% (Delavari et al., 2009); which concurs with other studies, suggesting that the worldwide prevalence is on the rise.

**Strengths**

Strengths in this study include the usage of information from NHANES which is a nationally representative dataset and characterizing both genders and multiple ethnicities. Due to rigorous NHANES methodology bias is limited, the national survey uses intensive training that helps with prevention of selection and interview bias and uses state of the art laboratory facilities. This study is high in internal validity; we adjusted for a number of confounding variables including age, annual income, race/ethnicity and smoking status. Since NHANES is an excellent representation of the general population it has external validity.

**Limitations**

Limitations of this study include the cross-sectional nature of the NHANES data which does not allow studying temporality, one of the criteria for causality. The sample size for males and females was a little over 500 participants for each. In future studies a larger sample size could possibly be used by combining data from different survey cycles. Future areas of study could look at the impact of lead exposure in those younger than 20 years of age, as chronic diseases have been on the rise in children and adolescents.

**Conclusion**

Based on the results of our study, lead exposure in U.S. adults aged 20 years and older does not have a statistically significant association with the prevalence of MetS in both males and females. Further analysis and identification of factors that contribute to the lack of significance will need additional evaluation.
References


Appendix A: Human Subjects Regulations Decision Chart

Chart 1: Is an Activity Research Involving Human Subjects Covered by 45 CFR part 46?

- Start here. Is it research?
  - Yes
    - Is the activity a systematic investigation designed to develop or contribute to generalizable knowledge? [45 CFR 46.102(d)]
      - No
        - Activity is not research, so 45 CFR part 46 does not apply.
      - Yes
        - Activity is research. Does the research involve human subjects?
          - Yes
            - Does the research involve obtaining information about living individuals? [45 CFR 46.102(f)]
              - Yes
                - Is the information individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information)? [45 CFR 46.102(f)(2)]
                  - No
                    - Activity is research involving human subjects. Is it covered by the regulations?
                      - Yes
                        - Is it conducted or supported by HHS? [45 CFR 46.101(a)(1)]
                          - Yes
                            - The research involving human subjects is covered by the regulations.
                              - Other Federal, State and local laws and/or regulations may apply to the activity. [45 CFR 46.101(f)]
                              - Go to Chart 2
                            - No
                              - The research involving human subjects is NOT covered by the regulations.
                                - AND
                                - Unless exempt under 45 CFR 46.101(b), 45 CFR part 46, subpart A applies to the research, and as appropriate subparts B, C, and D also apply.
                                - BUT
                                - Go to Chart 2
                          - No
                            - Does the institution hold an FWA under which it applies 45 CFR 46 to all of its human subjects research regardless of the source of support?
                              - Yes
                                - The research involving human subjects is covered by the regulations.
                              - No
                                - The research involving human subjects is NOT covered by the regulations.
                      - No
                        - The research is not research involving human subjects, and 45 CFR part 46 does not apply.
          - No
            - Does the research involve intervention or interaction with the individuals? [45 CFR 46.102(f)(1), (2)]
              - Yes
                - Is the information private? (About behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, or provided for specific purposes by an individual and which the individual can reasonably expect will not be made public.) [45 CFR 46.102(f)(2)]
                  - No
                    - Activity is research involving human subjects. Is it covered by the regulations?
                      - Yes
                        - Is it conducted or supported by HHS? [45 CFR 46.101(a)(1)]
                          - Yes
                            - The research involving human subjects is covered by the regulations.
                          - No
                            - The research involving human subjects is NOT covered by the regulations.
                      - No
                        - The research is not research involving human subjects, and 45 CFR part 46 does not apply.
              - No
                - Activity is research involving human subjects. Is it covered by the regulations?
                  - Yes
                    - Is it conducted or supported by HHS? [45 CFR 46.101(a)(1)]
                      - Yes
                        - The research involving human subjects is covered by the regulations.
                      - No
                        - The research involving human subjects is NOT covered by the regulations.
                    - No
                      - The research is not research involving human subjects, and 45 CFR part 46 does not apply.
Appendix B: List of Competencies Met in Integrative Learning Experience

**CEPH Foundational Competencies Checklist**

<table>
<thead>
<tr>
<th>Evidence-based Approaches to Public Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Select quantitative and qualitative data collection methods appropriate for a given public health context</td>
</tr>
<tr>
<td>3. Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate</td>
</tr>
<tr>
<td>4. Interpret results of data analysis for public health research, policy or practice</td>
</tr>
</tbody>
</table>

**Communication**

| 19. Communicate audience-appropriate public health content, both in writing and through oral presentation |

**Concentration Specific Competencies Checklist**

<table>
<thead>
<tr>
<th>Population Health Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Demonstrate application of an advanced quantitative or qualitative research methodology.</td>
</tr>
<tr>
<td>3. Demonstrate the ability to contextualize and integrate knowledge of specific population health issues.</td>
</tr>
</tbody>
</table>