

# Selenium, Copper, Zinc and Hypertension: An Analysis of the National Health and Nutrition Examination Survey (2011-2016)

Mrigendra Mani Bastola (✉ [manitola@gmail.com](mailto:manitola@gmail.com))

National Institutes of Health <https://orcid.org/0000-0002-5696-674X>

Craig Locatis

National Institutes of Health

Richard Maisiak

University of Alabama

Paul Fontelo

National Institutes of Health

---

## Research article

**Keywords:** Selenium serum levels, Hypertension, NHANES, Reference levels, Trace elements, Copper, Zinc

**Posted Date:** August 30th, 2019

**DOI:** <https://doi.org/10.21203/rs.2.12017/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

**Version of Record:** A version of this preprint was published at BMC Cardiovascular Disorders on January 31st, 2020. See the published version at <https://doi.org/10.1186/s12872-020-01355-x>.

# Abstract

**Abstract:** Background: Hypertension is a major cardiovascular illness worldwide with many underlying causes. The role of trace elements selenium, copper, and zinc in hypertension is uncertain with only a few studies reported. The objective of this study was to evaluate the role of these trace elements in hypertension. Method: Data from 6683 National Health and Nutrition Examination Survey (NHANES) participants from 2011 to 2016 were analyzed using Statistical Analytical System (SAS, version 9.4) software for the role of trace elements in hypertension in age range 8 to 80 years, irrespective of the antihypertensive medication taken. Results: Findings showed a significant positive association between serum selenium levels and hypertension but not with serum copper and zinc. At optimal levels for transport and distribution, serum selenium levels of 120 µg/L or higher (reference level 70 -150 µg/L) were significantly associated with hypertension (OR = 1.56, 95% CI= 1.38 – 1.76) after adjusting for confounding factors. At serum selenium greater than 150 µg/L, the association with hypertension strengthened (OR= 1.91, 95% CI = 1.54-2.36). Conclusion: A positive association was found between serum selenium and hypertension, irrespective of age or anti-hypertensive medications intake. These findings also suggest that the reference levels of serum selenium levels in healthy individuals may need to be re-determined. If validated, patients with hypertension may also need to be cautioned about selenium intake.

## Background

Hypertension is a major cardiovascular illness, affecting more than a billion individuals worldwide and causing millions of deaths each year. Although researchers have studied micronutrients such as sodium, potassium, chloride, magnesium, and calcium and their effects on hypertension, there is not much evidence available on micronutrients such as selenium, copper, and zinc [1, 2]. The roles of the trace elements selenium, copper and zinc on hypertension were analyzed using data from National Health and Nutrition Examination Survey (NHANES) participants from 2011 to 2016, following recent American Heart Association (AHA) guidelines for blood pressure categories [3, 4].

Selenium is an essential trace element. It is a cofactor required for glutathione peroxidase, an enzyme that protects the body against reactive oxygen species and free radical-mediated cell membrane damage. The Institute of Medicine (IOM) recommended daily allowance for selenium for both men and women is 55 µg/day [5]. In a recent study, the average daily selenium intake in U.S. population was more than 100 micrograms [6], suggesting an intake level much higher than required, with some authors implicating high selenium in American soil as a possible reason [5, 6].

Selenium is reported to have some protective role on upper gastrointestinal tract cancers and colorectal adenoma for smokers [7, 8]. Lesser depressive symptoms among young adults occurred with optimal serum selenium levels [9]. Low selenium also has been associated with increased prevalence of thyroid disease [10]. Selenium deficiencies related to total parenteral nutrition has been linked to intramural fibrosis of cardiac muscles [11]. In a recently published NHANES and Canadian Health Measure Survey

based study, circulating selenium has also been found to be inversely associated with prevalence of stroke [12]. Another recent study reported that a low selenium concentrations measured in toenail samples was associated with increased risk of hypertension in Chinese adults [13].

Higher selenium levels have been associated with diseases such as hypertension, hypercholesterolemia and diabetes mellitus. A recent longitudinal study suggests that selenium may have a harmful role in the development of hypertension in the elderly [14]. High selenium levels have been associated with high serum cholesterol levels [15], and increased risk for diabetes mellitus [16, 17]. A previous study on dietary selenium intake in 2638 NHANES participants revealed a positive association of increments in serum selenium and blood pressure in the U.S. population [18]. However, no recent studies with a large number of participants address the role of selenium on hypertension or in younger people, using the revised AHA guidelines for adults and revised practice guidelines for pediatric hypertension.

Zinc has a role in cell division and enhances the action of insulin, but only a few publications discuss its role in blood pressure. In some animal studies, the role of zinc in hypertension is conflicting, with some studies suggesting higher levels, while others suggesting lower levels causing hypertension. Tubek et al. suggested alternations in zinc metabolism where zinc might be absorbed and excreted more in urine with hypertension [19]. Kim et al. showed a negative correlation between zinc and systolic blood pressure, and that serum and urinary concentrations of zinc were not significantly associated with blood pressure [20]. A study in an animal model suggested that excessive zinc intake increases systemic blood pressure and decreases renal blood flow [21]. However, inverse correlations of blood pressure and serum zinc have also been observed, while higher levels of serum copper were associated with hypertension [22]. A recently published article has implicated zinc deficiency to hypertension in animal models [23]. In another study, excessive zinc intake elevated systemic blood pressure levels in animal models and was presumably associated with oxidative stress [24]. Dietary zinc was inversely associated with the systolic blood pressure in young obese women, but both serum and urinary zinc concentrations were not found to be correlated with either systolic or diastolic blood pressure after adjustments to dietary intake [20].

Copper is an essential component for lysyl oxidase and superoxide dismutase enzymes, which are involved in collagen and elastin and free radical metabolism needed for healthy arteries [25]. The role of copper and zinc in hypertension is inconclusive, with some studies showing links to hypertension while others do not [26, 27]. A recently published study based on NHANES indicated that the serum levels of copper and zinc might not correlate with blood pressure, although zinc and copper metabolism imbalance has been hypothesized as a hypertension cause [22, 26, 28]. Copper has been found to inhibit the activity of angiotensin converting enzyme, a key enzyme for blood pressure regulation, and a study found low blood copper levels in hypertensive group compared to normal controls in animal model [29]. Patients with both low and high serum copper were associated with hypertension in a study [30], but others reported no association of copper with hypertension after adjustment for confounding factors [31].

## Methods

## **Study design and population characteristics:**

The NHANES 2011-2016 database on trace elements having 31 522 total participants was the study's data source. After excluding entries with missing data sets, 6683 participants were included. The study population consisted of 3289 males, 3394 females. Of these, 976 were smokers, 49 were pregnant and 1314 were on blood pressure lowering medications. NHANES categories were used to classify participants by reported race. There were 1060 Hispanics, 2338 Caucasians, 1465 blacks, 789 Asians and 744 were in "another Hispanic" category.

## **Data collection and processing:**

Blood pressure was calculated as the average of the three subsequent observations for systolic and diastolic blood pressure, irrespective of the anti-hypertensive medication status of the participants. Serum levels of the trace elements in the NHANES participants were measured by inductively coupled plasma-dynamic reaction cell-mass spectrometry [3].

## **Outcome assessment:**

Normal clinical values for trace elements published by Mayo Clinic Laboratories (2019) were used as reference values. According to its reference website for currently practiced lab values, the normal serum selenium, copper and zinc values were 70 to 150 µg/L, 75 to 145 µg/L and 65 to 105 µg/L respectively [32-34]. The reference values were used as cutoffs in analysis for all trace elements. Additionally, high normal selenium was defined as serum selenium values more or equal to 120 µg/L.

In accordance with the American Heart Association 2018 guidelines, hypertension was defined as either having a diastolic > 79 mmHg or systolic > 129 mmHg for ages 13 or above [4]. For the age range 8 to 12 years, having a systolic or diastolic above the 95<sup>th</sup> percentile in accordance with the age, gender, and height was classified as hypertensive in accordance to the recently published guidelines on pediatric hypertension [35].

## **Statistical analysis:**

Statistical Analysis System (SAS, version 9.3) software was used for data analysis. The trace elements were characterized in mean values, maximum, minimum and median values. odds ratios (OR) with Wald confidence limits, polynomial logistic regression and quantile regression were sequentially used in the analysis.

Highest and lowest quantiles of serum trace elements were screened for possible association with hypertension. Un-adjusted odds ratios for the demographic variables were represented in forest plots as obtained from logistic regressions. Also, the highest and lowest quantiles of the serum trace elements were analyzed with logistic regression and odds ratios were calculated. A quantile regression model was selected to observe the effects of serum selenium on each quantile of the heterogeneous study

population, since the only the higher quantiles in serum selenium showed association with hypertension among the trace elements under study.

## Results

### Study participants characteristics:

Median values of the study participants were age 38 years, body mass index (BMI) 26.4, and waist circumference 91.7 cm. The median serum copper level was 113.6 µg/L, median selenium level of 126.1 µg/L and the median serum zinc level was 80.7 µg/L (Table 1). Other demographics, blood pressure and laboratory parameters relevant to this study are shown in Table 1 (see Supplementary Files).

### Unadjusted odds ratios of relevant variables and the trace elements with hypertension:

Lowest and highest quantiles for each of the trace elements were screened for their association with hypertension. The lowest quantile of serum selenium and serum copper negatively correlated with hypertension, while the highest quantile of serum selenium was positively correlated with hypertension (Table 2 in the Supplementary Files).

Unadjusted odds ratios were calculated for each of the relevant variables for hypertension causation and the serum trace elements (Table 2). The results of the unadjusted odds ratios with 95% confidence intervals (CI) are shown in Figure 1. The median serum selenium among hypertensives was 126.1 µg/L, but only 9.3% of the participants (n=625) had serum selenium higher than the normal range (70 – 150 µg/L) [33]. Studies suggested that at or around 120µg/L, selenium values are optimal for distribution and transport [36]. In this analysis, at high normal range of serum selenium value at 120 µg/L or more, the serum selenium level was significantly associated with hypertension (unadjusted OR = 1.78, 95% CI= 1.58 – 2.022). Interestingly, serum selenium higher than 150 µg/L strengthened the association with hypertension (unadjusted OR= 1.84, 95% CI = 1.55-2.18). Estimated probabilities comparisons of serum trace elements selenium, zinc and copper are shown in Figure 2. Increased probability for hypertension was noted only in case of high serum selenium levels.

### Predicted probabilities for the serum trace elements with hypertension

The predicted probabilities of serum selenium, serum copper and serum zinc as an output from logistic regression analysis revealed no significant association of serum copper and serum zinc levels with hypertension (Figure 2). However, there was a significant positive association of high serum selenium with high blood pressure (Table 2, Figures 1 and 2). These initial findings of association concurred with subsequent analyses. Although lower than normal serum zinc levels showed odds ratio of 1.4 (1.01 – 1.51) (Figure 1), the subsequent polynomial regression procedure with adjustments for confounding factors on low serum zinc did not show strong association with hypertension (Figure 1 and Table 3 in the Supplementary Files) and was not analyzed further.

### Confounding factors adjustments with polynomial regression models

Confounding factors considered for multinomial logistic regression model were smoker, gender (male), BMI > 24, borderline high cholesterol, high serum cholesterol, high waist circumference for males and females, daily sodium and cholesterol intake and taking anti-hypertensive medications (Figure 1). Among the different races, being in the black population of non-Hispanic origin was considered as a confounding factor in the analysis, but pregnancy was not (Figure 1).

After adjusting for confounders, serum selenium levels of 120 µg/L or higher (reference level 75 -150 µg/L) were significantly associated with high blood pressure (OR = 1.56(1.38 – 1.76)). Also, at serum selenium greater than 150 µg/L, the association with high blood pressure strengthened (OR = 1.91 (1.54 – 2.36)) with hypertension after adjusting for confounding factors (Table 3). The adjusted odds ratios of hypertension with serum selenium at highest quantile versus lowest quantile were significant at 1.34 (95% CI= 1.17 -1.53) and 0.63(95% CI= 0.55-0.72) respectively.

When confounding factors were taken into account, serum copper and zinc were no longer significantly associated with hypertension, with either higher or lower than normal values or at their highest and lowest quantiles (Table 3). The adjusted odds ratios of hypertension with serum copper at highest versus lowest quantiles were 1.03(95% CI=0.9-1.19) and 1.05(95% CI=0.91-1.2) respectively. For serum zinc, the adjusted odds ratios of hypertension at highest versus lowest quantiles were 0.99(95% CI = 0.87-1.13) and 1.15(95% CI=1.00-1.31) respectively.

Since the association of increments in serum selenium was not linear at all serum selenium levels and the association with hypertension increased from values at 150ug/L compared to 120ug/L (Figure 2 and Table 3), quantile regression models were also analyzed for serum selenium, systolic blood pressure, diastolic blood pressure, age of the participants and total serum cholesterol levels (Figures 3 and 4). Looking closer at the effect of serum selenium on systolic and diastolic blood pressure, the results of quantile regression revealed stronger increments in associations of diastolic blood pressure with the higher quantiles of selenium compared to systolic blood pressure, where the strength of association remained mostly at the same level in all the quantiles of serum selenium (Figure 3). Also, the quantile regression models for serum levels of selenium showed a positive association on all the quantiles of serum selenium with increments of the participant age, and a stable but stronger association with total serum cholesterol levels persisted at all quantiles of serum selenium (Figure 4), as some studies suggest [15].

## Discussion

Findings show the higher values of serum selenium, including those in the high normal range, are associated with hypertension, but high levels of trace elements copper or zinc and low levels of any of these trace elements are not (Table 3). The association of high serum selenium levels with hypertension persisted after adjustment of various confounding factors. In addition, the results of quantile regression indicate that the effect of per unit increments in serum selenium's on hypertension was stronger with diastolic blood pressure compared to systolic blood pressure (Figures 2 and 3). Interestingly, this finding

also supports the study by Mark et al. where a group of nutritionally deprived population was supplemented with dietary selenium and the population developed diastolic but not systolic hypertension [37]. Although several studies suggest a potential role of copper and zinc in hypertension, this study did not show an association.

This study's findings support previous studies reporting higher daily selenium intake in U.S. population than the rest of the world. Its results extend those of an earlier NHANES study (2003-2004), showing a positive association of serum selenium with hypertension [18], by having a larger sample size, a later and longer time period, a more inclusive age range of 8 to 80 years, and accounting for potential confounding factors. The association of higher serum selenium levels, irrespective of the participant's anti-hypertensive medicine intake further strengthens the association. The finding that the increments in selenium values were observed with stable increments in total serum cholesterol over all the quantiles of serum selenium suggests the possibility of selenium accumulation with consumption of high cholesterol containing food, which are also good sources of selenium, such as eggs and meat, causing uniform association with hypertension, in both the serum selenium and serum cholesterol concurrently [38].

Although not the main objective of the study, the analysis also found a significant positive correlation of high blood pressure among smokers and males while there was a significant negative correlation of hypertension with pregnancy (Figure 1). Also, high sodium intake was not associated with hypertension as expected, presumably because normotensives were consuming high sodium diets compared to hypertensives who were probably restricting their sodium intake [39]. Studies showed that the total parenteral nutrition patients in hospitals and chronic malnutrition are more likely to develop selenium deficiency which could be replenished by food or supplements rich in selenium [38, 40]. Since there are few publications about the metabolism and excretion of selenium, no definitive predictions can be made regarding its physiology and excretion mechanism. Therefore, avoiding selenium sources in food and water is the only method advisable to gain lower levels of selenium in blood. More focused and controlled studies including animal models need to be done to confirm the pathogenesis of hypertension linked with higher blood selenium levels at a molecular and cellular level.

### **Limitations:**

One limitation of this study is the inclusion criteria of the hypertensive patients, where hypertensive cases were defined according to their blood pressure at examination, irrespective of their status of hypertensive medications intake status. This could have included hypertensive patients with well-controlled blood pressure as normotensives, if they had presented as a normotensive at the time of data collection. Any participants who were taking anti-hypertensives would have potentially contributed as confounding factors in this study, if they were included as hypertensives despite their normal blood pressure at examination. Also, participants with incidental findings of high blood pressure at the time of examination might have been included in the hypertensives group. Although a recent publication showed protective role of selenium for stroke, whether the selenium is a protective factor for stroke despite its association

with hypertension is still unanswered [12]. Although not a limitation of the study, there were limited publications about the normal reference values used.

## Conclusion

The study suggests that higher values of serum selenium including the high normal values may be associated with hypertension. These findings require confirmation from larger population studies so that the hypertensives may be advised to lower their daily selenium intake. The current reference levels of serum selenium may need to be redetermined if these study results are further validated.

## Abbreviations

AHA= American Heart Association

BMI= Body Mass Index

CI= Confidence Interval

DBP= Diastolic Blood Pressure

NHANES = National Health and Nutrition Examination Survey

OR = Odds ratio

Q1-4 = Quantiles 1 to 4

SBP = Systolic Blood Pressure

## Declarations

### **Ethics approval and consent to participate:**

The data used in this study is publicly available and deidentified data from Centers for Disease Control and Prevention website, under National Health and Nutrition Examination Survey 2011-2016 sections. According to its website, serum and plasma specimens are obtained from NHANES study participants ages six years and older who have given consent for their specimens to be used in future research studies. An additional ethics approval and consent to participate is not applicable.

### **Consent for publication:**

Not applicable. An additional parental consent is not applicable in this study.

### **Availability of data and materials:**

The data used in this study is publicly available and downloadable from Centers for Disease Control and Prevention website, under National Health and Nutrition Examination Survey 2011-2016 sections. Additionally, the datasets used are available from the corresponding author.

### **Competing interests:**

Authors declare no competing interests.

### **Funding:**

This research was supported by the Intramural Research Program of the National Institutes of Health (NIH), National Library of Medicine (NLM) and Lister Hill National Center for Biomedical Communications (LHNCBC).

### **Authors' contributions:**

We would like to thank statistician Dr. Richard Maisiak for his expert opinions on this paper.

### **Acknowledgements:**

The views and opinions of the authors herein do not necessarily state or reflect those of the National Library of Medicine, National Institutes of Health or the US Department of Health and Human Services.

## **References**

1. Ascherio A, Hennekens C, Willett WC, Sacks F, Rosner B, Manson J, et al. Prospective study of nutritional factors, blood pressure, and hypertension among US women. *Hypertension*. 1996;27(5):1065-72.
2. Karppanen H. Minerals and blood pressure. *Ann Med*. 1991;23(3):299-305.
3. CDC. National Health and Nutrition Examination Survey. 2003. [Accessed on: July 12, 2019]
4. Association AH. Blood Pressure Categories 2018 [Available from: <https://www.health.harvard.edu/heart-health/reading-the-new-blood-pressure-guidelines>.] [Accessed on: July 12, 2019]
5. IOM. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium and Carotenoids. 2000. p. 284.
6. Supplements OoD. Selenium: ODS/NIH; 2018 [Available from: <https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional%20/>.] [Accessed on: July 12, 2019]
7. Peters U, Chatterjee N, Church TR, Mayo C, Sturup S, Foster CB, et al. High serum selenium and reduced risk of advanced colorectal adenoma in a colorectal cancer early detection program. *Cancer Epidemiol Biomarkers Prev*. 2006;15(2):315-20.
8. Knekt P, Aromaa A, Maatela J, Alfthan G, Aaran RK, Teppo L, et al. Serum vitamin E, serum selenium and the risk of gastrointestinal cancer. *Int J Cancer*. 1988;42(6):846-50.

9. Conner TS, Richardson AC, Miller JC. Optimal serum selenium concentrations are associated with lower depressive symptoms and negative mood among young adults. *J Nutr.* 2015;145(1):59-65.
10. Wu Q, Rayman MP, Lv H, Schomburg L, Cui B, Gao C, et al. Low Population Selenium Status Is Associated With Increased Prevalence of Thyroid Disease. *J Clin Endocrinol Metab.* 2015;100(11):4037-47.
11. de Lorgeril M, Salen P. Selenium and chronic heart failure. *Circulation.* 2000;101(5):E74.
12. Hu XF, Stranges S, Chan LHM. Circulating Selenium Concentration Is Inversely Associated With the Prevalence of Stroke: Results From the Canadian Health Measures Survey and the National Health and Nutrition Examination Survey. *J Am Heart Assoc.* 2019;8(10):e012290.
13. Liu L, Lin G, Wang H, Zhang B, Du S. Selenium Exposure and Incident Hypertension Among Chinese Adults (P24-020-19). *Curr Dev Nutr.* 2019;3(Suppl 1).
14. Su L, Jin Y, Unverzagt FW, Liang C, Cheng Y, Hake AM, et al. Longitudinal Association between Selenium Levels and Hypertension in a Rural Elderly Chinese Cohort. *J Nutr Health Aging.* 2016;20(10):983-8.
15. Chen C, Jin Y, Unverzagt FW, Cheng Y, Hake AM, Liang C, et al. The association between selenium and lipid levels: a longitudinal study in rural elderly Chinese. *Arch Gerontol Geriatr.* 2015;60(1):147-52.
16. Stranges S, Sieri S, Vinceti M, Grioni S, Guallar E, Laclaustra M, et al. A prospective study of dietary selenium intake and risk of type 2 diabetes. *BMC Public Health.* 2010;10:564.
17. Lu CW, Chang HH, Yang KC, Kuo CS, Lee LT, Huang KC. High serum selenium levels are associated with increased risk for diabetes mellitus independent of central obesity and insulin resistance. *BMJ Open Diabetes Res Care.* 2016;4(1):e000253.
18. Laclaustra M, Navas-Acien A, Stranges S, Ordovas JM, Guallar E. Serum selenium concentrations and hypertension in the US Population. *Circ Cardiovasc Qual Outcomes.* 2009;2(4):369-76.
19. Tubek S. Role of zinc in regulation of arterial blood pressure and in the etiopathogenesis of arterial hypertension. *Biol Trace Elem Res.* 2007;117(1-3):39-51.
20. Kim J. Dietary zinc intake is inversely associated with systolic blood pressure in young obese women. *Nutr Res Pract.* 2013;7(5):380-4.
21. Kasai M, Miyazaki T, Takenaka T, Yanagisawa H, Suzuki H. Excessive zinc intake increases systemic blood pressure and reduces renal blood flow via kidney angiotensin II in rats. *Biol Trace Elem Res.* 2012;150(1-3):285-90.
22. Bergomi M, Rovesti S, Vinceti M, Vivoli R, Caselgrandi E, Vivoli G. Zinc and copper status and blood pressure. *J Trace Elem Med Biol.* 1997;11(3):166-9.
23. Williams CR, Mistry M, Cheriyan AM, Williams JM, Naraine MK, Ellis CL, et al. Zinc deficiency induces hypertension by promoting renal Na(+) reabsorption. *Am J Physiol Renal Physiol.* 2019;316(4):F646-F53.

24. Yanagisawa H, Sato M, Nodera M, Wada O. Excessive zinc intake elevates systemic blood pressure levels in normotensive rats–potential role of superoxide-induced oxidative stress. *J Hypertens.* 2004;22(3):543-50.
25. Klevay LM. Cardiovascular disease from copper deficiency—a history. *J Nutr.* 2000;130(2S Suppl):489S-92S.
26. Vivoli G, Bergomi M, Rovesti S, Pinotti M, Caselgrandi E. Zinc, copper, and zinc- or copper-dependent enzymes in human hypertension. *Biol Trace Elem Res.* 1995;49(2-3):97-106.
27. Carpenter WE, Lam D, Toney GM, Weintraub NL, Qin Z. Zinc, copper, and blood pressure: Human population studies. *Med Sci Monit.* 2013;19:1-8.
28. Yao J, Hu P, Zhang D. Associations Between Copper and Zinc and Risk of Hypertension in US Adults. *Biol Trace Elem Res.* 2018;186(2):346-53.
29. Loyke HF. Copper and zinc in experimental hypertension. *Biol Trace Elem Res.* 1991;29(1):45-9.
30. Darroudi S, Saberi-Karimian M, Tayefi M, Tayefi B, Khashyarmanesh Z, Fereydouni N, et al. Association Between Hypertension in Healthy Participants and Zinc and Copper Status: a Population-Based Study. *Biol Trace Elem Res.* 2019;190(1):38-44.
31. Lee YK, Lyu ES, Oh SY, Park HR, Ro HK, Heo YR, et al. Daily Copper and Manganese Intakes and Their Relation to Blood Pressure in Normotensive Adults. *Clin Nutr Res.* 2015;4(4):259-66.
32. Laboratories MC. Serum, Selenium 2019 [Available from: <https://spectrumhealth.testcatalog.org/show/LAB579>] [Accessed on: July 12, 2019]
33. Laboratories MC. Serum, Copper 2019 [Available from: <https://spectrumhealth.testcatalog.org/show/LAB8170>] [Accessed on: July 12, 2019]
34. Laboratories MC. Serum, Zinc 2019 [Available from: <https://spectrumhealth.testcatalog.org/show/LAB581-1>] [Accessed on: July 12, 2019]
35. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics.* 2017;140(3).
36. Kipp AP, Strohm D, Brigelius-Flohe R, Schomburg L, Bechthold A, Leschik-Bonnet E, et al. Revised reference values for selenium intake. *J Trace Elem Med Biol.* 2015;32:195-9.
37. Mark SD, Wang W, Fraumeni JF, Jr., Li JY, Taylor PR, Wang GQ, et al. Do nutritional supplements lower the risk of stroke or hypertension? *Epidemiology.* 1998;9(1):9-15.
38. Kieliszek M. Selenium-Fascinating Microelement, Properties and Sources in Food. *Molecules.* 2019;24(7)
39. Ha SK. Dietary salt intake and hypertension. *Electrolyte Blood Press.* 2014;12(1):7-18.
40. von Stockhausen HB. Selenium in total parenteral nutrition. *Biol Trace Elem Res.* 1988; 15:147-55.

## Figure And Table Legends

## Figure Legends

Figure 1: Unadjusted odds ratios (95% CI) for hypertension with serum trace elements, demographic, dietary and lab variables.

Figure 2: Estimated probabilities of hypertension at increasing levels of serum selenium (a), serum copper (b) and serum zinc (c).

Figure 3: Estimated parameter plots with 95% CI for systolic (SBP) and diastolic (DBP) blood pressures for the four quantiles of serum selenium. (Q1 = <115.9 µg/L, Q2 = 116- 126.1 µg/L, Q3=126.2-137.2 µg/L, Q4 =137.3-<299.1 µg/L).

Figure 4: Estimated parameter levels with 95% CI by quantile levels (Q1-4) of serum selenium and its effects on incremental age and total serum cholesterol (Q1 = <115.9 µg/L, Q2 = 116- 126.1 µg/L, Q3=126.2-137.2 µg/L, Q4 =137.3-<299.1 µg/L).

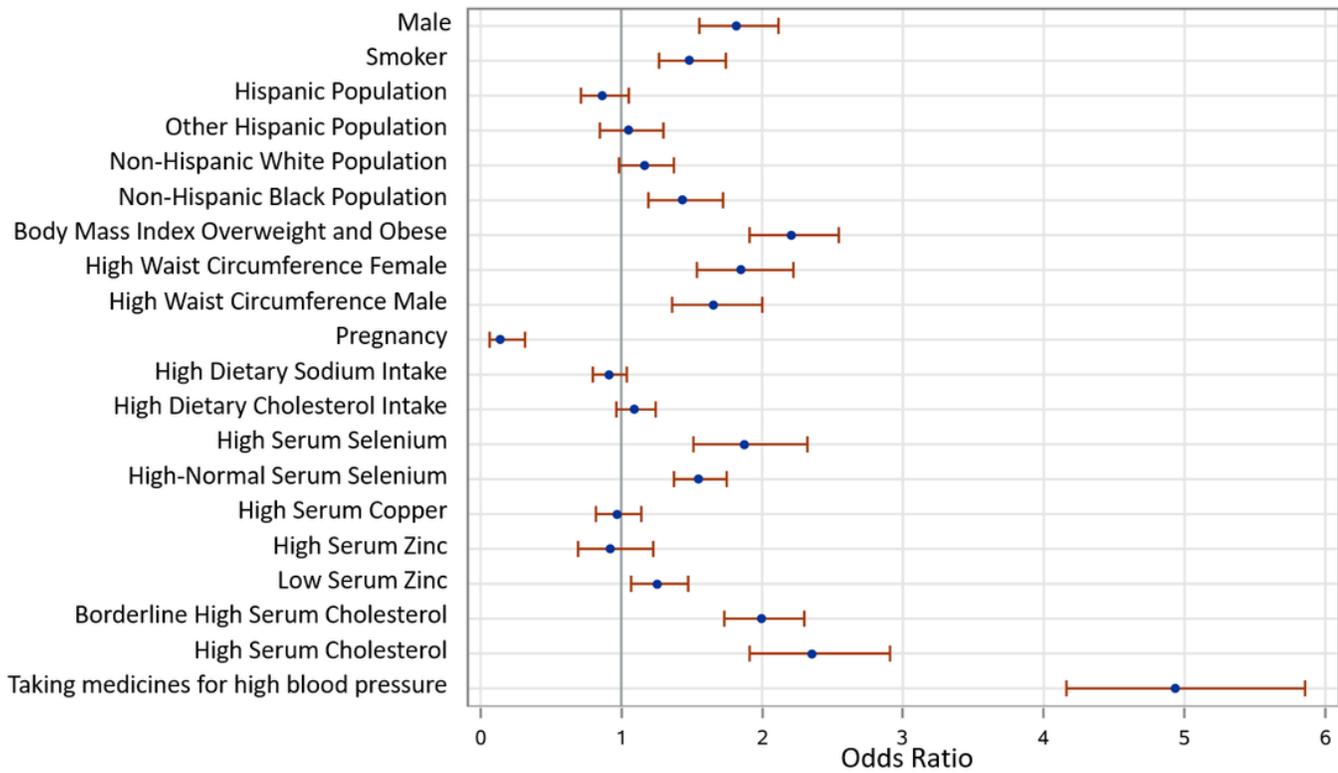
## Table Legends

Table 1: Summary statistics of relevant variables in the study population (NHANES, 2011 – 2016 data).

Table 2: Unadjusted odds ratios of the lowest quantiles and the highest quantiles of serum trace elements with hypertension. \*\* Significant p <0.01 \* Significant p <0.05.

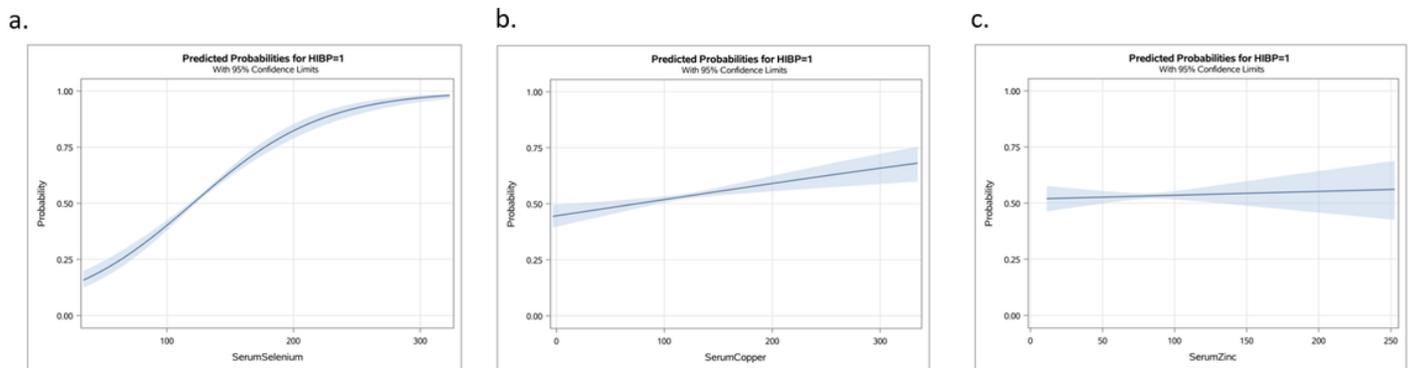
Table 3: odds ratios for hypertension and serum selenium, serum copper and serum zinc levels adjusted for confounding factors. High and low values refer to normal lab range values for trace elements. Q1= Lowest Quantile, Q4 = Highest Quantile. \*Significant at p <0.01.

## Figures



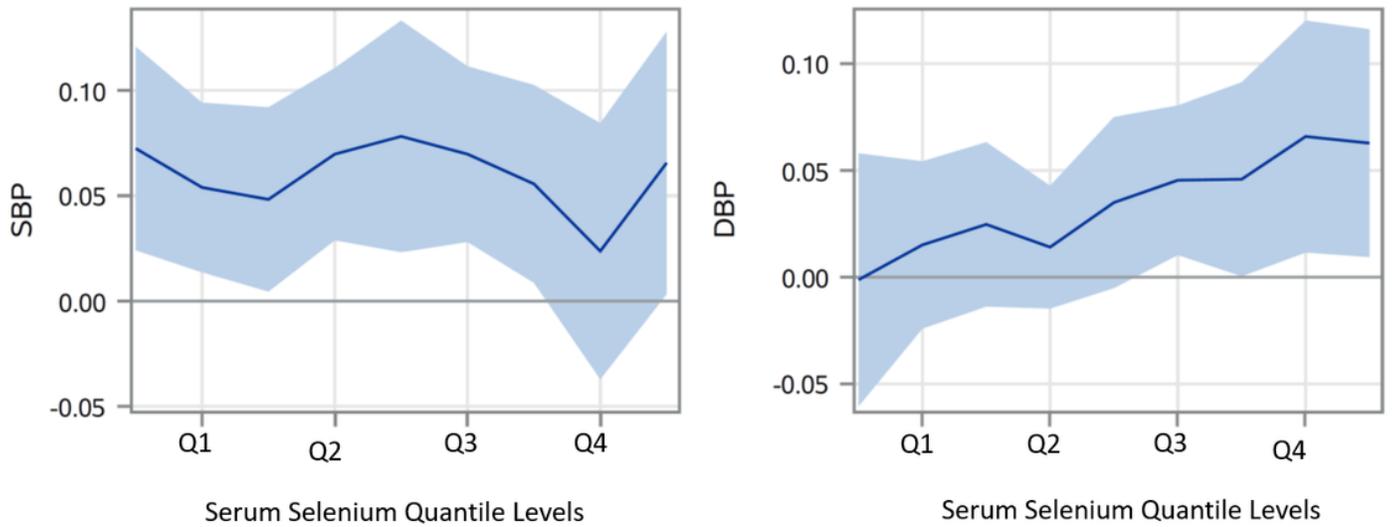
**Figure 1**

Unadjusted odds ratios (95% CI) for hypertension with serum trace elements, demographic, dietary and lab variables.



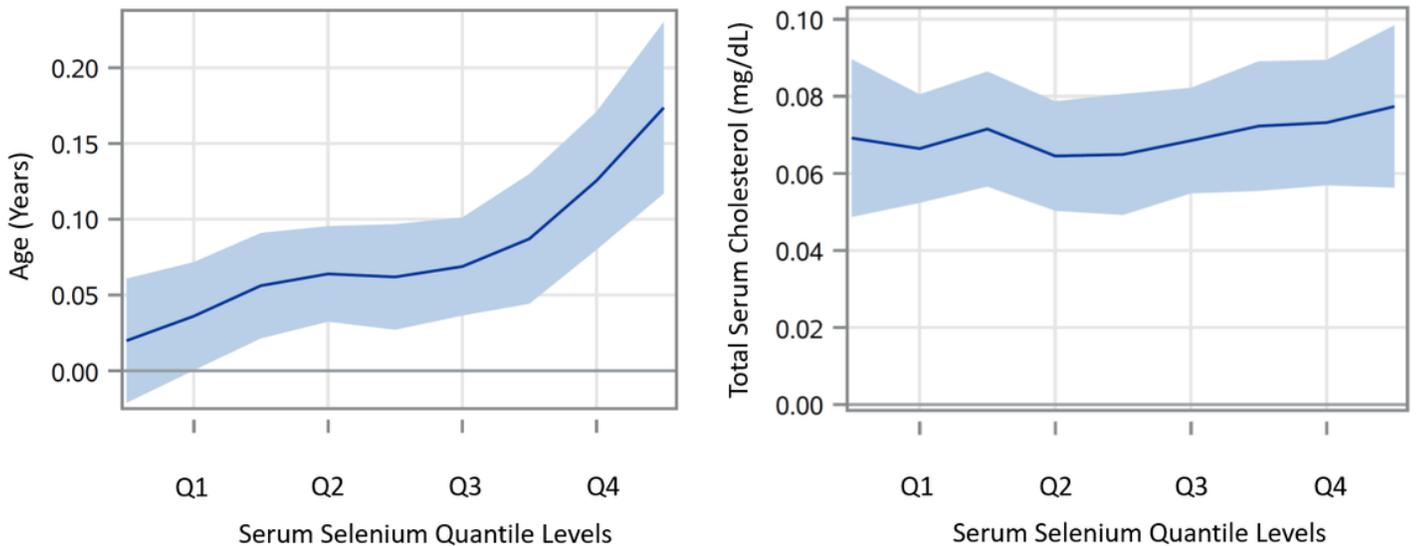
**Figure 2**

Estimated probabilities of hypertension at increasing levels of serum selenium (a), serum copper (b) and serum zinc (c).



**Figure 3**

Estimated parameter plots with 95% CI for systolic (SBP) and diastolic (DBP) blood pressures for the four quantiles of serum selenium. (Q1 =  $\leq 115.9 \mu\text{g/L}$ , Q2 =  $116-126.1 \mu\text{g/L}$ , Q3 =  $126.2-137.2 \mu\text{g/L}$ , Q4 =  $137.3- < 299.1 \mu\text{g/L}$ ).



**Figure 4**

Estimated parameter levels with 95% CI by quantile levels (Q1-4) of serum selenium and its effects on incremental age and total serum cholesterol (Q1 = <115.9 µg/L, Q2 = 116- 126.1 µg/L, Q3=126.2-137.2 µg/L, Q4 =137.3-<299.1 µg/L).

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table2.jpg](#)
- [Table1.jpg](#)
- [Table3.jpg](#)