Nutrition 62 (2019) 169–176

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Is selenium intake associated with the presence of depressive symptoms among US adults? Findings from National Health and Nutrition Examination Survey (NHANES) 2011–2014

Saruna Ghimire M.P.H. [a,*], Binaya Kumar Baral M.Sc. [b], Du Feng Ph.D. [c], Francisco S. Sy Dr. P.H. [a], Rachelle Rodriguez Ph.D. [d]

[a] School of Community Health Sciences, University of Nevada, Las Vegas, Las Vegas, Nevada, USA
[b] Department of Biochemistry, Nepal Medical College and Teaching Hospital, Kathmandu, Nepal
[c] School of Nursing, University of Nevada, Las Vegas, Las Vegas, Nevada, USA
[d] Purdue Pharma, L.P., Stamford, Connecticut, USA

ARTICLE INFO

Article History:
Received 24 July 2018
Received in revised form 1 December 2018
Accepted 15 December 2018

Keywords:
Selenium
Depressive symptoms
NHANES

ABSTRACT

Objectives: This study aimed to examine the cross-sectional association between dietary and serum selenium measures and depressive symptoms among a nationally representative sample of US adults.
Methods: Dietary selenium intake and serum selenium concentration were evaluated on 7725 adult participants from National Health and Nutrition Examination Survey (NHANES) 2011–2014. Participants' selenium intake, assessed by 24-h recall, was classified based on the recommended dietary allowance (dietary selenium intake ≥ 55 μg/d) and estimated average requirement (dietary selenium intake ≥ 45 μg/d) criteria. Serum selenium and depressive symptoms were assessed using inductively coupled plasma mass spectrometry and a patient health questionnaire or use of an antidepressant, respectively. Univariate and multivariate logistic regression, accounting for the complex survey design of NHANES, were employed to estimate the cross-sectional association between measures of selenium and the presence of depressive symptoms.
Results: The median selenium concentration was 193.9 μg/L (interquartile range = 179.3-209.3). Approximately 8% of the participants met the case definition for depressive symptoms. Based on the recommended dietary allowance of selenium, participants not meeting the recommended dietary intake, compared with those meeting the requirement, had higher odds of depressive symptoms (odds ratio [OR] = 1.57, 95% confidence interval [CI]: 1.03–2.38). When analyzing by quintile of dietary selenium intakes, compared with the first quintile, participants in higher quintiles had significantly lower odds of depressive symptoms. However, based on quintiles of serum selenium and using the first quintile as referent category, except for quintile 3, results indicated a higher but not significant association (quintile 2 [OR = 1.08, 95% CI: 0.73–1.61], quintile 4 [OR = 1.17, 95% CI: 0.89–1.55], and quintile 5 [OR = 1.14, 95% CI: 0.83–1.58]). Power analysis indicated sufficient power. Notably, study participants had a very high serum selenium concentration. The findings, although not significant, between serum selenium concentrations and depressive symptoms had a U-shaped association, supported by the current literature.
Conclusions: Our study supports an inverse association between participants recommended dietary intake of selenium and depressive symptoms. Although results were not statistically significant for the association by quartile of serum selenium concentrations and depressive symptoms, a U-shaped association was identified.

Introduction

Depression, the leading cause of poor health and disability, increased more than 18% in global prevalence between 2005 and 2015 [1]. By setting the theme for World Health Day 2017 as "Depression, Let's Talk" [2], the World Health Organization urged people to talk about depression in 2017. With more than 300 million

Dr. Rachelle Rodriguez is a current employee at Purdue Pharma, L.P., Stamford, CT, but the study was completed, under her supervision, while she was a faculty member at University of Nevada, Las Vegas.

* Corresponding author. Tel.: 702-831-3776.
E-mail address: saruna.ghimire@unlv.edu (S. Ghimire).

https://doi.org/10.1016/j.nut.2018.12.007
0899-9007/

people worldwide [1] and 1 in 10 adults in the United States [3] diagnosed, depression is undoubtedly an important issue to address.

Selenium is an essential micronutrient, positively associated with type 2 diabetes [4,5] and inversely associated with the risk of coronary heart disease [6] and cancer [7]. Selenium deficiency has also been linked to neurologic conditions and cognitive decline [8,9]. However, its causal role in disease etiology has yet to be established. Selenium, in the form of selenoprotein, protects the brain against oxidative damage [10] and is involved in the regulation of the inflammatory response [11]. A biologically plausible pathway to depression involves inflammation, oxidative stress, and lower antioxidant levels [12]. Because selenium acts both as an antioxidant and anti-inflammatory agent [13], increased risk of depression at a lower level of selenium is possible via an inflammatory and oxidative pathway. In accord with the proposed biological pathway, epidemiologic studies consistently reported an increased risk of depressive symptoms among those with lower selenium concentration in serum [14,15] and nail samples [16] and among those with lower dietary selenium intake [17]. Recently, studies suggested an increased risk of depressive symptoms with elevated selenium levels in serum [14] and toenail samples [18]. The most recent study from New Zealand [14], among 978 young adults ages 17 to 25 y, identified an optimal range of serum selenium between 82 and 85 μg/L to be associated with reduced risk of depressive symptoms. The finding is alarming because the average serum selenium concentration of US adults has been estimated at 125.7 μg/L to 136.7 μg/L [19,20], which is much higher than the upper limit of the protective range, reported by the study from New Zealand [14]. A similar study from the United States, among 3,735 young adults ages 20 to 32 y, reported 56% higher odds of having depressive symptoms with a doubling of the selenium concentration in toenail samples [18]. However, this study was limited to young adults and did not measure depression at baseline. A double-blinded, randomized controlled trial (RCT) from the UK found no evidence of the benefits of selenium supplementation on mood in the elderly [21].

The average selenium intakes among the US population age 2 y and older is 108.5 μg/d from foods and 120.8 μg/d from both foods and supplements [22]; most Americans meet the daily recommended intake of 55 μg/d [23]. The high selenium intake among the US population is attributable to the high soil content, and subsequently high food content [24], and greater use of nutrient supplementation among the US population [25]. In the United States, approximately 50% of the population take dietary supplements [25], and around 18% to 19% of adults and children use a dietary supplement containing selenium [25]. In the light of recent evidence suggesting an increased risk of depression with elevated serum selenium concentrations, and given that both selenium intake and blood concentration are high among US populations, it becomes more compelling to provide more evidence on the possible association between selenium and depression risk among the US population. Therefore this study aims to assess the association between selenium measures, in terms of dietary intake and concentrations in serum, and depressive symptoms among a representative sample of US adults in National Health and Nutrition Examination Survey (NHANES) 2011 to 2014. Use of NHANES is well suited for our study because it provides a nationally representative sample of noninstitutionalized US adults and has a rigorous methodology, high response rate, and comprehensive quality control procedures.

Materials and methods

Study design of NHANES 2011 to 2014

NHANES is a cross-sectional survey of a nationally representative US civilian noninstitutionalized population of children and adults. The details of NHANES 2011 to 2014 have been reported elsewhere [26–28]. In brief, NHANES uses a complex, multistage, stratified, clustered sampling to obtain a nationally representative sample of the US civilian noninstitutionalized population [26–28]. We used data from the cycles 2011 to 2012 and 2013 to 2014 and combined them following the National Center for Health Statistics recommendations [29].

Study participants

NHANES 2011 to 2012 included a total of 9338 participants, and NHANES 2013 to 2014 included a total of 9813 participants in the mobile examination. For the final analyses, we included a total of 7725 individuals, ages 20 and older, who had a blood selenium measurement available. Individuals were excluded if they were younger than 20 y ($n = 8244$) and had missing serum selenium data ($n = 3182$). The NHANES sample weighting, taken into consideration during data analyses, corrects for differential selection probabilities, compensates for possible inadequacies in the eligible population and adjusts for non-coverage and non-response [29].

Ethical approval

The study procedure for NHANES was approved by the National Center for Health Statistics Research Ethics Review Board (Protocol #2011-17 and Continuation of Protocol #2011-17) [30]. In NHANES, all participants provided written informed consent.

Measurements

Depressive symptoms

Depressive symptoms were screened in NHANES 2011 to 2014 by using the validated Patient Health Questionnaire (PHQ-9) [31]. The PHQ-9 is a nine-item depression screening instrument that asks about the frequency of symptoms of depression over the past 2 wk [31]. Each of the nine items' response included "not at all," "several days," "more than half the days," and "nearly every day" and were scored from 0 (not at all) to 3 (nearly every day). The cumulative total of all question ranged from 0 to 27. The validity and reliability of PHQ-9 have already been established [31]. A PHQ-9 score ≥10 was considered to indicate depressive symptoms, following the approach recommended by the National Quality Forum [32]. In addition, participants using antidepressants were also included in the "depressive symptoms" category. Antidepressants included selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors, and others (clomipramine, mirtazapine nefazodone, and trazodone), identified from the predefined medication list in the Lexicon Plus, a proprietary database of Cerner Multum, Inc., used for the NHANES datasets.

Selenium measurements

Two measures of selenium were used: dietary intake and serum concentration. Dietary intake of selenium was measured via 24-h dietary recall interviews. During the interview, participants provided details (including the description, amount, and nutrient content) of food and beverages consumed in the 24-h (midnight to midnight) period before the interview. For each participant, estimates of nutrient intake from each food or beverage, including selenium intake, were calculated using the US Department of Agriculture's Food and Nutrient Database for Dietary Studies [33]. The nutrient estimates do not include nutrients obtained from dietary supplements or medications. The protocol and data collection methods are documented elsewhere [34]. Two dietary guidelines for US adults, the recommended dietary allowance (RDA) and the estimated average requirement (EAR), were used as references to categorize participants' dietary intakes. Accordingly, the dietary intake of selenium was considered EAR adequate if the estimated selenium intake for the participant was ≥45 μg/d [35]. Based on RDA recommendation, if the estimated selenium intake for the participant was ≥55 μg/d, it was considered RDA adequate [35].

Likewise, serum selenium concentrations were measured using inductively coupled plasma mass spectrometry in the Division of Laboratory Sciences, National Center for Environmental Health. The details of the NHANES laboratory procedure are described elsewhere [36]. Briefly, the NHANES quality assurance and quality control protocols meet the 1988 Clinical Laboratory Improvement Act mandates [36]. The lower detection limits for selenium was 30 μg/L [36]. As stated in the laboratory documentation, values less than the limit of detection were replaced with the value (limit of detection / $\sqrt{2}$) [36].

Other Covariates

Sociodemographic characteristics

Selection of covariates (age, sex, race or ethnicity, education, marital status, body mass index [BMI], socioeconomic status [SES], smoking, alcohol drinking, physical activity, and various comorbidities), were based on existing literature. Depression is directly associated with increasing age, female gender, race, and lower SES [37]. Likewise, marital status and educational attainment are correlates of major depressive disorder, lifetime or at 12 mo [38]. Depression is also associated with body weight status, smoking, alcohol consumption, and physical

activities [39]. Depression has also been associated with numerous morbidities such as diabetes, cardiovascular disease, and cancer [39,40].

Age (in years), sex (binary: male and female), race or ethnicity (categorical: non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, and other race or multiracial); educational level (categorical: less than high school, high school graduate or equivalent, some college, and college graduate or higher) were self-reported by the participants. Marital status included never married; married or living with a partner; and widowed, divorced, or separated. BMI, the ratio of weight-to-height^2 measured in kg/m^2, was available as a continuous measure. SES was quantified in terms of poverty income ratio (PIR), a measure of the ratio of family income to the poverty threshold. PIR is calculated following the US Department of Health and Human Services' poverty guidelines, described in detail elsewhere [41]. We categorized smoking into three categories: never smoker (smoked <100 cigarettes during their lifetime), former smoker (smoked ≥100 cigarettes during lifetime but did not smoke at the time of interview), and current smoker (smoked ≥100 cigarettes during lifetime and reported smoking at the time of interview). We assessed alcohol intake by lifetime and current alcohol use and classified into three categories of abstainers, occasional/moderate drinkers, and heavy drinkers. Those reporting fewer than 12 alcoholic drinks in a lifetime were considered abstainers. The drinking levels for alcoholic beverages for men and women was determined based on the *Dietary Guidelines for Americans, 2005* [42]. The guidelines recommend a sex-specific cut point of one drink or fewer per day for women and two drinks or fewer per day for men. Therefore respondents who consumed alcohol more than the recommended levels were considered heavy drinkers, whereas the remainder of drinkers were classified as occasional or moderate drinkers. Physical activity (categorical: inactive, low, moderate, and high activity) was assessed by the Global Physical Activity Questionnaire, which includes the frequency and duration of physical activity performed during daily activities, leisure time activities, and sedentary activities [43]. The total metabolic equivalents (METS)–hours per week of their reported activity was assessed. As recommended in NHANES [44], vigorous and moderate activities were assigned a MET score of 8 and 4, respectively. The cumulative MET-hours per week was divided into tertiles, whereby the lowest, middle, and highest tertiles represented the low, medium, and high level of physical activity, respectively. Participants were considered physically inactive if they reported not doing any types of vigorous or moderate work or leisure activity in a typical week. Dietary supplement use (dichotomized, yes or no) was based on participants' self-reported use of any vitamins, minerals, or dietary supplements in the past month. Participants' total calorie intake, estimated via 24-h food recall, was the average calorie intake reported for first and second days of the interview.

Participants were also classified in terms of their health outcomes. Diabetes was defined as the previous diagnosis of diabetes, current use of diabetic pills or insulin, a hemoglobin A1c level of ≥6.5%, a fasting plasma glucose level of ≥126 mg/dL, or 2-h plasma glucose level of ≥200 mg/dL [45]. Heart disease was a self-reported diagnosis of congestive heart failure, coronary heart disease, angina pectoris, heart attack, and stroke. Cancer was a self-reported diagnosis of any cancer. Kidney disease was defined by ever diagnosis of weak or failing kidneys, received dialysis in past 12 mo, a glomerular filtration rate <60 mL/min [46], or presence of microalbuminuria (urine albumin-to-creatinine ratio of ≥30 mg/g) [47]. Lung and liver diseases were a self-reported diagnosis of a liver condition and lung disease (asthma and chronic bronchitis), respectively.

Statistical analyses

Sample weights were adjusted according to NHANES guidelines to generate a nationally representative sample [29]. Total serum selenium concentration and dietary selenium intakes were divided into quintiles based on the weighted population distribution. Covariate characteristics were compared between those with and without depressive symptoms, those with and without adequate dietary selenium intakes, and between the quintiles of serum and dietary selenium using Rao-Scott χ^2 test. Odds ratios (ORs) and 95% confidence interval (CI) of depressive symptoms were computed, in univariate and multivariate logistic regression, first using a binary category of participants meeting and not meeting the recommended dietary intake of selenium. Again, the analyses were repeated to compare quintiles of serum and dietary selenium, using the first quintile as the referent category. Three different models were used to examine the cross-sectional association between each measure of selenium and depressive symptoms. Model 1 was adjusted for demographic variables (age, sex, race or ethnicity, and marital status). In addition to covariates from model 1, model 2 was also adjusted for education, PIR, BMI, smoking, alcohol, physical activity, and use of dietary supplements. In the final model, model 3, comorbidities (diabetes, kidney disease, cancer, and heart disease) and total energy intake were added to the covariates from model 2. Akaike information criterion and area under the receiver operating characteristic curve were used as the metrics to assess each model's performance. A two-tailed P value <0.05 was considered statistically significant. Data analyses were performed using the survey procedures that accounted for the weights and complex survey design of NHANES, in SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

In addition, a power calculation, sensitivity, and subgroup analyses were done. Given that antidepressant use may also be reported by individuals with anxiety disorders, in a sensitivity analysis we restricted our definition of depressive symptoms in terms of a PHQ-9 score ≥10 only to verify if the inclusion of antidepressant use had any impact on the findings. To verify whether our results also held true for healthy populations, we performed a sensitivity analysis, restricting the analysis to individuals without a chronic disease (diabetes, heart disease, cancer, kidney disease, lung, and liver disease). Because the previous studies reporting an increased risk of depression at elevated concentrations of serum selenium had young participants, we performed a subgroup analysis based on age, whereby we categorized participants into younger (<32 y) and older adults (≥32 y). Additional subgroup analyses were performed based on sex and the use of dietary supplements.

Results

A total of 7725 participants were included in the analyses. The median PHQ-9 score was 0.9 (interquartile range [IQR]: 0–3.6) and ranged from 0 to 27. Approximately 8% (n = 1200) of the participants met the case definition for depressive symptoms (PHQ-9 ≥ 10 or using antidepressant). Table 1 provides detailed characteristics of the study population by depressive symptoms status. On average, participants with depressive symptoms were older, female, less educated, had higher BMI and lower PIR, were current smokers and heavy alcohol users, were without a partner, and were physically inactive. The median selenium concentration was 192.2 μg/L (IQR = 176.9–208.9) in participants with depressive symptoms and 194.1 μg/L (IQR = 179.7–209.3) in those without depressive symptoms (Table 1).

Overall, the median selenium concentration was 193.9 μg/L (IQR = 179.3–209.3) (Table 1) and ranged from 118.5 μg/L to 391.5 μg/L. The proportion of participants with inadequate daily selenium intake was 8.4% (n = 646) according to RDA criteria and 4.3% (n = 339) according to EAR criteria. Tables 2 and 3 provide characteristics of the study population by dietary selenium intake (RDA and EAR criteria) and by serum selenium quintiles, respectively. Participants with inadequate dietary selenium intake, based on both RDA and EAR criteria, were more likely to be older, female, not married or living with a partner, physically inactive or low activity, and depressed (Table 2). Based on quintiles of dietary intake, the proportion of participants with depressive symptoms gradually decreased in higher quintiles (Appendix A).

Likewise, participants in the lowest quintile of serum selenium were more likely to be older, female, and not married or living with a partner; have lower PIR; and be a current smoker (Table 3). A slightly higher proportion of participants were depressed in both the highest (fourth and fifth) and lowest (first and second) quintiles of serum selenium compared with the middle quintile (third), but findings were not statistically significant (Table 3).

Both Akaike information criterion and area under the curve suggested that the model improved with the addition of covariates. When analyzing data based on dietary intake of selenium, participants not meeting the RDA of selenium, compared with those meeting the requirement, had higher odds of depressive symptoms (OR = 1.57, 95% CI: 1.03–2.38) (Table 3). Similarly, participants not meeting the EAR recommendations were at elevated risk, but the findings were not statistically significant. When analyzing by quintiles of dietary selenium intake, compared with the first quintile, participants in higher quintiles had significantly lower odds of depressive symptoms (quintile 2 [OR = 0.64, 95% CI: 0.48–0.85), quintile 3 [OR = 0.69, 95% CI: 0.49–0.96], quintile 4 [OR = 0.57, 95% CI: 0.36–0.90], and quintile 5 [OR = 0.60, 95% CI: 0.39–0.94]) (Table 4).

When analyzing in terms of quintiles of serum selenium and using the first quintile as referent category, results, except for quintile 3, indicated a higher but not significant association (quintile 2 [OR = 1.08, 95% CI: 0.73–1.61], quintile 4 [OR = 1.17, 95% CI: 0.89–1.55], and quintile 5 [OR = 1.14, 95% CI: 0.83–1.58]) (Table 4).

Table 1
Sociodemographic characteristics of the study participants by depression status, NHANES 2011 to 2014

	Overall (n = 7725)		Depressive symptoms		
	n	% (95% CI)	Absent (n = 6525; 92.1%) % (95% CI)	Present (n = 1200; 7.9%) % (95% CI)	P
Age, y, median (IQR)	7725	46.4 (32.5–59.7)	45.3 (31.6–59.0)	50.3 (38.2–62.5)	<0.001
Sex: Female	3955	51.8 (50.7–53.0)	48.9 (47.6–50.2)	66.1 (63.6–68.6)	<0.001
Race					<0.001
Non-Hispanic White	866	8.3 (5.5–11.0)	9.0 (6.0–12.0)	4.6 (2.9–6.4)	
Non-Hispanic Black	758	6.2 (4.0–8.4)	6.4 (4.3–8.5)	5.5 (2.8–8.2)	
Mexican American	3054	66.9 (61.2–72.6)	64.8 (59.1–70.4)	77.3 (71.4–83.2)	
Other Race or Multiracial	1815	10.9 (7.7–14.1)	11.5 (8.2–14.7)	8.0 (4.8–11.3)	
Other Hispanic	1232	7.8 (6.2–9.3)	8.4 (6.6–10.2)	4.6 (3.4–5.8)	
Marital status					<0.001
Married/living with partner	4438	61.9 (59.1–64.7)	63.4 (60.1–66.8)	54.3 (51.0–57.7)	
Widow, divorced, or separated	1698	18.7 (17.5–19.9)	16.7 (15.6–17.8)	28.6 (24.9–32.4)	
Never married	1587	19.4 (16.2–22.6)	19.9 (16.2–23.6)	17.0 (14.7–19.3)	
Educational status					<0.001
Less than high school	1736	15.8 (13.2–18.4)	15.2 (12.6–17.7)	19.0 (15.2–22.7)	
High school graduate	1675	21.1 (19.1–23.1)	20.5 (18.8–22.3)	23.9 (19.1–28.8)	
Some college	2350	31.9 (29.6–34.1)	31.8 (29.2–34.3)	32.5 (29.0–35.9)	
College graduate or above	1961	31.2 (27.5–34.9)	32.5 (28.9–36.2)	24.6 (19.5–29.7)	
PIR, median (IQR)	7104	2.8 (1.3–5.0)	3.0 (1.4–5.0)	2.1 (1.2–4.2)	<0.001
BMI, kg/m^2, median (IQR)	7631	27.6 (24.1–32.1)	27.3 (24.0–31.7)	29.2 (24.7–34.3)	<0.001
Smoking					<0.001
Never smokers	4402	56.1 (53.7–58.5)	58.4 (55.8–61.0)	44.6 (40.9–48.4)	
Former smokers	1786	24.8 (22.7–26.8)	24.1 (21.8–26.4)	28.1 (25.5–30.7)	
Current smokers	1531	19.2 (17.5–20.9)	17.5 (15.9–19.2)	27.3 (23.8–30.8)	
Alcohol use					0.026
Nondrinker/abstainers	1027	12.9 (10.7–15.0)	12.7 (10.7–14.8)	13.5 (10.1–16.8)	
Moderate/occasional	2357	43.4 (41.0–45.9)	44.4 (41.7–47.1)	38.5 (34.4–42.7)	
Heavy	2377	43.7 (41.5–45.9)	42.9 (40.3–45.4)	48.0 (43.5–52.4)	
Physical activity					<0.001
Inactive	1948	22.5 (20.4–24.6)	19.7 (17.5–21.8)	36.4 (32.1–40.6)	
Low	2015	24.9 (23.6–26.2)	24.9 (23.6–26.2)	25.2 (21.7–28.7)	
Moderate	1841	25.9 (24.2–27.6)	27.0 (25.0–28.9)	20.8 (17.5–24.1)	
High	1908	26.6 (24.6–28.7)	28.5 (26.1–30.8)	17.6 (15.1–20.1)	
Used dietary supplements	3827	52.7 (50.7–54.7)	51.8 (49.7–53.8)	57.5 (54.1–60.9)	<0.001
Selenium (μg/L), median (IQR)	7725	193.9 (179.3–209.3)	194.1 (179.7–209.3)	192.2 (176.9–208.9)	0.003

BMI, body mass index; CI, confidence interval; IQR, interquartile range; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.
Values are % (95% CI) unless otherwise mentioned.

Power analysis (results not shown) for the crude estimates reported in Table 3 indicated that our study had sufficient power (>99%).

In the sensitivity analysis, based on the definition of depressive symptoms in terms of a PHQ-9 score only or excluding antidepressant users, the findings for dietary selenium intake were consistent with the main findings in crude and demographic adjusted models (Appendix B). Again, restricting the analysis to healthy individuals (without diabetes, heart disease, cancer, kidney disease, lung, and liver disease), increased odds of depressive symptoms among participants not meeting the dietary selenium requirement compared with those meeting the requirement (OR = 2.47, 95% CI: 1.52–4.01), were noted (Appendix C). In subgroup analyses based on age, sex, and dietary supplements use, increased odds of depressive symptoms among participants not meeting the dietary selenium requirement were noted for older age group (32–80 y), men, and dietary supplement users (Appendix C).

For serum selenium levels, the null findings persisted in the subgroup analyses based on age, sex, and dietary supplements use, and in all the sensitivity analyses—first defining depressive symptoms in terms of a PHQ-9 score only, and second restricting the analysis to healthy individuals (without diabetes, heart disease, cancer, kidney disease, lung, and liver disease) (Appendixes B and C).

Discussion

Using the data from NHANES 2011 to 2014, we aimed to examine the association between measures of selenium (dietary intake and serum concentrations) and presence of depressive symptoms among US adults and found increased odds of depressive symptoms among participants not meeting the RDA of selenium (compared with those who met the recommendations) and decreased odds of depressive symptoms in higher quintiles of dietary selenium (compared with the first quintile). Although the results were not statistically significant for the association by quintiles of serum selenium concentrations and depressive symptoms, a U-shaped association was identified.

Our finding of higher odds of depressive symptoms among participants with lower dietary selenium intakes is consistent with a previous nested case-control study that reported an increased risk of de novo major depressive disorder with lower dietary selenium intakes [17]. The findings pertaining to the EAR criteria also indicated an elevated risk among participants not meeting the recommendations, but the findings were not statistically significant, which may be explained by the small number of (n = 339) participants not meeting the EAR recommendations. An inverse association between selenium and depression risk, at a lower concentration, is biologically possible and could be mediated via selenoproteins through multiple pathways such as inflammation, oxidative stress, and a decrease in antioxidant levels [12,13]. However, such a pathway at the elevated concentrations of serum selenium is not clear.

Our results of a null association between serum selenium concentrations and depressive symptoms are in line with a double-blinded RCT from the UK, the largest RCT to date to investigate the

Table 2
Sociodemographic characteristics of the study participants by dietary selenium intake with reference to estimated average requirement (EAR) and the recommended dietary allowance (RDA), NHANES 2011 to 2014

Characteristics	Dietary selenium intake			Dietary selenium intake		
	Inadequate RDA (n = 646, 8.4%) % (95% CI)	Adequate RDA (n = 6396, 91.6%) % (95% CI)	P*	Inadequate EAR (n = 339, 4.3%) % (95% CI)	Adequate EAR (n = 6703, 95.7%) % (95% CI)	P†
Age, y, median (IQR)	47.2 (33.7–63.0)	46.3 (32.1–59.4)	<0.001	47.7 (38.1–63.4)	46.3 (32.1–59.5)	<0.001
Sex: Female	77.2 (72.6–81.8)	49.1 (47.6–50.5)	<0.001	75.7 (70.3–81.1)	50.3 (49.0–51.7)	<0.001
Race			0.095			0.064
Non-Hispanic white	6.9 (4.0–9.9)	8.2 (5.4–11.0)		7.8 (4.2–11.3)	8.1 (5.3–10.9)	
Non-Hispanic black	6.0 (2.8–9.2)	5.9 (4.0–7.9)		7.5 (3.5–11.5)	5.9 (4.0–7.8)	
Mexican American	67.3 (58.7–75.9)	68.1 (62.7–73.5)		65.9 (56.7–75.2)	68.1 (62.6–73.6)	
Other race or multiracial	13.6 (8.8–18.5)	10.4 (7.3–13.5)		14.0 (8.4–19.7)	10.5 (7.3–13.6)	
Other Hispanic	6.2 (3.7–8.6)	7.4 (6.0–8.8)		4.8 (2.7–6.9)	7.4 (6.0–8.8)	
Marital status			<0.001			0.001
Married or living with a partner	51.7 (46.2–57.2)	63.4 (60.4–66.3)		50.2 (40.1–60.3)	62.9 (60.0–65.8)	
Widow, divorced, or separated	28.2 (24.4–32.1)	17.3 (16.1–18.5)		29.0 (22.9–35.1)	17.7 (16.5–19.0)	
Never married	20.0 (15.0–25.1)	19.4 (16.1–22.7)		20.8 (13.5–28.1)	19.4 (16.1–22.6)	
Educational status			<0.001			<0.001
Less than high school	21.1 (17.3–24.9)	14.7 (12.1–17.3)		22.1 (16.0–28.2)	15.0 (12.3–17.6)	
High school graduate	23.1 (18.6–27.7)	21.0 (18.9–23.2)		29.8 (23.3–36.2)	20.8 (18.7–23.0)	
Some college	37.7 (32.0–43.4)	31.6 (29.4–33.8)		35.3 (27.4–43.3)	32.0 (29.7–34.3)	
College graduate or above	18.1 (12.6–23.5)	32.6 (28.9–36.4)		12.8 (7.4–18.1)	32.2 (28.5–36.0)	
PIR, median (IQR)	1.9 (1.0–3.7)	3.0 (1.4–5.0)	<0.001	2.0 (1–3.6.0)	2.9 (1.4–5.0)	<0.001
BMI, kg/m^2, median (IQR)	27.4 (23.9–32.0)	27.7 (24.1–32.2)	0.415	27.2 (23.9–30.8)	27.7 (24.1–32.3)	0.561
Smoking			0.001			0.196
Never smokers	52.8 (46.8–58.8)	56.2 (53.9–58.5)		54.5 (46.0–63.0)	56.0 (53.6–58.4)	
Former smokers	21.8 (16.0–27.6)	25.3 (23.3–27.4)		20.8 (12.0–29.7)	25.2 (23.1–27.3)	
Current smokers	25.4 (21.8–29.1)	18.5 (16.8–20.1)		24.7 (17.2–32.3)	18.8 (17.1–20.4)	
Alcohol use			<0.001			<0.001
Nondrinker or abstainers	20.6 (15.5–25.6)	11.7 (9.7–13.7)		24.8 (17.9–31.7)	11.9 (9.8–13.9)	
Moderate or occasional	34.5 (29.5–39.4)	44.4 (41.8–47.0)		27.6 (20.8–34.4)	44.3 (41.8–46.8)	
Heavy	45.0 (38.9–51.1)	43.9 (41.6–46.1)		47.6 (39.6–55.5)	43.8 (41.7–45.9)	
Physical activity			0.036			0.052
Inactive	27.0 (22.7–31.3)	21.4 (19.1–23.7)		30.4 (23.2–37.5)	21.5 (19.1–23.8)	
Low	26.5 (22.2–30.8)	24.6 (23.2–26.0)		23.2 (17.1–29.3)	24.8 (23.6–26.1)	
Moderate	23.0 (18.8–27.2)	26.2 (24.3–28.1)		23.7 (18.0–29.5)	26.0 (24.2–27.8)	
High	23.5 (19.3–27.7)	27.8 (25.5–30.2)		22.7 (16.4–28.9)	27.7 (25.5–29.9)	
Used dietary supplements	53.5 (48.4–58.6)	53.1 (51.0–55.2)	0.854	52.0 (44.3–59.6)	53.2 (51.0–55.4)	0.750
Depression status: Yes	27.9 (21.3–34.5)	16.0 (14.3–17.6)	<0.001	24.9 (19.9–30.0)	16.6 (15.0–18.3)	<0.001
Selenium (μg/L), median (IQR)	190.3 (172.8–205.1)	194.3 (179.8–209.7)	<0.001	190.2 (175.3–207.3)	194.2 (179.6–209.4)	0.0248

BMI, body mass index; CI, confidence interval; IQR, interquartile range; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.
Values are % (95% CI) unless otherwise mentioned.
*P values comparing participants with adequate and inadequate dietary selenium intakes based on RDA.
†P values comparing participants with adequate and inadequate dietary selenium intakes based on EAR.

effect of selenium on mood in healthy individuals [21]. In contrast, it differs from a previous study from the United States [18] and another study from the New Zealand [14], both of which reported an increased risk of depressive symptoms with higher concentrations. The discrepancies may be explained by many factors, such as age range, selenium status, use of dietary supplements, and type of biospecimen used for assessing selenium concentrations. First, both the previous studies [14,18] had younger participants. Second, the participants in the New Zealand study [14] had much lower serum selenium concentrations (82 μg/L) than our participants; only 4.7% of our study participants were within their range of 49 to 158 mg/L. Nevertheless, other studies from the United States, using different cycles of NHANES data, have indicated that Americans have higher serum selenium concentrations [5,20,48]. High serum selenium concentrations among US populations was expected given that their daily selenium intake is high [22] and often exceeds the daily recommended intake [23]. In addition, 53% of the participants in our study reported taking dietary supplements, which is in line with previous estimates, from NHANES 1999 to 2000 [49] and NHANES 2003 to 2006 [25], that found around 50% of the US population take dietary supplements. The recent study from New Zealand suggested an inverted J-shaped relationship between serum selenium concentrations and depressive symptoms [14]. Furthermore, the current literature suggests an "inextricable U-shaped link hypothesis" around potential benefits and harms of selenium [50]. Thus it is possible to identify null findings among the selenium-replete populations like ours when using linear models or binary variables.

Notably, inconsistent findings were found for the two methods of selenium measurement (i.e., dietary versus serum). The inconsistent findings may be explained by the fact that dietary selenium intake may not accurately reflect the estimates of serum selenium [51,52]. In general, of the two types of biomarkers—recovery and concentration—recovery types provide more reliable measures of intake and excretion of nutrients [53], whereas the concentration biomarkers, such as serum micronutrient levels, cannot provide an absolute measure of food intake. Rather, they provide correlations with intake levels [53]. Previous studies provide evidence of no or weak association between dietary, plasma, and serum selenium [51,54,55], suggesting that serum selenium level may not be a good biomarker for selenium intake estimation [51]. Several facts may explain this weak or absent association between selenium intakes and concentration in serum. First, although 24-h recall technique is widely used in epidemiologic studies and surveys, it is

Table 3
Sociodemographic characteristics of the study participants by serum selenium quintiles, NHANES 2011 to 2014

Characteristics	Serum selenium quintiles					
	Quintile 1 (n = 1662) % (95% CI)	Quintile 2 (n = 1558) % (95% CI)	Quintile 3 (n = 1538) % (95% CI)	Quintile 4 (n = 1447) % (95% CI)	Quintile 5 (n = 1520) % (95% CI)	P
Age, y, median (IQR)	47.6 (33.8–61.4)	46.7 (31.9–60.5)	44.1 (31.7–58.0)	46.3 (32.6–60.1)	47.5 (33.2–58.8)	<0.001
Sex: Female	59.5 (56.9–62.0)	55.5 (52.4–58.6)	53.3 (49.0–57.5)	46.5 (43.0–50.1)	44.4 (41.3–47.6)	<0.001
Race						0.012
Non-Hispanic white	7.1 (3.9–10.2)	8.1 (5.5–10.8)	9.2 (5.9–12.4)	8.8 (5.4–12.3)	8.1 (4.5–11.8)	
Non-Hispanic black	7.6 (4.6–10.6)	6.1 (3.2–9.0)	6.6 (3.8–9.3)	5.5 (3.5–7.6)	5.2 (3.4–7.1)	
Mexican American	64.4 (54.4–74.3)	65.6 (59.6–71.5)	65.8 (59.9–71.8)	69.7 (64.5–75.0)	69.0 (62.8–75.2)	
Other Race/multiracial	14.0 (8.1–19.8)	12.1 (8.2–16.1)	10.7 (7.9–13.6)	8.7 (6.5–11.0)	8.8 (6.4–11.2)	
Other Hispanic	7.0 (4.4–9.6)	8.1 (6.2–9.9)	7.7 (5.9–9.5)	7.2 (5.5–8.9)	8.8 (6.9–10.7)	
Marital status						<0.001
Married or living with a partner	57.0 (52.1–61.8)	61.5 (58.1–64.9)	63.5 (60.6–66.4)	63.9 (60.6–67.3)	63.6 (59.6–67.6)	
Widow, divorced, or separated	24.7 (22.1–27.4)	19.4 (16.6–22.2)	18.1 (15.9–20.4)	16.0 (13.4–18.7)	15.3 (12.7–18.0)	
Never married	18.3 (13.6–23.0)	19.1 (15.5–22.7)	18.4 (14.9–21.9)	20.0 (17.0–23.1)	21.1 (16.4–25.8)	
Educational status						0.030
Less than high school	20.0 (14.9–25.2)	16.1 (12.5–19.7)	15.4 (12.5–18.3)	13.0 (10.4–15.7)	14.6 (12.1–17.1)	
High school graduate	23.1 (20.1–26.1)	21.3 (18.2–24.4)	21.7 (19.2–24.1)	19.0 (15.8–22.2)	20.5 (15.6–25.5)	
Some college	29.4 (25.1–33.7)	31.2 (27.0–35.4)	32.5 (29.3–35.8)	34.4 (30.8–37.9)	31.9 (28.1–35.7)	
College graduate or above	27.5 (21.9–33.0)	31.4 (25.9–36.9)	30.4 (26.8–34.0)	33.6 (29.5–37.8)	32.9 (27.2–38.7)	
PIR, median (IQR)	2.1 (1.1–4.4)	3.0 (1.4–5.0)	2.8 (1.4–5.0)	3.1 (1.5–5.0)	3.0 (1.3–5.0)	<0.001
BMI, kg/m^2, median (IQR)	27.5 (23.9–32.6)	27.0 (23.6–31.4)	28.1 (24.2–32.5)	27.7 (24.2–31.8)	27.8 (24.6–32.2)	<0.001
Smoking						<0.001
Never smokers	54.7 (50.2–59.2)	57.4 (53.6–61.3)	56.3 (52.7–59.8)	57.6 (53.1–62.0)	54.4 (50.2–58.5)	
Former smokers	22.6 (20.0–25.3)	21.5 (17.5–25.6)	23.6 (19.8–27.3)	27.9 (23.9–32.0)	28.1 (24.3–31.9)	
Current smokers	22.7 (18.8–26.6)	21.0 (17.8–24.3)	20.2 (17.9–22.4)	14.5 (12.1–16.9)	17.5 (14.3–20.7)	
Alcohol use						<0.001
Nondrinker/abstainers	18.2 (14.5–22.0)	14.1 (10.7–17.4)	12.0 (9.0–15.1)	9.7 (6.5–12.8)	11.0 (8.8–13.2)	
Moderate/occasional	39.2 (35.1–43.3)	41.2 (37.2–45.1)	42.7 (37.7–47.7)	47.0 (43.2–50.7)	46.5 (41.6–51.4)	
Heavy	42.5 (38.0–47.1)	44.8 (40.6–48.9)	45.3 (41.0–49.5)	43.4 (39.6–47.2)	42.5 (37.5–47.5)	
Physical activity	57.0 (52.1–61.8)	61.5 (58.1–64.9)	63.5 (60.6–66.4)	63.9 (60.6–67.3)	63.6 (59.6–67.6)	0.012
Inactive	26.9 (24.0–29.8)	23.1 (19.7–26.5)	20.9 (18.1–23.8)	19.7 (15.6–23.8)	21.9 (18.9–24.9)	
Low	24.4 (21.4–27.3)	22.8 (19.4–26.2)	25.4 (22.1–28.7)	26.6 (23.6–29.5)	25.4 (22.5–28.3)	
Moderate	27.4 (24.2–30.6)	25.7 (22.0–29.4)	24.5 (20.4–28.6)	25.3 (21.3–29.4)	26.7 (23.0–30.4)	
High	21.3 (18.0–24.6)	28.4 (25.1–31.6)	29.1 (24.9–33.4)	28.4 (25.3–31.6)	26.0 (22.7–29.3)	
Used dietary supplements	51.2 (47.9–54.5)	52.6 (49.0–56.1)	50.9 (47.5–54.2)	52.8 (49.4–56.3)	56.2 (52.3–60.1)	0.126
Depression status: Yes	19.6 (16.8–22.3)	17.2 (13.9–20.4)	14.4 (11.8–17.0)	17.3 (14.0–20.7)	16.4 (13.9–19.0)	0.094
Selenium (μg/L), median (IQR)	165.7 (158.2–171.2)	182.3 (179.3–185.4)	193.8 (191.0–196.7)	205.4 (202.2–209.3)	226.6 (219.1–238.1)	<0.001

BMI, body mass index; CI, confidence interval; IQR, interquartile range; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.
Values are % (95% CI) unless otherwise mentioned.

well evident that such recalls are subjected to bias and generally they underreport actual dietary intakes [56]. Second, the dietary selenium intakes in this study were estimated only from food and beverages and excluded dietary supplements. Dietary supplement use is high among the US population, and thus the selenium concentration in serum is expected to be higher [25]. Further, the availability of dietary selenium in serum may be influenced by various metabolic and physiological processes.

Selenium supplementation has been effective especially among those with lower concentrations of plasma selenium. In the Nutritional Prevention of Cancer trial in the United States, selenium supplement therapy was found to be most effective in reducing the risk of different cancer, particularly in participants entering the trial with low plasma selenium concentration (<106 μg/L), and there was no cancer-protective benefit of supplementation among participants entering the trial with plasma selenium >121 μg/L [57]. Therefore the implications of the findings from the present study and others suggest that people whose serum selenium concentration is already higher should not supplement with selenium [50]. More research, specifically dose-controlled RCTs, are needed to determine more precisely the optimal concentrations for a protective effect, especially among the selenium-replete population.

This study has several strengths and limitations. The strengths of the study include large sample size, a nationally representative sample of non-institutionalized US adults, rigorous methodology, and the comprehensive quality control procedures of NHANES. The statistical analyses have been adjusted for study weights and complex survey design to reduce the errors in estimation. Many different covariates were adjusted into the models, which may rule out the possible confounding role of identified covariates in the estimation of the effect size. The cross-sectional design of the study is the primary limitation, and no causation should be inferred from this study. Although the biological pathways linking selenium to depression could be mediated by inflammation and oxidation [12,13], we could not adjust for biomarkers like interleukin-6 and C-reactive protein in our model because their measurement was not available in NHANES 2011 to 2014 at the time of this study. Our study participants had high concentrations of selenium, so the findings cannot be extrapolated to populations with depleted selenium status.

Conclusions

In conclusion, our study supports the hypothesis that inadequate dietary selenium intake may increase the risk of depressive symptoms. However, our results do not provide evidence to support the possible association between serum selenium concentrations and the presence of depressive symptoms. Furthermore, our study also does not support that serum selenium, at higher

Table 4
Multivariable logistic regression for depressive symptoms by dietary selenium intake and quintiles of serum selenium levels, NHANES 2011 to 2014

			n	Crude OR OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Dietary selenium intake	**Recommended dietary allowance criteria**						
	Adequate RDA (≥55 μg/d)		6396		**Reference**		
	Inadequate RDA (<55 μg/d)		646	2.03 (1.46–2.83)	1.65 (1.16–2.35)	1.38 (0.90–2.12)	1.57 (1.03–2.38)
	AIC			13.8×10^7	13.2×10^7	9.4×10^7	9.3×10^7
	AUC			0.53	0.68	0.73	0.74
	Estimated average requirement criteria						
	Adequate EAR (≥45 μg/d)		6703		**Reference**		
	Inadequate EAR (<45 μg/d)		339	1.67 (1.28–2.17)	1.35 (1.00–1.81)	1.30 (0.84–2.00)	1.45 (0.97–2.17)
	AIC			13.9×10^7	13.3×10^7	9.4×10^7	9.3×10^7
	AUC			0.51	0.68	0.73	0.74
	Dietary selenium intake quintiles						
	Quintiles	**Range (μg/d)**					
	1	*≤72.5*	1490		**Reference**		
	2	*>72.5 to ≤95.5*	1451	0.59 (0.48–0.73)	0.63 (0.51–0.79)	0.70 (0.52–0.94)	0.64 (0.48–0.85)
	3	*>95.5- ≤118.1*	1356	0.58 (0.45–0.75)	0.68 (0.53–0.88)	0.79 (0.59–1.05)	0.69 (0.49–0.96)
	4	*>118.1- ≤149.8*	1328	0.52 (0.38–0.72)	0.66 (0.46–0.94)	0.69 (0.44–1.10)	0.57 (0.36–0.90)
	5	*>149.8*	1417	0.42 (0.32–0.54)	0.63 (0.47–0.85)	0.83 (0.57–1.21)	0.60 (0.39–0.94)
	AIC			13.8×10^7	13.3×10^7	9.3×10^7	9.3×10^7
	AUC			0.58	0.68	0.73	0.74
Serum selenium	**Quintiles**	**Range (μg/L)**					
	1	≤175.8	1665		**Reference**		
	2	>175.8 to ≤188.1	1555	0.85 (0.61–1.18)	0.91 (0.63–1.30)	1.10 (0.74–1.63)	1.08 (0.73–1.61)
	3	>188.1- ≤199.4	1531	0.69 (0.52–0.91)	0.75 (0.57–0.99)	0.80 (0.56–1.15)	0.77 (0.53–1.11)
	4	>199.4- ≤213.6	1454	0.86 (0.70–1.05)	0.98 (0.80–1.20)	1.18 (0.90–1.55)	1.17 (0.89–1.55)
	5	>213.6	1520	0.81 (0.61–1.06)	0.93 (0.68–1.26)	1.14 (0.82–1.59)	1.14 (0.83–1.58)
	AIC			14.9×10^7	14.2×10^7	9.6×10^7	9.6×10^7
	AUC			0.53	0.69	0.74	0.74

AIC, Akaike information criterion; AUC, area under the receiver operating characteristic curve; EAR, estimated average requirement; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; RDA, recommended dietary allowance.
Model 1 is adjusted for age, sex, race or ethnicity, and marital status.
Model 2 is adjusted for model 1 variables and educational status, family poverty income ratio, body mass index, smoking, alcohol use, physical activity, and use of dietary supplements.
Model 3 is adjusted for model 2 variables and comorbidities (diabetes, kidney disease, cancer, and heart disease) and total energy intake.

concentrations, may increase the risk of depressive symptoms as some other studies have found. In light of the current literature, benefits of additional selenium intake in the form of food or supplements may be limited to participants with low selenium status. However, people with adequate intake or high serum selenium status may have no such benefit.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2018.12.007.

Reference

[1] World Health Organization. Depression and other common mental disorders: global health estimates. Geneva: World Health Organization; 2017.
[2] World Health Organization. World Health Day—7 April 2017: Depression: let's talk. Date Accessed: November 2017. Available at: http://www.who.int/campaigns/world-health-day/2017/en/.
[3] Centers for Disease Control Prevention. Current depression among adults—United States, 2006 and 2008. MMWR Morb Mortal Wkly Rep 2010;59:1229.
[4] Wang XL, Yang TB, Wei J, Lei GH, Zeng C. Association between serum selenium level and type 2 diabetes mellitus: a non-linear dose-response meta-analysis of observational studies. Nutr J 2016;15:48.
[5] Bleys J, Navas-Acien A, Guallar E. Serum selenium and diabetes in U.S. adults. Diabetes Care 2007;30:829–34.
[6] Flores-Mateo G, Navas-Acien A, Pastor-Barriuso R, Guallar E. Selenium and coronary heart disease: a meta-analysis. Am J Clin Nutr 2006;84:762–73.
[7] Cai X, Wang C, Yu W, Fan W, Wang S, Shen N, et al. Selenium exposure and cancer risk: an updated meta-analysis and meta-regression. Sci Rep 2016;6:19213.
[8] Akbaraly TN, Hininger-Favier I, Carriere I, Arnaud J, Gourlet V, Roussel AM, et al. Plasma selenium over time and cognitive decline in the elderly. Epidemiology 2007;18:52–8.
[9] Shahar A, Patel KV, Semba RD, Bandinelli S, Shahar DR, Ferrucci L, et al. Plasma selenium is positively related to performance in neurological tasks assessing coordination and motor speed. Mov Disord 2010;25:1909–15.
[10] Mostert V. Selenoprotein P: properties, functions, and regulation. Arch Biochem Biophys 2000;376:433–8.
[11] Van Cauwenbergh R, Robberecht H, Van Vlaslaer V, Deelstra H. Comparison of the serum selenium content of healthy adults living in the Antwerp region (Belgium) with recent literature data. J Trace Elem Med Biol 2004;18:99–112.
[12] Maes M, Yirmyia R, Noraberg J, Brene S, Hibbeln J, Perini G, et al. The inflammatory & neurodegenerative (I&ND) hypothesis of depression: leads for future research and new drug developments in depression. Metab Brain Dis 2009;24:27–53.
[13] Rayman MP. The importance of selenium to human health. Lancet 2000;356:233–41.
[14] 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;145:59–65.
[15] Ibarra O, Gili M, Roca M, Vives M, Serrano MJ, Pareja A, et al. The Mediterranean diet and micronutrient levels in depressive patients. Nutr Hosp 2014;31:1171–5.
[16] Gao S, Jin Y, Unverzagt FW, Liang C, Hall KS, Cao J, et al. Selenium level and depressive symptoms in a rural elderly Chinese cohort. BMC Psychiatry 2012;12:72.
[17] Pasco JA, Jacka FN, Williams LJ, Evans-Cleverdon M, Brennan SL, Kotowicz MA, et al. Dietary selenium and major depression: a nested case-control study. Complement Ther Med 2012;20:119–23.
[18] Colangelo LA, He K, Whooley MA, Daviglus ML, Morris S, Liu K. Selenium exposure and depressive symptoms: the Coronary Artery Risk Development in Young Adults Trace Element Study. Neurotoxicology 2014;41:167–74.
[19] Bleys J, Navas-Acien A, Stranges S, Menke A, Miller 3rd ER, Guallar E. Serum selenium and serum lipids in US adults. Am J Clin Nutr 2008;88:416–23.
[20] Laclaustra M, Stranges S, Navas-Acien A, Ordovas JM, Guallar E. Serum selenium and serum lipids in US adults: National Health and Nutrition Examination Survey (NHANES) 2003-2004. Atherosclerosis 2010;210:643–8.

[21] Rayman M, Thompson A, Warren-Perry M, Galassini R, Catterick J, Hall E, et al. Impact of selenium on mood and quality of life: a randomized, controlled trial. Biol Psychiatry 2006;59:147–54.
[22] National Institute of Health. Selenium: Fact Sheet for Health Professionals. Date Accessed: January 2017. Available at: https://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/#en14.
[23] Moshfegh A, Goldman J, Cleveland L. What we eat in America, NHANES 2001–2002: usual nutrient intakes from food compared to dietary reference intakes. Washington, DC: U.S. Department of Agriculture, Agricultural Research Service; 2005.
[24] Combs Jr GF. Selenium in global food systems. Br J Nutr 2001;85:517–47.
[25] Bailey RL, Gahche JJ, Lentino CV, Dwyer JT, Engel JS, Thomas PR, et al. Dietary supplement use in the United States, 2003-2006. J Nutr 2011;141:261–6.
[26 Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey 2013-2014 Overview. Date Accessed: January 2017. Available at: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/Overview.aspx?BeginYear=2013.
[27] Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey 2011-2012 Overview. Date Accessed: January 2017. Available at: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/Overview.aspx?BeginYear=2011.
[28] Johnson C, Dohrmann S, Burt V, Mohadjer L. National Health and Nutrition Examination Survey: sample design, 2011–2014. Vital Health Stat 2014;2(162).
[29] Chen T, Parker J, Clark J, Shin H, Rammon J, Burt V. National Health and Nutrition Examination Survey: estimation procedures, 2011–2014. Vital Health Stat 2018;2(177).
[30 Centers for Disease Control Prevention. Research ethics review board (erb) approval. Date Accessed: December 2017. Available at: https://www.cdc.gov/nchs/nhanes/irba98.htm.
[31] Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–13.
[32] National Quality Measures Clearinghouse. Measure summary: depression: percent of clinically significant depression patients who attain a 5 point or greater reduction in Patient Health Questionnaire (PHQ) score within 6 months after their New Episode PHQ. Rockville, MD: Agency for Healthcare Research and Quality, National Quality Measures Clearinghouse; 2005.
[33] Montville JB, Ahuja JK, Martin CL, Heendeniya KY, Omolewa-Tomobi G, Steinfeldt LC, et al. USDA food and nutrient database for dietary studies (FNDDS), 5.0. Procedia Food Sci 2013;2:99–112.
[34] Centers for Disease Control and Prevention. Dietary interview—total nutrient intakes, first day (DR1TOT_H). Date Accessed: January 2017. Available at: https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/DR1TOT_H.htm.
[35] Prabhu KS, Lei XG. Selenium. Adv Nutr 2016;7:415–7.
[36] Centers for Disease Control and Prevention. Cadmium, lead, total mercury, selenium, & manganese—blood (PbCd_G). Date Accessed: January 2017. Available at: https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/PBCD_G.html.
[37] Centers for Disease Control and Prevention. Depression in the US Household Population, 2009-2012. Date Accessed: March 2017. Available at: https://www.cdc.gov/nchs/data/databriefs/db172.pdf.
[38] Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003;289:3095–105.
[39] Strine TW, Mokdad AH, Balluz LS, Gonzalez O, Crider R, Berry JT, et al. Depression and anxiety in the United States: findings from the 2006 Behavioral Risk Factor Surveillance System. Psychiatr Serv 2008;59:1383–90.
[40] Chapman DP, Perry GS, Strine TW. The vital link between chronic disease and depressive disorders. Prev Chronic Dis 2005;2:A14.
[41] The poverty guidelines updated periodically in the Federal Register. Date Accessed: March 2017. Available at: https://aspe.hhs.gov/2013-poverty-guidelines.
[42] U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2005. 6th ed. Washington, DC: U.S. Department of Health and Human Services and U.S. Department of Agriculture; 2005.
[43] Armstrong T, Bull F. Development of the World Health Organization Global Physical Activity Questionnaire (GPAQ). J Public Health 2006;14:66–70.
[44 Centers for Disease Control and Prevention. 2013-2014 Data documentation, codebook, and frequencies: physical activity (PAQ_H). Date Accessed: January 2017. Available at: https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/PAQ_H.htm.
[45] Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988-2012. JAMA 2015;314:1021–9.
[46] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461–70.
[47] Ricardo AC, Fischer MJ, Peck A, Turyk M, Lash JP. Depressive symptoms and chronic kidney disease: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. Int Urol Nephrol 2010;42:1063–8.
[48] Niskar AS, Paschal DC, Kieszak SM, Flegal KM, Bowman B, Gunter EW, et al. Serum selenium levels in the US population: Third National Health and Nutrition Examination Survey, 1988-1994. Biol Trace Elem Res 2003;91:1–10.
[49] Radimer K, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: data from the National Health and Nutrition Examination Survey, 1999-2000. Am J Epidemiol 2004;160:339–49.
[50] Rayman MP. Selenium and human health. Lancet 2012;379:1256–68.
[51] Karita K, Sasaki S, Ishihara J, Tsugane S. Validity of a self-administered food frequency questionnaire used in the 5-year follow-up survey of the JPHC Study to assess selenium intake: comparison with dietary records and blood levels. J Epidemiol 2003;13:S92–7.
[52] Duffield AJ, Thomson CD. A comparison of methods of assessment of dietary selenium intakes in Otago, New Zealand. Br J Nutr 1999;82:131–8.
[53] Kaaks R, Ferrari P, Ciampi A, Plummer M, Riboli E. Uses and limitations of statistical accounting for random error correlations, in the validation of dietary questionnaire assessments. Public Health Nutr 2002;5:969–76.
[54] Snook JT, Palmquist DL, Moxon AL, Cantor AH, Vivian VM. Selenium status of a rural (predominantly Amish) community living in a low-selenium area. Am J Clin Nutr 1983;38:620–30.
[55] Lane HW, Warren DC, Taylor BJ, Stool E. Blood selenium and glutathione peroxidase levels and dietary selenium of free-living and institutionalized elderly subjects. Proc Soc Exp Biol Med 1983;173:87–95.
[56] Ahluwalia N, Dwyer J, Terry A, Moshfegh A, Johnson C. Update on NHANES dietary data: focus on collection, release, analytical considerations, and uses to inform public policy. Adv Nutr 2016;7:121–34.
[57] Combs Jr. GF, Clark LC, Turnbull BW. An analysis of cancer prevention by selenium. Biofactors 2001;14:153–9.