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Serum Zinc Concentrations in the US Population Are Related to Sex, Age, and Time of Blood Draw but Not Dietary or Supplemental Zinc

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Abstract

Background: Serum zinc concentration is used to assess the zinc status of populations. Cutoffs for serum zinc were developed on the basis of data from the second NHANES (1976–1980).

Objective: The objective of this study was to evaluate serum zinc concentrations in the US population and to determine factors affecting serum zinc with the use of NHANES 2011–2014.

Methods: Serum zinc was determined in males and females aged ≥6 y with the use of NHANES 2011–2014 ($n = 4347$). Dietary zinc intake was determined, and factors affecting serum zinc were identified with the use of regression models adjusting for sex, age, fasting status, and time of blood draw. ORs were calculated to identify factors associated with the risk of being below the serum zinc cutoff, and the prevalence of low serum zinc in the US was calculated. $P < 0.01$ was considered significant.

Results: Mean ± SE serum zinc concentrations in males and females were 84.9 ± 0.8 and 80.6 ± 0.6 μg/dL, respectively ($P < 0.0001$). Regression models with serum zinc as the dependent variable indicated that afternoon and evening blood draws ($\beta = -9.7$ and -15.3; $P < 0.0001$) were negatively associated with serum zinc concentrations and serum albumin ($\beta = 16.1$; $P < 0.0001$) and hemoglobin ($\beta = 1.0$; $P = 0.0048$) were positively associated with serum zinc concentrations. Hypoalbuminemia (OR = 11.2; 99% CI: 3.4, 37.3), anemia in females (OR: 3.4; 99% CI: 1.7, 6.9), and pregnancy (OR: 9.6; 99% CI: 2.9, 31.9) increased the odds of being below the serum zinc cutoff ($P < 0.0001$ for all). Zinc from diet or supplements did not affect serum zinc ($P > 0.01$). Approximately 3.8% of children (<10 y), 8.6% of males (≥10 y), and 8.2% of females (≥10 y) were below the serum zinc cutoff.

Conclusions: Factors such as sex, age, and time of blood draw should be considered when using serum zinc concentration to determine the zinc status of a population. Caution is advised when interpreting serum zinc concentration in populations with a high prevalence of hypoalbuminemia or anemia. This trial was registered at http://www.isrctn.com as ISRCTN96013840. *J Nutr* 2018;148:1341–1351.

Keywords: plasma zinc, zinc status, zinc deficiency, NHANES, zinc metabolism

Introduction

Zinc is a nutritionally essential trace mineral required as a coenzyme for >300 metalloproteins and enzymes, as a structural component for ~2500 transcription factors, and in the regulation of gene expression for thousands of genes. In contrast to overt zinc deficiency, which is generally limited to developing nations, marginal or moderate zinc deficiency may be widespread (1). Pregnant and lactating women and exclusively breastfed infants are at particular risk due to increased physiologic zinc demands (2). In humans, mild or moderate zinc deficiency may lead to stunted growth and delayed puberty in adolescents, hypogonadism in males, dermatitis, reduced appetite, mental lethargy, and delayed wound healing (3).

Assessing zinc nutriture is challenging because zinc homeostasis is tightly regulated. The Biomarkers of Nutrition for Development Zinc Expert Panel and the International Zinc Nutrition Consultative Group recommend plasma or serum zinc concentration (hereafter referred to as "serum zinc") as a biomarker of zinc status (4). Although serum zinc is not considered to be a reliable indicator of zinc status of an individual, it is the most widely used and available indicator of risk of zinc deficiency in populations. Moreover, serum zinc is the only indicator of zinc status for which adequate

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reference data and suggested lower cutoff values are available. The suggested lower cutoffs for serum zinc are as follows—children aged <10 y: morning/nonfasting, 65 μg/dL; afternoon 57 μg/dL; females aged ≥10 y: morning/fasting, 70 μg/dL; morning/nonfasting, 66 μg/dL; afternoon, 59 μg/dL; and males aged ≥10 y: morning/fasting, 74 μg/dL; morning/nonfasting, 70 μg/dL; afternoon, 61 μg/dL (4). However, caution is advised when interpreting serum zinc concentrations because many factors have been identified to affect serum zinc independent of an individual's zinc status, such as meal consumption (5–7), time of day (5, 6, 8, 9), and inflammation and infection (10).

The percentage of the population with serum zinc concentrations below the cutoff and those with usual dietary zinc intakes below the Estimated Average Requirement are 2 criteria recommended by international organizations, such as the WHO, UNICEF, and the International Zinc Nutrition Consultative Group, to determine the population risk of zinc deficiency (11). The cutoffs for serum zinc were established on the basis of serum zinc values obtained from the second NHANES in the United States (1976–1980) (12). In subsequent years, serum zinc was excluded from NHANES and was not reintroduced as a biochemical measurement until the 2011–2012 survey cycle. Beyond the importance of having contemporary data from a population survey on zinc intake and status measures, changes in lifestyle and dietary habits in the US have occurred over the past 30 y. In particular, Americans are eating less red meat (13, 14), a major contributor to zinc intake, and are consuming more dietary supplements, including multivitamin and mineral supplements that contain zinc (15). Thus, the objective of the current study was to evaluate serum zinc concentrations in the US population and to determine factors affecting serum zinc with the use of NHANES 2011–2012 and 2013–2014.

Methods

Study overview, population, and analytic sample. The plan and operations, sample design, response rates, and analytical guidelines of NHANES have been published (16–18). Data from those aged ≥6 y participating in NHANES 2011–2014 with serum zinc values (approximately one-third of the sample) were used for these analyses. Data for pregnant ($n = 34$) or lactating ($n = 20$) females were analyzed separately. The final analytic sample of those aged ≥6 y excluding those who were pregnant or lactating was 4347 participants. The National Center for Health Statistics Research Ethics Review Board approved the use of human subjects for NHANES studies (19) and additional institutional review was unnecessary (20). This study was registered at isrctn.com (ISRCTN96013840).

Dietary intake assessment. Zinc intake from food was obtained from 24-h dietary recalls using an Automated Multiple-Pass Method (21) via in-person dietary interviews (day 1) (22) and then again via telephone 3–10 d later. A dietary supplement questionnaire that assessed the usage of vitamins, minerals, botanicals, and other dietary supplements over the past 30 d was administered as part of the NHANES household interview and the consumption frequency, duration, and amount consumed were recorded for each supplement (23). The complete product information, including labeled dosage or serving size, ingredients, and the amounts of ingredients per serving, was also recorded. The average daily intake of nutrients from dietary supplements was calculated by using the supplement consumption frequency and dosage. Individual usual intake was estimated by using the National Cancer Institute method (NCI version 2.1) (24) and with the use of the 1-part model, given that zinc was consumed on most days during the 24-h recalls. Covariates in the models included age, day (weekend: Friday–Sunday; weekday: Monday–Thursday) of recall, recall-day sequence (day 1 or day 2), and dietary supplement use (yes or no). Total zinc intake was the sum of individual usual intake from food plus zinc from dietary supplements.

Demographic characteristics, anthropometric measurements, and biomarkers. Demographic information (age, sex, race/ethnicity, poverty-income ratio) was collected via interview with the use of questionnaires (23). Height, weight, and waist circumference were obtained according to NHANES protocols (25). BMI was calculated as body weight (kilograms) divided by height (meters) squared. Physical activity was classified as sedentary, moderate activity, or active on the basis of self-report. Participants who reported "7 days active at least 60 minutes in the past 7 days" or who gave a positive response to 2 questions about vigorous recreational or work-related activity were considered active. Moderately active participants reported between 4 and 6 "days active at least 60 minutes in the past 7 days" or gave a positive response to 2 questions on moderate recreational or work-related activity. All other participants were classified as sedentary (23). Those with diabetes were determined on the basis of response (yes or no) to the question 'have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes' (23). Smoking was determined on the basis of response (yes or no) to a question regarding current smoking (23). Alcohol intake was determined by using day 1 dietary recall information. White blood cell counts and serum albumin and hemoglobin concentrations were obtained from relevant NHANES laboratory files (26). Hormone, steroid, and oral contraceptive use (yes or no) was obtained from questions regarding prescription medications (23).

Statistical analysis. NHANES survey weights (subsample A for all serum zinc analyses), strata, and primary sampling units were used in all calculations, thus providing nationally representative estimates. All of the statistical analyses were performed with SAS software (version 9.2; SAS Institute, Inc.) and SUDAAN (version 11; Research Triangle Institute). Means ± SEs were determined by using PROC SURVEYMEANS. Regression analyses using PROC SURVEYREG were used to assess differences between groups after adjusting for age, sex (when analyses included both sexes), and session (including morning/fasting, morning/nonfasting, afternoon, and evening). Logistic regression (PROC RLOGIST) was used to determine the percentage of the population below accepted cutoffs of serum zinc. The cutoffs for serum zinc were defined as follows—children aged <10 y: morning/nonfasting, 65 μg/dL; afternoon 57 μg/dL; females aged ≥10 y: morning/fasting, 70 μg/dL; morning/nonfasting, 66 μg/dL; afternoon, 59 μg/dL; and males aged ≥10 y: morning/fasting, 74 μg/dL; morning/nonfasting, 70 μg/dL; afternoon, 61 μg/dL (4). $P < 0.01$ was considered significant; a cutoff below $P < 0.05$ was chosen to prevent type I errors, given the large sample size. The prevalence of the population with serum zinc values below the cutoffs was also determined.

Results

Demographic characteristics and dietary information. Serum zinc was added to NHANES in the 2011 survey cycle

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TABLE 1 Demographic characteristics of NHANES 2011–2014 participants with serum zinc concentrations[1]

	Children	Males						Females						Pregnant	Lactating
	6–8 y ($n = 280$)	9–13 y ($n = 246$)	14–18 y ($n = 219$)	19–30 y ($n = 368$)	31–50 y ($n = 519$)	51–70 y ($n = 490$)	≥71 y ($n = 203$)	9–13 y ($n = 244$)	14–18 y ($n = 233$)	19–30 y ($n = 334$)	31–50 y ($n = 522$)	51–70 y ($n = 490$)	≥71 y ($n = 199$)	20–44 y ($n = 34$)	≥19 y ($n = 20$)
Age, y	7.2 ± 0.0	11.1 ± 0.1	15.8 ± 0.1	24.4 ± 0.3	40.5 ± 0.2	59.4 ± 0.3	75.8 ± 0.3	11.0 ± 0.1	16.0 ± 0.1	24.2 ± 0.3	41.2 ± 0.4	59.6 ± 0.3	76.5 ± 0.3	28.0 ± 1.1	30.6 ± 0.5
Male, %	55.7 ± 3.2	—	—	—	—	—	—	—	—	—	—	—	—	—	—
BMI, kg/m^2	17.4 ± 0.2	20.5 ± 0.4	24.7 ± 0.4	26.6 ± 0.4	29.4 ± 0.3	29.4 ± 0.5	27.7 ± 0.4	21.6 ± 0.5	25.1 ± 0.7	27.3 ± 0.5	29.2 ± 0.5	30.4 ± 0.6	28.2 ± 0.6	29.0 ± 1.5	24.1 ± 0.8
Ethnicity, %															
Hispanic	23.1 ± 3.4	27.1 ± 4.8	21.3 ± 3.0	21.2 ± 3.1	18.4 ± 2.9	9.7 ± 1.3	3.5 ± 1.0	29.4 ± 4.3	17.4 ± 3.2	20.6 ± 3.0	17.6 ± 3.2	8.5 ± 1.5	4.2 ± 1.4	12.6 ± 5.1	16.2 ± 8.2
White	54.4 ± 5.1	50.1 ± 4.5	52.0 ± 5.3	58.5 ± 3.5	62.5 ± 3.3	76.1 ± 2.4	86.0 ± 2.6	50.2 ± 5.7	61.8 ± 5.3	58.6 ± 3.7	61.1 ± 3.7	74.1 ± 3.0	86.2 ± 2.4	53.6 ± 10.6	61.7 ± 13.1
Black	14.9 ± 2.2	15.0 ± 3.0	16.4 ± 3.0	11.2 ± 2.0	10.7 ± 1.6	9.7 ± 1.5	6.3 ± 1.6	12.8 ± 2.3	12.8 ± 2.9	11.5 ± 2.1	13.1 ± 1.7	11.3 ± 2.2	5.3 ± 1.0	21.4 ± 5.7	4.8 ± 4.7
Asian	4.3 ± 0.7	2.9 ± 0.9	5.0 ± 1.1	4.7 ± 0.9	5.2 ± 0.8	3.2 ± 0.5	4.0 ± 1.0	4.2 ± 0.9	4.7 ± 0.8	4.9 ± 1.1	5.1 ± 0.8	4.2 ± 0.8	2.8 ± 0.8	9.8 ± 3.8	10.1 ± 5.8
Other	3.3 ± 1.2	4.9 ± 1.5	5.2 ± 2.2	4.5 ± 1.1	3.3 ± 0.9	1.2 ± 0.7	0.3 ± 0.3	3.4 ± 0.6	3.3 ± 1.2	4.4 ± 1.3	3.1 ± 0.7	1.8 ± 0.9	1.5 ± 1.0	2.6 ± 2.5	7.3 ± 5.4
PA, %															
Sedentary	9.8 ± 2.6	10.8 ± 1.9	7.3 ± 2.1	7.9 ± 1.4	13.5 ± 2.1	20.5 ± 2.5	37.9 ± 4.1	16.1 ± 2.2	13.7 ± 3.3	18.0 ± 2.8	19.0 ± 2.3	31.2 ± 2.8	43.0 ± 4.5	32.9 ± 11.2	6.9 ± 4.5
Moderate	20.2 ± 3.4	16.9 ± 3.6	17.4 ± 3.4	24.2 ± 4.4	29.2 ± 2.8	39.8 ± 3.2	41.5 ± 4.3	37.1 ± 3.8	35.6 ± 4.4	36.2 ± 3.4	44.7 ± 2.5	48.5 ± 2.7	48.6 ± 4.7	53.7 ± 13.4	34.3 ± 12.4
Vigorous	70.1 ± 3.4	72.3 ± 4.4	75.3 ± 3.6	67.9 ± 4.6	57.3 ± 2.9	39.7 ± 3.3	20.5 ± 3.7	46.8 ± 3.5	50.7 ± 4.7	45.8 ± 3.6	36.3 ± 2.2	20.4 ± 2.2	8.4 ± 1.7	13.4 ± 6.3	58.8 ± 14.7
PIR, %															
<1.35	37.9 ± 4.7	38.2 ± 4.6	34.5 ± 4.1	33.7 ± 4.3	21.1 ± 2.1	19.4 ± 2.8	16.2 ± 3.0	36.9 ± 4.6	32.2 ± 5.3	41.0 ± 5.1	23.4 ± 3.0	22.9 ± 2.3	26.6 ± 3.6	30.7 ± 8.2	28.0 ± 11.3
1.35–1.85	15.4 ± 2.6	9.4 ± 2.2	13.4 ± 4.1	9.7 ± 2.4	12.3 ± 2.3	7.0 ± 1.2	12.1 ± 3.6	9.8 ± 2.9	10.0 ± 2.4	11.6 ± 2.6	8.0 ± 1.6	7.0 ± 1.7	17.1 ± 3.7	17.2 ± 10.3	2.7 ± 2.8
> 1.85	46.7 ± 4.6	52.4 ± 5.0	52.0 ± 5.0	56.5 ± 5.4	66.7 ± 3.1	73.6 ± 3.0	71.6 ± 4.3	53.2 ± 4.1	57.7 ± 4.9	47.4 ± 4.9	68.6 ± 3.6	70.2 ± 3.4	56.3 ± 5.8	52.2 ± 10.7	69.2 ± 11.8

[1]Values are estimated demographic means ± SEs and population percentages for children aged 6–8 y, males and females separated by age ranges used in the Institute of Medicine DRIs (27), and pregnant and lactating women. PA, physical activity; PIR, poverty-income ratio.

TABLE 2 Dietary, supplemental, and total zinc intakes in the US population: NHANES 2011–2014[1]

	Children	Males					Females					Pregnant	Lactating
	6–8 y (n = 280)	9–13 y (n = 246)	14–18 y (n = 219)	19–30 y (n = 368)	31–50 y (n = 519)	51–70 y (n = 490)	≥71 y (n = 203)	9–13 y (n = 244)	14–18 y (n = 233)	19–30 y (n = 334)	31–50 y (n = 522)	51–70 y (n = 490)	≥71 y (n = 199)	20–44 y (n = 34)	≥19 y (n = 20)
Zinc, mg/d															
Diet	10.07 ± 0.14	11.75 ± 0.16^{a}	12.27 ± 0.26^{a,b}	14.04 ± 0.22^{d}	13.48 ± 0.09^{c}	12.73 ± 0.19^{b}	12.01 ± 0.18^{a,b}	9.38 ± 0.12^{b,c}	8.88 ± 0.18^{a,b}	9.45 ± 0.11^{c}	9.47 ± 0.12^{b,c}	9.31 ± 0.12^{a,bc}	8.92 ± 0.11^{a}	10.30 ± 0.44	10.50 ± 0.24
Supplement	0.56 ± 0.12	0.99 ± 0.27^{a}	1.76 ± 0.51^{a,b}	2.25 ± 0.38^{a,b}	3.02 ± 0.40^{b}	5.10 ± 0.50^{c}	9.56 ± 2.44^{bc}	0.72 ± 0.22^{a}	1.09 ± 0.38^{a}	2.25 ± 0.42^{b}	3.46 ± 0.77^{b,c}	5.37 ± 0.44^{c}	5.98 ± 0.93^{c}	8.11 ± 2.29	13.95 ± 2.72
Total	10.63 ± 0.14	12.74 ± 0.32^{a}	14.04 ± 0.62^{a}	16.28 ± 0.39^{b}	16.50 ± 0.40^{b}	17.83 ± 0.50^{b}	21.57 ± 2.43^{b}	10.10 ± 0.21^{a}	9.96 ± 0.40^{a}	11.71 ± 0.45^{b}	12.93 ± 0.78^{b,c}	14.68 ± 0.50^{c}	14.90 ± 0.99^{c}	18.42 ± 2.17	24.46 ± 2.79
RDA	5	8	11	11	11	11	11	8	9	8	8	8	8	11	12

[1]Values are means ± SEs for children aged 6–8 y, males and females separated by age ranges used in the Institute of Medicine DRIs (27), and pregnant and lactating women. Data were analyzed by using PROC SURVEY REG (SAS Institute, Inc.), and differences in means were detected with t tests. Labeled means within a row and without a common letter within ages 9–13 and ≥71 y differ, $P < 0.01$. No differences between pregnant and lactating women were observed.

and was measured in one-third of survey participants aged ≥6 y. Demographic and dietary intake data from survey participants with serum zinc values are shown in Tables 1 and 2. Data are shown for children aged 6–8 y (n = 280) and for males (n = 2045) and females (n = 2076) separated based on age ranges used in the Institute of Medicine DRIs (27). Mean dietary and total daily zinc (dietary + supplemental zinc) intakes were at or above the RDA for zinc for all age groups. Children aged 6–8 y consumed approximately twice the RDA for zinc, with the majority of zinc derived from dietary sources. Mean dietary zinc intake in males increased from 11.8 mg/d in those aged 9–13 y to 14.0 mg/d in those aged 19–30 y ($P < 0.01$) and declined thereafter to 12.0 mg/d in those aged ≥71 y (compared with age 19–30 y, $P < 0.01$). Mean dietary zinc intake in females did not follow a discernable pattern and varied only slightly across age groups, with a 0.6-mg/d difference between the highest (age 19–50 y) and lowest (ages 14–18 y and ≥71 y) intakes. There was a pattern of increasing zinc intake from supplements with age. This ranged from 1.0 to 9.6 mg zinc/d in males and from 0.7 to 6.0 mg zinc/d in females aged 9–13 y compared with those aged ≥71 y ($P < 0.01$ for both). Mean total daily zinc intake was higher in males than in females (17.3 ± 0.3 and 13.4 ± 0.4 mg/d; $P < 0.0001$) and tended to increase with age in both males and females, from 12.7 to 21.6 mg/d in males and from 10.1 to 14.9 mg/d in females aged 9–13 y compared with those aged ≥71 y ($P < 0.01$ for both). Pregnant and lactating women consumed less than the RDA for zinc from diet alone; however, both groups consumed approximately twice the RDA with the addition of zinc from supplements.

Factors affecting serum zinc concentrations. Mean serum zinc concentrations are shown in Table 3. Serum zinc concentrations were higher in males than in females ($P < 0.0001$). Overall, there was no difference in serum zinc in those aged 6–9 y compared with those aged ≥10 y ($P = 0.59$). When separated on the basis of sex and age, serum zinc concentrations increased in males from early childhood to age ~30 y and declined thereafter with increasing age, but this trend was not significant ($P = 0.02$). Serum zinc concentrations in females were not affected by age ($P = 0.45$). Ethnicity, poverty-income ratio, physical activity, diabetes, and smoking or alcohol use did not affect serum zinc concentrations ($P > 0.01$).

Participants with a morning appointment were asked to provide a fasting blood sample. The majority of these participants arrived in a fasted condition (94%), whereas the remaining participants had not fasted. This is in contrast to NHANES II, where the proportion of fasting and nonfasting morning samples was equivalent. Serum zinc concentrations were 9% lower in afternoon blood draws ($P < 0.01$) and declined even further in evening blood draws ($P < 0.01$) compared with nonfasting morning blood draws; no difference was observed between fasting and nonfasting morning samples ($P > 0.01$).

Participants with hypoalbuminemia (serum albumin ≤3.5 g/dL) and females with anemia (hemoglobin ≤12 g/dL) had significantly lower serum zinc concentrations ($P < 0.0001$ for both). High white blood cell count, hormone or steroid use, and BMI and waist circumference did not affect serum zinc concentrations ($P > 0.01$). Zinc intake was not associated with serum zinc; there was no difference in serum zinc concentrations when the population (male or female) was divided into those consuming less than or greater than the RDA for zinc from diet, supplements, or total zinc ($P > 0.01$).

TABLE 3 Geometric mean and selected percentiles of serum zinc concentrations in the US population: NHANES 2011–2014[1]

				Serum zinc, μg/dL				
	Serum zinc, μg/dL	***n***	***P***	**2.5th**	**5th**	**50th**	**95th**	**97.5th**
All participants	82.7 ± 0.6	4347		57.7 ± 0.5	60.7 ± 0.6	81.3 ± 0.6	109.2 ± 1.2	116.9 ± 1.7
Demographic characteristics								
Sex[2]			<0.0001					
Male	84.9 ± 0.8[b]	2193		58.6 ± 0.8	61.5 ± 0.8	83.4 ± 0.6	113.1 ± 1.9	120.9 ± 2.7
Female	80.6 ± 0.6[a]	2154		57.1 ± 0.8	59.6 ± 0.9	79.5 ± 0.7	103.9 ± 1.0	111.3 ± 1.9
Age[3]			0.59					
6–9 y	81.1 ± 1.1	378		56.1 ± 1.8	60.6 ± 1.9	79.8 ± 1.0	104.7 ± 3.5	112.7 ± 3.3
≥10 y	82.8 ± 0.6	3969		57.7 ± 0.6	60.7 ± 0.7	81.3 ± 0.6	109.3 ± 1.2	117.4 ± 1.7
Sex/age[4]								
Male			0.02					
6–8 y	80.5 ± 1.1	148		54.7 ± 4.8	60.3 ± 3.9	80.8 ± 1.4	97.5 ± 1.7	102.2 ± 4.0
9–13 y	83.3 ± 1.1	246		58.8 ± 2.3	61.8 ± 1.9	81.7 ± 1.2	108.5 ± 2.9	112.2 ± NA
14–18 y	87.2 ± 1.6	219		61.2 ± 2.2	65.6 ± 1.5	85.5 ± 2.3	115.5 ± 2.3	116.2 ± NA
19–30 y	87.0 ± 1.4	368		58.8 ± 1.8	61.0 ± 1.5	84.9 ± 1.4	121.7 ± 3.8	129.0 ± NA
31–50 y	85.9 ± 1.3	519		59.4 ± 2.7	64.1 ± 1.8	84.4 ± 0.7	110.2 ± 3.1	118.9 ± 6.3
51–70 y	83.7 ± 1.5	490		58.2 ± 1.2	60.3 ± 1.3	82.4 ± 1.9	110.0 ± 2.7	113.7 ± 3.7
≥71 y	81.8 ± 1.8	203		53.9 ± 2.3	58.4 ± 2.3	78.7 ± 2.3	111.6 ± 7.6	120.3 ± 10.2
Female			0.45					
6–8 y	80.5 ± 1.8	132		53.3 ± NA	57.9 ± 4.9	77.7 ± 0.9	111.8 ± 4.2	114.1 ± NA
9–13 y	82.8 ± 1.0	244		58.4 ± 1.4	60.9 ± 1.9	81.1 ± 1.6	104.8 ± 4.1	117.0 ± NA
14–18 y	81.2 ± 1.3	233		54.8 ± 2.9	59.7 ± 3.0	81.3 ± 1.9	101.9 ± 1.2	104.1 ± 3.4
19–30 y	79.0 ± 1.1	334		55.6 ± 1.5	58.8 ± 1.4	77.9 ± 1.3	103.8 ± 2.5	111.9 ± NA
31–50 y	80.0 ± 0.8	522		55.2 ± 1.7	58.4 ± 1.2	79.6 ± 0.7	103.5 ± 1.7	108.1 ± 4.2
51–70 y	81.2 ± 1.3	490		58.1 ± 1.2	61.0 ± 1.3	79.8 ± 1.5	102.5 ± 3.3	111.3 ± 5.8
≥71 y	81.5 ± 1.2	199		55.9 ± 2.8	59.3 ± 2.7	80.5 ± 1.5	103.9 ± 3.4	112.1 ± NA
Ethnicity			0.19					
Hispanic	82.9 ± 1.1	1065		56.5 ± 1.4	60.0 ± 1.1	81.0 ± 1.0	112.4 ± 2.9	119.3 ± 2.9
White	83.2 ± 0.8	1628		57.9 ± 0.7	61.0 ± 1.0	82.0 ± 0.7	108.9 ± 1.8	116.5 ± 2.4
Black	80.8 ± 0.9	1020		55.7 ± 1.2	58.9 ± 1.1	78.8 ± 0.9	107.9 ± 1.7	113.5 ± 4.2
Asian	81.9 ± 0.9	471		54.4 ± 2.1	58.7 ± 1.5	80.4 ± 1.3	109.4 ± 1.8	113.6 ± 1.7
Other	80.9 ± 1.6	163		60.5 ± 0.6	63.1 ± 1.2	79.7 ± 1.4	107.9 ± 5.3	113.6 ± 4.1
Poverty-income ratio			0.33					
<1.35	83.1 ± 0.8	1602		56.2 ± 1.1	60.2 ± 0.9	82.0 ± 1.2	110.6 ± 1.5	118.1 ± 2.7
1.35–1.85	81.9 ± 1.1	442		58.1 ± 2.7	61.1 ± 1.6	80.1 ± 0.9	107.9 ± 3.4	115.4 ± NA
>1.85	82.5 ± 0.7	1985		57.8 ± 0.6	60.7 ± 0.9	81.1 ± 0.6	108.6 ± 1.8	116.3 ± 2.1
Physical activity			0.06					
Sedentary	81.1 ± 0.9	892		54.0 ± 1.6	58.0 ± 1.0	80.1 ± 1.0	106.3 ± 2.0	112.4 ± 5.1
Moderate	82.3 ± 0.7	1545		57.6 ± 0.7	60.2 ± 1.0	81.2 ± 0.7	108.9 ± 1.3	114.7 ± 1.5
Vigorous	83.8 ± 0.6	1898		59.3 ± 0.7	62.1 ± 0.8	82.0 ± 0.7	110.9 ± 1.9	118.5 ± 3.0
Diabetes			0.69					
No	82.8 ± 0.6	3856		57.5 ± 0.6	60.7 ± 0.7	81.2 ± 0.5	109.7 ± 1.2	117.5 ± 1.6
Yes	82.3 ± 1.1	487		58.3 ± 1.0	60.9 ± 1.0	82.0 ± 1.3	106.4 ± 2.2	109.8 ± 2.6
Smoker			0.43					
No	82.4 ± 0.6	3616		57.6 ± 0.5	60.7 ± 0.7	81.0 ± 0.6	108.5 ± 1.3	115.9 ± 1.8
Yes	84.0 ± 1.3	608		59.0 ± 2.2	62.1 ± 0.9	82.7 ± 0.9	111.3 ± 3.6	120.6 ± 4.7
Alcohol use			0.03					
No	82.2 ± 0.6	3582		57.4 ± 0.6	60.3 ± 0.7	81.0 ± 0.5	107.8 ± 1.4	114.4 ± 2.0
Yes	84.4 ± 1.1	765		58.7 ± 1.4	62.5 ± 1.1	82.4 ± 1.1	114.4 ± 2.3	120.5 ± 5.8
Biological								
Time/fasting status[5]			<0.0001					
Morning, fasting	88.6 ± 0.7[c]	1423		64.1 ± 0.9	67.6 ± 1.1	86.8 ± 0.8	115.0 ± 1.9	121.8 ± 1.8
Morning, nonfasting	86.6 ± 2.7[c]	89		56.5 ± NA	60.9 ± 3.8	85.0 ± 3.1	114.0 ± 3.8	117.6 ± 7.5
Afternoon	78.6 ± 0.8[b]	1124		55.5 ± 1.4	58.1 ± 0.7	76.9 ± 0.9	101.3 ± 2.0	109.2 ± 3.1
Evening	74.2 ± 0.8[a]	489		53.7 ± 1.4	57.3 ± 1.1	73.8 ± 0.9	94.5 ± 3.1	102.1 ± 4.3
Serum albumin			<0.0001					
≤3.5 g/dL	66.6 ± 2.7[a]	38		NA	NA	68.4 ± 3.5	80.9 ± 0.7	81.0 ± 3.2
>3.5 g/dL	82.8 ± 0.7[b]	3048		57.8 ± 0.6	60.8 ± 0.7	81.4 ± 0.6	109.1 ± 1.4	117.4 ± 2.0
Hemoglobin								
Females			<0.0001					
≤12 g/dL	74.3 ± 1.4[a]	218		51.6 ± 1.4	52.9 ± 1.7	71.9 ± 2.4	95.6 ± 3.6	110.7 ± NA
>12 g/dL	81.0 ± 0.7[b]	1325		57.6 ± 0.9	61.0 ± 1.1	80.2 ± 0.7	103.9 ± 1.1	111.2 ± 2.3
Males			0.03					
≤13 g/dL	77.1 ± 3.2	121		NA	49.8 ± NA	74.3 ± 4.1	106.2 ± 4.4	109.8 ± 4.5
>13 g/dL	85.5 ± 0.9	1459		59.3 ± 0.7	62.8 ± 1.0	83.8 ± 0.6	113.8 ± 2.4	122.2 ± 2.9
WBC count			0.24					
<11.5 $\times 10^9$/L	82.8 ± 0.7	3015		57.7 ± 0.6	60.6 ± 0.6	81.3 ± 0.6	109.4 ± 1.3	118.1 ± 1.8
≥11.5 $\times 10^9$/L	79.1 ± 2.1	108		48.6 ± 4.2	49.6 ± 3.8	79.9 ± 2.4	103.6 ± 4.1	109.4 ± 4.3

(*Continued*)

TABLE 3 (*Continued*)

	Serum zinc, μg/dL	*n*	*P*	Serum zinc, μg/dL				
				2.5th	5th	50th	95th	97.5th
Hormone use			0.17					
No	83.0 ± 0.7	2733		57.6 ± 0.8	60.7 ± 0.7	81.6 ± 0.7	109.8 ± 1.7	118.7 ± 2.1
Yes	81.0 ± 0.8	392		57.5 ± 0.9	58.9 ± 1.1	80.2 ± 0.8	104.3 ± 2.4	111.2 ± 2.7
Steroid use			0.02					
No	82.7 ± 0.7	3078		57.6 ± 0.7	60.6 ± 0.7	81.3 ± 0.6	109.4 ± 1.2	117.6 ± 1.8
Yes	78.4 ± 1.8	47		60.5 ± NA	62.1 ± 2.3	80.2 ± 2.7	97.6 ± 3.3	101.6 ± 2.8
Physical								
BMI			0.54					
<18.5 kg/m^2	84.1 ± 2.6	57		59.9 ± 2.5	60.4 ± 2.8	82.8 ± 1.6	109.0 ± NA	123.2 ± NA
18.5–24.9 kg/m^2	83.0 ± 0.9	917		57.3 ± 1.3	60.2 ± 1.0	80.8 ± 1.1	113.6 ± 2.4	118.7 ± 4.1
25–29.9 kg/m^2	83.6 ± 0.9	966		58.8 ± 1.5	62.1 ± 0.8	82.7 ± 0.8	108.5 ± 1.9	116.7 ± 2.3
≥30 kg/m^2	81.6 ± 0.8	1151		57.4 ± 1.0	59.6 ± 1.0	80.2 ± 0.9	107.3 ± 1.9	113.0 ± 3.0
Waist circumference								
Females			0.89					
<88 cm	80.2 ± 1.0	480		57.3 ± 1.2	58.7 ± 1.1	79.3 ± 1.1	103.7 ± 1.7	112.1 ± 3.0
≥88 cm	80.5 ± 0.8	1002		56.4 ± 1.4	59.6 ± 1.2	79.5 ± 0.9	102.9 ± 1.7	110.8 ± 4.8
Males			0.90					
<102 cm	85.9 ± 1.3	880		59.2 ± 0.9	62.2 ± 1.1	84.2 ± 0.8	116.7 ± 3.5	126.4 ± 7.8
≥102 cm	84.2 ± 1.2	661		58.1 ± 2.0	61.0 ± 1.4	83.2 ± 1.6	110.8 ± 3.1	120.6 ± 6.4
Diet								
Dietary zinc								
Females			0.31					
<RDA	80.5 ± 0.9	581		55.4 ± 2.8	59.2 ± 1.3	79.5 ± 1.0	103.9 ± 1.6	110.0 ± 4.3
≥RDA	80.6 ± 0.6	1573		57.3 ± 0.7	60.2 ± 0.9	79.5 ± 0.8	103.8 ± 1.1	111.4 ± 1.9
Males			0.04					
<RDA	83.0 ± 0.7	532		56.9 ± 3.5	62.1 ± 1.7	82.1 ± 1.0	108.6 ± 2.5	116.5 ± 4.4
≥RDA	85.5 ± 0.9	1661		58.6 ± 0.7	61.3 ± 0.9	83.9 ± 0.7	113.8 ± 2.3	122.1 ± 2.9
Total zinc								
Females			0.29					
<RDA	80.5 ± 1.0	481		57.4 ± 1.0	59.5 ± 1.2	79.1 ± 1.0	105.0 ± 2.2	111.2 ± 3.6
≥RDA	80.6 ± 0.6	1673		56.9 ± 0.9	59.6 ± 0.9	79.7 ± 0.7	103.7 ± 1.0	111.3 ± 1.9
Males			0.04					
<RDA	83.1 ± 0.7	429		59.5 ± 3.2	62.0 ± 1.1	82.8 ± 1.1	108.4 ± 3.0	116.2 ± 5.0
≥RDA	85.3 ± 0.9	1764		58.6 ± 0.9	61.3 ± 0.9	83.5 ± 0.8	113.7 ± 2.1	121.9 ± 3.0
Supplemental zinc								
Females			0.14					
Nonusers	80.1 ± 0.6	1618		57.4 ± 0.7	59.8 ± 0.9	78.9 ± 0.7	104.0 ± 1.4	111.7 ± 2.0
Users	81.6 ± 0.9	536		55.6 ± 2.0	58.9 ± 2.0	81.6 ± 1.1	103.6 ± 1.4	108.4 ± 3.5
Males			0.23					
Nonusers	84.9 ± 0.8	1661		59.3 ± 0.6	61.3 ± 0.9	83.4 ± 0.7	111.1 ± 2.0	120.5 ± 7.0
Users	85.1 ± 1.3	532		57.7 ± 2.3	62.4 ± 1.6	83.3 ± 1.1	115.8 ± 3.3	122.0 ± 5.5
Females								
Pregnant			0.0004					
Nonpregnant[6]	79.1 ± 0.9[b]	659		55.7 ± 1.4	58.8 ± 1.0	78.7 ± 0.9	102.9 ± 1.5	107.9 ± 3.2
Pregnant	69.1 ± 2.0[a]	34		47.4 ± NA	48.1 ± NA	64.8 ± 3.3	98.9 ± NA	NA
Lactating			0.07					
Nonlactating[6]	78.8 ± 0.9	673		54.3 ± 1.4	57.9 ± 1.1	78.2 ± 1.0	103.3 ± 1.5	108.3 ± 3.6
Lactating	74.3 ± 2.5	20		57.1 ± NA	60.3 ± NA	71.6 ± 3.9	92.0 ± NA	NA
Oral contraceptives			0.99					
Nonusers[6]	78.7 ± 0.9	627		54.1 ± 1.5	57.9 ± 1.1	78.3 ± 1.1	103.2 ± 2.0	109.8 ± 3.9
Users	78.4 ± 1.9	66		54.9 ± 3.2	56.3 ± 1.7	77.1 ± 1.3	102.4 ± NA	104.6 ± NA

[1]Values are means and selected percentiles ± SEs and were adjusted for age, sex (when analyses included both sexes), and session (including morning fasting, morning nonfasting, afternoon, and evening). Pregnant and lactating women were excluded except when stratified by oral contraceptive use and pregnancy and lactation. Data were analyzed by using PROC SURVEYREG (SAS Institute, Inc.), and differences in means were detected with *t* tests. Labeled means within a variable and without a common letter differ, $P < 0.01$. NA, percentiles or SE not estimated due to insufficient sample size; WBC, white blood cell.
[2]Adjusted for age and time/fasting status.
[3]Adjusted for sex and time/fasting status.
[4]Adjusted for fasting status.
[5]Morning: samples collected before 1200; afternoon: samples collected 1200–1800; evening: samples collected after 1800.
[6]Age-matched population.

Pregnant women had lower serum zinc concentrations ($P < 0.0004$) than did age-matched, nonpregnant women. Lactating women had 6% lower serum zinc concentrations; however, due to the low sample size ($n = 20$), this was not significantly different from age-matched, nonlactating women ($P = 0.07$). Serum zinc concentrations did not differ in oral contraceptive users compared with nonusers ($P = 0.99$).

Regression models with serum zinc as dependent variable. Regression models with serum zinc as the dependent variable are shown in Table 4. Afternoon and evening blood draws were negatively associated with serum zinc concentrations ($\beta = -9.7$ and -15.3; $P < 0.0001$ for both), and serum albumin ($\beta = 16.1$, $P < 0.0001$) and hemoglobin ($\beta = 1.0$, $P = 0.0048$) were positively associated with serum

TABLE 4 Association of serum zinc concentration with selected variables in the US population: NHANES 2011–2014[1]

Variable	n[2]	$\beta \pm$ SE	99% CI	P
Intercept		1.07 ± 7.60	−19.88, 22.03	0.89
Sex				
Male	1397	0	0	
Female	1319	0.60 ± 1.13	−2.52, 3.72	0.60
Age	2716	0.00 ± 0.02	−0.05, 0.06	0.92
Ethnicity				
Hispanic	559	1.69 ± 1.29	−1.87, 5.25	0.20
White	1174	0	0	
Black	593	1.23 ± 1.10	−1.82, 4.27	0.28
Asian	308	0.16 ± 0.98	−2.55, 2.87	0.87
Other	82	−0.96 ± 1.92	−6.26, 4.34	0.62
Poverty-income ratio	2716	−0.40 ± 0.20	−0.97, 0.16	0.06
Physical activity				
Sedentary	611	0	0	
Moderate	1091	−0.49 ± 0.86	−2.86, 1.87	0.57
Vigorous	1014	0.05 ± 0.99	−2.67, 2.77	0.96
BMI	2716	−0.05 ± 0.09	−0.31, 0.21	0.61
Time/fasting status				
Morning, fasting	1250	0	0	
Morning, nonfasting	67	−1.38 ± 2.43	−8.09, 5.33	0.58
Afternoon	969	−9.66 ± 0.71	−11.61, −7.71	<0.0001
Evening	430	−15.26 ± 0.73	−17.25, −13.26	<0.0001
Waist circumference	2716	0.08 ± 0.05	−0.05, 0.21	0.10
Diabetes				
No	2313	0	0	
Yes	403	1.24 ± 0.74	−0.80, 3.27	0.10
Smoking				
No	2203	0	0	
Yes	513	0.80 ± 0.82	−1.46, 3.06	0.34
WBC count	2716	−0.27 ± 0.21	−0.85, 0.31	0.21
Serum albumin	2716	16.06 ± 0.87	13.66, 18.45	<0.0001
Hemoglobin	2716	1.02 ± 0.33	0.10, 1.94	0.0048
Hormone use				
Nonusers	2479	0	0	
Users	237	−0.01 ± 0.99	−2.74, 2.72	0.99
Steroid use				
Nonusers	2676	0	0	
Users	40	−3.60 ± 1.81	−8.59, 1.39	0.06
Oral contraceptives				
Nonusers	2642	0	0	
Users	74	1.18 ± 2.12	−4.67, 7.03	0.58
Supplemental zinc	2716	0.12 ± 0.07	−0.07, 0.31	0.09
Dietary zinc	2716	−0.08 ± 0.17	−0.55, 0.40	0.66
Alcohol	2716	0.10 ± 0.05	−0.03, 0.22	0.04
Fiber	2716	−0.31 ± 0.14	−0.69, 0.07	0.03
Dietary iron	2716	0.19 ± 0.17	−0.27, 0.65	0.27
Supplemental iron	2716	0.06 ± 0.05	−0.07, 0.20	0.20
Fruit	2716	−0.26 ± 0.42	−1.41, 0.88	0.53
Vegetables	2716	−0.01 ± 0.90	−2.48, 2.46	0.99
Protein foods[3]	2716	−0.01 ± 0.32	−0.90, 0.89	0.98
Whole grains	2716	1.40 ± 0.69	−0.51, 3.30	0.05

[1] Values are means ± SEs and 99% CIs. $P < 0.01$ indicates an association with serum zinc concentration. Data were analyzed with PROC SURVEYREG (SAS Institute, Inc.). WBC, white blood cell.
[2] n represents the number of participants with data for all variables evaluated.
[3] Protein foods include meat, poultry, seafood, organ meat, and cured meats in ounce equivalents.

zinc concentrations. No other significant associations were observed.

Factors affecting odds of serum zinc concentrations below the cutoff. Participants were separated on the basis of sex, age, fasting status, and time of blood draw, and ORs of having serum zinc concentrations below the established cutoffs were calculated (Table 5). Adolescents were 43% less likely ($P < 0.01$) to have serum zinc concentrations below the cutoff compared with adults. Those who reported vigorous physical activity were 45% less likely ($P < 0.001$) to have serum zinc concentrations below the cutoff compared with sedentary individuals. Those with hypoalbuminemia (OR: 11.2; 99% CI: 3.4, 37.3; $P < 0.0001$) or anemia (females—OR: 3.4; 99% CI: 1.7, 6.9; $P < 0.0001$; males—OR: 3.4; 99% CI: 1.1, 10.1; $P < 0.01$) were more likely to have low serum zinc concentrations. Consuming less than the RDA for zinc (diet alone, supplements alone, or total zinc) did not increase ($P > 0.01$) the odds of having a serum zinc concentration below the cutoff. Pregnant woman were 9.6 times more likely to have serum zinc concentrations below the cutoff than nonpregnant women (99% CI: 2.9, 31.9; $P < 0.0001$).

Prevalence of low serum zinc concentrations in the US. The prevalence of low serum zinc concentrations in the US was estimated by using the established cutoffs for serum zinc (Table 6). With the use of the appropriate cutoffs on the basis of sex, age, fasting status, and time of blood draw, 3.8% of children (<10 y), 8.6% of males (≥10 y), and 8.2% of females (≥10 y) were below the cutoff for serum zinc.

Discussion

This study reevaluated serum zinc concentrations and determined factors affecting serum zinc in US males and females aged ≥6 y with the use of the nationally representative NHANES 2011–2012 and 2013–2014 surveys. Zinc intake from diet, supplements, or both was carefully characterized; and factors known to affect serum zinc, including sex, age, time of blood draw, and pregnancy, were confirmed. The prevalence of low serum zinc concentrations in the US was estimated and indicated that ~4% and 8% of children and adults, respectively, have low serum zinc concentrations and may be at risk of zinc deficiency.

This is the first study, to our knowledge, to characterize concomitantly both zinc intake and serum zinc concentration using the NHANES data set. Females consumed less zinc per day than did males. All age groups in both sexes and pregnant and lactating women had mean intakes above the RDA. These data are in general agreement with previous estimates of dietary zinc intake in the US population using NHANES II (1976–1980) and NHANES III (1988–1994) (28, 29). NHANES III, the first survey with quantitative data on supplement intake, reported intakes of 3.3 and 3.6 mg Zn/d from supplements in men and women aged ≥71 y, respectively (29), which is 66 and 40% lower, respectively, than the current survey. This is consistent with data that show that dietary supplement use increases with age and that men and women in the US are consuming more supplements compared with the 1970s (30). With the use of NHANES 2003–2006 data, Bailey et al. (15) reported an increased prevalence of zinc-containing dietary supplement use in men and women aged ≥51 y compared with younger persons. Collectively, these data suggest that zinc intake from the diet has remained relatively constant over the past 30 y, whereas zinc

TABLE 5 Adjusted ORs for serum zinc concentration below the cutoff in the US population: NHANES 2011–2014[1]

	n	Adjusted OR (99% CI)	*P*
Demographic characteristics			
Sex[2]			
Male	2193	1.00 (reference)	
Female	2154	0.97 (0.67, 1.40)	0.80
Age[3]			
6–13 y	770	0.45 (0.15, 1.33)	0.05
14–18 y	452	0.57 (0.34, 0.94)	0.0047
≥19 y	3125	1.00 (reference)	
Ethnicity			
Hispanic	1065	1.14 (0.65, 2.01)	0.51
White	1628	1.00 (reference)	
Black	1020	1.47 (0.84, 2.57)	0.07
Asian	471	1.21 (0.60, 2.43)	0.46
Other	163	1.21 (0.60, 2.46)	0.45
Poverty-income ratio			
<1.35	1602	1.00 (reference)	
1.35–1.85	442	0.77 (0.40, 1.47)	0.27
>1.85	1985	0.83 (0.57, 1.23)	0.20
Physical activity			
Sedentary	892	1.00 (reference)	
Moderate	1545	0.70 (0.44, 1.12)	0.04
Vigorous	1898	0.55 (0.34, 0.91)	0.0026
Diabetes			
Nondiabetic	3856	1.00 (reference)	
Diabetic	487	0.77 (0.42, 1.42)	0.25
Smoker			
No	3616	1.00 (reference)	
Yes	608	1.36 (0.82, 2.26)	0.11
Alcohol use			
No	3582	1.00 (reference)	
Yes	765	0.79 (0.45, 1.40)	0.27
Biological			
Time/fasting status[4]			
Morning, fasting	1423	1.00 (reference)	
Morning, nonfasting	89	1.20 (0.34, 4.17)	0.70
Afternoon	1124	0.68 (0.40, 1.17)	0.06
Evening	489	1.07 (0.60, 1.93)	0.74
WBC count			
$<11.5 \times 10^9$/L	3015	1.00 (reference)	
$\geq 11.5 \times 10^9$/L	108	1.25 (0.46, 3.38)	0.54
Serum albumin			
≤3.5 g/dL	38	11.18 (3.35, 37.34)	<0.0001
>3.5 g/dL	3048	1.00 (reference)	
Hemoglobin			
Females			
≤12 g/dL	218	3.39 (1.67, 6.86)	<0.0001
>12 g/dL	1325	1.00 (reference)	
Males			
≤13 g/dL	121	3.36 (1.11, 10.14)	0.0052
>13 g/dL	1459	1.00 (reference)	
Hormone use			
Nonusers	2859	1.00 (reference)	
Users	266	1.10 (0.52, 2.33)	0.72
Steroid use			
Nonusers	3078	1.00 (reference)	
Users	47	0.94 (0.08, 10.61)	0.95
Physical			
BMI			
<18.5 kg/m^2	57	0.67 (0.06, 7.95)	0.66
18.5–24.9 kg/m^2	917	1.00 (reference)	
25–29.9 kg/m^2	966	0.66 (0.33, 1.32)	0.11
≥30 kg/m^2	1151	0.78 (0.45, 1.33)	0.21
Waist circumference			
Females			
<88 cm	484	1.00 (reference)	
≥88 cm	998	0.68 (0.32, 1.43)	0.16
Males			
<102 cm	883	1.00 (reference)	
≥102 cm	658	0.77 (0.36, 1.62)	0.34
Diet			
Dietary zinc			
Females			
<RDA	581	1.04 (0.59, 1.84)	0.84
≥RDA	1573	1.00 (reference)	
Males			
<RDA	532	1.25 (0.74, 2.12)	0.25
≥RDA	1661	1.00 (reference)	
Total zinc			
Females			
<RDA	481	1.07 (0.57, 2.01)	0.77
≥RDA	1673	1.00 (reference)	
Males			
<RDA	429	1.33 (0.77, 2.28)	0.16
≥RDA	1764	1.00 (reference)	
Supplemental zinc			
Females			
Nonusers	1618	1.00 (reference)	
Users	536	1.05 (0.46, 2.40)	0.88
Males			
Nonusers	1661	1.00 (reference)	
Users	532	0.75 (0.45, 1.25)	0.13
Females			
Oral contraceptives			
Nonusers	627	1.00 (reference)	
Users	66	0.69 (0.23, 2.07)	0.36
Pregnant			
Nonpregnant	659	1.00 (reference)	
Pregnant	34	9.60 (2.88, 31.94)	<0.0001
Lactating			
Nonlactating	673	1.00 (reference)	
Lactating	20	0.43 (0.05, 4.04)	0.31

[1] Values are ORs (99% CIs), adjusted for sex, age, and time/fasting status. $P < 0.01$ indicates different from reference. Serum zinc cutoffs were as follows—children aged <10 y: morning/nonfasting, 65 μg/dL; afternoon, 57 μg/dL; females aged ≥10 y: morning/fasting, 70 μg/dL; morning/nonfasting, 66 μg/dL; afternoon, 59 μg/dL; males aged ≥10 y: morning/fasting, 74 μg/dL; morning/nonfasting, 70 μg/dL; afternoon, 61 μg/dL. WBC, white blood cell.
[2] Adjusted for age and time/fasting status.
[3] Adjusted for sex and time/fasting status.
[4] Adjusted for age and sex.

intake from supplements has increased compared with previous years, particularly in those aged ≥51 y.

Serum zinc concentrations were not related to dietary zinc or zinc intake from supplements. These findings are consistent with meta-analyses of randomized controlled trials, before and after supplementation trials, and before and after depletion trials that showed that serum zinc is a useful biomarker to assess severe zinc restriction (<1 mg zinc/d) and zinc supplementation

TABLE 6 Prevalence of low serum zinc concentrations in the US population: NHANES 2011–2014[1]

	Sample size, *n*	Prevalence, %	Estimated number in NHANES with low serum zinc, *n*	Estimated number in US population with low serum zinc, *N*
Children aged <10 y	378	3.8 ± 1.5	10	434,051
Males aged ≥10 y	1989	8.6 ± 0.9	182	9,877,988
Females aged ≥10 y	1980	8.2 ± 1.2	170	9,838,678

[1] Values are means ± SEs unless otherwise indicated. Serum zinc cutoffs were as follows—children aged <10 y: morning/nonfasting, 65 μg/dL; afternoon, 57 μg/dL; females aged ≥10 y: morning/fasting, 70 μg/dL; morning/nonfasting, 66 μg/dL; afternoon, 59 μg/dL; males aged ≥10 y: morning/fasting, 74 μg/dL; morning/nonfasting, 70 μg/dL; afternoon, 61 μg/dL.

but is less responsive to dietary zinc (31–33). The lack of responsiveness is likely due to mechanisms that maintain homeostasis, such as the decrease in endogenous zinc loss observed with zinc restriction (34–36). As such, it is likely that serum zinc is only affected when homeostasis cannot be maintained and zinc must be drawn from the exchangeable zinc pool (34, 35, 37), which is estimated to be ~5–6 mg dietary zinc/d (34).

Previously identified factors that affect serum zinc concentration that were confirmed in the current analysis include sex and time of blood draw. Pinna et al. (38) showed that the size of the exchangeable zinc pool is positively correlated ($r = 0.9$) to fat-free mass. Thus, lower serum zinc concentrations in females compared with males may be related to decreased body size and lean mass. Previous studies have shown that regular meal consumption affects serum zinc concentration, with the timing and size of meals contributing to the variation in serum zinc (5–9). Serum zinc concentrations begin to decline 0.5–1.5 h after a meal and are lowest 3–4 h after a meal (5). Thus, serum zinc concentrations tend to decline throughout the day with regular meal consumption (e.g., meals at 0700, 1200, and 1700) and increase overnight with the typical 12- to 14-h fast (5, 9). Interestingly, King et al. (7) reported that serum zinc concentrations did not increase overnight, and continued to decline, in those who consumed meals at regular 6-h intervals (0600, 1200, 1800, and 2400) compared with an overnight fast. These data confirm findings that show that larger and more frequent meals augment the decline in serum zinc (6).

Zinc in the circulation is predominantly (>70%) bound to albumin. In the current analysis, participants with hypoalbuminemia (serum albumin ≤3.5 g/dL) had lower serum zinc concentrations and were more likely to have a serum zinc concentration below the cutoff than those with serum albumin concentrations >3.5 g/dL. Even with low serum albumin concentrations, only ~2% of circulating albumin molecules are bound to zinc (39, 40). Thus, conditions resulting in hypozincemia concurrent with hypoalbuminemia, such as liver disease, inflammation, and infection, are likely independent of an individual's zinc status. Alternatively, zinc deficiency may affect the synthesis of albumin and other proteins identified in the current study, such as hemoglobin. For example, previous studies have shown that serum albumin concentrations respond to zinc supplementation in severely zinc-deficient individuals (41), although this has not been shown in marginally zinc-deficient individuals (42). Moreover, zinc is required for heme synthesis through incorporation into Δ-aminolevulinic acid dehydratase and erythropoiesis through the zinc finger transcription factor GATA-binding protein 1; and although zinc and iron deficiency often coexist (43), increasing evidence suggests that serum zinc may affect hemoglobin concentrations independent of iron status (44–46).

Pregnant women had significantly lower serum zinc concentrations and were more likely to have a serum zinc concentration below the cutoff than age-matched, nonpregnant women. These findings are consistent with findings from NHANES II, which reported serum zinc concentrations of 69.8 μg/dL in pregnant women (12). The interpretation of serum zinc concentrations during pregnancy is difficult due to plasma volume expansion (47, 48). As such, lower cutoffs of serum zinc concentration were tentatively proposed on the basis of the 2.5th percentiles of serum zinc concentration for pregnant women in the first (56 μg/dL) and second and third (50 μg/dL) trimesters (12). Further reference data are required to confirm and develop lower cutoffs for pregnant and lactating women.

Overall mean serum zinc concentrations in the US population were ~86 μg/dL in 1976–1980 (12, 49) and ~83 μg/dL in the current study, which indicate a decline of ~4% in serum zinc concentrations over the past 30 y. One possible explanation for the decline in serum zinc is the methodology used, because NHANES II used flame atomic absorption spectroscopy and NHANES 2011–2014 used dynamic reaction cell inductively coupled plasma mass spectrometry to determine serum zinc concentrations. With the use of the NHANES 2011–2014 survey population, it is possible to develop cutoffs on the basis of the 2.5th percentiles of serum zinc concentration from children aged 6–9 y and males and females aged ≥10 y, defined for serum zinc as follows—in children aged <10 y: morning/nonfasting, 63 μg/dL; afternoon, 50 μg/dL; evening, 57 μg/dL; in females aged ≥10 y: morning/fasting, 63 μg/dL; morning/nonfasting, 56 μg/dL; afternoon, 56 μg/dL; evening, 52 μg/dL; and in males aged ≥10 y: morning/fasting, 66 μg/dL; morning/nonfasting, 62 μg/dL; afternoon, 57 μg/dL; evening 54 μg/dL. With the use of these cutoffs, the estimated prevalences of individuals in the US below the cutoff was reduced to 1.6% of children aged <10 y and 2.3% and 2.2% of males and females aged ≥10 y, respectively, which are consistent with estimates from Pilch and Senti (49) using NHANES II.

As with any epidemiologic study, the current study cannot infer causation. Moreover, dietary data in NHANES are limited to 24-h dietary recall interviews, which are self-reported and therefore have the inherent limitation of over- and underreporting (50). NHANES also does not assess the intake of phytate, an inhibitory component that affects the bioavailability of zinc. Last, NHANES 2011–2014 did not determine serum zinc concentrations in children aged <6 y and had a limited sample of pregnant and lactating women. These were also limitations in NHANES II, although NHANES II did include serum zinc concentrations for children as young as 3 y. This is particularly concerning because children and pregnant and lactating women are most at risk of zinc deficiency (2). Until a suitable biomarker to assess zinc status is identified, future

studies should carefully characterize serum zinc concentrations in these populations.

In conclusion, the current study characterized serum zinc concentrations in the US population and factors that contribute to the variability in serum zinc. Factors such as sex, age, and time of blood draw, but not dietary zinc and/or zinc intake from supplements, affected serum zinc concentrations and should be considered when using serum zinc concentration to determine zinc status of a population. Caution is advised when interpreting serum zinc concentration in populations with a high prevalence of hypoalbuminemia or anemia. Although serum zinc concentrations may be used to estimate populations at risk of zinc deficiency, the development of alternative biomarkers such as DNA damage (51, 52) or expression of metallothionein or zinc transporters (53) in leukocytes to accurately and sensitively assess zinc status of individuals is imperative.

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