Nutritional Epidemiology and Public Health

The Nutritional Status of HIV-Infected US Adults

Sowmyanarayanan V Thuppal, Shinyoung Jun, Alexandra Cowan, and Regan L Bailey

Department of Nutrition Science, Purdue University, West Lafayette, IN

Abstract

Background: Nutrition is critical to HIV mortality and morbidity. Improved treatment modalities have increased life expectancy of HIV-infected individuals. More than 1 million US adults are living with HIV, but little is known about their nutritional status.

Objective: We aimed to characterize the nutritional status of those living with HIV with the use of the NHANES 2003–2014.

Methods: The NHANES is a nationally representative, cross-sectional survey of the US population and includes a household interview, medical examination, and two 24-h dietary recalls; survey weights are applied to make the data nationally representative. HIV antibodies were ascertained initially by immunoassay and confirmed with Western blot. NHANES 2003–2014 data were analyzed for HIV-positive (n = 87) and HIV-negative (n = 15,868) US adults (aged 19–49 y). Body mass index (BMI), waist circumference, dietary intakes, and nutritional biomarkers were estimated and compared by HIV status, stratified by sex.

Results: HIV-infected men and women had higher serum protein, lower serum albumin, and lower serum folate than did non–HIV-infected adults. HIV-positive women had significantly higher BMI, prevalence of overweight or obesity, and waist circumference risk and substantially lower serum 25-hydroxyvitamin D concentrations (44 compared with 65 nmol/L) than did HIV-negative women. When compared with HIV-negative women, HIV-positive women had lower intakes of some key nutrients such as fiber, vitamin E, vitamin K, magnesium, and potassium but had higher intakes of protein and niacin.

Conclusions: The NHANES data suggest that HIV infection is associated with poorer markers of some nutritional status indicators; however, the US population prevalence of HIV is <0.5%. Given the small sample size, not only in this study but also in the United States, much more targeted research is needed to better understand the multitude of factors that influence the nutritional status among those living with HIV in the United States, especially among women. *Curr Dev Nutr* 2017;1:e001636.

Introduction

Poor nutritional status can both be a cause of and exacerbate infection and inflammation (1); nutrition is an independent predictor of mortality among those with HIV infection (2, 3). The malnutrition of HIV has been associated with various factors: increased likelihood of food insecurity, high costs of prescription medications, nutrient-drug interactions, weight loss due to diarrhea and vomiting, alterations in metabolism and absorption of nutrients, and increased caloric requirements (4, 5). Medical advances in the treatment of HIV/AIDS, such as antiretroviral therapy (ART), have dramatically improved HIV survival rates and also reduced many of the acute malnutrition—related concerns associated with the disease. Meanwhile, with increased life expectancy, people living with HIV are now facing the challenges of chronic diseases. HIV-positive adults were reported to have higher risks of metabolic syndrome, cardiovascular disease, and type 2 diabetes, which have the potential to be reduced with optimal nutrition (6–8). Thus, public health concerns over nutrition and HIV have shifted from acute





Keywords: HIV, nutrition, obesity, biomarker, NHANES

Copyright © 2017, Thuppal et al. This is an open access article distributed under the terms of the CCBY-NC License http://creativecommons.org/licenses/by-nc/4.0/, which permits noncommercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

Manuscript received July 6, 2017. Initial review completed August 30, 2017. Revision accepted September 27, 2017. First published September 27, 2017.

This research received no specific grant from any funding agency.

Author disclosures: SVT, SJ, AC, and RLB, no conflicts of interest.

Address correspondence to SVT (e-mail: tvsowmy@gmail.com) or RLB (e-mail: regan.bailey@gmail.com).

Abbreviations used: ART, antiretroviral therapy; NCHS, National Center for Health Statistics; PIR, poverty-income ratio.

malnutrition to providing optimal nutrition to enhance the quality of life and health of infected individuals (9).

Currently, \sim 1.2 million Americans are living with HIV (10–12), but very little is known about the nutritional status of those living with HIV in the United States that is national in scope. The purpose of this analysis was to characterize the nutritional status of those living with HIV in the United States by using the NHANES 2003-2014, a nationally representative cross-sectional survey of the health and nutrition status of Americans.

Methods

NHANES is a cross-sectional survey of the noninstitutionalized civilian US-resident population conducted to assess the health and nutrition status of the US population (13). The survey is conducted by the National Center for Health Statistics (NCHS), CDC. All of the study methods were approved by the NCHS research ethics review board. All of the participants provided informed consent. NHANES participants are selected by using a complex multistage sampling design (14). The NHANES includes an in-home health interview, a physical examination in a mobile examination center, and a follow-up telephone interview. This analysis includes data from NHANES 2003 to 2014, from all nonpregnant adult participants aged 19-49 y who did not refuse the HIV antibody testing, representing a total of both HIV-positive (n = 87) and HIV-negative (n = 15,868) adults. Participants up to the age of 49 y were eligible for the HIV testing from 2003 to 2008 and participants up to the age of 59 v were eligible from 2009 to 2014. For consistency, we limited the sample size to the corresponding age range in the earlier

Demographic data were collected during the interview in participants' homes via a computer-assisted personal interview, interviewer-administered questionnaire. Across most NHANES cycles, self-reported race/ethnicity is categorized as non-Hispanic white, non-Hispanic black, Hispanic and Mexican American, and "other." Education was dichotomized as less than high school or high school diploma or GED (General Equivalency Diploma) or higher than high school. The poverty-income ratio (PIR) is a measure that represents the ratio of household income to the poverty threshold after adjustments for geographic location and family size, developed by the Department of Health and Human Services.

Three PIR categories were constructed: <130%, 130% to <350%, and ≥350%. A PIR <130% is the income eligibility criterion for participation in the Supplemental Nutrition Assistance Program (SNAP; i.e., the former Food Stamps Program), and these cutoffs have been previously used in NHANES analyses because they have been shown to differentiate between health and nutrition indicators (15).

Height and weight were measured during the health examination at the mobile examination center, and BMI was calculated as weight (kilograms)/height (meters squared). Participants were classified as nonoverweight or nonobese [BMI (kg/m²) <25] or overweight or obese (BMI ≥25). Waist circumference was measured at the uppermost lateral border of the iliac crest by using a tape measure (16). Waist circumference risk was calculated by using NIH guidelines: >88 cm for women and >102 cm for men

During the examination, a blood sample was drawn by a trained phlebotomist from all participants who did not refuse the HIV antibody test. HIV status was ascertained on the basis of the presence of antibody to HIV in blood (by using the synthetic peptide enzyme immunoassay technique for HIV-1 or HIV-2 or both). Specimens that were reactive in the initial screening were retested in duplicate with the Genetic Systems HIV-1/HIV-2 peptide enzyme immunoassay (Bio-Rad Laboratories). Specimens that were reactive in either one or both of the duplicates were then tested again for confirmation by using the Western blot technique (Calypte Biomedical Corporation). A limited number of nutritional biomarkers with sufficient survey years available for analysis were available. Therefore, this analysis was limited to serum protein, serum albumin, total cholesterol, TGs, serum glucose, and vitamin D (25-hydroxyvitamin D) (NHANES 2003-2010) and serum and RBC folate (NHANES 2003-2012). Differences in analytical methods across survey years were standardized as recommended by the NCHS. A timed-rate biuret method, a bichromatic digital endpoint method, and the timed-endpoint method were used to measure the concentrations of total protein, albumin, and cholesterol, respectively, with the use of the DxC Synchron Clinical Systems analyzer (Beckman Coulter). A modified microbiological assay method was used for measuring RBC folate. A diluted whole-blood sample was added to an assay medium containing Lactobacillus casei (National Collection of Industrial Bacteria 10463) and all of the nutrients necessary for the growth of L. casei, except for folate. Because the growth of L. casei is proportional to the amount of total folate present in the sample, the total folate concentration was assessed by measuring the turbidity of the inoculated medium in a PowerWave X340 Microplate reader (Bio-Tek Instruments). Serum folate was measured by using isotope-dilution HPLC coupled to tandem MS (LC-MS/MS). Ultra-HPLC-tandem MS was used for measuring vitamin D concentration. Detailed laboratory methods are publicly available (18).

Two 24-h dietary recalls were collected by using the USDA's automated multiple-pass method (19, 20). The first 24-h recall was collected in person during the health examination. The second was collected via telephone. The NHANES protocol attempts to have an even distribution of weekdays and weekend days. The USDA Food and Nutrient Database for Dietary Studies was used to convert foods and beverages as reported to determine their respective energy and nutrient values. The dietary data are presented for individuals with complete data on both dietary recalls. The average of nutrient intakes from both dietary recalls was calculated. Supplement use was classified as any dietary supplements taken during the past month.

All of the statistical analysis were performed by using SAS software (version 9.4; SAS Institute, Inc.) and SAS-callable SUDAAN software (version 11.0; RTI International). The sample design includes oversampling in order to obtain reliable estimates of health and nutritional measures for population subgroups. Sample weights, which account for differential probabilities of selection, nonresponse, and noncoverage, were calculated for 12 y for the

examination and dietary data to produce unbiased national estimates. Means were estimated for BMI, dietary components, and biomarkers by HIV status within sexes and by sex within HIV status for infected adults by using contrast statements in Proc Descript. SE estimates were calculated by using Taylor series linearization. The relative SE was calculated for each estimate, and the estimates with relative SEs >40% could be interpreted as statistically unreliable (12). Significance was set at P < 0.05.

Results

HIV infection represented <0.5% of the US adult population in NHANES 2003-2014 (data not shown). Men had a higher prevalence of HIV than did women (77% compared with 23%), and non-Hispanic blacks were more likely than other race/ethnic groups to be HIV positive (Table 1). The mean age of HIV-positive individuals was slightly higher (37.7 y) than that of HIV-negative individuals (34.3 y). Educational attainment did not differ by sex within infected individuals or between infected and noninfected adults when sex was combined. Most infected adults were at <350% of the PIR; none of the HIV-positive women belonged to the ≥350% PIR category compared with 38% of noninfected women. There was no consistent or significant pattern of marital status in infected adults, although the distributions differed from those of the noninfected US adult population.

HIV-positive women had a significantly higher BMI (mean ± SE: 34.3 \pm 2.3) than did both HIV-negative women (28.4 \pm 0.1) and HIV-positive men (26.2 \pm 0.7) (**Table 2**). HIV-positive men had a significantly lower BMI than did HIV-negative men (28.3 \pm 0.1). Indeed, the percentage of those who were overweight or obese was significantly higher for HIV-positive women compared with both HIV-negative women and HIV-positive men and was significantly lower for HIV-positive men compared with HIV-negative men. A similar trend was found with regard to waist circumference and the percentage of those at metabolic risk on the basis of waist circumference.

Consistent in both sexes, HIV-infected adults had higher serum protein, lower serum albumin, and lower serum folate than did non-HIV-infected adults. No significant differences were observed for TGs, glucose, or RBC folate within sexes by HIV status or within HIV-infected individuals by sex. HIV-positive men had lower concentrations of total cholesterol than did HIV-negative men (4.7 compared with 5.0 mmol/L). HIV-positive women had substantially lower serum 25-hydroxyvitamin D concentrations than did HIV-negative women (43.7 compared with 64.9 nmol/L).

No differences in energy intake were observed within sexes by HIV status (Table 3). HIV-positive women had significantly different intakes of fiber (mean \pm SEM: 9.2 \pm 1.5 g compared with 14.7 \pm 0.2 g) and protein (83.5 \pm 6.1 g compared with 71.3 \pm 0.5 g) than did HIV-negative women. Among men, no significant differences in dietary intakes were observed by HIV status, except for vitamin B-6, which was lower in HIV-positive men than in HIVnegative men. Compared with HIV-negative women, HIVpositive women had higher intakes of niacin and lower intakes of vitamin E, vitamin K, magnesium, and potassium. No significant difference in the prevalence of dietary supplement use was noted within HIV status and sexes: HIV-positive (mean \pm SE: 37% \pm 7%) and HIV-negative (38% \pm 1%) men and HIV-positive (53% \pm 13%) and HIV-negative (49% \pm 1%) women (data not shown).

TABLE 1 Baseline demographic characteristics of US adults aged 19–49 y by HIV status and sex¹

	HIV-positive adults: group A				HIV-negative adults: group B				
						Men	Women		P (group A
	All (n = 87)	Men ($n = 67$)	Women ($n = 20$)	Р	All $(n = 15,868)$	(n = 7907)	(n = 7961)	Р	vs. group B)
Age, y, mean ± SEM	37.7 ± 1.0	36.8 ± 1.3	40.7 ± 1.6	0.05	34.3 ± 0.15	34.1 ± 0.2	34.7 ± 0.2	0.001	0.001
Sex, %									< 0.001
Male	76.6 ± 4.5	_	_		49.2 ± 0.4	_	_		
Female	23.4 ± 4.5	_	_		50.8 ± 0.4	_	_		
Education, %				0.525				< 0.001	0.113
Less than high school	25.2 ± 5.5	23.4 ± 6.0	31.0 ± 10.8		16.4 ± 0.6	17.5 ± 0.7	15.2 ± 0.6		
High school or more	74.8 ± 5.5	76.6 ± 6.0	69.0 ± 10.8		83.6 ± 0.6	82.5 ± 0.7	84.8 ± 0.6		
Race/ethnicity, ² %				0.013				< 0.001	< 0.001
Non-Hispanic white	26.3 ± 6.8	32.2 ± 8.1	7.1 ± 6.7		63.5 ± 1.5	63.9 ± 1.5	63.3 ± 1.6		
Non-Hispanic black	55.3 ± 6.7	47.1 ± 7.2	82.1 ± 11.1		12.0 ± 0.8	10.8 ± 0.7	13.1 ± 0.9		
Hispanic and Mexican	15.9 ± 3.6	20.7 ± 5.0	_		17.2 ± 1.1	18 ± 1.1	16.4 ± 1.1		
Poverty-income ratio, %				0.023				< 0.001	0.003
<130%	40.3 ± 6.7	37.0 ± 7.3	51.0 ± 13.9		24.8 ± 0.8	22.7 ± 0.8	26.9 ± 0.9		
130% to <350%	40.0 ± 6.3	37.3 ± 6.7	49.0 ± 13.8		35.2 ± 0.8	35.8 ± 0.9	34.7 ± 0.8		
≥350%	19.7 ± 6.5	25.7 ± 7.8	_		39.9 ± 1.0	41.5 ± 1.0	38.4 ± 1.2		
Marital status, %				0.183				< 0.001	< 0.001
Married/living together	44.1 ± 6.4	39.4 ± 7.9	58.6 ± 10.4		68.2 ± 0.8	69.2 ± 1.0	67.1 ± 0.8		
Widowed/divorced/	16.4 ± 4.2	16.0 ± 4.4	17.6 ± 9.2		14.1 ± 0.4	12.5 ± 0.5	15.8 ± 0.5		
separated									
Never married	39.5 ± 6.0	44.6 ± 7.2	23.8 ± 8.5		17.7 ± 0.9	18.3 ± 1.1	17.1 ± 0.9		

¹ Values are estimated percentages ± SEs unless otherwise indicated. Data are from NHANES 2003–2014. Proc Descript was used for mean age comparison and Proc Crosstab procedure was used for comparing all categorical percentages by sex and by HIV status (SAS-Callable SUDAAN; RTI International).

TABLE 2 Biomarkers of nutritional status and biochemistry profile in US adults aged 19–49 y by HIV status and sex¹

	HIV-positive adults		HIV-neg	ative adults	P			
	Group A (men; $n = 65$)	Group B (women; $n = 20$)	Group C (men; <i>n</i> = 7838)	Group D (women; <i>n</i> = 7869)	Group A vs. group C	Group B vs. group D	Group A vs. group B	
BMI, kg/m ²	26.2 ± 0.7	34.3 ± 2.3	28.3 ± 0.1	28.3 ± 0.1	0.0042	0.0091	0.0009	
Overweight or obese, ² %	50.5 ± 6.1	83.5 ± 10.7	68.9 ± 0.8	59.4 ± 0.9	0.0039	0.0273	0.0090	
Waist circumference, cm	93.7 ± 2.2	107.4 ± 5.4	98.2 ± 0.3	93.0 ± 0.3	0.0463	0.0089	0.0220	
At risk, ³ %	15.2 ± 5.2	81.6 ± 11.8	35.3 ± 0.8	55.0 ± 0.9	0.0004	0.0280	< 0.0001	
Total protein, g/L	76.0 ± 1.3	79.3 ± 1.5	72.3 ± 0.1	71.2 ± 0.1	0.0042	< 0.0001	0.0864	
Albumin, g/L	41.7 ± 0.6	38.6 ± 0.8	44.6 ± 0.1	42.0 ± 0.1	< 0.0001	< 0.0001	0.0023	
Cholesterol, mmol/L	4.7 ± 0.2	4.7 ± 0.2	5.0 ± 0.0	4.9 ± 0.0	0.0412	0.3221	0.8164	
TGs, mmol/L	2.1 ± 0.2	2.1 ± 0.4	1.9 ± 0.0	1.4 ± 0.0	0.5248	0.0526	0.8322	
Serum glucose, mmol/L	5.1 ± 0.1	7.6 ± 2.4	5.3 ± 0.0	5.1 ± 0.0	0.2439	0.2921	0.2968	
Vitamin D, nmol/L	57.8 ± 4.3	43.7 ± 7.1	62.7 ± 0.8	64.6 ± 0.8	0.2821	0.0044	0.1107	
RBC folate, nmol/L	765.9 ± 62.0	914.9 ± 210.9	852.8 ± 10.3	897.7 ± 10.2	0.1843	0.9350	0.4996	
Serum folate, nmol/L	26.7 ± 2.1	24.9 ± 3.4	31.6 ± 0.5	36.3 ± 0.5	0.0261	0.0015	0.6494	

 $^{^{1}}$ Values are means \pm SEs. Data from NHANES 2003–2014 were combined. The sample sizes shown are for participation in the mobile examination center. For vitamin D, the data were available only from 2003 to 2010 (n = 10,538); for RBC folate and serum folate, data were available only from 2003 to 2012 (n = 13,600).

Discussion

In this cross-sectional national survey, HIV-positive status in women but not in men was associated with poor nutritional status, including high BMI and waist circumference, lower mean dietary intakes of many key nutrients, and suboptimal concentrations of some biomarkers of nutritional status, compared with HIV-negative adults. The mean BMI of HIV-infected women falls within the grade II obese range, indicating substantially increased risk of

cardiovascular disease, hypertension, and type 2 diabetes. Interestingly, the nutritional status of men with HIV did not differ substantially when compared with HIV-negative men; in fact, HIV-positive men had a mean BMI that more closely approximated the normal range, with a much lower waist circumference risk than any of the other groups. Indeed, men with HIV are very different than women with HIV in many ways and have >3 times higher prevalence than women (12). The CDC estimates that the majority (83%) of new HIV infection in men is among men who have sex

TABLE 3 Daily energy and nutrient intakes of US adults aged 19–49 y by sex and HIV status¹

	HIV-positive adults		HIV-neg	ative adults	P		
	Group A (men; <i>n</i> = 56)	Group B (women; <i>n</i> = 18)	Group C (men; <i>n</i> = 6410)	Group D (women; <i>n</i> = 6715)	Group A vs. group C	Group B vs. group D	
Energy, kcal	2820.4 ± 158.3	2002.2 ± 213.9	2643.3 ± 18.6	1859.5 ± 10.1	0.2621	0.5049	
Macronutrients, g							
Carbohydrate	341.1 ± 29.9	251.6 ± 32.3	315.7 ± 2.3	231.1 ± 1.4	0.3927	0.5255	
Protein	104.9 ± 6.0	83.5 ± 6.1	104.4 ± 0.7	71.3 ± 0.5	0.9305	0.0469	
Fat	105.5 ± 5.7	67.9 ± 8.6	98.7 ± 0.9	70.1 ± 0.6	0.2407	0.8044	
Fiber	17.9 ± 1.8	9.2 ± 1.5	18.7 ± 0.2	14.7 ± 0.2	0.6816	0.0004	
Micronutrients							
Vitamin A (RAEs²), μg	689.5 ± 83.1	439.9 ± 77.0	671.7 ± 9.4	568.2 ± 10.1	0.8296	0.0988	
Thiamin, mg	2.0 ± 0.2	1.4 ± 0.1	2.0 ± 0.0	1.4 ± 0.0	0.9131	0.9369	
Riboflavin, mg	2.4 ± 0.2	1.7 ± 0.2	2.6 ± 0.0	1.9 ± 0.0	0.3897	0.1438	
Niacin, mg	29.6 ± 1.7	25.7 ± 1.5	32.7 ± 0.3	21.8 ± 0.1	0.0700	0.0112	
Folate, μg	466.4 ± 49.7	347.8 ± 28.4	488.5 ± 4.8	362.0 ± 4.2	0.6514	0.6212	
Vitamin B-6, mg	2.3 ± 0.1	1.8 ± 0.2	2.6 ± 0.0	1.8 ± 0.0	0.0410	0.7467	
Vitamin B-12, μg	5.6 ± 0.6	6.3 ± 1.3	6.6 ± 0.1	4.4 ± 0.1	0.0853	0.1476	
Vitamin C, mg	89.3 ± 12.2	74.7 ± 18.3	92.4 ± 1.7	77.4 ± 1.5	0.8026	0.8805	
Vitamin E, mg	8.9 ± 0.8	4.6 ± 0.6	9.1 ± 0.1	7.2 ± 0.1	0.7101	0.0001	
Vitamin K, μg	102.4 ± 15.5	48.5 ± 9.2	106.0 ± 2.4	101.2 ± 2.4	0.8114	< 0.0001	
Calcium, mg	1171.2 ± 92.6	711.8 ± 78.6	1140.6 ± 11.5	863.3 ± 8.7	0.7439	0.0582	
Iron, mg	18.8 ± 1.6	14.6 ± 1.3	18.6 ± 0.2	13.5 ± 0.1	0.9394	0.3743	
Magnesium, mg	337.2 ± 23.9	194.7 ± 22.1	345.2 ± 3.0	261.1 ± 2.7	0.7402	0.0036	
Phosphorus, mg	1714.5 ± 106.4	1149.4 ± 104.3	1678.2 ± 13.1	1191.1 ± 8.6	0.7356	0.6884	
Sodium, mg	4818.7 ± 262.9	2927.3 ± 276.5	4343.8 ± 31.9	3070.5 ± 18.2	0.0767	0.6060	
Potassium, mg	3069.5 ± 174.2	1877.1 ± 157.3	3085.2 ± 23.7	2319.8 ± 18.5	0.9291	0.0058	
Zinc, mg	14.6 ± 1.0	10.9 ± 1.1	14.8 ± 0.2	10.1 ± 0.1	0.9044	0.4552	

¹ Values are means ± SEs. Dietary data from NHANES 2003–2014 were combined to estimate mean total nutrient intakes.

²Overweight (BMI >25) and obese (BMI >30) were combined for this analysis.

³Waist circumference: >88 cm for women and >102 cm for men.

²RAE, retinol activity equivalent.

with men, whereas infection rates in women are not as related to sexual orientation (21). Data from multiple sources indicate that HIV infection is higher in non-Hispanic blacks than in other race/ethnic groups in both men and women (12, 21, 22).

Before the availability of ART, weight loss was an important diagnostic criterion for HIV and a distinguishing feature of AIDS (23, 24). However, in this post-ART analysis, the risk of overweight and obesity, specifically for women, was observed. A study by Sharma et al. (25) suggested that HIV-positive women receiving ART treatment gain weight, although ART use was associated with only modest change in BMI. A cohort study that followed HIV-infected adults in the United States and Canada also reported that HIV-positive white women had a higher BMI after 3 y of ART compared with their age-matched NHANES controls, whereas no such difference was observed for HIV-positive men or nonwhite women (26). Previous CDC reports indicate that approximately half of US adults with HIV report the use of ART (12). Given the dramatic differences in the BMI of men and women with HIV, the use of ART alone is unlikely responsible for the obesity observed in women with HIV. Future work should seek to understand the relations of HIV and overweight and obesity in women, and whether the association is driven by race/ethnicity or other factors. Previous studies have not observed an association of BMI and HIV status but have documented higher waist circumferences in HIV-infected adults than in HIV-negative adults (27).

Total protein concentrations were higher and albumin concentrations were lower in both men and women with HIV when compared within sexes with noninfected adults, which is consistent with other studies (9, 28, 29). Lower serum albumin may be indicative of poor nutritional status or other health conditions and is an independent predictor of mortality in HIV-infected women (30). Among both men and women with HIV, lower concentrations of serum folate were observed, with no differences in RBC folate, when compared with HIV-negative adults. Although HIV infection is associated with anemia of chronic disease, we were unable to confirm the antecedents of low serum folate alone. Both HIV status (31-33) and ART (34-36) are individual predictors of vitamin D status and bone health. HIV-infected women with vitamin D deficiency have a higher risk of developing osteoporosis than do HIV-negative controls with vitamin D deficiency (37-42). Similar to other studies, this NHANES analysis also suggests that HIV-positive women are at higher risk of vitamin D inadequacy (<50 nmol/L), defined by the National Academy of Medicine, which could be one of the contributing causes of the high prevalence of osteopenia or osteoporosis among HIV-infected adults receiving ART (43).

To our knowledge, this is the first study to characterize the nutritional status of people living with HIV in a nationally representative sample of US adults. However, this national survey is not designed specifically for HIV and diseases with a low population prevalence. Furthermore, a limited number of nutritional biomarkers were available across multiple years in NHANES. Limitations exist with selfreported dietary intake, including a well-known and characterized energy underreporting bias (44). Due to the small number of participants who were HIV positive, it would not be possible to provide reliable estimates by stratifying on other factors beyond sex; however, given the strong association with infection and race/ ethnicity, future work should seek to address how race/ethnicity influences nutrition and infection. Similarly, the very small sample sizes, particularly among women, indicate that much more data are needed to understand the nutritional needs associated with HIV infection in the United States. Our results should be considered with these caveats in mind. The findings of this report should be a call to action that much more data are needed on the nutritional aspects of living with HIV in America.

Acknowledgments

We thank Victor Fulgoni (Nutrition Impact LLC) and Jaime Gahche (NIH/Office of Dietary Supplements) who provided unpaid consultation on the NHANES methodology and provided guidance on the data analysis. The authors' responsibilities were as follows-SVT: designed the project and performed the preliminary data analysis; SJ and AC: prepared the tables and confirmed the data presented within this manuscript that were originally prepared by SVT; and all authors: performed the literature search, drafted sections of the manuscript, aided in data interpretation, and read and approved the final manuscript.

References

- 1. Hughes S, Kelly P. Interactions of malnutrition and immune impairment, with specific reference to immunity against parasites. Parasite Immunol 2006;28:577-88.
- 2. Guenter P, Muurahainen N, Simons G, Kosok A, Cohan GR, Rudenstein R, Turner JL. Relationships among nutritional status, disease progression, and survival in HIV infection. J Acquir Immune Defic Syndr 1993;6:1130-8.
- 3. Tang AM, Quick T, Chung M, Wanke CA. Nutrition assessment, counseling, and support interventions to improve health-related outcomes in people living with HIV/AIDS: a systematic review of the literature. J Acquir Immune Defic Syndr 2015;68(Suppl 3):S340-9.
- 4. WHO. Nutrient requirements for people living with HIV/AIDS: report of a technical consultation. Geneva (Switzerland): WHO; 2003.
- 5. Young JS. HIV and medical nutrition therapy. J Am Diet Assoc 1997;97: S161-6.
- 6. Islam FM, Wu J, Jansson J, Wilson DP. Relative risk of cardiovascular disease among people living with HIV: a systematic review and metaanalysis. HIV Med 2012;13:453-68.
- 7. Gutierrez J, Albuquerque ALA, Falzon L. HIV infection as vascular risk: a systematic review of the literature and meta-analysis. PLoS One 2017;12:e0176686.
- 8. Gutierrez AD, Balasubramanyam A. Dysregulation of glucose metabolism in HIV patients: epidemiology, mechanisms, and management. Endocrine 2012;41:1-10.
- 9. Fields-Gardner C, Campa, A; American Dietetic Association. Position of the American Dietetic Association: nutrition intervention and human immunodeficiency virus infection. J Am Diet Assoc 2010;110:1105-19.
- 10. CDC. Today's HIV/AIDS epidemic [Internet]. [cited 2016 Apr 1]. Available from: https://www.cdc. gov/nchhstp/newsroom/docs/factsheets/todaysepidemic-508.pdf.
- 11. McQuillan GM, Kruszon-Moran D. HIV infection in the United States household population aged 18-49 years: results from 1999-2006. NCHS Data Brief 2008;4:1-8.
- 12. Woodring J, Kruszon-Moran D, McQuillan G. HIV infection in U.S. household population aged 18-59: data from the National Health and Nutrition Examination Survey, 2007-2012. Natl Health Stat Report 2015;83:1-13.

- Zipf G, Chiappa M, Porter KS, Ostchega Y, Lewis BG, Dostal J. National health and nutrition examination survey: plan and operations, 1999-2010. Vital Health Stat 1 2013;56:1–37.
- Mohadjer LMJ, Waksberg J. National Health and Nutrition Examination Survey III: weighting and examination methodology. Hyattsville (MD): Westat, Inc.; 1996.
- 15. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA 2014;311:806–14.
- 16. US Department of Health and Human Services; National Center for Health Statistics; CDC. NHANES III anthropometric procedures video, stock number 017-022-01335-5. Washington (DC): US Government Printing Office; 1996.
- 17. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. Obes Res 1998;6(Suppl 2):51S–209S.
- CDC. National Health and Nutrition Examination Survey (NHANES) MEC laboratory procedures manual. Hyattsville (MD): CDC; 2013.
- Blanton CA, Moshfegh AJ, Baer DJ, Kretsch MJ. The USDA automated multiple-pass method accurately estimates group total energy and nutrient intake. J Nutr 2006;136:2594–9.
- 20. Moshfegh AJ, Rhodes DG, Baer DJ, Murayi T, Clemens JC, Rumpler WV, Paul DR, Sebastian RS, Kuczynski KJ, Ingwersen LA, et al. The US Department of Agriculture automated multiple-pass method reduces bias in the collection of energy intakes. Am J Clin Nutr 2008;88:324–32.
- CDC. HIV infection among gay and bisexual men [Internet]. [cited 2017 Sep 3]. Available from: https://www.cdc. gov/hiv/group/msm/index.html.
- CDC. Characteristics associated with HIV infection among heterosexuals in urban areas with high AIDS prevalence—24 cities, United States, 2006-2007. MMWR Morb Mortal Wkly Rep 2011;60: 1045-9.
- CDC. HIV among people aged 50 and over. Hyattsville (MD): CDC;
 2014
- 24. Atkinson BE, Krishnan S, Cox G, Hulgan T, Collier AC. Anthropometric differences between HIV-infected individuals prior to antiretroviral treatment and the general population from 1998-2007: the AIDS Clinical Trials Group Longitudinal Linked Randomized Trials (ALLRT) cohort and NHANES. PLoS One 2013;8:e65306.
- Sharma A, Bynum SA, Schneider MF, Cox C, Tien PC, Hershow RC, Gustafson D, Plankey MW. Changes in body mass index following HAART initiation among HIV-infected women in the Women's Interagency HIV Study. J AIDS Clin Res 2014;5:1000323.
- 26. Koethe JR, Jenkins CA, Lau B, Shepherd BE, Justice AC, Tate JP, Buchacz K, Napravnik S, Mayor AM, Horberg MA, et al. Rising obesity prevalence and weight gain among adults starting antiretroviral therapy in the United States and Canada. AIDS Res Hum Retroviruses 2016;32:50–8.
- Lo J, You SM, Wei J, Canavan B, Grinspoon S. Relationship of peak growth hormone to cardiovascular parameters, waist circumference, lipids and glucose in HIV-infected patients and healthy adults. Clin Endocrinol (Oxf) 2009;71:815–22.
- Linares ME, Bencomo JF, Perez LE, Torrez O, Barrera O. [Influence of HIV/AIDS infection on some biochemical indicators of the nutritional status.] Biomedica 2002;22:116–22 (in Spanish).
- Mehta SH, Astemborski J, Sterling TR, Thomas DL, Vlahov D. Serum albumin as a prognostic indicator for HIV disease progression. AIDS Res Hum Retroviruses 2006;22:14–21.

- 30. Feldman JG, Burns DN, Gange SJ, Bacchetti P, Cohen M, Anastos K, Nowicki M, Delapena R, Miotti P. Serum albumin as a predictor of survival in HIV-infected women in the Women's Interagency HIV Study. AIDS 2000;14:863–70.
- Bearden A, Abad C, Gangnon R, Sosman JM, Binkley N, Safdar N. Cross-sectional study of vitamin D levels, immunologic and virologic outcomes in HIV-infected adults. J Clin Endocrinol Metab 2013;98: 1726–33.
- Panayiotopoulos A, Bhat N, Bhangoo A. Bone and vitamin D metabolism in HIV. Rev Endocr Metab Disord 2013;14:119–25.
- 33. Mangili A, Murman DH, Zampini AM, Wanke CA. Nutrition and HIV infection: review of weight loss and wasting in the era of highly active antiretroviral therapy from the nutrition for healthy living cohort. Clin Infect Dis 2006;42:836–42.
- 34. Paton NI, Sangeetha S, Earnest A, Bellamy R. The impact of malnutrition on survival and the CD4 count response in HIV-infected patients starting antiretroviral therapy. HIV Med 2006;7:323–30.
- 35. Klassen K, Martineau AR, Wilkinson RJ, Cooke G, Courtney AP, Hickson M. The effect of tenofovir on vitamin D metabolism in HIV-infected adults is dependent on sex and ethnicity. PLoS One 2012;7: e44845.
- 36. Schwartz JB, Moore KL, Yin M, Sharma A, Merenstein D, Islam T, Golub ET, Tien PC, Adeyemi OM. Relationship of vitamin D, HIV, HIV treatment, and lipid levels in the Women's Interagency HIV Study of HIV-infected and uninfected women in the United States. J Int Assoc Provid AIDS Care 2014;13:250–9.
- 37. Brown TT. Challenges in the management of osteoporosis and vitamin D deficiency in HIV infection. Top Antivir Med 2013;21:115–8.
- 38. Lo Re V III, Lynn K, Stumm ER, Long J, Nezamzadeh MS, Baker JF, Hoofnagle AN, Kapalko AJ, Mounzer K, Zemel BS, et al. Structural bone deficits in HIV/HCV-coinfected, HCV-monoinfected, and HIVmonoinfected women. J Infect Dis 2015;212:924–33.
- 39. Mehta S, Mugusi FM, Spiegelman D, Villamor E, Finkelstein JL, Hertzmark E, Giovannucci EL, Msamanga GI, Fawzi WW. Vitamin D status and its association with morbidity including wasting and opportunistic illnesses in HIV-infected women in Tanzania. AIDS Patient Care STDS 2011;25:579–85.
- Schafer JJ, Manlangit K, Squires KE. Bone health and human immunodeficiency virus infection. Pharmacotherapy 2013;33:665– 82
- 41. Yin M, Dobkin J, Brudney K, Becker C, Zadel JL, Manandhar M, Addesso V, Shane E. Bone mass and mineral metabolism in HIV+postmenopausal women. Osteoporos Int 2005;16:1345–52.
- 42. Haug CJ, Aukrust P, Haug E, Morkrid L, Muller F, Froland SS. Severe deficiency of 1,25-dihydroxyvitamin D3 in human immunodeficiency virus infection: association with immunological hyperactivity and only minor changes in calcium homeostasis. J Clin Endocrinol Metab 1998; 83:3832–8.
- 43. Escota GV, Mondy K, Bush T, Conley L, Brooks JT, Onen N, Patel P, Kojic EM, Henry K, Hammer J, et al. High prevalence of low bone mineral density and substantial bone loss over 4 years among HIV-infected persons in the era of modern antiretroviral therapy. AIDS Res Hum Retroviruses 2016;32:59–67.
- 44. Subar AF, Freedman LS, Tooze JA, Kirkpatrick SI, Boushey C, Neuhouser ML, Thompson FE, Potischman N, Guenther PM, Tarasuk V, et al. Addressing current criticism regarding the value of self-report dietary data. J Nutr 2015;145:2639–45.