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The relationship of 25-hydroxyvitamin D concentrations and individual-level socioeconomic status

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Abstract

Socioeconomic status (SES), defined as the ability to access desired resources, is associated with behaviors that may affect vitamin D status. Most studies of the effect of vitamin D status on outcomes do not account for individual-level SES. The ability to adjust for SES in epidemiologic studies, when data on conventional SES measures have not been obtained, would be advantageous. We identified all serum 25(OH)D measurements in adults age 18 years and older residing in Olmsted County, MN, a mixed urban-rural setting, between January 1, 2005 and December 31, 2011, through the Rochester Epidemiology Project. The first 25(OH)D measurement was considered the index measurement for each subject. SES was determined for each subject by the HOUSing-based SocioEconomic Status (HOUSES) index, derived from real property data. The HOUSES index is an aggregated z-score of assessed housing value, area of living space, number of bedrooms, and number of bathrooms, with higher scores indicating higher SES. Multivariable analyses were adjusted for age, BMI, sex, race, season of 25(OH)D measurement, and Charlson comorbidity index. HOUSES was matched for 10,378 of 11,002 subjects (94%) with 25(OH)D measurements available. The mean (SD) age was 54.3 (17.1) years with 26.9% ≥ 65 years; 77.3% were women, and 12.1% were non-white. The mean 25(OH)D concentration was 30.0 (12.9) ng/mL, and 598 (5.8%) had a 25(OH)D value < 12 ng/mL. The mean (SD) HOUSES was -1.55 (3.09), -0.97 (3.34), 0.14 (3.52), 0.24 (3.51) for serum 25(OH)D categories of <12, 12–19, 20–50, and >50 ng/mL, respectively (P=0.12 for trend). 25(OH)D increased by 0.43 (95% CI 0.36–0.50) ng/mL for each unit increase in HOUSES in univariate analysis and by 0.28 (0.21–0.35; P<0.001) ng/mL in multivariable analysis. This represents a change of 4 ng/mL across the entire range of observed HOUSES, an effect similar in magnitude to the seasonal variation of 25(OH)D values. SES was independently associated with serum 25(OH)D concentrations in a dose-response manner

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after adjustment for important covariates. HOUSES is a useful tool to assess the role of individual-level SES in health outcomes when other SES measures are unavailable and to control for confounding by SES in examining the effect of 25(OH)D on clinical and metabolic outcomes.

Keywords

vitamin D; epidemiology; mortality; nutrition; health disparities

1. Introduction

Socioeconomic status (SES) is defined as one's ability to access to desired resources,¹ which may be associated with behaviors that affect vitamin D status. These behaviors can affect vitamin D status through diet, exercise, sun exposure, and supplement use. Serum 25-hydroxyvitamin-D [25(OH)D] concentrations are used to assess vitamin D status. Epidemiologic studies have examined the effects of 25(OH)D values on clinically important outcomes like mortality, cardiovascular disease, fractures, and cancer incidence. SES is associated with these outcomes and may be an important confounder in epidemiologic studies. Furthermore, SES has an impact on pathways underlying health disparities from biological effects to social policy.²

Most studies of the effect of vitamin D status on outcomes do not account for individual-level socioeconomic status (SES).^{3–11} Studies based on the Third National Health and Nutrition Examination Survey (NHANES III) data assessed SES with the ratio of a family's income to the poverty threshold of a family of the same size (poverty:income ratio),¹² which was an important covariate in adjustment for the effect of 25(OH)D on mortality. A lower poverty:income ratio was associated with 25(OH)D < 10 ng/mL (25 nmol/L).¹² When this ratio was dichotomized, with low SES defined as 200% of the poverty index or lower, low SES was associated with a higher risk of vitamin D deficiency in unadjusted analysis but lower risk in an adjusted analysis that included race and physical activity.¹³ Others have used education as a proxy for SES.¹⁴ While these measures may reflect individual level SES, they could be subject to social desirability, recall bias from self-report, and within-group heterogeneity (ie, variability of earnings in each educational category),^{15,16} which could be reason for inconsistent results in the literature. Additionally, large retrospective studies (e.g., registry or electronic health record-based studies), without survey data for SES, generally lack individual level SES. Accurately adjusting for individual level SES in epidemiologic studies of vitamin D is necessary to evaluate the independent effect of vitamin D status on outcomes.

The HOUsing-based SocioEconomic Status (HOUSES) index is a validated individual level SES measure for large-scale clinical and epidemiological studies, associated with numerous health outcomes, health behaviors, health care access and care quality in adults and children.^{17–20} A patient's address information, available in medical records, is directly linked to publicly available real property data, reflecting a patient's current wealth or income, thus conceptually it can be used as an objective SES measure. It does not require completion of questionnaires by study subjects to obtain socioeconomic data, and socioeconomic status

can be calculated through simple linkage to the subject's address. Our objective was to determine the relationship of vitamin D status with socioeconomic status as measured by HOUSES index.

2. Methods

2.1 Olmsted County and the Rochester Epidemiology Project

We selected study subjects from the Rochester Epidemiology Project (REP) database, a population-based medical record linkage system that includes health care utilization, diagnostic and laboratory data for virtually all medical care within Olmsted County, Minnesota, covering 98% of all health care services provided for Olmsted County residents.^{21,22} Over 95% of the Olmsted County population has granted authorization for their records to be used for research.^{23,24} Olmsted County, MN is a mixed urban-rural setting located in the Upper-Midwestern United States with limited sun exposure in winter (44° north latitude). The Olmsted County population was 148,700 in 2011, and in the 2010 census, the proportions of Olmsted County residents classified as white, black, Asian and Hispanic were 86%, 4.8%, 5.5%, and 4.2%, respectively. Compared with the entire U.S. 2010 population, the county is less ethnically diverse (72% versus 86% white), more educated (85% versus 94% high school graduates) and wealthier (\$51,914 versus \$64,090 median household income). However, characteristics of the population are very similar to the overall population of the Upper-Midwestern United States.²⁴

2.2 Patient Selection and Outcomes

We identified all initial serum 25(OH)D measurements in persons age 18 years and older residing in Olmsted County, MN between 01/01/2005 and 12/31/2011. We collected data on age, sex, race, Charlson Comorbidity Index (CCI), smoking status, and body mass index (BMI) at the time of initial 25(OH)D measurement. Diagnoses of hypertension, hyperlipidemia, and osteoporosis in the medical record prior to the date of 25(OH)D measurement were recorded.

2.3 HOUSES Index and Psychometric Properties

We used HOUSES index data to assess individual SES at the time of initial 25(OH)D measurement. For generating the HOUSES index, we retrieved subject addresses from the REP, which collects and maintains all historical individual addresses during residence in Olmsted County. The HOUSES index is a robust individual measure of SES represented by a single factor made up of four items (number of bedrooms, number of bathrooms, square footage of the unit, and estimated building value of the unit) ascertained from the county Assessor's office.²⁵

Variables were aggregated into an overall z-score such that a higher HOUSES score indicated higher SES. HOUSES index has demonstrated criterion validity with moderate to good correlations with education, income, Hollingshead Index, and Nakao-Treas Index (NT) in Olmsted County, MN and Jackson County, MO.²⁵ HOUSES index has construct validity, predicting a broad range of health behavior (e.g. smoking exposure) and outcomes (e.g. obesity, preterm birth, and general health), conceptually and empirically associated with

SES.²⁵ While HOUSES has moderate to good correlation with other conventional SES measures, it better predicts health outcomes than other SES measures.^{25–27}

2.4 Laboratory Methods

All 25(OH)D tests ordered in Olmsted County during the study interval were measured at the Mayo Clinic Laboratory using isotope-dilution liquid chromatography tandem mass spectrometry (LC-MS/MS).²⁸ For this study, 25(OH)D refers to the sum of 25(OH)D₂ and 25(OH)D₃. Interassay coefficients of variation (CV) for 25(OH)D₂ were 6–14% and for 25(OH)D₃ were 6–13% in control samples. The recovery of analyte spiked into patient samples was 82–115% (mean, 102%) of predicted for 25(OH)D₂ and 88–115% (mean, 103%) for 25(OH)D₃. The limit of detection was 4 ng/mL. Throughout the study interval, Mayo Clinic Laboratory participated in the CDC Vitamin D standardization program. The relationship between serum 25(OH)D and all-cause and cause-specific mortality in this cohort are reported elsewhere.¹⁰

2.5 Statistical Analysis

All analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC). Serum 25(OH)D was examined as a continuous variable and as a categorical variable using predetermined ranges of interest: 25(OH)D values <12, 12–19, 20–50 (reference category), and >50 ng/mL. The association between serum 25(OH)D and SES was assessed using bivariate and multivariable linear regression. Non-linear models were tested but did not provide substantial improvement in fit. Multivariable analysis was adjusted for age, sex, race, month of 25(OH)D measurement, and Charlson comorbidity index at the time of 25(OH)D measurement. These variables were selected to provide the simplest model that maintained the maximum R². Local regression was used to create a smoothed fit of the data to help us determine if linear regression was appropriate for this data.

3. Results

3.1 Study Subjects

HOUSES was successfully geocoded for 10,378 of 11,002 subjects (94%) with 25(OH)D measurements between 2005 and 2011. The mean (\pm SD) serum 25(OH)D concentration for the population was 30.0 \pm 12.9 ng/mL with a mean age of 54.3 \pm 17.1 y (Table 1). A total of 598 (5.7%) had 25(OH)D values <12 ng/mL. The cohort was mostly female (77.3%) and white (87.9%). In comparison with the overall population of Olmsted County (Table 2), those who had 25(OH)D measurements were more likely older, female, white, smokers, and have hypertension,

3.2 Association of HOUSES with Subject Characteristics

In bivariate regression analysis, greater HOUSES Index was associated with younger age, male sex, and white race (Table 3). Health risk factors, including Charlson Comorbidity Index, greater BMI, smoking, hypertension, hyperlipidemia, and osteoporosis, were associated with lower HOUSES Index. Lower serum 25(OH)D values were associated with lower HOUSES Index.

3.3 Association of 25(OH)D with HOUSES and Subject Characteristics

Serum 25(OH)D values were positively associated with advancing age, female sex, white race, Charlson Comorbidity Index, hyperlipidemia, osteoporosis, and greater HOUSES Index (Table 4). Greater BMI, smoking, and hypertension were associated with lower serum 25(OH)D values.

A multivariable analysis was performed to identify the optimal model of subject characteristics independently associated with serum 25(OH)D concentrations (Table 5). In the final model, advancing age, female sex, white race, and greater HOUSES Index were associated with greater serum 25(OH)D values, while Charlson Comorbidity Index, BMI, and winter season were associated with lower 25(OH)D values. Greater HOUSES Index remained positively associated with serum 25(OH)D values in the model controlling for these other characteristics ($R^2=0.13$ for complete model). The variables not in the final model were smoking, hypertension, hyperlipidemia, and osteoporosis. The multivariable model including these additional variables had the same $R^2=0.13$ and had minimal effect on the coefficient (0.25) or significance of the HOUSES Z.

SES was independently associated with serum 25(OH)D concentrations in a dose-response manner. Serum 25(OH)D increased by 0.28 (0.21–0.35; $P<0.001$) ng/mL per unit change in HOUSES in multivariable analysis. This represents a change of 4 ng/mL over the range of observed HOUSES indices, which is similar in magnitude to the effect of summer season compared with winter, based on adjusted seasonal data from our cohort (Table 5). A local regression/smoothed fit analysis demonstrated greater decrease in serum 25(OH)D values with HOUSES Index below -1.0 than with the linear regression fit (Figure 1).

4. Discussion

We found that serum 25(OH)D values were positively associated with individual-level SES as assessed by the HOUSES Index. This positive relationship remained significant after adjusting for important covariates affecting 25(OH)D values, and the magnitude of the effect over the range of observed SES statuses was similar to the seasonal variation of 25(OH)D values. The clinical significance of this magnitude of variation needs to be determined in the context of subgroups and outcomes of interest to be examined in the future.

Other studies have assessed the relationship of vitamin D status with aspects of socioeconomic status in varying populations. Among healthy schoolgirls in Delhi, stratified by upper or lower socioeconomic status, those in the upper socioeconomic stratum had lower 25(OH)D levels and lower sun exposure.²⁹ In a study of socioeconomic factors associated with vitamin D deficiency in young adults (18–25 years old) in Copenhagen, Denmark, less exercise, greater BMI, alcohol abstinence, and smoking were modifiable risk factors independently associated with vitamin D deficiency.³⁰ We observed a magnitude of seasonal variation in 25(OH)D values (3.9 ng/mL) that was similar to values reported in other studies, ranging from 2.6 to 6.9 ng/mL, with differences based on sex, age, and geographic location.^{31–33}

The prevalence of 25(OH)D values <20 ng/mL in our cohort was 20.4%. This is similar to a representative sample of the Canadian population (20%), which has similar racial/ethnic diversity to Olmsted County, MN.³² The prevalence is lower than the United States sample from the 2001–2006 NHANES survey (32%).³⁴ However, the NHANES report included a much higher proportion of non-white patients (30.2%, compared to 12.1% in our study), which likely accounts for this difference.

Many observational studies and meta-analyses have assessed the association of vitamin D status with various outcomes, including mortality, fractures, cardiovascular disease, and cancers.^{3–11,13} These studies generally confirm an association of low vitamin D status with mortality, fractures, cardiovascular disease, and cancer. However, vitamin D deficiency may be a marker of disease risk but not causally related to the risk of these events.

It is difficult to assess SES without collecting additional data through subject questionnaires, which makes retrospective cohort studies difficult to perform if SES data were not previously collected. HOUSES has the advantage of permitting determination of SES using only the subject's address and publically available individual-level real property data, and unlike neighborhood level data, it can be determined at the individual level. HOUSES is useful for overcoming the absence of conventional SES measures in commonly used datasets in epidemiological research. SES is associated with many important outcomes, like mortality and cancer. Adjustment for SES may help overcome some of the limitations of observational studies by capturing the effects of some unmeasured variables associated with both vitamin D status and outcomes.

This study had several limitations. The specific behaviors that were associated with SES and vitamin D status were not identified. We did not obtain data regarding behaviors related to vitamin D status, like dietary intake of vitamin D, supplement use, exercise, and sun exposure, which likely differ by SES. The relationship of SES with vitamin D status is likely explained in part by these behaviors. The sample is not a true population sample, as it included only those who presented for care and had 25(OH)D measured, and women are overrepresented. Women are at greater risk of osteoporosis than men, likely leading to more 25(OH)D measurements in women. Osteoporosis was associated with greater 25(OH)D values, likely due to vitamin D supplementation. Although we found a relationship of 25(OH)D with SES in those with indications for 25(OH)D measurement, this relationship may not be generalizable to the population that did not have 25(OH)D measured. This sampling bias would be unlikely to directly affect the relationship of 25(OH)D with SES, but we do not have data in those without 25(OH)D measurements to conclusively demonstrate this. The population was representative of the upper Midwest, but the findings may be difficult to generalize more broadly to other socioeconomic contexts and ethnic groups. Another limitation is that HOUSES has not been validated outside of the United States.

We conclude that HOUSES is a useful tool for assessing the role of individual-level SES in health outcomes, especially when other SES measures are not available, and could be used to control for confounding by SES in examining the effect of 25(OH)D on clinical and metabolic outcomes.

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Highlights

- Socioeconomic factors are associated with behaviors that may affect vitamin D status.
- Socioeconomic status (SES) measured with HOUSES was independently associated with serum 25(OH)D in a dose-response manner, with an effect similar in magnitude to the seasonal variation of 25(OH)D values.
- HOUSES is a useful tool to assess the role of individual-level SES in health outcomes when other SES measures are unavailable and to control for confounding by SES in examining the effect of 25(OH)D on clinical and metabolic outcomes.

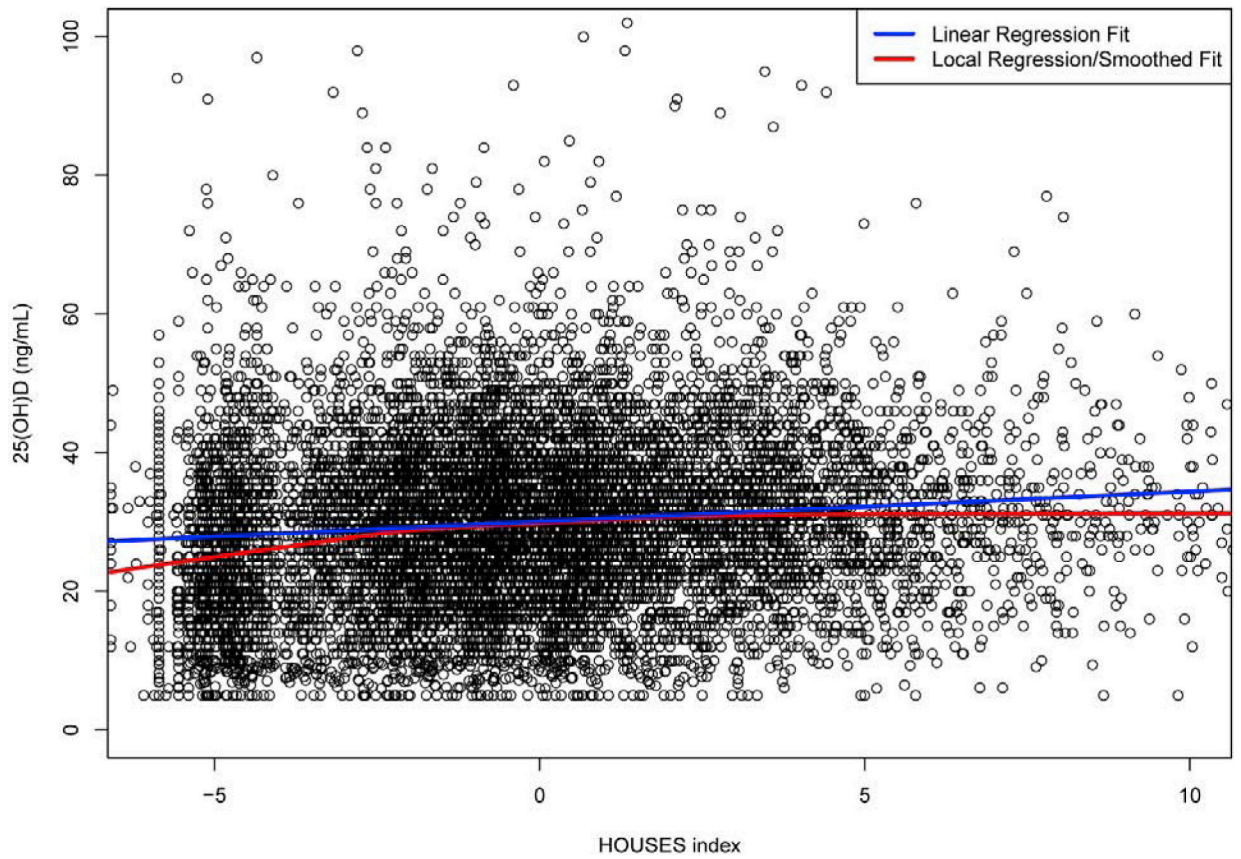


Figure 1.
Relationship of Serum 25(OH)D with HOUSES Index.

Table 1.

Characteristics of study subjects.

	25(OH)D Categories (ng/mL)				
	Total (N=10378)	<12 (N=598)	12–19 (N=1514)	20–50 (N=7749)	>50 (N=517)
25(OH)D, Mean (SD), ng/mL	30.01 (12.86)	8.48 (2.06)	15.85 (2.28)	32.36 (7.65)	61.07 (15.81)
Age, mean (SD), years	54.28 (17.09)	51.09 (18.09)	51.77 (16.97)	54.91 (16.91)	55.91 (17.82)
Age groups, n (%)					
18–49 yr	3986 (38.4%)	293 (49.0%)	682 (45.0%)	2831 (36.5%)	180 (34.8%)
50–64 yr	3603 (34.7%)	179 (29.9%)	519 (34.3%)	2733 (35.3%)	172 (33.3%)
65 yr	2789 (26.9%)	126 (21.1%)	313 (20.7%)	2185 (28.2%)	165 (31.9%)
Sex, n (%)					
Female	8019 (77.3%)	436 (72.9%)	1112 (73.4%)	6010 (77.6%)	461 (89.2%)
Male	2359 (22.7%)	162 (27.1%)	402 (26.6%)	1739 (22.4%)	56 (10.8%)
Race, n (%)					
White	9120 (87.9%)	393 (65.7%)	1149 (75.9%)	7081 (91.4%)	497 (96.1%)
Non-white	1257 (12.1%)	205 (34.3%)	365 (24.1%)	667 (8.6%)	20 (3.9%)
Season, n (%)					
Winter, Dec–Feb	2596 (25.0%)	210 (35.1%)	461 (30.4%)	1825 (23.6%)	100 (19.3%)
Spring, Mar–May	2713 (26.1%)	201 (33.6%)	478 (31.6%)	1891 (24.4%)	143 (27.7%)
Summer, Jun–Aug	2355 (22.7%)	80 (13.4%)	231 (15.3%)	1911 (24.7%)	133 (25.7%)
Fall, Sept–Nov	2714 (26.2%)	107 (17.9%)	344 (22.7%)	2122 (27.4%)	141 (27.3%)
Charlson index, mean (SD)	3.38 (3.40)	3.73 (4.12)	3.24 (3.47)	3.37 (3.34)	3.52 (3.22)
BMI, mean (SD)	28.83 (7.47)	31.69 (10.03)	31.13 (8.30)	28.37 (6.98)	25.68 (6.03)
HOUSES Z, mean (SD)	–0.12 (3.51)	–1.55 (3.09)	–0.98 (3.35)	0.14 (3.52)	0.24 (3.50)
Ever Smoked					
Missing	697	44	110	520	23
No	4918 (50.8%)	244 (44.0%)	649 (46.2%)	3768 (52.1%)	257 (52.0%)
Yes	4763 (49.2%)	310 (56.0%)	755 (53.8%)	3461 (47.9%)	237 (48.0%)
Hypertension					
No	5977 (57.6%)	300 (50.2%)	846 (55.9%)	4518 (58.3%)	313 (60.5%)
Yes	4401 (42.4%)	298 (49.8%)	668 (44.1%)	3231 (41.7%)	204 (39.5%)
Hyperlipidemia					
No	4768 (45.9%)	309 (51.7%)	724 (47.8%)	3517 (45.4%)	218 (42.2%)
Yes	5610 (54.1%)	289 (48.3%)	790 (52.2%)	4232 (54.6%)	299 (57.8%)
Osteoporosis					
No	8265 (79.7%)	511 (85.6%)	1291 (85.3%)	6089 (78.7%)	374 (72.6%)
Yes	2102 (20.3%)	86 (14.4%)	223 (14.7%)	1652 (21.3%)	141 (27.4%)

Table 2.

Comparison of subject characteristics between those who had 25(OH)D measurements and the entire Olmsted County population, ages 18 years and older on January 1, 2010.

Characteristic	25(OH)D Cohort (N=11,002)	Olmsted (N=106,869)	P value
Age groups, n (%)			<0.001
18–49 yr	4235 (38.5)	62400 (58.4)	
50–64 yr	3779 (34.3)	26483 (24.8)	
65 yr	2988 (27.2)	17986 (16.8)	
Sex, n (%)			<0.001
Women	8482 (77.1)	57472 (53.8)	
Men	2520 (22.9)	49397 (46.2)	
Race, n (%)			<0.001
White	9637 (87.6)	91587 (85.7)	
Non-white	1365 (12.4)	15282 (14.3)	
Ever Smoked, n (%)			<0.001
No	5204 (50.8)	62839 (58.8)	
Yes	5050 (49.2)	44030 (41.2)	
Hypertension, n (%)			<0.001
No	6344 (57.7)	76304 (71.4)	
Yes	4658 (42.3)	30565 (28.6)	

Table 3:

Bivariate Linear Regression Analysis of Subject Characteristics Associated with HOUSES Index.

Characteristic	Estimate (95% CI)	R ²	p-value
Age (per decade)	-0.15 (-0.19, -0.11)	0.005	<0.001
Sex (M vs F)	0.30 (0.14, 0.46)	0.001	<0.001
Race (White vs Non-White)	1.02 (0.81, 1.22)	0.01	<0.001
Charlson Comorbidity Index (per unit)	-0.14 (-0.16, -0.12)	0.02	<0.001
BMI (per unit)	-0.07 (-0.08, -0.07)	0.03	<0.001
Ever Smoked (Y vs N)	-1.10 (-1.24, -0.96)	0.02	<0.001
Hypertension (Y vs N)	-0.93 (-1.07, -0.80)	0.02	<0.001
Hyperlipidemia	-0.30 (-0.44, -0.16)	0.002	<0.001
Osteoporosis	-0.58 (-0.75, -0.41)	0.004	< 0.001
Serum 25(OH)D (per 10 ng/mL)	0.32 (0.27, 0.37)	0.01	< 0.001
Serum 25(OH)D (ng/mL)		0.02	
20 – 50	Reference		
<12	-1.69 (-1.98, -1.40)		<0.001
12 – 19	-1.11 (-1.31, -0.92)		<0.001
> 50	0.10 (-0.21, 0.41)		0.52

Table 4.

Bivariate Linear Regression Analysis of Subject Characteristics Associated with Serum 25(OH)D Concentrations.

Characteristic	Estimate (95% CI)	R ²	p-value
Age (per decade)	0.76 (0.62, 0.90)	0.01	<0.001
Sex (M vs F)	-3.42 (-3.99, -2.85)	0.01	<0.001
Race (White vs Non-White)	8.55 (7.84, 9.27)	0.05	<0.001
Charlson Comorbidity Index (per unit)	0.11 (0.04, 0.18)	0.001	0.003
BMI (per unit)	-0.37 (-0.40, -0.34)	0.05	<0.001
Ever Smoked (Y vs N)	-1.26 (-1.76, -0.76)	0.002	<0.001
Hypertension (Y vs N)	-0.52 (-1.00, -0.03)	0.000	0.038
Hyperlipidemia	0.96 (0.48, 1.44)	0.001	<0.001
Osteoporosis	3.56 (2.97, 4.15)	0.01	<0.001
Houses Z	0.43 (0.36, 0.50)	0.01	<0.001

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Table 5.

Multivariable Linear Regression Analysis of Characteristics Associated with 25(OH)D concentrations (ng/mL). $R^2=0.13$ for complete model.

Characteristic	Estimate (95% CI)	p-value
Age (per decade)	0.82 (0.64, 1.01)	<0.001
Sex (M vs F)	-3.02 (-3.58, -2.46)	<0.001
Race (White vs Non-White)	7.98 (7.25, 8.70)	<0.001
Charlson Comorbidity Index (per unit)	-0.16 (-0.26, -0.07)	<0.001
BMI (per unit)	-0.34 (-0.37, -0.31)	<0.001
Season		
Winter	Reference	
Spring	0.98 (0.33, 1.63)	0.003
Summer	3.86 (3.19, 4.54)	<0.001
Fall	2.98 (2.33, 3.63)	<0.001
Houses Z	0.28 (0.21, 0.35)	<0.001

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