Vitamin D Deficiency in Older Men

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Context: Vitamin D deficiency is not adequately evaluated in older men.

Objective: The aim of the study was to determine the prevalence of vitamin D deficiency and identify risk factors for its occurrence.

Design and Setting: We conducted a cross-sectional evaluation of 1606 older men in the general community who were enrolled in the Osteoporotic Fractures in Men Study.

Participants: A randomly selected subcohort of a large population of men from six U.S. communities participated in the study.

Main Outcome Measures: Serum concentrations of 25-hydroxyvitamin D_2 [25(OH)D_2] and 25(OH)D_3 were measured using mass spectrometry.

Results: Deficiency [25(OH)D <20 ng/ml] was present in 26%, and insufficiency (<30 ng/ml) was present in 72%. Deficiency was particularly common among men during the winter and spring (especially in the northern communities) and in the oldest and more obese men. For instance, in Caucasian men in winter or spring who were >80 yr old, did not engage in lawn/garden work, and had a body mass index greater than 25 kg/m^2 and vitamin D intake below 400 IU/d, the prevalence of vitamin D deficiency was 86%. 25(OH)D_2 levels were present in a small fraction of men and accounted for a low proportion of total 25(OH)D levels. The use of vitamin D supplements was reported by 58% of men, but supplement use had a small effect on total 25(OH)D levels and, despite supplement use, low levels remained frequent.

Conclusions: Vitamin D deficiency is common in older men and is especially prevalent in obese, sedentary men living at higher latitudes. Use of vitamin D supplements at levels reported here did not result in adequate vitamin D nutrition. ***(J Clin Endocrinol Metab* 94: 1214–1222, 2009)**

Vitamin D is necessary for a wide variety of essential biological functions such as bone and mineral metabolism, muscle function, and immunity (1). Moreover, vitamin D insufficiency has been noted to be present in a variety of populations (2) and is implicated in the causation of common disorders including osteoporosis and fractures, falls, cancer, psoriasis, and others (3). Vitamin D deficiency is of particular interest because it is easily, safely, and inexpensively corrected with adequate supplementation. Although findings have been somewhat inconsistent, trials of the effects of vitamin D supplementation suggest beneficial effects on important clinical outcomes (2, 4, 5). As a result, increased attention has been directed at improving vitamin D nutrition, including recent recommendations to increase the routine intake of vitamin D (6).

Complicating the assessment of vitamin D status are concerns about measurement technique. Immunoassay and protein bind-

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Abbreviations: BMI, Body mass index; 25(OH)D, 25-hydroxyvitamin D.

ing based methods have yielded discrepant results (7), and some of these assays may yield spurious levels when compared with liquid chromatography/mass spectrometry (8–10).

Despite concerns about vitamin D adequacy in the elderly, there remain too few large, community-based studies that use accurate and precise 25-hydroxyvitamin D [25(OH)D] assays to determine the extent of deficiency and identify those at risk. For instance, there are inadequate data about vitamin D levels in older men, a group commonly affected by disorders linked to vitamin D insufficiency (*e.g.* falls, fractures, cancer). To understand more completely the vitamin D status in a large population of elderly men and identify factors with potential for clinical intervention, we measured levels of 25(OH)D_2 (a sterol produced in yeast and obtained primarily from nutritional supplements and supplemented foods) and 25(OH)D_3 (obtained from nutritional supplements, supplemented foods, food, and UV irradiation of the skin).

Subjects and Methods

Study participants

Participants were enrolled in the Osteoporotic Fractures in Men Study (MrOS). From March 2000 through April 2002, a total of 5995 community-dwelling men at six clinical centers in the United States (Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Monongahela Valley near Pittsburgh, PA; Portland, OR; and San Diego, CA) agreed to participate in a study of healthy aging, with a focus on osteoporosis and fractures. Eligible men were at least 65 yr old, without bilateral hip replacements, and able to walk without assistance from another person. Details of the MrOS design and cohort have been described (11, 12). The Institutional Review Board at each center approved the study, and written consent was obtained from all participants.

Baseline serum for 25(OH)D assays were from 1608 participants who were randomly chosen from 5908 participants in the cohort who had at least one vial of serum available. One participant had insufficient serum to complete the assays. Another man had 25(OH)D levels more than 3 SD above the mean (75.6 ng/ml) and was omitted for analyses, leaving results from 1606 participants.

In addition, assays were performed on a second serum sample from men who volunteered for a follow-up visit an average of 1.9 yr after baseline. The results from those men who were also in the random sample selected at baseline (n = 352) were used to examine the stability of 25(OH)D levels over time.

25(OH)D assays

Fasting morning blood was collected, and serum was prepared immediately after phlebotomy and stored at −70 C in vials foil-wrapped to prevent light exposure. Samples remained frozen until assay. Measures for 25(OH)D_2 (derived from ergocalciferol) and 25(OH)D_3 (derived from cholecalciferol) were performed at the Mayo Clinic using mass spectrometry as previously described (13). Deuterated stable isotope [d3-25(OH)D] was added to a 0.2-ml serum sample as internal standard. 25(OH)D_2, 25(OH)D_3, and the internal standard were extracted using acetonitrile precipitation. The extracts were further purified online and analyzed by liquid chromatography/tandem mass spectrometry using multiple reaction monitoring. 25(OH)D_2 and 25(OH)D_3 were reported individually. The minimum detectable limit was 4 ng/ml for 25(OH)D_2 and 2 ng/ml for 25(OH)D_3. Aliquots of a single serum pool were included in alternate assay runs. Using the pooled serum, the interassay coefficient of variation for 25(OH)D_3 was 4.4%, and the intraassay coefficient of variation was 4.9%. In the study of stability of 25(OH)D levels over time, baseline and follow-up samples were run sequentially within an assay run, and the order of the pair in the run was randomly determined.

Total 25(OH)D was the sum of 25(OH)D_3 and 25(OH)D_2 levels. Baseline total 25(OH)D levels were categorized as normal, insufficient, or deficient according to the definitions proposed by Holick (3). Deficiency was defined as less than 20 ng/ml, insufficiency as 20–29 ng/ml, and sufficiency as 30–149 ng/ml. No participant had "toxic" levels (>150 ng/ml). We also report the proportion of participants with levels below 10 ng/ml.

Other measures

Demographic factors, smoking, alcohol consumption, and medications were determined by questionnaire. Physical activity was assessed with the Physical Activity Score for the Elderly (PASE) (14). In PASE, walking for exercise was estimated from the questions "Over the past 7 d, how often did you take a walk outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, *etc.*?" During the clinic interview, an additional question was asked: "Do you take walks for exercise, daily or almost every day?" Outdoor activity was determined from the question "During the past 7 d, did you engage in any of the following activities: lawn work or yard care, including snow or leaf removal, wood chopping, *etc.*? Outdoor gardening?" A modified Block food frequency questionnaire was administered to assess usual dietary and supplement intake over the past year (Block Dietary Data Services, Berkeley, CA) (15). Vitamin D intake from food and supplements was determined, but information did not include whether vitamin D supplements included D_3 or D_2; hence, only total 25(OH)D content was considered. Participants brought in all medications they used within the last 30 d. A computerized dictionary, based on the original Established Populations for Epidemiologic Studies of the Elderly (EPESE) coding system (16) was used to categorize the medications. Each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA). Height (centimeters) was measured on Harpenden stadiometers, and weight (kilograms) was measured on standard balance beam or digital scales. Body mass index (BMI) was calculated as kilograms per meter squared.

Statistical analyses

The distributions of 25(OH)D, 25(OH)D_3, and detectable 25(OH)D_2 levels were approximately normal. However, because the majority of 25(OH)D_2 results were undetectable, the variable was examined both as dichotomous (detectable or not) and as continuous if in the detectable range (>4 ng/ml), and both results are reported. Analyses using 25(OH)D_2 as a continuous variable used only participants with detectable levels. Pearson correlations were calculated for each 25(OH)D measure and continuous variables collected at baseline, including age, body size measures, and reported intake of vitamin D and calcium from diet and supplements. Means and SD values of baseline total 25(OH)D, 25(OH)D_2, and 25(OH)D_3 were calculated by participant characteristics, including demographic and physical activity variables, collected at the baseline exam. ANOVA and *t* tests were used to compare means, and χ^2 tests were used to compare proportions.

Mean 25(OH)D concentrations were evaluated by season and clinic site. Season of baseline visit was coded as winter (January-March), spring (April-June), summer (July-September), and fall (October-December). Clinic sites also differed in their climate and latitude, which may affect participants' exposure to sunlight; therefore, 25(OH)D levels were evaluated by site. Absolute change in 25(OH)D levels between baseline and a subsequent visit (1.9 ± 0.4 yr later) were calculated for 352 participants who had baseline and follow-up measures, and these levels were normalized for season of collection. Seasonal normalization was accomplished as follows. A five-category "season change" variable was created to describe whether a participant's follow-up visit was: 1) in the same season as baseline; 2) in a "lighter" season than baseline (*e.g.* baseline visit was in winter and follow-up was in spring); 3) in a "much lighter" season (*e.g.* baseline visit was in winter and follow-up was in summer), and so on for "dark" and "much darker" season changes. Mean differences between baseline and follow-up in 25(OH)D and 25(OH)D_3 were calculated for participants in each of the five categories of the season change variable. The mean differences were added to each follow-up value. For example, participants whose follow-up visit was in a much darker season had an average 5.55 ng/ml lower $25(OH)D_3$ value at follow-up than at baseline. Therefore, 5.55 ng/ml was added to each participant's $25(OH)D_3$ value in that season change category. Values in other season-change categories were adjusted similarly.

Factors associated with vitamin D deficiency were identified using log-binomial models (PROC GENMOD). This method provides better estimates of prevalence ratios than does logistic regression for common outcomes, such as vitamin D deficiency (17). That is, logistic regression would be expected to overestimate strengths of association reported in this study (18). Prevalence ratio estimates for deficiency were calculated for each of several baseline characteristics alone and after adjustment for age, season, and race. Upon this basic model adjusted for these three variables, a multivariable model was constructed using each of the variables associated with vitamin D deficiency with a $P < 0.10$ in bivariate analysis. A likelihood ratio test was used to determine whether model fit improved significantly ($P < 0.05$) with the addition of new variables. Additional variables were added to the multivariate model in the order of lowest to highest P value (among those with $P < 0.05$) until no additional variable significantly improved the model fit as assessed by the likelihood ratio test.

All analyses were conducted using SAS version 9.1.2 (SAS Institute, Cary, NC).

TABLE 1. Baseline characteristics of participants (n = 1606)

	No. of participants (%) or mean ± SD
Age category (yr)	
65–69	474 (29.5)
70–74	436 (27.2)
75–79	408 (25.4)
80–84	213 (13.3)
>85	75 (4.7)
BMI category (kg/m²)	
<25	424 (26.4)
25–29 (overweight)	858 (53.4)
30–34 (obese)	264 (16.4)
>35	60 (3.7)
Race	
White	1441 (89.7)
Black	54 (3.4)
Asian	51 (3.2)
Hispanic	42 (2.6)
Other	18 (1.1)
Education	
Graduate school	566 (35.2)
College	642 (40.0)
High school	288 (17.9)
<High school	110 (6.9)
Season	
Winter (Jan-Mar)	320 (19.9)
Spring (Apr-Jun)	418 (26.0)
Summer (Jul-Sep)	461 (28.7)
Fall (Oct-Dec)	407 (25.3)
Site	
Birmingham	258 (16.1)
Minneapolis	239 (14.9)
Palo Alto	278 (17.3)
Pittsburgh	280 (17.4)
Portland	276 (17.2)
San Diego	275 (17.1)
Daily intake of vitamin D from diet (IU)	
<600	1574 (99.4)
>600	10 (0.6)
Daily intake of vitamin D from supplements (IU)[a]	
0–199	730 (46.1)
200–399	104 (6.6)
400–599	644 (40.7)
600	106 (6.7)
Daily intake of calcium from diet and supplements (mg)	1153.1 ± 594.3
Measures in serum	
Total 25(OH)D (ng/ml)	25.1 ± 7.9
$25(OH)D_3$ (ng/ml)	22.9 ± 8.4
$25(OH)D_2$, if detectable (ng/ml)	8.4 ± 3.3
$25(OH)D_2$ detectable, n (%)	420 (26.2)

[a] No men reported the use of more than 600 IU/d.

Results

Characteristics of study participants are shown in Table 1. The average age was 73.8 ± 5.9 yr, with a range of 65–99. Most were Caucasian; 10.3% were from other racial and ethnic groups. The average serum total 25(OH)D level was 25.1 ± 7.9 ng/ml (range, 3.1–58.3 ng/ml). A total of 71.1% had 25(OH)D levels below 30 ng/ml, 25.7% had levels below 20 ng/ml, and 2.9% had levels below 10 ng/ml.

A total of 352 men had measures of 25(OH)D in serum obtained on two occasions 1.9 ± 0.4 yr apart. After adjusting for season, there were no statistically significant differences in the means of the two measurements, and differences between measures in individuals were generally small. The partial correlation coefficient for baseline and second visit total 25(OH)D, adjusted for season change, was 0.72 ($P < 0.0001$). All the 151 men with two measures who were classified as deficient at baseline were also deficient at the second visit.

Almost all circulating 25(OH)D was derived from vitamin D_3; only 26% of subjects had detectable levels of $25(OH)D_2$, and mean levels were low (8.4 ± 3.3 ng/ml) in those in whom it was detectable. The level of total 25(OH)D was weakly associated with the amount of vitamin D reported from supplement use (r = 0.28; $P < 0.0001$). Those who reported supplement use had slightly higher total 25(OH)D levels and more often had detectable levels of $25(OH)D_2$ (43.6% *vs.* 1.5%).

Age, obesity, and race

Total 25(OH)D levels tended to be lower in older men (r = −0.09; $P = 0.0002$) (Table 2). In men aged 80–84 yr, 31% had levels below 20 ng/ml, and in men at least 85 yr old, 40% were deficient (Fig. 1A). Levels of $25(OH)D_3$ were lower as age increased (r = −0.10; $P < 0.0001$), but older men tended to have slightly higher $25(OH)D_2$ levels (r = 0.11; $P = 0.03$).

Obesity was also associated with lower total 25(OH)D levels (Table 2). Of those with BMI in the normal range (<25 kg/m²), 21% had 25(OH)D levels below 20 ng/ml; in overweight men (BMI = 25–29 kg/m²), 24.5% had vitamin D deficiency; and in obese men (BMI ≥ 30 kg/m²), 33.6% had vitamin D deficiency and 4.3% had levels below 10 ng/ml. Of those who were very obese (BMI ≥35 kg/m²), 53.3% were deficient (Fig. 1B).

TABLE 2. 25(OH)D concentrations by participant characteristics (n = 1606)

	Total 25(OH)D (ng/ml)	*P*	25(OH)D_3 (ng/ml)	*P*
Age category (yr)				
65–69	25.7 ± 8.3		23.8 ± 8.6	
70–74	25.6 ± 8.2		23.4 ± 8.7	
75–79	25.0 ± 7.2		22.4 ± 7.7	
80–84	23.5 ± 7.8		21.3 ± 8.0	
>85	23.0 ± 7.2	0.001	20.9 ± 8.0	0.0004
BMI category (kg/m^2)				
<25	26.0 ± 8.0		23.4 ± 8.7	
25–29 (overweight)	25.3 ± 7.9		23.1 ± 8.3	
30–34 (obese)	24.0 ± 7.6		22.2 ± 8.1	
>35	20.2 ± 7.5	<0.0001	18.7 ± 7.3	0.0003
Race				
White	25.5 ± 7.8		23.3 ± 8.2	
Black	18.5 ± 8.8		15.8 ± 8.3	
Asian	24.3 ± 6.7		21.7 ± 7.7	
Hispanic	20.9 ± 7.7		19.3 ± 8.5	
Other	24.4 ± 8.6	<0.0001	23.8 ± 9.2	<0.0001
Education				
Graduate school	25.6 ± 8.0		22.9 ± 8.5	
College	25.1 ± 7.9		23.0 ± 8.4	
High school	24.8 ± 7.5		23.2 ± 8.0	
<High school	22.9 ± 8.3	0.01	21.2 ± 8.2	0.2
Season				
Winter (Jan-Mar)	22.2 ± 7.7		20.1 ± 8.0	
Spring (Apr-Jun)	24.3 ± 7.4		21.7 ± 7.6	
Summer (Jul-Sep)	27.5 ± 7.8		25.6 ± 8.4	
Fall (Oct-Dec)	25.3 ± 7.9	<0.0001	23.2 ± 8.4	<0.0001
Site				
Birmingham	24.5 ± 7.5		22.9 ± 7.7	
Minneapolis	23.9 ± 7.1		22.0 ± 7.5	
Palo Alto	25.4 ± 7.6		22.9 ± 8.5	
Pittsburgh	24.2 ± 7.3		22.2 ± 7.5	
Portland	24.3 ± 8.7		21.9 ± 8.9	
San Diego	28.0 ± 8.5	<0.0001	25.3 ± 9.3	<0.0001
Alcoholic drinks per week				
0	24.2 ± 7.8		22.3 ± 8.2	
1–7	25.3 ± 7.4		22.9 ± 8.0	
>7	25.9 ± 8.8	0.005	23.6 ± 9.0	0.04
Smoking status				
Never	25.2 ± 7.7		23.0 ± 8.3	
Past	23.0 ± 8.0		22.9 ± 8.4	
Current	22.6 ± 8.9	0.05	21.4 ± 9.1	0.4
Daily intake of vitamin D from diet and supplements (IU)				
<400	22.9 ± 8.1		22.6 ± 8.1	
≥400	27.3 ± 7.2	<0.0001	23.2 ± 8.6	0.2
Daily intake of vitamin D from supplements (IU)				
0–199	22.7 ± 8.0		22.5 ± 8.0	
200–399	25.5 ± 7.6		24.3 ± 8.3	
400–599	27.4 ± 7.2		22.8 ± 8.8	
600	27.8 ± 7.3	<0.0001	24.8 ± 8.1	0.02
PASE score quartile				
1 (lowest)	23.6 ± 8.3		21.2 ± 8.5	
2	25.2 ± 7.2		22.8 ± 8.0	
3	25.4 ± 8.0		23.4 ± 8.2	
4	26.1 ± 8.0	<0.0001	24.2 ± 8.5	<0.0001
Walking				
Never	23.5 ± 7.9		21.3 ± 8.0	
Rarely	24.5 ± 8.3		22.2 ± 8.5	
Sometimes	25.1 ± 7.4		23.0 ± 8.0	
Often	25.7 ± 8.1	0.004	23.5 ± 8.5	0.007
Daily walks for exercise				
No	24.3 ± 7.8		22.3 ± 8.2	
Yes	25.8 ± 8.0	0.0002	23.4 ± 8.5	0.009
Lawn work and/or gardening				
No	23.2 ± 8.2		20.3 ± 8.7	
Yes	25.6 ± 7.8	<0.0001	23.6 ± 8.1	<0.0001

Data are expressed as mean ± SD. *P* values are for ANOVA or *t* test.

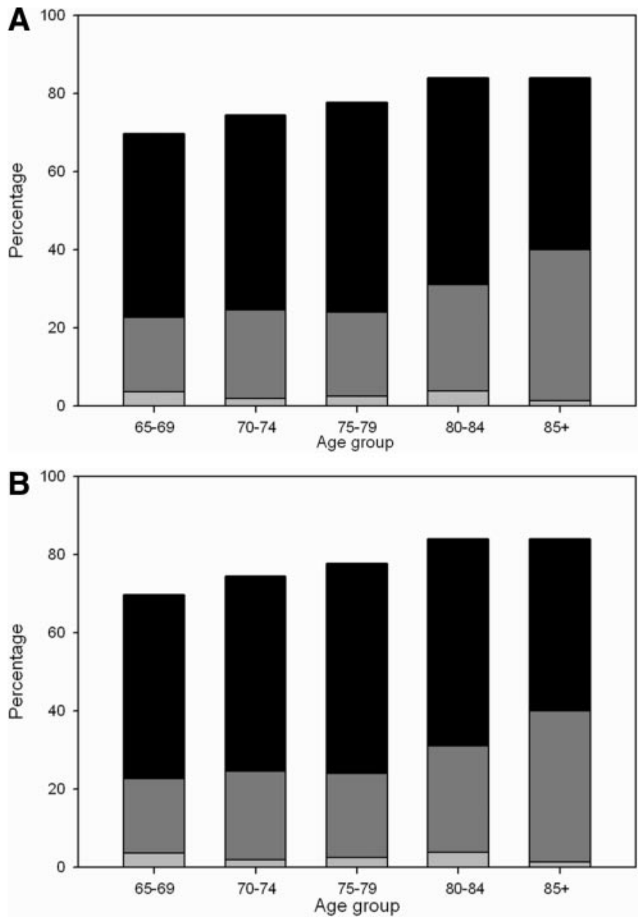

FIG. 1. A, Vitamin D deficiency and insufficiency by age group for three total 25(OH)D cut points. B, Vitamin D deficiency and insufficiency by BMI category for three total 25(OH)D cut points.

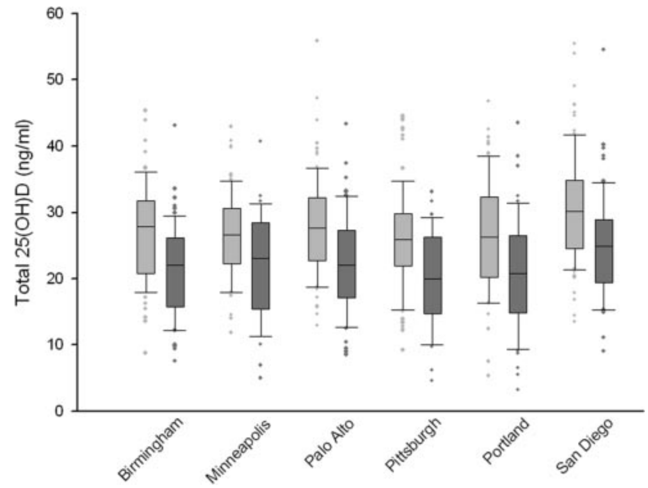

FIG. 2. Summer to winter comparison of total 25(OH)D by site.

Total 25(OH)D levels were lower in African-Americans (18.5 ± 8.8 ng/ml) than in Caucasians (25.5 ± 7.8 ng/ml). Whereas average $25(OH)D_2$ levels were similar (27.8% detectable, mean = 9.6 ng/ml, *vs.* 26.6% detectable, mean = 8.3 ng/ml, respectively), $25(OH)D_3$ levels were lower in African-Americans (15.8 *vs.* 23.3 ng/ml). A total of 64.8 and 22.2% of African-Americans had 25(OH)D levels below 20 and 10 ng/ml, respectively, whereas 23.2 and 1.8% of Caucasians were below those levels. Hispanics also had lower 25(OH)D levels (Table 2).

Geography and season

Geography and season did not have major effects on vitamin D levels. Slightly higher total 25(OH)D levels were present in San Diego and Palo Alto, whereas levels were slightly lower in Minneapolis. Moreover, mean total 25(OH)D levels were highest in summer and lowest in winter, although the mean differences between seasons were small (27.5 *vs.* 22.2 ng/ml, respectively) (Table 2 and Fig. 2). In men with two measurements who had the first one in summer and the second one during winter, there were no differences in mean $25(OH)D_2$ levels, but average $25(OH)D_3$ levels were 5.6 ng/ml lower during winter.

Despite the modest seasonal and geographical differences, these factors affected the proportion of men identified with vitamin D deficiency. For instance, the proportion with vitamin D deficiency (<20 ng/ml) was higher in winter (30.9%) than in spring or fall (28.2% and 22.8%, respectively), and was lowest in summer (18.1%). Vitamin D deficiency was more common at the more northern clinical sites. In winter, the mean total 25(OH)D level in Minneapolis was 21.9 ng/ml (37.8% deficient) and in summer was 26.3 ng/ml (13.5% deficient). In contrast, for San Diego the winter mean was 25.0 ng/ml (26.8% deficient), and the summer mean was 30.8 ng/ml (5.0% deficient).

Physical activity

Higher activity level (PASE score) and amount of outside activity were associated with higher 25(OH)D levels (Table 2). For instance, for those who reported no lawn work or gardening, mean total 25(OH)D was 23.2 ng/ml, and 35.2% were deficient; whereas men who reported at least one outdoor yard activity had a mean 25(OH)D of 25.6 ng/ml ($P < 0.0001$), and 22.6% were deficient.

Vitamin D from diet and supplements

Diet supplied small amounts of vitamin D (mean intake, 163 ± 115 IU/d); only 10 subjects (0.6%) received the recommended daily allowance of 600 IU/d from diet alone (Table 1), and dietary intake correlated weakly with total 25(OH)D levels (r = 0.08). The use of vitamin D supplements was reported by 58.5% of subjects, but none reported taking more than 600 IU/d. Supplements were associated with higher total 25(OH)D levels (Table 2). The 15.5% who reported supplement use had 25(OH)D levels below 20 ng/ml, whereas 39.6% who did not report supplement use had concentrations below that level. Nevertheless, a high proportion had vitamin D insufficiency with all supplement doses (percent of subjects with 25(OH)D levels <30 ng/ml: supplement intake <200 IU/d, 83.6%; 200 to <400 IU, 68.3%; 400 to <600 IU, 69.3%, and 600 IU, 61.3%).

Multivariable analyses

In bivariate analyses, several factors were associated with vitamin D deficiency (<20 ng/ml) (Table 3). After adjustment for these factors, older age, obesity, Black or Hispanic race, and winter or spring season remained independently associated with

TABLE 3. Factors associated with vitamin D deficiency [total 25(OH)D <20 ng/ml] in bivariate analyses

	Prevalence ratio	95% CI	Age-, season-, and race-adjusted prevalence ratio	95% CI
Age range (yr)				
65–69	ref		ref	
70–74	1.08	0.83–1.41	1.17	0.90–1.54
75–79	1.06	0.80–1.39	1.14	0.87–1.51
80–84	1.35	0.99–1.83	1.54	1.13–2.10
>85	1.74	1.16–2.61	2.13	1.41–3.21
BMI category (kg/m^2)				
<25	ref		ref	
25–29 (overweight)	1.16	0.91–1.49	1.22	0.95–1.57
30–34 (obese)	1.39	1.03–1.88	1.48	1.09–2.03
>35	2.51	1.68–3.76	2.56	1.69–3.87
Race				
White	ref		ref	
Black	2.76	1.95–3.90	3.16	2.21–4.51
Asian	1.08	0.62–1.89	1.26	0.72–2.20
Hispanic	1.83	1.13–2.93	1.85	1.15–2.98
Other	1.65	0.78–3.49	1.89	0.89–4.00
Education				
Graduate school	ref		ref	
College	1.10	0.87–1.38	1.11	0.88–1.40
High school	1.16	0.87–1.53	1.17	0.89–1.55
<High school	1.61	1.13–2.29	1.32	0.92–1.90
Season				
Winter (Jan-Mar)	2.44	1.83–3.25	2.52	1.89–3.35
Spring (Apr-Jun)	1.69	1.26–2.26	1.69	1.27–2.27
Summer (Jul-Sep)	ref		ref	
Fall (Oct-Dec)	1.43	1.06–1.94	1.37	1.01–1.86
Site				
Birmingham	ref		ref	
Minneapolis	1.05	0.75–1.46	1.14	0.81–1.59
Palo Alto	0.88	0.64–1.24	0.79	0.55–1.13
Pittsburgh	1.00	0.72–1.38	1.16	0.83–1.62
Portland	1.19	0.87–1.63	1.15	0.84–1.59
San Diego	0.56	0.38–0.83	0.58	0.39–0.85
Alcoholic drinks per week				
0	ref		ref	
1–7	0.78	0.63–0.98	0.80	0.64–1.01
>7	0.87	0.68–1.11	0.89	0.70–1.14
Ever smoked				
Never	ref		ref	
Past	1.00	0.82–1.23	1.04	0.85–1.28
Current	1.48	0.95–2.31	1.43	0.91–2.26
Daily intake of vitamin D from diet and supplements (IU)				
<400	ref		ref	
>400	0.36	0.29–0.45	0.38	0.31–0.48
Daily intake of vitamin D from supplements (IU)				
0–199	ref		ref	
200–399	0.67	0.45–0.99	0.69	0.46–1.03
400–599	0.33	0.26–0.42	0.35	0.27–0.44
600	0.32	0.18–0.55	0.36	0.21–0.63
PASE score quartile				
1 (lowest)	ref		ref	
2	0.73	0.56–0.95	0.77	0.59–1.00
3	0.71	0.55–0.93	0.78	0.60–1.01
4	0.65	0.50–0.85	0.74	0.56–0.98
Walking				
Never	ref		ref	
Rarely	0.94	0.68–1.31	1.03	0.74–1.44
Sometimes	0.68	0.50–0.93	0.74	0.54–1.02
Often	0.69	0.52–0.91	0.76	0.57–1.01
Daily walks for exercise				
No	ref		ref	
Yes	0.81	0.66–0.98	0.82	0.67–1.00
Lawn work and/or outdoor gardening				
No	ref		ref	
Yes	0.65	0.53–0.80	0.73	0.59–0.90

CI, Confidence interval.

a greater prevalence of deficiency (Table 4). For instance, the risk of vitamin D deficiency approximately doubled with age of at least 85 yr, BMI of at least 35 kg/m^2, Black race, and winter season. Dietary intake of vitamin D of at least 400 IU and lawn work/gardening were both associated with a lower prevalence of deficiency. The additive impact of these risk factors was considerable. In Caucasian men who were older than 80 yr, with a BMI greater than 25 kg/m^2, who had a vitamin D intake below 400 IU/d, did not engage in lawn/garden work, and who were sampled in winter or spring, the prevalence of vitamin D deficiency was 86%; whereas there was a prevalence of 24% in younger, thinner men who had higher vitamin D intakes, who were sampled in summer or fall, and who engaged in lawn/garden work.

Discussion

In a cohort of older men in the United States, vitamin D deficiency and insufficiency were common. Approximately one fourth had a 25(OH)D level below that commonly considered to represent frank deficiency (<20 ng/ml), and the majority had levels considered insufficient (<30 ng/ml). Deficiency was particularly common during the winter and spring months (especially in the northern communities) and in the oldest and more obese subjects. In fact, 86% with multiple risk factors were deficient. Because vitamin D deficiency has been linked to a variety of common diseases, these results may be of considerable public health relevance. Importantly, our data demonstrated that the level of 25(OH)D varied little in sera obtained approximately 2 yr apart, indicating that vitamin D status is stable over time and suggesting that many have longstanding vitamin D deficiency.

There is uncertainty concerning the levels of 25(OH)D levels that are adequate, but because measures of serum PTH tend to be higher in those with 25(OH)D levels below 30 ng/ml (19), that concentration is considered sufficient to prevent secondary hyperparathyroidism. Less than 30% of our population achieved that goal. One fourth of older men had 25(OH)D levels below 20 ng/ml, concentrations associated with more severe consequences (3). These results are similar to those reported in other studies (20–22) and confirm that vitamin D deficiency is widespread.

Considerable variation has been noted in measurements of 25(OH)D levels in multicenter comparisons of assay performance (7–9), apparently reflecting inconsistency between methods or laboratories. Thus, some of the difficulty in estimating what levels of 25(OH)D are adequate, and in surveying the population burden of vitamin D deficiency, may result from the lack of standardization of assay approaches. We measured 25(OH)D levels using liquid chromatography/mass spectrometry, and assay quality control revealed excellent performance.

$25(OH)D_3$ was present in much higher concentrations than was $25(OH)D_2$. In fact, only one fourth of these men had detectable levels of $25(OH)D_2$, and few who did not take supplements had detectable $25(OH)D_2$. These results suggest that many older men in the United States have minimal exposure to vitamin D_2. Vitamin D deficiency is thought to be less common in the United States because of vitamin D supplementation of dairy products (21, 23, 24); many of the men in the MrOS reported using daily vitamin D supplements, and in fact the levels of total 25(OH)D in these men were higher. Nevertheless, the prevalence of vitamin D deficiency remained high even in supplement users, and 39.6% of supplement users were deficient (<20 ng/ml). These results strengthen the impression (25) that commonly used supplement doses are inadequate to ensure vitamin D nutrition. To some extent this is not surprising because Holick *et al.* (26) recently reported that for every 100 IU of vitamin D_2 or vitamin D_3 ingested, there is an increase in circulating 25(OH)D levels of only 1 ng/ml, providing some explanation for why men reporting supplement use have marginally higher concentrations. In addition, we also estimated the intake of vitamin D from diet. On average, it was small and probably contributed little to overall vitamin D nutrition. In combination, the apparently small effects of supplements and diet support the fact that endogenous production from skin UV exposure is the primary source of vitamin D in older men.

Other studies reported that aging (2, 27), obesity (28–30), and winter season (31) are associated with lower 25(OH)D levels. We demonstrate that those factors have important effects on the prevalence of vitamin D deficiency; 53.3% of the most obese men were deficient, and almost half of those 85 yr or older were

TABLE 4. Factors independently associated with deficiency [total 25(OH)D <20 ng/ml]

	New model for clinical prediction use (AUC, 0.77)	
	Relative risk	**95% CI**
Age (yr)		
<80	ref	
80–84	1.30	0.99–1.71
>85	1.99	1.35–2.94
Race/ethnicity		
White or Asian	ref	
Black	2.40	1.66–3.45
Hispanic or other	1.78	1.18–2.69
BMI (kg/m^2)		
<25	ref	
25–29 (overweight)	1.14	0.88–1.46
30–34 (obese)	1.34	0.98–1.82
>35	2.10	1.38–3.20
Season		
Winter (Jan-Mar)	2.19	1.64–2.92
Spring (Apr-Jun)	1.63	1.22–2.18
Summer (Jul-Sep)	ref	
Fall (Oct-Dec)	1.29	0.95–1.76
Latitude[a]		
Low	ref	
High	1.37	1.12–1.67
Vitamin D supplement use		
Yes	ref	
No	2.36	1.92–2.90
Lawn work and/or gardening		
Yes	ref	
No	1.44	1.16–1.79

CI, Confidence interval.

[a] For model fitting, "high" latitude clinic sites were Minneapolis (44°), Pittsburgh (40°), and Portland (45°). "Low" latitude sites were Birmingham (33°), Palo Alto (37°), and San Diego (32°).

deficient. The winter season considerably increased the proportion classified as deficient. Moreover, we showed that these are independent predictors of vitamin D deficiency and that the cumulative effects of these factors are impressive. The great majority with multiple risk factors were deficient. This information suggests that obese, older men may particularly benefit from vitamin D supplementation, especially in the winter and spring, and that trials are warranted to assess the potentially widespread benefits.

The study has several major strengths. To our knowledge this is the largest study of 25(OH)D levels in elderly men. It draws from a cohort of community-dwelling men from diverse geographical regions of the United States and includes the availability of information concerning relevant seasonal, nutritional, and lifestyle factors. In addition, 25(OH)D measurements were performed using mass spectrometry-based assays with high precision, thus avoiding potential artifacts associated with other approaches (8, 9, 32, 33). These assay methods also allowed us to determine independently both 25(OH)D_2 and 25(OH)D_3 levels. On the other hand, study weaknesses included the volunteer nature of the participants, which limits the generalizability of the results. For instance, the prevalence of vitamin D deficiency would be expected to be higher in less healthy men (34). Nevertheless, the likelihood that our results apply to other older U.S. men is strengthened by the observation that means for height, weight, and BMI among Black, Hispanic, and White men studied here are nearly identical to the race/ethnicity-specific means from the National Health and Nutrition Examination Survey 1999–2000 reference data for men aged 60 yr or older (35). Finally, no women were studied, and the proportion of non-White participants was limited.

In summary, vitamin D deficiency is very common in older U.S. men, especially among the most elderly and obese, and during the winter in northern latitudes. In many, prevalent vitamin D deficiency appears to be a long-standing condition, rather than a recent occurrence. Because older men are commonly afflicted with disorders potentially linked to vitamin D deficiency and some studies have suggested benefit from supplementation, there is a need to further examine the usefulness of vitamin D supplements in clinical trials with adequate power to address multiple outcomes.

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