Association of Vitamin D–Related Information from a Telephone Interview with 25-Hydroxyvitamin D

Harleen Sahota,[1,3] Heidi Barnett,[1] Maia Lesosky,[1] Janet M. Raboud,[1,3,5] Reinhold Vieth,[2,5] and Julia A. Knight[1,3]

[1]Prosserman Centre for Health Research, Samuel Lunenfeld Research Institute; [2]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital; Departments of [3]Public Health Sciences and [4]Laboratory Medicine and Pathobiology, University of Toronto; [5]University Health Network, Toronto, Ontario, Canada

Abstract

Vitamin D may be associated with reduced risks of several types of cancer, including colon, prostate, and breast. We examined the relationship between vitamin D–related questions administered in a telephone interview and serum 25-hydroxyvitamin D [25(OH)D]. Three hundred and eight eligible women were randomly selected from controls in a breast cancer case-control study. Questions pertaining to sun exposure and dietary sources of vitamin D over the previous 4 weeks were asked in both summer and winter. We assessed the association between questionnaire-derived items and 25(OH)D using multiple linear regression. There were 217 participating women, 203 in summer and 213 in winter. Models were adjusted for age, body mass index, and skin color. Number of days when more than 0.5 hour was spent outdoors per week (''7'' versus ''<7'' β = 11.12; P = 0.01), limb coverage (''no'' β = 24.90 and ''partial'' β = 8.15 versus ''yes''; P = 0.0001), and milk intake (glasses/wk; ''>10'' β = 18.94, ''>5-10'' β = 9.16, and ''1-5'' β = 7.90 versus ''<1''; P = 0.02) best predicted 25(OH)D in the summer. The best predictors in the winter were sunlamp use (''yes'' β = 27.97 versus ''no''; P = 0.01), milk intake (glasses/wk; ''>10'' β = 14.54, ''>5-10'' β = 11.54, and ''1-5'' β = 2.15 versus ''<1''; P = 0.01), and vitamin D–containing supplements (''high'' β = 17.30 and ''moderate'' β = 13.82 versus ''none''; P = 0.0006). The R^2 was 0.29 for the summer model and was 0.21 for the winter model. Overall, there was evidence to suggest that questions designed to assess vitamin D exposure were in fact related to serum 25(OH)D. (Cancer Epidemiol Biomarkers Prev 2008;17(1):232–8)

Introduction

Vitamin D (cholecalciferol), a hormone that regulates bone development, metabolism, and calcium homeostasis, can be obtained through the diet or through endogenous pathways (photolysis of vitamin D precursors in the skin; refs. 1-3). It also plays an important role in the regulation of cell growth and differentiation (4). Vitamin D is produced on exposure to UV light, which converts 7-dihydrocholesterol to vitamin D (1). Within 2 days, vitamin D is converted to 25-hydroxyvitamin D [25(OH)D], which has a half-life of at least 2 months, making it an acceptable measure of vitamin D status (2, 3). Other major sources of vitamin D include fortified milk, some types of fish, particularly salmon and to a lesser extent tuna, and vitamin D–containing supplements (1-3). Latitude, season, age, skin color, and skin coverage can all potentially influence the amount of circulating 25(OH)D (5). Body mass index (BMI) may also play a role (6).

There is accumulating evidence that vitamin D may be associated with reduced risks of several types of cancer, including colon, prostate, and breast (6-8), or cancer in general (9). In many studies, information regarding vitamin D exposure is inferred from questions related to sun exposure, diet, and dietary supplement use. There have been few attempts to validate the types of questions used. In a previous validation study of sun exposure questions used in a case-control study of multiple sclerosis, Van der Mei et al. found significant correlation between reported time in the sun or activities outside in the last 3 years and serum 25(OH)D (P < 0.01 for both and r = 0.22 and 0.31, respectively; ref. 10).

In this study, we examined the relationship between vitamin D–related questions (sun exposure as well as dietary and supplemental vitamin D) administered in a telephone interview and circulating levels of 25(OH)D to validate the questionnaire used in a population-based case-control study of breast cancer and vitamin D (8).

Materials and Methods

Study Population. A population-based case-control study to examine the association between vitamin D and breast cancer was conducted in the province of Ontario, Canada from 2003 to 2005 (8). Control women who had never been diagnosed with breast cancer and who were ages 20 to 69 years were recruited by calling randomly selected residential telephone numbers. Of the 1,135 participating controls from the original study, 315 were

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Requests for reprints: Julia A. Knight, Prosserman Centre for Health Research, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 60 Murray Street, Box 18, Toronto, Ontario, Canada M5T 3L9. Phone: 416-586-8701; Fax: 416-586-8404. E-mail: knight@mshri.on.ca

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randomly selected to participate in the validation study. Three hundred and eight participants were eligible, of which 84 chose not to participate and 7 participants could not be contacted. This left 217 (70%) women who participated in at least one season with blood samples and an interview. The total number of participants for the summer was 203 and the total number for the winter was 213.

Participants were asked to complete a telephone interview with questions based on the main questionnaire but focused on vitamin D–related exposures during the previous 4 weeks in both summer and winter. They were also asked to give a blood sample within 2 weeks of the interview in each season. The summer was classified as the months of June, July, August, and September. The winter included the months of January, February, March, and April. Wintertime sun exposure variables were based on whether a trip to a warm, sunny climate had been taken. Specific dietary sources of vitamin D were assessed through a question on the number of times per day, week, or month the participant had glasses of milk, fish other than tuna or salmon, and tuna or salmon. Tuna or salmon was considered as a separate category as these are some of the most commonly consumed fish with relatively high levels of vitamin D. Other food items contain very little vitamin D, and cereal is not fortified with vitamin D in Canada. There was also a question on whether cod liver oil had been taken at least once per week and the number of times per week it was taken and a question on whether any other vitamin and/or mineral supplements had been taken at least once a week. Participants were then asked to list any they had taken.

Variable Descriptions. The questionnaire included questions pertaining to sun exposure and dietary sources of vitamin D over the previous 4 weeks alongside potentially confounding variables. Overall, the following variables were included in the analysis for both questionnaires: age in years (continuous), skin color (classified as ''very fair,'' ''fair,'' ''light,'' ''light medium,'' or ''dark medium/brown/very dark brown/black''), BMI in kg/m^2 (continuous), sunlamp use (classified as ''yes'' or ''no''), milk (glasses/wk; classified as ''<1,'' ''1-5,'' ''>5-10,'' or ''>10''), fish (other than tuna or salmon; times per week; classified as ''<1,'' ''1-2,'' or ''>2''), tuna or salmon (times per week; classified as ''0,'' ''>0-1,'' or ''>1''), and vitamin D–containing supplements (classified as ''none,'' ''moderate,'' or ''high''). The summer questionnaire also included the following items: outdoor job (working outdoors between 9 a.m. and 5 p.m.; classified as ''yes'' or ''no''), days outside per week (where at least 0.5 hour each day was spent outdoors; classified as ''<7'' or ''7''), limb coverage (coverage of arms and legs; classified as ''yes,'' ''partial,'' or ''no''), and sunscreen use (classified as ''yes'' or ''no''). The winter questionnaire contained additional items on a trip to a warm, sunny climate in the winter (classified as ''yes'' or ''no''), limb coverage while on trip (coverage of arms and legs; classified as ''yes,'' ''partial,'' or ''no''), and sunscreen use while on trip (classified as ''did not go on trip,'' ''yes,'' or ''no'').

The variable for vitamin D–containing supplements in each season was defined as ''none'' (participants who did not take any multivitamins, vitamin D supplement, or cod liver oil), ''moderate'' based on an approximate estimated intake of 200 to 400 IU (participants taking vitamin D capsules or multivitamins or cod liver oil only), or ''high'' based on an approximate estimated intake of more than 400 IU (individuals taking more than one source of a vitamin D–containing supplements).

The number of outdoor activity episodes per week for the summer questionnaire was calculated based on participation (number of times per week or month) in specific outdoor activities (sunbathing, swimming, walking, biking, running or jogging, hiking, canoeing/kayaking, sailing, motor boating, tennis, golf, team sports such as soccer, gardening, or other outdoor activities).

Assay for 25(OH)D. The Diasorin RIA kit was used to measure serum 25(OH)D. Duplicate aliquots were obtained for 15% of the total for the summer and winter, and the between-assay coefficient of variation for each season was 12.6% and 8.6%, respectively.

Statistical Analysis. Linear regression models were used to determine which independent variables best predicted the levels of 25(OH)D in three stages: simple linear regression for each independent variable, adjusted multiple linear regression (single independent variables adjusted for age, BMI, and skin color), and a comprehensive model including all independent variables with a two-sided $P < 0.10$. At each stage, separate models were created for the summer and winter data. The process to determine a comprehensive model was a backward selection procedure eliminating variables with $P > 0.10$ until all remaining variables were significant or marginally significant. All models included age, BMI, and skin color. Reproductive factors were not included as they were not significantly related to 25(OH)D. Analyses were conducted using SAS version 9.1. Two-sided P values < 0.05 were considered significant.

Results

Mean Levels of 25(OH)D. Table 1 provides the levels of 25(OH)D by potential indicators of exposure and by potential confounders for both summer and winter. As expected, the mean levels of 25(OH)D were higher in the summer than in the winter and decreased with increasing BMI. Levels increased with increasing age, although the differences were not large. There was a nonlinear relationship between skin color and 25(OH)D in the summer, with the lowest values occurring in those with the darkest and lightest skin tones. There were no clear relationships between 25(OH)D and any of the reproductive variables for either season. Mean 25(OH)D increased with increasing exposure to the sun as indicated by all sun exposure variables in both seasons (only a trip to a warm, sunny climate was considered in the winter). Levels also increased with increasing milk consumption in the summer and winter. There were no clear trends in 25(OH)D related to either salmon and tuna or other fish consumption. In both seasons, as vitamin D–related supplement use increased, levels of 25(OH)D also increased.

Linear Regression Analysis: Summer. Table 2 presents the regression coefficient and univariate P values for the adjusted and unadjusted variables in the summer. Skin color was significantly associated with 25(OH)D ($P = 0.009$), with light skin tones (but not fair ones) being associated with the highest levels of

Table 1. Mean 25(OH)D levels (nmol/L) and standard deviations for characteristics of the summer and winter questionnaire samples

	Summer (n = 203), n (%)	Summer mean 25(OH)D (SD)	Winter (n = 213), n (%)	Winter mean 25(OH)D (SD)
Age (y)				
<40	9 (4)	83.3 (25.5)	13 (6)	58.5 (28.1)
40-49	54 (27)	85.1 (30.8)	61 (29)	54.1 (27.8)
50-59	87 (43)	89.9 (37.3)	92 (43)	59.9 (29.0)
≥60	53 (26)	92.1 (31.6)	47 (22)	67.4 (28.2)
Skin color				
Very fair	17 (8)	87.1 (40.0)	18 (8)	56.5 (26.8)
Fair	57 (28)	81.3 (27.8)	62 (29)	63.5 (32.2)
Light	38 (19)	105.5 (37.7)	40 (19)	61.6 (32.1)
Light medium	76 (37)	88.6 (32.0)	77 (36)	56.2 (24.9)
Dark medium/brown/very dark brown/black	15 (7)	79.6 (33.2)	16 (8)	62.2 (23.9)
BMI (kg/m^2)				
<25	72 (36)	96.0 (35.7)	78 (37)	63.7 (32.6)
25 to <30	71 (35)	87.5 (33.3)	75 (35)	60.7 (22.6)
≥30	58 (29)	81.4 (30.4)	60 (28)	53.6 (29.2)
Ever parous				
Yes	185 (91)	88.7 (33.7)	195 (92)	60.7 (29.1)
No	18 (9)	91.1 (33.3)	18 (8)	49.4 (19.8)
Menopause status				
Premenopausal	83 (41)	83.3 (30.1)	91 (43)	54.4 (27.6)
Postmenopausal	111 (55)	91.9 (34.7)	112 (53)	63.9 (29.1)
Unknown	9 (4)	104.7 (43.6)	10 (5)	63.0 (26.6)
Days outside/wk*				
<7	100 (49)	82.1 (30.1)	—	—
7	103 (51)	95.5 (35.6)		
Limbs covered				
Yes	22 (11)	71.0 (26.1)	—	—
Partial	59 (29)	78.9 (29.7)		
No	122 (60)	97.0 (34.3)		
Sunscreen use †				
Yes	63 (31)	89.0 (32.7)	—	—
No	140 (69)	88.9 (34.2)		
Sun trip in the winter ‡				
Yes	—	—	16 (8)	74.6 (25.4)
No			197 (92)	58.6 (28.6)
Limbs covered while on trip				
Did not go on trip	—	—	194 (91)	58.1 (28.4)
Yes			2 (1)	55.5 (34.7)
Partial			5 (2)	68.2 (24.3)
No			12 (6)	83.5 (24.4)
Sunscreen use while on trip †				
Did not go on trip	—	—	194 (91)	58.1 (28.4)
Yes			10 (5)	68.2 (23.1)
No			9 (4)	85.8 (26.6)
Outdoor job§				
Yes	25 (12)	100.4 (38.1)	—	—
No	178 (88)	87.3 (32.8)		
Outdoor activity episodes/wk‖				
<7	79 (39)	81.3 (29.7)	—	—
7-10	64 (32)	85.5 (33.4)		
>10	60 (30)	102.6 (35.1)		
Sunlamp use				
Yes	6 (3)	110.6 (40.2)	6 (3)	85.8 (25.0)
No	196 (97)	88.1 (33.4)	207 (97)	59.0 (28.4)
Milk (glasses/wk)				
<1	50 (25)	79.4 (36.4)	54 (25)	52.3 (28.4)
1-5	50 (25)	84.3 (36.1)	51 (24)	54.8 (23.8)
>5-10	52 (26)	89.5 (27.0)	54 (25)	64.3 (28.6)
>10	51 (25)	102.2 (31.0)	54 (25)	67.5 (30.9)
Fish/wk				
<1	127 (63)	89.90 (35.67)	139 (65)	60.74 (30.90)
1-2	67 (33)	87.42 (28.17)	66 (31)	56.35 (23.45)
>2	9 (4)	86.04 (43.78)	8 (4)	71.33 (24.07)
Tuna or salmon/wk				
0	38 (19)	85.1 (35.2)	35 (16)	60.7 (27.4)
>0-1	120 (59)	89.5 (34.0)	130 (61)	57.3 (28.1)
>1	45 (22)	90.6 (31.7)	48 (23)	65.7 (30.6)

(*Continued on the following page*)

Table 1. Mean 25(OH)D levels (nmol/L) and standard deviations for characteristics of the summer and winter questionnaire samples (Cont'd)

	Summer (n = 203), n (%)	Summer mean 25(OH)D (SD)	Winter (n = 213), n (%)	Winter mean 25(OH)D (SD)
Vitamin D–containing supplements¶				
None	104 (51)	82.8 (32.8)	105 (49)	51.2 (25.5)
Moderate	80 (39)	94.8 (34.3)	84 (39)	66.6 (30.3)
High	19 (9)	97.5 (30.2)	24 (11)	73.3 (24.7)

NOTE: Questions were based on vitamin D intake and UVB exposure in the 4 weeks before interview.
*Number of days outside for at least 0.5 hour.
† Question asked if sunscreen was usually worn.
‡ Trip to warm climate.
§Question asked if more than 0.5 hour was spent outdoors at work between 9 a.m. and 5 p.m.
∥Based on the total number of specific outdoor activities (e.g., swimming and sunbathing) reported as number of times per week or month.
¶''None'' = 0 IU (no multivitamins, vitamin D supplement, or cod liver oil intake), ''Moderate'' = 200 to 400 IU (took vitamin D capsules or multivitamins or cod liver oil only), and ''High'' = greater than 400 IU (took more than one source of a vitamin D–containing supplements).

25(OH)D. BMI was significantly negatively associated with 25(OH)D (P = 0.004), and age was marginally positively associated (P = 0.08). After adjustment for age, skin color, and BMI, indicators of sun exposure were associated with 25(OH)D, including higher levels significantly associated with spending at least 0.5 hour outside every day (11.81 nmol/L versus less than every day; P = 0.009) and a greater number of outdoor activity episodes (18.72 nmol/L in those doing outdoor activities >10 times versus <7 times; P = 0.002). Higher levels were also associated with keeping arms and legs uncovered (25.36 nmol/L versus keeping limbs covered; P = 0.0001). Working outdoors was marginally significant when unadjusted but no longer significant after adjustment, and sunscreen use was not related to 25(OH)D. There was no effect of sunlamp use in the summer. Higher intake of milk was significantly related to 25(OH)D levels (19.09 nmol/L in those drinking >10 glasses/wk versus <1 glasses/wk; P = 0.02), and vitamin D–containing supplement use was marginally associated with increased 25(OH)D (11.49 nmol/L with high intake and 10.75 nmol/L with moderate intake versus none; P = 0.06) in the summer after adjustment. There was no relationship between salmon and tuna or other fish consumption and 25(OH)D. We also considered potential interactions between vitamin D–related items and BMI, with adjustment for age and skin color, but none of these were statistically significant.

In the multivariate model (Table 2), days outside per week (''7'' 11.12 nmol/L versus ''<7''; P = 0.01), limbs covered (''no'' 24.90 nmol/L and ''partial'' 8.15 nmol/L versus ''yes''; P = 0.0001), and milk intake (glasses/wk; ''>10'' 18.94 nmol/L, ''>5-10'' 9.16 nmol/L, and ''1-5'' 7.90 nmol/L versus ''<1''; P = 0.02) best predicted 25(OH)D levels. Vitamin D–containing supplement use was marginally associated (''high'' 7.51 nmol/L and ''moderate'' 10.22 nmol/L versus ''none''; P = 0.08). The summer model explained 29% of the variance in serum 25(OH)D.

Linear Regression Analysis: Winter. In the winter, age was significantly positively (P = 0.02) associated and BMI significantly negatively associated (P = 0.01) with 25(OH)D (Table 3). There was no relationship with skin color in the winter. Sun exposure in the winter was limited to sun exposure while on a trip to a warm, sunny climate. Although after adjustment for age, BMI, and skin color taking a trip was only marginally associated with increased 25(OH)D (13.55 nmol/L versus no trip; P = 0.07), there was some evidence that leaving limbs uncovered (22.98 nmol/L versus no trip; P = 0.05) or not using sunscreen (25.52 nmol/L versus no trip; P = 0.02) while on a trip was associated with higher 25(OH)D. Sunlamp use was significantly associated with increased levels of 25(OH)D (25.68 nmol/L versus no sunlamp use; P = 0.03). Use of vitamin D–containing supplements was highly significantly related to 25(OH)D in the winter (17.83 nmol/L for high intake and 13.16 nmol/L for moderate intake versus none; P = 0.0001). Milk consumption was also associated with higher 25(OH)D (15.39 nmol/L for >10 glasses/wk and 10.91 for >5-10 glasses/wk versus <1; P = 0.01), but salmon and tuna consumption or other fish consumption were not. As in the summer, there was no evidence for interaction between vitamin D–related items and BMI.

Based on the multivariate model, the best predictors in the winter were sunlamp use (''yes'' 27.97 nmol/L versus ''no''; P = 0.01), milk intake (glasses/wk; ''>10'' 14.54 nmol/L, ''>5-10'' 11.54 nmol/L, and ''1-5'' 2.15 nmol/L versus ''<1''; P = 0.01), and vitamin D–containing supplement use (''high'' 17.30 nmol/L and ''moderate'' 13.82 nmol/L versus ''none''; P = 0.0006). The winter model accounted for 21% of the variation in serum 25(OH)D.

Discussion

The aim of this study was to assess the association between vitamin D–related variables derived from a summer and winter questionnaire with serum levels of 25(OH)D, considered the best indicator of vitamin D status (2, 3). In the summer, spending at least 0.5 hour outdoors every day, leaving limbs uncovered, participating in more outdoor activities, and drinking more milk were significantly associated with increased 25(OH)D after adjustment for age, BMI, and skin color. Taking vitamin D–containing supplements was marginally associated. The variables that best predicted higher levels of 25(OH)D in a multivariate model in the summer were as follows: skin color, BMI, spending 0.5 hour outdoors every day, less coverage of the limbs, and increased milk consumption. Age and intake of vitamin D–containing supplements remained marginally associated with 25(OH)D. In the winter, sunlamp use, higher milk intake, and taking vitamin D–containing supplements were all significantly associated with higher 25(OH)D after adjustment for age, BMI, and skin color.

Going on a trip to a warm climate was marginally associated with higher 25(OH)D, but the relationship was more significant for those who did not use sunscreen or left their limbs uncovered while on the trip. In the winter multivariate model, 25(OH)D levels were best predicted by age, sunlamp use, milk consumption, and vitamin D–containing supplement use, with BMI remaining marginally associated. Although BMI contributed to the overall circulating 25(OH)D, there was no evidence in this study that BMI influenced the effect of the other variables.

In general, sun exposure–related questions were strongly associated with 25(OH)D in the summer. This is consistent with the previous work of Van der Mei et al. in Tasmania (10). Sunlamp use was associated in the winter, although relatively few people reported using them (3%). This study was conducted in Ontario at latitudes greater than 43° where exposure to UVB radiation occurs largely in the summer because of the angle of the sun (11). Skin exposure is also limited in the winter because of lower temperatures. Being exposed to enough UVB to cause a slight pinkness to the skin

Table 2. Association between self-reported indicators of UVB exposure and dietary vitamin D with serum 25(OH)D (nmol/L) in the summer in 203 women (R^2 = 0.29; P < 0.0001 for whole multivariate model)

	Unadjusted		Adjusted*		Multivariate†		
	Regression coefficient	P	Regression coefficient	P	Regression coefficient	P	R^2
Age (y)	0.51	0.08	—	—	0.47	0.07	0.01
Skin color							
Very fair	7.46	0.009	—	—	23.99	0.02	0.04
Fair	1.66				14.00		
Light	25.84				28.56		
Light medium	8.92				17.40		
Dark medium to black	Reference				Reference		
BMI (kg/m^2)	−1.26	0.004	—	—	−1.09	0.007	0.03
Days outside/wk‡							
<7	Reference	0.004	Reference	0.009	Reference	0.01	0.03
7	13.45		11.81		11.12		
Limbs covered							
Yes	Reference	<0.0001	Reference	0.0001	Reference	0.0001	0.07
Partial	7.87		7.70		8.15		
No	25.92		25.36		24.90		
Sunscreen use§							
Yes	Reference	0.66	Reference	0.62	—	—	—
No	−0.16		1.31				
Outdoor job‖							
Yes	13.11	0.07	10.19	0.14	—	—	—
No	Reference		Reference				
Outdoor activity episodes/wk¶							
<7	Reference	0.0005	Reference	0.002	—	—	—
7-10	4.22		2.74				
>10	21.29		18.72				
Sunlamp							
Yes	22.41	0.11	16.51	0.23	—	—	—
No	Reference		Reference				
Milk (glasses/wk)							
<1	Reference	0.004	Reference	0.02	Reference	0.02	0.04
1-5	4.89		4.98		7.90		
>5-10	10.11		8.51		9.16		
>10	22.84		19.09		18.94		
Fish/wk							
<1	Reference	0.89	Reference	0.92	—	—	—
1-2	2.40		0.33				
>2	0.27		−2.40				
Tuna or salmon/wk							
0	Reference	0.73	Reference	0.99	—	—	—
>0-1	4.35		−0.27				
>1	5.50		−0.96				
Vitamin D–containing supplements**							
None	Reference	0.01	Reference	0.06	Reference	0.08	0.02
Moderate	11.93		10.75		10.22		
High	14.64		11.49		7.51		

NOTE: Questions were based on vitamin D intake and UVB exposure in the 4 weeks before interview.
*Adjusted for age, BMI, and skin color.
† Model includes all variables shown.
‡ Number of days outside for at least 0.5 hour during the summer.
§Question asked if sunscreen was usually worn.
‖Question asked if more than 0.5 hour was spent outdoors at work between 9 a.m. and 5 p.m.
¶Based on the total number of specific outdoor activities (e.g., swimming and sunbathing) reported as number of times per week or month.
**''None'' = 0 IU (no multivitamins, vitamin D supplement, or cod liver oil intake), ''Moderate'' = 200 to 400 IU (took vitamin D capsules or multivitamins or cod liver oil only), and ''High'' = greater than 400 IU (took more than one source of a vitamin D–containing supplements).

Table 3. Association between self-reported indicators of UVB exposure and dietary vitamin D with serum 25(OH)D (nmol/L) in the winter in 213 women (R^2 = 0.21; P < 0.0001 for whole model)

	Unadjusted		Adjusted*		Multivariate †		
	Regression coefficient	P	Regression coefficient	P	Regression coefficient	P	R^2
Age (y)	0.57	0.02	—	—	0.50	0.03	0.02
Skin color							
Very fair	−5.66	0.60	—	—	−5.01	0.71	0.01
Fair	1.27				1.52		
Light	−0.64				−3.58		
Light medium	−6.03				−4.36		
Dark medium/brown/very dark brown/black	Reference				Reference		
BMI (kg/m^2)	−0.92	0.01	—	—	−0.66	0.06	0.01
Sun trip in the winter ‡							
Yes	16.05	0.03	13.55	0.07	—	—	—
No	Reference		Reference				
Limbs covered while on trip							
Did not go on trip	Reference	0.02	Reference	0.05	—	—	—
Yes	−2.64		−4.29				
Partial	10.06		8.14				
No	25.36		22.98				
Sunscreen use while on trip§							
Did not go on trip	Reference	0.01	Reference	0.02	—	—	—
Yes	10.06		7.49				
No	27.64		25.52				
Sunlamp use							
Yes	26.81	0.02	25.68	0.03	Reference	0.01	0.03
No	Reference		Reference		27.97		
Milk (glasses/wk)							
<1	Reference	0.01	Reference	0.01	Reference	0.01	0.04
1-5	2.57		1.57		2.15		
>5-10	12.06		10.91		11.54		
>10	15.21		15.39		14.54		
Fish/wk							
<1	Reference	0.95	Reference	0.93	—	—	—
1-2	1.33		0.63				
>2	1.41		−1.70				
Tuna or salmon/wk							
0	Reference	0.22	Reference	0.1	—	—	—
>0-1	−3.35		−6.61				
>1	5.06		3.03				
Vitamin D−containing supplements‖							
None	Reference	<0.0001	Reference	0.0001	Reference	0.0006	0.06
Moderate	15.34		13.16		13.82		
High	22.07		17.83		17.30		

NOTE: Questions were based on vitamin D intake and UVB exposure in the 4 weeks before interview.
*Adjusted for age, BMI, and skin color.
† Model includes all variables shown.
‡ Trip to warm climate.
§Question asked if sunscreen was usually worn.
‖"None" = 0 IU (no multivitamins, vitamin D supplement, or cod liver oil intake), "Moderate" = 200 to 400 IU (took vitamin D capsules or multivitamins or cod liver oil only), and "High" = greater than 400 IU (took more than one source of a vitamin D−containing supplements).

(1 minimal erythemal dose) produces vitamin D equivalent to 20,000 IU (6). A maximal dose of vitamin D can be reached in less than 0.5 hour in individuals with lighter skin tones, although longer is needed for individuals with darker skin tones (12). Indicator questions to determine whether some time is spent outdoors every day or the number of outdoor activities per week in the summer were highly associated with 25(OH)D. Going to a lower latitude in the winter did increase 25(OH)D to some extent, but only those who reported not using sunscreen or leaving their limbs uncovered. Only 8% of the women traveled south in the winter.

Milk was associated in both seasons, but vitamin D from supplements was more relevant in the winter. Milk contributes ~100 IU/glass (13). Although this is not a large dose, regular milk drinking did contribute significantly to the circulating 25(OH)D in both seasons. Approximately 25% of the women drank more than 10 glasses of milk per week. Salmon and tuna, which provide about 360 and 200 IU/serving, respectively [NIH Office of Dietary Supplements], did not contribute significantly to 25(OH)D likely because they were not eaten sufficiently frequently to have much effect. As we would expect, women who took vitamin D−containing supplements had higher levels of 25(OH)D compared with women who did not take vitamin D−containing supplements. Supplement use contributed much more to 25(OH)D levels in the winter compared with the summer. We estimated the total amount of IU consumed in supplements based on the supplement reported and available information on formulation. Supplemental intake was analyzed in categories because most respondents either took no supplements containing vitamin D or consumed vitamin D in the range of 200 to 400 IU with a few taking more than this, usually from multiple sources.

In this study, as BMI increased, the levels of 25(OH)D decreased as has been observed previously (6). Unexpectedly, as age increased, 25(OH)D levels increased as well, although the significance was marginal in the summer. We would expect levels to decline as the ability of the skin to synthesize vitamin D deteriorates with age (5), although a previous study also found that older women had similar or higher levels of 25(OH)D (14). The majority of women were under 60 years old, and it is possible that the ageing effect is more apparent at older ages. The older women may have had greater sun exposure or dietary and supplemental exposure to vitamin D that was imperfectly accounted for by the other variables. Individuals with darker skin tones tend to have lower levels of 25(OH)D because melanin blocks UVB radiation, and individuals with darker skin tones may require 10 to 50 times the exposure to UVB compared with individuals with lighter skin tones (6, 12). This general observation was seen more clearly in the summer where it is more relevant. The lower levels of 25(OH)D we observed in women with fairer skin tones may be associated with sun avoidance to help prevent sun burns.

The R^2 values indicate that the multivariate models accounted for ~29% of the variation in circulating 25(OH)D in the summer and 21% in the winter. These are likely underestimates given that there is some random error in the measurements of 25(OH)D. Given that many of the exposure indicators were fairly crude, this is quite a high degree of variance accounted for.

Overall, there was evidence that questions designed to assess vitamin D exposure were in fact related to 25(OH)D. This provides reassurance that studies based on similar questions are capturing relevant vitamin D information, including the case-control study from which this validation study sample was drawn (8). This study found reduced breast cancer risks associated with increasing sun exposure and increasing milk consumption particularly during ages 10 to 19 years. Although we do not know how well recalled exposure earlier in life correlates with circulating 25(OH)D, it is likely that extreme categories of indicators, such as outdoor activities and milk drinking, do differentiate those with higher and lower levels of 25(OH)D.

As well as providing some validation for questionnaire-based assessment of vitamin D, this study may be useful to determine how to optimize 25(OH)D levels in the body and to create targeted preventive interventions in future studies.

Limitations of this study include small sample sizes for some variables, which made it difficult to completely evaluate some factors and limited the power to detect effect modification. More detailed information on some of the vitamin D indicators would increase understanding of their relationship to 25(OH)D, particularly for dietary supplements. Only specific dietary items were assessed (milk, tuna or salmon, and other fish). However, other food items contain relatively little vitamin D and/or are rarely consumed. These items reflect the questions that were used in the larger study. Currently, most food frequency questionnaires do not collect detailed information on type of fish consumed. Milk is the primary dietary contributor to dietary vitamin D, as fish is rarely consumed on a daily basis. In future studies, additional information on supplements would be beneficial, including whether the supplement contained vitamin D_2 or vitamin D_3. However, this level of detail may be challenging to obtain. Also, we only requested recent information and the relevance of longer term recall was not evaluated. There were differences in sample composition between the summer and the winter participants because individuals who completed the summer questionnaire did not necessarily complete the winter questionnaire, but the two seasons were evaluated independently. This study is likely relevant primarily for populations at higher latitudes (above 40°), but this area includes large populations. It is likely that the main contributors to circulating 25(OH)D will vary to some degree by population and geographic location.

In summary, this study found that indicator questions on vitamin D exposure related to sun exposure and major dietary sources, such as milk as well as supplements, are highly related to circulating 25(OH)D, a biomarker of vitamin D exposure. These types of questions will be useful for future studies on the health effects of vitamin D. These results provide a guide for the refinement of questions for future studies and also for the development of interventions.

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