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Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors[1–3]

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ABSTRACT

Background: Increased awareness of the importance of vitamin D to health has led to concerns about the prevalence of hypovitaminosis D in many parts of the world.

Objectives: We aimed to determine the prevalence of hypovitaminosis D in the white British population and to evaluate the influence of key dietary and lifestyle risk factors.

Design: We measured 25-hydroxyvitamin D [25(OH)D] in 7437 whites from the 1958 British birth cohort when they were 45 y old.

Results: The prevalence of hypovitaminosis D was highest during the winter and spring, when 25(OH)D concentrations <25, <40, and <75 nmol/L were found in 15.5%, 46.6%, and 87.1% of participants, respectively; the proportions were 3.2%, 15.4%, and 60.9%, respectively, during the summer and fall. Men had higher 25(OH)D concentrations, on average, than did women during the summer and fall but not during the winter and spring ($P = 0.006$, likelihood ratio test for interaction). 25(OH)D concentrations were significantly higher in participants who used vitamin D supplements or oily fish than in those who did not ($P < 0.0001$ for both) but were not significantly higher in participants who consumed vitamin D–fortified margarine than in those who did not ($P = 0.10$). 25(OH)D concentrations <40 nmol/L were twice as likely in the obese as in the nonobese and in Scottish participants as in those from other parts of Great Britain (ie, England and Wales) ($P < 0.0001$ for both).

Conclusion: Prevalence of hypovitaminosis D in the general population was alarmingly high during the winter and spring, which warrants action at a population level rather than at a risk group level. *Am J Clin Nutr* 2007;85:860–8.

KEY WORDS 25-Hydroxyvitamin D, vitamin D status, vitamin D supplements, vitamin D deficiency, seasonality, fortified food, population studies, Great Britain

INTRODUCTION

The thinking about the actions of vitamin D have made an important shift during the past 10 y. In addition to its well-established role in the regulation of calcium metabolism, the active form of vitamin D has been shown to have antiproliferative and immunomodulatory effects that are thought to influence the development of several serious conditions, including diabetes, cardiovascular disease, and cancer (1–6). Vitamin D is a nutrient that functions as a hormone precursor, and wide-ranging health effects are supported by the presence of vitamin D receptors in several cell types and tissues of the body (eg, lymphocytes and monocytes, brain, heart, pancreas, intestine, and placenta; 2). With this increasing knowledge, a reconsideration of the cutoffs for adequate vitamin D status has occurred. 25-Hydroxyvitamin D [25(OH)D] is the best available indicator for vitamin D status (7), and concentrations ≥25 nmol/L are sufficient to prevent the severe hypovitaminosis D that leads to softening of bone tissue, which manifests as rickets in children and as osteomalacia in adults (1, 4, 8). Furthermore, it is now understood that even less severe forms of hypovitaminosis D have short- and long-term health implications, and accordingly, in a recent consensus statement, concentrations of ≥75 nmol/L were identified as necessary for optimum bone health (9). This cutoff was based on a threshold required for a range of functional outcomes, including maximal suppression of circulating parathyroid hormone, greatest calcium absorption, and highest bone mineral density.

Concerns exist that hypovitaminosis D may be common in many parts of the world; some discussion has been held of possible epidemics in Western populations, and calls have been heard for screening of vitamin D status in routine health care surveillance (2). We aimed to evaluate the magnitude of hypovitaminosis D as a public health problem in Great Britain (ie, England, Scotland, and Wales), because several reasons exist for suspicion that it is particularly prevalent there. Skin synthesis of vitamin D (the major source of the vitamin) is likely to be affected by Western lifestyles, which increasingly involve working indoors during daylight hours, and this may be particularly important when combined with residence in northern latitudes and a cloudy climate (10). Moreover, dietary intake of vitamin D may be low in Great Britain, where vitamin D fortification is mandatory only for margarine. This situation contrasts with that in other countries, such as the United States and Canada, where milk is also fortified (11). With the exception of oily fish, most foods naturally contain very little vitamin D (2, 3). Intake in the form of supplements is limited to the availability of over-the-counter products. Finally, the high prevalence of obesity in Great Britain

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(12), a well-known risk factor for hypovitaminosis D (13, 14), may adversely affect vitamin D status in the population.

Alarmingly high rates of hypovitaminosis D have been found in ethnic minorities living in Great Britain (15–17). Case reports document a reemergence of rickets in infants (18), children (19), and adolescents (20); in addition, hypovitaminosis D is common in the elderly, particularly those living in institutions (21, 22). We measured serum 25(OH)D in 2002–2004 in a nationwide sample of whites (aged 45 y) who are participants in the 1958 birth cohort study. Our aims here were to report current prevalence rates and to examine seasonal, demographic, and lifestyle influences on hypovitaminosis D.

SUBJECTS AND METHODS

Subjects

Participants are from the 1958 British birth cohort; all were born in England, Scotland, or Wales during the same week of March 1958 (n = 16 751; 23, 24). Cohort members were most recently contacted between September 2002 and April 2004 (24). The target population for this survey consisted of 12 069 persons currently living in Great Britain. Seventy-eight percent (n = 9349) of participants completed questionnaires, and 7591 (81%) also provided a blood sample, which was used to determine their vitamin D status. The cohort is mainly white (98%); immigrants born during the target week were included in the birth cohort study only up to 1974. The current study is restricted to whites (including British, ethnically Irish living in Great Britain, and other whites); persons of other ethnic origins (n = 154) were excluded.

Written informed consent for the use of information in medical studies was obtained from the cohort members. The 2002–2004 survey was approved by the South-East Multi-Centre Research Ethics Committee.

Methods

Weight and standing height at age 45 y were measured without shoes and in light clothing by the nurse using scales and a stadiometer. Body mass index (BMI; in kg/m^2) was calculated, and obesity was defined as BMI ≥ 30. The season in which the blood sample was obtained was classified as winter (December through February), spring (March through May), summer (June through August), and fall (September through November). Geographic location was based on current region of residence, which, for presentation and analyses of north-south gradient, was grouped as follows (denoted by using the standard British terminology for regional boundaries in Great Britain): South (South East, South West, and Greater London), Middle (East Anglia, Midlands, and Wales), North (North, North West, and Yorkshire and the Humber), and Scotland. Socioeconomic status (SES) was assessed by using the Registrar General's occupational classification based on current or most recent occupation at age 42 y and categorized as I and II (professional and managerial), III (skilled) nonmanual, III (skilled) manual, and IV and V (partly skilled and unskilled). Persons who were institutionalized, retired, or unemployed over a long period were classified separately (n = 319; 4.3%).

Information on selected dietary and lifestyle influences on 25(OH)D was collected by using a structured food-frequency questionnaire (FFQ). Frequencies of dietary intake were reported as never, occasionally, <1 d/wk, 1–2 d/wk, 3–6 d/wk, 1 time/d, 1–4 times/d, and >4 times/d. Consumption of oily fish (eg, salmon, trout, and mackerel) was classified as weekly, less than weekly, and never, and margarine use was classified as daily, weekly, and less than weekly. Vitamin D fortification of margarine (7.05–8.82 μg/100 g) is mandatory in the United Kingdom (25). Participants reported their use of cod liver or fish oil or other supplements containing vitamin D [typical vitamin D concentration in over-the-counter supplements sold in the United Kingdom (D_3 or D_2) is 200 IU]. The usual time per day spent outdoors in daylight hours during the previous month was reported as no time, <15 min, 15–30 min, 30–60 min, 1–2 h, 3–4 h, and >4 h. Protection of skin with the use of sunscreen or clothing during sunny weather in the United Kingdom or abroad was reported as "often," "sometimes," "rarely," and "never." Information on holidays outside of Great Britain was not available. Skin color (inner arm) was reported as light (white, fair, or ruddy), medium (olive or light or medium brown), and dark (dark brown or black). Participants reported the average time per day that they watched television (TV) or used a personal computer (PC) as none, <1 h, 1–2 h, 2–3 h, 3–4 h, and >4 h; data from these separate questions were combined for the current analyses.

Measurement of vitamin D status

25(OH)D was measured by using automated application of an enzyme-linked immunosorbent assay (IDS OCTEIA Elisa; IDS, Bolton, United Kingdom) and an analyzer (BEP 2000; Dade-Behring, Milton Keynes, United Kingdom) with sensitivity of 5.0 nmol/L, linearity ≤155 nmol/L, and intraassay CV 5.5–7.2% (26, 27). The heterogeneity of 25(OH)D concentrations measured by different assay methods is well known (7, 28). To apply previously recommended cutoffs for hypovitaminosis D, 25(OH)D concentrations were standardized according to the mean of the values found by the Vitamin D External Quality Assurance Survey (DEQAS) of >100 laboratories around the world (9, 28). Standardization was based on quality-control data compared on 5 occasions during the study period; evaluations were conducted at the start of the fieldwork and then at 3-mo intervals. Hypovitaminosis D was defined by using 3 thresholds for 25(OH)D concentrations: <25, <40, and <75nmol/L. Cutoffs were selected on the basis of *1*) concentrations sufficient to prevent rickets and osteomalacia (ie, <25 nmol/L) (1, 4, 8); *2*) a lower reference concentration suggested to reflect the need for vitamin D supplementation according to most laboratories carrying out vitamin D assays (ie, <40 nmol/L) (3, 28); and *3*) current judgment as to the concentration required for optimal bone health (ie, <75 nmol/L) (4, 9).

Statistical analysis

Natural log transformation was used to achieve normal distribution for 25(OH)D. Log-transformed values were used in calculating geometric means and for determining the outcome in linear regression analyses. For descriptive purposes, mean 25(OH)D concentrations and the proportion of persons with hypovitaminosis D are presented after standardization by sex and season. Comparisons of seasonal and demographic factors with dietary and lifestyle indicators of vitamin D status were analyzed by chi-square test and by nonparametric test for trend in the case of ordinal categorized variables. $P < 0.05$ was considered significant. Log likelihood ratio tests (LRT) and LRTs for trend were used to determine associations with serum 25(OH)D. All

TABLE 1
Demographic characteristics and associations with the use of vitamin D supplements and time spent outdoors in the 1958 British birth cohort at age 45 y

		Vitamin D supplements[1]			Time spent outdoors/d[2]			
	Subjects	No (n = 6080)	Yes (n = 1187)	P[3]	<30 min (n = 764)	30 min–3 h (n = 3133)	≥3 h (n = 2953)	P[3]
	n (%)	*n*				*n*		
All	7437 (100)	83.7	16.3		11.2	45.7	43.1	
Sex				<0.0001				<0.0001
Men	3725 (50.1)	87.1	12.9		9.2	42.0	48.9	
Women	3712 (49.9)	80.2	19.8		13.1	49.4	37.5	
Obese[4]				<0.0001				0.02
No	5598 (76.3)	81.9	18.1		11.4	46.4	42.2	
Yes	1740 (23.7)	89.3	10.7		10.4	43.6	46.1	
Season[5]				0.17				<0.0001
Winter	1290 (17.4)	81.5	18.5		21.1	49.9	29.0	
Spring	1560 (21.0)	84.4	15.6		15.3	51.1	33.6	
Summer	1748 (23.5)	84.0	16.0		5.5	42.1	52.4	
Fall	2839 (38.2)	84.0	16.0		8.0	43.2	48.8	
Region[6]				<0.0001				0.007
South	2853 (38.4)	80.1	19.9		11.0	48.3	40.7	
Middle	1928 (26.0)	84.5	15.5		11.1	45.2	43.7	
North	1937 (26.1)	85.9	14.1		12.2	43.3	44.5	
Scotland	712 (9.6)	89.3	10.7		8.8	43.6	47.6	
Socioecomic status (British occupational classifications)[7]				<0.0001				<0.0001
I and II	3011 (40.5)	80.4	19.6		13.6	53.7	32.8	
III Nonmanual	1528 (20.6)	81.6	18.4		12.4	49.9	37.7	
III Manual	1421 (19.1)	87.8	12.2		7.3	30.9	61.8	
IV and V	1158 (15.6)	88.7	11.3		8.0	37.7	54.4	
Unclassified[8]	319 (4.30)	87.8	12.2		10.7	45.6	43.8	

[1] Use of cod liver or fish oil or other supplements containing vitamin D. n = 170 with missing data.
[2] During daylight hours in the previous month. n = 587 with missing data.
[3] Chi-square test: nonparametric trend test was used for ordinally grouped variables.
[4] Defined as BMI (kg/m^2) ≥30. n = 99 with missing data.
[5] Winter, December through February; spring, March through May; summer, June through August; fall, September through November.
[6] n = 7 with missing data.
[7] I and II, professional or managerial; III, Nonmanual or manual, skilled; IV and V, partly skilled and unskilled.
[8] Includes cohort members who are institutionalized, retired, unemployed, and other.

analyses of serum 25(OH)D were done by using linear regression after adjustment for sex and month of measurement.

Influences on hypovitaminosis D were evaluated by logistic regression after adjustment of all models for sex and month of measurement. Odds ratios and corresponding 95% CIs were used to describe the influence of demographic, dietary, and lifestyle indicators on the risk of hypovitaminosis D. LRTs and LRT trend tests were used to test the significance of each factor in the models. The first model included adjustment for sex and month of measurement only. The fully adjusted model included, in addition, all other indicators of hypovitaminosis D. Logistic regression analyses were repeated by using the 3 thresholds for hypovitaminosis D to evaluate whether influences on hypovitaminosis D were similar regardless of the level of severity. Multiple imputation (10 cycles) was used for missing information on obesity, dietary, or lifestyle indicators in the final models of hypovitaminosis D (29). Information on obesity was missing for 99 participants (1.3%), and 1117 cohort members (15.0%) were missing data on skin color or ≥1 dietary or lifestyle indicator (eg, vitamin D supplementation, intake of oily fish, margarine consumption, use of sun protection, time spent outdoors, or watching TV or using a PC). Analyses were repeated for the sample with complete data, and results were unaffected by the treatment of missing information unless otherwise indicated. Results are presented with imputed data. Statistical analyses were carried out by using STATA software (version 9.1; Stata Corp, College Station, TX), and maps were constructed with the use of EPIMAP software (version 3.3.2; Epi Info, Atlanta, GA).

RESULTS

Demographic characteristics and associations with supplement use and time spent outdoors are presented in **Table 1**. Women and nonobese participants (BMI < 30) were significantly more likely to use vitamin D supplements and to spend less time outdoors than were others. Variations in the frequency of oily fish consumption were similar to those observed for supplement use: compared with others, fish consumption was significantly more frequent in females, the nonobese, participants living in Southern England, and those in SES classification I and II ($P \leq 0.001$ for all comparisons, chi-square test). Women were significantly more likely to use sun protection than were men: 70% and 49%, respectively, classified their use as "often" and 5% and 15%, respectively, classified their use as "rarely or

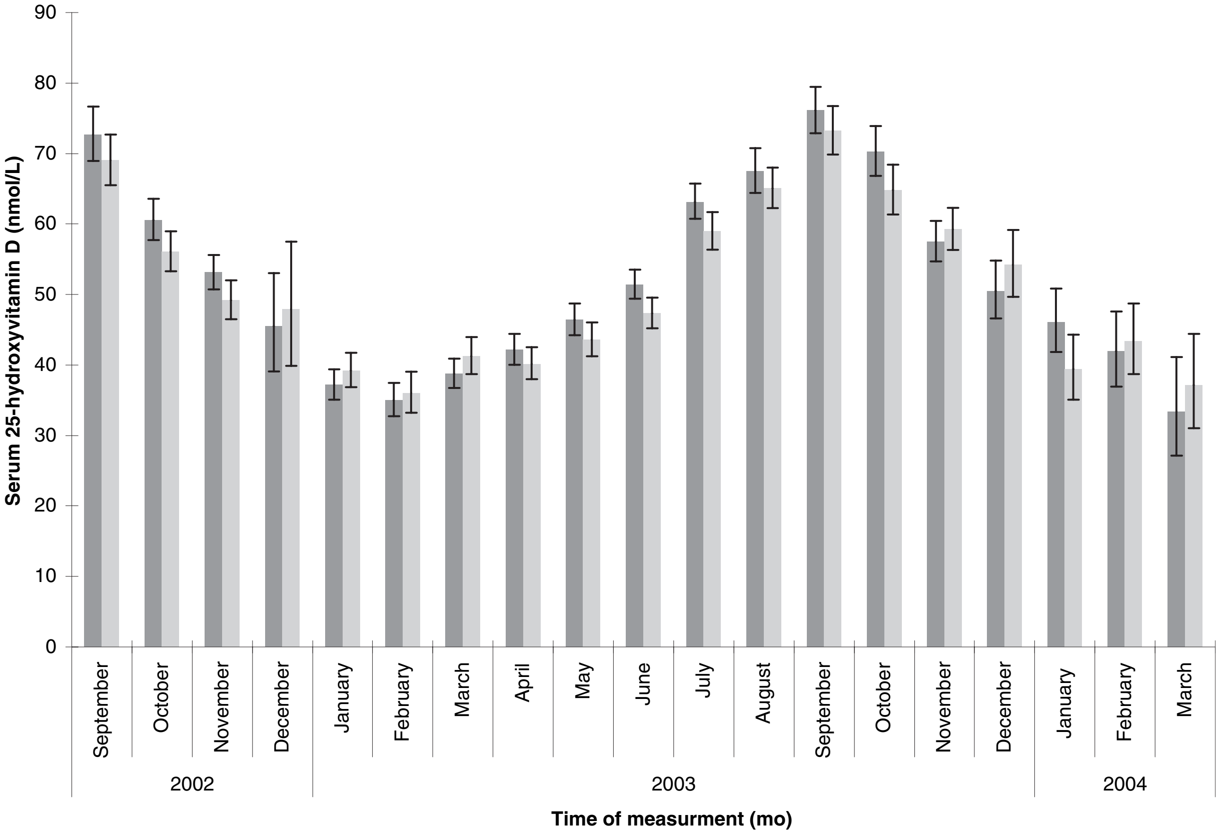

FIGURE 1. Geometric mean (95% CI) monthly variation in serum 25-hydroxyvitamin D [25(OH)D] concentrations in men (■; n = 3725) and women (▨; n = 3712) in the 1958 British birth cohort at age 45 y. The interaction between sex and month was significant [P = 0.02, linear regression analyses on log 25(OH)D]. n per sex and month ranged from 17 to 340: 98 in December 2003 for women and <100 for both sexes in December 2002 (n = 40 M, 37 F), January 2004 (n = 95 M, 75 F), February 2004 (n = 58 M, 70 F), and March 2004 (n = 22 M, 17 F).

never" ($P < 0.0001$, chi-square test). SES differences were seen in the use of sun protection: the proportion of participants reporting use "often" and "rarely or never," respectively, was 63% and 8% in SES classification I and II, 67% and 7% in SES classification III (skilled) nonmanual, 50% and 15% in SES classification III (skilled) manual, 57% and 12% in SES classification IV and V, and 57% and 14% in the unclassified group ($P < 0.0001$, chi-square test). Variation in sun protection by BMI was modest: "often" and "rarely or never" in 58% and 12%, respectively, of the obese compared with 61% and 9%, respectively, of the others ($P = 0.03$, chi-square test), whereas no significant variations were seen by region (data not presented) ($P = 0.07$, chi-square test).

Serum 25(OH)D concentrations peaked in September and were at their lowest from January through April (**Figure 1**). Month of blood sampling was the strongest predictor; it explained 21.5% of the variation in 25(OH)D ($P < 0.0001$, LRT). The association between 25(OH)D and sex varied by month of measurement; concentrations tended to be lower in women during the summer and fall (June through November), whereas no consistent monthly sex differences were apparent during the winter and spring (December through May; Figure 1). The use of vitamin D supplements and the consumption of oily fish but not (fortified) margarine showed the expected associations with 25(OH)D (**Figure 2**). Time spent outdoors was strongly associated with 25(OH)D during the summer and fall, but no association was apparent during the winter months ($P < 0.0001$, LRT interaction).

Because the 25(OH)D concentration was largely predicted by the month of blood sampling, the prevalence of hypovitaminosis D, as shown in **Table 2**, is stratified by season. Hypovitaminosis D at all thresholds was more common in women than in men during the summer and fall, whereas, during the winter and spring, women were overrepresented among those with 25(OH)D <25nmol/L and ≥75nmol/L. The prevalence of hypovitaminosis D was markedly higher in the obese than in the others in all severity groups and regardless of season. There was a significant north-south gradient in the prevalence of hypovitaminosis D in all severity groups (Table 2). Regional variation in the prevalence of 25(OH)D concentrations <40 nmol/L during the 4 seasons is represented in **Figure 3**.

As reported in Table 2, the association between sex and hypovitaminosis D was dependent on season. Women had a risk of having 25(OH)D < 25nmol/L during the summer or fall twice that of men, whereas women's risk of concentrations < 40 nmol/L and < 75 nmol/L were only 40% greater than that of men after full adjustment for available background indicators (LRT $P < 0.0001$ for all comparisons adjusted for month of measurement, skin color, obesity, region, SES, supplement use, fish consumption, time spent outdoors, sun protection and time spent watching TV or using a PC). During winter, the only threshold at which the risk of hypovitaminosis D was increased in women was the threshold of <25nmol/L ($P = 0.001$; adjusted OR: 1.50; LRT). Persons who were obese or who lived in Scotland had a risk of 25(OH)D concentrations <40 nmol that was twice that of nonobese persons or those who did not live in

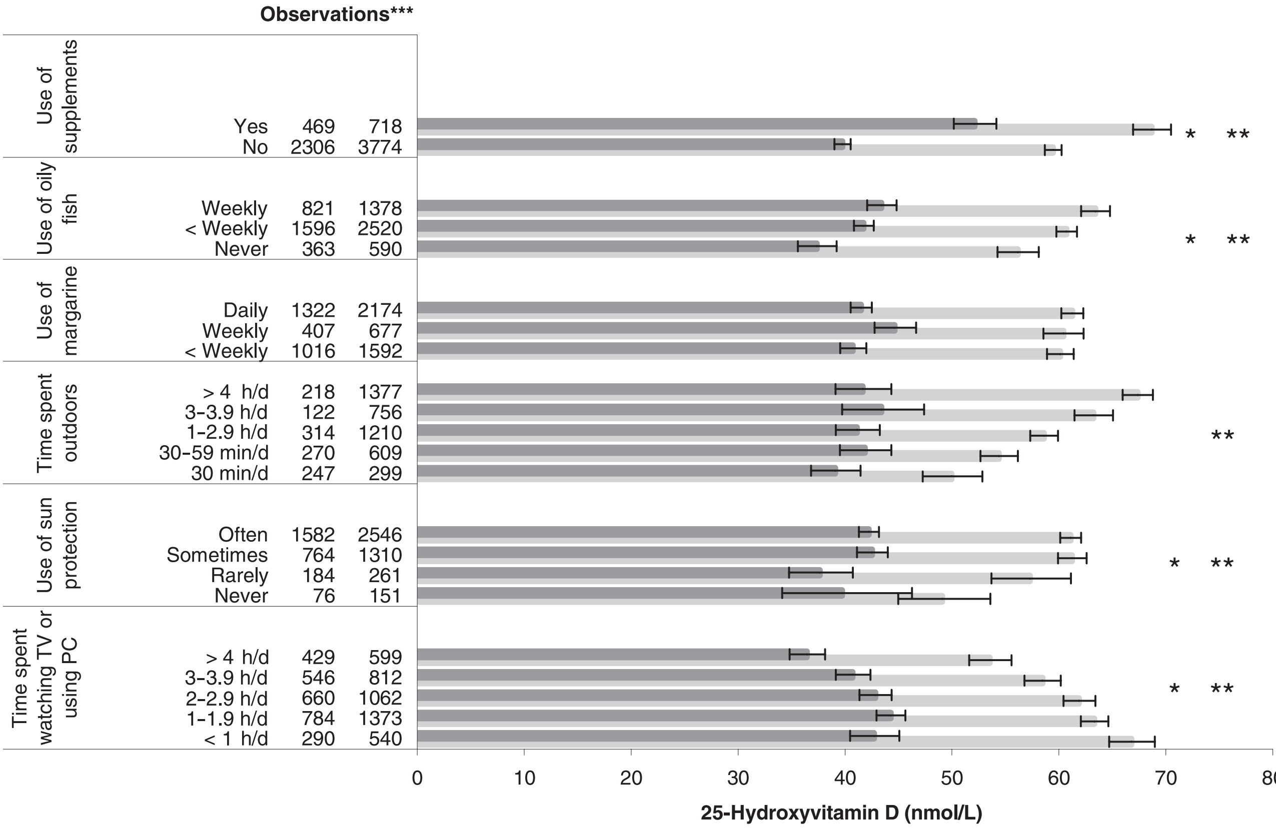

FIGURE 2. Geometric mean (95% CI) 25-hydroxyvitamin D [25(OH)D] concentrations by dietary and lifestyle indicators, standardized by sex and season. ▩; winter and spring (December through May); ▨, summer and fall (June through November) in Great Britain. *December through May: log likelihood ratio test, $P < 0.0001$ for supplementation; log likelihood ratio trend test, $P < 0.0001$ for fish consumption and time spent watching television (TV) or using a personal computer (PC), $P = 0.002$ for sun protection. **June through November: log likelihood ratio test, $P < 0.0001$ for supplementation; log likelihood ratio trend test, $P < 0.0001$ for fish consumption, time spent outdoors, and time spent watching TV or using a PC, $P = 0.007$ for sun protection. All tests were adjusted for sex and month of measurement. 25(OH)D concentrations for time spent outdoors are presented for December through February, and those for all other indicators are presented for December through May. ***Number of unknown observations for December through May (first column) and for June through November (second column), respectively: supplementation, 95 and 75; fish consumption, 99 and 70; margarine use, 144 and 105; time spent outdoors, 336 and 251; sun protection, 319 and 244; and time spent using a PC or watching TV, 201 and 141.

Scotland (**Table 3**). The strength of the association with vitamin D supplementation and margarine consumption varied according to the severity of hypovitaminosis D. Use of vitamin D supplements was associated significantly more strongly with the 2 lowest thresholds (fully adjusted OR for <25 nmo/L: 0.33; 95% CI: 0.2, 0.5; OR for <40 nmol/L: 0.36; 95% CI: 0.3, 0.4) than with a threshold of <75 nmol/L (OR: 0.52; 95% CI: 0.5, 0.6). Margarine consumption was not associated with 25(OH)D concentrations <75 nmol/L and was not robustly associated with those <40 nmo/L (Table 3), but the risk of a concentration <25 nmol/L was less in cohort members who consumed margarine daily (adjusted OR: 0.69; 95% CI: 0.6, 0.8) or weekly (adjusted OR: 0.68; 95% CI: 0.5, 0.9) than in those with less frequent consumption (adjusted LRT for trend, $P = 0.003$). As suggested by Figure 2, time spent outdoors during winter did not affect the risk of hypovitaminosis D ($P \geq 0.18$), however, there was a strong linear association for all severity groups at other times of the year (adjusted LRT for trend, $P < 0.0001$ for all comparisons).

DISCUSSION

Previous studies have highlighted the emerging problems of hypovitaminosis D in the elderly in Great Britain (21, 22) and ethnic minority groups (15–17). Our results suggest that the problem is widespread also in middle-aged British whites. It is striking that nearly half of the population had 25(OH)D concentrations <40 nmol/L during the winter and spring (3, 28); this showed that, for part of the year at least, the problem is not restricted to high-risk groups. With the use of the higher cutoff from a recent consensus on optimal status (ie, <75 nmol/L) (9), it is disturbing from the viewpoint of future bone health that nearly 90% of the current study population was affected by hypovitaminosis D during the winter and spring, and 60% had suboptimal concentrations year-round.

Old age is a well-established risk factor for hypovitaminosis D (2) and as expected our middle-aged population compares favorably to Britons aged >65 y (21, 22). It is reassuring that our results are confirmed by statistics for 35–49-y-olds in the National Diet and Nutrition survey (mean concentration for both men and women: 48 nmol/L) (30). Nonetheless, the mean 25(OH)D concentration was lower and the prevalence of hypovitaminosis D higher in our study than in the general adult population in Canada or the United States. For example, in a study from Calgary, Canada (latitude 51°N) 20% of participants had 25(OH)D concentrations <40 nmol/L during the winter (31), whereas, in the current study, that proportion was 46%. In the 2

TABLE 2
Average 25-hydroxyvitamin D [25(OH)D] and the prevalence of hypovitaminosis D at 3 thresholds (<25, <40, and <75 nmol/L) stratified by season and demographic characteristics[1]

Characteristics and season	Subjects	Average	25(OH)D <25 nmol/L (n = 148/439)	25(OH)D <40 nmol/L (n = 705/1327)	25(OH)D <75 nmol/L (n = 2794/2481)
	n	*nmol/L*		%	
All[2]					
Winter and spring	2850	41.1 (40.4, 41.8)[3]	15.5	46.6	87.1
Summer and fall	4587	60.3 (59.5, 61.0)	3.2	15.4	60.9
Sex					
Winter and spring					
Men	1413	41.1 (40.2, 42.1)	13.9	47.0	88.7
Women	1437	41.2 (40.2, 42.3)	17.1	46.3	85.4
P		0.91	0.009	0.72	0.005
Summer and fall					
Men	2312	61.9 (60.9, 62.9)	2.2	13.4	58.1
Women	2275	58.6 (57.6, 59.6)	4.3	17.4	63.7
P		<0.0001	<0.0001	0.0001	<0.0001
Obesity[4]					
Winter and spring					
No	2129	42.8 (41.9, 43.6)	13.5	43.3	84.9
Yes	674	36.7 (35.5, 38.0)	21.4	56.4	93.2
Summer and fall					
No	3469	62.8 (62.0, 63.7)	2.8	12.3	57.3
Yes	1066	52.7 (51.4, 54.0)	4.5	25.3	72.7
P		<0.0001	<0.0001	<0.0001	<0.0001
Region of residence[5]					
Winter and spring					
South	1226	42.6 (41.5, 43.7)	12.5	43.8	86.2
Midlands and Wales	690	40.6 (39.3, 42.0)	16.1	46.9	87.9
North	676	41.2 (39.7, 42.7)	17.5	46.6	85.9
Scotland	256	35.4 (33.4, 37.5)	23.5	60.0	92.2
Summer and fall					
South	1627	62.4 (61.2, 63.6)	2.7	12.3	56.7
Midlands and Wales	1238	60.4 (59.1, 61.8)	2.1	14.8	62.4
North	1261	60.9 (59.5, 62.3)	3.3	15.7	60.0
Scotland	456	50.9 (48.9, 53.0)	8.3	27.5	74.9
P for trend		<0.0001	<0.0001	<0.0001	<0.0001
Socioeconomic status (British occupational classifications)[6]					
Winter and spring					
I and II	1165	41.8 (40.7, 42.9)	14.2	45.6	86.3
III Nonmanual	596	42.0 (40.1, 43.9)	15.7	44.9	86.3
III Manual	521	39.9 (37.9, 42.0)	17.8	46.4	88.0
IV and V	453	40.2 (38.5, 42.0)	16.1	48.9	88.4
Unemployed/other[5]	115	36.0 (33.1, 39.1)	26.8	59.1	89.0
P for trend		0.004	0.01	0.04	0.09
Summer and fall					
I and II	1846	60.9 (59.8, 62.0)	3.2	14.0	60.0
III Nonmanual	932	59.9 (58.0, 61.8)	2.5	15.8	62.9
III Manual	900	62.4 (60.2, 64.6)	2.7	13.2	56.9
IV and V	705	58.2 (56.3, 60.1)	4.2	16.7	65.1
Unemployed or other[7]	204	55.1 (51.6, 58.9)	7.3	26.5	62.4
P for trend		0.006	0.04	0.008	0.17

[1] All means and proportions are standardized by sex and season (winter and spring = December through May; summer and fall = June through November). *P* values for differences in 25(OH)D or prevalence of hypovitaminosis D from log likelihood ratio tests or log likelihood ratio trend tests as indicated. Sex, obesity, and socioeconomic status were distributed equally across seasons ($P \geq 0.41$ for all comparisons, chi-square test). A small difference was found between regions of interviews carried out in the summer and fall: 54% in southern England compared with 64% in the Midlands and 65% in northern England compared with 64% in Scotland ($P < 0.0001$, chi-square test). Season modified the association between sex and 25(OH)D ($P < 0.0006$) and socioeconomic status and 25(OH)D ($P = 0.01$); no interaction was observed for other factors.

[2] The number of subjects with hypovitaminosis D in December through May and June through November.

[3] Geometric $\bar{x}$ standardized by sex and season; 95% CI in parentheses (all such values).

[4] Defined as BMI (in kg/m^2) ≥30. Unknown: December through May, $n = 47$; June through November, $n = 52$. *P* value from test including data for full year.

[5] Unknown: December through May, $n = 2$; June through November, $n = 5$. *P* value from test including data for full year.

[6] I and II, professional or managerial; III, nonmanual or manual, skilled; IV and V, partly skilled and unskilled.

[7] Includes cohort members who were institutionalized, retired, unemployed, and other.

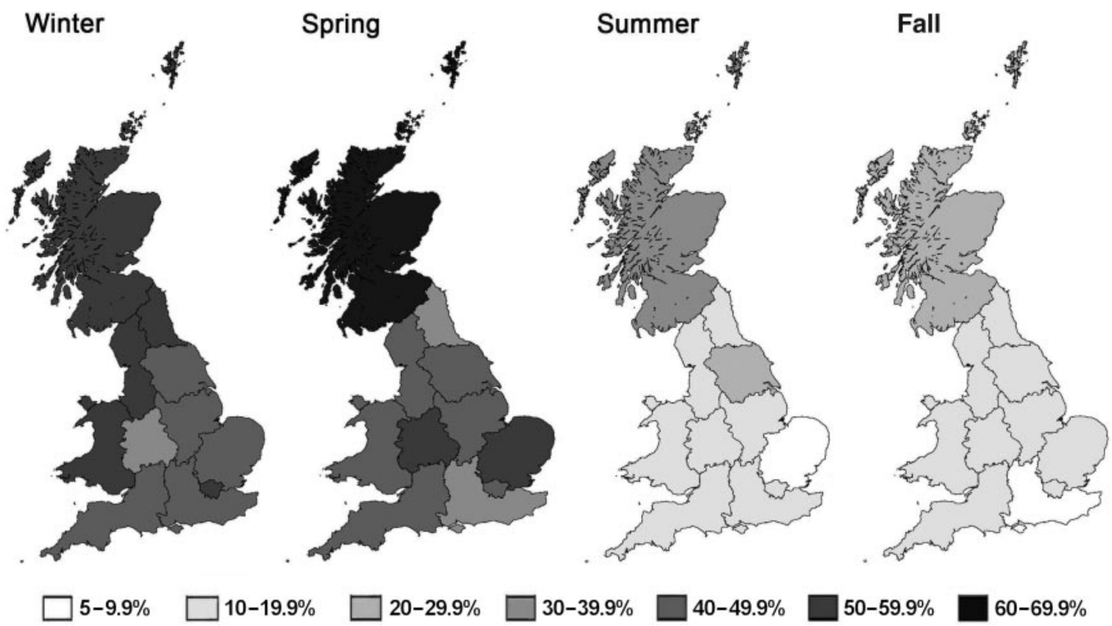

FIGURE 3. Seasonal and geographical variation in the prevalence of hypovitaminosis D (25-hydroxyvitamin D <40 nmol/L) in Great Britain.

seasonal subpopulations participating in the third National Health and Nutrition Examination Survey (NHANES III), the average 25(OH)D concentration was 66 nmol/L during winter in the southern group (median latitude 32°N) and 73 nmol/L during the summer in the northern group (median 39°N) (32). The prevalence of 25(OH)D concentrations <25nmol/L was low (≤3%) in NHANES III (32). The vitamin D status of the general US population is increasingly acknowledged to be unsatisfactory (2, 32, 33), and thus the even higher prevalence of hypovitaminosis D in the British population in the current study than in the US population highlights the urgency of the situation in Great Britain.

The high prevalence of hypovitaminosis D observed in British 45 y-olds is not surprising. First, Great Britain is located between 50°N and 60°N, which corresponds to the latitude of Canada up to the southern tip of Alaska. North of London, no cutaneous vitamin D synthesis occurs in December and January, and, even during the remainder of the year, cloud cover can block up to 99% of vitamin D production (10). The effect of latitude on production was apparent within the current study; the highest rates of hypovitaminosis D were observed in Scottish participants. Second, vitamin D supplements appear to be taken less frequently in Great Britain than in other countries. We found that 13% of men and 20% of women used supplements, whereas the corresponding proportions reported for the United States were 30% and 40% (11). Estimates of supplement use from the current study agree well with those reported from the National Diet and Nutrition Survey (12% and 24%, respectively) (34). Limited availability of supplements (eg, lack of over-the-counter single vitamin D products) is likely to contribute to these differences. In addition, the average dietary intake of vitamin D in the British National Diet and Nutrition Survey was only half of that reported for the United States, which may at least partly reflect differences in food fortification policy (11, 34). Unlike the situation in the United States, milk is not fortified with vitamin D in the United Kingdom, and only fortification of margarine is mandatory. The amount of added vitamin D is relatively low, because the purpose of the fortification is only to increase the vitamin D concentration of margarine to concentrations that occur naturally in butter (25). In the current study, the frequency of margarine consumption was not associated with the average 25(OH)D concentration, but the risk of 25(OH)D concentrations <25nmol/L was slightly reduced. This suggests that, whereas fortification of margarine is largely ineffective in improving vitamin D status at population level, it may be sufficient to raise 25(OH)D concentrations in the extreme state of deficiency. However, we acknowledge that only relatively crude information on margarine use was available; hence, we cannot exclude the possibility that underlying measurement error contributed to these observations.

Methodologic considerations

Cutoffs for adequate vitamin D status are a key influence on our perception of the extent hypovitaminosis D. For this reason, we presented data for 3 thresholds that are in part defined by known health outcomes [ie, <25 nmol/L to reflect calcium malabsorbtion and rickets (1, 4, 8) and <75 nmol/L from a consensus statement on requirements for bone health (4, 9)]. For an intermediate cutoff (<40 nmol/L), we relied on the view of most laboratories carrying out vitamin D assays that <40 nmol/L was the concentration reflecting the need for vitamin D supplementation, and it is commonly used as the lower reference level by the laboratories (3, 28). An alternative strategy would have been to use a higher threshold of 50 nmol/L (4). Furthermore, 25(OH)D concentrations can vary with assay method (7, 28). We used an automated application that is particularly suitable for large population surveys because of its excellent repeatability and the lack of variation by the operator carrying out the assay (26). Standardization of values to data from DEQAS facilitated the use of previously determined cutoffs for hypovitaminosis D.

The main strength of the study lies in the large sample of whites for whom information on 25(OH)D concentrations was available. With nationwide coverage and measures spanning the year, the current study provides valuable information on the

TABLE 3
Adjusted odds ratios (95% CIs) for selected risk factors of hypovitaminosis D (25-hydroxyvitamin D <40 nmol/L) in the 7437 participants of the 1958 British birth cohort[1]

	Simple[2]	Adjusted[3]
Obesity[4]		
No	Reference	Reference
Yes	2.03 (1.8, 2.3)	1.83 (1.6, 2.1)
P	<0.0001	<0.0001
Region of residence		
South	Reference	Reference
Midlands and Wales	1.22 (1.1, 1.4)	1.13 (1.0, 1.3)
North	1.19 (1.0, 1.4)	1.09 (0.9, 1.3)
Scotland	2.38 (2.0, 2.9)	2.13 (1.7, 2.6)
P for trend	<0.0001	<0.0001
Use of vitamin D supplements		
No	Reference	Reference
Yes	0.33 (0.28, 0.40)	0.36 (0.30, 0.44)
P	<0.0001	<0.0001
Margarine consumption		
Less than weekly	Reference	Reference
Weekly	0.82 (0.69, 0.98)	0.83 (0.69, 0.99)
Daily	0.92 (0.82, 1.04)	0.87 (0.77, 0.99)
P for trend	0.23	0.04[5]
Oily fish consumption		
Never	Reference	Reference
Less than weekly	0.62 (0.53, 0.74)	0.68 (0.57, 0.82)
Weekly	0.49 (0.41, 0.59)	0.59 (0.48, 0.71)
P for trend	<0.0001	<0.0001
Time spent outdoors (March through November)[6]		
< 30 min/d	Reference	Reference
30–59 min/d	0.77 (0.60, 0.98)	0.74 (0.57, 0.95)
1–2.9 h/d	0.64 (0.51, 0.80)	0.62 (0.49, 0.78)
3–3.9 h/d	0.56 (0.44, 0.73)	0.48 (0.36, 0.63)
≥4 h/d	0.47 (0.37, 0.59)	0.37 (0.29, 0.48)
P for trend	<0.0001	<0.0001
Use of sun protection		
Usually	Reference	Reference
Sometimes	0.97 (0.85, 1.11)	0.97 (0.84, 1.12)
Rarely or never	1.61 (1.31, 1.97)	1.63 (1.32, 2.01)
P for trend	0.0003	0.0006
Television viewing or use of computer		
<1 h/d	Reference	Reference
1–1.9 h/d	1.00 (90.81, 1.23)	0.92 (0.74, 1.14)
2–2.9 h/d	1.13 (0.91, 1.40)	0.98 (0.78, 1.24)
3–3.9 h/d	1.40 (1.12, 1.75)	1.19 (0.95, 1.50)
≥4 h/d	2.27 (1.80, 2.85)	1.78 (1.40, 2.26)
P for trend	<0.0001	<0.0001

[1] Analyses were done by using logistic regression. 25-Hydroxyvitamin D was <40 nmol/L in 2035 participants. *P* values from log likelihood ratio test or log likelihood trend test as indicated.

[2] Adjusted for sex and month of measurement.

[3] Adjusted for sex, month of measurement, BMI, region, socioeconomic status, skin color, and other variables in the table. Multiple imputation was used to fill in information from participants with unknown values of ≥1 background indicators ($n = 1117$).

[4] Defined as BMI (in kg/m^2) ≥30.

[5] The association was not significant after restriction of data to sample with complete data on all background indicators ($n = 6320$), $P = 0.35$ (log likelihood ratio trend test).

[6] A significant interaction was found between season and time spent outdoors, $P < 0.0001$ (log likelihood ratio test). $n = 6147$; 1420 participants with 25-hydroxyvitamin D <40 nmol/L). No association was found between time spent outdoors and hypovitaminosis D during December through February (*P* for trend = 0.67).

current prevalence of hypovitaminosis D in British adults. Although the 1958 cohort provides a representative sample of the current adult white population, it is not representative of immigrant ethnic minorities (24). Nevertheless, in agreement with previous reports for ethnic minority groups living in Great Britain (15–17), the prevalence of hypovitaminosis D in 154 nonwhites in the cohort was markedly high: 50% had concentrations <25 nmol/L, 80% had concentrations <40 nmol/L, and 100% had concentrations <75 nmol/L during the winter and spring. A further limitation is the self-reported information on dietary vitamin D intake, supplementation, and sun exposure. However, the strong associations observed between the available indicators and serum 25(OH)D concentrations add face validity to our findings, as do the clear seasonal trends.

Use of sun protection is known to reduce vitamin D production in the skin (2). However, in the current study, the use of sun protection was associated with slightly higher (rather than lower) 25(OH)D concentrations. This suggests that the use of sun protection partly reflects levels of sun exposure. The lack of any apparent adverse effects of sun protection on vitamin D status in the current study could indicate that, at the population level, sun screen and protective clothing are used by those who need them, rather than being seen as an excessively cautious measure strongly interfering with vitamin D synthesis.

Public health implications and conclusions

Data from the 1958 birth cohort suggest that, at different cutoffs for hypovitaminosis D, a substantial public health problem exists in British whites. Obese participants and those living in Scotland were at the highest risk of hypovitaminosis D. However, the prevalence in the general population was very high during the winter and spring, which suggests that, to improve the situation, action is required at a population level rather than at a risk-group level. In the United States, calls have gone out for an increase in vitamin D fortification of foods (11), and the data from the current study suggest that such action is also warranted in the United Kingdom. Vitamin D is currently available without prescription as a dietary supplement only as part of cod liver oil or multivitamin products; hence, a need clearly exists to consider increased availability of over-the-counter supplements. Hypovitaminosis D has been implicated in the development of serious conditions, including diabetes, various types of cancer, and cardiovascular diseases, in addition to its essential role in maintaining bone health (1, 2). The high rates of hypovitaminosis D reported in this study suggest that immediate action is needed to improve the vitamin D status of the British population.

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