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Original article

Ambient ultraviolet-B radiation, supplements and other factors interact to impact vitamin D status differently depending on ethnicity: A cross-sectional study

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SUMMARY

Background & aims: Many determinants of vitamin D status have been well-described, yet supplementation guidelines largely follow a one-size-for-all model and deficiency remains common. We hypothesised that accounting accurately for ultraviolet-B (UVB) radiation and considering interactions could advance understanding of vitamin D status.

Methods: Asian, Black, and White participants from the UK Biobank cohort were included (N = 438,978). The Tropospheric Emission Monitoring Internet Service provided UVB data which we linked to participants' place of residence. UVB dose over 135 days prior to blood draw was weighted and added, yielding cumulative and weighted UVB (CW-D-UVB). The association between 25(OH)D and selected variables was assessed in multivariable linear regression models with and without interactions, stratified by ethnicity. Predictors were ranked using standardised β-coefficients.

Results: Median 25(OH)D differed by ethnicity (Asian: 25.4 nmol/L (10.2 ng/mL), Black: 30.6 nmol/L (12.2 ng/mL), White: 47.9 nmol/L (19.2 ng/mL), p-value < 0.001). CW-D-UVB was strongly associated with 25(OH)D in all ethnicities. It was the most important predictor in White ($\beta_{Asian} = 0.15$, $\beta_{Black} = 0.20$, $\beta_{White} = 0.35$), whereas supplementation was in Asian and Black participants ($\beta_{Asian} = 0.30$, $\beta_{Black} = 0.24$, $\beta_{White} = 0.21$). We identified statistically significant interactions between BMI:supplementation (all), CW-D-UVB:sex (Asian and White), and CW-D-UVB:age (Black and White), and in White population between CW-D-UVB and supplementation, BMI, and cholesterol.

Conclusion: Vitamin D deficiency was widespread, particularly among non-White individuals. UVB was a strong predictor of 25(OH)D and the effect was modified by other factors. Findings suggest that accurately measured ambient-UVB radiation and interactions could improve 25(OH)D prediction models, and support personalised approaches to vitamin D optimisation.

1. Introduction

While it is increasingly recognised that vitamin D is important for health, deficiency is widespread. The prevalence in Europe ranges from 13 to 40%, with substantial differences between subpopulations; for example, the prevalence of vitamin D deficiency amongst darker-skinned individuals is 3- to 71-fold higher than white ethnicities [1].

Vitamin D is synthesised in the skin following exposure to ultraviolet-B (UVB) solar radiation. Multiple factors affect dermal synthesis including sunlight intensity [2–4], age, and skin tone. Pigment limits the light that penetrates the skin [5,6] underpinning the link between ethnicity and vitamin D status [1]. Dermal synthesis is further affected by lifestyle factors such as seeking/

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avoiding sunshine [7], sunscreen [6], and clothing. Nonetheless, it is estimated that UVB-induced dermal synthesis can meet 80–100% of vitamin D requirements, making sunshine the most important natural source of vitamin D for many [2,7–9]. Vitamin D can also be ingested via supplements [7,10], and natural or fortified foods [11]. Once it reaches the circulation, vitamin D is converted into 25-hydroxyvitamin D (25(OH)D), the best biomarker of vitamin D status [9,12].

Exclusive of a few subgroups (e.g., pregnant women, older adults, and people with dark skin) [13], a one-size-fits-all approach to vitamin D supplementation is typically adopted [14]. Yet, the profound differences between and within populations, documented in observational studies and trials [1,15–20] underscore a varied need for supplementation. Indeed, changes in 25(OH)D response vary between individuals [10,15–17]. For example, the response to supplementation is attenuated in overweight and obese individuals, dermal production of vitamin D decreases with age [6], and baseline 25(OH)D level is a major determinant of the increase in 25(OH)D after irradiation: the lower the baseline, the greater the increase [9]. Moreover, we previously identified an interaction between vitamin D supplementation and UVB [7], and Sutherland described interactions between season and lifestyle indicators [18].

We hypothesise that prediction of vitamin D status could be improved by using accurately captured ambient UVB radiation and by considering predictors and their interactions jointly. To investigate this, we used a large cohort of free-living adults from the UK Biobank. We utilised data on a range of important factors and calculated ambient UVB dose at a place of residence for each participant via linkage to solar radiation data. We examined and quantified the role supplements and other determinants have on 25(OH)D status, once UVB is accounted for, and investigated interactions in different ethnicities. The findings are practically relevant, because improved prediction can enable a more nuanced approach to vitamin D supplementation and prevention of deficiency in diverse populations.

2. Material & methods

2.1. Study design

In this cross-sectional study, the UK Biobank (UKBB) was linked to the Tropospheric Emission Monitoring Internet Service (TEMIS) database [21]. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed.

2.2. Participants and setting

UKBB recruited approximately half-a-million participants from England, Scotland and Wales [22,23]. During baseline assessments (2006–2010), participants completed a questionnaire and interview, underwent physical measurements and provided biological samples [22,23]. UKBB ethical approval was granted by the North West Multi-centre Research Ethics Committee [24].

2.3. Vitamin D status

25(OH)D concentration was measured from blood samples using chemiluminescent immunoassay (DiaSorin, Stillwater, USA; detectable range: 10–375 nmol/L). We categorised vitamin D status as: 25(OH)D < 25 (deficiency), 25–39.99 (high deficiency risk), 40–50 (low deficiency risk) and >50 (sufficiency, as defined by the 2011 Institute of Medicine report), but use 25(OH)D in continuous form unless stated otherwise. Participants with missing or outlier log-transformed 25(OH)D values (Z scores > +/− 3) were excluded (N = 54,753) (Figure S1).

2.4. UVB and CW-D-UVB dose

Ambient daily UVB doses at wavelengths that can induce synthesis (D-UVB) adjusted for cloud attenuation, surface elevation and UV reflectivity were extracted from TEMIS. To account for 25(OH)D accumulation and utilisation, a cumulative and weighted estimate of D-UVB (CW-D-UVB) was calculated based on participant residential locations as described previously [7]. In brief, the contribution of D-UVB (kJ/m^2) is added up over 135 days preceding blood draw, with doses immediately before contributing more to the estimate than those from longer before, assuming 25(OH)D half-life of 35 days (Equation (1)).

$$CW\text{-}D\text{-}UVB(x) = \sum_{x=1:135} (D\text{-}UVB(x)) * e^{-\left(\frac{ln2}{y}\right)x} \quad (1)$$

Equation (1) used to calculate CW-D-UVB; x represents the number of days preceding the blood 25(OH)D measurement, y the rate of disappearance of the effect of UVB in days and $e^{(-\ln 2/y)x}$ is the weighting formula applied.

2.5. Covariates

Covariates were chosen as known 25(OH)D predictors or potential confounders of the UVB-25(OH)D relationship from existing literature.

Ethnicity was self-reported. We analysed Asian (Indian, Pakistani, Bangladeshi, Chinese and any other Asian background), Black (Caribbean, African and any other Black background) and White (British, Irish and Any other White Background) UKBB subpopulations. Other ethnicities were excluded (N = 8684) (Figure S1). Body mass index (BMI) was categorised as per the World Health Organization (WHO) [25]. Time spent outdoors in the summer (April to September) and winter (October to March) was recategorized as: < 1 h, 1–2 h, or ≥3 h per day. From time spent outdoors and the month of blood sampling, we generated a new variable: time outdoors in season of sample (referred to as "time outdoors" in text). We formed a new binary variable for vitamin D supplementation by merging data from Mineral and other dietary supplements, and Vitamin and mineral supplements. Positive responses include self-reported intake of vitamin D, multivitamins, or fish oil, which were reported by 17,405, 89,433, and 75,112 UKBB participants, respectively. Oily fish intake was recategorized to less than once, once, or twice or more per week. C-reactive protein (CRP) was summarised as a continuous variable and dichotomised as < 2 and ≥2 (mg/L). We also included age, sex, Townsend deprivation index, cholesterol, use of UV protection, smoking status and alcohol intake frequency. Responses of "Do not know" or "Prefer not to answer" were treated as missing observations, except for vitamin D supplementation, where these were re-coded as "no supplementation". See data dictionary (Table S1).

2.6. Statistical methods

Median and interquartile range (IQR) were calculated for continuous variables, counts and proportions for categorical, followed by cross-tabulation. Correlation matrices and generalised variance inflation factors (GVIF) assessed multicollinearity. All covariates were retained since none exceeded correlation coefficient≥0.5 or GVIF≥5 (Tables S2-3).

Determinants of 25(OH)D concentration were investigated in multivariable linear regression models (Equation S1), stratified by ethnicity (Asian, Black and White). Participants with missing data were excluded from regression models to facilitate a complete case analysis (Table S4). Raw 25(OH)D and log-transformed 25(OH)D were both investigated as outcome variables given right-skew of 25(OH)D. To facilitate interpretation, raw unstandardised coefficients (b) are presented in the main paper and log-transformed in supporting information (Tables S5-7). We evaluated effect modification with interaction terms (between CW-D-UVB and age, sex, BMI, supplementation and cholesterol, and between BMI and supplementation; Equation S2). Analyses were conducted within each stratum of variables assessed for effect modification (Equation S3). The relative contribution of variables to 25(OH)D was evaluated with standardised beta coefficients (β) and the proportion of variance in 25(OH)D attributable to each variable with ANOVA. Multivariable models with and without interactions, were compared using adjusted R^2, Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and ANOVA. To account for multiple testing, a Bonferroni correction was applied to each set of multivariable models. R version 4.3.1 was used.

3. Results

3.1. Baseline characteristics

The study population included 438,978 participants (53.5% female, median age 58 years) (Tables 1 and S8). Median CW-D-UVB exposure was 90.1 kJ/m^2 (IQR: 28.9–166.1), 41.5% reported taking vitamin D supplements, and 66.9% were categorised as overweight or obese. A higher proportion of the Black subpopulation reported supplementation (47.6%), compared to Asian and White (42% and 41.3%, respectively). Median 25(OH)D concentration was 47.1 nmol/L (IQR: 32.7–62.6) overall, but this varied significantly by ethnicity (Asian: 25.4 nmol/L, Black: 30.6 nmol/L, White: 47.9 nmol/L; p-value < 0.0001) (Table S9).

25(OH)D status improved with increasing CW-D-UVB exposure but this varied by ethnicity and age (Table 2 and S10, respectively). The change in 25(OH)D (Δ25(OH)D (nmol/L) = median(25(OH)D)$_{Q4}$ - median(25(OH)D)$_{Q1}$) was most prominent for the White group, particularly among those who were male (Δ25(OH)D = 24.8), younger (26.1), underweight or normal BMI (23.1 and 23.5), spent more time outdoors (23.1) and were not taking supplements (25). Differences were approximately two- to four-fold smaller in the Asian and Black groups.

3.2. Predictors associated with 25(OH)D

25(OH)D concentration was significantly associated with CW-D-UVB, supplementation, age, and oily fish consumption, and negatively with increasing BMI and cholesterol across all ethnicities (Table 3).

The largest contributor to 25(OH)D concentration was CW-D-UVB in the White group (β = 0.35), followed by supplementation (β = 0.21) and BMI (β = −0.15). For Asian and Black subgroups, the strongest contributor was supplementation (β = 0.30 and 0.24, respectively), followed by CW-D-UVB (β = 0.15 and 0.20), BMI (β = −0.15 and −0.08) and oily fish intake (β = 0.12 and 0.18 for ≥2 portions a week). Age was more relevant in Asian and Black (β = 0.13 and 0.12, respectively) than White subgroups (β = 0.03). A single SD increase in CW-D-UVB (71.7 kJ/m^2), corresponded to 25(OH)D increase of 7.3 nmol/L in White, 3.2 nmol/L in Black and 2.3 nmol/L in Asian groups (βxSD 25(OH)D). The largest proportion of variance in 25(OH)D was explained by CW-D-UVB (14%) in White participants, and by supplementation in Asian and Black participants (9.7% and 6.5%, respectively, Table 4).

Of note, CRP was considered as an independent variable but no significant associations were found (Table S11-12) nor was there a change in overall model explanatory power, therefore CRP was not retained in final models. CRP levels were low overall (median 1.3 mg/L, IQR: 0.7–2.7 mg/L; Table 1).

3.3. Interactions in 25(OH)D

A significant interaction was observed between BMI and supplementation across ethnicities. Additionally, we observed interactions between CW-D-UVB and sex (Asian and White), and CW-D-UVB and age (Black and White). In White population only, we also noted interactions between CW-D-UVB and supplementation, CW-D-UVB and BMI, and CW-D-UVB and cholesterol (Table 4).

Adjusted R^2 for models without interactions involving Asian, Black and White subgroups was 20.9%, 19.3% and 25.2%, respectively. When interactions were included, R^2 increased to 21.3%, 19.6% and 26.0%, respectively. Variance explained by models with and without interactions were significantly different across ethnicities (p-values < 0.001). Overall, this suggests models with interactions are preferred (Table S13).

We examined the differential association of CW-D-UVB and BMI with 25(OH)D concentration in stratified analysis according to selected factors (Table 5).

3.4. Interactions with CW-D-UVB

Among White individuals, there was a clear trend of weakening impact of CW-D-UVB on 25(OH)D with increasing age. In each ethnic group, the contribution of CW-D-UVB was larger in males than females. This was particularly pronounced in the Black subgroup, where it was almost doubled (b = 0.17 vs. 0.10, Table 5). Similar, albeit less pronounced, differences were observed in Asian and White individuals. In the White subgroup, those not taking supplements experienced a larger rise in response to CW-D-UVB exposure compared to those who did (0.28 vs. 0.21). The opposite pattern was seen in those of Black ethnicity (0.11 vs. 0.14) while results were not significant for the Asian group. Lastly, a declining trend across BMI and cholesterol tertiles was evident in the White subgroup only.

3.5. Interactions with BMI

In every ethnic group, increasing BMI was associated with decreases in 25(OH)D concentration. More substantial declines in 25(OH)D levels were exhibited in those taking supplementation compared to those who did not, possibly reflecting higher baseline 25(OH)D (Table 5).

4. Discussion

We investigated associations and interactions between UVB, supplementation and other factors that influence 25(OH)D in a large UK cohort. Specifically, we examined how sociodemographic factors modified the relationship between precisely measured ambient UVB radiation or BMI and 25(OH)D concentrations within three different ethnic groups. We observed substantial variation in 25(OH)D concentrations between ethnic groups with nearly 50% of Asian and 35% of Black individuals deficient in vitamin D (< 25 nmol/L), compared to 12% of White participants, consistent with other reports [1,18,20].

Table 1
Baseline characteristics of UK Biobank analytical cohort[a] and stratified according to ethnicity.

	Overall	Asian (n = 9262)	Black (n = 7032)	White (n = 422,684)
Variables	N (%)/Median (IQR)			
Age (years)	58 (50.00–63.00)	53 (46–60)	51 (45–58))	58 (50–63)
Sex: Female	234,922 (53.52)	4453 (48.08)	4020 (57.17)	226,449 (53.57)
25(OH)D (nmol/L)	47.10 (32.70–62.60)	25.40 (17.40–37.08)	30.60 (21.70–42.20)	47.90 (33.50–63.20)
<25	57,335 (13.06)	4518 (48.78)	2430 (34.56)	50,387 (11.92)
25–39.99	107,498 (24.49)	2820 (30.45)	2589 (36.82)	102,089 (24.15)
40–50	76,936 (17.53)	970 (10.47)	937 (13.32)	75,029 (17.75)
>50	197,209 (44.93)	954 (10.30)	1076 (15.30)	195,179 (46.18)
CW-D-UVB (kJ/m^2)	90.11 (28.88–166.14)	108.78 (42.51–182.90)	93.41 (36.26–164.62)	89.69 (28.50–165.92)
Q1 (5.69–28.88)	12.33 (9.52–17.54)	1789 (19.55)	1517 (21.97)	105,479 (25.20)
Q2 (28.88–90.11)	54.78 (40.41–72.15)	2134 (23.32)	1824 (26.41)	104,753 (25.02)
Q3 (90.14–166.13)	128.03 (108.53–148.61)	2366 (25.86)	1892 (27.40)	104,336 (24.92)
Q4 (166.14–245.17)	195.18 (181.10–209.63)	2861 (31.27)	1673 (24.23)	104,078 (24.86)
Season of sample				
Spring	126,649 (28.85)	2378 (25.68)	2094 (29.78)	122,177 (28.91)
Summer	116,435 (26.52)	3040 (32.82)	1944 (27.65)	111,451 (26.37)
Autumn	106,722 (24.31)	2263 (24.43)	1619 (23.02)	102,840 (24.33)
Winter	89,172 (20.31)	1581 (17.07)	1375 (19.55)	86,216 (20.40)
UV protection				
Never/rarely	42,891 (9.79)	3879 (43.23)	3614 (52.57)	35,398 (8.38)
Sometimes	145,949 (33.30)	3262 (36.35)	2104 (30.60)	140,583 (33.28)
Most of the time	156,092 (35.62)	1012 (11.28)	600 (8.73)	154,480 (36.57)
Always	90,794 (20.72)	630 (7.02)	419 (6.10)	89,745 (21.45)
No sun exposure	2546 (0.58)	191 (2.13)	138 (2.01)	2230 (0.53)
Time outdoors				
<1 h/day	50,375 (12.14)	1755 (20.92)	840 (13.77)	47,780 (11.93)
1–2 h/day	183,141 (44.12)	3698 (44.08)	2115 (34.67)	177,328 (44.27)
≥3 h/day	181,557 (43.74)	2936 (35.00)	3146 (51.57)	175,475 (43.81)
Smoking				
Current	45,333 (10.37)	857 (9.34)	871 (12.47)	43,605 (10.35)
Previous	152,589 (34.89)	1266 (13.79)	1226 (17.56)	150,097 (35.64)
Never	239,429 (54.75)	7057 (76.87)	4886 (69.97)	227,486 (54.01)
Alcohol				
Daily or almost daily	89,616 (20.43)	630 (6.84)	442 (6.31)	88,544 (20.96)
3/4 times a week	102,502 (23.37)	768 (8.34)	884 (9.77)	101,050 (23.92)
1/2 times a week	114,385 (26.08)	1310 (14.22)	1404 (20.05)	111,671 (26.44)
1–3 times a month	48,852 (11.14)	755 (8.19)	919 (13.12)	47,178 (11.17)
Special occasions only	49,577 (11.30)	1976 (21.45)	1990 (28.42)	45,611 (10.80)
Never	33,669 (7.68)	3775 (40.98)	1564 (22.33)	28,330 (6.71)
BMI (kg/m^2)				
<18.5	2192 (0.50)	63 (0.69)	9 (0.13)	2120 (0.50)
18.5–24.99	142,739 (32.64)	3396 (37.31)	1295 (18.70)	138,048 (32.76)
25–29.99	186,106 (42.55)	3969 (43.60)	2867 (41.41)	179,270 (42.55)
≥30	106,327 (24.31)	1675 (18.40)	2753 (39.76)	101,899 (24.19)
Deprivation[b]	−2.18 (−3.67 to 0.43)	0.06 (−2.40 to 2.35)	2.90 (0.03–5.59)	−2.27 (−3.70 to 0.25)
Supplement				
No	257,028 (58.55)	5372 (58.00)	3682 (52.36)	247,974 (58.67)
Yes	181,950 (41.45)	3890 (42.00)	3350 (47.64)	174,710 (41.33)
Oily fish				
<1 per week	192,734 (44.15)	4791 (53.25)	2335 (34.13)	185,608 (44.12)
1 per week	165,194 (37.84)	2832 (31.47)	2408 (35.20)	159,954 (38.02)
≥2 per week	78,602 (18.01)	1375 (15.28)	2098 (330.67)	75,129 (17.86)
Cholesterol (mmol/L)	5.60 (4.88–6.32)	5.31 (4.58–6.02)	5.15 (4.46–5.88)	5.61 (4.89–6.33)
CRP (mg/L)	1.3 (0.65–2.74)	1.33 (0.64–2.85)	1.36 (0.64–3.06)	1.31 (0.65–2.73)
<2	284,663 (65.03)	5906 (64.02)	4412 (62.89)	274,345 (65.09)
≥2	153,095 (34.97)	3320 (35.99)	2604 (37.12)	147,171 (34.92)

Footnote: 25(OH)D: 25-hydroxyvitamin D, CW-D-UVB: cumulative and weighted daily ultraviolet-B; BMI: body mass index; Time outdoors = time outdoors in season of sample (summer defined as April to September and winter as October to March). Supplement = vitamin D supplementation. CRP = C-reactive protein.

[a] Only participants with available 25(OH)D measurements and ethnicity are included. 25(OH)D outliers (defined as log-transformed observations with Z scores > +/− 3) and ethnicities other than those listed were excluded. Analytical cohort n = 438978.

[b] Deprivation: Townsend index of deprivation. Zero represents national average and positive scores correspond to relatively higher levels of deprivation.

4.1. Key determinants

In the White subgroup, CW-D-UVB was the most important 25(OH)D predictor. Overall, 25(OH)D increased by about 1 nmol/L for every 10 kJ/m^2 increase in CW-D-UVB in the White group, comparable to similar studies [2,7,26]. CW-D-UVB explained 14% of 25(OH)D variability. This is substantially more than reported in studies that approximated UVB dose: 3% was explained by 91-day UVB [26], 1% by mean annual regional solar irradiance [27] and 7% by season [28]. These findings correspond to our previous work [2,7,19,29], and highlight that CW-D-UVB may currently be the best ambient predictor of 25(OH)D concentration for epidemiological studies. This is likely driven by accurate measurement of UVB radiation and by capturing vitamin D accumulation and diminution [2,9,19]. Vitamin D supplementation ranked second in the White group, but the proportion of variance explained was 3-fold less

Table 2
Median 25(OH)D in subgroups stratified by ethnicity and quartiles of cumulative and weighted daily ultraviolet-B (CW-D-UVB) at the time of blood sampling.

	Asian					Black					White				
	CW-D-UVB														
	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	
Median	16	75	149	215		15	66	131	198		12	54	128	195	
(IQR)	(11-27)	(59-92)	(130-166)	(196-234)	Δ25(OH)D	(10-21)	(50-81)	(111-148)	(181-217)	Δ25(OH)D	(10-17)	(40-72)	(108-148)	(181-209)	Δ25(OH)D
Sex															
Female	25.4	26.2	29.2	29.9	4.5	28.2	28.2	31.9	36.8	8.6	37.7	42.6	50.8	57.7	20
Male	20.1	22	25.2	28.4	8.3	24.7	26.6	31.3	34.1	9.4	35.2	42.3	52.3	60	24.8
Age															
37-49	19.8	21.9	24.2	27.9	8.1	23.7	24.7	29.8	33.3	9.6	32.5	38.7	49.9	58.6	26.1
50-61	22.6	24.4	27.3	28.9	6.3	28.6	28.6	32	36.8	8.2	35.9	41.9	50.8	58.1	22.2
62-73	27.5	27.7	30.4	32	4.5	*32.3*†	*34.8*†	*36.6*†	*39.9*†	7.6†	40.3	45.8	53.5	59.7	19.4
BMI															
<18.5	*22.4*†	*38.6*†	*32*†	*42.6*†	20.2†	*28.1*†	*51*†	*18.9*†	*24.8*†	-3.3†	36.7	41.9	48.7	59.8	23.1
18.5-24.99	26.1	26.6	30	32.4	6.3	*26.2*†	26.1	30.4	37.2	11	38.9	45.5	54.9	62.4	23.5
25-29.99	20.8	23.1	26.4	28.8	8	26.9	29.1	33.3	36.5	9.6	37.4	43.5	52.7	59.4	22
≥30	19.2	20.2	23	25.8	6.6	26.8	26.8	31	34	7.2	32.3	37.3	45.6	52.3	20
Supplement															
No	18.2	20.1	22.8	24.7	6.5	23.4	23.8	28	31	7.6	30.9	37	47.2	55.9	25
Yes	29.6	30.8	35	34.9	5.3	31.8	33.3	36.6	39.9	8.1	45.6	50.5	57.3	62.6	17
Time outdoors															
<1hours/day	21.3	24.9	25.2	*27.4*†	6.1†	26.3	*25.2*†	*31.9*†	*35.2*†	8.9†	34	40.3	46	48	14
1-2hours/day	22.7	23.5	26.6	29	6.3	26.9	28.4	32.2	35.6	8.7	36.8	42.4	50.3	55.6	18.8
≥3hours/day	22.1	23.5	28	29.3	7.2	26.3	27.8	31.4	36.3	10	38.6	43.7	53.7	61.7	23.1

Legend: 25(OH)D <25 nmol/L | 25(OH)D = 25-39.99 nmol/ | 25(OH)D= 40-50 nmol/ | 25(OH)D>50nmol/L

Footnote: 25(OH)D: 25-hydroxyvitamin D; CW-D-UVB: cumulative and weighted daily ultraviolet-B dose; Δ25(OH)D: difference in median 25(OH)D between quartile 4 and 1 of CW-D-UVB; IQR: interquartile range; BMI: body mass index; Supplement= vitamin D supplementation. Time outdoors: time spent outdoors in season of blood sample (summer defined as April to September and winter October to March); † Interpret with caution because median is based on a small number of observations (bottom 10% of cells with the lowest n are highlighted [1-308 participants])

(4.9%). This suggests that including advice on healthy sun exposure in vitamin D guidelines could have a meaningful impact for White individuals, even at UK latitudes.

Within Asian and Black individuals, vitamin D supplementation was the most important predictor, followed by BMI in Asian, and CW-D-UVB in Black individuals. This suggests that at UK latitudes, UVB exposure is less likely to raise 25(OH)D in Asian and Black individuals. This is unsurprising since skin pigmentation blocks UVB, diminishing its availability for vitamin D synthesis [6,30]. Thus, combating vitamin D deficiency in these ethnicities will primarily depend on supplementation [30]. To address substantial ethnic disparities, recommended daily doses likely need to be higher in non-White groups.

4.2. Interactions

Supplementation:UVB. White participants who did not take supplements exhibited a stronger 25(OH)D response to CW-D-UVB. As this is a cross-sectional study, we cannot discern whether supplement-taking limits dermal synthesis, or *vice versa*; or

Table 3
Predictors of 25(OH)D concentration in the UK Biobank cohort in each ethnic group.

	Asian N = 7764				Black N = 5656				White N = 392,184			
Predictor	b	p-value	β	β rank	b	p-value	β	β rank	b	p-value	β	β rank
Age	0.23	<0.001*	0.13	**4**	0.24	<0.001*	0.12	**4**	0.08	<0.001*	0.03	13
Sex												
Female	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Male	−2.48	<0.001*	−0.08	6	−0.73	0.076	−0.02		1.09	<0.001*	0.03	15
CW-D-UVB	0.03	<0.001*	0.15	**3**	0.05	<0.001*	0.20	**2**	0.10	<0.001*	0.35	**1**
Supplement												
No	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Yes	9.23	<0.001*	0.30	**1**	7.64	<0.001*	0.24	**1**	8.71	<0.001*	0.21	**2**
BMI	−0.53	<0.001*	−0.15	**2**	−0.24	<0.001*	−0.08	7	−0.67	<0.001*	−0.15	**3**
Time outdoors												
<1 h/day	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
1–2 h/day	0.61	0.143	0.02		−0.25	0.683	−0.01		1.80	<0.001*	0.04	11
≥3 h/day	0.73	0.102	0.02		−0.44	0.462	−0.01		4.94	<0.001*	0.12	**4**
UV protection												
Never	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Sometimes	2.18	<0.001*	0.07	9	0.59	0.182	0.02		2.65	<0.001*	0.06	9
Mostly	2.35	<0.001*	0.05	11	1.08	0.129	0.02		3.55	<0.001*	0.08	7
Always	3.06	<0.001*	0.05	10	0.63	0.444	0.01		4.14	<0.001*	0.08	8
No sun exposure	0.02	0.985	0.00		1.47	0.311	0.01		−8.17	<0.001*	−0.03	14
Smoking												
Never	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
Previous	1.27	0.006	0.03		−1.99	<0.001*	−0.05	9	0.72	<0.001*	0.02	16
Current	−0.53	0.345	−0.01		−3.55	<0.001*	−0.07	8	−2.97	<0.001*	−0.04	10
Deprivation	−0.06	0.231	−0.01		−0.20	<0.001*	−0.04	10	−0.58	<0.001*	−0.08	6
Oily fish												
<1/week	Ref	Ref	Ref		Ref	Ref	Ref		Ref	Ref	Ref	
1/week	2.49	<0.001*	0.07	7	2.91	<0.001*	0.09	6	1.27	<0.001*	0.03	14
≥2/week	5.21	<0.001*	0.12	**5**	6.16	<0.001*	0.18	**3**	2.29	<0.001*	0.04	12
Cholesterol	−1.02	<0.001*	−0.07	8	−1.77	<0.001*	−0.11	**5**	−1.99	<0.001*	−0.10	**5**

Footnote: 25(OH)D: 25-hydroxyvitamin D; CW-D-UVB: cumulative and weighted daily ultraviolet-B dose; Supplement: vitamin D supplementation, BMI: body mass index; Time outdoors: time spent outdoors in season of blood sample (summer defined as April to September and winter October to March); UV: ultraviolet; b: unstandardized coefficient reflects the change in 25(OH)D (without logarithmic transformation) associated with a one-unit change in the predictor variable; β: standardised (beta) coefficient indicates the expected change in 25(OH)D in standard deviation units, given a corresponding one standard deviation change in the predictor variable. β rank is shown to highlight the most influential predictors by ethnicity.
*p-value < 0.005 is considered significant, as per Bonferroni correction (0.05/11).

whether the dependency is bidirectional. Our findings correspond to an Irish study that found a seasonality effect on 25(OH)D in individuals who did not supplement but not in those who did [10]. Similarly, a UKBB study reported smaller seasonal 25(OH)D differences in those who supplemented or regularly ate oily fish [18]. A meta-analysis showed that baseline 25(OH)D concentration significantly impacted levels after UVB exposure [9] and similarly the increase due to supplementation gradually diminishes as 25(OH)D rises [31]. There may be a feedback mechanism through which baseline 25(OH)D determines the rise; for example, 25(OH)D may inhibit 25-hydroxylase in the liver [32]. These interactions suggest that the relationship between 25(OH)D and supplementation or UVB exposure is not linear, which should inform supplementation policies and development of personalised recommendations.

Age:UVB and *Sex:UVB.* We found a clear trend of weakening association between CW-D-UVB and 25(OH)D with increasing age in the White subgroup, in line with previous research showing diminished dermal synthesis with ageing [6]. Another study found the impact within younger age groups (age-group 12–19) was approximately twice that amongst those aged 20–59 or 60–79 years [26]. While these findings support the higher recommended daily vitamin D dose for older adults, it appears that a decline in the ability to synthesize vitamin D happens at relatively younger ages. Hence a more nuanced approach to age-based dosing is advised. The association was stronger in males possibly due to gender differences in time outdoors ($p < 0.001$, data not shown). UVB interaction effects were less pronounced in Asian and Black individuals. Apart from the smaller samples, darker pigmentation likely attenuates the UVB [30], rendering the effective dose lower and variability decreased.

BMI:supplementation and *BMI:UVB*. BMI weakened the association between both UVB and supplementation and 25(OH)D. Overall, our findings align with a substantial evidence base recognising obesity as a risk factor for vitamin D deficiency possibly due to sequestration in body fat compartments [33], and lend support to the hypothesis that vitamin D supplementation recommendation may need to be adjusted according to BMI [34,35]. Future research should investigate optimal weight-based dosing for vitamin D supplementation.

Cholesterol:UVB. Similar to BMI, higher cholesterol levels diminished CW-D-UVB impact on 25(OH)D in White individuals. This contrasts with evidence of a positive correlation between total cholesterol and 25(OH)D following irradiation [36] but corresponds with a study reporting higher cholesterol was associated with lower 25(OH)D six years later [37]. While 7-dehydrocholesterol isa key substrate in dermal vitamin D synthesis it is also aprecursor for de novo cholesterolbiosynthesis in the epidermis [38]. Higher cholesterol may be an indicator of an underlying condition associated with an increased demand or depletion of vitamin D that we did not adjust for.

Our findings suggest that accounting for interactions could improve 25(OH)D prediction models. However, the difference in the total variability in 25(OH)D between models with and without

Table 4
Interactions between sociodemographic factors, CW-D-UVB and BMI by ethnicity.

Predictor	Asian			Black			White		
	b	p-value	SS/TSS (%)	b	p-value	SS/TSS (%)	b	p-value	SS/TSS (%)
Age	0.30	<0.001*	2.94	0.35	<0.001*	3.27	0.23	<0.001*	0.59
Sex			1.75			0.31			0.00
Female	Ref	Ref		Ref	Ref		Ref	Ref	
Male	−4.390	<0.001*		−1.22	0.085		−1.30	<0.001*	
CW-D-UVB	0.06	0.007	1.79	0.12	<0.001*	4.39	0.26	<0.001*	14.01
Supplement			9.68			6.51			4.89
No	Ref	Ref		Ref	Ref		Ref	Ref	
Yes	18.76	<0.001*		13.73	<0.001*		18.11	<0.001*	
BMI	−0.38	<0.001*	2.25	−0.02	0.833	0.53	−0.42	<0.001*	2.39
Time outdoors			0.08			0.01			0.67
<1 h/day	Ref	Ref		Ref	Ref		Ref	Ref	
1–2 h/day	0.56	0.176		−0.22	0.727		1.72	<0.001*	
≥3 h/day	0.68	0.123		−0.46	0.440		4.95	<0.001*	
UV protection			0.63			0.07			0.56
Never	Ref	Ref		Ref	Ref		Ref	Ref	
Sometimes	2.16	<0.001*		0.61	0.168		2.66	<0.001*	
Mostly	2.24	<0.001*		1.11	0.120		3.56	<0.001*	
Always	2.99	<0.001*		0.58	0.477		4.09	<0.001*	
No sun exposure	0.06	0.955		1.38	0.340		−8.08	<0.001*	
Smoking			0.13			0.80			0.38
Never	Ref	Ref		Ref	Ref		Ref	Ref	
Previous	1.25	0.007		−2.02	<0.001*		0.71	<0.001*	
Current	−0.49	0.381		−3.56	<0.001*		−2.97	<0.001*	
Deprivation	−0.06	0.255	0.00	−0.20	0.001*	0.08	−0.58	<0.001*	0.59
Oily fish			1.39			2.31			0.16
<1/week	Ref	Ref		Ref	Ref		Ref	Ref	
1/week	2.43	<0.001*		2.88	<0.001*		1.27	<0.001*	
≥2/week	5.18	<0.001*		6.19	<0.001*		2.32	<0.001*	
Cholesterol	−1.00	<0.001*	0.45	−2.03	<0.001*	1.24	−1.36	<0.001*	0.91
CW-D-UVB: sex			0.19			0.02			0.20
Female	Ref	Ref		Ref	Ref		Ref	Ref	
Male	0.02	<0.001*		0.01	0.361		0.02	<0.001*	
CW-D-UVB: cholesterol	−0.00	0.845	0.00	0.00	0.400	0.01	−0.01	<0.001*	0.06
CW-D-UVB: supplement			0.03			0.00			0.30
No	Ref	Ref		Ref	Ref		Ref	Ref	
Yes	−0.01	0.197		0.00	0.692		−0.03	<0.001*	
CW-D-UVB: age	−0.00	0.013	0.06	−0.00	0.002*	0.015	−0.00	<0.001*	0.17
CW-D-UVB: BMI	−0.00	0.853	0.00	−0.00	0.021	0.07	−0.00	<0.001*	0.06
BMI: supplement			0.21			0.13			0.07
No	Ref	Ref		Ref	Ref		Ref	Ref	
Yes	−0.34	<0.001*		−0.22	0.003		−0.24	<0.001*	

Footnote: b: unstandardized coefficients reflect the change in 25(OH)D (without logarithmic transformation) associated with a one-unit change in the predictor variable; SS: Sum Squares or partitioned variance; TSS: Total Sum of Squares. SS/TSS: ratio of individual SS to the TSS for a predictor variable, i.e., the proportion of the total variability that is explained by that predictor. : Double colon indicates an interaction term (e.g. CW-D-UVB:sex); CW-D-UVB: cumulative and weighted daily ultraviolet-B dose; BMI: body mass index; Supplement = vitamin D supplementation. Time outdoors = time outdoors in season of sample (summer defined as April to September and winter October to March). *p-value < 0.003 is considered significant, as per Bonferroni correction (0.05/17).

interactions was smaller than we expected, given that highly significant interactions were found. This could be because only two-way interactions were examined, leaving more complex interactions unaccounted for.

4.3. Strengths

The sample size and availability of comprehensive high-quality lifestyle and biomarker data increases robustness of our findings. Even though the Black and Asian subgroups are dramatically smaller than the White subgroup, resulting in comparatively weaker study power, the sample sizes remain notably larger than most othervitamin D studies, where non-White individuals are often underrepresented. The availability of residential locations enabled us to calculate a specific UVB dose for each participant, resulting in an approximation superior to season, sunshine hours or latitude used in similar studies [18,20].

4.4. Limitations

A healthy volunteer effect has been reported in the UKBB, indicating that it is not representative of the sampling population [22], and it is possible that levels of vitamin D deficiency and ethnic disparities may be even more pronounced amongst the wider adult population [20]. Secondly, the majority of Black (66%) and Asian (54%) individuals were recruited via four and three (out of twenty-one) assessment centres, respectively (Table S14), which suggests these participants were clustered regionally. This is fortunately not a problem for the CW-D-UVB variable, because variability is primarily driven by the date of sampling. The 25(OH)D assay used is limited to a range of 10–375 nmol/L [39,40]. Consequently, those most deficient (< 10) are excluded. Comparing those with available 25(OH)D observations to those missing, there were important differences in CW-D-UVB and cholesterol levels (Table S15). We lacked information on the dose of vitamin D supplementation; thus, a dose

Table 5
Stratified analysis examining the differential association of (A) CW-D-UVB, and (B) BMI with 25(OH)D concentration in each ethnic group, according to selected socio-demographic factors.

	Asian		Black		White	
	b	p value	b	p value	b	p value
A. CW-D-UVB						
Age[a]						
Q1	0.01	0.671	0.08	0.065	0.22	<0.001*
Q2	0.00	0.912	−0.02	0.695	0.18	<0.001*
Q3	−0.00	0.964	0.06	0.206	0.17	<0.001*
Q4	0.08	0.104	0.02	0.635	0.16	<0.001*
Q5	0.04	0.412	0.14	0.024	0.15	<0.001*
Sex						
Female	0.06	0.073	0.10	0.004	0.26	<0.001*
Male	0.09	0.005	0.17	0.001*	0.29	<0.001*
Supplement						
No	0.06	0.0145	0.11	0.001*	0.28	<0.001*
Yes	0.05	0.170	0.14	0.001*	0.21	<0.001*
Cholesterol[b]						
T1	0.07	0.035	0.12	0.005	0.23	<0.001*
T2	0.08	0.009	0.15	0.005	0.23	<0.001*
T3	0.04	0.225	0.11	0.001*	0.21	<0.001*
BMI[c]						
T1	0.04	0.086	0.109	0.001*	0.22	<0.001*
T2	0.06	0.008	0.079	0.010	0.18	<0.001*
T3	0.07	0.002*	0.107	0.001*	0.15	<0.001*
B. BMI						
Supplement						
No	−0.44	<0.001*	−0.04	0.650	−0.35	<0.001*
Yes	−0.64	<0.001*	−0.18	0.065	−0.76	<0.001*

Footnote: 25(OH)D: 25-hydroxyvitamin D; CW-D-UVB: cumulative and weighted daily ultraviolet-B dose; Supplement = vitamin D supplementation. BMI: body mass index; b: unstandardized coefficient which reflect the change in the outcome variable (25(OH)D without logarithmic transformation) associated with a one-unit change in the predictor variable.
*p value < 0.003 is considered significant, as per Bonferroni correction (0.05/17).
[a] quintiles for age (range) by ethnicity: Asian: Q1 (40–45), Q2 (46–50), Q3 (51–56), Q4 (57–62), Q5(63–72); Black: Q1 (39–44), Q2 (45–48), Q3 (49–53), Q4 (54–60), Q5 (61–70); White: Q1 (38–48), Q2 (49–55), Q3 (56–60), Q4 (61–64), Q5 (65–73).
[b] tertiles of cholesterol (range) by ethnicity: Asian: T1 (2.04–4.84), T2 (4.84–5.77), T3 (5.77–8.72); Black: T1 (1.80–4.70), T2 (4.70–5.61), T3 (5.61–8.17); White: T1 (0.60–5.15), T2 (5.15–6.07), T3 (6.08–10.82).
[c] tertiles of BMI (range) by ethnicity: Asian: T1(14.87–24.54), T2 (24.54–27.81), T3 (27.81–60.00); Black T1 (16.15–26.80), T2 (26.80–30.88), T3 (30.88–68.13), T2, T3; White: T1 (12.12–24.99), T2 (24.99–28.63), T3 (28.63–74.68).

effect could not be investigated. Finally, only the level of UVB radiation occurring in the UK could be investigated, which is generally quite low. Therefore, we cannot generalise the role UVB plays in other parts of the world with different (stronger) levels of solar radiation. Examination of non-linear effects was beyond the scope of this study; however future research should consider this.

5. Conclusion

UVB radiation at place of residence explained a large proportion of the variance in 25(OH)D concentration, particularly in White individuals at UK latitudes. Vitamin D deficiency is widespread with notable disparities between ethnic groups in the UKBB cohort. Our study provides valuable insights that can be used to inform tailored population approaches to vitamin D optimisation. Based on our findings, renewed efforts to optimise vitamin D supplementation in older adults and weight-based vitamin D supplementation strategies for those of higher BMI should be evaluated.

Data availability

UK Biobank data is available to users on application. https://www.ukbiobank.ac.uk/enable-your-research/apply-for-access.

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Patient consent

Not applicable.

Ethical approval

UK Biobank has approval from the North West Multi-centre Research Ethics Committee (MREC) as a Research Tissue Bank (RTB) approval. This approval means that researchers do not require separate ethical clearance and can operate under the RTB approval. This RTB approval was granted initially in 2011 and is renewed on a 5-yearly cycle. UK Biobank successfully renewed its ethical approval in 2016 and 2021. These renewal applications and approvals are shown on the website [24].

Conflict of interest

None declared.

Contributorship

Margaret M. Brennan: Methodology, Formal Analysis, Writing - Original draft preparation.

Jos van Geffen: Data Curation, Writing - Review & Editing.

Michiel van Weele: Data Curation, Writing - Review & Editing.

Lina Zgaga: Resources, Conceptualization, Methodology, Data Curation, Writing - Review & Editing, Supervision.

Rasha Shraim: Resources, Conceptualization, Methodology, Data Curation, Formal Analysis, Writing - Review & Editing, Supervision.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2024.04.006.

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