Supplemental Material can be found at:
http://jn.nutrition.org/content/suppl/2017/03/22/jn.116.244079.DCSupplemental.html

The Journal of Nutrition
Nutritional Epidemiology

Ambient UVB Dose and Sun Enjoyment Are Important Predictors of Vitamin D Status in an Older Population[1–3]

Fiona O'Sullivan,[4] Eamon Laird,[5] Dervla Kelly,[4] Jos van Geffen,[6] Michiel van Weele,[6] Helene McNulty,[7] Leane Hoey,[7] Martin Healy,[8] Kevin McCarroll,[9] Conal Cunningham,[9] Miriam Casey,[9] Mary Ward,[7] JJ Strain,[7] Anne M Molloy,[5] and Lina Zgaga[4]*

[4]Department of Public Health and Primary Care and [5]School of Medicine, Trinity College, University of Dublin, Dublin, Ireland; [6]Royal Netherlands Meteorological Institute, De Bilt, Netherlands; [7]Northern Ireland Centre for Food and Health, School of Biomedical Sciences, Ulster University, Coleraine, Northern Ireland, United Kingdom; and [8]Department of Biochemistry and [9]Mercer's Institute for Successful Ageing, St. James's Hospital, Dublin, Ireland

Abstract

Background: UVB-induced skin synthesis is considered the key source of vitamin D, yet exposure to UVB is poorly accounted for in epidemiological studies.

Objectives: The aim of this study was to examine the association of serum 25-hydroxyvitamin D [25(OH)D] concentration with accurately measured ambient UVB dose, sun enjoyment, supplements, and other factors.

Methods: An all-Irish cohort of community-dwelling participants aged >60 y [median age: 73; 67% female; median 25(OH)D: 54.5 nmol/L] was used. Participants from this large, cross-sectional study completed a questionnaire to provide information on demographic factors and lifestyle (including supplement use and sun enjoyment). The Tropospheric Emission Monitoring Internet Service database was used to extract the daily ambient UVB dose at wavelengths that could induce vitamin D synthesis (D-UVB) over Ireland (latitude: 51°N–55°N). Blood sampling occurred throughout the year. Ambient exposure at the place of residence was calculated for each participant individually. Associations between determinants and serum 25(OH)D concentration were examined in a multivariate model. Random forest analysis was used to establish prediction models of vitamin D deficiency, and area under the curve (AUC) is shown.

Results: In total, 5138 individuals were included. Median D-UVB was 63 mJ/cm^2, which varied between seasons and latitudes, despite the small latitude differential. Vitamin D supplementation ($\beta = 27.7$; $P < 10 \times 10^{-10}$), D-UVB ($\beta = 1.58$ per 1000 mJ/cm^2; $P < 10 \times 10^{-10}$), and sun enjoyment ($\beta = 6.6$; $P < 0.001$) were strongly positively associated with serum 25(OH)D. Those who avoided sunshine were largely at risk of deficiency (<40 nmol/L), whereas those who enjoyed sunshine tended to be vitamin D sufficient (≥50 nmol/L). D-UVB and sun enjoyment improved prediction of deficiency in non–supplement-taking individuals; the overall AUC improved by 3.5%.

Conclusion: D-UVB and sun enjoyment are important predictors of vitamin D status, even in this elderly population at northern latitudes. Accurate estimation of ambient UVB can help to further clarify the role of other determinants of vitamin D status and inform sunshine recommendation guidelines. *J Nutr* 2017;147:858–68.

Keywords: UVB, vitamin D, vitamin D supplementation, sun enjoyment, Tropospheric Emission Monitoring Internet Service

Introduction

Vitamin D deficiency is highly prevalent worldwide (1, 2). Apart from the well-established role for bone health (3), studies have also linked vitamin D deficiency to a wide array of other illnesses, including metabolic, cardiovascular, and autoimmune conditions and cancers. Reports of a beneficial role for vitamin D in the risk and survival of these conditions have resulted in a reignited interest in vitamin D (4–7).

[1] Supported by grant FP7-PEOPLE-2013-MARIE CURIE CAREER INTEGRATION GRANTS (631041) (to FO); the Irish Department of Agriculture, Food and the Marine [07FHRIUCD1 (JINGO 2007–2013)] and [13F407 (JINGO-JPI/ENPADASI 2014–2016)]; and the Northern Ireland Department for Employment and Learning.
[2] Author disclosures: F O'Sullivan, E Laird, D Kelly, J van Geffen, M van Weele, H McNulty, L Hoey, M Healy, K McCarroll, C Cunningham, M Casey, M Ward, JJ Strain, AM Molloy, and L Zgaga, no conflicts of interest.
[3] Supplemental Methods, Supplemental Tables 1–4, and Supplemental Figures 1–3 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.
*To whom correspondence should be addressed. E-mail: zgagal@tcd.ie.

© 2017 American Society for Nutrition.

Manuscript received November 11, 2016. Initial review completed December 1, 2016. Revision accepted February 21, 2017.
First published online March 22, 2017; doi:10.3945/jn.116.244079.

JN THE JOURNAL OF NUTRITION

Downloaded from jn.nutrition.org by guest on May 8, 2017

Sources of vitamin D include synthesis in the skin after exposure to sunshine, diet, and supplementation. However, food sources of vitamin D are rare, and fortification of products is not routinely done in Ireland; therefore, fortified-product consumption is rare (8). The key contribution of cutaneous synthesis is evident from the annual undulation: peak vitamin D concentrations closely follow peak solar radiation. Vitamin D production in the skin depends on the exposure to UVB at wavelengths of 280–315 nm, but the peak conversion occurs only at a very narrow range between 295 and 298 nm (9). Synthesis is initiated when UVB photons are absorbed by 7-dehydrocholesterol in the epidermal layer, and pre–vitamin D is formed. Spontaneous isomerization subsequently occurs, and inactivated vitamin D is created (10). This molecule is subsequently hydroxylated in the liver, yielding 25-hydroxyvitamin D [25(OH)D],[10] the main storage form of the vitamin that is also used for vitamin D status assessment (11).

Although UVB is by far the most important natural source of vitamin D, fulfilling ≤80–100% of the requirement in some cases (12), it is difficult to measure the natural exposure in free-living individuals and consequentially to determine the contribution of sunshine to 25(OH)D concentration. UVB dose can vary dramatically depending on latitude, altitude, time of day, season, weather, ozone column, and pollution, which can all strongly affect the potential for cutaneous vitamin D synthesis (13, 14). Latitude and altitude do not change at any given location, and solar angle (determined by the time of day and time of year) can be easily modeled (15). However, given the erratic nature of the ozone and cloud cover and their major effect on UVB dose, previous estimates of UVB dose have been limited in their ability to account for such variability. This limitation is why most epidemiological studies settle for using the season of sampling as a (poor) proxy for exposure to UVB. However, without the accurate account of ambient UVB dose, it is impossible to study the role of natural sun exposure, sun enjoyment, or even supplements and other determinants on vitamin D deficiency or to determine sensible sun exposure for preventing vitamin D deficiency (16).

In this study, the most accurate estimate of the daily ambient UVB dose at wavelengths that can induce vitamin D synthesis (D-UVB) in free-living individuals to date was used. The UVB dose over a 135-d period before blood sampling was calculated, while accounting for physiological accumulation and deterioration of vitamin D, to investigate the impact of the UVB dose at a place of residence and sun enjoyment on vitamin D deficiency in older, free-living individuals at a high, northerly latitude. Furthermore, we re-examined the role of other key determinants of vitamin D status while adjusting for the ambient UVB radiation.

Methods

Study population. Data from an all-Irish cohort of participants was used in this project. The cohort (n = 5186) was recruited as a part of the Trinity, University of Ulster and Department of Agriculture Study (2008–2011) and described previously (17–19). Briefly, inclusion criteria included age >60 y, no diagnosis of dementia, and ethnically Irish parents. A 90-min interview was performed at a hospital outpatient department by trained researchers, and all participants completed a detailed sociodemographic, lifestyle, and health questionnaire. Information on various factors was collected, including age, sex, smoking status

[10] Abbreviations used: cw-D-UVB, cumulative and weighted daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; D-UVB, daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; HBP, high blood pressure; MEDDS, median daily dose per season; TEMIS, Tropospheric Emission Monitoring Internet Service; 25(OH)D, 25-hydroxyvitamin D.

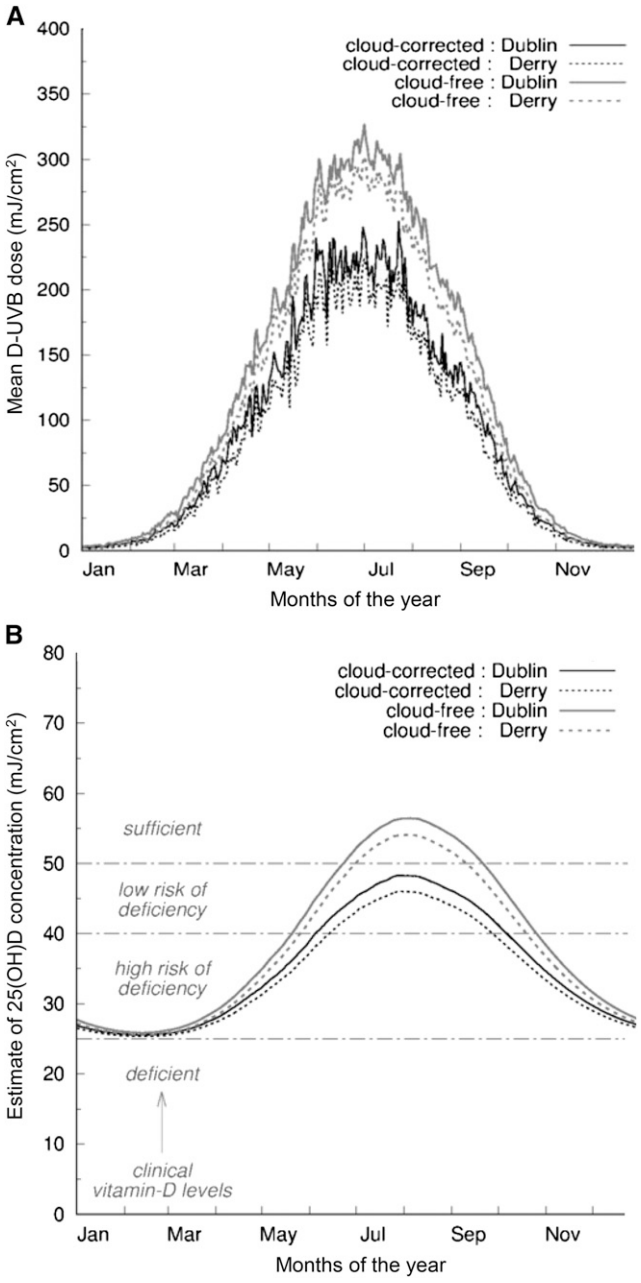

FIGURE 1 Mean daily D-UVB dose and estimated serum 25(OH)D concentration for the grid cells of Dublin and Derry, Ireland (Supplemental Table 1). (A) The daily D-UVB dose averaged over July 2005 through June 2015. (B) An estimate of the 25(OH)D concentrations by using the relation mentioned in Figure 3C in the study by Kelly et al. (23) and the cumulative and weighted D-UVBs derived from the data in panel A; horizontal lines indicate the levels of deficiency mentioned in Methods, Vitamin D measurement. Curves are shown for the cloud-corrected data (solid line) as well as for when cloud correction was not applied. On average, the daily cloud attenuation factor for both towns is ≈0.73. Note: The D-UVB data are determined with the vitamin-D action spectrum taken from the draft of the study by Bouillon et al. (9). If the action spectrum from that study is used instead, the D-UVB values increase by a factor of ≈2.2 in panel A, as discussed in the Discussion. The scale of panel B, however, is not affected by this, as the relation of Figure 3C in Kelly et al. (23) would then have a slope that is smaller by a factor of ≈2.2. D-UVB, UVB dose at wavelengths appropriate for vitamin D synthesis; 25(OH)D, 25-hydroxyvitamin D.

Downloaded from jn.nutrition.org by guest on May 8, 2017

TABLE 1 Baseline characteristics of entire cohort overall and after stratification according to quartiles of cw-D-UVB[1]

Characteristic	All	D-UVB				P^2
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	
D-UVB, mJ/cm^2	3650 (1216–7182)[3]	431 (326–625)	2420 (1854–3035)	5278 (4415–6211)	8334 (7922–8687)	
Serum 25(OH)D,[4] nmol/L	54.5 (34–81)	47.6 (28–74)	49.5 (32–76)	57.0 (36–81)	65.0 (43–88)	$<2 \times 10^{-16}$
<40	1634 (32)	539 (33)	450 (27)	375 (23)	270 (17)	
≥40	3504 (68)	747 (21)	833 (24)	910 (26)	1014 (29)	
Sex						0.18
Female	3452 (67)	879 (25)	827 (24)	864 (25)	882 (25)	
Male	1686 (33)	407 (24)	456 (27)	421 (25)	402 (24)	
Age, y						0.0002
<75	2885 (56)	705 (25)	777 (27)	740 (26)	663 (23)	
≥75	2253 (44)	581 (26)	506 (22)	545 (24)	621 (28)	
BMI,[5] kg/m^2						0.44
Underweight, <18.5	109 (2)	26 (24)	25 (24)	23 (20)	35 (32)	
Normal weight, 18.6–24.9	1430 (28)	361 (25)	328 (23)	360 (25)	381 (26)	
Overweight, 25–29.9	2003 (39)	505 (25)	524 (26)	490 (25)	484 (24)	
Obese, 30–39.9	1435 (28)	348 (24)	359 (25)	376 (26)	352 (25)	
Extremely obese, ≥40	136 (3)	37 (28)	38 (28)	33 (24)	28 (20)	
Cohort						2.8×10^{-10}
Cognitive impairment	1699 (33)	485 (29)	377 (22)	376 (22)	461 (27)	
HBP	2073 (40)	422 (20)	605 (29)	563 (28)	483 (23)	
Bone	1366 (27)	379 (28)	301 (22)	346 (25)	340 (25)	
Supplement use[6]						0.14
Yes	2437 (47)	633 (26)	571 (23)	605 (25)	628 (26)	
No	2447 (48)	582 (24)	650 (27)	624 (25)	591 (24)	
Oily fish consumption[7]						0.012
Yes	3060 (60)	735 (24)	757 (25)	760 (25)	808 (26)	
No	2076 (40)	550 (27)	526 (25)	524 (25)	476 (23)	
Sun holiday in the last 6 mo[8]						0.42
Yes	894 (17)	201 (23)	225 (25)	235 (26)	234 (26)	
No	4235 (83)	1083 (25)	1055 (25)	1049 (25)	1048 (25)	
Province[9]						$2 \times 10^{-11, 10}$
Ulster	2063 (40)	418 (20)	603 (29)	560 (27)	482 (23)	
Leinster	3058 (60)	865 (28)	676 (22)	722 (24)	795 (26)	
Munster and Connacht	17 (3)	3 (18)	4 (24)	3 (18)	7 (41)	
Season of blood draw						$<2 \times 10^{-16}$
Winter	1044 (20)	830 (80)	214 (20)	0	0	
Spring	1290 (25)	456 (35)	580 (45)	254 (20)	0	
Summer	1310 (26)	0	0	302 (23)	1008 (79)	
Autumn	1494 (29)	0	489 (33)	730 (49)	276 (18)	
Year of blood draw						$<2 \times 10^{-16, 11}$
2008	6 (0.1)	2 (40)	4 (60)	0	0	
2009	1430 (28)	196 (14)	399 (28)	407 (28)	428 (30)	
2010	2309 (45)	522 (23)	615 (27)	601 (25)	571 (25)	
2011	1156 (23)	452 (39)	201 (17)	251 (22)	252 (22)	
2012	237 (5)	114 (48)	64 (27)	26 (11)	33 (14)	
Smoking status[12]						0.44
Current	615 (12)	155 (25)	159 (26)	157 (26)	144 (23)	
Never	2387 (46)	580 (24)	614 (26)	575 (24)	618 (26)	
Past	2134 (41)	551 (26)	510 (24)	552 (26)	521 (24)	
Alcohol consumption[13]						0.14
Current	2946 (57)	720 (25)	743 (25)	743 (25)	740 (25)	
Past	916 (18)	218 (24)	238 (26)	222 (24)	238 (26)	
Never	1274 (25)	353 (28)	295 (23)	324 (25)	302 (24)	
Sun enjoyment[14]						0.0005
Avoid direct sunshine	1679 (33)	389 (23)	376 (22)	450 (27)	464 (28)	
Sometimes enjoy sunshine	1965 (38)	492 (24)	524 (27)	480 (25)	469 (24)	
Enjoy staying in sunshine	1492 (29)	404 (27)	382 (25)	355 (24)	351 (24)	

(Continued)

Downloaded from jn.nutrition.org by guest on May 8, 2017

TABLE 1 *Continued*

Characteristic	All	D-UVB				P^2
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Sun protection[15]						0.0002
Always	853 (17)	240 (28)	212 (25)	204 (24)	197 (23)	
Usually	711 (14)	179 (25)	201 (29)	158 (22)	173 (24)	
Sometimes	771 (15)	175 (23)	223 (29)	208 (27)	165 (21)	
Rarely	314 (6)	86 (27)	85 (27)	67 (22)	76 (24)	
Never	2486 (48)	605 (24)	561 (23)	648 (26)	672 (27)	
Age finished education,[16] y						0.11
≤14	2187 (43)	544 (25)	514 (24)	573 (26)	556 (25)	
15–18.9	1787 (35)	466 (26)	480 (27)	426 (24)	415 (23)	
19–24.9	1057 (21)	255 (24)	267 (26)	258 (24)	277 (26)	
≥25	97 (2)	19 (21)	22 (23)	26 (26)	30 (31)	

[1] Values are *n* (%) unless otherwise specified. cw-D-UVB, cumulative and weighted daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; D-UVB, daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; HBP, high blood pressure; NA, not available; 25(OH)D, 25-hydroxyvitamin D.
[2] All *P* values represent the results of chi-square analysis. This was carried out to determine differences in the number of participants for each quartile of D-UVB for each of the variables, e.g., difference in the number of female-to-male participants for each quartile. Differences between groups were significant at $P < 0.05$.
[3] Median; IQR in parentheses (all such values).
[4] NA = 15.
[5] NA = 25.
[6] NA/don't know = 254.
[7] NA = 2.
[8] NA = 8.
[9] Ulster is located in the north of Ireland, Leinster is in the east-to-southeast of Ireland, Connacht is located in the west of Ireland, and Munster is located in the south-to-southwest of Ireland.
[10] Because of the low count, Connacht and Munster were not included in this analysis.
[11] Because of the low count, years 2008 and 2012 were not included in this analysis.
[12] NA = 2.
[13] NA = 2.
[14] NA = 2.
[15] NA = 3.
[16] NA = 10.

(never, past, or current smoker), alcohol intake (never, past, or current drinker), oily fish use (yes or no), sun holidays in the past 6 mo (yes or no; the majority of which were taken in Spain, the Canary Islands, and other warmer European countries), vitamin D supplement use (yes or no), BMI (in kg/m^2), sun enjoyment (enjoy staying in sunshine, sometimes staying in sunshine, or avoiding sunshine), and sun protection (always, usually, sometimes, rarely, or never). A residential address was needed for the calculation of UVB and was not known for 48 participants so they were excluded from this analysis.

Three subcohorts of patients were independently recruited within this Trinity, University of Ulster and Department of Agriculture Study: those with cognitive impairment (n = 1699), bone disorders (n = 1366), and high blood pressure (HBP; n = 2073). Further details on each subcohort are described in **Supplemental Methods**. Because of the known link between bone disorders and vitamin D, the cohort with bone disorders was closely monitored for vitamin D deficiency and treated as necessary, resulting in a high prevalence of vitamin D supplementation in this cohort. Those in the cohorts with cognitive impairment and bone disorders were recruited from St. James's Hospital, Dublin, Republic of Ireland, and those in the cohort with HBP were recruited from general practitioners' clinics in Northern Ireland, United Kingdom. Ethical approval was granted by the relevant authorities in each jurisdiction: the Research Ethics Committee of St. James's Hospital, The Adelaide and Meath Hospital, Dublin, and the Office for Research Ethics Committees Northern Ireland (reference 08/NI/RO3113) with corresponding approvals from the Northern and Western Health and Social Care Trusts, Northern Ireland. All participants provided written, informed consent at the time of enrolment. All blood samples and questionnaire data were coded, and the identifiers were removed before analysis.

Vitamin D measurement. A 50-mL blood sample was taken from nonfasting participants, and samples were centrifuged at 3000 rpm for 15 min and refrigerated within 3 h of collection. Total 25(OH)D (25-hydroxyergocalciferol and 25-hydroxycholecalciferol) was measured by LC-tandem mass spectrometry (API 4000 and AB SCIEX; Chromsystems GmbH) with an interassay CV of <5.7% from serum samples at the Biochemistry Department of St. James's Hospital, Dublin, Ireland, which is verified by the Vitamin D External Quality Assessment Scheme and National Institute of Standards and Technology. Concentrations of ≥50 nmol/L 25(OH)D indicated sufficiency, 40–49 nmol/L 25(OH)D indicated a low risk of deficiency, 25–39 nmol/L 25(OH)D indicated a high risk of deficiency, and >25 nmol/L 25(OH)D indicated vitamin D deficiency (20).

Ambient UVB radiation. UV dose data from the Tropospheric Emission Monitoring Internet Service (TEMIS) database (www.temis.nl/uvradiation/UVdose.html; version 1.4) was used. The daily UV dose is determined by way of an integration between sunrise and sunset in steps of 10 min with a correction for the attenuation of the UV radiation by clouds and a correction for the surface elevation and surface UV reflectivity (UV albedo). At each time step the amount of UV radiation is a function of the total ozone column (taken from the daily global total ozone column geographical distribution, which is determined from satellite observations) and the solar zenith angle (the angle between the local vertical and the position of the sun in the sky). The coefficients of this function depend on the action spectrum (21, 22). The attenuation by clouds during the day is determined from the cloud cover fraction for every 0.5 h, which is derived from geostationary Meteosat Second Generation satellite observations. For the UV dose data used in this study, the action spectrum of the final draft version from the study by Bouillon et al. (9), dated September 2005, was used. The TEMIS data are given in kilojoules per square meter. For this study, the daily D-UVB data are converted to millijoules per square centimeter, where 1 kJ/m^2 = 100 mJ/cm^2. The data are provided on a 0.5° × 0.5° (longitude × latitude) grid, each cell covering an area of ~55 km (north–south) × ~33 km (east–west). In this study we use the D-UVB estimates for the 69 grids that cover the island of Ireland from July 2005 to June 2015.

JN THE JOURNAL OF NUTRITION

Downloaded from jn.nutrition.org by guest on May 8, 2017

Descriptive analysis of D-UVB over Ireland. To facilitate descriptive analysis of D-UVB over Ireland, we calculated the following measures for each location.

By the addition of daily D-UVB in each month, we calculated the cumulative dose for all months. Because data for 10 y were available, we next found the mean monthly cumulative D-UVB for each calendar month, and we report this as the monthly cumulative dose.

For each day of the year (e.g., 31 August), the mean dose for that day over the 10-y period was found. These estimates were then grouped by month, and the mean D-UVB was found for the 12 mo, giving the mean daily dose for each month. The median daily dose for each month was calculated in a similar manner. For each season, the mean of median daily dose for each month was then found to give the median daily dose per season (MEDDS).

Individual cumulative D-UVB estimation calculation. We assigned a TEMIS grid cell to each participant based on his or her residential address. Next, we found daily D-UVBs over 135 d before the blood draw independently for each participant, depending on their location and date of blood draw. Vitamin D accumulates and is metabolized in the body, so we weighted the daily D-UVB contributions before summing them up because D-UVB exposure immediately preceding blood sampling contribute more than exposure from a more distant past. The weighting equation is shown below, where x = the number of days preceding the blood draw (starting day before and ≤135 d before sampling), y = the rate of disappearance of effect of D-UVB in days [half-life set at 35 d (23)], and $e^{(-\ln 2)(x/y)}$ is the weighing formula applied. This calculation provided estimates of cumulative and weighted D-UVB (cw-D-UVB) for each participant.

$$\text{Cumulative and weighted D-UVB}(X) = \sum_{x=1:135} [\text{vitDUVB(X)}] \times e^{-(\ln 2/y)(X)} \quad (1)$$

The annual mean daily D-UVB (shown in **Figure 1** for 2 grid cells) was used to estimate the mean cw-D-UVB for each day of the year from the above weighting equation. The relation derived in Figure 3C in the study by Kelly et al. (23) was then used to find an estimate of the deficiency levels of serum 25(OH)D concentrations associated with the cw-D-UVB.

Statistical analysis. We used chi-square tests to determine if there was a statistical difference between numbers within UVB quartiles for each category within a certain variable. Multivariable backward stepwise linear regression analysis was used to examine the association between cw-D-UVB and serum 25(OH)D after adjustment for supplementation use, age, sex, patient cohort, smoking status, and BMI. We split cw-D-UVB into quartiles and determined the median serum 25(OH)D concentrations in each quartile according to the participants' reported sun enjoyment. We stratified our cohort into those who were aged 60–74 y (younger old) and ≥75 y (older old) and by supplementation to more accurately portray the relation between cw-D-UVB, sun enjoyment, and 25(OH)D.

Random forest analyses were then used to assess the contribution of cw-D-UVB and sun enjoyment in predicting vitamin D deficiency. Different models were run for those aged <75 y and those aged ≥75 y—the cutoff was chosen because the mean age of the cohort was just over 74 y—and because older individuals have been shown to have reduced cutaneous vitamin D production (24). Data were split into 2 groups with part of the cohort randomly selected for the training data set and the remainder for the testing data set. Classification analysis was undertaken by using the training data set with data split into 0 or 1 by using the deficiency cutoff (<25 nmol/L). Receiver operating characteristic curves were then plotted by using the testing data set to measure the performance of the random forest analysis. The AUC demonstrates the ability of the test to accurately classify each binary pair from each category. The higher the AUC, the better the prediction model was at classifying each participant correctly. Model 1 included age, sex, BMI, cohort type, season of blood draw, and sun holiday in the last 6 mo; model 2 in addition included sun enjoyment and cw-D-UVB variables. Mann-Whitney *U* tests were carried out to determine statistical differences between those who enjoyed the sun compared with those who avoided the sun. All analyses were performed in R (R Development Core Team, 2011). Differences were considered significant at $P < 0.05$.

Results

Basic cohort characteristics. In total, 5138 older individuals (median age: 73 y; 67% female) with cognitive impairment, HBP, or bone impairment were included in the study. The median serum 25(OH)D concentration was 54.5 nmol/L (IQR: 34–81 nmol/L). Overall, 32% of this cohort were deficient or at high risk of deficiency [<40 nmol/L 25(OH)D; this was 38.6% in the cohort with cognitive impairment, 39.4% in the

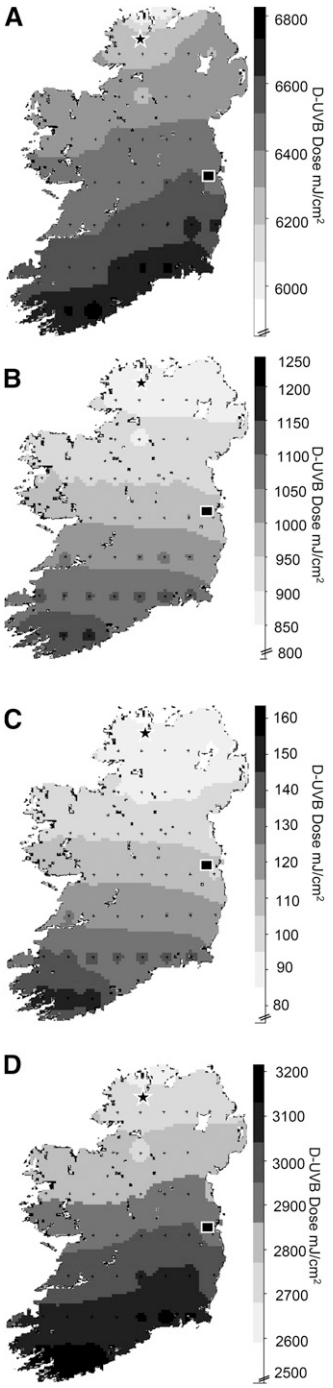

FIGURE 2 D-UVB on the island of Ireland. The monthly cumulative D-UVB was calculated by the addition of the D-UVB in each month, which was then averaged from 2005 to 2015. (A) June. (B) October. (C) January. (D) April. The star (★) denotes Derry, and the square (■) denotes Dublin, where the majority of the participants were located. D-UVB, daily ambient UVB dose at wavelengths that can induce vitamin D synthesis.

Downloaded from jn.nutrition.org by guest on May 8, 2017

cohort with HBP, and 11.8% in the cohort with bone impairment]. Overall, 47.4% took supplements, but prevalence was particularly high in the cohort with bone impairment (80%). Women were more likely to take supplements than men (55% compared with 32%; $P < 2.2 \times 10^{-16}$). Cohort characteristics are shown in **Table 1**, and further relevant information can be found elsewhere (18, 19).

Descriptive results for D-UVB over Ireland. The yearly integrated D-UVB on the island of Ireland was found to be 31,668 mJ/cm^2, and the median daily dose was 63 mJ/cm^2; this was 206 mJ/cm^2 in summer and 3.6 mJ/cm^2 in winter. Despite the narrow range of latitude (51°30'N–55°24'N), it was found that the ambient D-UVB was statistically significantly inversely related to latitude (51°00'N–51°30'N compared with 55°00'N–55°30'N) (**Figure 2**, **Supplemental Tables** 1 and **2**). When comparing the most northerly point (Malin Head) with the most southerly point (Mizen Head), the difference in total yearly D-UVB was 5694 mJ/cm^2 (a 19.8% higher D-UVB at Mizen); the difference was most prominent during the summer months (**Figures** 2 and **3**): a mean daily dose difference of 27 mJ/cm^2 was observed in June. Large differences were also observed between the seasons, with D-UVBs being a mean of 172 mJ/cm^2 higher in the summer than in the winter (winter MEDDS = 16.7 mJ/cm^2; spring MEDDS = 96.9 mJ/cm^2; summer MEDDS = 188.3 mJ/cm^2; and autumn MEDDS = 89.4 mJ/cm^2).

The mean cw-D-UVB for each day of the year demonstrated that people in Ireland have a high risk of 25(OH)D deficiency for the majority of the year (Figure 1). Using D-UVB to estimate serum 25(OH)D concentrations, only during 3 mo of the year did we observe a low risk of deficiency or sufficiency (>40 nmol/L) when cloud correction was taken into account. Furthermore, it was demonstrated that sufficiency (>50 nmol) only taking into account cw-D-UVB was not possible throughout the whole year when cloud correction was taken into account (Figure 1).

The determinants of 25(OH)D concentration. Dramatic effects of vitamin D supplementation on the circulating concentration were observed in all instances ($P < 2 \times 10^{-16}$). Serum 25(OH)D concentration was also significantly positively associated with cw-D-UVB, sun holiday in the last 6 mo, sun enjoyment, oily fish consumption, and patient cohort, and it was inversely associated with BMI and smoking (**Table 2**). A strong relation between cw-D-UVB and serum 25(OH)D concentration was further confirmed in all stratified analyses, except in individuals whose blood samples were taken in winter (**Table 3**).

Ambient D-UVB, sun enjoyment, and vitamin D status. We consistently observed higher serum 25(OH)D concentrations among those who enjoyed sunshine than in those who avoided sunshine for all levels of cw-D-UVB (**Supplemental Figure 1**, **Supplemental Table 3**, and **Figure 4**); differences were largely statistically significant (**Supplemental Table 4**). Very large differences in serum 25(OH)D concentration of >20 nmol/L were observed in some instances, particularly with higher ambient D-UVB radiation among individuals aged <75 y who were not taking supplements. Among those who were not taking supplements, it was observed that those who were in the lower quartiles of cw-D-UVB (quartiles 1 and 2) and avoided the sun were typically within the insufficient range (<40 nmol/L 25(OH)D), whereas those who were in the higher quartiles of cw-D-UVB (quartiles 3 and 4) and enjoyed the sun were typically in the sufficient range of (≥50 nmol/L 25(OH)D).

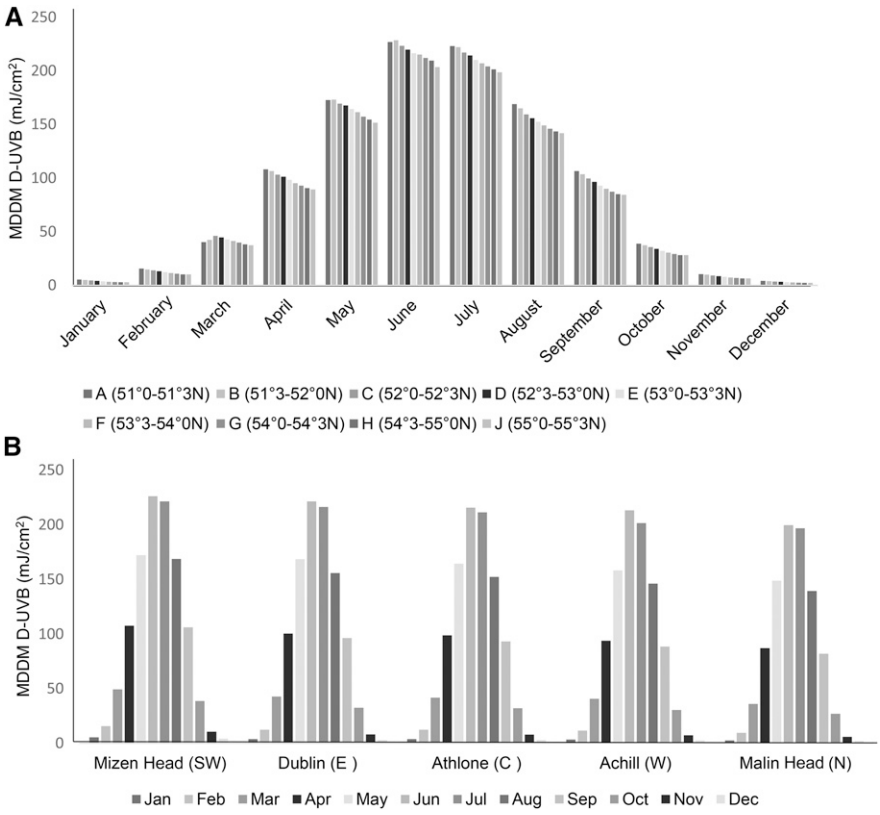

FIGURE 3 The differences in D-UVB over different regions and seasons in Ireland. (A) MDDM over latitude groups in Ireland shown in bars A–J. (B) MDDM over 5 areas in Ireland. Mizen Head (51.45°N, 9.82°W); Dublin (53.35°N, 6.26°W); Athlone (53.43°N, 7.95°W); Achill (53.96°N, 10.00°W); Malin Head (55.38°N, 7.37°W). C, center; D-UVB, daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; E, east; MDDM, mean daily ambient UVB dose at wavelengths that can induce vitamin D synthesis per month; N, north, SW, southwest; W, west.

Downloaded from jn.nutrition.org by guest on May 8, 2017

TABLE 2 Associations between serum 25(OH)D concentrations and select variables in older adults (N = 5138)[1]

Variable	n	β± SE	P[2]
Age	5138	0.02 ± 0.05	0.74
cw-D-UVB,[3] mJ/cm^2	5138	1.58 ± 0.12	$<2 \times 10^{-16}$
BMI, kg/m^2	5113	−0.56 ± 0.07	8×10^{-16}
Supplement use			
No	2447	Ref	Ref
Yes	2437	27.7 ± 0.8	$<2 \times 10^{-16}$
Patient cohort			
Bone	1366	Ref	Ref
Cognitive	1699	−10.3 ± 1	$<2 \times 10^{-16}$
HBP	2073	−8.6 ± 1	$<2 \times 10^{-16}$
Sun enjoyment			
Avoid direct sunshine	1679	Ref	Ref
Sometimes enjoy sunshine	1965	3.0 ± 0.9	4.5×10^{-4}
Enjoy staying in sunshine	1492	6.6 ± 0.9	2.2×10^{-12}
Sex			
Male	1686	Ref	Ref
Female	3452	−0.12 ± 0.8	0.88
Smoking status			
Current	615	Ref	Ref
Past	2387	5.1 ± 1.2	1.9×10^{-5}
Never	2134	6.4 ± 1.2	8.2×10^{-8}
Recent sun holiday			
No	4235	Ref	Ref
Yes	892	10.5 ± 1	$<2 \times 10^{-16}$
Oily fish consumption			
No	3060	Ref	Ref
Yes	2076	2.1 ± 0.7	5.3×10^{-3}

[1] cw-D-UVB, cumulative and weighted daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; HBP, high blood pressure; Ref, reference; 25(OH)D, 25-hydroxyvitamin D.
[2] Multivariable linear regression was used to test associations. Adjusted for the age, cw-D-UVB, BMI, supplementation, patient cohort, sun enjoyment, sex, smoking status, recent sun holiday, and oily fish consumption.
[3] β per 1000 mJ/cm^2.

Using cw-D-UVB quartiles to predict deficiency levels of individuals. We observed that the addition of cw-D-UVB and sun enjoyment to the random forest model gave a 5.7% higher AUC when classifying deficient and sufficient patients aged 60–74 y and a 1.4% higher AUC in those aged >75 y who did not take supplements (**Figure 5**). These improvements in prediction were less obvious in older individuals and among those taking supplements (**Supplemental Figures 2** and **3**).

Discussion

In this article we demonstrated an important contribution of natural sun exposure to vitamin D status in an older cohort of free-living individuals residing at high, northerly latitudes. This finding is contrary to the prevailing view that the potential for skin synthesis is of marginal importance at high latitudes for large parts of the year (14, 25, 26). Moreover, this study extends our understanding of skin synthesis in older individuals because we show that both ambient UVB and sun enjoyment affect vitamin D status even in individuals aged >60 y. A similar study found a strong association between the UVB estimate and 25(OH)D concentration measurements but only in participants aged <60 y (27), a null finding that may be due to the poorer UVB exposure estimate and/or a much smaller cohort. Although we demonstrated a strong association between UVB and 25(OH)D even among supplement takers, in a study that used global solar radiation, an association with serum 25(OH)D concentration in supplemented participants was not found (28); this might be explained by the lack of adjustment for important determinants of UVB exposure.

Evidence suggests that the role of natural synthesis decreases with age (24, 29). Our findings also note this trend as the association between cw-D-UVB and serum 25(OH)D concentration was reduced in older-old (≥75 y) participants. However, we argue that the importance of natural exposure to sunshine is still of consequence even among this group. Previous studies have also demonstrated this; seasonal variation in serum 25(OH)D concentration is commonly observed in older individuals (30), and older individuals who undertook outdoor activities, such as gardening and cycling, had higher serum 25(OH)D concentrations than those who did not (31).

The effect sizes we observed were of clinical importance: sun enjoyment and ambient UVB dose were clearly linked to vitamin D status, particularly among non–supplement takers. For example, we demonstrated in a subset of nonsupplemented individuals aged 60–74 y that sun enjoyment (avoided compared with sometimes enjoyed and avoided compared with enjoyed) was clearly linked with clinical vitamin D deficiency categories for all doses of UVB. For instance, the median serum 25(OH)D concentrations for quartile 1 were 24, 30, and 36 nmol/mL, whereas they were found to be 46, 54, and 67 nmol/mL in quartile 4 for each of the 3 sun enjoyment levels, respectively. This highlights that those who avoided sunshine had a dramatically lower serum 25(OH)D concentration than did those who sometimes enjoyed sunshine and those who enjoyed sunshine.

Supplement use has been shown to be a critical source of vitamin D particularly in high-latitude countries (32, 33). Calculation of each individual's background UVB dose, accounting for the date of blood sample and residential address, allowed us to bring all participants to the same denominator, facilitating a more accurate assessment of the contribution of other factors, such as supplements or sun enjoyment to 25(OH)D concentration. Accurately adjusting for UVB dose is particularly important when individuals from different countries or a wider geographical area sampled throughout the year are analyzed in the same study. Our study confirms the impact of vitamin D supplementation on maintaining a healthy vitamin D status across all levels of ambient radiation at this northerly location, irrespective of sun enjoyment and across all examined age groups. By stratifying according to doses of ambient UVB and sun enjoyment, we were able to estimate that the increase in serum 25(OH)D concentration due to taking any dose of vitamin D supplement was ~35–40 nmol/L in this cohort.

We found a substantial improvement in the prediction of vitamin D–deficient individuals among the nonsupplemented younger old (60–74 y) with the addition of UVB dose and sun behaviors to the model. Consistent with the notion that UVB-induced synthesis decreases with age (24), classification was less successful among the older old. Unfortunately, the dosage of vitamin D supplementation taken was not known, and the heterogeneity in this predictor is likely to have affected the performance of models that included supplemented individuals.

The total yearly D-UVB amounts we found (31,668 mJ/cm^2) are comparable to those reported for Scotland (27,806 mJ/cm^2) (23). Although a large variation in ambient D-UVB has been shown across Europe (34), we found that notable differences

Downloaded from jn.nutrition.org by guest on May 8, 2017

TABLE 3 Associations between cw-D-UVB and serum 25(OH)D concentrations in older adults stratified by select variables[1]

Stratification variable	*n*	Median 25(OH)D, nmol/L	β, per 1000 mJ/cm^2	*P*[2]
Supplement use				
Yes	2437	74.9	1.10	2.4×10^{-9}
No	2066	38.46	2.14	$<2 \times 10^{-16}$
Age, y				
<75	1720	54.1	2.18	$<2 \times 10^{-16}$
≥75	1706	54.45	0.91	6×10^{-7}
Cohort				
Cognitive	1699	50.7	1.16	1×10^{-8}
HBP	2073	76.7	2.44	$<2 \times 10^{-16}$
Bone	1366	45.7	1.09	5×10^{-6}
Sex				
Male	1686	48.5	2.36	$<2 \times 10^{-16}$
Female	3452	59.5	1.23	$<2 \times 10^{-16}$
BMI, kg/m^2				
Underweight, <18.5	109	65.4	3.33	7×10^{-4}
Normal weight, 18.6–24.9	1430	67.3	1.01	2×10^{-5}
Overweight, 25–29.9	2003	55.19	1.91	$<2 \times 10^{-16}$
Obese, 30–39.9	1435	45.9	1.53	4×10^{-14}
Extremely obese, ≥40	136	39	1.98	3×10^{-3}
Smoking				
Current	614	46	2.19	6×10^{-10}
Past	2133	53.7	1.62	$<2 \times 10^{-16}$
Never	2380	58.2	1.29	8×10^{-14}
Alcohol consumption				
Current	2940	57	1.97	$<2 \times 10^{-16}$
Past	914	51.8	1.41	2×10^{-7}
Never	1273	52.15	0.82	7×10^{-3}
Enjoy the sun				
Avoid direct sunshine	1675	47.85	1.32	4×10^{-11}
Sometimes stay in sunshine	1963	54.4	1.48	10×10^{-15}
Enjoy staying in sunshine	1489	62.6	2.01	$<2 \times 10^{-16}$
Season				
Winter	1204	49.3	1.93	0.26
Spring	1220	49	1.43	2×10^{-3}
Summer	1300	55.8	2.98	6×10^{-6}
Autumn	1414	63.02	0.77	3×10^{-2}
Sun protection use[3]				
Yes	2335	61.68	2.02	$<2 \times 10^{-16}$
No	2800	48.8	1.28	7×10^{-16}

[1] cw-D-UVB, cumulative and weighted daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; HBP, high blood pressure; 25(OH)D, 25-hydroxyvitamin D.
[2] Multivariable linear regression was used to determine associations. Adjusted for the age, sex, BMI, supplementation, cohort type, sun enjoyment, smoking status, recent sun holiday, and oily fish consumption, minus the variable that is used for stratification.
[3] Those who answered always, usually, and sometimes were classified as yes, and those who answered rarely and never were classified as no.

exist across Ireland despite a relatively small geographical area. The implications of these findings are especially relevant for regions that stretch over a wider range of latitudes, altitudes, or climates because determining UVB dose at single or a few locations, assuming similar exposure over a wider geographic area as is commonly done, is likely to affect the precision of the estimate and thus bias association analysis findings toward the null because of error in the estimate (28, 35, 36).

Establishing the role of cutaneous vitamin D synthesis is topical (37, 38) because of the current conflicting guidelines. On one hand, studies have highlighted the need to avoid sunshine because of the risks of skin cancer (39). Contrarily, multiple reports acknowledge the need for sunshine exposure to prevent vitamin D deficiency and recommend 5–15 min of sunlight exposure 3 times/wk (16, 40–42). As a result, mixed and even contradictory health messages are being communicated to the public (43). Furthermore, there have been multiple reports suggesting a beneficial role of vitamin D in the risk and survival of numerous conditions, such as cancers, cardiovascular disease, and bone and immunological conditions (4–7). The combined mortality for certain cancers (breast, colorectal, and prostate) far outweigh the mortality of melanoma skin cancer patients in Europe (438,233 compared with 12,051) (44), yet the general population is unaware of the potential benefit it could be neglecting by strict sun avoidance practices.

The UK Scientific Advisory Committee on Nutrition, which assesses current vitamin D reference values, recently published guidelines noting that UVB is the most important

Downloaded from jn.nutrition.org by guest on May 8, 2017

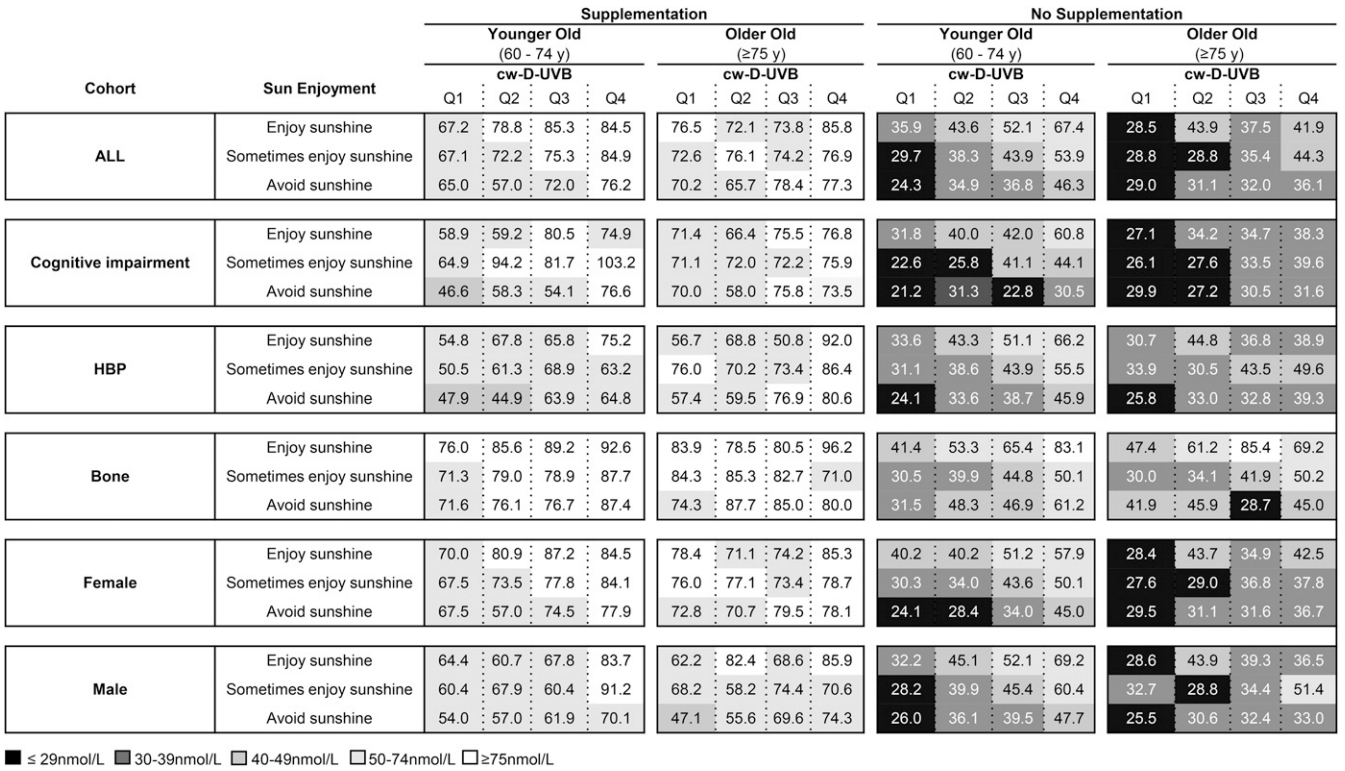

FIGURE 4 Median 25(OH)D concentration in older adults stratified by cw-D-UVB quartiles and sun enjoyment. More analysis of these data is provided in the supplemental material: median, mean, and IQR of serum 25(OH)D concentration are shown for each cw-D-UVB quartile according to the sun enjoyment data in Supplemental Table 2 and statistical analysis of the differences in Supplemental Table 3. cw-D-UVB, cumulative and weighted daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; HBP, high blood pressure; Q, quartile; 25(OH)D, 25-hydroxyvitamin D.

source of vitamin D (45). However, no recommendations could be made regarding how much sunlight exposure is needed to prevent deficiency because of endogenous factors with vitamin D production, which further reiterates the confusion on the topic and emphasizes the relevance and contribution of approaches taken in our study. Most attempts to reconcile the skin cancer–vitamin D deficiency conundrum come from Australia and New Zealand, where skin cancer is highly prevalent because of the intensity of solar radiation; yet a large proportion of the population is vitamin D deficient (46–48). One-size-fits-all global sun behavior guidelines cannot be achieved because of the extreme differences in the background exposure doses. An accurate understanding of UVB radiation and its relation to 25(OH)D concentration is key to providing appropriate regional sun behavior recommendations. Determination of the ambient UVB dose at which the majority of individuals are at risk of vitamin D deficiency can inform the recommended duration of sun exposure or time of year when seasonal supplementation should commence, and this could be personalized by region and personal characteristics.

The precision of the ambient UVB estimate used presents an important strength of this study. Briefly, we calculated the individual ambient UVB exposure dose for each participant separately using the greatest spatial and temporal resolution to date (15, 34). We focused on D-UVB only, and we accounted for the accumulation as well as diminution of vitamin D in the body, offering critical improvements over similar studies (27, 49–52). Additionally, we recruited only individuals with ethnically Irish parents [the majority of whom are shown to have skin types I and II (53)], to ensure similar cutaneous vitamin D production abilities. Further strengths include a large cohort and the best available assay for the measurement of serum 25(OH)D concentrations.

There are some limitations to the current study. First, the dose of vitamin D supplement taken was not known. Second, sun enjoyment was taken as a proxy of utilization of ambient UVB; unfortunately we were unable to capture other personal factors that affect skin synthesis, such as time spent outdoors, clothing choices, or angle of exposed skin to the sun rays. Although these factors are important when estimating cutaneous synthesis, they are nearly impossible to capture correctly in contrast to the ambient UVB dose, which is accurately measurable. The TEMIS UV data from this study were calculated by using a peak action spectrum of 295 nm, which was derived from the final draft version of the study by Bouillon et al. (9); however, the published version of their report has a peak of 298 nm. This leads to daily UV dose values that are higher by a factor of ~2.2 (2.1 and 2.3 in summer and winter, respectively). The use of a different action spectrum does not affect the statistical relation (regressions and correlations) presented in this study, merely the absolute value of the presented cw-D-UVB.

Ambient D-UVB and sun enjoyment are important predictors of vitamin D status, even in this elderly, northern population. The accurate estimation of ambient UVB can help further clarify the role of other determinants of vitamin D status and inform sunshine recommendation guidelines. Future epidemiologic studies should use readily available UVB data to improve assessment of skin synthesis contribution to 25(OH)D concentration and enhance association studies focused on vitamin D.

Downloaded from jn.nutrition.org by guest on May 8, 2017

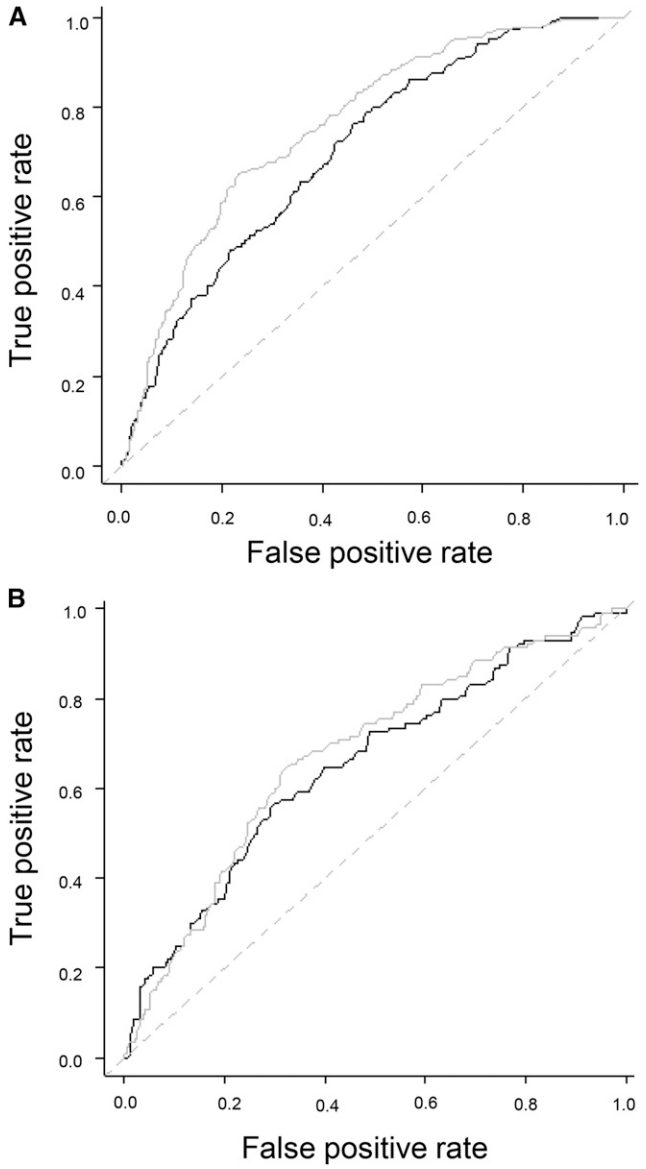

FIGURE 5 Receiver operating characteristic curves predicting vitamin D deficiency (<25 nmol/L) in nonsupplemented older adults. (A) Data shown for those aged 60–74 y [total n = 1491; <25 nmol/L 25(OH)D, n = 293]; AUC model 1: 70.5%; AUC model 2: 76.2%. (B) Data shown for those aged ≥75 y [total n = 920; <25 nmol/L 25(OH)D, n = 277]; AUC model 1: 67.7%; AUC model 2: 69.1%. Model 1 (black line) is adjusted for age, sex, BMI, cohort type, season of blood draw, and sun holiday in the last 6 mo. Model 2 (gray line) is adjusted for variables in model 1 plus cw-D-UVB quartiles and sun enjoyment. cw-D-UVB, cumulative and weighted daily ambient UVB dose at wavelengths that can induce vitamin D synthesis; 25(OH)D, 25-hydroxyvitamin D.

Acknowledgments

EL, HM, LH, KM, CC, MC, MW, JJS, and AMM conducted the research; JvG and MvW provided and analyzed the data; FO and DK analyzed the data and performed the statistical analysis; FO and LZ wrote the manuscript; and LZ had primary responsibility for the final content. All authors read and approved the final manuscript.

References

1. Cashman KD, Dowling KG, Skrabakova Z, Gonzalez-Gross M, Valtuena J, De Henauw S, Moreno L, Damsgaard CT, Michaelsen KF, Molgaard C, et al. Vitamin D deficiency in Europe: pandemic? Am J Clin Nutr 2016;103:1033–44.
2. Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc 2006;81:353–73.
3. Cranney A, Horsley T, O'Donnell S, Weiler H, Puil L, Ooi D, Atkinson S, Ward L, Moher D, Hanley D, et al. Effectiveness and safety of vitamin D in relation to bone health. Evid Rep Technol Assess (Full Rep) 2007 Aug:1–235.
4. Pittas AG, Chung M, Trikalinos T, Mitri J, Brendel M, Patel K, Lichtenstein AH, Lau J, Balk EM. Systematic review: vitamin D and cardiometabolic outcomes. Ann Intern Med 2010;152:307–14.
5. Gandini S, Boniol M, Haukka J, Byrnes G, Cox B, Sneyd MJ, Mullie P, Autier P. Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. Int J Cancer 2011;128:1414–24.
6. Autier P, Boniol M, Pizot C, Mullie P. Vitamin D status and ill health: a systematic review. Lancet Diabetes Endocrinol 2014;2:76–89.
7. Theodoratou E, Tzoulaki I, Zgaga L, Ioannidis JP. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ 2014;348:g2035.
8. Flynn A, Hirvonen T, Mensink GB, Ocke MC, Serra-Majem L, Stos K, Szponar L, Tetens I, Turrini A, Fletcher R, et al. Intake of selected nutrients from foods, from fortification and from supplements in various European countries. Food Nutr Res 2009 Nov 12.
9. Bouillon R, Eisman J, Garabedian M, Holick MF, Kleinschmidt J, Suda T, Terenetskaya I, Webb AR. Action spectrum for the production of previtamin D3 in human skin. Vienna (Austria): International Commission on Ilumination; 2006.
10. Jovičić S, Ignjatović S, Majkić-Singh N. Biohemija i metabolizam vitamina D. [Biochemistry and metabolism of vitamin D.] J Med Biochem 2012;31:309–15.
11. Cannell JJ, Vieth R, Umhau JC, Holick MF, Grant WB, Madronich S, Garland CF, Giovannucci E. Epidemic influenza and vitamin D. Epidemiol Infect 2006;134:1129–40.
12. Kimlin MG. Geographic location and vitamin D synthesis. Mol Aspects Med 2008;29:453–61.
13. Lubin D, Frederick JE. The ultraviolet radiation environment of the Antarctic Peninsula: the roles of ozone and cloud cover. J Appl Meteorol 1991;4:478–93.
14. Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. J Clin Endocrinol Metab 1988;67:373–8.
15. Kazantzidis A, Smedley A, Kift R, Rimmer J, Berry JL, Rhodes LE, Webb AR. A modeling approach to determine how much UV radiation is available across the UK and Ireland for health risk and benefit studies. Photochem Photobiol Sci 2015;14:1073–81.
16. British Association of Dermatologists CRU, Diabetes UK, the Multiple Sclerosis Society, the National Heart Forum, the National Osteoporosis Society and the Primary Care Dermatology Society. Consensus vitamin D position statement. 2010. [cited 2016 Oct 10]. Available from: http://www.nhs.uk/livewell/summerhealth/documents/concensus_statement%20_vitd_dec_2010.pdf.
17. McCarroll K, Beirne A, Casey M, McNulty H, Ward M, Hoey L, Molloy A, Laird E, Healy M, Strain JJ, et al. Determinants of 25-hydroxyvitamin D in older Irish adults. Age Ageing 2015;44:847–53.
18. Laird E, McNulty H, Ward M, Hoey L, McSorley E, Wallace JM, Carson E, Molloy AM, Healy M, Casey MC, et al. Vitamin D deficiency is associated with inflammation in older Irish adults. J Clin Endocrinol Metab 2014;99:1807–15.
19. Molloy AM, Pangilinan F, Mills JL, Shane B, O'Neill MB, McGaughey DM, Velkova A, Abaan HO, Ueland PM, McNulty H, et al. A common polymorphism in HIBCH influences methylmalonic acid concentrations in blood independently of cobalamin. Am J Hum Genet 2016;98:869–82.
20. Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, Durazo-Arvizu RA, Gallagher JC, Gallo RL, Jones G, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab 2011;96:53–8.
21. Allaart M, van Weele M, Fortuin P, Kelder H. An empirical model to predict the UV-index based on solar zenith angles and total ozone. Meteorol Appl 2004;11:59–65.

Downloaded from jn.nutrition.org by guest on May 8, 2017

22. van Geffen J, van der AR, van Weele M, Allaart M Eskes H. Surface UV radiation monitoring based on GOME and SCIAMACHY. Proceedings of the ENVISAT & ERS Symposium (SP-572:10); 2004 Sep 10; Salzburg, Austria. Paris: ESA Publications; 2004.
23. Kelly D, Theodoratou E, Farrington S, Fraser R, Campbell H, Dunlop MG, Zgaga L. The contributions of adjusted ambient UVB at the place of residence and other determinants to serum 25-hydroxyvitamin D concentrations. Br J Dermatol 2016;174:1068–78.
24. MacLaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. J Clin Invest 1985;76:1536–8.
25. Engelsen O. The relationship between ultraviolet radiation exposure and vitamin D status. Nutrients 2010;2:482–95.
26. Kimlin MG, Olds WJ, Moore MR. Location and vitamin D synthesis: is the hypothesis validated by geophysical data? J Photochem Photobiol B 2007;86:234–9.
27. Greenfield JA, Park PS, Farahani E, Malik S, Vieth R, McFarlane NA, Shepherd TG, Knight JA. Solar ultraviolet-B radiation and vitamin D: a cross-sectional population-based study using data from the 2007 to 2009 Canadian Health Measures Survey. BMC Public Health 2012;12:660.
28. Romero-Ortuno R, Cogan L, Browne J, Healy M, Casey MC, Cunningham C, Walsh JB, Kenny RA. Seasonal variation of serum vitamin D and the effect of vitamin D supplementation in Irish community-dwelling older people. Age Ageing 2011;40:168–74.
29. Holick MF. Environmental factors that influence the cutaneous production of vitamin D. Am J Clin Nutr 1995;61:638S–45S.
30. McKenna MJ, Freaney R, Meade A, Muldowney FP. Hypovitaminosis D and elevated serum alkaline phosphatase in elderly Irish people. Am J Clin Nutr 1985;41:101–9.
31. De Rui M, Toffanello ED, Veronese N, Zambon S, Bolzetta F, Sartori L, Musacchio E, Corti MC, Baggio G, Crepaldi G, et al. Vitamin D deficiency and leisure time activities in the elderly: are all pastimes the same? PLoS One 2014;9:e94805.
32. Hennessy Á, Browne F, Kiely M, Walton J, Flynn A. The role of fortified foods and nutritional supplements in increasing vitamin D intake in Irish preschool children. Eur J Nutr 2016 Feb 19 (Epub ahead of print; DOI: 10.1007/s00394-016-1171-7).
33. Zgaga L, Theodoratou E, Farrington SM, Agakov F, Tenesa A, Walker M, Knox S, Michael Wallace A, Cetnarskyj R, McNeill G, et al. Diet, environmental factors, and lifestyle underlie the high prevalence of vitamin D deficiency in healthy adults in Scotland, and supplementation reduces the proportion that are severely deficient. J Nutr 2011;141:1535–42.
34. O'Neill CM, Kazantzidis A, Ryan MJ, Barber N, Sempos CT, Durazo-Arvizu RA, Jorde R, Grimnes G, Eiriksdottir G, Gudnason V, et al. Seasonal changes in vitamin D-Effective UVB availability in Europe and associations with population serum 25-Hydroxyvitamin D. Nutrients 2016;8E533.
35. Boscoe FP, Schymura MJ. Solar ultraviolet-B exposure and cancer incidence and mortality in the United States, 1993–2002. BMC Cancer 2006;6:264.
36. Grant WB. An ecologic study of cancer mortality rates in Spain with respect to indices of solar UVB irradiance and smoking. Int J Cancer 2007;120:1123–8.
37. de Gruijl FR. Sufficient vitamin D from casual sun exposure? Photochem Photobiol 2011;87:598–601.
38. Diffey BL. Is casual exposure to summer sunlight effective at maintaining adequate vitamin D status? Photodermatol Photoimmunol Photomed 2010;26:172–6.
39. Barysch MJ, Hofbauer GF, Dummer R. Vitamin D, ultraviolet exposure, and skin cancer in the elderly. Gerontology 2010;56:410–3.
40. Irish cancer society. Vitamin D and the sun [Internet]. [cited 2016 Jul 24]. Available from: http://www.cancer.ie/reduce-your-risk/sunsmart/vitamin-D#sthash.k81DN3yU.dpbs.
41. WHO. The known health effects of UV: are there beneficial effects of UV radiation? [Internet]. [cited 2016 Jun 11]. Available from: http://www.who.int/uv/faq/uvhealtfac/en/index1.html.
42. Glossmann H. Vitamin D, UV, and skin cancer in the elderly: to expose or not to expose? Gerontology 2011;57:350–3.
43. Reeder AI, Jopson JA, Gray AR. "Prescribing sunshine": a national, cross-sectional survey of 1,089 New Zealand general practitioners regarding their sun exposure and vitamin D perceptions, and advice provided to patients. BMC Fam Pract 2012;13:85.
44. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, Forman D, Bray F. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374–403.
45. Public Health England. The Scientific Advisory Committee on Nutrition (SACN) recommendations on vitamin D [Internet]. [cited 2016 Jul 21]. Available from: https://www.gov.uk/government/publications/sacn-vitamin-d-and-health-report.
46. Ministry of Health. Vitamin D status of New Zealand adults findings from the 2008/09 New Zealand adult nutrition survey. 2008. [cited 2016 Nov 5]. Available from: https://www.health.govt.nz/system/files/documents/publications/vit-d-status-nzadults.pdf.
47. Boyages S, Bilinski K. Seasonal reduction in vitamin D level persists into spring in NSW Australia: implications for monitoring and replacement therapy. Clin Endocrinol (Oxf) 2012;77:515–23.
48. Tran B, Armstrong BK, McGeechan K, Ebeling PR, English DR, Kimlin MG, Lucas R, van der Pols JC, Venn A, Gebski V, et al. Predicting vitamin D deficiency in older Australian adults. Clin Endocrinol (Oxf) 2013;79:631–40.
49. Tran B, Lucas R, Kimlin M, Whiteman D, Neale R. Association between ambient ultraviolet radiation and risk of esophageal cancer. Am J Gastroenterol 2012;107:1803–13.
50. Sayers A, Tilling K, Boucher BJ, Noonan K, Tobias JH. Predicting ambient ultraviolet from routine meteorological data; its potential use as an instrumental variable for vitamin D status in pregnancy in a longitudinal birth cohort in the UK. Int J Epidemiol 2009;38:1681–8.
51. Nair-Shalliker V, Clements M, Fenech M, Armstrong BK. Personal sun exposure and serum 25-hydroxy vitamin D concentrations. Photochem Photobiol 2013;89:208–14.
52. Bertrand KA, Giovannucci E, Liu Y, Malspeis S, Eliassen AH, Wu K, Holmes MD, Laden F, Feskanich D. Determinants of plasma 25-hydroxyvitamin D and development of prediction models in three US cohorts. Br J Nutr 2012;108:1889–96.
53. Gibson GE, Codd MB, Murphy GM. Skin type distribution and skin disease in Ireland. Ir J Med Sci 1997;166:72–4.

Downloaded from jn.nutrition.org by guest on May 8, 2017