Seasonality of UV-radiation and vitamin D status at 69 degrees north

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The main purpose with this study was to assess the seasonal variation in measured UV-radiation and its impact on vitamin D status throughout one year in subjects living at high latitude. Blood samples drawn from 60 volunteers (44 women, 16 men) living at Andenes (69° N), Norway, were collected throughout one year, at two-month intervals. The blood samples were analysed for 25-hydroxy vitamin D [25(OH)D]. Data on dietary intakes of vitamin D, time spent in daylight, use of sun beds and sun seeking holidays were collected by using questionnaires. The ambient vitamin D effective UV-radiation was measured at a site near by Andenes, and the number of hours spent outdoors with sufficient radiation for cutaneous vitamin D production (UV-hours) was estimated for each day. The mean 25(OH)D values were significantly higher at the end of the summer and in December, 2004 and varied from 42.0 nmol L^{-1} in October, 2004 and April, 2005 to around 47 nmol L^{-1} in December, 2004 and September, 2005. For the whole group, a positive relationship between UV-hours and 25(OH)D was found at UV-hours \geq 3.5. However, for subjects with lower 25(OH)D levels *i.e.* at least one blood measurement with 25(OH)D < 37.5 nmol L⁻¹, the positive relationship were found at around 1.5 UV-hours and more, whereas for the group of subjects that had all their vitamin D values above 37.5 nmol L⁻¹, positive relationship was found at UV-hours \geq 4.0, when adjusting for vitamin D intake, sun bed use and sun seeking holidays. The generally high dietary intakes of vitamin D, especially in winter, mask largely the effect of seasonal variation in UV-exposure, causing an atypical seasonal variation in vitamin D status. The UV-hour variable significantly predicted 25(OH)D levels in blood when adjusted for intakes and artificial UV-radiation exposure and sun holidays abroad.

Introduction

The solar induced cutaneous production has long been recognised as the main source to vitamin D.¹The synthesis in skin consists of two basic stages. In the first stage, initial provitamin D (7dehydrocholesterol, 7-DHC) is converted to previtamin D by radiation at wavelengths mainly in the range 290–315 nanometers. At the second stage, the latter undergoes heat-induced isomerization to vitamin D (cholecalciferol), which is specifically translocated by the vitamin-D-binding protein into the circulation.²

Concern has been raised regarding the risk of insufficient vitamin D status among populations at latitudes where the solar radiation part of the year is insufficient for cutaneous vitamin D production.³ The duration of the so called "vitamin D winter" increases with increasing latitude. Engelsen *et al.*⁴ have, by utilising estimation models, computed that at 51 degrees and higher, cutaneous vitamin D production can be suppressed part of the year.

Surprisingly, studies have shown that in Europe, there is a positive correlation between vitamin D levels in blood and increasing latitude.^{5,6} This correlation has been explained by a higher intake of vitamin D in the north. Vitamin D is found in

a limited number of food items like fatty fish, cod-liver oil and fortified margarine, butter, and milk.⁷

In northern Norway, traditional vitamin D rich marine diet has compensated for lack of solar induced cutaneous vitamin D production during winter.⁸ However, people living at high latitudes and who do not consume food containing vitamin D are at risk of not getting enough vitamin D.

The vitamin D status of populations have gained increased attention driven by a growing body of literature suggesting that vitamin D has health promoting effects far beyond the well established impact on bone-metabolism and calcium and phosphorous homeostasis.⁹ Vitamin D insufficiency has been suggested, however not yet well documented, to contribute to increased risk of cancer, in particular colon cancer,¹⁰ and some autoimmune diseases like multiple sclerosis¹¹ and type I diabetes.¹²

In order to study vitamin D and health in large epidemiological prospective studies, methodological improvements are needed to develop models that provide valid exposure data at the individual level on both the dietary and sun-induced vitamin D. Here we explore the applicability of the statistical parameter "UV-hours"¹⁴ for such studies. Although some *in vivo* studies exist in the literature, much is still unclear regarding sunlight and vitamin D production in skin, especially for populations living at high latitudes.¹³ We have previously collected single blood samples throughout one winter and spring from 300 women situated in northern Norway.¹⁴ These samples were analysed for 25-hydroxy vitamin D (25(OH)D) and were found to be statistically significant in relation to both dietary intake and estimates for exposure of ultraviolet radiation.

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The main purpose of this study was to further assess seasonal variation measured UV-radiation and its impact on vitamin D status throughout one year in subjects living at high latitude by using a repeated measurement design.

Methods

Sample

The study was carried out at Andenes municipality in Nordland County, Norway (69.2° N, 16.2° E). Subjects were recruited by advertising as well as journalistic coverage in the local newspaper. Inclusion criteria were subjects between 20 and 60 years and resident in Andenes municipality. Altogether 60 subjects; 44 women and 16 men participated in the study. All participants signed a consent form. The study was approved by the Regional Committee for Research Ethics.

Data collection

An overview of the data collection is presented in Table 1. Blood samples were drawn from the participants at two-month intervals throughout one year, *i.e.* altogether six blood samples per person. Each participant answered a food frequency questionnaire at the first (October 2004) and the last blood sampling (September 2005) (Questionnaire I). The questionnaire was a slightly altered version of the NOWAC (Norwegian Women and Cancer Study) food frequency questionnaire, and was used to estimate usual daily vitamin D intake. The questionnaire also contained questions on gender, age, height, and weight of the respondents. Both the NOWAC questionnaire and the altered version have been described in detail elsewhere.^{8,15-16}

At each blood sample collection, the participants answered questions on how many hours they spent in daylight the previous week, as well as sun-seeking holidays and use of sun beds during the last month prior to blood sampling (Questionnaire II). These questions have been validated.¹⁴

UV-measurements

The participants' records on how many hours they spent in daylight (DL-hours) the previous week were registered at the time of blood sampling. The tabulated responses above were converted to a continuous function of time spent outdoors *vs.* time of year by application of cubic spline interpolation.

In order to find a measure for each subject's exposure of vitamin D effective UV-radiation, we measured the ambient UV-radiation every half hour at the ALOMAR atmospheric observatory near Andenes. The Brewer UV instrument and its

Table 1 Overview of the data collection

calibration is described in Edvardsen *et. al.*¹⁷ By application of cubic spline interpolation we reduced the time interval of the vitamin D effective UV doses to one-minute. From the calculated time series we established a value for how many hours per day there were vitamin D effective UV-radiation (UV-hours) available, and compared the available UV-hours with the subjects' data on DL-hours. The UV-hours assigned to each subject were then set equal to the DL-hours, but were then not allowed to exceed the calculated maximum available number of UV-hours (Fig. 1). 'UV-hours' has hereafter this definition only.

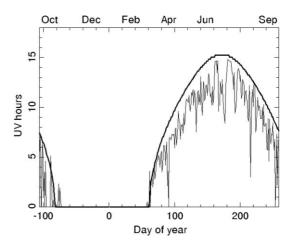


Fig. 1 Number of available daily hours with sufficient UV-radiation for cutaneous vitamin D production to take place (skin type II) by time of year from October 2004 to September 2005. The thin, erratic line are real measurements and the solid, thick line indicates simulations of an ideal clear sky situation with a constant ozone layer of 350 DU.

Determination of 25-hydroxy vitamin D

The blood plasma samples were kept at -80 °C until analysis for 25(OH)D according to a modified version of the method described by Aksnes.¹⁸ Briefly, 0.25 mL plasma samples were extracted with methanol and *n*-hexane. The *n*-hexane phase was collected, evaporated to dryness and ejected into a reverse-phase high performance liquid chromatography system. Elution of 25(OH)D was performed with methanol–water (85:15, v/v) and the elute was monitored at 265 nm by a diode-array detector (UV6000; ThermoFinnigan, San Jose, CA, USA) equipped with a 5 cm detector cuvette. The mean recovery of 25(OH)D was 77.2% (SD 3.9%) and the interassay variation was 6%, with a detection limit of 6.0 nmol L⁻¹. The method determined the sum of 25(OH)D₂ and 25(OH)D₃.

	Questionnaire I	Questionnaire II		
Time	Food frequency/basic characteristics	Sun exposure	Blood samples collected	
October 2004	\checkmark	\checkmark	\checkmark	
December 2004		\checkmark	\checkmark	
February 2005		\checkmark	\checkmark	
April 2005		\checkmark	\checkmark	
June 2005		\checkmark	\checkmark	
September 2005	\checkmark	\checkmark	\checkmark	

Statistical analysis

SAS version 9.1 (SAS Institute, Cary NC, USA) was used for nutrient calculations and statistical analysis. Multiple linear regression models were used to assess the association between 25(OH)D and body mass index (BMI, kg m⁻²) at each time point. The association between repeated measurements of 25(OH)Dand UV-hours was assessed using linear mixed models (Proc Mixed in SAS). The 25(OH)D was fitted as a cubic polynomial function of UV-hours, adjusting for covariates. The within subjects dependence due to repeated observations was controlled for by including the Toeplitz covariance structure. The model are given as (when UV and age are the independent variables)

$$25(OH)D_{ij} = \beta_0 + \beta_1 UV_{ij} + \beta_2 UV_{ij}^2 + \beta_3 UV_{ij}^3 + \beta_4 age_i + \varepsilon_{ij} \quad (1)$$

 $i = 1, \ldots, 60; j = 1, \ldots, 6$, where OHD_{*ij*} is subject *i*'s 25(OH)D value at time *j*, β_0 is the intercept, β_1 , β_2 , β_3 are the regression coefficients for UV-hours, β_4 is the regression coefficient for age, and ε_{ij} is the variance component.

Results

Vitamin D status by different characteristics

The overall mean values for 25(OH)D, throughout the study period, are presented in Table 2, together with mean 25(OH)D levels by different selected characteristics. For the total study sample, 25(OH)D values were significantly highest in the summer and in December and varied from 42 nmol L^{-1} in October and April to around 47 nmol L^{-1} in September and December. When excluding subjects that had either been on sun holiday or used sun-bed, the 25(OH)D values were stable at around 40 nmol L^{-1}

throughout the whole blood sampling period except for a slightly elevated level in December, 2004 at 43.8 nmol L^{-1} , which was significantly higher than the other points, except the September 2005 mean.

Vitamin D status was inversely related to BMI for all blood sampling points, except for June when no significant relationship was found (*p* for trend = 0.10). Average levels of 25(OH)D close to 50 nmol L^{-1} were found among subjects with BMI < 25, cod-liver oil supplement users, and subjects consuming fish-liver more than once per season.

The number of subjects reporting use of cod-liver oil supplements was doubled during the study period (n = 6 to n = 12). However, the average intake of vitamin D for the total group remained the same at the start (October 2004) and the end (September 2005) of the study period, *i.e.* 8.6 µg d⁻¹.

UV-light and UV-hours during the actual time period for the study

The thin erratic line in Fig. 1 presents the estimated daily vitamin D-effective UV-hours from October 2004 to September 2005 (for skin type II). The thin erratic line is real, high accuracy, Brewer measurements of solar UV-radiation at Andenes and the solid, thick line is simulations of the same conditions except for ideal cloudless sky with a constant ozone layer of 350 Dobson Units (DU). The strong modulation of the thin line (*i.e.* measurements) is mainly a direct result of change in cloud conditions and the amount of atmospheric ozone during the measurement period. The sums of the measured number of UV-hours and ideal theoretical UV-hours were 1867 h and 2413 h, respectively. This means that the varying cloud conditions in combination with the change in atmospheric ozone content over the period reduced the

 Table 2
 Mean 25(OH)D levels during the time period by different characteristics

Variables	October, 2004 mean, (Std)	December, 2004 mean, (Std)	February, 2005 mean, (Std)	April, 2005 mean, (Std)	June, 2005 mean, (Std)	September, 2005 mean, (Std)
All	42.3 (13.3)	47.2 (17.6)	43.8 (16.2)	42.0 (15.6)	45.6 (18.7)	46.7 (13.7)
Subjects never using sun-bed or been on sun holiday $[n]^{\alpha}$	41.2 (12.5)	43.8 (13.7)	40.1 (14.6)	38.9 (14.8)	40.6 (14.6)	41.7 (13.2)
	[51]	[47]	[41]	[41]	[36]	[29]
Age						
-50 (n = 40)	43.4 (13.8)	45.5 (15.0)	42.4 (16.0)	40.4 (16.0)	44.8 (18.0)	46.9 (13.4)
>50 (n = 20)	40.0 (12.4)	50.6 (22.1)	46.4 (16.6)	45.2 (14.7)	47.2 (20.3)	45.9 (14.6)
Sex						
Female $(n = 44)$	41.8 (14.0)	47.7 (18.9)	43.8 (16.5)	42.4 (16.1)	46.4 (21.0)	45.4 (12.6)
Male $(n = 16)$	43.6 (11.5)	46.0 (13.9)	43.7 (15.7)	40.9 (14.5)	43.2 (9.0)	49.8 (16.2)
BMI						
<25 (n = 29)	44.9 (14.5)	52.1 (19.4)	49.3 (17.2)	47.8 (16.1)	50.0 (22.2)	48.8 (14.6)
25-30 (n = 22)	43.8 (10.9)	46.5 (13.3)	42.1 (13.1)	39.1 (13.5)	44.1 (13.9)	47.9 (11.9)
>30 (n = 9)	30.1 (7.7)	33.0 (13.8)	30.6 (11.7)	31.3 (11.7)	35.7 (13.0)	35.9 (10.6)
Test for tend	p < 0.001	p = 0.001	p = 0.001	p = 0.003	p = 0.10	p = 0.02
Cod-liver oil supplement						
Yes $(n = 12)$	43.3 (13.0)	51.1 (13.9)	47.2 (16.1)	46.6 (17.9)	48.9 (20.7)	48.5 (15.0)
No $(n = 48)$	42.0 (13.5)	46.2 (18.4)	42.9 (16.3)	40.9 (14.9)	44.8 (18.3)	46.1 (13.4)
Vitamin D intake						
$<7.5 \ \mu g \ d^{-1} \ (n=38)$	42.4 (14.5)	46.9 (19.8)	42.6 (16.2)	41.9 (16.0)	45.4 (20.2)	47.3 (14.2)
\geq 7.5 µg d ⁻¹ (<i>n</i> = 22)	42.1 (11.3)	47.8 (13.5)	45.9 (16.3)	42.3 (15.2)	46.0 (16.3)	45.4 (12.9)
Fish-liver more than one time p	ber season					
Yes $(n = 31)$	45.6 (12.0)	53.3 (17.6)	47.7 (14.7)	45.5 (14.1)	49.0 (17.1)	51.8 (12.2)
No $(n = 29)$	38.7 (13.9)	40.7 (15.5)	39.5 (16.8)	38.5 (16.5)	41.9 (20.0)	40.9 (13.1)

^a All subjects that have either been on sun holiday or used sun-bed prior to the blood sampling were excluded.

number of available UV-hours by almost 30% with respect to a typical ideal clear sky situation.

UV-hours and predicted mean 25(OH)D in blood

The estimated UV-hour variable was significantly associated with 25(OH)D levels in blood when adjusting for other sources of vitamin D like intake, sun holiday and sun-bed use. In Table 3, the relationship between UV-hours and difference in 25(OH)D levels relative to zero UV-hours are given. For the total group, a positive relationship between UV-hours and 25(OH)D was found at UV-hours \geq 3.5. However, for subjects with lower 25(OH)D levels *i.e.* at least one blood measurement with 25(OH)D < 37.5 nmol L⁻¹, the positive relationship was found at around UV-hours \geq 1.5, whereas for the group of subjects that had all their vitamin D values above 37.5 nmol L⁻¹, positive relationship was found at UV-hours \geq 4.0.

Discussion

The main finding in the present study was the absence of the clear seasonal variation pattern in the blood values of 25(OH)D (Table 2) and this contradicts some former findings. However, the estimated UV-hours variable based on time spent in daylight at Andenes, did predict vitamin D status when adjusted for vitamin D intake and use of sun-bed and sun holidays. Furthermore, we found that subjects below the suggested limit for moderate hypovitaminosis D (37.5 nmol L^{-1})¹⁹ responded more to UV-exposure than those above this limit (Table 3).

Large seasonal variations in 25(OH)D levels have been found in some studies. Guillemant *et al.*²⁰ found a difference between summer and winter levels to be around Δ 50 nmol L⁻¹ in French male adolescents. Vieth *et al.*²¹ found an average difference between summer and winter levels at Δ 30 nmol L⁻¹ in a study among Canadian women (n = 702) at 43° N. One would expect greater seasonal variation in 25(OH)D in populations living at higher latitudes compared to lower latitudes, due to larger differences in sun light and the long "vitamin D winter". However, former studies from Norway shows only a modest difference between summer and winter levels at around Δ 10 nmol L^{-1} 14,22 and less. 23 This contradicts claims that solar UV radiation is the main source of vitamin D.1

Seasonal variation in vitamin D levels in blood has been suggested as an explanation to seasonal variation in survival after a cancer diagnosis in ecological studies.^{22,24-26} However, our findings from this northern, coastal community support former findings of only a modest seasonal variation in 25(OH)D levels. A large variation in available UV-radiation (Fig. 1) was not accompanied by a pronounced seasonal variation in vitamin D status throughout the blood sampling period.

Relatively stable 25(OH)D levels throughout different seasons, were most likely caused by high intakes of vitamin D in general, and much clothes in a cold climate.¹⁷ Due to the low summer temperatures (generally 5–15 °C) in coastal northern Norway, it is likely that in general only face, neck, and hands were exposed. The observed elevated mean level in December, also when subjects who had been on sun holiday or used sun beds were excluded, strengthens the suggested contribution of diet to relatively high levels of 25(OH)D during winter.

The importance of diet to vitamin D status in the north has been found in other population based investigations.¹⁴ Increased use of fish-liver and cod-liver oil supplements were associated with higher vitamin D levels and were in agreement with studies conducted in rural coastal areas of Northern Norway where these items were shown to be important food sources to vitamin D.^{8,16} Both fishliver and cod-liver oil use are according to food traditions, mainly consumed during winter from December to March. Subjects living at high latitudes and who do not consume food items with vitamin D and with less UV-exposure, are at risk of acquiring unfavourable vitamin D levels.

Average intake of vitamin D was above recommendations at 7.5 µg d^{-1.27} Based on a review of available literature, the Norwegian expert working group of vitamin D status in the population, has suggested levels for optimal vitamin D status to be plasma 25(OH)D levels \geq 50 nmol L^{-1.28} Average levels close to this limit where found in the group consuming fish-liver more

Table 3 Differences in predicted mean 25(OH)D according to increases UV-hours d⁻¹

	Total		$25(OH)D > 37.5^{b}$		$25(OH)D < 37.5^{\circ}$	
UV-hours d ⁻¹	25(OH)D	95% CI	25(OH)D	95% CI	25(OH)D	95% CI
0.0	0.0	Ref	0.0	Ref	0.0	Ref
0.5	-1.1	-2.4, 0.2	-3.0	-5.4, -0.6	-0.1	-1.8, 1.7
1.0	-1.7	-3.9, 0.5	-4.8	-8.9, -0.8	-0.1	-2.9, 2.8
1.5	-1.9	-4.7, 0.9	-5.6	-10.7, -0.6	0.0	-3.3, 3.4
2.0	-1.7	-4.8, 1.4	-5.5	-11.2, 0.1	0.2	-3.5, 3.8
2.5	-1.2	-4.6, 2.2	-4.7	-10.7, 1.4	0.4	-3.5, 4.4
3.0	-0.4	-4.0, 3.2	-3.1	-9.6, 3.3	0.8	-3.5, 5.1
3.5	0.6	-3.3, 4.6	-1.1	-8.3, 6.1	1.3	-3.5, 6.2
4.0	1.8	-2.6, 6.2	1.3	-6.9, 9.6	2.0	-3.4, 7.4
4.5	3.1	-1.9, 8.0	4.0	-5.7, 13.7	2.8	-3.1, 8.7
5.0	4.4	-1.3, 10.1	6.8	-4.6, 18.2	3.7	-2.7, 10.2
5.5	5.7	-0.7, 12.2	9.6	-3.5, 22.8	4.9	-2.3, 12.0
6.0	7.0	-0.3, 14.2	12.3	-2.6, 27.2	6.2	-2.4, 14.8
<i>p</i> value	< 0.0001	,	< 0.0001	-	< 0.0001	<i>,</i>
Predicted mean values at UV-hours $= 0$	43.7	40.6, 46.9	54.4	47.8, 60.9	37.9	34.3, 41.6

^{*a*} Adjusted for sex, age, BMI, vitamin D intake, solarium and sun vacation. The 25(OH)D was fitted as cubic polynomial function of UV-hours. ^{*b*} All 25(OH)D values > 37.5. ^{*c*} The lowest 25(OH)D values < 37.5.

than once per season, cod-liver oil users and normally weighted, subjects (BMI < 25). The increased risk of low vitamin D status at high BMI is well established,²⁹ however the metabolic explanation for this remains uncertain.

Around half the study sample used sun-beds or travelled on sun-seeking holidays abroad during one year, and thus increased their sun induced vitamin D production beyond the available UVradiation corresponding to living at high latitude. This proportion was higher than what was found among 300 randomly selected northern Norwegian women¹⁴ (26% used sun-beds or travelled on sun holidays).

Use of solar UV dosimeters to measure individual UV radiation is possible, but is not realistic to use in large population based prospective studies due to high costs and practical considerations. Furthermore, we indeed tried out dosimeters at these latitudes (69° N) during the study presented in our previous paper.¹⁷ We found the dosimeters had some UV-A sensitivity which influenced the dosimeter readings long time before there were adequately intense vitamin D effective UV-B radiation present to cause any apparent synthesis of vitamin D. This is because the dosimeters measure erythemally weighted radiation, not vitamin D effective radiation. The former is more sensitive to UV-A than the latter, which is roughly speaking only sensitive to UV-B radiation. When the sun approaches the horizon, UV-B radiation disappears much more quickly than UV-A. This will of course introduce an error which is not systematic and cannot easily be accounted for accurately. This was evident in the numbers we got, and also confirmed by the manufacturer of the dosimeters (Viospor from Biosense). At mid and low latitudes this is not a problem because the vitamin D effective radiation detected with the dosimeter will be much stronger than the UV-A radiation detected by the dosimeter. Our study suggests that it is possible to use the "UV-hours" parameter based on questionnaire data in further large epidemiological investigations.

We have in this study shown that UV-hours can be a possible predictor for plasma 25(OH)D levels when adjusted for vitamin D intake, but it is important to note that one UV-hour is not a fully quantitative measure of the vitamin D effective UV-dose. For the same atmospheric conditions during a day, one UVhour at noon will be more effective than one UV-hour in the morning (or evening) as the UV-radiation is highly dependent on the solar zenith angle (SZA). Equally, one UV-hour at noon mid summer is more effective than one UV-hour at noon in the spring (or autumn). Also, knowing that the cloud conditions at Andenes is highly variable (Fig. 1), it is possible that one clear sky UV-hour in the morning (or evening) is more effective than one overcast UV-hour at noon. This suggests that a seasonal weighting function could have been applied to each subject's estimated UVhour in order to get a better quantitative predictor. However, it will not be possible, based on available data from this study, to get the full quantitative picture of the UV-hours since the only time information we have is "when it was daylight", and only six samples during one year (described in the methods section). But as a measure in large prospective epidemiological studies, it seems to be a simple and valuable parameter to use.

Our results of a basal plasma vitamin D level-dependent response to UV-radiation has been found in several other studies.^{17,30,31} The finding that 3.5 or more UV-hours was needed for a positive relationship between UV-hours and 25(OH)D-levels

in blood, indicates that at group level this order of magnitude in UV-hours was needed to obtain an actual raise in plasma vitamin D level. Our results show that dietary traditions patterns with a high intake of vitamin D rich food during "the vitamin D winter", when UV-hours were zero, contributed to the maximum vitamin D levels. UV-hours > 3.5 were required at group level to compensate for this high winter intake and prevent decline in 25(OH)D levels.

The very modest effect of UV exposure is consistent with the findings in Edvardsen *et al.*,¹⁷ which speculated that the small effect of UV exposure could be attributed to limited facial skin exposure at freezing temperatures.

In summary, the impact of UV-radiation on vitamin D production in skin is dependent on several factors such as individual characteristics like skin type, clothing, use of sun screen, time spent in daylight, BMI, age in addition to external factors like season (zenith angle), clouds, ozone, aerosols, surface reflection.¹⁷

Conclusions

Our results suggest that for this coastal population living at high latitude, vitamin D status was determined by the sum of diet and UV-radiation (both when residing at Andenes, but also when using artificial UV-sources and travelling on sun holidays), but that dietary contribution to vitamin levels in blood neutralises the contribution of seasonal variation in sun exposure. Our work indicates that the vitamin D efficient "UV-hour" may be a useful and valid parameter for large prospective epidemiological investigations on vitamin D exposure and health outcomes.

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