Daily Duration of Vitamin D Synthesis in Human Skin with Relation to Latitude, Total Ozone, Altitude, Ground Cover, Aerosols and Cloud Thickness.<sup>‡</sup>

Ola Engelsen<sup>1\*</sup>, Magritt Brustad<sup>2</sup>, Lage Aksnes<sup>3</sup> and Eiliv Lund<sup>2</sup>

<sup>1</sup> Norwegian Institute for Air Research (NILU), Norway.

<sup>2</sup> Institute of Community Medicine, University of Tromsø, Norway.

<sup>3</sup> Department of Clinical Medicine, Section of Peadiatrics, University of Bergen.

NILU, The Polar Environmental Centre, H. Johansens gate 14, N-9296 Tromsø, Norway

> Phone: +47 77750375 Fax: +47 77750376 E-mail: ola.engelsen@nilu.no

**Abbreviations:** BED, biologically effective dose; DU, Dobson unit (1 DU = 1matm-cm, equivalent to the thickness of 0.01 mm of pure ozone at standard conditions of temperature [273.15K] and pressure [1013.25 Pa]); FWHM, full width half maximum of a spectrometer's spectral response function; HPLC, high performance liquid chromatography; UV-B, ultraviolet radiation of wavelengths in the range 280-315 nanometers; 25(OH)D, blood serum circulating 25-hydroxyvitamin D; 7-DHC, 7-dehydrocholesterol = provitamin D.

<sup>&</sup>lt;sup>‡</sup> Published in the journal website (www.ASPjournal.com) on xx-xxx-xxx.

#### ABSTRACT

Vitamin D production in human skin occurs only when incident UV radiation exceeds a certain threshold. From simulations of UV irradiances worldwide and throughout the year, we have studied the dependency of the extent and duration of dermal vitamin D production in terms of latitude, time, total ozone, clouds, aerosols, surface reflectivity and altitude. For clear atmospheric conditions, no dermal vitamin D production occurs at 51 degrees latitude and higher during some periods of the year. At 70 degrees latitude, vitamin D synthesis can be absent for five months. Clouds, aerosols and thick ozone events reduce the duration of vitamin D synthesis considerably, and can suppress vitamin D synthesis completely even at the equator. A web page allowing the computation of the duration of dermal vitamin D production worldwide throughout the year, for various atmospheric and surface conditions, is available on the Internet at <u>http://zardoz.nilu.no/~olaeng/fastrt/VitD.html</u> and

http://zardoz.nilu.no/~olaeng/fastrt/VitD-ez.html. Its methodology is outlined here.

#### **INTRODUCTION**

Vitamin D is essential for natural bone metabolism and for the calcium and phosphorus homeostasis. In addition, a protective effect of vitamin D on cancer in colon, prostate, and breast has been suggested based on both epidemiological (1-4) and experimental studies (5). Vitamin D is obtained either from the skin when exposed to ultraviolet radiation or through a few dietary sources, mainly fatty fish, cod-liver oil, and fortified margarine or butter. A dramatic effect of seasonal and latitudinal changes of solar UV radiation on vitamin D synthesis was revealed by Webb et al. (6). They found that below a certain threshold of UV radiation, corresponding to cloudless conditions in Boston, USA  $(42^0 \text{ N})$  in mid February near solar noon, no photoconversion of provitamin D to previtamin D was detected. Models (7) and experiments (8-9) describing photoconversion of provitamin D to previtamin D exist, but are not well validated or associated with critically low vitamin D weighted irradiances at which vitamin D production in human skin is initiated under natural daylight conditions. The period when there is not sufficient UV radiation outdoors for a person to produce vitamin D is termed the "vitamin D winter". The potential health risk due to the presence of "vitamin D winter" is real: moderate hypovitaminosis D was found in one quarter of the North Norwegian population  $(25(OH)D < 37.5 \text{ nmol } l^{-1})$ . Two thirds had blood plasma concentrations below the recommended level (25(OH)D  $\leq$  50 nmol l<sup>-1</sup>) (10).

From simulations of UV irradiances worldwide and throughout the year, we estimated the daily time period when UV radiation exceeds the required threshold (6)(10). The duration of vitamin D production depends not only on latitude and time, but also on several other

parameters, most importantly total ozone, clouds, aerosols, surface reflectivity and altitude. To our knowledge we are first to investigate dermal synthesis of vitamin D in terms of all these other parameters that describe the major optical properties of the terrestrial surface and atmosphere in the UV spectral region.

This paper presents a novel method to estimate the maximum daily duration of vitamin D synthesis in human skin at any location worldwide throughout the year. The estimates are available through a web browser, or from a computer script freely available from the author. The manuscript constitutes a reevaluation of the extent of the vitamin D winter, i.e. the period when no dermal vitamin D synthesis exists. Its findings may have implications for future general public advice on nutrition and UV exposure.

## MATERIALS AND METHODS

Based on (6), we established a biologically effective UV dose rate (BED) for photoconversion of 7-dehydrocholesterol (7-DHC, (Aldrich Chemical Co., Milwaukee, WI.) to previtamin D in skin (10). Webb et al. (6) found no detectable photoconversion of 7-DHC to previtamin D for mid-February and only a small production of previtamin D at mid-March in Boston. For mid-February within a half hour of the solar noon at the maximum intensity of the day, they measured surface irradiances of 0.024, 1.0 and 10 mW m<sup>-2</sup> nm<sup>-1</sup> with an Optronics 742 spectroradiometer (Optronic Laboratories Inc., Orlando, FL.) at wavelengths of 300, 306 and 316 nm, respectively. The BED was established by adding the measured surface irradiances weighted by the relative efficiencies for converting 7-DHC to previtamin D. The weighting

factors are 0.92, 0.45 and 0 for 300, 306 and 316 nm, respectively (6). Below the threshold: BED<sub>threshold</sub>=0.024\*0.92+1.0\*0.45=0.472, we assumed that no photoconversion to previtamin D took place. We applied the fast, yet accurate UV simulation tool FastRT (11) to simulate surface irradiances at 300 and 306 nm as would be measured by an Optronics 742 spectroradiometer similar to the one used by (6). For each day throughout the year we simulated the amount of time the BED exceeded the UV radiation threshold for vitamin D production described above for the whole globe for various atmospheric and surface conditions. We assumed a very clear "base case" atmosphere over a non-reflecting surface with an ozone layer thickness fixed at a typical level (300 Dobson Units) and a rural aerosol optical depth given by  $\tau = \beta^* \lambda^{-\alpha}$  where the Ångström coefficients  $\alpha$  and  $\beta$  were set to 1.3 and 0.02, respectively, and the wavelengths ( $\lambda$ ) are in micrometers. The Ångström coefficient  $\beta$ was related to visibility  $R_m/km$  using the parameterization of (12), i.e.,  $\beta = 0.55^{1.3} (3.912/km)$  $R_m/km/-0.01162$  [0.02472\*( $R_m/km/-5$ )+1.132]. For cloudy, overcast conditions we assumed homogeneous alto-stratus type clouds (13) of variable densities at 2-7 km above ground. In case of snow-covered ground, we assumed an albedo of 0.9, which pertains to fresh new snow. Otherwise, for all simulations we assumed a US standard atmosphere (14).

#### RESULTS

In clear atmospheric conditions, a vitamin D winter occurs at 51 degrees latitude and higher (figure 1, table 1). At 70 degrees latitude, dermal vitamin D synthesis can be absent from 5 October through 10 March. The main parameters influencing UV radiation (ozone, aerosols, clouds, albedo and altitude) roughly speaking shifts the extent of the dark field, i.e. the vitamin D

winter, in figure 1 up or down while the essential shape is preserved.

Ozone strongly absorbs UV-B radiation. Extremely high/low ozone levels (500 DU / 100 DU) can decrease / increase the latitude of vitamin D winter incidence by about 10 degrees, and extend / shorten its period of duration by about two months.

Atmospheric aerosols attenuate surface UV-B radiation. On the other hand, reflection of UV radiation from the Earth's surface enhances UV-B radiation. Snow cover or a turbid atmosphere (5 km visibility, i.e. Ångström  $\beta = 0.4$ ) can change the lower latitude of occurrence for the vitamin D winter by a couple of degrees and alter the duration of dermal vitamin D synthesis by about 1-2 weeks. Increasing the surface elevation to 3000 m has about the same effect as covering the ground with snow at sea level.

Clouds generally attenuate UV-B radiation. Thick clouds can reduce surface UV-B radiation to as much as 1% of clear sky levels. Even scattered clouds on the horizon may lower the UV radiation significantly. Dermal vitamin D synthesis can halt completely at the equator for a very thick overcast cloud with a liquid water column of 3600 g m<sup>-2</sup> or higher (not shown in table 1). At 70 degrees latitude the vitamin D production in skin can disappear even at mid-summer for a medium thick cloud cover with a liquid water column of 2000 g m<sup>-2</sup>.

#### DISCUSSION

### Uncertainties

As mentioned before, we used a threshold pertaining to cloudless conditions in Boston, USA  $(42^0 \text{ N})$  within a half hour of the solar noon for the closest cloudless day to  $15^{\text{th}}$  February 1986,

for which spectral UV irradiances are available (6). Those measured irradiances are somewhat lower than those we would normally obtain for corresponding cloudless sky simulations at that time and location. Using the FastRT simulation tool, we could only reproduce the measurements in (6) at mid February 1986 by assuming an extremely high ozone column (~600 DU) and a very turbid atmosphere (visibility of ~5 km). According to the Total Ozone Mapping Spectrometer (TOMS) satellite instrument, Boston had ozone columns ranging from 280 to 450 DU in February 1986. These ozone values would not attenuate cloudless sky UV radiation as much as observed in (6) except during extreme, low visibility events (e.g. volcanic eruptions or haze). According to our calculations, the period of vitamin D winter seems thus somewhat overestimated in (6). It is important to note, however, that completely cloudless days are rare. There are almost always some scattered clouds in the sky dome, even on days that most people would call cloudless. Since most of UV radiation is diffuse, scattered clouds, even those near the horizon and not occluding the sun, influence the surface irradiance. Likewise, nearby building structures and other surroundings can block and thus abate radiation. Unfortunately there are no relevant sky dome images available for Boston in February 1986, so it is not possible to verify if conditions were truly cloudless.

The FastRT UV simulation tool is by no means perfect. The program is designed to have uncertainties better than current high quality UV measurements when all input parameters are known (11).

Another source of uncertainty is the lack of a confirmed spectral response function for the Optronics 742 instrument used in Boston in 1986. We have assumed the spectral response function measured for another Optronics 742 instrument currently located in Reading, England. Assuming instead a triangular spectral response function with a full width half maximum of 1.5

nm, i.e. the nominal FWHM of the Optronics 742 instrument, reduces the threshold solar zenith angle for a clear atmosphere by 0.7° (compare to table 1, column 1). The uncertainty caused by the missing spectral response functions is somewhat reduced by the construction of the BED. This problem would have been reduced further if other irradiances from the vitamin D effective spectral range were available. Furthermore, this would have provided a better BED and a more accurate threshold for vitamin D synthesis.

Measurement uncertainties for UV radiation always exist, and may have influenced the BED threshold. Even high quality UV-B measurements have uncertainties  $(\pm 2\sigma)$  of about 13% (300 nm wavelength at 60° solar zenith angle) (15). The spectral UV measurements made in Boston in 1986 may not have been subject to the same advanced quality controls as one would expect today and consequently may have even higher uncertainties. In order to evaluate the measurements forming the basis for the BED threshold further, we simulated irradiances corresponding to those measured by the Optronics 742 instrument of (6) throughout 1986 in Boston for cloudless atmospheres but assuming a global average visibility of 25 km and taking ozone columns from the Total Ozone Mapping Spectrometer (TOMS). The ratios of the measured irradiances with respect to simulations revealed no systematic bias neither for the 300 nm channel  $(0.70 \pm 2.48)$  nor for the 306 nm band  $(0.57 \pm 1.21)$ .

In the event that the measured irradiances were incorrect and our cloudless sky simulations for mid-February represent the real radiation threshold, duration of vitamin synthesis in human skin would be far less extensive (table 2, fig. 2), and more in line with the vitamin D winter extent found for Boston and Edmonton (52 °N, vitamin D winter about two months longer than Boston) in (6). Nonetheless, the vitamin D solutions at the centre of the experiments in (6) give the best indication of whether any previtamin D was formed at that time and those conditions, and not

whatever the UV measurements or the FastRT model predict.

Note that the measured UV radiation thresholds determined by (6) were determined on the basis of in vitro samples. The effect of clothes and skin were ignored. The spectral effectiveness of conversion from 7-DHC to previtamin D in human skin and in vitro solutions may also deviate somewhat. Furthermore, the radiation threshold pertained to the last monthly measurement where no photoconversion to previtamin D was detected in spring. The initiation of photoproduction of vitamin D actually took place sometime during the following month. In addition, the figures and tables in this paper present results for very clear, pristine atmospheres, which rarely occur. In summary, the real UV radiation threshold for dermal vitamin D synthesis may be expected to be higher, but as we have selected a conservative value in this manuscript. The real vitamin D winter is thus likely to be longer than shown here. Tests on excised human skin samples (6), and with a more sensitive HPLC system to detect previtamin D (A. Webb, personal communication), indicated an extension and reduction respectively of a couple of weeks for the vitamin D winter in Boston.

### **Public health implications**

Vitamin D status is determined by the sum of exposure to UV radiation and dietary intake. When considering vitamin D status in a population, lifestyle, culture, and behavioral parameters need to be addressed. Studies have found intake of vitamin D to increase with increased latitude (16) and that traditional diets, with increased intake of vitamin D rich food items during winter, can compensate for lack of sun induced vitamin D (17). The total contribution of UV radiation on vitamin D levels in blood is affected both by clothing and sun-exposure behavior. An illustrative

example is that high prevalence of vitamin D deficiency has been found among women and neonates in Saudi Arabia due to clothing traditions (18).

To further investigate the role of vitamin D in health and diseases in humans, methodological approaches need to be improved where both the quantitative and qualitative aspects of UV radiation are included in addition to actual skin exposure and diet in populations living in different geographical and cultural settings. Most epidemiological studies on vitamin D and health lack information either on UV exposure or dietary intake data. The data obtained by the method described in this present paper could, in combination with questionnaire data on diet and sun-exposure behavior, contribute to a methodological improvement for prospective epidemiological investigations into vitamin D and different health outcomes.

### CONCLUSION

We have described a method to estimate the duration of vitamin D synthesis in terms of time and location as well as surface- and atmospheric conditions. The quality and availability of information on the relevant surface and atmospheric parameters such as total ozone, clouds, aerosols and snow cover has now greatly improved from recent advances in computer science, meteorological models and satellite data.

Our studies show that dermal vitamin D production cannot be sustained throughout the year for latitudes of about 50 degrees and higher. In the Arctic vitamin D production can be absent for several months. Our conclusions are somewhat less dramatic than previous studies. The vitamin D winter seems not as extensive as in (6). Conversely, clouds, aerosols and thick ozone events reduce the duration of vitamin D synthesis considerably, and can force a "vitamin D winter" even at the equator.

We have reexamined the irradiance measurements presented in (6), and found that they may not pertain to perfectly cloudless conditions as stated. If the measurements (6) were incorrect, and the in vitro samples were exposed to sunlight under idealized cloudless conditions as simulated by us, the vitamin D winter is indeed very extensive (table 2, fig. 2). The real vitamin D winter period probably lies somewhere between those indicated in tables 1 and 2 (A. Webb, personal communication).

*Acknowledgments*—We thank Ann Webb for her insightful review comments, and for providing details about her experiments in Boston and her Optronics 742 spectroradiometer. This work was funded by the Norwegian Research Council (COZUV project) and the Institute for Community Medicine at the University of Tromsø.

#### REFERENCES

- Garland, C. F., G. W. Comstock, F. C. Garland, K. J. Helsing, E. K. Shaw and E. D. Gorham (1989) Serum 25-hydroxyvitamin D and colon cancer: eight-year prospective study. *Lancet* 2, 1176-1178.
- 2. Grant, W.B. (2002a) An ecologic study of dietary and solar ultraviolet-B links to breast carcinoma mortality rates. *Cancer* **94**, 272-281.
- 3. Grant, W.B. (2002b) An estimate of premature cancer mortality in the U.S. due to inadequate doses of solar ultraviolet-B radiation. *Cancer* **94**, 1867-1875.
- John, E.M., G. G. Schwartz, D. M. Dreon and J. Koo (1999) Vitamin D and breast cancer risk: the NHANES I Epidemiologic follow-up study, 1971-1975 to 1992. National Health and Nutrition Examination Survey. *Cancer Epidemiol.Biomarkers Prev.* 8, 399-406.
- Banwell, C. M., R. Singh, P. M. Stewart, Uskokovic M. R. and M. J. Campbell (2003) Antiproliferative signalling by 1,25(OH)2D3 in prostate and breast cancer is suppressed by a mechanism involving histone deacetylation. *Recent Results Cancer Res.* 164, 83-98.
- Webb, A. R., L. Kline and M. F. Holick (1988) Influence of season and latitude on the cutaneous synthesis of vitamin D<sub>3</sub>: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D<sub>3</sub> synthesis in human skin. *J. Clin. Endocrinol. Metab.* 67, 373-378.
- 7. Galkin, O. N. and I. P. Terenetskaya (1999) Vitamin D' biodosimeter: basic characteristics and potential applications. *J. Photochem. Photobiol. B: Biol.* **53**, 12-19.

- Obi-Tabot, E. T., X. Q. Tian, T. C. Chen and M. F. Holick (2000) A human skin equivalent model that mimics the photoproduction of vitamin D<sub>3</sub> in human skin. *In vitro Cell. Dev. Biol. –Animal.* 36, 201-204.
- Matsuoka, L. Y. J. Wortsman, J. G. Haddad and B. W. Hollis (1989) In vivo threshold for cutaneous synthesis of vitamin D<sub>3</sub>. *J. Lab. Clin. Med.* 114, 301-305.
- Brustad, M., E. Alsaker, O. Engelsen, L. Aksnes, and E. Lund (2004a) Vitamin D status in middle-aged women at 65-71 °N in relation to dietary intake and exposure to ultraviolet radiation. *Publ. Health Nutr.* 7, 327-335.
- Engelsen, O. and A. Kylling (2005) A fast simulation tool for ultraviolet radiation at the Earth's surface. Accepted for publication in the Journal of Optical Engineering. (http://nadir.nilu.no/~olaeng/fastrt/fastrt.html)
- 12. Iqbal, M. (1983) An Introduction to Solar Radiation, Academic, San Diego, CA.
- Shettle, E. P. (1989) Models of aerosols, clouds, and precipitation for atmospheric propagation studies. *AGARD Conf. Proc.* 454, 15-32.14. Anderson, G. P., S. A. Clough, F. X. Kneizys, J. H. Chetwynd and E. P. Shettle (1986) AFGL atmospheric constituent profiles (0-120 km). *Tech. Rep. AFGL-TR-86-0110*, Air Force Geophys. Lab., Hanscom AFB, Mass.
- 15. Bernhard, G. and G. Seckmeyer (1999) Uncertainty of measurements of spectral solar UV irradiance. *J. Geophys. Res.* **104**, 14321-14345.
- Johansson, L. and K. Solvoll (1999). Norkost 1997 National dietary survey among men and women at age 16-79 years. Oslo. Norwegian State Council for Nutrition and Physical Activity (in Norwegian).

- Brustad, M., T. Sandanger, L. Aksnes, and E. Lund (2004b). Vitamin D status in a rural population of northern Norway with high fish liver consumption. *Publ. Health Nutr.* 7, 783-790.
- Holick, M. F. (1995) Environmental factors that influence the cutaneous production of vitamin D. Am. J Clin. Nutr. 61(suppl) 638S-645S.

### **TABLE LEGENDS**

**Table 1.** Duration of vitamin D winter. The rightmost column is the threshold of perpetual

 vitamin D winter.

**Table 2.** Same as Table 1 but using a simulated weekly mean BED radiation threshold centered at 12th February 1986 (BED<sub>threshold</sub> = 3.46) for cloudless sky conditions at solar noon in Boston with a visibility of 25 km and total ozone obtained from the TOMS satellite instrument. The weekly mean ozone column at this time was 388 DU (for reference only). The weekly mean BED was computed in order to reduce the effect of inexact dates of exposure for the 7-DHC solutions in (6).

### **FIGURE LEGENDS**

**Figure 1**. Daily period (in hours) of vitamin D production in terms of time and latitude for a clear atmosphere and no surface reflection and for a typical level of total ozone (300 DU). The austral vitamin D winter is identical to the vitamin D winter at northern latitudes.

**Figure 2.** Same as figure 1, but using the higher simulated radiation threshold as described in the table 2 legend (BED<sub>threshold</sub> = 3.46).

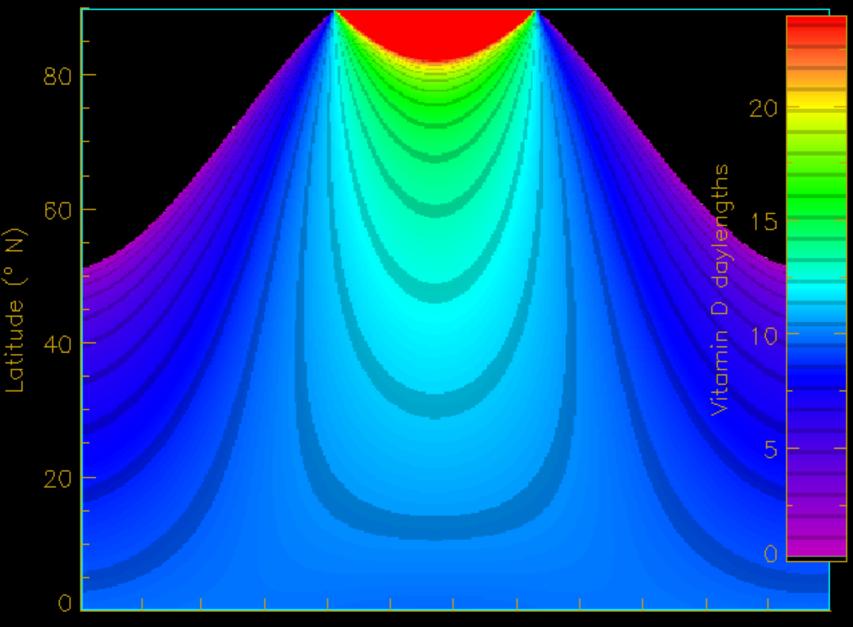
# Tables

| Vitamin D winter      | Minimum       | Period at 70 °N   | Cloud liquid water         |
|-----------------------|---------------|-------------------|----------------------------|
|                       | latitude [°N] |                   | column threshold at        |
|                       | (solar zenith |                   | 70 °N (g m <sup>-2</sup> ) |
|                       | angle [°]) of |                   |                            |
|                       | incidence     |                   |                            |
| Clear atmosphere      | 51 (74.3)     | 5 Oct. – 10 Mar.  | 2000                       |
| Low ozone (100 DU)    | 63 (85.8)     | 6 Nov. – 6 Feb.   | >4000                      |
| High ozone (500 DU)   | 42 (64.7)     | 10 Sep. – 4 Apr.  | 700                        |
| Low visibility (5 km) | 49 (72.0)     | 29 Sep. – 16 Mar. | 2000                       |
| High altitude (3 km)  | 52 (75.0)     | 7 Oct. – 8 Mar.   | 2000                       |
| Snow covered ground   | 53 (76.0)     | 9 Oct. – 6 Mar.   | >4000                      |

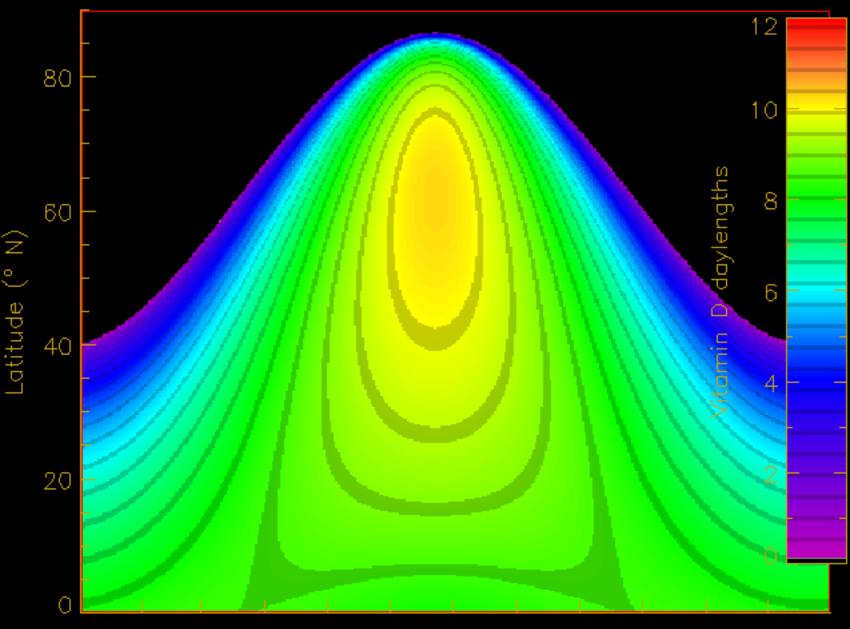
# Table 1.

| Vitamin D winter      | Minimum<br>latitude [°N]<br>(solar zenith<br>angle [°]) of<br>incidence | Period at 70 °N   | Cloud liquid water<br>column threshold at<br>70 °N (g m <sup>-2</sup> ) |
|-----------------------|---|-------------------|---|
| Clear atmosphere      | 40 (63.3)   | 6 Sep. – 8 Apr.   | 400   |
| Low ozone (100 DU)    | 55 (78.5)   | 16 Oct. – 28 Feb. | 1900  |
| High ozone (500 DU)   | 27 (49.8)   | 22 Jul. – 23 May  | <100  |
| Low visibility (5 km) | 36 (58.9)   | 25 Aug. – 19 Apr. | 400   |
| High altitude (3 km)  | 42 (64.7)   | 10 Sep. – 4 Apr.  | 400   |
| Snow covered ground   | 43 (66.1)   | 13 Sep. – 31 Mar. | 1200  |

# Table 2.



Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec



Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec