CHAPTER

# 56

# Determinants of vitamin D levels from sun exposure: a global perspective

*William B. Grant*[1], *Harjit P. Bhattoa*[2] *and Pawel Pludowski*[3]

[1]Sunlight, Nutrition, and Health Research Center, San Francisco, CA, United States [2]University of Debrecen, Debrecen, Hungary [3]The Children's Memorial Health Institute, Warsaw, Poland

**OBJECTIVES**

- Understand the importance of sun exposure in determining 25-hydroxyvitamin D (25(OH)D) concentrations.
- Understand the seasonal nature of serum 25(OH) D concentrations.
- Learn about atmospheric effects on vitamin D production.
- Learn about endogenous effects on vitamin D production.
- Learn about behavioral effects on vitamin D production.

## 1. Introduction

Globally, serum 25-hydroxyvitamin D (25(OH)D) concentrations average about 50–55 nmol/L—nearly independent of latitude [1–6]. Although that similarity may seem paradoxical, the primary reason is that skin pigmentation varies inversely with latitude in general and that summer daylight times increase with latitude. The variation in pigmentation serves to balance production of vitamin D with protection against damage from free radicals and folate destruction by UV radiation [7]. Many observational studies report that adverse health outcomes are more likely as 25(OH)D concentrations decrease [8–11]. The Endocrine Society defines vitamin D deficiency as a 25(OH)D concentration below 50 nmol/L; vitamin D insufficiency is a 25(OH)D concentration of between 50 and 75 nmol/L [12]. Thus, about half the world's population is vitamin D deficient.

An estimate of the natural 25(OH)D concentration can be obtained from indigenous populations living in east Africa. A study examined two traditionally living populations there, one the pastoral Maasai and the other Hadzabe hunter-gatherers. Subjects had skin type VI, wear a moderate degree of clothing, and spend most of the day outdoors—but they avoid direct exposure to sunlight when possible. They had mean 25(OH)D concentrations of 115 nmol/L [13]. A study of pregnant women from five east African ethnic groups who consumed different amounts of fish found that solar ultraviolet B (UVB) exposure determined 25(OH)D concentrations and that the mean concentration was 115 nmol/L [14]. Those values correspond to an estimated daily production of vitamin D of 2000 IU [15]. On the other hand, a study in South Australia found that UV exposure led to a mean maximum 25(OH)D concentration of 89 nmol/L and was associated with an estimated mean weekly solar erythemal UV exposure of 1230 $mJ/cm^2$ [16]. Solar UV radiation at wavelengths 290–330 nm can destroy some vitamin D metabolites [17]. That effect limits the maximum 25(OH)D concentration resulting from solar UV exposure so that one cannot overdose on vitamin D from solar UVB exposure, as seen in the results from east Africa.

## 2. Vitamin D production from solar UVB exposure

An excellent systematic review and metaanalysis reported the impact of several factors on cutaneous vitamin D synthesis from UVB exposure [18]. One factor

*Feldman and Pike's Vitamin D, Fifth Edition*
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is the part of the body exposed. The hands and face, which account for 3% of total body surface area (BSA), are eight times more effective in synthesizing vitamin D than the whole-body surface area. Another factor is that the increase in serum 25(OH)D concentration depends on baseline concentration. When the baseline is 21 nmol/L, the increase in terms of Δ25(OH)D/SED/%BSA is 0.093 where SED is standard erythemal dose, dropping to 0.004 for baseline 25(OH)D = 72 nmol/L.

Another review reported the change in 25(OH)D concentration with respect to simulated solar radiation [19]. It found that the change was linear in a logarithmic fashion: 10 standard vitamin D doses (SDDs), equivalent to about 12 SED, increased 25(OH)D by about 20 nmol/L, 100 SDDs by about 32 nmol/L, 500 SDDs by 46 nmol/L, and 1000 SDDs by about 52 nmol/L. A study in India found that men with a mean age of 48 ± 6 years with 27% deficient and 41% insufficient 25(OH)D required greater than 1 h/day casual midday sunlight exposure to maintain 25(OH)D above 50 nmol/L and greater than 2 h/day for above 75 nmol/L [20].

## 3. Factors affecting 25-hydroxyvitamin D concentrations

Factors that affect 25(OH)D concentrations related to sun exposure fall under three broad categories [1]: atmospheric and environmental determinants [2]; endogenous characteristics such as genetics and obesity; and [3] behavioral determinants. A recent paper reviewed the determinants of trends in vitamin D status [6]. Factors associated with decline include reduced sun exposure, increasing BMI, reduced consumption of vitamin D-containing foods, and the effects of urbanization, air pollution, less outdoor occupation, and poor socioeconomic status. Factors associated with increase include sun exposure on holidays, food fortification, increases in vitamin D supplementation, and increased physical activity.

### 3.1 Seasonal changes in 25-hydroxyvitamin D

Solar UVB exposure is the major source of vitamin D for most people [21]. Table 56.1 shows winter and summer mean 25(OH)D concentrations for a representative sample of countries. The criteria for inclusion included that the 25(OH)D data were obtained after 2000, that they were for adults with data for elderly preferred, that the assays used were considered relatively accurate, and that a sufficient number of participants were included. The data from the various countries have some differences such as the age ranges of the participants, the selection of participants, and the periods considered summer and winter. Nonetheless, the data are very useful.

**TABLE 56.1** Seasonal changes in 25-hydroxyvitamin D (25(OH)D) concentrations.

| | | | 25(OH)D concentration (nmol/L) in: | | |
|---|---|---|---|---|---|
| **Country, latitude** | **Population** | **Period** | **Winter** | **Summer** | **References** |
| Australia<br>19 to 43 degrees S | ~250 in each of 4 cities, 18–75 years | 2009–10 | 51 ± 23 | 74 ± 24 | [22] |
| Australia 35 degrees S | 3523 | | M 67<br>F 63 | M 84<br>F 71 | [23] |
| China 23 degrees N | M & F, <18 to>80 years | 2018–19 | 73 ± 25 | 88 ±25 | [24] |
| Denmark 56 degrees N | F, 70–75 years | 2002–03 | 49 | 67 | [25] |
| Estonia 59 degrees N | 367 M, F, mean 49 ± 12 years | 2006 | 44 ± 15 | 59 ± 18 | [26] |
| Germany 48.4 degrees N | 1418 M + F, >65 years | 2009–10 | 39 ± 3 | 63 ± 4 | [27] |
| Great Britain 52 degrees N | M, 45 years<br>F, 45 years | 2002–04 | 34<br>36 | 74<br>71 | [28] |
| Greece 39 degrees N | 970 M & F | 2010–12 | 48 ± 19 | 52 ± 20 | [29] |
| Iceland 64 degrees N | | | 56 | 74 | [30] |
| India<br>29 degrees N | 26,339 assays | 2008–2017 | 52 ± 58 | 58 ± 56 | [31] |
| Iran 38 degrees N | 541 M & F, 5–60 years | 2015 | 46 ± 24 | 55 ± 37 | [32] |

**TABLE 56.1** Seasonal changes in 25-hydroxyvitamin D (25(OH)D) concentrations.—cont'd

| Country, latitude | Population | Period | 25(OH)D concentration (nmol/L) in: | | References |
|---|---|---|---|---|---|
| | | | Winter | Summer | |
| Ireland 53 degrees N | 1132 adults | 2008–10 | 42 | 72 | [33] |
| Italy, 45 degrees N | 2558 M, 8592 F, med age 62 years | 2014 | 50 (IQR, 30–70) | 68 (IQR, 47–89) | [34] |
| Japan 33 degrees N | 312 M, 217 F, 21–67 years | 2006 | 43 (Nov) | 68 (July) | [35] |
| Japan 33 & 43 degrees N | 107 M & F, 20–60 years | 2018 | 37 | 53 | [36] |
| Mongolia 48 degrees N | 320 M, F, 20–58 years | 2011, 2013 | 19 ± 8 | 56 ± 23 | [37] |
| Netherlands 52 degrees N | 201 M, 338 F | Ca 2010? | 48 | 82 | [38] |
| New Zealand 41 degrees S | 2946, 18+ years | 1996–97 | 40 | 75 | [39] |
| Norway 60 degrees N | | 1999–2005 | 51 | 67 | [40] |
| Portugal 41 degrees N | 18–67 years | 2015, 2016 | 42 ± 17 | 68 ± 22 | [41] |
| Slovenia 46 degrees N | 280 M&F | 2017–18 | 35 | 77 | [42] |
| Sweden 60 degrees N | M & F, 210 in summer, 58 in winter | 2010–11 | 55 ± 18 | 66 ± 18 | [43] |
| Switzerland 47 degrees N | 1308 M + F | 2010–11 | 42 ± 3 | 72 ± 3 | [44] |
| Switzerland 46 degrees N | M&F, BMI = 25 | 2003–08 | 35 | 66 | [45] |
| Turkey 40 degrees N | F, 21–52 years, office workers | 2008 | 35 | 71 | [46] |
| United Arab Emirates 24 degrees N | M & F, university students | 2009–10 | 31 | 21 | [47] |
| United States 26–48 degrees N | Adults | 2007–09 | 54 | 71 | [48] |

Fig. 56.1 also raises the question of what determines serum 25(OH)D concentrations in winter in the absence of solar UVB. Two recent articles made the case that the primary mechanism for maintaining 25(OH)D concentrations in the absence of solar UVB is the storage of 25(OH)D in muscle cells [49,50]. They proposed that parathyroid hormone controlled the recirculation process. The linear regressions in Fig. 56.1 can also be used to estimate the relative contributions of oral vitamin D intake and solar UVB in winter. Let us assume that all of the oral intake of vitamin D is from food. Animal sources are the only source of vitamin D, ignoring that from fungi, with meat and fish accounting for the largest share [51]. Data from the Food and Agriculture Organization can be used to estimate the amount of animal products in the national diets (https://www.fao.org/faostat/en/#data, accessed June 15, 2022). Fig. 56.1 is a plot of summer and winter serum 25(OH)D concentrations for European countries using the data from Table 56.1. What is interesting is that summertime mean concentrations for adults are near 68 nmol/L for all latitudes, while wintertime concentrations have a U-shaped relationship with latitude. The summertime effect can probably be explained as due to a combination of decreasing amount of skin pigmentation [7] and increased length of daily sunlight in summer with increasing latitude. The wintertime effect at high latitudes can be explained by the higher consumption of animal products that serve as sources of vitamin D at higher latitudes [51–53] as well as higher intake of vitamin D supplements [30] and food fortification such as in Finland [54]. The slight increase in 25*+(OH)D at lower latitudes can be explained by a longer duration of producing vitamin D from solar UVB exposure (see Ref. [55]). The finding regarding winter concentrations suggests that more countries should consider vitamin D fortification of food to raise wintertime 25(OH)D concentrations [56–58].

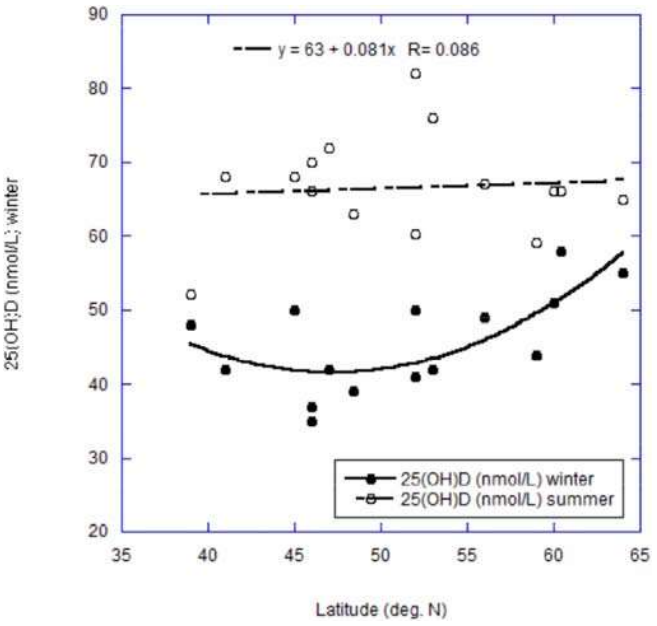


**FIGURE 56.1 Latitudinal dependence of summertime and wintertime 25(OH)D concentrations for adults in European countries using data in Table 56.1.** The equation for the winter regression fit is 25(OH)D (nmol/L) = (170−5.4 × Latitude + 0.057 × Latitude$^2$ (nmol/L), r = 0.72.

## 3.2 Geographic location and ultraviolet B doses: seasonal variations

The most important factor affecting vitamin D production from solar UVB exposure is the solar zenith angle (SZA). The spectral region for solar UVB reaching the earth's surface is 290−315 nm. Given the short wavelength, UVB is strongly scattered by atmospheric molecules. According to Rayleigh's model, scattering varies as the inverse fourth power of wavelength. In addition, stratospheric ozone affects UVB transmission. Thus, the longer the atmospheric path, the less UVB reaches earth's surface. A graph shows that UVB radiation at 310 nm reaching earth's surface drops by an order of magnitude in going from an SZA of 25−75 degrees [55]. For San Francisco on June 8, the SZA reaches 25 degrees at 1300 h (1:00 p.m.), falling to 75 degrees at 0745 and 1750 (http://keisan.casio.com/exec/system/1224682277). The general rule is that one can produce a reasonable amount of vitamin D for SZA <45 degrees. The SZA reaches these values that day at 0930 and 1610.

Figure 3 in Engelsen [55] indicates that vitamin D can be produced rapidly from solar UVB the entire year for latitudes <20 degrees, rising to 65 degrees in summer. However, it is impossible to produce vitamin D at the end of the year for latitudes >46 degrees, rising to 65 degrees by early March. From these calculations, it is estimated that for Fitzpatrick skin type III, one-quarter of a minimal erythemal dose over one-quarter of the body would produce 1000 IU [59]. In Florida, that would take 8−15 min near solar noon, depending on the season.

The calculations in Engelsen [55] were based on the International Commission on Illumination (CIE) action spectrum for previtamin D production [60]. A recent paper pointed out some of the problems with the CIE action spectrum such as the use of a bandwidth of several nanometers in its determination [61]. Another was developed by the Dutch National Institute for Public Health and the Environment (RIVM) in the Netherlands [62]. In addition, that paper points out that prolonged UVB exposure saturates vitamin D production and that wavelengths between 310 and 330 nm cause photodecay of vitamin D metabolites. Although an improved action spectrum would probably make a few days change vitamin D production rates, the general conclusions reached using the CIE action spectrum offer good guidance for now.

Additional factors to consider include altitude, surface type, and aboveground features. UVB intensity increases about 19% per 1000 m for an SZA of 20 degrees [63]. The effect of altitude is evident in maps of vitamin D-producing UVB doses in the United States [64]. Different surfaces reflect different amounts of solar UVB. For overhead sun, reflectance varies from 10% for water, 12% for land, 23% for an alpine pasture, to 87% for new dry snow [63]. However, reflectance varies as a function of SZA; anyone who has spent much time on the water in summer knows how easy it is to get sunburned because of the high reflectance at higher SZAs. Living in forested regions reduces UVB doses. As a result, populations inhabiting forested tropical regions for centuries to millennia have lighter pigmentation than those who live in tropical plain regions [7].

## 3.3 Meteorological factors

Clouds can reduce the amount of UVB radiation reaching earth's surface. The degree of attenuation depends on the optical thickness/density of the cloud, the amount of cloud cover, and the SZA [65]. UVB can penetrate thin clouds. Coastal regions also can have considerable fog, which also attenuates UVB radiation reaching the surface. A good example is San Francisco, where the marine air passes through the Golden Gate in summer to cool the Sacramento Valley, bringing both clouds and fog.

Air pollution reduces vitamin D production by attenuating solar UVB radiation reaching earth's surface [66] as well as by reducing time spent outdoors [67]. In addition, since air pollution particulate matter perturbs over 500 genes including multiple proinflammatory

cytokines which vitamin D can counter [68], and since smoking reduces 25(OH)D concentrations [69], it is very likely that air pollution also reduces 25(OH)D concentrations due to vitamin D combating the inflammation and oxidative stress caused by the pollution [68]. The effect of urban pollution has been documented in studies in Belgium [70], China [71], France [72], India [73], and Iran [41,42]. Although aerosols may contribute most of the attenuation, gases that absorb in the UVB spectral region such as ozone and sulfur dioxide also can contribute [70]. In highly industrial regions of China and India, pollution can attenuate UV radiation by up to 50% [71]. Air pollution may also help explain the higher rates of vitamin D deficiency in urban regions than in rural regions.

### 3.4 Urban versus rural residence

Living in urban regions is often associated with lower 25(OH)D concentrations. A study of the effect of urbanization on South African women explored the reasons for lower 25(OH)D concentrations for urban dwellers. Several factors were investigated. The most important ones identified were higher urban rates of obesity, lower urban rates of physical activity levels, and greater urban alcohol consumption [74]. Another study from South Africa reported lower 25(OH)D concentrations among adolescents with alcohol use disorder [75]. Another reason for lower 25(OH)D concentrations in urban regions is due to a greater preponderance of indoor occupations [76]. High-rise buildings also reduce the UVB radiation reaching the surface [77]. A study of women of childbearing age in Vietnam found slightly higher 25(OH)D concentrations in the Hai Dong province (85 nmol/L) than in Hanoi City (78 nmol/L) [78]. A study in Malaysia found that rural women spent much more time in the sun than urban women (~8 vs. ~3 hour/day, respectively, resulting in higher 25(OH)D concentrations, ~70 versus ~32 nmol/L, respectively), even though urban women exposed more skin surface area than rural women [79]. A study of elderly Koreans found higher 25(OH)D concentrations in rural than in urban residence (66 vs. 43 nmol/L, respectively) [80].

### 3.5 Travel to sunny locations in winter

People who live at high latitudes and travel to sunny locations during winter have higher 25(OH)D concentrations. A study of Swedish women found that a winter sun vacation was associated with a 14.5-nmol/L increase in 25(OH)D concentration—greater than the 11.0-nmol/L increase associated with a daily intake of 300 IU of vitamin D from reduced fat dairy products [81]. A study in Europe found that sun holidays increased 25(OH)D concentrations from 49 to 71 nmol/L for Danes and from 56 to 73 nmol/L for Spaniards; ski holidays increased 25(OH)D concentrations for Danes from 51 to 59 nmol/L [82]. However, the study also found significant increases in T−T dimers (also known as thymine−thymine or pyrimidine dimers), a biomarker of DNA damage, measured in the urine.

## 4. Endogenous characteristics

### 4.1 Effect of age

Vitamin D is produced in the skin when UVB acts on 7-dehydrocholesterol, followed by a thermal reaction [83]. As people age, the amount of 7-dehydrocholesterol in the skin changes. On the basis of those concentrations in the dermis and epidermis [84], the ability to produce vitamin D in the skin decreases linearly with time from 10 years of age, falling to about 50% lower ability by 70 years of age [83]. A study in Hungary found that August 25(OH)D concentrations decreased with age, from 42 nmol/L for those aged 0−9 years to 21 nmol/L for those aged 80−89 years [85]. This finding is probably due to a combination of younger people spending more time in the sun and producing vitamin D from solar UVB more efficiently. However, a study found that the US children do not generally spend enough time in the sun to meet nominal vitamin D requirements [86].

### 4.2 Obesity

The higher the body mass index (BMI), the lower the 25(OH)D concentration is likely to be [87]. One plausible explanation for this finding is vitamin D sequestration in adipose tissue [88]. Another is volumetric dilution [89]. A third is decreased hepatic 25-hydroxylase activity due to decreased expression of CYP2R1 [90]. Given the worldwide increases in rates of obesity, global 25(OH)D concentrations related to obesity will continue to decline.

### 4.3 Genetics

In a study of exposure to UVB lamps in winter in Denmark, 22 healthy participants achieved 25(OH)D concentrations from 85 to 216 nmol/L [91]. Baseline 25(OH)D concentrations accounted for 55% of the variance, whereas age, polymorphisms in the vitamin D receptor gene, height, and constitutive skin pigmentation accounted for 15% of the variance. Genes involved in the vitamin D metabolic pathway also can affect 25(OH)D concentrations. Alleles of these genes are associated with different 25(OH)D concentrations. The candidate genes are *DHCR7*, *CYP2R1*, and *GC* as shown by Brouwer-Brolsma [62]. *DHCR7* encodes the enzyme

7-dehydrocholesterol reductase. This enzyme catalyzes the conversion of 7-dehydrocholesterol into cholesterol in the skin, thus preventing that 7-dehydrocholesterol from being metabolized into previtamin D. *CYP2R1* encodes the liver enzyme that converts vitamin D to 25(OH)D. *GC* encodes the vitamin D-binding protein, which transports vitamin D metabolites to different organs, tissues, and cells. In a study involving 2857 Dutch men and women older than 65 years, 35% of 25(OH)D concentrations were explained by a model including sun exposure, oral vitamin D intake, and genetic factors [62]. In the model adjusted for age, BMI, years of education, smoking, alcohol consumption, physical activity, and self-reported health, the factors significantly affecting 25(OH)D concentration were the *GC* gene ($P = 0.005$), being outside in the past 2 weeks ($P = 0.01$), and sunlamp use ($P = 0.03$). *CYP2R1* was marginally insignificant ($P = 0.07$).

Another paper found that people with certain alleles of *CYP2R1* and *GC* had the smallest increases in 25(OH)D concentrations after UVB exposures and the largest decreases in 25(OH)D concentrations after 6 months of consumption of vitamin $D_3$-fortified bread and milk [92]. Thus, genetics can modestly affect 25(OH)D concentrations from UVB exposure and oral vitamin D intake. Genome-wide association studies (GWAS) have identified genes associated with 25(OLH)D concentration. A GWAS involving up to 79,366 participants of European descent added two loci harboring genome-wide significant variants of 25(OH)D concentration, rs8018720 in *SEC23A*, and rs10745742 in *AMDHD1* to four already known (*GC*, *NADSYN1/DHCR7*, *CYP2R1*, *CYP24A1*) [93]. Another GWAS involving 417,580 Europeans identified 143 independent loci [94].

## 5. Behavioral determinants

### 5.1 Use of sunscreen

Sunscreens generally block erythemal wavelengths (<325 nm) well. The thicker the layer of sunscreen applied, the less the UVB reaches the skin [95]. Thus, if not applied thickly enough, some UVB will reach the skin [96]. In addition, sunscreen wears off. People who habitually apply sunscreen when in the sun will have lower 25(OH)D concentrations than those who do not, assuming similar sun exposures [97]. Many women's cosmetics contain sunscreen (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=700.35). The primary reason for putting sunscreen in cosmetics is probably to reduce the risk of elastosis (wrinkling) [98].

An alternative to the use of sunscreen to reduce risk of erythema and DNA damage is to raise serum 25(OH)D concentrations using vitamin $D_3$ supplements. An intervention study conducted in Cleveland, OH, United States, found that raising 25(OH)D concentration to above 100 nmol/L using 200,00 IU of vitamin $D_3$ resulted in very little erythema for a sunburning UV dose compared with those supplemented with 100,000 IU vitamin D and achieving 25(OH)D near 75 nmol/L [99]. The mechanism indicated was inhibition of inducible nitric oxide synthase and TNF-α by activated macrophages [100], thereby reducing risk of inflammation. The Cleveland group also suggested using high-dose vitamin $D_3$ to treat sunburn [101]. The work was endorsed in an editorial by Bikle [102].

### 5.2 Shade

Atmospheric molecules and aerosols strongly scatter UVB radiation. There are two types of scatter involved: Rayleigh scattering is involved for particles up to about a 10th of the wavelength of light, while Mie scattering occurs for larger particles. Atmospheric molecules have a diameter of 0.4 nm, which is much smaller than 300 nm. Rayleigh scattering varies as the inverse fourth power of wavelength, whereas aerosols scatter to a lower extent, depending on particle size. The effect of scattering explains why the clear sky is blue and clouds are white during midday and orange at sunrise and sunset. Thus, UV exposure is related to direct, diffuse, and reflected UV radiation. A model calculation for Payerne, Switzerland, estimated that direct UV erythemal radiation contributed 15%–24% of annual exposure, whereas diffuse radiation explained about 80% of cumulative erythemal dose [103]. A study reported that for SZA between 35 and 60 degrees, previtamin D production under trees and umbrellas was about half of that in full sun [104]. A later paper reported that in Australia, the best time to expose the body to UV radiation while using a shaded environment with a sky view of >40% was when the SZA was <45 degrees [105]. Using that approach would reduce total UV exposure by 37%–58%.

### 5.3 Messages to get UV exposure mornings and afternoons (the shadow rule)

The UV index (UVI) is a commonly used indicator of erythemal (skin reddening) potential of solar radiation introduced in Canada in 1992 [64]. The UVI is an irradiance scale computed by multiplying the erythemal irradiance in Watts/$m^2$ by 40. The erythemal action spectrum for solar radiation has the highest value for below 300 nm and then decreases by a factor of 500 from 300 to 327 nm, and then more slowly out to 39 nm. The UVI multiplies the erythemal action spectrum by the solar UV spectrum reaching the earth's

surface, which starts at 290 nm. The UVI peaks from 305 to 310 nm. Satellite instrument data are used to determine two important components of the UVI, total ozone, cloud, and aerosol effects. Surface altitude and latitude are also included. The UVI is given for solar noon.

In Australia, most people have skin pigmentation much lighter than appropriate for the UVB doses. Most people have Anglo-Celtic ethnic backgrounds. In the United Kingdom, the UVI often reaches 6 in summer, and people with Fitzpatrick skin type 2 could be in the sun for 30–60 min without burning (http://www.weatheronline.co.uk/reports/wxfacts/The-UV-Index.htm).

As a result, 25(OH)D concentrations for 45-year-old people living in England increase from 37 nmol/L in winter to 75 nmol/L at the end of summer just by going about their lives [28]. However, the Cancer Council of Victoria urges Australians to be "SunSmart" and cover up when the UVI is 3 or higher (http://www.cancervic.org.au/preventing-cancer/be-sunsmart). As a result, 25(OH)D concentrations of Australians are not as high as might be expected. A study based on serum 25(OH)D concentrations from women younger than 60 years in the period 1993–2001 found mean peak, monthly peak, and monthly trough values for three locations: South East Queensland (67.0, 75.3, and 54.6 nmol/L, respectively); Geelong region (75.5, 92.5, and 57.1 nmol/L, respectively); and Tasmania (51.1, 62.1, and 40.3 nmol/L, respectively) [106]. The authors' concluding statement was "Current sun exposure practices and dietary intake do not seem to fully prevent vitamin D insufficiency and deficiency, and consideration should be given to modification of sun exposure advice or pursuing other means to achieve vitamin D adequacy."

Dermatologists often recommend the shadow rule; i.e., use sun protection when one's shadow is shorter than one's height [107]. However, following the shadow rule greatly reduces the production of vitamin D and is associated with increases in risk of melanoma from the higher UVA to UVB ratio [108]. The abstract of the European Code Against Cancer 4th Edition: Ultraviolet Radiation and Cancer states: "Excessive exposure from natural sources can be avoided by seeking shade when the sun is strongest, by wearing appropriate clothing, and by appropriately applying sunscreens if direct sunlight is unavoidable. Exposure from artificial sources can be completely avoided by not using sunbeds. Beneficial effects of sun or UVR exposure, such as for vitamin D production, can be fully achieved while still avoiding too much sun exposure and the use of sunbeds" [109]. The Canadian guidelines for the prevention of nonmelanoma skin cancer (NMSC) recommend precautions when the UVI is 3–5, using protection (shade, cover up, wear a hat and sunglasses, use sunscreen) when the UVI is 6–7, using extra precaution for UVI 8–10, and avoiding the sun more for UVI >11 [110].

Danish sun exposure guidelines recommend seeking shade, wearing a sun hat, wearing protective clothing, or using sunscreen. Adherence to the guidelines regarding seeking shade or wearing protective clothing always or often was associated with approximately 7–10 nmol/L lower 25(OH)D concentrations for adults in spring and autumn [111]. No clear associations were evident for children.

## 5.4 Sun avoidance because of concern about skin cancer, melanoma

Public interest in the role of solar UV exposure and risk of melanoma and NMSC seems to have been sparked by reports that stratospheric ozone concentrations would be reduced by widespread use of chlorofluorocarbons [112]. In 1980, Australia began its "Slip! Slop! Slap!" campaign to get Australians to avoid the sun for UV indices above 3 [113]. A paper published in the *Journal of the American Academy of Dermatology* in 1982 reviewed the use of sunscreens for protection against the harmful effects of solar radiation [114]. People diagnosed with NMSC are more likely to try to minimize sun exposure through various means, including seeking shade, wearing clothing that exposes less of the body, and using sunscreen [115]. That effect also has been reported in an analysis of cancer rates among participants in the Women's Health Initiative in the United States [116]. Women diagnosed with NMSC tended to have lower sun exposure in the decade of the study as well as increased risk of several cancers for which UVB reduces risk [117].

## 5.5 Occupation (outdoors vs. indoors)

People who work outdoors generally have higher 25(OH)D concentrations than those who work indoors. A study in Israel found that outdoor workers had an average daily solar UVB exposure of $4.4 \pm 1.6$ h, whereas indoor workers had $0.9 \pm 0.5$ h, resulting in much higher 25(OH)D concentrations for the outdoor workers [118]. Rates of cancer incidence in Nordic countries offer another example of occupation's effect on 25(OH)D concentrations. Workers in the occupations with most time outdoors, such as farmers, forestry workers, and gardeners, had the lowest rates of cancers for which UVB and vitamin D are associated with reduced risk [119]. Vitamin D production by solar UVB exposure is the only mechanism proposed to explain the link between UVB exposure and reduced cancer risk. A study of professional ballet dancers with mean age of 26 years in the United Kingdom found winter

and summer 25(OH)D concentrations of 37 and 60 nmol/L, respectively [120]. The dancers also had higher injury rates in winter. A study of males in Delhi in August–September found that outdoor, mixed outdoor–indoor, and indoor workers had sun indices of $12.0 \pm 6.3$, $4.3 \pm 2.2$, and $0.7 \pm 0.6$, respectively, and mean serum 25(OH)D concentrations of $73 \pm 22$, $48 \pm 14$, and $27 \pm 11$ nmol/L, respectively [121]. The sun index was calculated as the product of sunshine exposure in hour/week and fraction of body surface exposed.

Working at night is also associated with reduced 25(OH)D concentrations. A study in Jordan found that female night shift workers had significantly lower 25(OH)D concentrations than day shift workers ($50 \pm 38$ vs. $73 \pm 35$ nmol/L) [122]. Male night shift workers had nonsignificantly lower 25(OH)D concentrations than day shift workers ($55 \pm 25$ vs. $65 \pm 33$ nmol/L). Also, a review of 10 studies found that shift workers and indoor workers were the occupational groups most likely to have vitamin D deficiency [123].

## 5.6 Outdoor recreational activities

Recreational activities, especially outdoors, can increase 25(OH)D concentrations. Younger people spend more free time outdoors. Analysis of NHANES data from 6370 people older than 18 years from 2003 to 2006 found that 10 min of objectively measured moderate to vigorous activities during the day were associated with an increase in serum 25(OH)D of 0.80 (95% confidence interval (CI) = 0.43–1.20) nmol/L [124]. A study in Italy found that serum 25(OH)D concentrations were about 25% higher for the elderly who regularly engaged in outdoor activities including brisk walking, cycling, gardening, and fishing [125].

## 5.7 Lack of knowledge of the benefits of vitamin D

A study in Hong Kong found that health literacy was directly associated with sunlight exposure, suggesting that health literacy training might be more effective than just providing information about vitamin D and sunlight exposure [126].

An important reason for low 25(OH)D concentrations appears to be lack of knowledge of the benefits of vitamin D, of the risks associated with vitamin D deficiency, and that the sun is an important source of vitamin D. A study of adults aged 20–40 years in Sharjah, United Arab Emirates, found that 39% knew about vitamin D deficiency and 43% of them knew that sunlight is the main source of vitamin D [127]. On the other hand, the elderly are becoming increasingly aware of the role of vitamin D in reducing risk of osteoporotic fractures and are increasing their oral vitamin D intake. A study in France found that the ratio of 75-year-old women with 25(OH)D concentration <25 nmol/L fell from 69% before 2009 to 35% thereafter [128]. In the United States, analysis of data from NHANES found that age-adjusted mean 25(OH)D concentrations increased from 61 to 63 nmol/L between 1988–94 and 2005–06–67 nmol/L for the period 2007–10 [129]. The increase was attributed to increased vitamin D supplementation.

A study of 208 adult participants in the United Kingdom in 2018 found that 42% answered 4 or 5 of 10 vitamin D questions correctly, while 36% answered 6–10 correctly and 22% answered 1–4 correctly [130]. Forty four percent of the participants reported taking vitamin D supplements. Knowledge score was the strongest predictor of supplement use (odds ratio = 2.5 (95% CI, 1.2–5.3)). The most commonly reported reasons for use were insufficient sun exposure (57%), health benefits (51%), and insufficient amounts from food (46%). Another study conducted online in the United Kingdom during June 17–18, 2019 surveyed public awareness and behavior regarding vitamin D and sunlight exposure in the United Kingdom [131]. Among the findings was that 71% thought that the risks of sun exposure were well promoted versus 22% that thought the benefits of sun exposure were well promoted. Fifty two percent had increased awareness of the risks of sun exposure during the preceding 10 years, but only 24% noticed increased promotion of the benefits of sun exposure during the same period.

Unfortunately, an important reason for lack of knowledge about the health benefits of vitamin D is that the public health and medical systems consider randomized controlled trials (RCTs) to provide the most accurate information on health benefits of pharmaceutical drugs and, by extension, nutrients. Results of observational studies are generally not accepted for setting policies and guidelines. Unfortunately, RCTs of vitamin D for various health outcomes have generally not been designed, conducted, or analyzed properly. As outlined by Heaney [132], the guidelines for nutrients studies (such as for vitamin D supplementation to increase 25(OH)D concentration) include starting with an understanding of the nutrient concentration–health outcome relationship, measure the concentrations for prospective participants, try to enroll participants with low concentrations, supplement with sufficient nutrient to raise concentrations enough to have significant health benefits, and then measure the achieved concentrations. See, also [133]. Unfortunately, most vitamin D RCTs do not restrict their study populations to individuals with vitamin D deficiency [134]. Also, they generally use small vitamin D doses and do not base the analyses on achieved 25(OH)D concentrations. For example, an RCT regarding progression from prediabetes to diabetes

enrolled participants with a mean baseline 25(OH)D concentration of 28 ng/mL and gave participants in the treatment arm 4000 IU/d vitamin $D_3$ [135]. The hazard ratio for progression to diabetes according to intention to treat was insignificant, 0.88 (95% CI, 0.75−1.04, $P = .12$). However, a subsequent secondary analysis, based on achieved 25(OH)D concentration in the treatment arm, found that the hazard ratio for conversion to diabetes was 0.75 (95% CI, 0.68−0.82) for every 10 ng/mL increase in 25(OH)D concentration above 20 ng/mL to >50 ng/mL [136]. Since it was a secondary analysis, it had little impact on health policy.

In addition, the medical systems such as in the United States consider vitamin D information and supplementation an obstacle to income and profits. As a result, the Disinformation Playbook has been used to discourage the dissemination of information regarding the benefits of vitamin D [137]. The five approaches include promoting bad vitamin D studies, harassing leading vitamin D researchers, manufacturing uncertainty, buying credibility for nonvitamin D approaches to health with academia and professional societies, and capturing government health policy agencies. Examples of these approaches are given in the posted analysis.

## 5.8 Lifestyle factors associated with reduced sun exposure

Both clothing and sun exposure behavior influence the effect of UV on vitamin D concentrations. Extremes of temperature, i.e., both hot and cold, have an impact. Although clothing traditions in equatorial societies are mainly highlighted, the same is true where the temperature is cold. Bedouins and Native Alaskans are traditionally clad from head to toe to prevent themselves from the harsh climate peculiar for their habitats and as such the temperature extremes that they are exposed to. Eventually, irrespective of the hours of sunshine theoretically available for endogenous vitamin D synthesis, the environmental temperature is a major determinant in sun exposure behavior. Studies from sunny countries such as Brazil have found that one of the major contributors of vitamin D insufficiency is seclusion to indoor activity [138].

Furthermore, clothing norms are dictated primarily by cultural following. Conservative societies, as is typical for the Arab world, demand a dress code that restricts the parts of the body exposed. Therefore, even with ample sunshine, type of clothing contributes to vitamin D deficiency. For example, vitamin D deficiency is prevalent among women and neonates in Saudi Arabia because of clothing traditions [139]. Lifestyle choices, such as sun avoidance, indoor work, and covered transport, also may be implicated in the prevalence of vitamin D insufficiency in countries with abundant sunshine. For women in Morocco, lack of sun exposure and veiled clothing style were the most important factors that influenced hypovitaminosis D [140]. Skin pigmentation, religious belief, and lifestyle were among the major determinants contributing to the prevalence of vitamin D deficiency in South Asia and Southeast Asia [141]. Prevalence of vitamin D deficiency has likewise also been linked to less exposure to sunshine among healthy schoolchildren in central Ethiopia [142] and among Iranian adolescents [143]. A study listed the aforementioned as the major contributors in Cambodian women, despite their living close to the equator [144].

Pale skin has historically been prized as beautiful in China, and that concept is widespread in other Asian countries, such as India (http://asiasociety.org/blog/asia/china-long-tradition-dodging-sun-photos). Thus, aesthetically the preference of fair complexion has also retarded sun exposure in several Asian communities [145].

Cultural beliefs tend to prevail independently of country of domicile—particularly for the Asian diaspora. A study on South Asian women residing in Auckland, New Zealand, reported that deliberate sun avoidance and an indoor lifestyle were the major causes of hypovitaminosis D [146]. More sun protection behavior, shorter sun exposure on weekends, and less acculturation to the Australian lifestyle all were associated with vitamin D deficiency in East Asian women living in Sydney, Australia [147]. Primary healthcare patients of African and Asian origin in Sweden were at high risk of vitamin D deficiency [148]. A study of East Asian women living in Australia reported the following: "These women reported a number of cultural factors related to their attitudes and behaviors regarding sun exposure. They expressed preference for fair skin, a tradition of covering skin when outdoors, and no sunbathing culture. They believed that fair skin was more beautiful than tanned skin. They reported that beauty was the reason for active avoidance of sunlight exposure. Although they reported knowledge of the need for sun avoidance due to skin cancer risk, few reported knowledge about the benefits of sun exposure for adequate vitamin D levels" [147,149].

## 5.9 Migration/migrants

The global migrant/refugee crisis will probably exacerbate vitamin D deficiency. An increasing number of countries were recently confronted with hundreds of thousands of immigrants. In Germany, for example, the number of immigrants of European origin increased 1.3-fold between 2008 and 2015 [104,105]. At the same time, the number of immigrants from Africa increased 1.6-fold, whereas that from Middle East and Asia

increased 1.9-fold. Furthermore, the second generation from overseas-born migrants should be also considered a group at high risk for vitamin D deficiency because of darker skin pigmentation than the host population and reduced rate of full assimilation to the host society and its habits (lifestyle and diet). Dark-skinned immigrants in Europe have a significantly increased rate of rickets [150]. In the United States, African Americans have significantly lower 25(OH)D concentrations than European Americans and, therefore, increased risk for many types of disease [151].

Compared with the migrants' sunny homelands, most of the host countries (high income) are at higher latitudes with reduced efficacy of UVB, cloudy skies, pollution, low average temperatures, and short summer season (except Australia). As a consequence, clothing effectively prevents skin synthesis of vitamin D because of weather conditions or cultural and religious reasons. Unfortunately, the dietary preferences of migrants who relocated to higher latitudes may intensify their risk for vitamin D deficiency. Only a few natural food products are rich in vitamin D, so vitamin D-fortified foods and vitamin D supplements can serve as an alternative source. However, because of dietary preferences or economic status, immigrants may not consume commonly fortified staple foods or supplements [152]. Therefore, displacement from tropical regions to high-latitude countries puts immigrants at even greater risk of vitamin D deficiency than in their country of origin.

As shown by Mughal and colleagues [153], prolonged breastfeeding without maternal vitamin D supplementation to benefit the infant is another problem within immigrant societies that increase the risk of vitamin D deficiency and its consequences. Thus, exclusively breastfed infants consuming 750−1000 mL of breast milk per day from vitamin D-deficient mothers fail to receive the 10 μg/day of vitamin D needed to at least prevent bone mineralization defects [153]. A clinical trial showed that nursing women supplemented with 6400 IU/day of vitamin $D_3$ delivered 400 IU/day vitamin $D_3$ to the nursing infants [154].

In a study from Italy, severe vitamin D deficiency [25(OH)D $<$ 25 nmol/L] was noted in 76% of migrant newborns and 48% of migrant mothers [155]. Both migrant newborns and migrant mothers had very low 25(OH)D concentrations ($18 \pm 14$ and $30 \pm 17$ nmol/L, respectively). Among the studied mother−infant pairs, a linear decrease of 25(OH)D concentrations was observed with increasing skin pigmentation (phototype I, $42 \pm 18$ nmol/L, vs. phototype VI, $18 \pm 10$ nmol/L; $P < .0001$) [155]. For data analyzed by country of origin, host country newborns from Italy had 25(OH)D concentrations higher than all migrant groups ($P < .0001$) such as North African, African, Asian, Central−South American, and East European. The same results were found in host country mothers, and North African mothers and their offspring had the lowest 25(OH)D concentrations of $22 \pm 11$ and $13 \pm 10$ nmol/L, respectively [155]. In the Netherlands, 25(OH)D concentrations <50 nmol/L were identified in 82% of Surinamese, 92% of Turkish, and 93% of Moroccan pregnant women compared with 28% of native Dutch women [156].

In Belgium, 90% of Moroccans and 77% of Congolese had serum 25(OH)D concentrations <50 nmol/L [157]. In Norway, 92% of Pakistanis had 25(OH)D concentrations below 50 nmol/L [158], and 81% of newly arrived immigrants from the Middle East, 75% from South Asia, and 73% from Africa had 25(OH)D concentrations lower than 50 nmol/L [159]. Furthermore, from aforementioned regions, approximately one-third had 25(OH)D $<$ 25 nmol/L [160]. Vitamin D deficiency appeared common among Pakistani immigrant children in Denmark [161]. Somali immigrant women had a high prevalence of vitamin D deficiency, defined as 25(OH)D $<$ 50 nmol/L, with rates of 90% in Norway [162] and Finland [163].

A recent metaanalysis of dark-skinned migrant populations showed that immigrants from the extended Middle East and sub-Saharan Africa had a high prevalence of vitamin D deficiency (65% and 56%, respectively) [164]. Refugees are considered particularly at risk for vitamin D deficiency because of staying indoors to avoid potential harm from conflict in native countries and dangers associated with refugee camps [165]. Longer time spent in the host country is an additional risk factor for vitamin D deficiency, as suggested in the literature. In one study, the length of time living in Melbourne, Australia, was associated with increased risk of vitamin D deficiency (defined as 25(OH)D $<$ 25 nmol/L) in African migrants, with a prevalence of 77% for those living >2 years in Melbourne compared with a prevalence of 38% for those living less than 2 years in that city [166]. The aforementioned phenomenon might be linked to asylum seekers dressing more conservatively since immigrating to Australia as well as reporting apartment-style accommodation and reduced time spent outdoors, further reducing sun exposure from that before they immigrated [166].

In migrant and refugee subpopulations, major risk factors for vitamin D deficiency include darker skin, Muslim religion, full body−covering clothing, longer stay in host country, decreased daylight exposure, living in an urban environment, and coming from a socioeconomically disadvantaged background. Prevention

programs with vitamin D supplementation should be considered in host countries, and migrants/refugees at high risk should be educated, screened, and monitored for vitamin D deficiency.

## 6. Predicting vitamin D deficiency

Diffey developed a model to estimate 25(OH)D concentrations from UV exposure in summer in the United Kingdom. He found that then-current advice to spend 10–20 min in the sun did little to boost overall 25(OH)D concentrations [167]. He extended that model later to include oral intake, finding that a combination of increased oral vitamin D intake in winter and increased summer sun exposure could improve vitamin D status for the adult British population [168]. His models were used to develop an integrated predictive model of population 25(OH)D concentration for Ireland on the basis of UVB data and vitamin D from food sources (4.4 μg/day or 180 IU/day). That model predicted well the 18%–19% of the population with 25(OH)D concentration <30 nmol/L in winter [169]. Evidently, 25(OH)D has a very slow decay rate, as shown by the fact that elderly patients who received vitamin $D_3$ in the form of fortified bread achieved a 25(OH)D concentration of 127 nmol/L, which decayed to 65 nmol/L after 1 year without the bread and 48 nmol/L at the end of 3 years [170].

Some researchers tried to predict vitamin D deficiency on the basis of several demographic characteristics and lifestyle factors. A cross-sectional study of 644 60- to 84-year-old participants in Australia found that use of "time outdoors, physical activity, vitamin D intake and ambient UVR, and inversely correlated with age, BMI, and poor self-reported health status" explained 21% of the variance in 25(OH)D concentration [171].

Another study in Amsterdam involved 1509 elderly Dutch participants in the development sample and 1100 in the validation sample [172]. "The final model for the prediction of vitamin D concentrations <30 nmol/L consisted of 10 predictors: older age, smoking, alcohol consumption (<13 drinks/wk), season, no vitamin supplement use, no bicycling, no gardening, medication use, limitations in the use of own or public transportation, and the inability to remember the present year, etc. The final prediction model for serum 25(OH)D < 50 nmol/L consisted of the following 13 variables: older age, sex (female), BMI (>30), smoking, alcohol consumption (<13 drinks/wk), season, no vitamin supplement use, no bicycling, no sporting, no gardening, medication use, poor appetite, and without a partner." The resulting model was sensitive to the upper 25(OH)D concentration cutoff. Table 4 in that article showed that the lower the cutoff concentration, the lower the specificity and the higher the sensitivity. Analysis of data from the Nurses' Health Study and Nurses' Health Study II in the United States found that for women, >10 g/day alcohol consumption raised 25(OH)D concentration by about the same amount as 7.5 μg/d (300 IU/d) vitamin $D_3$ intake [173].

A recent study based on analysis of 201 healthy individuals between the ages of 20 and 40 years identified male sex ($P < .001$), taking 50,000 IU vitamin $D_3$ supplement monthly ($P < .001$), and lower waist circumference ($P = .02$) were identified as effective factors in increasing serum 25(OH)D levels [174]. It is difficult to predict serum 25(OH)D concentration with respect to vitamin D supplementation due to several factors including solar UVB exposure, BMI, dietary sources of vitamin D, and genetics. A figure posted at Grassrootshealth.net based on values for their volunteer cohort shows that while 25(OH)D concentration rises in a nonlinear manner from 100 nmol/L with no vitamin D supplementation to 240 nmol/L for 20,000 IU/d, there is considerable variability for any supplementation amount (https://www.grassrootshealth.net/document/serum-25ohd-vs-vitamin-d-supplement-intake/ accessed March 22, 2022).

The question is often raised whether it is worthwhile to measure 25(OH)D concentrations especially given cost considerations. One analysis suggested that it is when targeted at people likely to have vitamin D deficiency such as those with chronic diseases, having dark skin living at higher latitudes, and the elderly [175]. Regarding darker skin, see Ames et al. [151].

## 7. Nonvitamin D benefits from solar UV exposure

There is now good evidence that there are important health benefits from solar UV exposure in addition to vitamin D production. The primary mechanism is liberation of nitric oxide (NO) from intracutaneous nitrogen compounds, primarily nitrate, by UVA [176,177]. NO is known to reduce the risk of cardiovascular disease [178], and fight viral infections [179], among other things. In fact, it appears to explain the seasonality of many health outcomes with highest rates in winter and lowest in summer [180]. Solar UVA has been found to reduce risk of autoimmune diseases [181,182], blood pressure

[183], metabolic dysfunction [184], and COVID-19 [185]. The COVID-19 study was done in winter in Italy, the United Kingdom, and the United States, in locations where solar UVB doses were so low that vitamin D could not be produced. Thus, the additional health benefit of NO liberation should be considered an added incentive to spend time in the sun. For those who have limited access to sun exposure in any season, a UV lamp can be used to produce both vitamin D and NO [186].

## 8. Conclusion

Although solar UVB exposure is the most important source of vitamin D for most people, many factors affect 25(OH)D concentrations related to solar UVB doses. Some of these factors are physical, relating to solar, atmospheric, and surface properties and time of day. Others are related to lifestyle, such as time spent outdoors, clothing worn, and use of sunscreen. These factors are subject to societal factors, including attitudes toward sun exposure. Genetic factors play a role in skin pigmentation and are involved in the metabolism and transport of vitamin D. Since solar UVB exposure is subject to physical, cultural, and personal restraints, vitamin D food fortification and vitamin D supplementation would be required to have everyone avoid vitamin D deficiency [8,12,169].

## 9. Summary points

- Solar UVB exposure is the most source of vitamin D.
- Many factors affect 25(OH)D concentrations associated with solar UVB exposure including solar elevation angle, duration of sun exposure, amount of skin exposed, genetics, age, body mass, skin pigmentation including that from tanning.
- In Europe, the mean 25(OH)D concentration is near 68 nmol/L in summer for all countries; in winter there is a U-shaped relationship between 25(OH)D concentration and latitude, with lowest concentrations near 45–50 degrees N latitude. For all latitudes, 25(OH)D stored in muscles is recirculated in winter; concentrations are higher at the lower latitudes in winter due to longer duration of vitamin D production, and higher at the higher latitudes due to greater consumption of dietary sources of vitamin D including ocean fish and meat, as well as taking vitamin D supplements.
- An important reason for low 25(OH)D concentrations is that the medical and health systems have not embraced vitamin D supplementation for nonskeletal health effects due to the paucity of successful vitamin D supplementation RCTs. The failure of most vitamin D RCTs is due to poor design, conduct, and analysis tied to not basing the trials on 25(OH)D concentration instead of vitamin D dose.
- There are additional health benefits from solar UV exposure due to nonvitamin D effects of UVB and increases in NO concentrations in the serum from UVA exposure.

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