

Contributions of Sunlight and Diet to Vitamin D Status

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Abstract Vitamin D is made in the skin using ultraviolet radiation of specific low wavelength, 290–315 nm (UVB). For many parts of the world there is a period when there is insufficient intensity of UVB to make vitamin D, which is reflected by a clear seasonal variation in vitamin D status. Sun avoidance practices, melanin in pigmented skin, and sun protection creams (sunscreen), if used properly, can dramatically reduce vitamin D synthesis. Few foods naturally contain vitamin D, although some countries fortify foods with vitamin D. Regulatory mechanisms in the skin mean there is no danger of vitamin D toxicity through sunlight synthesis. Although oral vitamin D is potentially toxic with high-dose supplements, there is a wide safety margin. Long-term safety data covering a range of potential adverse outcomes are limited.

Keywords Steroid hormones · Vitamin D · Age · Aging · Rickets · Osteomalacia

Introduction

Vitamin D and sunlight go hand in hand. Vitamin D is sometimes referred to as the “sunshine” vitamin; and the “D-lightful vitamin” is one of the many “D” puns quoted in the context of vitamin D. Ultraviolet radiation of a specific wavelength, 290–315 nm (UVB), is required for the

cutaneous synthesis of vitamin D. But how much sunlight do we need to make sure we have enough vitamin D? There are models which have been adapted to tell us how long we need to be outside, based on location and time of day. All the models are based on assumptions, the main assumption being the amount of vitamin D that can be made if we are completely exposed to sunlight of the correct wavelength to enable synthesis of vitamin D in the skin. This is dependent on going outside with at least some skin uncovered and on geographical location and time of year. It also depends on how much melanin pigment is in the skin, how high up you are, cloud color, shade, and how much light is reflected from the ground surface. If there is no cutaneous synthesis of vitamin D, the only source of vitamin D is what comes from the diet. Few foods naturally contain vitamin D, although many countries fortify some foods with it.

Sunlight and dietary recommendations for optimal vitamin D is an area of controversy, with public health advice trying to balance requirements for vitamin D against cancer risk from too much UV light.

Are minutes a day sufficient, or do current lifestyles mean that we cannot meet our requirements based on sunlight alone? This short review will explore and evaluate some of the evidence (see Box 1).

Brief History of Vitamin D

Although there is evidence that rickets, due to vitamin D deficiency, has been around since Roman times, it became a recognized problem in the mid-seventeenth century and by the early twentieth century had emerged into an epidemic throughout the industrialized countries of Europe. The anti-rachitic factor in diet was discovered in the early 1920s [1–3].

In the late nineteenth century the beneficial effects of sunlight were recognized, and sunlight or heliotherapy was

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Box 1 Units of vitamin D

Vitamin D intake is measured in micrograms or IU, with 1 μg equivalent to 40 IU.

25-Hydroxyvitamin D is measured in ng/mL or nmol/L, with 1 ng/mL equivalent to 2.5 nmol/L.

used as a cure for tuberculosis, which continued into the twentieth century as UV treatment with the use of sunlamps that could emit UV radiation (<http://www.sciencemuseum.org.uk/broughttolife/techniques/heliotherapy.aspx>). In the early 1920s, sunlamp treatment was proven to be effective in treating rickets. There are numerous examples of children undergoing UV treatment in Scotland. A photograph of children being treated in the orthopedic ward in Aberdeen, UK, circa 1920 is shown in Fig. 1. As diets improved, UV treatment fell out of favor. However, there are documented reports of UV treatment for children continuing until the late 1960s in Aberdeen, and school medical service reports exist up to 1965 which detail the use of mobile UV clinics in schools in Sutherland (north of Scotland) where children between the ages of 5 and 12 years received courses of UV radiation.

As concern has mounted about the cancer risks of UV radiation from excessive sunlight exposure, the advice has been to cover up to avoid sunlight exposure, leading to some groups not getting enough vitamin D.

A simplified schematic diagram (Fig. 2) illustrates that both sunlight and diet can provide vitamin D (the latter mainly as vitamin D₃, with a small amount of vitamin D₂ coming from the diet). This is converted to 25-hydroxyvitamin D

(25[OH]D) in the liver (by a cytochrome P-450–dependent enzyme, CYP2R1). Circulating 25(OH)D reflects how much vitamin D has been made or consumed and is currently accepted as the best marker of vitamin D status [4]. The active form of the vitamin, 1,25(OH)₂D, is produced in the kidney and released systemically as part of the homeostatic mechanism for controlling circulating calcium and phosphate [5, 6]. Other tissues have the potential for producing 1,25(OH)₂D locally. There are also mechanisms for degrading unwanted vitamin D, which is excreted in the bile [7]. This also shows that sunlight causes degradation of previtamin D and vitamin D into inactive metabolites, ensuring that with sunlight synthesis of vitamin D, toxic amounts of the vitamin are never reached. It is possible to overdose on oral vitamin D; although short-term studies show that the safety margin for toxicity is wide [8], longer-term data in a wide range of population groups are lacking.

Current Sunlight Advice

There have been concerns that sun avoidance leads to inadequate vitamin D; and it has been argued that sunlight exposure saves more deaths through preventing other cancers than might arise from skin cancer [9] and that there are other health benefits [10]. In Australia the Web page giving the daily UV index discusses the need for balance (<http://www.bom.gov.au/uv>). In the United Kingdom, where UV radiation is generally less intense, a joint statement from leading charity stakeholders (National Osteoporosis Society, Cancer Research UK, British Society of Dermatologists)

Fig. 1 Simplified schematic diagram of vitamin D sources

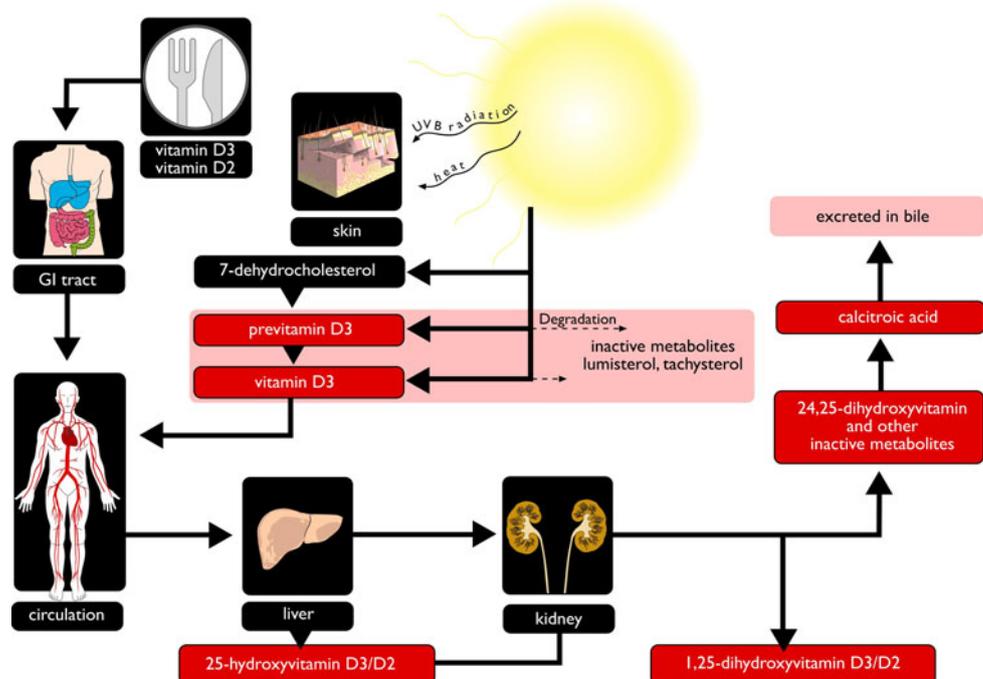




Fig. 2 UV treatment for vitamin D in Woodend Orthopaedic Hospital, Aberdeen, NE Scotland, 1927–1928. Reproduced with permission from NHS Grampian

was issued in 2011 to help clarify what sunlight exposure is considered safe (to limit skin cancer risk) and what is acceptable (for adequate vitamin D synthesis) based on current evidence (<http://info.cancerresearchuk.org/news/archive/cancernews/2010-12-16-Joint-position-statement-issued-to-provide-vitamin-D-clarity->). The main point was to ensure that people do not avoid the sun completely but take care not to burn.

However, this approach is still being debated by opposing groups: on the one hand, by evidence showing that even small amounts of sun may be damaging [11] and, on the other, that we cannot obtain enough vitamin D with current lifestyles [12].

How Much Vitamin D Do We Get from Sunlight?

There are many who advocate limited sunlight exposure to make enough vitamin D [13]. Holick and Jenkins [13] suggest exposing one-quarter of the body surface (e.g., the hands, face, and arms) to summer sunlight in the United Kingdom two or three times a week for up to 10 min (longer for darker skins) and then the skin should be protected from further sunlight exposure. This makes 1,000 IU vitamin D/day, which should be sufficient to last the winter months [13]. These values are based on the assumption that whole-body exposure to sunlight can result in synthesis of 10,000–25,000 IU (or 250–625 μg) vitamin D in a single day [14] and is equivalent to the vitamin D content of 3–8 kg of oily fish (or 2–5 kg of vitamin D-rich Pacific salmon) [15].

There are Web sites to help determine what period of exposure is necessary: some consider the outside conditions in detail [16] (http://nadir.nilu.no/~olaeng/fastrt/VitD_quartMEDandMED_v2.html), and others can be used on a day-by-day basis to determine whether sun protection is

required (<http://www.sunsmart.com.au/vitamin-d/tracker-tool.asp>). The computer models are based on the same assumptions that Holick and Jenkins [13] used. This original FASTRT model overestimated the sunlight required by one-third [17], but the current model has been adjusted (http://nadir.nilu.no/~olaeng/fastrt/README_VitD_quartMEDandMED_v2.html). However, none of the models allow for changes in an individual's capacity to make vitamin D, which will change according to how much has been produced (or consumed). This may not be important if the goal is to obtain vitamin D. However, for pale skins, cancer risk may be increased unnecessarily if little additional vitamin D is synthesized through successive sunlight exposures.

Skin color has a role to play, with melanin blocking sunlight of the wavelength required to synthesize vitamin D, in addition to providing protection against UV radiation [18]. It has been known for several decades that skin color affects vitamin D status [19]. Although it took longer for Indian and Pakistani immigrants living in Boston to synthesize vitamin D, when exposed to UV radiation their capacity to synthesize vitamin D was the same as that of Caucasians [20]. In practice, the equivalent of half an hour's sunlight exposure three times a week for 6 weeks was shown to increase mean 25(OH)D in south Asians to less than half the value seen in whites living in the north of England [21]. The prevalence of osteomalacia in south Asians in Britain is a recognized concern [22]. It is suggested that dietary calcium is "vitamin D sparing," and it is known that calcium alone can cure rickets [23]. There is evidence that black adolescents living in the United States handle calcium differently from whites, which may be the reason for the former group having higher bone mineral density [24]. Nevertheless, there are still reports of rickets in black Afro-Caribbean children living in the United Kingdom [25].

Theoretically, although sunscreen use reduces vitamin D production, as shown under experimental conditions when sunscreen product is applied at the required coverage prior to UV exposure [26], it has not always been observed in practice [27, 28]. This is probably due to sunscreen not being applied as thickly or frequently as recommended. Clothing [29] and keeping in the shade (shadows of tall buildings shade the sun in cities) contribute to less sunlight reaching the skin. We found that change in skin color was the major predictor of change in 25(OH)D but that it did not predict the final wintertime circulating 25(OH)D, suggesting that other factors are involved [27].

Estimation of Sunlight Exposure

Sunlight exposure can be estimated from badges that are sensitive to UV light (either UVA and UVB [30] or UVB only [polysulfone film] [31, 32]). Skin color change can be

Table 1 Exposure to sunlight

Do you go outside during the day?	Yes <input type="checkbox"/> No <input type="checkbox"/>
If “Yes”—at what time of day do you normally go outside?	
How long do you stay outside? (please indicate below)	_____
(i) Less than 15 min	<input type="checkbox"/>
(ii) Between 15–30 min	<input type="checkbox"/>
(iii) Between 30 min and 2 h	<input type="checkbox"/>
(iv) More than 2 h	<input type="checkbox"/>
Which parts of the body/skin have been exposed:	
(i) Face only	Yes <input type="checkbox"/>
(ii) Hands and face	Yes <input type="checkbox"/>
(iii) Hands and face plus arms and/or legs	Yes <input type="checkbox"/>
(iv) Hands and face plus arms and/or legs and some/all of trunk	Yes <input type="checkbox"/>
Have you been on holiday abroad in the last 2 months?	Yes <input type="checkbox"/> No <input type="checkbox"/>
Destination:	Duration of stay:

used as an estimate of how much sunlight someone has received [27]. We have collected data from sunlight diaries, which included time spent outside and body surface area exposed each day [33], and found these can be burdensome on both the subject and the researcher. Questions about sunlight exposure can be asked once (or more than once) to cover a longer period, although there are limited data on the validity of this approach [34]. Using aggregates of how much time a day people living in Tasmania spent in the sun (<1 h daily, 1–2, 2–3, 3–4 h, and >4 h daily), a significant correlation ($r = 0.22$) was found with recent sun exposure and 25(OH)D [35]. In a Danish study, the question asked was “How frequently do you expose yourself to sunlight lightly dressed, either with the purpose of getting sun-tanned or during the course of various outdoor activities like sport or gardening?” with the options of “never” (which included some exposure), “occasionally,” and “regularly.” They dichotomized the variable to never and whole-body exposure (which included “occasionally” and “regularly”) and found significantly higher 25(OH)D with exposure ($r = 0.21$ for December–May, $r = 0.29$ for June–October). For a large longitudinal study, we asked “Whilst living in Scotland, how often are you usually out-doors in sunny weather?” (optional answers: “often,” “occasionally,” and “seldom/never,” coded as 3, 2, and 1, respectively) and “Which parts of the body do you usually expose?” (tick boxes for head, hands, arms, legs, stomach/back, coded as head = 1; head and hands = 2; head, hands, arms, or legs = 3; head, hands, arms, and legs = 4; and stomach/back = 5). Using a multiplicative score for sunlight exposure, we found significant associations with 25(OH)D ($r = 0.17$ for summer and $r = 0.16$ for autumn) [36].

The questions in Table 1 (adapted from the sunlight exposure diary) were asked at each 2-monthly visit of an intervention trial in Scotland. Sunlight exposure (expressed as standard erythemal dose, SED) was also assessed using

polysulfone badges during 1 week of the 2-month period, and 25(OH)D was measured by tandem mass spectrometry. In the sunnier months, there was a clear association between SED and time spent outside (<15 min, 15–30 min, 30 min–2 h, >2 h), and 25(OH)D was significantly associated with body surface area exposed (as face 5 %; hands and face 10 %; hands, face, plus arms or legs 25 %; plus some or all of the trunk 60 %) (Fig. 3). The relationship between time outside and 25(OH)D was not as strong as that with SED. We did not find that the additional question, relating to time of day (morning, midday, afternoon, evening), provided any additional information. It should be noted that the relationship is dominated by those at the extremes of exposure or time outside, where there are fewer people.

It is recommended that information also be collected about holidays abroad and sunscreen use. Paradoxically, as mentioned earlier, the use of sunscreen may be associated with higher 25(OH)D [27], which suggests that protective creams are not being applied thickly or often enough to block out UVB; and they give an indication of deliberate sun exposure (see Box 2).

Data from Extreme Groups

Submariners ($n = 11$) who spent 3 months devoid of sunlight had a decrease in 25(OH)D of 39 % compared to 0.3 % for a comparable group ($n = 11$) who were given a vitamin D supplement of 600 IU (15 μg) [37]. Halfway through the study (1.5 months) the decreases were 37 and 17 %, respectively, showing that there was little additional decrease for the nonsupplemented group from 1.5 to 3 months. Unfortunately, the half-life cannot be calculated as the “before and after” 25(OH)D measurements were not provided. For both groups, there was an increase in 25(OH)D 1 month after returning from the trip (44 and 21 %, respectively). The study was performed in 1984, but

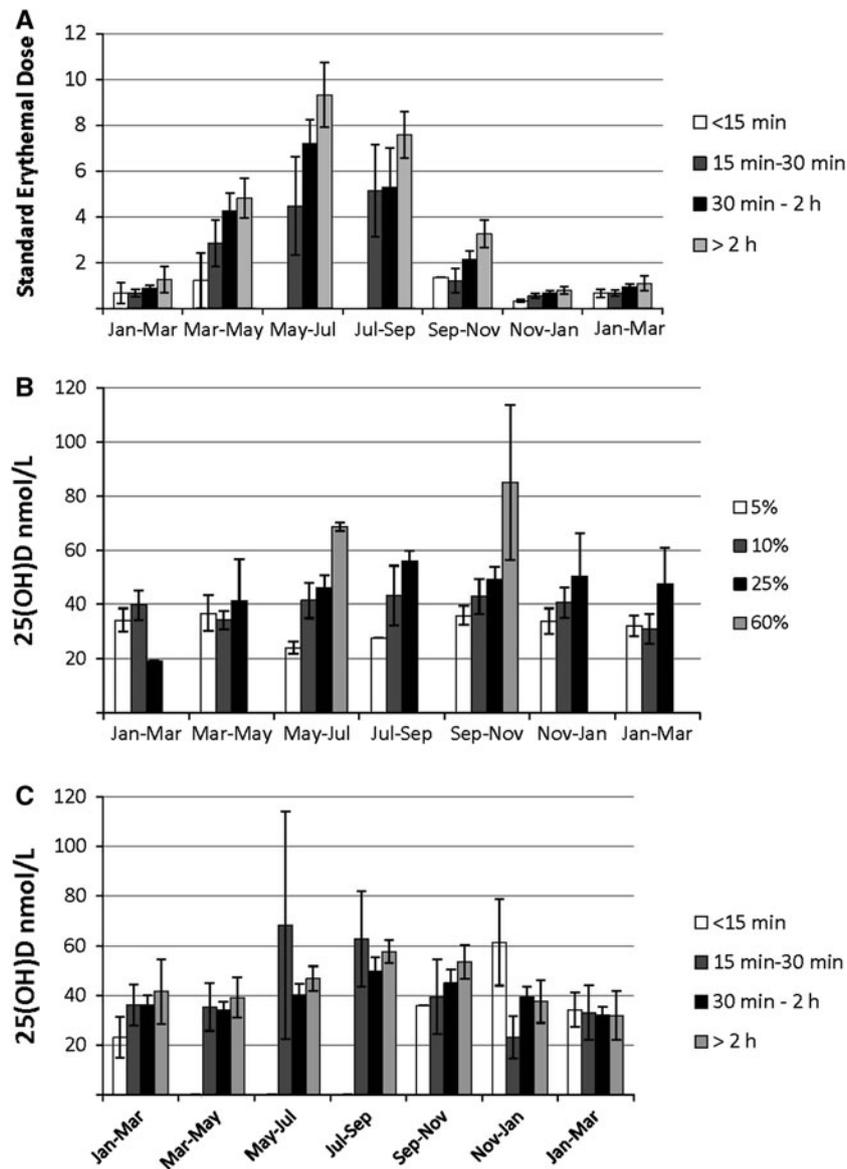


Fig. 3 Association between data obtained from simple questions on sun exposure, SED estimated from polysulfone film badges, and 25(OH)D. **a** Time spent outside and SED (all women). Significance value associations by one-way ANOVA: March–April ($p = 0.011$), May–June ($p = 0.059$), July–August ($p = 0.001$), September–October ($p = 0.017$), November–December ($p = 0.030$). Numbers for time spent outside <15, 15–30 min, 30 min–2 h, >2 h: March–April (2, 25, 171, 72), May–June (0, 12, 101, 150), July–August (0, 6, 108, 150), September–October (1, 9, 118, 132), November–December (9, 27, 176, 38). **b** Body surface area exposed and 25(OH)D (placebo only). Significance value associations by one-way ANOVA: March–April ($p = 0.540$), May–June (0.006), July–August (0.019), September–October (0.003), November–December (0.057). Numbers for body surface area exposed 5% (face only), 10% (face and hands), 25% (hands, face, arms, or legs), 60% (plus all or part of trunk): March–April (21, 68, 8, 0), May–June (3, 33, 55, 3), July–August (1, 7, 87, 0), September–October (3, 34, 50, 5), November–December (40, 45, 4, 0). **c** Time spent outside and 25(OH)D (placebo

only). Significance value associations by one-way ANOVA: March–April ($p = 0.593$), May–June (0.084), July–August (0.045), September–October (0.160), November–December (0.001). Numbers for time spent outside <15, 15–30 min, 30 min–2 h, >2 h: March–April (0, 11, 67, 20), May–June (0, 3, 41, 50), July–August (0, 3, 37, 55), September–October (1, 5, 45, 41); November–December (3, 9, 64, 13). *Note:* Comparing sun exposure data at one visit with 25(OH)D at a later visit did not improve the associations. However, Spearman’s correlations between SED at spring visits (March–April, May–June) and 25(OH)D were stronger if offset by one visit. SED March–April with 25(OH)D March–April $r = 0.125$ (NS) and with 25(OH)D May–June $r = 0.208$ ($p = 0.046$); SED May–June with 25(OH)D May–June $r = 0.212$ ($p = 0.046$) and with 25(OH)D July–August $r = 0.248$ ($p = 0.020$); SED July–August with 25(OH)D July–August $r = 0.281$ ($p = 0.007$) and with 25(OH)D September–October $r = 0.268$ ($p = 0.011$); SED September–October with 25(OH)D September–October $r = 0.199$ ($p = 0.060$) and with 25(OH)D November–December $r = 0.130$ (NS)

Box 2 Measurement of sunlight exposure

Sunlight is measured in SEDs, where 1 SED is equivalent to 100 J m^{-2} UV radiation. The MED is the dose that causes erythema or pinkness.

This will differ according to individual, whereas SED is a standard measurement. For light-skinned Caucasians 1 MED is 2–3 SED.

Skin color is measured by light reflectance using specific color axes according to the CIE- $L^*a^*b^*$ system. Measurement of dark–light is represented by the L -axis, red–green by the a -axis, and blue–yellow by the b -axis. Although some researchers only use the dark–light measurement as an indication of change in pigmentation, the cosmetic industry and other researchers use a combination of the L - and b -axes for measuring melanin pigment, which is defined as the individual topology angle (ITA). The formula is $\text{ITA} = [\text{Arctangent}(L^*-50)/b^*] \times 180/\pi$; the larger the ITA, the lighter the skin color [18].

the time of year was not given. More recently, it was found that following a 30-day submersion exercise, 25(OH)D levels decreased significantly by $9.8 \pm 1.8 \text{ nmol/L}$ (from 62.5 ± 18.3 to $54.3 \pm 13.5 \text{ nmol/L}$, $p < 0.0005$) [38]. Using these data, the half-life of 25(OH)D would be 4.4 months.

During winter in Antarctica, there is no light available to make vitamin D. A small study ($n = 55$, with 18–19 subjects in each treatment group) carried out during the Antarctic winter showed that, with a starting point of 44 nmol/L , mean (SD) 25(OH)D increased to 57 (15), 63 (25), and 71 (23) nmol/L , respectively, with 400, 1,000, and 2,000 IU daily vitamin D for 5 months [39]. A similar study reported on 110 Antarctic expeditioners (mainly males) divided into three groups, with a mean starting 25(OH)D of between 55 (SD 14) and 63 (SD 12) nmol/L . It found (1) a single dose of 50,000 IU every month (equivalent to 1,600 IU/day) increased 25(OH)D by 7 nmol/L , (2) 50,000 IU every other month (800 IU/day) was sufficient to maintain circulating 25(OH)D, but (3) a single dose of 50,000 IU prior to departure (equivalent to 100 IU/day) was inadequate (as 25(OH)D decreased by 8 nmol/L) [40]. Populations living in the high latitude of the Arctic are also at risk of vitamin D deficiency [41].

At the opposite end of the spectrum, a study which is often quoted in support of higher circulating 25(OH)D involved eight lifeguards whose weekly average sunlight exposure was 53 (SD 10) hours with a mean 25(OH)D of 161 (SD 22) nmol/L [42]. This compared with an average 25(OH)D of 68 (SD 30) nmol/L in 40 normal volunteers, whose weekly sunlight exposure was 9 (SD 6) hours. Other populations that have more sunlight exposure include those with traditional lifestyles in Tanzania, who spend most of the day outside [43] and whose mean 25(OH)D was 115 nmol/L (range 58–171). High circulating 25(OH)D has been reported in the Gambia and South Africa, but in some areas of Africa there is vitamin D deficiency, illustrating the diversity of population lifestyles across the continent [44]. In a Hawaiian study, half the adults living an outdoor lifestyle with mean weekly sunlight exposures of 28.9 (SD 1.5) hours ($n = 93$) failed to reach circulating concentrations of 75 nmol/L 25(OH)D [45]. Mean 25(OH)D was 79 nmol/L , 10 % were below 50 nmol/L , and the maximum recorded

was 155 nmol/L . The weekly exposure without any sunscreen was 22.4 (SD 1.6) hours.

Other Factors

There is a clear genetic component to vitamin D status, even within race [46]. Variants in D-binding protein [47, 48] and cytochrome P-450 enzymes (CYP2R1 and CYP27B1) which are involved in the hydroxylation of vitamin D have been implicated [49, 50]. Obesity and diseases which affect vitamin D metabolism will also impact on vitamin D status. There have been several reports that obesity is linked to lower 25(OH)D [36, 51, 52]. One-year supplementation of adults over 65 years of age ($n = 275$) with vitamin D and calcium showed that the increase in 25(OH)D was inversely associated with body mass index (BMI); and in a longitudinal study of women in Scotland ($n = 314$), 25(OH)D was less for those in the highest quartile of BMI in spring, summer, and autumn [27], indicating that 25(OH)D is lower whether the source of vitamin D is oral or sunlight. It is suggested that adipose tissue may act as a sink for vitamin D, making it less accessible [52]. Others have suggested that obesity is associated with increased requirements for vitamin D [53] or that low vitamin D may even predispose to obesity [54].

As adipose tissue is also indicated as a storage depot of vitamin D that can be used to meet winter requirements for people living at high latitudes, there is some inconsistency in the message. Recent data from obese patients who underwent surgical bypass ($n = 17$) showed that despite a mean weight loss at 12 months of 54.8 kg, there was no increase in 25(OH)D (baseline 57.8 [SD 31.5] nmol/L ; 12 months 65.5 [SD 13.6] nmol/L) [55]. The authors suggest that because the breakdown of adipose tissue (estimated from fat biopsies to contain $297.2 \pm 727.7 \text{ mg}$ total vitamin D/kg of tissue) does not add to 25(OH)D, it is not an important source of vitamin D. The patients were supplemented with 2,500 IU/day throughout the study. Others suggest that the reason for continued low vitamin D status in these patients, despite being supplemented with vitamin D, is that they suffer from calcium malabsorption as a result of the bypass and that vitamin D and calcium metabolism are abnormally altered [56].

A recent report suggests that the phenomenon of low vitamin D status in obesity is simply a dilution effect [57].

Seasonal Variation

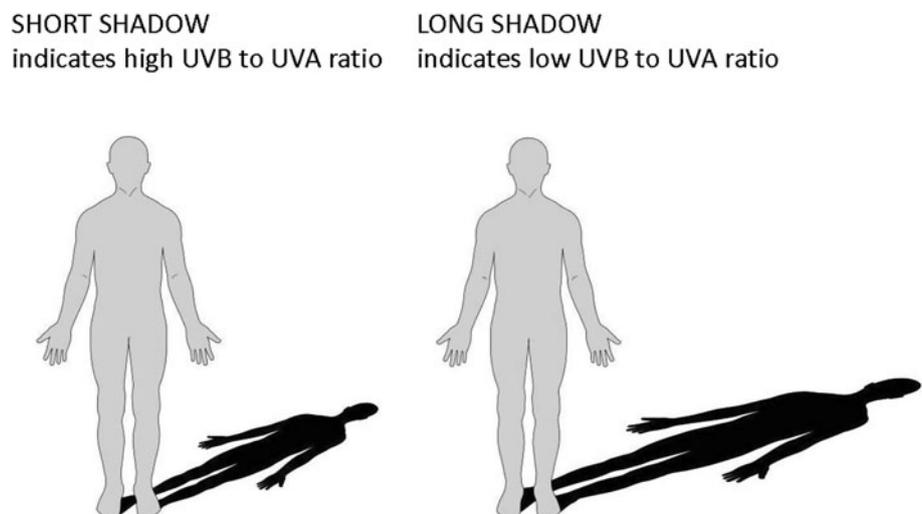
It is well documented that UVB radiation and, hence, vitamin D status vary according to season, depending on latitudinal position [58]. The action spectra for vitamin D and erythema overlap, but the spectrum continues into the UVA region for erythema, whereas there is a sharp cut-off at 315 nm for vitamin D. This means that measurements such as the UV index do not exactly match with vitamin D synthesis. It also means that as far as the risks and benefits of sunlight exposure are concerned, a few minutes' exposure in the middle of the day, when the UVB/UVA ratio is at its highest for vitamin D synthesis, may be preferable to prolonged exposure at other times of the day since the latter carries an increased risk of skin cancer [59] and UVA also degrades vitamin D [60] (Fig. 4). In addition, there is a lag between seasonal increases in sunlight exposure and 25(OH)D. Studies in Aberdeen showed SED increases from April to May but no increase in 25(OH)D until June; similarly, 25(OH)D remained high in October when SED had substantially decreased [27, 61].

Differences in 25(OH)D according to latitudinal position have been observed within countries [62, 63]. Diffey [12] modeled the seasonal variation in 25(OH)D using data from the 1959 birth cohort [63]. He suggested that sun exposure accounts for "20 % of overall serum 25(OH)D in winter and around 50 % during the winter" (presumably the latter "winter" is an error and refers to summer). This means that diet would contribute more than previously estimated. He assumed a constant value of 33 nmol/L 25(OH)D throughout the year, which he attributed to nonsolar factors. These may be partly genetic. In the Framingham study heritability accounted for 29 % of the variability in 25(OH)D [64].

Consistency in 25(OH)D measured at different seasons has been noted in other studies [27, 65]. We know that diet contributes only a small amount of vitamin D, so based on this, either our estimates of dietary vitamin D are too low or tissue stores of vitamin D make an important contribution (and the stored vitamin D may have originated from diet or sunlight). There is uncertainty about how much vitamin D is stored and whether this is accessible for future use. Heaney et al. [66] showed that daily oral vitamin D supplements of 500 IU were sufficient to maintain 25(OH)D at 70 nmol/L in men during winter. If diet were to add another 200 IU, the total would provide enough for 12 nmol/L 25(OH)D. On this basis they estimated that tissue stores would need to contribute 3,400 IU (85 µg)/day. An alternative interpretation of these data is that if daily vitamin D usage was equivalent to 12 nmol/L 25(OH)D (i.e., 700 IU oral vitamin D), the vitamin D intake would be equal to its expenditure and tissue stores would not be required. The group showed that at normal vitamin D intakes 25(OH)D is the dominant metabolite but with large, supraphysiological doses of vitamin D the native, nonmetabolized vitamin D would accumulate and could be added to tissue stores [67]. However, later estimates based on data from pigs [68] suggest that the total body store of vitamin D is small, and even at daily intakes of 2,000 IU, it probably only supplies a week's reserve of the vitamin [69]. As the reported half-life of 25(OH)D is much shorter than the periods where UVB is unavailable, it is unclear how people living at high latitudes, without adequate sunlight for months every year, manage to keep their 25(OH)D from reaching dangerously low concentrations. We have shown consistency between mean 25(OH)D in early spring 2006, 2007, and 2008, despite a poor summer in 2007 [61].

Although there was clear seasonal variation in 25(OH)D₃ (from 40.8 [SD 17.5] nmol/L in late winter to 78.0 [SD 21.3] nmol/L in early autumn), no seasonal variation in

Fig. 4 *Short shadow* requires a short time to make vitamin D (still taking care not to burn). Overall less UV exposure = less cancer risk. *Long shadow* requires a longer time to make vitamin D. Overall more UV exposure = more cancer risk



1,25(OH)₂D (the active form of the vitamin) was observed [70]. The authors comment that this shows the tight homeostatic control of 1,25(OH)₂D.

Studies of Sunlight and Vitamin D

Subliminal UV given over a period of 56–72 weeks increased 25(OH)D in nursing home residents, who had their faces and hands exposed. When given the equivalent of 15 min summer sun exposure a day, mean 25(OH)D had increased from 14 to 25.1 nmol/L in 12–24 weeks. For the latter part of the study, the equivalent of 30-minute exposure was given and the final mean 25(OH)D was 36 nmol/L [71]. The residents had the equivalent of 100–200 SED in a year as a result of the subliminal UV exposure, similar to that received by indoor workers in Denmark (going outside at weekends) [30, 72] and women living in North of Scotland [33]. Another study of female nursing home patients ($n = 45$) gave UV radiation (0.5 minimal erythral dose (MED)) directly to the lower back 3 times a week for 12 weeks, which resulted in a much larger increase in 25(OH)D, from a median of 18 nmol/L to 60 nmol/L [73].

Rhodes et al. [74] gave the equivalent of 30 min summer sunshine three times a week for 6 weeks during winter to 109 Caucasian adults (age 20–60 years) living in the north of England. Dressed in T-shirts and shorts their 25(OH)D increased from a mean of 44–70 nmol/L so that 90 % were above 50 nmol/L. One-quarter of their population would have 25(OH)D >75 nmol/L. They similarly treated a south Asian group living in the same region ($n = 15$) and found a much smaller increase in 25(OH)D (10.8 compared to 26.3 nmol/L increase in whites). The mean 25(OH)D in the south Asian group was 16 (SD 4.8) nmol/L at the start and 26.8 (SD 6.5) nmol/L after the treatment; the minimum had increased from 6.8 to 14.5 nmol/L and the maximum from 27.5 to 37.0 nmol/L. Although the treatment had ensured that the subjects below 12.5 nmol/L 25(OH)D had increased to above this value, none of the South Asian subjects reached 25(OH)D >50 nmol/L.

When UV was given to women as sessions of narrow band-UVB over 7 days, with a cumulative dose of 13 SED, 25(OH)D was shown to increase by 11.4 nmol/L when applied to the whole-body ($n = 19$); 11.0 nmol/L when applied to the face and arms ($n = 9$); and 4 nmol/L when applied only to the abdomen ($n = 14$) [75]. The study was performed in winter in Finland, with a mean starting 25(OH)D for each study group of between 35 and 44 nmol/L. Using broader wavelengths that mimicked solar radiation, the increase in 25(OH)D was 3.8 nmol/L when the radiation was applied to the face and arms ($n = 11$) [75]. When dermatology outpatients in Aberdeen (57°N) were given narrow band-UVB as treatment for skin conditions, the starting 25(OH)D increased from a mean 34 (SD 17) nmol/L to 78 (SD 19) nmol/L over 4 weeks [76]. The

median UV dosage of 39 SED was equivalent to a quarter of the sunlight dose obtained by an Aberdeen population during spring/summer [33] and would be achievable by most people.

A total of 13 days in the Canary Islands as heliotherapy treatment for atopic dermatitis ($n = 21$) in 2005 resulted in mean sunlight exposures of 75 SED in January and 131 SED in March, which corresponded to a mean increase in 25(OH)D of 9.7 (SD 12.0) and 26.0 (SD 18.7) nmol/L, respectively. It is clear that holidays abroad contribute to UV radiation exposure. For Danish indoor workers who wore time-stamped dosimeters for estimation of UV radiation exposure it was found that those who went on holiday for a median of 7 days received 26 SED [72]. Also, a total of 70 SED received by a subject in 14 days in Mexico in February or in Greece in October equals the total annual UV dose for subjects with low UV exposure. Holidays abroad also affected the vitamin D status of women living in the north of Scotland [36].

How Much from Diet?

The few foods that contain vitamin D include oily or fatty fish and eggs (egg yolk). In the United Kingdom, margarine is fortified (mandatory for hard margarines, and voluntarily by food manufacturers for other spreadable fats) [77] whereas milk is fortified in the US and parts of northern Europe. Some breakfast cereals are also fortified with vitamin D. The UK recommend 400 IU a day for groups at risk of deficiency because of limited sun exposure (the elderly, people who do not go outside or cover up, pregnant and lactating women) [77, 78]. It is recognised that these intakes will not be met by most people and can only be guaranteed by taking a supplement [78].

Although the diet can provide vitamin D as vitamin D₃ (cholecalciferol) and vitamin D₂ (ergocalciferol) it is vitamin D₃ that dominates. Vitamin D₂ is of particular importance when considering ergocalciferol supplements. There has been debate about the efficacy of vitamin D₂ compared to vitamin D₃ [79, 80]. A recent study found that vitamins D₂ and D₃ were equally bioavailable either from fortified orange juice or capsules [81] but differences found between vitamins D₂ and D₃ in the subcutaneous fat and circulation, with 50,000 IU weekly supplementation for 12 weeks, suggest that the vitamin D₃ is more effective [82]. This was also the conclusion reached by a recent meta-analysis although there was no significant difference between vitamin D₂ and vitamin D₃ when given daily, only when given as a large bolus [83].

The UK National Diet and Nutrition Survey (NDNS) data show intakes of 4.2 μg (170 IU) for men and 3.7 μg (150 IU) for women. For older adults, fish accounted for most of the vitamin D intake, followed by cereals (with fortified breakfast cereals), meat and fat spreads [84]. For

younger adults (19–24 years) it was meat that was the major contributor. In the UK meat can account for 10 % or more of vitamin D intake. This is partly because a potency factor has been included, which was added to food composition tables in 1995 and 1996, to include metabolites of vitamin D that are found in meat [77]. Using older databases without the potency factor the contribution from meat would be much lower (1 %) [85].

Other countries that fortify milk, e.g., the United States, find that milk has a greater contribution [86]. Fortification of milk in Finland, which started in 2003, was shown to have increased 25(OH)D in 65 men by 20 %, (the median increase in 25-OHD was 3.0 nmol/L overall and 9.5 nmol/L for the high milk-intake groups) [87]. U.S. intakes are 8.12 µg (330 IU) for men and 7.33 µg (290 IU) for women. The average intakes of around 6–7 µg (240–280 IU) a day are dominated by fish intake in Japan; and primarily dietary supplements and secondarily fish, in Norway [86].

Data from our own studies show that the main source of vitamin D is fish (Table 2) and fat spreads (which are fortified with vitamin D). Dairy produce (which includes eggs) contributed around 15 % of dietary vitamin D. Although the cereal food group apparently accounts for one-fifth of the vitamin D intake, this is a result of the fat contained in cakes, biscuits and pastries, and the vitamin D coming from fortified breakfast cereals. Again, this table illustrates the effect of adding the potency factor for meat.

The use of dietary supplements including cod liver oil also contributes to vitamin D intakes in the United Kingdom. The NDNS showed that overall mean daily intakes were 5.1 µg (200 IU), but without the addition of dietary supplements it was only 3.5 µg (140 IU) [84]. For free-living older people (>65 years) in NDNS, the cross-sectional associations between dietary vitamin D (which included vitamin D from supplements) and 25(OH)D were significant for the spring, autumn and winter waves of recruitment but not for the summer [88]. In early post-menopausal women living North of Scotland, where 16 % took cod liver oil supplements, dietary vitamin D alone was associated with 25(OH)D in spring and winter; but when including the contribution from supplements, the association was significant for all seasons [36]. A cod liver oil capsule usually provides 5 µg or 200 IU vitamin D in addition to *n* – 3 fatty acids and vitamin A. The latter, as preformed retinol, is thought to be detrimental to bone health but the Aberdeen Prospective Osteoporosis Screening Study showed cod liver oil to be beneficial, and it was only retinol intake from foods that was detrimental to bone [36]. Supplements can increase 25(OH)D in pregnant women. At their first antenatal visit 80 out of 160 women who were from a non-European ethnic minority population living in South Wales were found to have 25(OH)D <20 nmol/L. The 80 women were given supplements and of the 58 that were retested at delivery, mean 25(OH)D had increased from 15 to 27.5 nmol/L [89].

Table 2 Contribution of foods to vitamin D intakes

	NDNS		APOSS		ANSAViD			
	Men age 50–64 years	Women age 50–64 years	FFQ	FFQ	FFQ spring McCW v5	FFQ spring McCW v6	Food diary Summer	Food diary Winter
			McCW v5	McCW v6				
Vitamin D intake (µg/day)	4.2	3.5	4.2	3.8	4.4	3.9	2.9	2.7
Food contribution (%)								
Meat	20	15	1.6	12.8	1.6	11.9	21.0	24.1
Fish	28	37	37.7	31.5	50.0	41.6	26.6	23.5
Dairy/eggs			17.0	16.9	14.6	15.2	20.2	18.5
Fruit/vegetables			0	0	0	0	0.9	2.1
Cereals/pasta/bread	17	22	10.0	14.7	9.0	13.6	22.6	22.2
Biscuits/cakes/confectionery			8.6	7.4	7.9	6.8	2.7	3.7
Spreadable fats	18	13	23.1	16.0	15.0	10.3	3.3	4.0
Miscellaneous			2.0	0.7	1.9	0.6	2.7	1.9
Other	16	14						

NDNS UK National Diet and Nutrition Survey [73] used weighed food records and food composition database similar to McCance and Widdowson's Composition of Foods version 6, APOSS Aberdeen Prospective Osteoporosis Screening Study [46] and ANSAViD aberdeen nutrition sunlight and vitamin D study [26, 32] were analysed using McCance and Widdowson's Composition of Foods versions 5 and 6. Food diaries were analyzed by Windiets (Robert Gordon's, University, Aberdeen) using McCance and Widdowson's Composition of Foods version 6 *McCW v5* McCance and Widdowson's Composition of Foods version 5, *McCW v6* McCance and Widdowson's Composition of Foods version 6

An intervention study carried out during the winter in Ireland ($n = 221$) used different daily amounts of vitamin D supplementation (5, 10, and 15 μg) and a placebo group. The results were analyzed to estimate the vitamin D intake required to keep 25(OH)D above 25 nmol/L over winter. A healthy adult who regularly enjoyed sunlight exposure in the summer would require daily vitamin D intakes of 7.2 μg (290 IU), whereas someone who avoided the sun would need 12.3 μg (490 IU) [90]. Similar estimates for those over 64 years were 7.9 μg (320 IU) and 11.4 μg (460 IU), respectively [91]. The required amounts would be much greater if the deficiency cut-off were made higher.

Although it is understood that the 25(OH)D increase per unit of supplemental vitamin D may depend on the original starting 25(OH)D (the lower the starting point, the higher the increase in 25(OH)D), and that smaller incremental increases in 25(OH)D will be seen with increasing doses of vitamin D, there are differences across studies. These may be explained partly by the assay method used for 25(OH)D [92]. A meta-analysis of different studies showed the average slope of the relationship between vitamin D intake and 25(OH)D increase was 2.2 nmol/L/ μg vitamin D [93]. For the Irish study, described above, the slope was 1.96 nmol/L/ μg with a starting 25(OH)D of 70.3 nmol/L. With a similar starting 25(OH)D concentration of 70 nmol/L in October, a slope of 0.70 nmol/L/ μg was found across a wide range of vitamin D intakes (0–250 μg) given to men ($n = 67$) during winter in Omaha, US [66]. The increase seen in older nursing home patients ($n = 15$, starting 25(OH)D 18 nmol/L) given 10 μg (400 IU) vitamin D a day [94] was estimated by Heaney to give a slope of 5.5 nmol/L/ μg [66]. In another study, in Toronto, Canada ($n = 61$) the estimated slope was 1.15 nmol/L/ μg for 25 μg (1,000 IU); and 0.56 nmol/L/ μg for 100 μg (4,000 IU) vitamin D a day [95]. The mean starting 25(OH)D was 43.3 and 37.9 nmol/L, respectively. As the latter study started in January/February, and continued for 2–5 months there may be some confounding from ambient UV radiation. A 1-year vitamin D dosing study, which tested 400, 800, 1,600, 2,400, 3,200, 4,000, and 4,800 IU vitamin D in Caucasian postmenopausal women living in Omaha, Nebraska (41°N) with mean starting 25(OH)D of 39 nmol/L showed a quadratic response curve, with a plateau at 112 nmol/L [96]. The model predicted that 600 IU vitamin D would be sufficient for 97.5 % of the population to achieve 50 nmol/L 25(OH)D. The actual data for mean and range of 25(OH)D achieved for each dose were not provided; but using the prediction equation 400 and 800 IU vitamin D would result in 25(OH)D of 63.8 and 72.6 nmol/L, respectively; and starting at 38.9 nmol/L, the 25(OH)D increase per microgram of vitamin D would be 2.5 nmol/L for 400 IU, 1.7 nmol/L for 800 IU, and 1.2 nmol/L for 1,600 IU. The equation predicts that the reduction in increments of 25(OH)D with increasing dose

would continue so that for 4,800 IU the increase in 25(OH)D per μg vitamin D would be 0.6 nmol/L.

Optimal Vitamin D Status and Recommended Dietary Intakes of Vitamin D

What was considered optimal 25(OH)D has changed [97] and continues to change with different expert opinion [98]. Values that would have been considered adequate are now defined as deficient [97]. UK government advice was based on evidence that 25(OH)D can be maintained at satisfactory concentrations in winter, if summer concentrations are above 40 nmol/L [99]. However, what was considered satisfactory in the late 1970s (20 nmol/L), would be considered by many to be “at risk of vitamin D deficiency” today. Although there have been calls to raise both the 25(OH)D that defines deficiency, and the required intake in the population, as the many reported health benefits of vitamin D increase; the Food and Nutrition Board of the Institute of Medicine in the US ruled that the quality of evidence was insufficient to support these [4]. Their recommendations are that 400 IU/day is the estimated average requirement of vitamin D for people living in the United States and that 600 IU (800 IU for >70 years) would cover 95 % of the populations needs [4]. They also clarify that for defining deficiency according to 25(OH)D, individuals below 30 nmol/L would be at risk of deficiency; that 40 nmol/L would be an optimum population median; and that 50 nmol/L would cover most of the population in terms of benefit. This approach is similar to that used in the United Kingdom for defining nutritional recommendations: an estimated average requirement is sufficient for half the population; this value plus an additional 2 SD of the normal distribution (the reference nutrient intake) would cover 97.5 % of the populations requirements and subtracting 2 SD from the population mean would give the lower reference nutrient intake, a value below which, 97.5 % of the population would be considered deficient or be at risk of deficiency [100]. The UK Scientific Committee on Nutrition is similarly reviewing the evidence to reevaluate current vitamin D guidelines and consider whether further fortification of foods is necessary. The committee aims to report its findings in 2014.

The seasonal variation in 25(OH)D has led experts to advocate that wintertime supplementation may be required and the corollary is that we eliminate or minimize the variability in vitamin D status due to season at high latitudes. It is possible that populations living at high latitude have adapted to the short winter days, and to the complete absence of light in the wavelength range required to synthesize vitamin D, and these processes are interlinked. There are no published data on the potential interactions between changes in circadian rhythms (as a result of shortened

daylight hours) and vitamin D metabolism; and of any repercussions if this relationship is severed.

Diet and Sunlight

Global estimates of 25(OH)D show that vitamin D deficiency is of particular concern for young children, pregnant women, the elderly and immigrants [101]. The deficiency appears to be primarily linked with sun avoidance behavior, but diet may account for the better vitamin D status of Nordic countries [101, 102].

Based on Holick’s estimations [14], a few minutes sunlight a day can make 1,000 IU vitamin D, which is four times as much as 100 g (4 oz) of oily fish. It is suggested that sunlight accounts for 90 % of vitamin D and diet only 10 %, although this will vary, primarily according to location [58]. For most people, diet is a poor source of vitamin D. Population groups at risk of vitamin D deficiency include people who cover up or do not go outside. Sunlight exposure (estimated from sunlight badges, body surface exposed, and Holick’s assumption [14]) was the

major contributor to vitamin D in both the north and south of the United Kingdom, accounting for 80–90 % of the vitamin D received in summer [33] (Table 3). It follows on that people who do not get exposed to sunlight will be more likely to be at risk of vitamin D deficiency. This study highlighted the difference in vitamin D synthesis between the north and south of the United Kingdom, and the prevalence of low circulating 25(OH)D in Asian women living in the south of England (whose limited exposure to sunlight was compounded by poor vitamin D in the diet).

It is argued that because most of us do not spend the summer outside, we need much larger doses of vitamin D in our diet, either through fortified foods or taking dietary supplements [103]. A trial in pregnant women, in which daily doses of 2,000 and 4,000 IU of vitamin D were given (50 and 100 µg, respectively) [104] showed no adverse effects for mother or infant. However, it was noted that 25(OH)D for one woman in the 4,000 IU group had increased from 29.3 to 233.3 nmol/L within 1 month; and two others also had met “upper threshold levels” (>225 nmol/L) prior to delivery which was put down to recent sunbathing. Concerns have

Table 3 Estimates of vitamin D intake from diet and cutaneous (sunlight) sources

Region and season	n Sunlight estimate/n food diary	SED median/week (IQR)	Daily cutaneous (sunlight) and dietary vitamin D intake, median and interquartile range (IU)			
			Cutaneous source ^a	Dietary source	Total vitamin D	Cutaneous/total
Aberdeen (57°N): Caucasian						
Summer (Jun–Aug)	325/333	5.7 (7.1)	597 (1,271)	92 (84)	735 (1,274)	82 %
Autumn (Sep–Nov)	301/311	0.5 (1.6)	36 (154)	88 (75)	149 (200)	29 %
Winter (Dec–Feb)	306/309	0.3 (0.4)	16 (21)	93 (74)	120 (97)	15 %
Spring (Mar–May)	301/293	2.5 (4.0)	190 (339)	97 (91)	316 (368)	66 %
Overall						70 %
Surrey (51°N): Caucasian						
Summer (Jun–Aug)	89/133	8.7 (9.0)	1,558 (1,811)	100 (107)	1,608 (1,849)	94 %
Autumn (Sep–Nov)	97/130	0.7 (1.6)	49 (120)	82 (108)	90 (130)	38 %
Winter (Dec–Feb)	117/124	0.2 (0.4)	16 (29)	86 (108)	55 (57)	15 %
Spring (Mar–May)	104/121	4.0 (4.7)	315 (419)	84 (99)	363 (434)	79 %
Overall						85 %
Surrey (51°N): Asian						
Summer (Jun–Aug)	6/27	1.7 (3.1)	72 (748)	56 (40)	92 (245)	56 %
Autumn (Sep–Nov)	20/30	0.2 (0.5)	13 (56)	48 (74)	37 (50)	21 %
Winter (Dec–Feb)	18/27	0.4 (0.5)	29 (43)	59 (71)	51 (66)	32 %
Spring (Mar–May)	18/22	2.7 (4.7)	203 (557)	64 (110)	213 (706)	76 %
Overall						58 %

^a Estimated from (SED, from dosimeters) and body surface area exposed (from sunlight exposure diaries: Aberdeen daily, Surrey extrapolated from 1 week per visit) using the following conversion: 5,000 IU vitamin D is obtained from 1 SED of sunlight (equivalent to 0.5 MED for pale skin). Individual body surface exposure was used in the calculations (face only 5 %; face and hands 10 %; face, hands, plus arms or legs 25 %; and including some or all of the trunk 60 %). It has been suggested that 1,000 IU vitamin D is generated by exposing 25 % body surface area to sunlight equivalent to 0.25 MED. This is a conservative estimate based on total body exposure to 1 MED sunlight providing 10,000–25,000 IU vitamin D [16]. There will be an overestimate of IU from UVB in the Asian group if skin color is dark. Reproduced with permission from Macdonald et al. [33]

Box 3 Questions

How much sun is needed for vitamin D and minimal skin cancer risk?

How much vitamin D in the diet is bioavailable?

How long do vitamin D stores last and are they accessible?

Are there toxic effects besides hypercalcemia and hypercalciuria?

been raised that the long-term effects of high-dose supplementation are not known. Nevertheless, it is clear that many women who are pregnant or lactating are deficient in vitamin D, and do not know that supplements are advised if they are not getting enough vitamin D. In the United Kingdom the recommended intake would be 400 IU or 10 µg. Whether much higher doses are required is still the subject of debate.

Conclusions

It is clear that sunlight is important for vitamin D synthesis, although it remains a challenge to recommend the appropriate exposure to make sufficient vitamin D and minimize skin cancer risk. For those who do not get any sunlight, there continues to be uncertainty about the optimal dose and whether this differs according to population group or geographical location. There are still gaps in our knowledge. If we start recommending high vitamin D intakes that require further fortification or supplementation on a national or international scale we have to be sure that we are fully aware of potential adverse outcomes, particularly in subgroups of the population that may be at increased risk of toxicity (see Box 3).

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