Sunscreen photoprotection and vitamin D status

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Summary

Background Global concern about vitamin D deficiency has fuelled debates on photoprotection and the importance of solar exposure to meet vitamin D requirements.

Objectives To review the published evidence to reach a consensus on the influence of photoprotection by sunscreens on vitamin D status, considering other relevant factors.

Methods An international panel of 13 experts in endocrinology, dermatology, photobiology, epidemiology and biological anthropology reviewed the literature prior to a 1-day meeting in June 2017, during which the evidence was discussed. Methods of assessment and determining factors of vitamin D status, and public health perspectives were examined and consequences of sun exposure and the effects of photoprotection were assessed.

Results A serum level of ≥ 50 nmol L⁻¹ 25(OH)D is a target for all individuals. Broad-spectrum sunscreens that prevent erythema are unlikely to compromise vitamin D status in healthy populations. Vitamin D screening should be restricted to those at risk of hypovitaminosis, such as patients with photosensitivity disorders, who require rigorous photoprotection. Screening and supplementation are advised for this group.

Conclusions Sunscreen use for daily and recreational photoprotection does not compromise vitamin D synthesis, even when applied under optimal conditions.

What’s already known about this topic?

- Knowledge of the relationship between solar exposure behaviour, sunscreen use and vitamin D is important for public health but there is confusion about optimal vitamin D status and the safest way to achieve this.
- Practical recommendations on the potential impact of daily and/or recreational sunscreens on vitamin D status are lacking for healthy people.
The prevention of rickets and osteoporosis by vitamin D has long been established. More recently, vitamin D has been implicated in many metabolic and immunological disorders as well as many cancers. Its pleiotropic activity may be mediated by modulation of ~1000 genes via the vitamin D receptor (VDR), which is expressed by at least 60 human cell types. The VDR controls many cellular functions including growth, differentiation and apoptosis. However, the role of vitamin D in the prevention of nonskeletal diseases remains highly controversial.

Terrestrial ultraviolet radiation (UVR) is the main determinant of vitamin D status. Stratospheric ozone absorbs all solar UVC (100–280 nm), attenuates UVB (280–315 nm) but not UVA (315–400 nm). The sun’s height determines the UVR pathlength through the ozone layer. Thus, UVI intensity (irradiance) depends mainly on latitude, season and time of day. The ratio of UVA to UBV also varies with the sun’s height because of the differential effect of the ozone layer. Thus, terrestrial UVR typically contains ≤5% UBV (~295–315 nm) and ≥95% UVA.

The minor UBV component is responsible for vitamin D synthesis, the initiating event of which is the isomerization of the epidermal chromophore (a UVR-absorbing molecule) 7-dehydrocholesterol (7-DHC) into pre-vitamin D3, which is thermally converted into cholecalciferol (vitamin D3). Pre-vitamin D3 enters the circulation via the vitamin D binding protein (DBP) and is hydroxylated into 25-hydroxyvitamin D3 [25(OH)D3] in the liver [by vitamin D3–25-hydroxylase (CYP2R1)], and then in the kidney [by 25(OH)D3–1α-hydroxylase (CYP27B1)] to 1,25-dihydroxyvitamin D3 [1,25(OH)2D3], the active form of vitamin D (calcitriol), which in fact is a hormone. However, many tissues including the skin also contain both hydroxylases for the synthesis of calcitriol.

Multiple intrinsic and extrinsic factors modulate vitamin D synthesis and overall status, including genetic polymorphisms, age, geographical location, sun exposure behaviour, UVB dose, clothing, body surface area (BSA) exposed. These are summarized in Figure 1 and Appendix S1 (see Supporting Information). Vitamin D3 may also be obtained from supplementation and/or animal-based foods (e.g. oily fish) and undergoes the same hydroxylations. Alternatively, vitamin D3 from non-natural dietary intake (e.g. mushrooms), is hydroxylated into 25(OH)D3 and then converted into 1,25(OH)2D3 (ergocalciferol). However, in general, intake from diet is low. For example, food intake in the U.S.A. between 2005 and 2006 in 19–30-year-old males and females was 204 IU ± 12 (5·1 μg) and 144 IU ± 12 (3·6 μg), respectively, which represents 34% and 24% of the recommended dietary allowance (RDA).

Solar UVR has many adverse effects, the most obvious of which is sunburn (erythema). The World Health Organization has defined the global solar UV index (UVI) (http://www.who.int/uv/publications/en/UVIGuide.pdf) to allow comparisons of erythemal potential at various geographical locations (latitudes), seasons and times of day. This is a numerical index of the erythemally weighted irradiance of terrestrial UVR. It is divided into five bands: ‘low’ (1–2), ‘moderate’ (3–5), ‘high’ (6–7), ‘very high’ (8–10) and ‘extreme’ (≥11). The UVI is primarily an index of UVB irradiance because this spectral region is the main cause of erythema (see Conclusions and recommendations: Spectral considerations: Ultraviolet B, below) and sun protection is advised when the UVI is ≥3.

Global concern about vitamin D deficiency has fuelled debates on the importance of solar exposure to meet vitamin D requirements. The acute and chronic health benefits of using sunscreens are established but there has been concern about their possible impact on vitamin D status. An international panel was tasked to review the published evidence to reach a consensus on the influence of photoprotection by sunscreens on vitamin D status, considering other relevant factors.

Methods

The panel comprised experts from diverse disciplines including vitamin D, endocrinology, dermatology, photoprotection, experimental photobiology, epidemiology and anthropology. Panel members made a comprehensive search of literature published from January 1996 to May 2017, using the Scopus database, with the following search term categories individually and in combination: vitamin D, status, level, values, deficiency, measurement, assay, dosage, evaluation, polymorphisms, genetics, diet, phenotype, pigmentation, lifestyle, location, latitude, sun, UV, UVR, ultraviolet, health, diseases, sunscreen, photoprotection or sun protection. Members of the panel used
their specific areas of expertise to identify relevant papers and presented and discussed their results at a meeting in Paris in June 2017. The panel discussion was recorded by a scientific writer and used as the basis of the manuscript. Additional references were included during the writing process. This article summarizes the consensus and provides clinical recommendations in terms of photoprotection in order to ensure optimal vitamin D status.

**Conclusions and recommendations from panel discussions**

**What is optimal vitamin D status and the best method to determine it?**

Serum 25(OH)D is the best indicator of vitamin D status but there is no international consensus on its optimal value, with recommendations varying from 25 nmol L\(^{-1}\) to >100 nmol L\(^{-1}\). Figure 2 summarizes the definitions of vitamin D status by various international bodies. The most widely held consensus for the boundary between insufficiency and sufficiency is 50 nmol L\(^{-1}\). According to the Institute of Medicine (IOM), a serum concentration of 50 nmol L\(^{-1}\) 25(OH)D meets or exceeds the requirement of 97.5% of the U.S. population, but it is not possible to specify desired individual status. The determination of vitamin D status is discussed in Appendix S2 (see Supporting Information).

**Public health perspectives**

Hypovitaminosis D is prevalent globally. A systematic review covering 168,000 people from 44 countries reported serum 25(OH)D < 50 nmol L\(^{-1}\) in 37% of studies. This was mainly in the Middle East and Asia.

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**Fig 1.** Factors that affect the synthesis of vitamin D₃. Many factors determine vitamin D₃ production. The most important external factor is UVB dose, which is the product of UVB intensity (irradiance) and exposure time. Cutaneous pre-vitamin D₃ is synthesized from 7-dehydrocholesterol after UVB exposure. Thermally converted into vitamin D₃, it then binds to vitamin D binding protein (DBP) in the blood to be activated sequentially by the liver and kidney. Cytochrome P450 (CYP) enzymes are crucial for the synthesis of biologically active vitamin D₃ (calcitriol), which binds to intracellular vitamin D receptor (VDR) in most cells in the body. Adapted from Jolliffe et al. More details of these factors are given in the Supporting Information. BSA, body surface area; RXR, retinoid X receptor; VDRE, vitamin D response element.

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Despite high insolation, emphasizing the importance of human behaviour.

Medical conditions and treatments with high risk of vitamin D deficiency are summarized in Table S1 (see Supporting Information). Concern about vitamin D status has resulted in increased screening with financial consequences. Clinical practice guidelines from the Endocrine Society advise screening only for those at risk of deficiency. In France, the Research and Information Group on Osteoporosis (GRIO) recommends systematic vitamin D supplementation without screening in everyone over 65 years.

Disagreement on recommended doses for vitamin D supplementation arises, in part, from discrepancies of opinion on optimal serum 25(OH)D levels. The doses recommended for supplementation are discussed in Appendix S2 (see Supporting Information), but in case of deficiency, vitamin D supplementation should be 600–800 IU (15–20 µg) daily [but 400 IU (10 µg) in those less than 1-year-old] to achieve at least a target serum level of 50 nmol L⁻¹.

Sunscreens and sun protection indices

Sunscreens are topical formulations that contain chemicals that attenuate solar UVR. Global regulatory authorities have defined the sun protection factor (SPF) of a sunscreen as a universal quantitative index of protection against erythema, assessed after a single exposure of solar-simulated radiation (SSR; Fig. 3a). In effect, the SPF is the ratio of SSR dose necessary for a minimal erythema dose (MED) with and without sunscreen application. SPF should be the primary driver of sunscreen choice. These authorities also require UVA protection (see Spectral considerations: Ultraviolet A). A given sunscreen, applied according to prescribed SPF test conditions at 2 mg cm⁻², transmits 1/SPF of the erythemally effective UVR. One MED is equivalent to about three standard erythema doses (1 SED = 100 J m⁻² of erythemally weighted UVR) in a fair-skinned person. Thus, assuming a possible ambient exposure of 30 SED during a sunbathing session, the correct use of SPF 20 sunscreen will allow a suberythemal 1/5 SED to reach the skin. However, people typically apply very much less with a commensurate reduction of actual labelled SPF. For example, a study of Danes on holiday in Egypt reported a mean application thickness of 0.179 mg cm⁻². This paradoxically means that sunscreen use may be associated with sunburn as a result of more time in the sun. Additional protection factors have been proposed, such as immune protection factor, DNA protection factor and a protection factor for visible light.

The benefits of sunscreens in photoprotection strategies

The acute and chronic adverse effects of solar UVR, especially to those with fair skins, are well established and can be inhibited by effective sun protection. This includes (i) sun avoidance or seeking shade; (ii) clothing; and (iii) sunscreen use. When used optimally sunscreens can prevent erythema during a week-long holiday, even when the UVI is very high. Laboratory studies have shown that sunscreens can prevent UVR-induced immunosuppression and the formation of DNA damage [specifically cyclobutane pyrimidine dimers (CPD), the action spectrum of which is very similar to erythema].
CPD are thought to be important in many skin cancers. Those with cancer-prone fair skin are especially sensitive to CPD formation, whereas the higher melanin content in dark skin affords much better protection against CPD, especially in the basal layer.46–50 A recent study with a high SPF sunscreen and high-dose SSR for 5 consecutive days showed significant protection against CPD, even when the sunscreen was applied at 0.75 mg cm$^{-2}$ to simulate typical use.44 A large Norwegian cohort showed that sunscreen use reduced the risk of melanoma.51 Extensive randomized controlled trials in Australia, with long-term follow-up, have demonstrated the protective properties of a sunscreen against photoageing, melanoma and squamous cell carcinoma, but not basal cell carcinoma.52–56

Spectral considerations

Ultraviolet B Action spectroscopy shows that UVB is orders of magnitude more effective than UVA for erythema (see Fig. 3b$^{57,58}$).45 This means that the SPF is primarily, but not exclusively, a measure of UVB protection.31 Such protection is essential when UVB doses are high with recreational solar exposure, and in countries with high UVI.

Ultraviolet A There has been an increasing trend over recent years for better UVA protection, with the aim of designing the ideal ‘neutral density’ sunscreen with ‘spectral homeostasis’ that mimics shade, i.e. it does not distort the natural solar UVR spectrum.59 There is no global standard for UVA protection and requirements vary with regulatory domain.31 The U.S. Food and Drug Administration has recently proposed greater UVA protection.60 A UVA protection factor (UVA-PF) can be obtained using a sunscreen’s ability to inhibit persistent pigment darkening in vivo.61 Spectral approaches, based on UVB/UVA absorption ratios and bandwidth cover, give qualitative but not quantitative information on UVA protection.

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DNA repair enzymes. Increasing UVA protection for a high UVA-PF offer such protection (Table 1), compared with low UVA-PF, and that low SPF sunscreens with protection strategies, because good UVB protection, which inhibits sunburn, enables prolonged solar exposure and the accumulation of unnaturally high UVA doses. UVA1 (340–400 nm) preferentially induces CPD in the basal layer, which contains stem cells and melanocytes, as well as damaging DNA repair enzymes. Increasing UVA protection for a given SPF results in a de facto reduction of UVB protection, which might be expected to be beneficial for vitamin D synthesis.

Studies in vivo or in 3D skin models, have shown that for a given SPF a high UVA-PF sunscreen offers better protection against pigmentation, photaginge and DNA damage compared with low UVA-PF, and that low SPF sunscreens with high UVA-PF offer such protection (Table 1). One study, on a reconstructed skin model exposed to daily SSR, showed that a sunscreen with a lower SPF but strong UVA protection was more effective in preventing photodamage compared with a sunscreen with a higher SPF but low UVA protection. Thus, overall there seems to be biological and clinical advantages from increasing UVA protection for a given SPF.

### Does photoprotection by sunscreens have an influence on vitamin D status?

**Sunscreen use and vitamin D status**

Given that solar UVB is the main source of vitamin D, a possible adverse effect of sunscreen use on vitamin D synthesis has important public health implications. This has been studied using the different approaches described below. Reviews on sunscreen use and vitamin D synthesis have concluded that sunscreen use is likely to have minimal impact on vitamin D status, even though the action spectra (Fig. 3b) for erythema and pre-vitamin D show considerable UVB overlap. One reason suggested for this is suboptimal sunscreen application, which reduces its efficacy. However, little is known about the minimal UVB dose and exposed BSA requirements to maintain optimal vitamin D status.

Action spectroscopy shows that UVA protection will have no effect on vitamin D synthesis (Figs 3b, c), although one in vitro study has suggested that UVA2 (315–340 nm) may cause vitamin D degradation, in which case UVA protection may be beneficial for vitamin D production.

Laboratory and modelling studies have shown that serum 25(OH)D can be increased with repeated suberythemal UVR exposure, such doses can be as low as four exposures of

### Table 1 Daily photoprotection studies with solar type UVR sources and emphasis on impact of ultraviolet (UV) A protection; summary of main conclusions from laboratory photoprotection studies

| First author, year | Study model | Exposure | Sunscreen | Conclusion |
|--------------------|-------------|----------|-----------|------------|
| Young 2007 | Healthy volunteers FST I/II | Daily suberythemal SSR exposure (11 days) | Broad-spectrum SS: SPF 7.5 UVA 4* | Prevention of DNA damage, p53 accumulation and Langerhans cell depletion |
| Lejeune 2008 | 3D human skin models | DUVR® dose–response (0–90 J cm⁻²) | SS with SPF 15 but high and low UVA-PF with SPF/UVA-PF ratio ≤ 3 or > 3 | showed better prevention of dermal alterations |
| Seité 2010 | Healthy volunteers FST II/III | Daily suberythemal DUVR® exposure (19 days over 4 weeks) | Broad-spectrum SS: SPF 8 UVA-PF 7 UVA 3* | Prevention of p53-positive cells, melanin increase, loss of HLA-DR-positive cells and induction of dermal modifications (GAG) |
| Fournier 2012 | Asian (FST III) volunteers | DUVR® | SS with SPF 19, 30 and 50, each with high and low UVA-PF | Better inhibition of pigmentation (at 7 days) with high UVA-PF (SPF/UVA-PF ratio ≤ 3) |
| Marionnet 2012 | 3D human skin models | DUVR® exposure. 12 J cm⁻² | SS with SPF 13 and high UVA-PF (SPF/UVA-PF ratio ≤ 3) | Inhibition of gene expression for adverse effects of DUVR |

DUVR, daylight UVR; FST, Fitzpatrick skin type; GAG, glycosaminoglycans; HLA-DR, human leukocyte antigen – DR isotype; SPF, sun protection factor; SS, sunscreen; SSR, solar simulating radiation, UVA-PF, UV protection factor; UVR, ultraviolet radiation

*SPF/UVA-PF ratios from L’Oréal: ≤ 3, well-balanced UVB–UVA protection (according to EC requirements); > 3, unbalanced SS with low UVA protection.

UVA star (*) rating refers to a sunscreen’s UVA : UVB absorbance ratio (Boots star rating method). The higher the rating, the better the UVA protection with a maximal value of 5 (which represents a more or less neutral density sunscreen).

DUVR has a UVA/UVB ratio of ~ 27 (96.5% UVA, 3.5% UVB), which is more typical of temperate sunlight compared with SSR used for SPF testing.

The FST type is not given in Fourtianer et al., but those authors refer to a poster by Moyal, which gives further details.
| First author, year | Pathology and patients (a) | Follow-up | Location, latitude | Vit D intake | Photoprotection strategies | Vit D status/conclusions |
|--------------------|----------------------------|-----------|-------------------|--------------|---------------------------|--------------------------|
| Sollitto 1997⁸¹ | XP, n = 8 | 6 years | U.S.A.: all parts | 7.7 µg daily | SPF > 15 daily<br>Clothing, shade-seeking | Mean 25(OH)D: 44.5 nmol L⁻¹ |
| Quenings 2004⁸² | XP, n = 3<br>BCNS, n = 1 | End of winter | Germany: Homburg, 49° N | NA | Not specified | Mean 25(OH)D: 23.8 nmol L⁻¹ |
| Quenings 2006⁸³ | Patients with kidney transplant, n = 31<br>Controls, n = 31 | End of winter | Germany: Homburg, 49° N | NA | SS + clothing | Mean 25(OH)D: 27.3 nmol L⁻¹ vs. 50.0 nmol L⁻¹ in controls |
| Cusack 2008⁸⁴ | Cutaneous lupus erythematos, n = 52<br>FST I–IV | 3 months in summer | Ireland: Dublin, 53° N | 40-4% took minimum<br>10 µg daily | 4 groups: SS user<br>Shade seeker<br>Non-SS user<br>Non-shade seeker | 25(OH)D: 57.9 nmol L⁻¹<br>58.8 nmol L⁻¹<br>73.5 nmol L⁻¹<br>81.8 nmol L⁻¹ |
| Holme 2008⁸⁵ | Erythropoietic protoporphyria, n = 201<br>FST II–III | 7 months, January to July | U.K.: 51–57.5° N | 3 took fish liver oil daily | SPF 50⁺, 2 mg cm⁻² | 25(OH)D: 63% < 50 nmol L⁻¹<br>17% < 25 nmol L⁻¹. Note: these values are very high |
| Ulrich 2009⁸⁶ | Organ transplant recipients<br>Applied SS, n = 60<br>No SS, n = 60<br>FST I–IV | 2 years | Germany: Berlin, 53° N | NA | | 25(OH)D: lower in SS users (132.5 vs. 150.0 nmol L⁻¹). Note: these values are very high |
| DeLong 2010⁸⁷ | Skin cancer patients n = 143<br>FST I–II, 12 FST IV–VI, n = 144<br>FST I–IV | 2 years (September to December period) | U.S.A.: Atlanta, GA, 34° N | 94% < 10 µg daily<br>60% taking supplements | Adherent or no sun protection | Mean 25(OH)D: Adherent: 70 nmol L⁻¹ (18% < 50 nmol L⁻¹), Nonadherent: 73 nmol L⁻¹ (16% < 50 nmol L⁻¹) |
| Hoesl 2010⁸⁸ | XP, n = 15 | NA | Germany: Tubingen, 49° N | NA | Sun protection | Mean 25(OH)D: 27 nmol L⁻¹ |
| Tang 2010⁸⁹ | BCNS, n = 41<br>FST I–III | 2 years | U.S.A.: all parts | 34% daily<br>multivitamin | 80% used daily SPF > 15 daily | 25(OH)D: 56% with < 50 nmol L⁻¹ compared with 18% controls |
| Reid 2012⁹⁰ | Patients with photosensitivity, n = 165 (of which n = 35 with strict photoprotection)<br>n = 143 FST I–III, 12 FST IV–VI | 1 year | Scotland: Dundee, 56° N | Supplements used by 14 patients | None, sensible, strict | Mean 25(OH)D: 41.9 nmol L⁻¹<br>40% with < 50 nmol L⁻¹<br>25% with < 25 nmol L⁻¹<br>Supplementation associated with significantly higher 25(OH)D (57.5 vs. 39.5 nmol L⁻¹) Strict vs. sensible photoprotection |

(continued)
### Table 2 (continued)

| First author, year | Pathology and patients (n) | Follow-up | Location, latitude | Vit D intake | Photoprotection strategies | Vit D status/conclusions |
|--------------------|---------------------------|-----------|-------------------|--------------|---------------------------|--------------------------|
| Gentzsch 201491    | Gorlin (incl. multiple BCCs), NA Germany: Freiburg, 48°N | Supplementation initiated | SS + clothing and shade-seeking | 2 days for vit D intake | Mean dietary intake of 4 l day⁻¹ | Vit D associated with lower 25(OH)D₃ (33/4) vs. 42/1 nmol L⁻¹<br>Study initiated | <br>Vit D synthesis: <br>25(OH)D₃ median 56.8 nmol L⁻¹<br>Control: median 73.2 nmol L⁻¹ |
| Kuwabara 201592    | XP-A, n=21 Japan: Kobe, 35°N | Mean dietary intake | SPF>30 + clothing and has after study | 25(OH)D: 76% < 25 nmol L⁻¹<br>Japanese intake of 1 l day⁻¹<br>Mean 4 l day⁻¹ | SS + clothing and has | <br>Vit D synthesis: <br>Summer 25(OH)D₃: 8 ± 2 nmol L⁻¹<br>Mean 4 l day⁻¹ | <br>Summer 25(OH)D₃ synthesis: <br>8 ± 2 nmol L⁻¹<br>Japanese intake of 4 l day⁻¹<br>Mean 4 l day⁻¹ |
| Bogaczewicz 201693 | SLE: n=104, Controls: n=34 Poland: Lodz, 52°N | 16 weeks | SS + clothing and hats | After study | SS + clothing and hats | <br>Vit D synthesis: <br>25(OH)D₃ synthesis: <br>16 weeks<br>SS + clothing and hats | <br>Vit D synthesis: <br>25(OH)D₃ synthesis: <br>16 weeks<br>SS + clothing and hats |

25(OH)D₃: 25-hydroxyvitamin D₃, BCC, basal cell carcinoma; BCNS, basal cell naevus syndrome; ET, Fitzpatrick skin type; NA, data not available or not applicable; NHANES, National Health and Nutrition Examination Survey; SS, sunscreen; XP, xeroderma pigmentosum; vit, vitamin D.

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Sunscreen use and vitamin D status in patients with photosensitivity with strict photoprotection

Patients with genetic and acquired photosensitivity disorders, and those at risk of and/or with a history of skin cancer are advised to practice strict photoprotection, including sunscreen use. This population is an ideal group to assess the effects of rigorous photoprotection. Table 2 shows some of these conditions, in which patients present with low levels of 25(OH)D₃ except in the study of Ulrich et al. in which 25(OH)D₃ was >132-5 nmol L⁻¹ in 120 organ transplant recipients. However, it is impossible to attribute low serum 25(OH)D₃ to a given photoprotection strategy because more than one was used. Furthermore, for the most part there were no controls, and supplementation was given or taken in many of the studies. Overall, it is not possible to use these studies for sunscreen guidance for the general population.

Sunscreen use and vitamin D₃ synthesis in studies using nonsolar ultraviolet radiation from artificial sources

Laboratory studies offer an obvious way to study the effects of sunscreens under controlled conditions. Five studies have shown that sunscreen application (0.5–2 mg cm⁻²) inhibited the synthesis of vitamin D (Table 3). However, the sources used were mainly UVB-rich (Fig. 3a), including nonsolar UVB (<295 nm), which is very effective at pre-vitamin D production (Fig. 3b). Figure 3c shows that such nonsolar wavelengths have a disproportionally large effect, and thus do not reflect environmental reality. Of note, one study showed that 25(OH)D₃ synthesis is dependent on application thickness when 25% of BSA is exposed. It was recently shown that sunscreens block cutaneous vitamin D₃ (cholecalciferol) production with only a minimal effect on circulating 25(OH)D after a single narrowband UVB (~313 nm) exposure. In general, the UVR dose of these studies is low, e.g. this was 0-375 SED over 24% BSA. A study of Polish children, who did apply sunscreen, on holiday by the Baltic Sea showed that daily borderline erythemal exposure results in a highly significant increase of serum 25(OH)D₃. These studies suggest that vitamin D synthesis occurs with low UVR doses and therefore sufficient UVR may be transmitted through a sunscreen for vitamin D synthesis.
### Table 3: Sunscreen use and vitamin D status in studies using normal human volunteers (FST I–III) exposed to UVR from artificial sources

| First author, year | In vivo / ex vivo, n, age | UVR source | Dose | Exposed area | SPF | Amount of sunscreen | Time of assessment | Conclusions |
|-------------------|--------------------------|------------|------|--------------|-----|---------------------|-------------------|-------------|
| Matsuoka 1987⁷⁴   | In vivo, n = 8 (SS, n = 4; placebo, n = 4) 21–45 years | UVB phototherapy tubes (260–360 nm with peak at 313 nm) | 1 MED | Whole body | SPF 8 | Cannot say with confidence | 24 h, 2 h prior UVR, 1, 2, 3, 7, 14 days post exposure | Without SS there was a 17-fold increase in serum vit D peaking at 1 day post UVR. SS totally blocked serum vit D increase. Lack of SS on the legs and trunk allowed significant synthesis. But synthesis not significant when arms and head & neck were spared. |
| Matsuoka 1990⁷⁵   | In vivo, n = 27 23–32 years | UVB phototherapy tubes (260–360 nm with peak at 313 nm) | Slightly < 1 MED | Six groups with different SS application zones: G1, whole body; G2, except head & neck; G3, except arms; G4, except trunk; G5, except buttocks & legs; G6, whole body no SS | SPF 15 | No data | 1 h before and 24 h after exposure | In the absence of whole-body SS there was a ~5-fold significant increase of serum vit D. Whole-body SS totally blocked vit D formation. Lack of SS on the hands and trunk allowed significant synthesis. But synthesis not significant when arms and head & neck were spared. |
| Faurschou 2012⁷⁶  | In vivo, n = 37 18–49 years | UVB phototherapy tubes (290–360 nm with peak at 320 nm) | 4 × 3 SED 2–3 days interval | 25% BSA (upper front and back) | SPF 8 | 0, 0-5, 1-0, 1-5, 2-0 mg cm⁻¹ | 3 days after final irradiation | Increase of 25(OH)D is dependent on SS application thickness. All increases significantly greater than baseline apart from SS at 2-0 mg cm⁻¹ |
| Libon 2017⁷⁷     | In vivo, n = 72 19–25 years | Narrowband UVB phototherapy tubes (311–313 nm) | 0·8 MED | Different body areas with and without SS (9–96%) | SPF 50+ | 2 mg cm⁻¹² | Pre and post UVR up to 5 days | SS use decreased serum 25(OH)D by 8–13% and decreased cutaneous vit D by 76–93% |

25(OH)D, 25-hydroxyvitamin D; 7-DHC, 7-dehydrocholesterol; BSA, body surface area; MED, minimal erythema dose; NA, not applicable; PABA, para-aminobenzoic acid; SED, standard erythema dose; SPF, sun protection factor; SS, sunscreen; SSR, solar simulated radiation; vit D, vitamin D [not 25(OH)D]; UVR, ultraviolet radiation.
Table 4: Sunscreen use and vitamin D status/outcomes in real sun exposure (controlled studies) in skin cancer patients and healthy volunteers

| First author, year | Participants: n (age) | Location, latitude | SPF | Assessment period | Baseline values | UVR monitored | Conclusions |
|--------------------|------------------------|--------------------|-----|-------------------|----------------|--------------|-------------|
| Matsuoka 1988<sup>104</sup> | n = 20 (65 ± 3 years) | U.S.A: Springfield, IL, 40° N; Philadelphia, PA, 40° N | Not given | Summer after SS use > 1 year | No | No | 25(OH)D significantly lower (44%) in SS group than controls |
| Marks 1995<sup>105</sup> | n = 113 (≥ 40 years) | Australia: Maryborough, 37° S | SPF 17 Controls given base cream | 7 months (after summer) 1,25(OH)₂D also assessed | Yes | Yes | Dosimeter badges (last week) |
| Farrerons 1998<sup>106</sup> | n = 24 (71 ± 8 years) | Spain: Barcelona, 41° N | SPF 15 | 2 years, 4 time points 1,25(OH)₂D, PTH, bone markers also measured | Yes | No | Outdoors ≥ once daily |
| Farrerons 2001<sup>107</sup> | n = 10 (74 ± 18 years)<sup>a</sup> | Spain: Barcelona, 41° N | SPF 15 | 2 years Bone mass | Yes | No | Outdoors ≥ once daily |
| Azizi 2012<sup>108</sup> | Outdoor male workers (~ 40 years) 3 sun protection intervention groups:<sup>b</sup> | Israel, 30–33° N 3 locations | SPF 42 | Two successive winters (8 and 20 months) | No | Yes | Ambient SID/day 40 ± 10 spring 15 ± 4 winter |
| Jayaratne 2012<sup>110</sup> | n = 556 (daily sunscreen) vs. n = 557 (discretionary use) (19–70+ years) | Australia: Nambour, 26° S | SPF 16 | End of a 4.5-year RCT | No | No | 25(OH)D not significantly different in daily vs. discretionary SS use |
| Narbutt 2019<sup>111</sup> and Young 2019<sup>112</sup> | n = 79 (34 ± 8 years) | Participants: Spain: Tenerife, 28° N  Control: Poland: Łódź, 52° N | SPF 15 (≥ 2 mg cm⁻²) Intervention: (i) High UVA-PF | 1-week holiday in March | Yes | Yes | Personal electronic dosimeters measuring SID |

(continued)
provide reliable data on their effect on vitamin D synthesis for public health purposes. The only way to do such studies reliably would be to use SSR as used in SPF testing, or a fluorescent SSR source.99 It should be noted that the higher UVB content of SSR than ‘typical’ terrestrial UVR may also influence results.100 Furthermore, the SSR doses given should be environmentally realistic and represent a serious challenge to the sunscreen under test.

Sunscreen use for daily and recreational photoprotection and vitamin D status

Questionnaire-based studies Table S2 (see Supporting Information) shows that most questionnaire-based studies report no correlation between sunscreen use and serum 25(OH)D3 levels. However, two studies showed a negative correlation and a positive correlation was observed in three studies. The negative correlation, in a Brazilian study, reported that 25(OH)D3 was sufficient (73 nmol L⁻¹) in the sunscreen group.101 Godar et al reported, from a modelling study, that young Americans (≤ 19 years) using sunscreen with SPF > 15 had insufficient vitamin D3 status, and concluded that most American children may not get sufficient solar exposure to meet their minimal vitamin D requirements.102 One explanation for the positive correlations, including one large Danish study of 2625 adults and 569 children,103 is increased solar exposure without erythema.

Questionnaire-based studies have obvious limitations including compliance, unknown confounding factors, the use of nonsunscreen photoprotection and recall bias. UVR exposure was based on proxies such as time outdoors.

Controlled studies Controlled field studies with real sun exposure are the best way to determine the effect of sunscreen use on vitamin D synthesis. Such studies present ethical considerations when considering control groups because lack of sunscreen use could result in sunburn and increased skin cancer risk. Results of such studies are shown in Table 4.41,104–111 which reports that most studies showed no change in serum 25(OH)D3 with sunscreen use,106–108 but two showed reduction.104,105 These studies mostly ignore the most important factors that influence outcome, namely personal UVR exposure, sunscreen application thickness and BSA exposed. Marks et al.,105 who found no difference between sunscreen and control groups, measured UVR exposure in the last week of a 7-week study in Australia using polysulphone badge personal dosimeters. The UVR exposures in the sunscreen and control groups were not different, but the last week’s exposure is unlikely to have been critical for the outcome because serum 25(OH)D3 was best predicted in Australian adults by solar exposure 6 weeks prior to measurement.112

One factor that has been ignored in all types of study described above, except for the study of Faurschou et al.,96 is the effect of baseline 25(OH)D3 on the response to UVR. The lower the baseline, the greater the response to UVR113 and this must be considered in the statistical analyses. A similar observation has been made in vitamin D supplementation studies.114
A holiday study in Tenerife (Canary Islands) during a week of very high UVI was designed to take the above factors into account, including a discretionary sunscreen-use control group. This showed that intervention with optimal SPF 15 sunscreen use (≥ 2 mg cm$^{-2}$), which inhibited erythema, still enabled very considerable vitamin D production compared with the discretionary sunscreen-use group that had sunburn. A comparison of high vs. low UVA-PF showed greater vitamin D synthesis with the former. Thus, optimal sunscreen use may have increased sun exposure. Indeed, time spent outdoors and BSA exposed to sun have been positively correlated with vitamin D deficiency and supplementation and screening is therefore advised for this population.

In conclusion, effective sunscreens must attenuate UVB to prevent erythema. In theory, this should inhibit vitamin D$_3$ biosynthesis. However, the doses of UVB necessary are low (i.e. substantially suberythemal) so that typical sunscreen use does not lead to vitamin D insufficiency in practice in healthy people. Indeed, even optimal sunscreen use allows good vitamin D synthesis under high UVI conditions. Better UVA protection for a given SPF results in a de facto reduction of UVB protection. UVA protection will have no impact on vitamin D synthesis (see Fig. 3b), and indeed may prevent photodegradation. Increased UVB for a given SPF should in theory and in practice result in better vitamin D synthesis.

Studies done to date have been with lighter-skinned individuals, and conclusions may not apply to those with darker skin types IV–VI who use sunscreens. In such cases, oral supplementation may be advisable.

**Summary**

Cutaneous vitamin D$_3$ synthesis is initiated by terrestrial-range UVB and can be achieved with suberythemal exposures to a relatively small BSA. Daily sunscreen use, for nonintentional solar exposure, is mainly based on products with low SPF and high UVA-PF. This is unlikely to impact on vitamin D production. In fact, most studies published to date have shown no association between sunscreen use and vitamin D deficiency, even with regular use of SPF > 15. Some studies have even reported a positive association between sunscreen use and 25(OH)D$_3$, suggesting that their use may have increased sun exposure. Indeed, time spent outdoors and BSA exposed to sun have been positively correlated with vitamin D status. Overall, other photoprotective behaviours (such as seeking shade, wearing protective clothing and long sleeves) may have more impact on vitamin D status than sunscreen use. The recommendations of the panel for daily and recreational photoprotection, as well as the need for vitamin D screening and supplementation, are summarized in Table 5.
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References

1. Maestro MA, Molnar F, Mourino A et al. Vitamin D receptor 2016: novel ligands and structural insights. Expert Opin Ther Pat 2016; 26:1291–306.

2. Bouillon R, Carmeliet G, Verlinden L et al. Vitamin D and human health: lessons from vitamin D receptor null mice. Endor Rev 2008; 29:726–76.

3. Holick MF. Vitamin D deficiency. N Engl J Med 2007; 357:266–81.

4. Bjelakovic G, Gluud LL, Nikolova D et al. Vitamin D supplementation for prevention of mortality in adults. Cochrane Database Syst Rev 2014; 1:CD007470.

5. Cardoso AT, Nanji L, Costa J et al. Vitamin D metabolism and action (first of two parts). J Bone Miner Res 1997; 12:V83–3.

6. Winterkorn M, Heintz F, Malmstrom K et al. The nonskeletal effects of vitamin D: an Endocrine Society scientific statement. Endor Rev 2012; 33:456–92.

7. Autier P, Mullie P, Macacu A et al. Effect of vitamin D supplementation on non-skeletal disorders: a systematic review of meta-analyses and randomised trials. Lancet Diabetes Endocrinol 2014; 2:141–13.

8. Springbett P, Buglass S, Young AR. Sun protection and vitamin D status. J Photochem Photobiol B 2010; 101:150–8.

9. Haussler MR, McCain TA. Basic and clinical concepts related to vitamin D metabolism and action (first of two parts). N Engl J Med 1997; 279:974–83.

10. Holick MF, Chen TC, Lu Z et al. Vitamin D and skin physiology: a D-lightful story. J Bone Miner Res 2007; 22 (Suppl. 2):V28–33.

11. Bilek DD. Vitamin D metabolism and function in the skin. Mol Cell Endocrinol 2011; 347:80–9.

12. Petersen B, Wulf HC, Triguero-Mas M et al. Sun and ski holidays improve vitamin D status, but are associated with high levels of DNA damage. J Invest Dermatol 2014; 138:2806–13.

13. Jolliffe DA, Walton RT, Griffiths CJ et al. Single nucleotide polymorphisms in the vitamin D pathway associating with circulating concentrations of vitamin D metabolites and non-skeletal health outcomes: review of genetic association studies. J Steroid Biochem Mol Biol 2016; 154:18–29.

14. IOM (Institute of Medicine). Dietary Reference Intakes for Calcium and Vitamin D. Washington DC: The National Academies Press, 2011.

15. WHO. Global Solar UV Index: A practical guide. A joint recommendation of the World Health Organization, World Meteorological Organization, United Nations Environment Programme, and the International Commission on Non-Ionizing Radiation Protection. Geneva: WHO; 2002; 1–32.

16. McKenzie RL, Lucas RM. Reassessing impacts of extended daily exposure to low level solar UV radiation. Sci Rep 2018; 8:13805.

17. Reddy KK, Gilchrest BA. What is all this commotion about vitamin D? J Invest Dermatol 2010; 130:321–6.

18. Linos E, Keiser E, Kanzler M et al. Sun protective behaviors and vitamin D levels in the US population: NHANES 2003–2006. Cancer Causes Control 2012; 23:133–40.

19. Janda M, Kimlin MG, Whiteman DC et al. Sun protection messages, vitamin D and skin cancer: out of the frying pan and into the fire? Med J Aust 2007; 186:52–4.

20. Liang G, Nan H, Qureshi AA et al. Pre-diagnostic plasma 25-hydroxyvitamin D levels and risk of non-melanoma skin cancer in women. PLoS One 2012; 7:e35211.

21. Lucas RM, Yazar S, Young AR et al. Human health in relation to exposure to solar ultraviolet radiation under changing stratospheric ozone and climate. Photocem Photochem Sci 2019; 18:641–80.

22. Bouillon R. Comparative analysis of nutritional guidelines for vitamin D. Nat Rev Endocrinol 2017; 13:466–79.

23. Gel-H Fuleihan, Bouillon R, Serum Clarke B et al. 25-hydroxyvitamin D levels: variability, knowledge gaps, and the concept of a desirable range. J Bone Miner Res 2015; 30:1119–33.

24. United Nations Environment Programme, Environmental Effects Assessment Panel. Environmental effects of ozone depletion and its interactions with climate change: progress report, 2016. Photochem Photobiol Sci 2017; 16:107–45.

25. Hilger J, Friedel A, Herr R et al. A systematic review of vitamin D status in populations worldwide. Br J Nutr 2014; 111:23–45.

26. Lips P, Cashman KD, Lamberg-Allardt C et al. Management of endocrine disease: current vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency; a position statement of the European Calcified Tissue Society. Eur J Endocrinol 2019; https://doi.org/10.1530/EJE-18-0736.

27. Zhao S, Gardner K, Taylor W et al. Vitamin D assessment in primary care: changing patterns of testing. London J Prim Care (Abingdon) 2015; 7:15–22.

28. Holick MF, Binkley NC, Bischoff-Ferrari HA et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96:1911–30.

29. Bumhamou CL, Souberbielle JC, Corret B et al. for the Groupe de recherche et d’information sur les ostéoporoses (GRIIO). La vitamine D chez l’adulte: recommandations du GRIIO. Presse Med 2011; 40:673–82.

30. Young AB, Claveau J, Rossi AB. Ultraviolet radiation and the skin: photobiology and sunscreen photoprotection. J Am Acad Dermatol 2017; 76:S100–9.

31. Osterwalder U, Sohn M, Herzog B. Global state of sunscreens. Photodermatol Photoimmunol Photomed 2014; 30:62–80.

32. Diffey BL, Jansen CT, Urbach F et al. The standard erythema dose: a new photobiological concept. Photodermatol Photoimmunol Photomed 1997; 13:64–6.

33. Harrison GL, Young AR. Ultraviolet radiation-induced erythema in human skin. Methos 2002; 28:14–19.

34. Petersen B, Datta P, Philipsen PA et al. Sunscreen use and failures – on site observations on a sun-holiday. Photochem Photobiol Sci 2013; 12:190–6.

35. Petersen B, Thielen E, Philipsen PA et al. Determinants of personal ultraviolet-radiation exposure doses on a sun holiday. Br J Dermatol 2013; 168:1073–9.

36. Petersen B, Thielen E, Philipsen PA et al. A sun holiday is a sunburn holiday. Photodermatol Photoimmunol Photomed 2013; 29:221–4.

37. Duteil L, Esdaile J, Maberi Y et al. A method to assess the protective efficacy of sunscreens against visible light-induced pigmentation. Photodermatol Photoimmunol Photomed 2017; 33:260–6.

38. Lucas RM, Norval M, Neale RE et al. The consequences for human health of stratospheric ozone depletion in association with other environmental factors. Photochem Photobiol Sci 2015; 14:53–87.
40 Bais AF, Lucas RM, Bornman JF et al. Environmental effects of ozone depletion, UV radiation and interactions with climate change: UNEP Environmental Effects Assessment Panel, update 2017. Photochem Photobiol Sci 2018; 17:127–79.

41 Narbutt J, Philipson PA, Harrison GI et al. Sunscreen applied at ≥ 2 mg cm⁻² during a sunny holiday prevents erythema, a biomarker of ultraviolet radiation-induced DNA damage and suppression of acquired immunity. Br J Dermatol 2019; 180: 604–14.

42 Fourtanier A, Moyal D, Maccario J et al. Measurement of sunscreen immune protection factors in humans: a consensus paper. J Invest Dermatol 2005; 125:403–9.

43 Olsen CM, Wilson LF, Green AC et al. Prevention of DNA damage in human skin by topical sunscreens. Photodermatol Photoimmunol Photomed 2017; 33:135–42.

44 Young AR, Greenaway J, Harrison GI et al. Sub-optimal application of a high SPF sunscreen prevents epidermal DNA damage in vivo. Acta Dermato-Venereol 2018; 98:880–7.

45 Young AR, Chadwick CA, Harrison GI et al. The similarity of action spectra for thymine dimers in human epidermis and erythema suggests that DNA is the chromophore for erythema. J Invest Dermatol 1998; 111:982–8.

46 Del Bino S, Sok J, Bernerd F. Assessment of ultraviolet-radiation-induced DNA damage within melanocytes in skin of different constitutive pigmentation. Br J Dermatol 2013; 168:1120–3.

47 Del Bino S, Bernerd F. Variations in skin colour and the biological consequences of ultraviolet radiation exposure. Br J Dermatol 2013; 169 (Suppl. 3):33–40.

48 Fajusighe D, Lwin SM, Diffey BL et al. Melanin distribution in human epidermis affords localized protection against DNA photodamage and concurs with skin cancer incidence difference in extreme phototypes. FASEB J 2018; 32:3700–6.

49 Tadokoro T, Kobayashi N, Zmudzka BZ et al. UV-induced DNA damage and melanin content in human skin differing in racial/ethnic origin. FASEB J 2003; 17:1177–9.

50 Yamaguchi Y, Takahashi K, Zmudzka BZ et al. Human skin responses to UV radiation: pigment in the upper epidermis protects against DNA damage in the lower epidermis and facilitates apoptosis. FASEB J 2006; 20:1486–8.

51 Veierod MB, Thelle DS, Laake P. Diet and risk of cutaneous malignant melanoma: a prospective study of 50,757 Norwegian men and women. Int J Cancer 1997; 71:600–4.

52 Green A, Williams G, Neale R et al. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. Lancet 1999; 354:723–9.

53 van der Pols JC, Williams GM, Pandeya N et al. Prolonged prevention of squamous cell carcinoma of the skin by regular sunscreen use. Cancer Epidemiol Biomarkers Prev 2006; 15:2546–8.

54 Green AC, Williams GM, Logan V et al. Reduced melanoma after regular sunscreen use: randomized trial follow-up. J Clin Oncol 2011; 29:257–63.

55 Iannacone MR, Hughes MC, Green AC. Effects of sunscreen on skin cancer and photoaging. Photodermatol Photoimmunol Photomed 2014; 30:55–61.

56 Sanchez G, Nova J, Rodriguez-Hernandez AE et al. Sun protection for preventing basal cell and squamous cell skin cancers. Cochrane Database Syst Rev 2016; 7:CD011161.

57 CIE. Erythema Reference Action Spectrum and Standard Erythema Dos. Vienna, Austria: Commission Internationale de l’Eclairage (CIE) Central Bureau, 1998.

58 Bouillon R, Eisman J, Garabedian M et al. Action spectrum for production of previtamin D3 in human skin. Vienna, Austria: Commission Internationale de l’Eclairage (CIE) Central Bureau, 2006.

59 Stengel F. Homeostasis in topical photoprotection: getting the spectral balance right. Am J Clin Dermatol 2018; 19:40–4.

60 U.S. Food and Drug Administration. Sunscreen drug products for over the counter use. Proposed Rules (Document no. 2019-03019). Federal Register 2019; 84:6204–75.

61 Cole C. Sunscreens – what is the ideal testing model? Photodermatol Photoimmunol Photomed 2014; 30:81–7.

62 Dupont E, Gomez J, Bilodeau D. Beyond UV radiation: a skin under challenge. Int J Cosmet Sci 2013; 35:224–32.

63 Tewari A, Sarkany RP, Young AR. UVA1 induces cyclobutane pyrimidine dimers but not 6-4 photoproducts in human skin in vivo. J Invest Dermatol 2012; 132:394–400.

64 McAdam E, Brem R, Karran P. Oxidative stress-induced protein damage inhibits DNA repair and determines mutation risk and therapeutic efficacy. Mol Cancer Res 2016; 14:612–22.

65 Young AR, Orchard GE, Harrison GI et al. The detrimental effects of daily sub-erythemal exposure on human skin in vivo can be prevented by a daily-care broad-spectrum sunscreen. J Invest Dermatol 2007; 127:975–8.

66 Lejeune F, Christiaens F, Bernerd F. Evaluation of sunscreen products using a reconstructed skin model exposed to simulated daily ultraviolet radiation: relevance of filtration profile and SPF value for daily photoprotection. Photodermatol Photoimmunol Photomed 2008; 24:249–55.

67 Seité S, Christiaens F, Bredoux C et al. A broad-spectrum sunscreen prevents cumulative damage from repeated exposure to sub-erythematic solar ultraviolet radiation representative of temperate latitudes. J Eur Acad Dermatol Venereol 2010; 24:219–26.

68 Fourtanier A, Moyal D, Seite S. UVA filters in sun-protection products: regulatory and biological aspects. Photochem Photobiol Sci 2012; 11:81–9.

69 Moyal D. Prevention of pigmentation in Asian skin exposed to ultraviolet daylight. Proceedings of the International Federation of the Societies of Cosmetic Chemists (IFSCC) meeting, Osaka, Japan, October 2006 [poster].

70 Marionnet C, Pierard C, Lejeune F et al. Modulations of gene expression induced by daily ultraviolet light can be prevented by a broad spectrum sunscreen. J Photochem Photobiol B 2012; 116:37–47.

71 Ashwell M, Stone EM, Stolte H et al. UK Food Standards Agency Workshop Report: an investigation of the relative contributions of diet and sunlight to vitamin D status. Br J Nutr 2010; 104:603–11.

72 Jamil NA, Yew MH, Noor Hafizah Y et al. Estimated vitamin D synthesis and dietary vitamin D intake among Asians in two distinct geographical locations (Kuala Lumpur, 3 degrees N v Aberdeen, 57 degrees N) and climates. Public Health Nutr 2018; 21:3118–24.

73 Norval M, Wulf HC. Does chronic sunscreen use reduce vitamin D production to insufficient levels? Br J Dermatol 2009; 161:732–6.

74 Neale RE, Khan SR, Lucas RM et al. The effect of sunscreen on vitamin D: a review. Br J Dermatol 2019; https://doi.org/10.1111/bjd.17980.

75 Webb AR, DeCosta BR, Holick MF. Sunlight regulates the cutaneous production of vitamin D3 by causing its photodegradation. J Clin Endocrinol Metab 1989; 68:882–7.

76 Felton SJ, Cooke MS, Kiff R et al. Concurrent beneficial (vitamin D production) and hazardous (cutaneous DNA damage) impact
of repeated low-level summer sunlight exposures. Br J Dermatol 2016; 175:1320–8.

77 Farrar MD, Webb AR, Kifi R et al. Efficacy of a dose range of simulated sunlight exposures in raising vitamin D status in South Asian adults: implications for targeted guidance on sun exposure. Am J Clin Nutr 2013; 97:1210–16.

78 Webb AR, Kazantzidis A, Kifi RC et al. Meeting vitamin D requirements in white Caucasians at UK latitudes: providing a choice. Nutrients 2018; 10:e947.

79 Bogh MK, Schmedes AV, Philipsen PA et al. Vitamin D production depends on ultraviolet-B dose but not on dose rate: a randomized controlled trial. Exp Dermatol 2011; 20:14–18.

80 Narbutt J, Philipsen PA, Lesiak A et al. Children sustain high levels of skin DNA photodamage, with a modest increase of serum 25-hydroxyvitamin D3, after a summer holiday in Northern Europe. Br J Dermatol 2018; 179:490–50.

81 Sollitto RB, Kraemer KH, DiGiovanna JJ. Natural vitamin D levels can be maintained despite rigorous photoprotection: six years’ experience with xeroderma pigmentosum. J Am Acad Dermatol 1997; 37:942–7.

82 Querings K, Reichrath J. A plea for the analysis of vitamin-D deficiency in patients with basal cell nevus syndrome. Arch Dermatol 2009; 146:1105–10.

83 Querings K, Girndt M, Geisel J et al. A sunscreen’s labeled sun protection factor may overestimate protection at temperate latitudes: a human in vivo study. J Invest Dermatol 2010; 130:2457–62.

84 Cusack C, Danby C, Fallon JC et al. Photoprotective behaviour and sunscreen use: impact on vitamin D levels in cutaneous lupus erythematosus. Photodermatol Photoimmun Photomed 2008; 24:260–7.

85 Holzne SA, Anstey AV, Badminton MN et al. Serum 25-hydroxyvitamin D in erythrocytic protoporphyrin II. Br J Dermatol 1989; 121:213–13.

86 Ulrich C, Jürgens J, Deegen A et al. Prevention of non-melanoma skin cancer in organ transplant patients by regular use of a sunscreen: a 24 months, prospective, case–control study. Br J Dermatol 2009; 161 (Suppl. 3):78–84.

87 Delong LK, Wetherington S, Hill N et al. Vitamin D levels, dietary intake, and photoprotective behaviors among patients with skin cancer. Smin Cutan MD Sug 2010; 29:185–9.

88 Hoesl M, Dietz K, Rocken M et al. Vitamin D levels of XP-patients under stringent sun-protection. Eur J Dermatol 2010; 20:457–60.

89 Tang JY, Wu A, Linos E et al. High prevalence of vitamin D deficiency in patients with basal cell nevus syndrome. Arch Dermatol 2010; 146:1105–10.

90 Reid SM, Robinson M, Kerr AC et al. Prevalence and predictors of low vitamin D status in patients referred to a tertiary photodiagnostic service: a retrospective study. Photodermatol Photoimmun Photomed 2012; 28:91–6.

91 Gentzsch S, Kern JS, Loecherrmann S et al. Iatrogenic vitamin D deficiency in a patient with Gorlin syndrome: the conundrum of photoprotection. Acta Derm Venerol 2014; 94:459–60.

92 Kuwabara A, Tsugawa N, Tanaka K et al. High prevalence of vitamin D deficiency in patients with xeroderma pigmentosum-A under strict sun protection. Eur J Clin Nutr 2015; 69:693–6.

93 Bogatzewicz J, Karczmarewicz E, Pludowski P et al. Requirement for vitamin D supplementation in patients using photoprotection: variations in vitamin D levels and bone formation markers. Int J Dermatol 2016; 55:e176–83.

94 Matsuoka LY, Ide L, Wortsman J et al. Sunscreens suppress cutaneous vitamin D3 synthesis. J Clin Endocrinol Metab 1987; 64:1165–8.
Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Appendix S1 Intrinsic and extrinsic factors that determine serum 25(OH)D.
Appendix S2 What is optimal vitamin D status and the best method to determine it? Public health perspectives.
Table S1 Indications for 25(OH)D screening.
Table S2 Sunscreen use and vitamin D status in real sun exposure (questionnaire-based and modelled studies).