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The effect of sunscreen on vitamin D: a review

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Summary

Background Sunscreen use can prevent skin cancer, but there are concerns that it may increase the risk of vitamin D deficiency.
Objectives We aimed to review the literature to investigate associations between sunscreen use and vitamin D_3 or 25 hydroxyvitamin D [25(OH)D] concentration.
Methods We systematically reviewed the literature following the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines. We identified manuscripts published in English between 1970 and 21 November 2017. Eligible studies were experimental [using an artificial ultraviolet radiation (UVR) source], field trials or observational studies. The results of each of the experimental studies and field trials are described in detail. Two authors extracted information from observational studies, and applied quality scoring criteria that were developed specifically for this question. These have been synthesized qualitatively.
Results We included four experimental studies, three field trials (two were randomized controlled trials) and 69 observational studies. In the experimental studies sunscreen use considerably abrogated the vitamin D_3 or 25(OH)D production induced by exposure to artificially generated UVR. The randomized controlled field trials found no effect of daily sunscreen application, but the sunscreens used had moderate protection [sun protection factor SPF) ~16]. The observational studies mostly found no association or that self-reported sunscreen use was associated with higher 25(OH)D concentration.
Conclusions There is little evidence that sunscreen decreases 25(OH)D concentration when used in real-life settings, suggesting that concerns about vitamin D should not negate skin cancer prevention advice. However, there have been no trials of the high-SPF sunscreens that are now widely recommended.

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What's already known about this topic?

- Previous experimental studies suggest that sunscreen can block vitamin D production in the skin but use artificially generated ultraviolet radiation with a spectral output unlike that seen in terrestrial sunlight.
- Nonsystematic reviews of observational studies suggest that use in real life does not cause vitamin D deficiency.

What does this study add?

- This study systematically reviewed all experimental studies, field trials and observational studies for the first time.
- While the experimental studies support the theoretical risk that sunscreen use may affect vitamin D, the weight of evidence from field trials and observational studies suggests that the risk is low.
- We highlight the lack of adequate evidence regarding use of the very high sun protection factor sunscreens that are now recommended and widely used.

Skin cancers are the most commonly occurring cancers in white populations.[1–3] In addition to the mortality and morbidity burden, they have a very large economic impact.[4,5] Regular sunscreen use can prevent skin cancer[6,7] and is one of the most common sun protection strategies used.[8,9] Prevailing levels of sunscreen use in Australia have prevented an estimated 10–15% of all skin cancers from occurring,[10] and an intervention to increase sunscreen use by 5% per year over 10 years is estimated to reduce melanoma incidence by 10% cumulatively to 2031.[11] In light of these benefits, health advocacy organizations in Australia and New Zealand now recommend routine sunscreen application to prevent incidental sun exposure, in addition to protecting the skin during planned outdoors activities.[12]

The theoretical counterpoint to the benefits of sunscreen may be an increase in the risk of vitamin D deficiency. In people exposed to adequate solar ultraviolet radiation (UVR), the primary source of vitamin D is UVB-induced conversion of 7-dehydrocholesterol in the skin to pre-vitamin D_3. After skin synthesis, vitamin D_3 is hydroxylated in the liver to form 25 hydroxyvitamin D [25(OH)D], the primary circulating form of vitamin D and the indicator of vitamin D status. 25(OH)D is then converted, primarily in the kidney, to 1,25-dihydroxyvitamin D [$1,25(OH)_2D$], the biologically active form which plays pivotal roles in calcium homeostasis and has a range of other effects.

Sunscreens are designed to prevent erythema. The action spectra for vitamin D production and erythema overlap considerably in the UVB region.[13] Thus, in theory, sunscreens that are effective at preventing erythema should also decrease vitamin D_3 production and circulating $25(OH)D_3$ concentration. However, vitamin D production and change in serum 25(OH)D concentration are affected by factors such as the starting concentration of 25(OH)D and, critically, the body surface area exposed (unlike erythema which is a local effect at the site of exposure). Therefore, the capacity for sunscreen to affect vitamin D needs to be empirically tested. If sunscreen does decrease vitamin D production to an extent that is clinically important, the risks and benefits of sunscreen application need to be considered. If sunscreen has minimal impact on vitamin D status this information will decrease concern about vitamin D which has the potential to undermine sun protection messages; 20% of people in a 2015 U.S. survey agreed that regularly protecting the skin leads to a risk of not getting enough vitamin D.[14]

Two reviews published almost a decade ago concluded that sunscreen use can significantly reduce the production of vitamin D under controlled experimental conditions, but that normal usage does not result in vitamin D insufficiency.[15,16] Those reviews did not undertake a systematic assessment of observational studies, including selected studies only, and several additional studies have been published in the interim. We thus systematically reviewed the literature to address the question of whether *in vivo* sunscreen use in humans reduces vitamin D_3 or 25(OH)D concentration, or increases the risk of vitamin D deficiency.

Methods

The review was carried out in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.[17] We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to guide reporting.[18]

Data sources and searches

Eligible studies published between 1 January 1970 and 21 November 2017 were identified by searching: MEDLINE 1950 (U.S. National Library of Medicine, Bethesda, MD, U.S.A.) database using PubMed software; Embase 1966 database (Elsevier Science, Amsterdam, Holland) using Embase; and the ISI Science Citation Index using ISI Web of Science search. The searches are shown in the supplementary material (see Supporting Information, Search terms S1).

We did not search for abstracts, unpublished studies or other literature, or studies that were not published in English. We read the abstracts of all identified studies and excluded those that were clearly not relevant. The full text of all remaining studies was reviewed to determine whether or not they met the inclusion criteria. Eligible studies were also identified by searching the reference lists of retrieved studies.

Study inclusion criteria

We included three study types: (i) experimental studies that assessed the effect of sunscreen on the change in vitamin D_3 or 25(OH)D concentration following exposure to UVR from artificial sources; (ii) field trials in which sunscreen was provided to participants as an intervention and the vitamin D_3 or 25(OH)D concentration in the intervention group was compared with a placebo or no intervention group; and (iii) observational epidemiological studies that compared vitamin D_3 or 25(OH)D concentrations between groups according to categories of sunscreen use. S.R.K. and R.E.N. reviewed all potentially eligible manuscripts, and any discrepancies were resolved by joint evaluation of the manuscript and further consultation with C.M.O. and/or M.W.

Data extraction and quality assessment

For the experimental studies we extracted details about the study protocol, including the sample size, spectral distribution of the UVR source, the experimental protocol [number of exposures, surface area exposed, sunprotection factor (SPF) of the sunscreen and thickness of application if available, molecule measured, timing of measurement]. For field trials we documented the sample size, sunscreen intervention, control intervention, length of the trial and timing of the outcome measurement.

For each observational study we recorded: location; years of data collection; source and number of participants; age and sex of participants; sunscreen measure used; the method for

Table 1 Description of experimental studies using an artificial ultraviolet radiation (UVR) source

First author (year)	Study population and sample size	Age range (years) and sex	Spectral distribution of UVR source (nm)	Experimental protocol	SPF	Outcome measure and timing	Results (for group descriptions see experimental protocol column)	
Matsuoka (1987)[21]	White volunteers (n = 8)	21–45; 6 F, 2 M	260–360 peak 313	Participants randomly assigned to either: **(1)** no SS application; or **(2)** whole-body application of 10 mL of 5% PABA in 55% ethanol with water and emollients 1 h prior to UVR exposure All participants received a single total-body exposure to 1 MED UVR	8	Vitamin D_3, measured 24 h and 2 h before exposure and 1, 2, 3, 7 and 14 days after exposure	Time 0 h **(1)** 1·5 ng mL^{-1} **(2)** 5·6 ng mL^{-1}	Time 24 h (peak) 25·6 ng mL^{-1} ($P < 0·01$) 4·4 ng mL^{-1} (NS)
Matsuoka (1990)[20]	Medical students (Fitzpatrick skin type III) (n = 27)	23–32, 7 F, 20 M	260–360 peak 313	Participants randomly assigned to: **(1)** no SS application; **(2)** SS application to total body; **(3)** SS application to total body excluding head and neck; **(4)** SS application to total body excluding arms; **(5)** SS application to total body excluding trunk; **(6)** SS application to total body excluding legs and buttocks. Thickness of SS application not stated. All participants received a single total-body exposure to a fixed suberythemal dose of UVR (27 mJ cm^{-2})	15	Vitamin D_3, measured 1 h before and 24 h after exposure	Time 0 h[a] **(1)** 2·1 ng mL^{-1} **(2)** 1·2 ng mL^{-1} **(3)** 4·8 ng mL^{-1} **(4)** 3·1 ng mL^{-1} **(5)** 2·5 ng mL^{-1} **(6)** 3·0 ng mL^{-1}	Time 24 h[a] 12·5 ng mL^{-1} ($P < 0·05$) 1·7 ng mL^{-1} (NS) 5·9 ng mL^{-1} (NS) 5·0 ng mL^{-1} (NS) 13·5 ng mL^{-1}($P < 0·05$) 11·2 ng mL^{-1} ($P < 0·05$)
Faurschou (2012)[23]	Volunteers (Fitzpatrick skin type I–III) (n = 37)	18–49; 20 F, 17 M	290–360 peak 320	Participants randomly assigned to SS application on the upper body 20 min prior to UVR exposure in layers of: **(1)** 0 mg cm^{-2}; **(2)** 0·5 mg cm^{-2}; **(3)** 1 mg cm^{-2}; **(4)** 1·5 mg cm^{-2}; or **(5)** 2 mg cm^{-2} All participants received 3 SED to the front and back of the trunk. This procedure was repeated four times with a 2–3-day interval	8	$25(OH)D_3$ measured before first exposure and 3 days after final exposure	Mean difference from day 0 to day 3 (P-value) **(1)** 25·8 nmol L^{-1} **(2)** 12·5 nmol L^{-1} **(3)** 11·5 nmol L^{-1} **(4)** 10·2 nmol L^{-1} **(5)** 6·4 nmol L^{-1}	 (0·0001) (0·0059) (0·0009) (0·0028) (0·16)
Libon (2017)[22]	Volunteers (Fitzpatrick skin type III) (n = 72)	19–25; 47 F, 25 M	311–313	All participants (except an unexposed control group) received a single exposure of 0·8 MED on two occasions, 1 month apart, first without and then with SS (applied at 2 mg cm^{-2}). They were randomly assigned to exposure of different body parts: **(1)** head, neck, hands; **(2)** head, neck, arms, hands; **(3)** head, neck, arms, hands, legs, feet; **(4)** total body	50	Vitamin D_3 and $25(OH)D_3$ measured just before each exposure, and at days 1, 2 and 5 after exposure	Mean difference from day 0 to day 5 (P-value) With SS Vitamin D_3 (nmol L^{-1}) **(1)** −1·4 (0·41) **(2)** 0·1 (0·90) **(3)** 2·9 (0·14) **(4)** 1·2 (0·21) $25(OH)D_3$ (nmol L^{-1}) **(1)** 3·4 (0·009) **(2)** 3·9 (0·001) **(3)** 3·6 (0·010) **(4)** 2·3 (0·20)	Without SS 0·3 (0·64) 1·4 (0·007) 2·7 (0·018) 6·0 (0·018) 5·2 (0·0006) 7·8 (< 0·0001) 8·7 (< 0·0001) 10·7 (< 0·0001)

[a]Data extracted from published chart using Webplot digitizer software (https://automeris.io/WebPlotDigitizer/) 25(OH)D, 25 hydroxyvitamin D; MED, minimal erythemal dose; PABA, para-aminobenzoic acid; SED, standard erythemal dose; SPF, sun protection factor; SS, sunscreen; NS, not significant (P-value > 0·05).

measurement of 25(OH)D concentration; whether the laboratory performing the 25(OH)D measurement was reported to be participating in a quality-assurance scheme; study design; whether the study accounted (through either design or analysis) for sun exposure (e.g. time outdoors or UVR dose); skin type (phototype or ethnicity); season of 25(OH)D measurement; and vitamin D supplement use.

We did not apply quality scoring for the experimental studies or trials. Instead these are described in detail, including design characteristics that might influence their findings.

No existing quality assessment tool enabled adequate assessment of the quality of the observational studies with respect to this research question. Thus, we derived a quality assessment tool comprising five items, with a possible maximum score of 9 based on the quality of the sunscreen measure and the 25(OH)D assay used, whether descriptive data on 25(OH)D level by sunscreen category and an effect estimate or P-value for difference across categories were provided, and the level of adjustment for possible confounders. The details of the score are described in the supplementary material (see Supporting Information: Quality Assessment tool S1). S.R.K. and R.E.N. extracted relevant information and scored the studies, with any discrepancies resolved through joint evaluation and consultation with C.M.O. and/or M.W.

Synthesis of results

Due to the small number of experimental studies and field trials included in this review, these are described individually.

Substantial heterogeneity in study populations and design, and in reporting of results, precluded meta-analysis of the observational studies. Instead, these studies were cross-classified into categories defined according to the results of unadjusted and adjusted analyses of the association between sunscreen use and 25(OH)D concentration or vitamin D status. Although we considered adjustment for four variables as part of our quality score, when synthesizing results we categorized studies according to adjustment for a measure of sun exposure only, as this is the factor most likely to confound the association between sunscreen use and 25(OH)D concentration. That is, we classified analyses that did and did not account for sun exposure as adjusted and unadjusted, respectively.

Associations were classified as: (1) no significant association between use of sunscreen and 25(OH)D concentration or vitamin D status (using $P \geq 0{\cdot}1$ due to the small sample size in many studies); (2) sunscreen use was associated with higher 25(OH)D concentration or vitamin D status ($P < 0{\cdot}1$); (3) sunscreen use associated with lower 25(OH)D concentration or vitamin D status ($P < 0{\cdot}1$). We classified studies as having no significant association on adjusted analysis if sunscreen use was not selected in multivariable modelling, provided that sun exposure was considered in the model. If sunscreen was not offered to the multivariable model, we classified the study as having not calculated an adjusted estimate.

Results

We screened the title and abstracts of 2517 studies and reviewed the full text of 369, ultimately including 75 eligible studies (four experimental studies, three trials and 69 observational studies; one study presented the results of both a trial and an observational analysis[19]) (Fig. S1; see Supporting Information).

Experimental studies

All four experimental studies included white volunteers (Table 1). Two studies used a UVR source that extended from 260 nm (i.e. in the UVC range) to 360 nm, while one ranged from 290 to 360 nm. One used a narrowband source (311–313 nm), which covers only a small part of the action spectra for either erythema or pre-vitamin D production. Two studies found that whole-body application of sunscreen [with sun protection factors (SPFs) of 8 and 15] prior to UV irradiation [with 1 or just under 1 minimal erythemal dose (MED), respectively] almost completely abrogated the increase in vitamin D_3 that was seen after exposure without sunscreen application.[20,21] A third study also observed no significant increase in vitamin D_3 concentration when sunscreen (SPF 50+) was applied (at 2 mg cm^{-2}) prior to exposure to 0·8 MED, irrespective of the amount of body surface area exposed, whereas there was a significant increase in the absence of sunscreen.[22] The 25(OH)D concentration increased when sunscreen was applied, but that increase was markedly less than when no sunscreen was applied. The fourth study investigated the effect on 25(OH)D concentration of sunscreen application (SPF 8) at different thicknesses prior to irradiation.[23] With decreasing thickness there was an exponential increase in 25(OH)D concentration between baseline and 3 days after the final of four exposures (to 3 standard erythemal doses). At 2 mg cm^{-2} (the thickness at which sunscreen is tested) there was a four-fold reduction in the increase in 25(OH)D concentration following irradiation (6·4 with sunscreen vs. 25·8 nmol L^{-1} without sunscreen).

Field trials

Two Australian population-based randomized controlled trials of sunscreen application for actinic keratosis or skin cancer prevention compared 25(OH)D concentration between the study arms (Table 2).[19,24] Both supplied sunscreen (SPF ~16) to participants randomized to the intervention arm and instructed them to apply it daily to exposed skin.[19,24] One supplied a placebo cream to the control group;[24] the other advised discretionary sunscreen application.[19] The placebo-controlled trial measured 25(OH)D_3 concentration at the end of winter and the end of the following summer and found no difference in the mean increase between the sunscreen and placebo groups (mean difference 11·8 nmol L^{-1} and 12·8 nmol L^{-1}, respectively). In the other trial the 25(OH)D

Table 2 Description of field trials

First author (Year)	Study population	Sample size	Age range (years) and sex	Experimental protocol	SPF	Results
Marks (1995)[24]	Residents of Maryborough (Victoria, Australia) (latitude 37° south) selected from the general population	113 (58 SS; 55 placebo)	40–70+ 67 F, 46 M	Randomized placebo-controlled trial of daily SS application vs. matching placebo. 25(OH)D_3 measured in September 1991 and March 1992	17	Mean increase in 25(OH)D_3 over summer: SS group: 11·8 nmol L^{-1} Placebo group: 12·8 nmol L^{-1} P = 0·75
Jayaratne (2012)[19]	Residents of Nambour (Queensland, Australia) (latitude 27° south) selected from the general population	1113 (556 SS; 557 no SS)	18–70+ 613 F, 500 M	Randomized controlled trial of daily SS application to head, neck, arms and hands vs. discretionary SS use. 25(OH)D[a] measured after 4·5 years of intervention (samples collected in 1996)	16	Mean 25(OH)D Daily SS group: 65·4 nmol L^{-1} Discretionary SS group: 65·9 nmol L^{-1} P = 0·70
Farrerons (1998)[26]	Patients with a history of actinic keratosis or keratinocyte cancer recruited from a hospital dermatology department in Barcelona, Spain (latitude 41° north). A control group of volunteer women from the same town	14 patients with skin cancer assigned to daily SS application; 19 controls	SS group: mean 71 years; 14 F, 10 M Controls: mean 59 years; 19 F, 0 M	Patients were provided with SS and asked to apply it each morning during spring and summer of 2 years. They were also instructed to avoid sun exposure at noon and to wear adequate clothing. Controls were given no specific instructions. 25(OH)D[a] measured in spring and autumn of each year, with the first and final measurements in spring	15	25(OH)D (nmol L^{-1}) Control / SS T0 (spring) 56·2 / 49·7 T1 (autumn) 87·0 / 66·9 T2 (spring) 57·1 / 40·4 T3(autumn) 70·6 / 53·8 T4 (spring) 48·5 / 44·8

[a]Not stated if 25(OH)D is total or 25(OH)D_3 25(OH)D, 25 hydroxyvitamin D; SPF, sun protection factor; SS, sunscreen.

concentration [the study did not specify whether the assay specifically measured 25(OH)D_3] did not differ between the study arms at the end of the 4·5-year intervention period (mean 65·4 nmol L^{-1} and 65·9 nmol L^{-1}, respectively). In both trials the incidence of the primary end point was significantly lower in the daily sunscreen application groups than in the control groups.[6,25]

The third trial was not randomized.[26] Patients with a history of actinic keratosis or skin cancer were instructed to apply an SPF 15 sunscreen daily throughout spring and summer for 2 years and to use other sun-protection measures. A control group, recruited from the same town but with no information about how they were identified, was not given specific instructions in relation to sunscreen or other sun-protection measures. 25(OH)D concentration was measured at baseline in spring and then each autumn and spring for the following 2 years. At baseline the mean 25(OH)D concentration was 6 nmol L^{-1} higher in the control compared with the sunscreen group. The initial increase in 25(OH)D concentration from spring to autumn was lower in the sunscreen group than in the control group, but thereafter the variation with season was similar. At the end of the study the difference between the two groups was almost the same as at the beginning (4 nmol L^{-1}) (Table 2).

Observational studies

Sixty-nine observational studies were identified (Table S1, see Supporting Information). They were highly heterogeneous in terms of location, study population, the method used to measure and report sunscreen use, and the reporting of associations between sunscreen use and 25(OH)D concentration. The quality scores ranged from 0 to 9 (median = 4) (Table S2, see Supporting Information). Only 30 studies (43%) scored 5 or more. Over 90% of the studies (n = 63) were cross-sectional in design (Table S2, see Supporting Information); this is appropriate because 25(OH)D concentration is influenced by sun exposure over a period of 1–3 months.

Five studies included a statement of 'no association' in the manuscript text without providing descriptive data, effect estimates or P-values. Although we do not know the level of significance used to make this determination, we have classified these five studies as showing no association between sunscreen use and 25(OH)D concentration based on unadjusted analysis.

Exposure to UVR is the strongest determinant of 25(OH)D_3 concentration. Only 30 studies (43%) controlled for a measure of sun exposure; of these 17 also controlled for skin type, season and intake of supplements. However, control of these factors was frequently imperfect (for example, controlling for having been on a sunny holiday rather than for a measure of recent routine sun exposure, or controlling for African American vs. white ethnicity).

Due to the heterogeneity and suboptimal reporting, we have presented a qualitative synthesis of results. Table 3 provides an overview of results. Table S3 (see Supporting Information) shows the summary data for individual studies. Forty-five studies (65%) found no association between sunscreen use and 25(OH)D concentration (24 on the basis of unadjusted analysis only). Seventeen studies (25%) found that sunscreen use was associated with higher 25(OH)D concentration or vitamin D status (five after adjustment).

In seven studies (10%) sunscreen use was associated with lower 25(OH)D concentration; the four that had adjusted for a measure of sun exposure are explored in more detail below:

1 A study from the U.K.[27] was performed among men aged over 50 years. A significant inverse association was found with childhood but not with adulthood or recent sunscreen use. Given the short half-life of 25(OH)D this association is most likely due to bias or chance.
2 A study from Kuwait[28] controlled for time outdoors and skin type by matching sunscreen users (defined as daily application of an SPF 15–50 sunscreen continuously for at least the past 2 years) to nonusers on age, sex, skin phototype and daily outdoor activity. Approximately a quarter (24%) of the nonsunscreen users had a 25(OH)D concentration greater than 75 nmol L^{-1} compared with 9% of the sunscreen users (P = 0·002). There is little information about the questions used to measure daily activity, and no descriptive data are presented so the success of the matching cannot be determined.
3 In a study among children and adolescents from Pisa (Italy)[29] sunscreen use was categorized into 'regular' and 'nonregular'; 'regular' was defined as always applying a sunscreen with an SPF of 15 or higher at least 30 min before exposure to sunlight and reapplying every 2 h after swimming. Despite the stringent definition, 41% of children and 30% of adolescents reported regular use. Among those in the highest sun-exposure category, the 25(OH)D concentration was approximately 20 nmol L^{-1} lower in regular vs. nonregular sunscreen users (47 nmol L^{-1} vs. 66 nmol L^{-1}). There was no association in those who did not spend significant time outdoors. In a model including age, sex, season, body mass index, sun exposure and residence (urban vs. rural), the odds of having 25(OH)D concentration less than 75 nmol L^{-1} was seven times higher in regular compared with nonregular sunscreen users [odds ratio (OR) 7·06; 95% confidence interval (CI) 2·86–17·40]. There was no adjustment for clothing or shade-seeking behaviour.
4 The final study[30] included 8378 participants from Japan. In women, sunscreen users (43%) had lower odds of having a 25(OH)D concentration of 75 nmol L^{-1} or greater after adjustment for time outdoors (OR 0·71; 95% CI 0·52–0·97). There was no association in men, among whom sunscreen use was infrequent.

Discussion

There is limited evidence on which to base advice about the effect of sunscreen use on vitamin D. Our review identified four experimental studies, including 144 participants in total, all reporting that sunscreen use abrogated the increase in

Table 3 Summary of observational studies: the cells contain the number of studies in categories defined according to unadjusted (for sun exposure) and adjusted (for sun exposure) analyses

	Unadjusted			
Adjusted	No association	SS use associated with higher 25(OH)D	SS use associated with lower 25(OH)D	Not reported
No association	9[a]	7[a]	2[a]	3[a]
SS use associated with higher 25(OH)D	0	3[b]	0	2[b]
SS use associated with lower 25(OH)D	0	0	3[c]	1[c]
Not reported	24[a]	12[b]	3[c]	0

[a]Group 1 in Tables S1–3 [no association between SS use and 25(OH)D concentration in adjusted analyses or, if adjustment not performed, in unadjusted analyses]; [b]Group 2 in Tables S1–3 [SS use associated with higher 25(OH)D concentration in adjusted analyses or, if adjustment not performed, in unadjusted analyses]; [c]Group 3 in Tables S1–3 [SS use associated with lower 25(OH)D concentration in adjusted analyses or, if adjustment not performed, in unadjusted analyses]. See Supporting information. 25(OH)D, 25 hydroxyvitamin D; SS, sunscreen

vitamin D_3 or 25(OH)D_3 concentration that occurs following exposure to artificially generated UVR. The observational studies identified had considerable limitations, but most found no association between sunscreen application and 25(OH)D concentration. The most applicable evidence comes from two randomized controlled field trials, neither of which found any effect of regular sunscreen application on 25(OH)D concentration.

The experimental studies were mostly small, and used different UVR sources and doses, sunscreens and study designs, so are not directly comparable. Nevertheless, all were in line with the expectation that sunscreen, as used in experimental conditions, significantly reduces vitamin D production in the skin. Three studies found that with sunscreen use there was no significant increase in vitamin D_3 concentration after exposure to a single fixed dose of UVR.[20–22] One used an SPF 50 sunscreen applied at 2 mg cm^{-1},[22] but the other two found that even relatively low SPF sunscreen (resulting in effective UVR doses of approximately 0·123 and 0·06 MED) could largely abolish vitamin D_3 production.[20,21] Two of these three studies did observe a small, albeit nonsignificant, increase in vitamin D_3 concentration, suggesting that with regular UVR exposure a more marked increase would be observed.[20,22] A recent study observed a small increase in 25(OH)D concentration with a UVR dose as low as 0·2 MED (the lowest dose given).[31] We identified two studies that investigated the effect of sunscreen on 25(OH)D concentration. Both found that the increase in 25(OH)D concentration after irradiation was lower with than without sunscreen.[22,23] However, even with an ultra-high SPF sunscreen applied optimally, resulting in an effective UVR dose of only 0·02 MED, there was some increase in 25(OH)D concentration after a single exposure.[22] These findings suggest that with regular sun exposure sufficient UVR may be received to avoid vitamin D deficiency, even with sunscreen applied.

The UVR generated by the lamps in the experimental studies has a fixed ratio of UVA to UVB, and two studies used a source that extended into the UVC range.[20,21] In contrast, the UVA to UVB ratio in sunlight varies according to location, season and time of day, and does not include UVC. The UVR spectral output and dose delivered, combined with the sunscreen's absorption profile (i.e. matching of the sunscreen to the spectral output), will affect the impact of sunscreen use on vitamin D production. Thus, the results of these experimental studies cannot be used to inform public health policy.

In the two randomized field trials daily sunscreen application did not have any effect on circulating 25(OH)D concentration. The sunscreen in the largest of these trials was applied at a median thickness of 0·8 mg cm^{-2}.[32] The thickness in the other trial was not stated but many participants reported using less than the recommended amount. It is possible that thicker application would have influenced vitamin D production. Both field trials used an SPF ~16 sunscreen, which is significantly lower than the SPF 30 that is now recommended.[33,34] The largest of the studies took place in a subtropical environment where the average maximum UVR index is in the high-to-extreme range for at least 8 months of the year (and does not drop below 4 in any month), and temperatures are conducive to outdoors activities even in winter; these findings may not translate to other climates. In addition, sunscreens vary according to the UVR spectrum covered. At a given SPF, increasing UVA protection reduces protection from UVB wavelengths.[35] Thus, trials of a high-SPF broad-spectrum sunscreen in different ambient UVR environments are needed to determine the broader impact on vitamin D status of recommending routine sunscreen application.

Among the observational studies a key finding of the review was the substantial variation in study design, analytic approaches and reporting, considerably influencing the interpretation of these studies. Most of the observational studies had suboptimal assessment of both sunscreen use and key confounders, particularly skin type and UVR dose. Laboratories performing 25(OH)D assays were not necessarily taking part in a quality control scheme, possibly resulting in inaccurate or imprecise measurements leading to nondifferential measurement error. Many studies did not present descriptive 25(OH)D data and there was little consistency among those that did. Most analyses were not carefully designed to control for confounders;

further, 25(OH)D was analysed variably as either a continuous or a categorical variable with no uniformity in the cut points used. We thus performed a qualitative synthesis only.

Most observational studies found no association between sunscreen use and 25(OH)D concentration. Among those that did, the most common finding was that sunscreen was associated with increasing 25(OH)D concentration. Sunscreen is often used to facilitate outdoors activity,[36] so control of this factor is crucial. Self-reported time outdoors was the most common method of estimating exposure; nondifferential measurement error was therefore likely to be considerable, causing incomplete control of confounding. Nevertheless, these results suggest that sunscreen application does not mitigate the benefits to vitamin D production of spending time outdoors. Conversely, sunscreen may be used in people at high risk of skin cancer as part of a broader suite of protection activities. None of the four studies that found sunscreen use was associated with lower 25(OH)D concentration adjusted for clothing, hats or shade-seeking behaviour in their analyses.

Strengths of our study include the systematic approach to identifying and reviewing the extant literature, including identifying studies that were not specifically designed to explore this issue. Any observational studies that were not identified would most likely have found no association, so would not materially change our conclusions. Our quality scoring of studies was based on the information provided in the publication and may not reflect the true quality of the study.

It is important that both the risks and the benefits of sun exposure be considered when developing recommendations about sun protection. Sunscreens are designed to prevent erythema and have been shown to do so in real-life settings, particularly when applied at optimal thickness.[37] The action spectra for vitamin D production and erythema coincide, and while the experimental studies identified by our review suggest that there is a theoretical risk that sunscreen use will increase the risk of vitamin D deficiency, we found no evidence from studies in real-life settings that this occurs. The observational studies should be interpreted with caution, but most are in agreement with the two high-quality randomized field trials which found that sunscreen use did not influence 25(OH)D concentration. However, there have been no randomized field trials of a sunscreen with a very high SPF, and it is plausible that these may influence vitamin D, particularly when the UV index is relatively low but above the level at which sun protection is advised (e.g. UV index of 3–5). This needs to be investigated in future trials conducted among men and women of different ages and skin types and across a range of climate zones to ensure variation in ambient UVR. In the interim, these results suggest that the risk of vitamin D deficiency due to sunscreen use is low and is unlikely to outweigh the benefits of sunscreen for skin cancer prevention.

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Supporting Information

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

Search terms S1 Search terms used: MEDLINE/PubMed, Embase and Web of Science.

Quality Assessment Tool S1 Item, category and score.

Table S1. Characteristics of observational studies (grouped by findings and ordered by study year and then first author name).

Table S2 Sunscreen measure, 25(OH)D assay and scores for observational studies.

Table S3 Summary of results for observational studies (with relevant notes).

Fig S1. PRISMA flow diagram for study inclusion.