SACN: Draft Vitamin D and Health Report

Thank you very much indeed for giving me the opportunity to comment from my area of expertise. I also hugely appreciate the expertise, dedication and hard work of the SACN committee in producing this report. I'm very much hoping that my detailed input on the following pages is helpful, and that you appreciate hearing my genuine comments, which are made in the very best of spirit. You are most welcome to get back to me by email or phone on any points at all that aren't clear or where you'd like any other information.

General comments

It is appreciated that this document has involved much research and hard work, and that some areas are particularly challenging, including the photobiology/photodermatology of vitamin D. The report will provide a highly useful and well-read source of information. Comments made are to assist especially in the area of photodermatology/photobiology of vitamin D, where specialist input was sought by SACN to assist with specific tasks; more comprehensive discussion and integration of this area could have been provided by including members with this expertise within the regular working group. This is particularly salient as sunlight is acknowledged to be the major source of vitamin D for most people in the UK.

A conclusion of this document is that the sunlight source of vitamin D cannot be measured and therefore that this source cannot be taken into account when considering the vitamin D requirements of the UK population. There are indeed complexities when considering the sunlight source, however measurements have been made that assist with this question, albeit in units that do not fit well with the standard nutritional assessments and definitions for oral nutrients.

Ideally, the available UK human in vivo study data on the sunlight source of vitamin D should be taken into account to provide the UK population with information and common sense (as not fitting the standard nutritional definitions) on vitamin D sources. Providing this information will positively assist the health of the UK population and also importantly assist in avoidance of harm, for example, people who take too much sunlight exposure in their quest to obtain vitamin D, including those not wishing to take oral supplements.

At least, more information including the data from these UK human in vivo longitudinal and intervention studies, examining the relationship between amounts of sunlight exposure, and amounts of simulated sunlight exposure, with 25(OH)D outcomes, should be presented. These are acknowledged internationally to be the most robust human in vivo datasets available on the sunlight/vitamin D relationship. Currently the low information on these studies (e.g. see section 179) contrasts sharply with detail presented on some other smaller less robust studies, using ultraviolet sources unlike sunlight, to parts of the body unusually exposed, and estimates involving many assumptions (e.g. see sections 177, 178, 181, 182). The DRV chapter includes an important modelling section addressing a specific question set by SACN involving projections including 6 and 3 months sunlight exposure, however the Manchester in vivo studies had different objectives, a different setting (with 6 weeks duration), and their actual in vivo data, which could be projected in different ways, are important to present separately at the earlier stage in the document (such as 179), alongside the other less-realistic studies that are given prominence (177, 178, 181, 182).

One much more minor (thought should be corrected as it is definitely erroneous) matter is that "the dermis" or "dermal" cannot be used as a substitute for "skin". This is because the dermal layer of the skin is a specific structure, with the 2 skin compartments being the (upper) epidermis and the (lower) dermis, i.e. the epidermal and dermal layers. This mistake

occurs very many times throughout the document and is misleading. For example, vitamin D synthesis actually occurs predominantly in the epidermal layer of the skin not the dermal layer, so you can see the confusion that arises. “Dermal” can be corrected to “cutaneous” or “skin”.

3. Photobiology of Vitamin D
Effect of skin pigmentation on dermal synthesis
Page 19, paragraph 115

Current text of 115:
“darker skin has the same capacity to synthesise vitamin D if the dose of radiation is adjusted for the protective effect of melanin (Farrar et al, 2013)”.

LER comments:
The Farrar paper 2013 is not the most suitable to refer to in this context and I would suggest using an alternative.

Comment [LR1]: I can send you a reference if helpful

Page 19, paragraph 116

LER comments:
The Farrar et al 2013 dose-ranging study data (actual, in vivo, data) would be beneficial to present in its own right, and currently does not appear in the document.

Suggested new text (suggested to use/adapt to add immediately after the current 116 text):
“Farrar et al (2013) further reported a UVR-25(OH)D dose-response study using UVR (95% UVA, 5% UVB) closely simulating UK summer sunlight and performed in winter-time to avoid confounding by ambient UVB. South Asians (brown, skin type V, total n=60) received 1 of a range of 6 UVR doses (0.65-3.9 SED) 3 times weekly for 6 weeks to skin sites commonly exposed in summer (~1/3 body surface area) in a whole body irradiation cabinet. At baseline, 90% subjects had 25(OH)D <25 nmol L−1. While a final 25(OH)D level ≥50 nmol L−1 was reached in only a minority of subjects receiving the higher doses, of those receiving a UVR dose of ≥1.95 SED, 25(OH)D was raised above 25 nmol L−1 in most (94%) subjects, with a mean final level of 37.5 nmol L−1 (SD 12.5), and mean rise of 21.8 nmol L−1 (SD14.4; 95%CI: 17-26.5). This equates to ≥22.5 minutes (ranging from ≥19.5 mins if lying horizontal to 25.5 mins if standing vertical) x6 weekly, when wearing casual clothes to expose ~1/3 skin surface area, in unshaded midday summer sunlight. This estimate takes account that in real life, the dorsal and ventral body surfaces are not exposed simultaneously to sunlight, and people adopt postures ranging from horizontal to the vertical randomly orientated to the sun (Webb et al, 2011). This work shows that South Asians could enhance their vitamin D status through modest sun exposure practice in the UK.”

Comment [LR2]: Please see later comment re this highlighted text

4. Measuring vitamin D exposure (from diet and skin synthesis)
Relationship between UVB sunlight exposure and serum 25(OH)D
(i) Page 32, paragraph 179

Current text:
“ A UK group (University of Manchester) has examined and reported the efficacy of a dose range of simulated summer sunlight exposures in raising serum 25(OH)D concentrations in UK white-skinned adults (Farrar et al, 2011) and in adult of South Asian ethnicity (Farrar et al, 2011, 2013).”

LER comments:
The Manchester in vivo data are acknowledged internationally to be the most substantive human datasets examining the relationships between sunlight and simulated sunlight UVR with 25(OH)D outcomes, acquired under as realistic as possible conditions. All were

performed according to high quality peer reviewed protocols and competitively funded by national bodies (PI LE Rhodes). It is insufficient to refer to these so briefly, contrasting with the information given on much more artificial studies and estimates based on many assumptions and very little in vivo data. These data are not presented in the DRV chapter, where specific and different scenarios are addressed.
There are also inaccuracies in the above text, as firstly, the UK white skin adult study is that of Rhodes et al 2010, and secondly, a dose-range study has not been performed in white adults. I suggest the above text is corrected, as below, and that fuller information is given to record the information on the pivotal Rhodes et al 2010 study in white adults. There has also been no data presented from the Farrar et al 2013 S Asian dose-response study; I have now provided that earlier (following paragraph 116 on page 19).

Potential adjusted text:
"A UK group (University of Manchester) has examined and reported the efficacy of simulated summer sunlight exposures in raising serum 25(OH)D concentrations in UK white-skinned adults (Rhodes et al, 2010) and in adults of South Asian ethnicity (Farrar et al, 2011, 2013). These were performed in winter-time (latitude 53.5°N) to avoid confounding by UVR and with subjects wearing summer clothing to involve commonly exposed skin sites (thus avoiding the need for commonly made but unproven assumptions that all skin sites respond similarly and that 25(OH)D production is proportionate to surface area exposed).
It was found that in white adults (n=109), low dose, sub-erythemal UVR (1.3SED 3×weekly for 6 weeks, total 23.4SED) when exposing ~1/3 body surface area produced a mean final 25(OH)D of 70(SD16) nmol L^{-1}, with 90% subjects ≥50 nmol L^{-1} (Rhodes et al, 2010) and 26% reaching ≥80 nmol L^{-1}. The UVR dose equates to ~15 minutes (ranging from 13 mins if lying horizontal to 17 mins if standing vertical) x6 weekly, wearing casual clothes to expose ~1/3 skin surface area, in unshaded midday summer sunlight. This estimate takes account that in real life, the dorsal and ventral body surfaces are not exposed simultaneously to sunlight, and people adopt postures ranging from horizontal to the vertical randomly orientated to the sun (Webb et al, 2011). The findings coincide with a longitudinal study in similar subjects (n=109) living at the same location, where the polysulphone badges they wore revealed personal natural sunlight UVR exposures of ~3.4 SED/week in summer; mean end-summer 25(OH)D level was 71(SD26) nmol L^{-1}, with ≥50 nmol L^{-1} and ≥80 nmol L^{-1} reached in 82% and 24%, respectively."

Comment [LR3]: I expect you already have this definition/ a glossary somewhere, but in case helpful, here is definition:
1 standard erythemal dose (SED) is an erythemal effective radiant exposure of 100 Jcm^{-2}

Comment [LR4]: If in any of the studies you prefer to know the % subjects ≥*25 nmol L^{-1} then we can check and send you this*

Comment [LR5]: This text could potentially be deleted if you retain the current order of sections (i.e. with describing pigmented subjects before white subjects) as this is described earlier (as highlighted in turquoise).

However, it is important that the Rhodes 2010 and Webb 2011 papers are still referenced together here as they in tandem provide the fuller interpretation of the data.

5. Relationship between vitamin D exposure (from diet & skin synthesis) and serum 25(OH)D concentration
Relationship between UVB sunlight exposure and serum 25(OH)D, page 31 (172-181)
and
8. Dietary vitamin D intakes and serum/plasma 25(OH)D concentrations of the UK population
Serum 25(OH)D by season, page 106 (649-652)
Serum 25(OH)D concentration by region, page 106 (653-656)
Serum 25(OH)D concentration by ethnicity, page 107 (661-664)
9. Review of DRVs for vitamin D
At risk groups, page 118 (715)

LER comments:
Longitudinal studies in adults (x3) have been performed at mid-UK latitude (Greater Manchester) that examine the personal sunlight UVR exposure dose of mixed sex population groups throughout the year, and relationship to 25(OH)D level. I'd suggest that the main data of the first 2 studies below are inserted in the section **Relationship between UVB sunlight exposure and serum 25(OH)D** on page 31 (with appropriate elements appearing in the other sections listed above on page 106, 107), whereas the data from the

third group is suggested to be presented in: by season (p106), by region (p106) and in **At risk groups** (p118).

Additional suggested text:
Study 1
"Solar UVR exposure - serum 25(OH)D relationships were examined in a longitudinal study of male and female white Caucasians (n=109, skin type I-IV, aged 20-60 years) at mid-UK latitude (Greater Manchester, 53.5°N). Personal UV dosimeter badges showed they were exposed to ~2% of ambient UVR (Webb et al, 2010), with median exposures of 3.7 SED/week in spring/summer and 0.1 SED in winter. Monthly 25(OH)D measurements revealed a seasonal pattern with peak level (mean 71, SD 26 nmol L−1) in September and trough (45.8, SD21.8) in February, while estimated dietary vitamin D remained low in all seasons (median 3.27 μg day−1, range 2.76 - 4.14). Sun exposure diaries indicated that relatively short frequent solar exposures increased vitamin D status, subjects spending a mean daily time outdoors in spring/summer of 9 (SD13) minutes/day on weekdays and 18 (SD23) at weekends during peak ambient UVB times (11-00 to 13-00)."

Study 2:
"A longitudinal study examined year-round vitamin D status, sunlight exposure and other contributors in male and female adults of South Asian ethnicity (skin type V, aged 20-60 years, n=125) living at mid-UK latitude (Greater Manchester, 53.5°N) (Kift et al, 2013). Compared with white Caucasian adults at the same latitude, the South Asians had ~1/3 the vitamin D status year-round, with median summer and winter 25(OH)D of 22.5 nmol L−1 (IQR 16.8-34.3) and 14.5 (10-20.3). Fifty-eight% and 90% South Asians had 25(OH)D <25 nmol L−1 in summer and winter, respectively. In addition to skin type difference, the South Asians had lower dietary vitamin D (median 1.3 μg day−1), lower personal UV exposure as recorded by their dosimeter badges (~1% ambient UV), and smaller surface area exposed."

Study 3:
"A longitudinal study examined year-round vitamin D status in a sample of photosensitive patients (n=53) living in Greater Manchester, UK (53.5°N) (Rhodes et al, 2014). Photosensitive people, who restrict their sun exposure and employ photoprotective measures to avoid precipitating their condition, still showed seasonal 25(OH)D variation, but substantially less than in concurrently-assessed healthy adults at the same latitude, with 9% of patients at summer-peak and 32% at winter-trough having 25(OH)D levels below 25 nmol L−1. After adjustment for demographic factors, values for patients were lower than healthy volunteers by 18% (95% CI 4 to 29%) and 25% (7 to 39%) in summer and winter, respectively. Photosensitive patients are at high risk of year-round vitamin D deficiency, contrasting with seasonal lows in healthy adults."

9. Review of DRVs for vitamin D
Modelling exercise
Page 112, 681 onwards

Modelling the summer sunshine exposure required to maintain a winter serum 25(OH)D ≥25 nmol/L, 682-691

LER comments:
In this modelling study, Ann Webb was asked to perform specific estimations based on regular sunlight exposure across 6 months (spring to autumn, section **688**) or 3 months (June-August, section **690**) and a target of 95% population **≥**25nmol/l of 25(OH)D at winter trough. This is the only data presented here, and as commented earlier it will be appropriate to present the actual in vivo study data these were partly modelled from at an earlier stage in the document.

Modelling the vitamin D intakes required to achieve a protective serum 25(OH)D target concentration ≥25 nmol/L, 692 & onwards

LER comment:
While the dose from the sunlight/skin source clearly doesn't fit neatly within standard methods of nutrient assessment, sunlight remains the major source of vitamin D for most people, and it would be good to consider other, more pragmatic, ways that sunlight's input is viewed to produce recommendations benefiting UK health and avoiding the harm to human health of giving no guidance. Differential guidance would be required for different skin types, with provisos, and a typical scenario given, and this would benefit most people.

At risk groups, page 118

715: Please specifically add mention of people who avoid sunlight and are advised to photoprotect for medical reasons: photosensitive patients (see earlier information; Rhodes et al Br J Dermatol 2014 now provides substantive data) and those prone to skin cancer especially organ transplant patients. The patients usually do not take vitamin D supplementation (Stafford et al, 2010) and thus they and their physicians may not recognise that "at-risk group" applies to them, from the brief description given.

Comment [LR6]: Evidence for this in photosensitive patients is in Stafford et al BJD 2010

716 (this may also apply to an earlier section): There is scarce data examining responses to and contributions of sunlight to vitamin D status in older adults (longitudinal/seasonal cohort data, and data on biological responses of older skin to sunlight), and this is warranted particularly considering the UK's demographic changes.

Summary and Conclusions page 119

722: This sentence needs re-wording as quantification can be performed, though not in standard nutritional terms. For example, the sentence could be adjusted as follows:

"Sunlight UVB exposure could not be taken into account in setting the RNI because it is not possible to quantify the contribution it made to serum 25(OH)D concentrations within the general population *with the standard assessment methodology used for oral nutrients*."

Overall summary and conclusions p121

LER comment:
While the dose from the sunlight/skin source clearly doesn't fit neatly within standard methods of nutrient assessment and recommendation, it is recognised that sunlight remains the major source of vitamin D for most people, and it would be good to consider other, more pragmatic, ways that sunlight's input is viewed to produce recommendations benefiting UK health and avoiding the harm to human health of giving no guidance (for example white skin people taking more sunlight to satisfy their vitamin D than is needed, increasing the risk of skin cancer, and brown skin people being unaware that UK sunlight exposure can assist their vitamin D). Differential guidance would be required for different skin types, with provisos, and a typical scenario given, and this would benefit most UK people.

Thank you again very much indeed for giving me the opportunity to comment from my area of expertise. Hilary very kindly invited me to one of the working group's meetings, but unfortunately due to having cataract surgery that week I had to decline. I hugely appreciate the expertise, dedication and hard work of the SACN committee.

My kindest regards, Lesley