Main points

This comprehensive document has examined many health outcomes in relation to vitamin D and rightly focused on musculoskeletal outcomes as this is where the robust evidence base lies. In spite of new evidence since the previous SACN report, it is clear that we are still lacking sufficient knowledge in many areas.

1) Heart – blood pressure

The meta- analysis included blood pressure data collected at the start and at the end of treatment - and most studies were not designed to look at seasonal effects. One of the key findings in VICtORy study (Wood et al JCEM 2012), with all study participants starting between Jan-Feb, was that blood pressure decreased in summer and went back up again in winter – and this was pattern was identical for two vitamin D treatment groups and placebo. This provides evidence to support that other factors besides vitamin D are influencing blood pressure, and explains why associations with vitamin D are difficult to separate from sunlight exposure/ season unless the study is designed appropriately.

2) Population protective

Population protective cut-off (point 559) would indicate that below this level there is risk of deficiency for everyone, and this would seem to be more of an LRNI than RNI. Point 704 indicates that a population mean vitamin D intake of 10ug a day means that 97.5% will be >25 nmol/L. This is confusing especially as the report states that it is not the same as an RDA - yet RNI are usually the same as RDA. Can this be reworded to make more sense? Perhaps RNI is not the correct word – as it is clearly not the same approach used as for other nutrients. Also vitamin D is the only nutrient that cannot be met by a healthy balanced diet – and if insufficient sunlight will require supplementation or food fortification (or a combination).

3) Winter decrease in vitamin D status – and risk management

There does not appear to have been serious consideration that having 25(OH)D below 25 nmol/L in summer is much more of an issue than in winter. There is no evidence that bone turnover changes from season to season in the general population. The concern is reaching those who have low vitamin D status year round because of low sunlight exposure in summer. It is also not known whether giving vitamin D year round could potentially interfere with any natural adaptation to low vitamin D status especially in children/ adolescents.

In the ANSAViD study there were measurements in spring (nadir) for 3 years – 2006, 2007 and 2008. In spite of a poor summer in 2007, there was no difference in end of winter values (Mavroeidi PlosONE 2013), suggesting there may be an adaptation or that 25(OH)D has to be much lower than 25 nmol/L to affect bone turnover.

As stated in the report, it is not possible to determine easily who in the population is at risk from lack of sunlight exposure. However as none of the UK population can make vitamin D in the winter, it is only summer behaviour that determines who is going to be at risk of deficiency. If in considering the risk management of preventing vitamin D deficiency without causing potential harm, supplementation and not food fortification is the route taken – then taking vitamin D in the summer

might be the answer. If there is an adaptation to low vitamin D in winter, along with other changes with shortening day light hours, supplementation could interfere with this process. A campaign of taking supplements if you are at work/ putting sunscreen on may be an option rather than year round supplementation. Although this would differ from RNI approach it would be advantageous as an interim approach – as if it effectively reduced the risk of vitamin D deficiency, there may be no need to supplement year-round.

The alternative approach would be to supplement everyone in winter, but that would not reach the groups most at risk of vitamin D deficiency, who do not go out at all in summer or are covered up. They should continue to take vitamin D year-round as currently recommended.

It is important to protect musculoskeletal health through avoiding vitamin D deficiency. If year round supplementation is required and an RNI is set at 400 IU it needs to be clarified that this includes dietary intakes. It is likely if supplementation is required then 400 IU will be given, so population intakes would be 500-600 IU a day.

4) Cut-off of 25 nmol/L versus 30 nmol/L (point 556)

For consistency with other countries, and what most clinicians and IOM use currently it would have been preferable that the panel had chosen 30 nmol/L as the cut-off, rather than what had been used in the past. It is clear that the cut-off is not diagnostic of disease, but indicative of risk of poor musculoskeletal health, and therefore the higher cut-off would be preferable.

5) Balance with other nutrients

Is it assumed that calcium is adequate? The interaction with other nutrients has not been considered. In foods that naturally contain vitamin D3, vitamin A is also present, and there may be an optimal balance, which will be altered if vitamin D only is given either in foods or as supplements. This may affect some 'at risk' groups more than the general population.

<u>Minor comments – no response required</u>

92. Artificial tanning booths - UVR – the concern is that UVA is high – so although there is some UVB that can make vitamin D, there will be UVA that is damaging without benefiting vitamin D status.

144. Is anything known about the C-epimer binding to VDBP?

163. This is inconsistent with VICtORy study and dosing studies (Gallagher) showing that the increase in 25(OH)D diminishes with ever increasing doses of oral vitamin D.

171. 10 ug incr > 50 nmol/L in 97.5% white women – suggests that less than 10 ug a day vitamin D would be required for > 25 nmol/L 25(OH)D in white people. More is required for other ethnicities, but this is the group that currently has an RNI.

214. Rickets <30 or > 30nmol/L – useful to give the number of remaining studies and what they were.

241. splaying index – is there some controversy about this index?

293. Useful to include starting 25(OH)D, which was low (30-32 nmol/L)

400. OR 1.04 –is that not higher risk of prostate cancer rather than a reduction?

473. typo? (the how)

557. Population protective 97.5% Year round?? Concern?

570. typo? (including for)

582. Falls and fractures – increase in black women. Does this not indicate that low vitamin D status in Blacks may be appropriate for their needs. What is the OR for Asian women increased fracture risk?

617. Clarify whether 'meat and meat products' includes fish or not

636. Section x?

650. If summer < 25 nmol/L more of a concern than if winter<25 nmol/L

652. Cohort Caucasians in Scotland (ANSAViD) – had spring measurements for 3 years (see main point above)

680. Confusing. Does RNI really mean LRNI? RDA is equivalent to RNI. See main point above.

687. 85.8 nmol/L end of summer? This is higher than most women achieved in ANSAViD and VICtoRY (placebo) – and only seen for those who went on holiday abroad.

688. 9 minutes – danger of burning for some skin types especially if midday?

689. only hands and face

Concern – one author/ centre – but 25OHD mixed.

704. mentions 9 for immunoassay, 12 for tandem mass spec > 25 nmol/L in 97.5% of adults.

775. This states that 25(OH)D < 25 nmol/L is 20-34% England and 28-38% Scotland at any time of year. What are the two figures – different age groups or seasons?