Scientific Advisory Committee on Nutrition

6th MEETING

Vitamin D Working Group

7 December 2012, Wellington House, London

DRAFT MINUTES

Chair:	Dr Ann Prentice
Members:	Professor Kevin Cashman
	Professor Roger Francis
	Professor Tim Key
	Professor Susan Lanham-New
	Professor Harry McArdle
	Dr Stella Walsh
	Dr Tony Williams
	Professor Ian Young
Adviser (*UV exposure):*	Dr John O'Hagan (HPA)
Secretariat:	Dr Louis Levy (DH)
	Ms Mamta Singh (DH)
	Mr Heiko Stolte (DH)
Observers:	Dr Fiona Comrie (FSA Scotland)
	Mr Ian Chell (DH)
	Ms Cath Mulholland (FSA)

Agenda item 1: Chair's welcome

1. Dr Ann Prentice welcomed Members to the sixth meeting of the SACN Working Group (WG) on vitamin D. She explained that she would be chairing the meeting since apologies for absence had been received from the Chair of the WG, Professor Hilary Powers. Apologies for absence had also been received from Dr Alison Tedstone. The Chair welcomed Dr Louis Levy (Department of Health) who, in the absence of Dr Tedstone, was attending the meeting to provide support for the Secretariat.

2. The Chair also welcomed Professor Antony Young, a dermatologist and professor of experimental photobiology at King's College London and principal co-ordinator of ICEPURE[a], an EC project looking at beneficial & adverse effects of exposure to ultraviolet radiation (UVR). Professor Young had kindly agreed to give a presentation on the photobiology of vitamin D.

3. Members were reminded that, for logistical reasons, it had been agreed to discuss vitamin D & UV exposure in the morning session and other business in the afternoon session.

4. Before proceeding with the meeting, the Chair invited Members to declare any changes to their conflicts of interest.

   (a) Professor Roger Francis declared that he had been asked to serve as an adviser for a pharmaceutical company developing a pharmacological preparation of vitamin D. He also reminded the WG that he was the joint author of a critique of the paper by Priemel et al (2010)[b], relating serum 25(OH)D to bone histomorphometry, which has provisionally been accepted for publication[c]. The paper by Priemel et al (2010) had been considered by the WG at its previous meeting.

   (b) Professor Ian Young declared that he had received funding from two charities for research on UV light exposure and eye disease.

   (c) Professor Susan Lanham-New declared that she had provided one full day and two-half days consultancy with Danone discussing calcium and micronutrients in general. She also informed the WG that a formal documentation had been made relating to her work with D3Tex Ltd. on the use of UVB transparent material to prevent vitamin D deficiency in women dressing in cultural style. The UK patent had been granted and the Gulf Corporation Council Patent was pending.

Agenda item 2: Adverse effects of sun exposure (John O'Hagan) (SACNvitD/12/48)

5. The chair invited Dr John O'Hagan from the Health Protection Agency to give his presentation on the adverse effects of sun exposure. The main points covered in Dr O'Hagan's presentation are summarised below.

   (a) The sun is the main source of UVR. Solar UVR is categorised into three types according to

[a] Impact of climatic and environmental factors on personal ultraviolet radiation exposure and human health.
[b] Priemel M, von Domarus C, Klatte TO *et al*. Bone mineralization defects and vitamin D deficiency: histomorphometric analysis of iliac crest bone biopsies and circulating 25-hydroxyvitamin D in 675 patients. *J Bone Miner Res*. 2010; 25:305-312.
[c] Since meeting, this has been published online: Aspray TJ, Francis RM. What can we learn about vitamin D requirements from post-mortem data? *Osteoporos Int.* 2013. Jan 9 [Epub ahead of print].

wavelength (nm[d]): UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm). UV penetrance of skin is very low for UVC, medium for UVB and deepest for UVA.

(b) The spectrum of solar radiation is modified on its path through the atmosphere. Ozone is a key factor in reducing and modifying the UVR reaching ground level. As solar radiation passes through the atmosphere, UVC and 90% of UVB is absorbed by ozone. The amount of UVR reaching ground level is modified by factors such as altitude, ground reflection of UVR (e.g., sand reflects 25%; snow reflects 80%), cloud cover and shade.

(c) The Solar UV Index (1 to 20) is used to advise populations on the strength of the sun's UVR. In the UK, the UV Index does not usually exceed 8.

(d) Skin exposure to UVR is dependent on a number of factors, including exposure angle. An area of skin exposed to incoming radiation at a perpendicular angle receives a larger radiation dose than exposure at a higher or lower angle. This makes it difficult to measure a person's actual UV exposure. Skin exposure to UVR is also modified by clothes and sunscreen.

(e) Biological effects of UVR on skin include erythema[e], tanning, skin ageing, skin cancer and immune suppression.

(f) Skin type is classified into 6 categories according to its response to UVR: from most sensitive (type I/fair skin) to least sensitive (type VI/dark brown or black skin). Two measures are used to quantify erythema risk: the standard erythemal dose (SED) and the minimal erythemal dose (MED). SED is a fixed physical quantity, equal to 100 J/m^2. The MED varies in each person because the amount of UVR required to produce a just-measurable degree of erythema depends on skin type, time of year, behaviour and possibly age; one MED is the minimum dose of UVR that produces erythema in that person's skin.

(g) UVA and UVB are implicated in photoageing, which is caused by cumulative exposure to sun.

(h) Skin cancers are classified into non-melanoma skin cancers (NMSC) and malignant melanoma (MM). NMSCs include squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Epidemiological evidence suggests a link between SCCs and cumulative lifetime exposure in Caucasians. Although exposure to UVR is implicated in BCC risk, the link with cumulative exposure is less clear. The risk of MM is associated with excessive UVR exposure, however the risk of MM is greater in indoor than in outdoor workers; large

[d] Nanometers.
[e] Redness of skin/sunburn.

bursts of UVR may play a role in disease aetiology.

(i) Skin exposure to UVR can cause a suppressed immune response to cutaneously presented antigens.

(j) UVR can also cause eye damage. While UVC is absorbed at the cornea surface, UVB penetrates further into the cornea and UVA into the lens. Acute UV exposure of the eye may result in photokeratitis and photoconjunctivitis. The role of UVR in cataract is unclear. UVR does not appear to play a role in age-related macular degeneration.

6. The chair thanked Dr O'Hagan for his presentation.

Agenda item 3: The photobiology of vitamin D (SACNvitD/12/49)

7. The chair invited Professor Antony Young to give his presentation on the photobiology of vitamin D. The main points are summarised below.

(a) Action spectra (wavelength dependence) have been established by the Commission Internationale de l'Eclairage (CIE) for different endpoints (e.g., pre-vitamin D production, erythema).

(b) Biological efficacy is more important than the relative amounts of UVA and UVB in sunlight. There is much more UVA than UVB at any time of the year but, if it is biologically weighted with the erythema action spectrum, UVB is much more effective than UVA for erythema. In winter, the relative contribution of UVA and UVB is similar.

(c) The erythema action spectrum is based on a mathematical composite of several studies. However, the action spectrum for pre-vitamin D production in human skin is based on a single skin sample (skin type III) and recent reviews have queried its reliability.

(d) Laboratory studies use UVB phototherapy sources, which also contain non-solar UVB radiation (< 295 nm) that is very effective at vitamin D production but makes it difficult to make comparisons with solar UVR.

(e) Laboratory studies have shown an inverse relationship between baseline 25(OH)D status and response to UVB. There are also important interactions between UVR dose and body surface area; higher doses are needed if a small area of the body is exposed while lower doses are adequate if larger body surfaces are exposed. Studies conducted as part of the ICEPURE project, which determined vitamin D status before and after holidays, have shown an increase in 25(OH)D concentrations at an individual and mean level but little correlation between an individual's UVR exposure and increase in 25(OH)D concentration.

(f) It is assumed that melanin is photoprotective because epidemiological studies have shown that people with darker skin have lower 25(OH)D concentrations than those with lighter skins. However, the limited number of laboratory studies have given contradictory results.

(g) Although sunscreen is advocated for prevention of sunburn, overall, the data show that vitamin D synthesis is still possible when sunscreens are used at the application density used for sun protection factor testing.

(h) One study (Webb et al, 1989[f]) using *ex-vivo* neo-natal foreskin has suggested that UVA degrades vitamin D but this has not been investigated *in vivo*.

8. The Chair thanked Professor Young for his presentation.

Agenda item 4: Discussion

9. In the discussion that followed the two presentations, the following points were noted:

(a) The sun protection factor provided by a tan (i.e., induced pigmentation) is not as protective as naturally darker skin.

(b) Different skin types have different vitamin D binding protein profiles; however, studies do not usually take this into account.

(c) The extent of the effect of latitude on vitamin D synthesis in the UK is not clear. While it probably has some effect, it could be relatively small compared to other factors. A study[g] which compared 25(OHD) concentrations in postmenopausal women residing in Aberdeen (north) and Guildford (south) reported a difference of approximately 10 nmol/L; however this difference might not be due to solar radiation. Although UVB (as a proportion of UVR) lessens with increasingly northern latitudes, the weather also gets progressively colder so people go outdoors less. There are also differences in the area of skin exposed.

(d) The uncertainty of the official CIE action spectrum for pre-vitamin D production is not well understood.

10. The Chair again thanked Professor Young for attending the meeting and for his presentation on the photobiology of vitamin D, which had helped to increase the WG's understanding of this complex subject.

Agenda item 5: Minutes of 5th meeting on 18 September 2012 (SACNvitD/12/min05)

[f] Webb AR, DeCosta BR, Holick MF. Sunlight regulates the cutaneous production of vitamin D3 by causing photodegradation. *J Clin Endocrinol Metab.* 1989; 68: 882-887.
[g] Mavroeidi A, O'Neill F, Lee PA et al. 25-hydroxyvitamin D changes in British postmenopausal women at 57 degrees north and 51 degrees N: a longitudinal study. *J Steroid Mol Biol.* 2010; 121(1-2): 459-61.

11. Before the start of this agenda item, Dr Louis Levy informed Members that the SACN Secretariat would be transferring to Public Health England from 1 April 2013.

12. Members were invited to comment on the minutes of the meeting held on 18 September 2012. The following amendments were agreed:
    (a) paragraph 15b, 2nd sentence – replace *'intra-assay'* with *'inter-assay'*;
    (b) transpose paragraphs 17 and 18;
    (c) paragraph 22 – replace *'vitamin D dependent rickets'* with *'vitamin D deficiency rickets'*;
    (d) paragraph 23, 2nd sentence – append with *'and where calcium intakes were regarded as a primary aetiological factor'*;
    (e) paragraph 26, last sentence – replace *'available evidence'* with *'evidence presented at the meeting'*;
    (f) paragraph 30, last sentence – replace with *'Growth of the skeleton is also important in children, therefore bone mass is also a relevant measure'*;
    (g) paragraph 31, last sentence – replace *'35 nmol/L for bone health'* with *'35 nmol/L, reported by Winzenberg et al (2010), for bone health in children and adolescents'*;
    (h) paragraph 37, 1st sentence – replace *'which administered'* with *'that administered'*;
    (i) paragraph 37, 2nd sentence – replace *'results from these studies were inconsistent and provided some evidence that vitamin D increases fracture risk'* with *'results from these studies were inconsistent: 1 reported no effect of vitamin D supplementation on fracture risk; 1 reported a reduction in fracture risk; and 1 reported an increase in fracture risk'*;
    (j) paragraph 42, 2nd sentence – replace *'p<0.0026'* with *'p<0.003'*;
    (k) paragraph 50, 1st sentence – include ethnicity (South Asian) of study population;
    (l) paragraph 56, 2nd sentence – replace *'tertile'* with *'third'*;
    (m) paragraph 60, 2nd sentence – replace *'rate of falls'* with *'number of falls'* and replace *'risk of falling'* with *'risk of being a faller'*;
    (n) paragraph 60, 3rd sentence – replace *'did not reduce falls'* with *'did not reduce the risk of being a faller'* and replace *'rate of falls'* with *'the number of falls'*;
    (o) paragraph 62, last sentence – state the actual 25(OH)D concentration used to define *'vitamin D deficient'*;
    (p) paragraph 71 – replace *'management/prevention* with *'management and/or prevention'*.

13. Before proceeding to the next agenda item, the Chair thought that it would be helpful for Members to be reminded of the current position in relation to the WG's collaboration with the Committee on Toxicity (COT) and the Committee on Medical Aspects of Radiation in the Environment (COMARE).

14. Ms Cath Mulholland, from the COT secretariat, informed the WG that the next COT meeting (11/12/12) would be considering calcium homeostasis, regulation and analysis. More extensive discussions on vitamin D will take place at subsequent meetings in February and March 2013. It was agreed that a WG representative would attend the February and March meetings.

15. Dr O'Hagan informed the WG that the Advisory Group on Non-Ionising Radiation (AGNIR), which reports to the Health Protection Agency, intends to produce a report on the risks and benefits of UVR in relation to vitamin D. AGNIR is due to begin its considerations at its first meeting in January 2013. The Chair of the WG has been invited to attend this meeting.

16. Members were informed that, since AGNIR was now considering UV exposure and vitamin D, the Committee on Medical Aspects of Radiation in the Environment COMARE, which the Secretariat had initially consulted for advice on the risks associated with sunlight exposure, would have no further involvement with the WG.

17. It was agreed to discuss how to proceed with this matter at the next meeting.

Agenda item 6: Matters arising from the Minutes of the meeting of 18 September 2012 (SACNvitD/12/35)

SACNvitD/12/38: *Vitamin D & rickets*

18. *Include information on calcium intakes in table of studies on vitamin D & rickets* – The table had been amended to include information on calcium intakes (*SACNvitD/12/51a).* It was noted that since very few studies provided data on calcium intake, it had not been possible to clarify whether the rickets had been caused by vitamin D or calcium deficiency.

19. *Contact British Paediatric & Adolescent Bone Group to check if any information available on number of patients in UK hospitals being treated for rickets (and the proportion caused by vitamin D deficiency)* - Replies had been received from Dr Nick Shaw (Consultant Paediatric Endocrinologist, Birmingham) and Dr Paul Arundel (Consultant Paediatrician in Metabolic Bone Disease, Sheffield) (SACNvitD/12/51b). Dr Arundel did not have any useful local data. Dr Nick Shaw did not think there was any good information on the numbers of children being treated for vitamin D deficiency rickets in the UK. He had forwarded copies of two papers (Ahmed et al, 2011 & Moy et al, 2012). Ahmed et al (2011) documented cases of vitamin D deficiency presenting to a children's hospital in Glasgow, while Moy et al (2012) reported on the success of an initiative in Birmingham to promote vitamin D supplementation for all children under the age of 5 years. Members agreed that the both papers would be of more relevance to the National Institute for Health and Clinical Excellence (NICE), since NICE is

currently developing public health guidance on *Safe Implementation of existing evidence based guidance on Vitamin D*.

SACNvitD/12/39: *Vitamin D & bone health in children & adolescents – consideration of original studies in Winzenberg et al (2011) meta-analysis*

20. *Include information on compliance in the studies included in meta-analysis* – The table had been amended to include information on compliance with the intervention and variance for baseline 25(OH)D concentrations (SACNvitD/12/52).

SACNvitD/12/40: *Vitamin D & bone health in postmenopausal women & older men & women: consideration of baseline 25(OH)D in studies included in IOM report*

21. *Include information on variance in baseline 25(OH)D & reconsider evidence when this had been done* – The table had been amended to include information on variance in baseline 25(OH)D concentration (SACN/vitD/12/53).

SACNvitD/12/41: *Vitamin D & fracture prevention in postmenopausal women*

22. *Check findings from different meta-analyses/systematic reviews that have assessed effect of vitamin D alone or with calcium on fracture risk* – The findings from the various meta-analyses/systematic reviews had been tabulated (SACN/vitD/12/54a).

23. *Check that any RCTs published since the IOM report have not been missed* – The table of studies had been amended to include the number of events (fractures) in each study and 2 large studies that had not been included in the IOM table (Larsen et al, 2004[h]; Smith et al, 2007[i]) (SACN/vitD/12/54b). No further studies, published after the IOM report, could be identified; it was noted, however, that there was an additional RCT (Meyer et al, 2002[j]) that had used cod liver oil as the vitamin D intervention and cod liver oil with the vitamin D removed as the control.

SACNvitD/12/43a: *Vitamin D & falls reduction in older people*

24. *Since completion of position paper, 1 further RCT identified (Karkkainen et al, 2010)* – The paper by Karkkainen et al (2010) had been circulated to Members (SACNvitD/12/55a).

25. *Consult with external experts on the interpretation of 'risk of falling' and 'risk of being a faller'* – A reply had been received from Professor Julia Newton (Newcastle University). She explained that being a faller is a yes/no response and does not take account of the fact that some fallers might fall once, whereas some might fall on multiple occasions. Since any fall might be

[h] Larsen ER, Mosekilde L, Foldspang A. Vitamin D and calcium supplementation prevents osteoporotic fractures in elderly community dwelling residents: A pragmatic population-based 3-year intervention study. *J Bone Miner Res.* 2004; 19: 370-378.
[i] Smith H, Andersen F, Raphael H et al. Effect of annual intramuscular vitamin D on fracture risk in elderly men and women – a population-based, randomized, double-blind, placebo-controlled trial. *Rheumatology.* 2007; 46: 1852-1857.
[j] Meyer HE, Smedshaug GB, Kvaavik E et al. Can vitamin D supplementation reduce the risk of fracture in the elderly? A randomized controlled trial. *J Bone Miner Res.* 2002; 17: 709-715.

the one that leads to a fracture, stopping people falling at all is the ideal scenario, i.e., converting someone from being a faller to a non faller. Although it is easier to demonstrate a reduction in falls, a decrease in the risk of being a faller is probably more important and is generally regarded as a better marker of the efficacy of an intervention.

26. The Chair expressed her thanks to Professor Newton (on behalf of the WG) for providing clarification on the difference between the risk of falling and the risk of being a faller.

27. *Check Bischoff-Ferrari et al's response to IOM critique of their meta-analysis on vitamin D & fall reduction* – The WG noted the correspondence relating to the meta-analysis by *Bischoff-Ferrari et al* (2009)[k] (SACN/vitD/12/55b).

28. *Check baseline and post intervention 25(OH)D concentrations in the 2 trials referred to in Cochrane review (Gillespie et al, 2010[l]) as 'recruiting participants with lower vitamin D levels'* – Members noted the baseline and post-intervention concentrations 25(OH)D concentrations of Dhesi et al (2004)[m] and Pfeifer et al (2000)[n]. It was noted that a third study (Prince, 2008[o]) had also recruited participants with *'lower vitamin D levels'*.

29. An abstract of an RCT by Bischoff-Ferrari et al on vitamin D supplementation & falls[p] (due to be published in the *Journal of Bone & Mineral Research)*, was tabled for information.

Agenda item 8: Summary and conclusions on evidence relating to vitamin D and health outcomes (excluding bone) (SACNvitD/12/57)

30. Prior to consideration of the summary and conclusions relating to vitamin D and the health outcomes, the Chair thought it would be useful for Members to be reminded of the WG's Terms of Reference[q].

31. At this point in the proceedings, Professor Hilary Powers joined the meeting (by teleconference).

32. Members considered the tabulated summary of the IOM conclusions, the additional evidence considered by the WG and the conclusions reached by the WG for each of the health outcomes (excluding bone) considered (SACNvitD/12/57). For each health outcome, Members were

[k] Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised-controlled trials. *BMJ.* 2009; 339:b3692

[l] Gillespie LD, Robertson MC, Gillespie WJ et al. Interventions for preventing falls in older people living in the community. *Cochrane database of systematic reviews 2009.* Issue 2. Art. No: CD007146. DOI: 10.1002/14651858. CD007146.pub2. Copyright 2010 The Cochrane Collaboration.

[m] Dhesi JK, Jackson SHD, Bearne LM et al. Vitamin D supplementation improves neuromuscular function in older people who fall. *Age and Ageing*. 2004; 33:589-595.

[n] Pfeifer M, Begerow B, Minne HW et al. Effects of short-term vitamin D and calcium supplementation on body sway and secondary hyperparathyroidism in elderly women. *J Bone Miner Res.* 2000; 15(6):1113-8.

[o] Prince RL, Austin N, Devine A et al. Effects of ergocalciferol added to calcium on the risk of falls in elderly high-risk women. *Archives of Internal Medicine.* 2008; 168(1): 103-8.

[p] Bischoff-Ferrari H, Dawson-Hughes B, Orav3 JE et al. Effects of 3 monthly vitamin D supplementation strategies among fallers age 70 years and older: a double-blind randomized controlled trial. *Original communication (poster) at American Society Bone Mineral Research meeting, 2012.*

[q] http://www.sacn.gov.uk/meetings/working_groups/vitamin/index.html

asked to consider whether there was there was an association with vitamin D and whether there was sufficient evidence to inform a threshold effect, which could be used as a basis for setting Dietary Reference Values (DRVs) for vitamin D in the UK.

33. Members were informed that, for those health outcomes considered to be useful for setting DRVs, the 25(OH)D threshold concentrations associated with benefits would be considered at the next meeting in February 2013.

Cancer

34. Members noted that little information was available from randomised controlled trials. Observational studies suggest an inverse association between 25(OH)D and colorectal cancer risk, but not for other cancers. Association with colorectal cancer might be due to protective effect, reverse causality or residual confounding.

35. Members concluded that there was not sufficient evidence on cancers to inform the setting of DRVs for vitamin D.

Oral health

36. The WG noted that there was little quantitative information on amounts of vitamin D or 25(OH)D associated with oral health outcomes. Members concluded that the evidence on oral health was not sufficient to inform the setting of DRVs for vitamin D.

Pregnancy and lactation

37. Members noted that there were few UK data on 25(OH)D concentrations of pregnant and lactating women and infants (0-6 months).

38. *Maternal non-skeletal health outcomes* (including gestational diabetes mellitus, preeclampsia/pregnancy induced hypertension) – Members agreed that there was very limited evidence from RCTs and mixed evidence from observational studies that vitamin D improves maternal non-skeletal reproductive health outcomes. It was agreed to check an RCT (in India) which reported a positive effect of vitamin D supplementation on incidence of pregnancy induced hypertension (Marya et al, 1987[r]). It was also agreed to check the RCT by Hollis et al (2011)[s] on vitamin D supplementation during pregnancy.

39. *Non-skeletal outcomes in newborn* – Members agreed that evidence from RCTs suggested that maternal vitamin D supplementation might have beneficial effects on neonatal hypocalcaemia and merited further consideration; it was agreed to check if a threshold range for neonatal

[r] Marya RK, Rathee S, Manrow M. Effect of calcium and vitamin D supplementation on toxaemia of pregnancy. *Gynecol Obstet Invest.* 1987; 24(1): 38-42.
[s] Hollis BW, Johnson D, Hulsey TC et al. Vitamin D supplementation during pregnancy: double-blind, randomized clinical trials of safety and effectiveness. *J Bone Miner Res.* 2011; 26(10): 2341-57.

calcium could be identified. There was very little evidence from RCTs or observational studies to indicate any additional benefits of maternal vitamin D supplementation for babies.

All-cause mortality

40. Although evidence from a meta-analysis of 50 trials suggested vitamin D supplementation decreases mortality, the WG's initial conclusion was that all-cause mortality was not an informative health outcome for setting DRVs. This was because it represents a mix of diseases and most RCTs were of very small size and conducted in older women who are at greater risk of mortality. It was agreed to reflect further on the evidence for all-cause mortality before concluding on its suitability for informing the setting of DRVs.

Cardiovascular disease (CVD)

41. Members agreed that although prospective studies suggested low 25(OH)D concentrations were associated with increased CVD risk, there was also the suggestion of a U-shaped association. It was agreed that the very limited data from RCTs should be interpreted with caution because most were designed and powered to evaluate effects of vitamin D on musculoskeletal outcome. Members concluded that the evidence on CVD was not sufficiently strong to influence the setting of DRVs for vitamin D.

Hypertension

42. Although evidence from meta-analyses of observational studies suggests an inverse association, meta-analyses of RCTs are inconsistent. Members concluded that the evidence on hypertension was not sufficiently strong or consistent to inform the setting of DRVs for vitamin D.

43. Members were informed that five major RCTs on the effects of vitamin D on hypertension and CVD were due to report their results in 2016.

Infectious disease

44. Members noted that the data were mainly observational and that findings from trials and observational studies were inconsistent. It was also noted that most studies focused on the therapeutic effects of vitamin D in patients and that vitamin D might be affected by the acute phase inflammatory response. Members concluded that the evidence on infectious diseases was not sufficient to inform the setting of DRVs for vitamin D.

Autoimmune disease

45. Members noted that there was a paucity of prospective cohort studies and no RCTs on vitamin D and risk of developing autoimmune disease. Most of the evidence was based on cross-sectional and case-control studies. Members concluded that the evidence on autoimmune

disease was not sufficient to inform the setting of DRVs for vitamin D.

Age-related macular degeneration

46. Members noted that the evidence on vitamin D and age-related macular degeneration is mainly from cross-sectional studies, which are inconsistent. No data from longitudinal or intervention studies were identified. Members concluded that the evidence on age-related macular degeneration was not sufficient to inform the setting of DRVs for vitamin D.

Neuropsychological functioning

47. Members noted that the evidence for an effect of vitamin D on neuropsychological functioning was weak and mainly from cross-sectional and ecological studies. Although there were a small number of clinical trials, no evidence was available from robust clinical trials. The WG concluded that the evidence on neuropsychological functioning was not sufficient to inform the setting of DRVs for vitamin D.

Agenda item 7: Summary and conclusions on evidence relating to vitamin D and bone (SACNvitD/12/56)

48. Members considered the table, which summarised the IOM conclusions, the additional evidence considered by the WG and the conclusions reached by the WG on vitamin D and bone health (SACNvitD/12/56). It was agreed that, for each life-stage group, the following bone health outcomes would go forward for further consideration of threshold effects at the next meeting:

    (a) *Maternal:* osteomalacia.

    (b) *Fetal & newborn*: bone health indicators (e.g., BMC/BMD); bone growth;

    (c) *Infants (up to 12 months):* bone health indicators.

    (d) *Infants and children:* rickets.

    (e) *Children & adolescents:* bone health indicators.

    (f) *Postmenopausal women, older men & women:* bone health indicators; fractures; muscle strength & function; falls.

49. It was agreed that the following bone health outcomes would not go forward for further consideration of threshold effects: stress fractures in children, adolescents, young adults; muscle health in young & adult population groups; and bone health indicators in women of reproductive age.

50. It was noted that a study by Abrams et al (2012), which had been circulated to Members, reported that daily supplementation of children (n=64; mean age 6y) with 25 µg (1000 IU) of vitamin D3 had no effect on calcium absorption even though there was a significant increase in 25(OH)D concentration. It was agreed that the effect of vitamin D on calcium absorption was not a useful basis for setting DRVs for children. Members discussed whether the evidence on the effect of vitamin D supplementation on calcium absorption in older age groups should be considered as a possible basis for setting DRVs. It was agreed to check in previous minutes whether the WG had agreed that calcium absorption should be considered as an intermediate factor or a separate health outcome.

Agenda item 9: Agreement of health outcomes to use as basis for setting DRVs

51. It was agreed to take forward he following health outcomes for further consideration at the next meeting in February 2013:

- Neonatal hypocalcaemia
- Pregnancy-induced hypertension
- All-cause mortality
- Osteomalacia during pregnancy
- Bone health indicators (fetal/newborn, infants, children & adolescents, postmenopausal women, older men & women)
- Rickets in infants and children
- Fractures in postmenopausal women, older men and women
- Muscle strength and function in postmenopausal women, older men and women
- Falls in postmenopausal women, older men and women

52. For all the other health outcomes, it was agreed that the evidence was not sufficiently strong to use as a basis for setting DRVs for vitamin D.

Agenda item 10: AOB

53. The Chair reminded Members that the next WG meeting would take place on 19 February 2013.

54. The Chair thanked Members for their attendance before closing the meeting.

ANNEX

Key references considered by the WG prior to 6th meeting

Abrams SA, Hawthorne KM, Chen Z. Supplementation with 1000 IU vitamin D/d leads to parathyroid hormone suppression, but not increased fractional calcium absorption, in 4-8-y-old children: a double-blind randomized controlled trial. *AJCN.* 2012. Doi: 10.3945/ajcn.112.046102.

Advisory Group on Non-Ionising Radiation, 2002. *Health effects from ultraviolet radiation.* Documents of the Nationa Radiological Protection Board, Volume 13, No.1.

Bogh MKB, Schmedes AV, Philipsen PA et al. Vitamin D production after UVB exposure depends on baseline vitamin D and total cholesterol but not on skin pigmentation. *Journal of Investigative Dermatology.* 2010; 130:546-553.

National Radiological Protection Board. Health effects from ultraviolet radiation. Report of an Advisory Group on non-ionising radiation.

Springbett P. Buglass S, Young AR. Photoprotection and vitamin D status. *J Photochem Photobiol B.* 2010; 101(2): 160-8.