

**1<sup>st</sup> MEETING**

**Vitamin D Working Group**

**26 May 2011, Wellington House, London SE1 8UG**

**DRAFT MINUTES**

<b>Chair:</b>	Professor Hilary Powers
<b>Members:</b>	Professor Kevin Cashman Professor Roger Francis Professor Tim Key Professor Susan Lanham-New Professor Harry McArdle Dr Ann Prentice Dr Tony Williams
<b>Adviser (UV exposure):</b>	Dr John O'Hagan
<b>Secretariat:</b>	Dr Alison Tedstone (DH) Ms Mamta Singh (DH) Mr Heiko Stolte (DH) Ms Cath Mulholland (FSA) Dr Sheela Reddy (DH) Dr Elaine Stone (DH)
<b>Observers:</b>	Ms Fiona Comrie (FSA Scotland) Dr Stuart Conney (DH) Ms Rachel Stratton (DH)

**Agenda item 1: Chair's welcome and introduction**

1. The Chair welcomed Members to the first meeting of the SACN Working Group (WG) on vitamin D. Apologies of absence were received from Professor Ian Young.
2. Before the start of business, Dr Alison Tedstone from the SACN secretariat provided a brief introduction about SACN including its role, remit, procedures and current status. She explained that Members are appointed to the main SACN Committee by a public

appointment process and that additional members are co-opted to SACN Working Groups in agreement with the Chair.

### **Agenda item 2: Background to SACN's vitamin D review**

3. The Chair reminded Members that the evidence on vitamin D and health had previously been considered by SACN in 2007, resulting in the publication of SACN's position statement 'Update on Vitamin D'. The committee had concluded that there was insufficient evidence, at that time, to amend the existing vitamin D dietary reference values and that the evidence on the relationship between vitamin D status and chronic disease, other than the metabolic bone diseases rickets and osteomalacia, was inconclusive.
4. At its meeting in October 2010, SACN agreed to review the data on vitamin D because a substantial amount of evidence has subsequently become available since the position statement's publication in 2007, including: research commissioned by the Food Standards Agency (FSA); reports from the Institute of Medicine (IOM) on *Dietary Reference Intakes for Calcium and Vitamin D* in 2010 and from the International Association for Research on Cancer (IARC) on *Vitamin D and Cancer* in 2008; a number of studies on vitamin D and chronic disease. A list of papers published from the FSA funded studies and three workshops on vitamin D convened by the FSA was tabled (SACNvitD/11/11) for information.
5. Dr Tedstone explained that the overall purpose of the vitamin D review was to inform policy on vitamin D. The Department of Health (DH) and the Scottish government want to ensure that advice on vitamin D is appropriate to ensure vitamin D adequacy of the UK population. The WG should restrict its work to areas relevant to public health.
6. Dr Tedstone clarified that SACN's remit is scientific risk assessment and does not include risk management. DH will consider the policy implications of SACN's scientific assessment. Dr Sheela Reddy from the SACN secretariat explained that DH is keen for the WG to provide advice on the proportion of vitamin D obtained by diet and the proportion obtained by sun exposure.

7. The Chair informed Members that the purpose of the meeting was to consider: the terms of reference and scope of work; how to assess the evidence, the work programme, responses received to the call for evidence; vitamin D biology; and to agree the health outcomes to consider in relation to vitamin D status.

### **Agenda Item 3: SACN'S approach to assessing the evidence**

8. Dr Tedstone outlined SACN's approach to assessing the evidence. She informed Members that SACN's considerations now tended to be largely restricted to well-designed RCTs and prospective cohort studies for drawing conclusions in relation to dietary recommendations. While case-control studies, cross-sectional studies and animal studies are useful for providing background information and plausible mechanisms, they are not used as a basis for dietary recommendations.
9. Members were informed that data from the National Diet and Nutrition Survey (NDNS), the Health Survey for England (HSE) and the Scottish Health Survey would be used to assess the vitamin D status of the UK population. Blood samples from the HSE and Scottish Health Survey will be analysed in the same laboratory.
10. Dr Tedstone explained that the draft report prepared by the WG would need to be agreed at a full SACN meeting before being published on the SACN website for public consultation (usually 3 months). The WG would then consider all responses and the revised report would need to be agreed and finalised by SACN before being published.
11. In response to a question about what would happen to the conclusions of the WG, Members were informed that these would be carefully considered by health departments.

### **Agenda Item 4: Terms of Reference & Scope of Work**

12. The Chair presented Members with a diagrammatic representation of the conceptual

framework for the vitamin D review (tabled). The main components of this framework are vitamin D exposure (from dietary intake and sunlight), indicators of vitamin D status (e.g., 25-hydroxyvitamin D [25OHD]), intermediate disease endpoints, and health outcomes related to vitamin D status. The relationship between vitamin D exposure (diet, supplements and sunlight) and biochemical indicators of vitamin D status is complicated by modulators and there are difficulties associated with measuring indicators of vitamin D status. The relationship between indicators of vitamin D status and health outcomes/intermediate disease endpoints will also need careful consideration.

13. Members were invited to comment on whether any important work strand had been omitted from the *Scope of Work* (SoW).
14. There was some discussion about the note in point 1 of the SoW (*Vitamin D biology and health outcomes*) stating that calcium will be considered only in terms of how it modifies vitamin D requirement. It was noted that although calcium intake could be considered a modifier of vitamin D requirements, vitamin D status also affects calcium metabolism, which would therefore be considered an outcome. It was agreed that the work would need to be cognisant of both these interactions. It was agreed to amend the 5<sup>th</sup> bullet point to include effects of modifiers “and interactions” and to remove the sentence referring to calcium.
15. It was noted that the term *diet* (point 3 of SoW, 2<sup>nd</sup> bullet) does not distinguish between vitamin D intake from food constituents and from supplements. Vitamin D supplements are prescribed to some population groups, e.g., to the elderly, and it would be important to include these in the modelling. It was also agreed to refer to *sunlight exposure* rather than *UVB exposure* when discussing health or adverse outcomes. It was agreed to change the wording of this bullet from ‘*modelling relative contribution of UVB and diet to vitamin D status*’ to ‘*modelling relative contribution of sunlight and vitamin D intakes (from natural food sources, fortified foods and supplements) to vitamin D status*’.
16. A point was made about the importance of using appropriate terminology. For example, assessment of the relationship between vitamin D status and health outcomes actually refers to a reduction in risk of health outcomes, i.e., disease prevention rather than cure;

this was highlighted as an important distinction.

17. Members were then invited by the Chair to comment on the *Terms of Reference* (ToR). They were informed that the ToR were initially very detailed and specific but following comments received after the SACN meeting in February 2011, they had been made more general and less descriptive. The ToR were approved by the WG.

### **Agenda Item 5: Consideration of the evidence base**

#### *Use of IOM Report*

18. Members were referred to the table in paper SACNvitD/11/02 comparing the methods used to review the evidence in the IOM report and the two systematic analyses commissioned by the IOM which were carried out by the Agency for Healthcare Research and Quality (AHRQ): AHRQ Ottawa and AHRQ Tufts. The AHRQ reviews used different criteria for data selection and for quality assessment.
19. The IOM report synthesised the evidence from the Ottawa and Tufts reviews to set Dietary Reference Intakes (DRIs). The IOM conducted its own literature search and updated the AHRQ reviews. The report did not consider sun exposure and the dietary recommendations were formulated assuming minimal or no sunshine exposure.
20. Members were invited to discuss how the IOM report should be used, how to update the evidence base and how to judge the quality of the papers considered.
21. Members agreed that while the IOM report is an important and comprehensive database, there were some gaps in the evidence. For example, it did not take sunlight exposure into account in formulating its recommendations. It was agreed that the IOM report would be a useful reference resource and a good starting point for consideration of the evidence on vitamin D, however the WG would make its own judgements and conclusions.
22. The WG was informed that the secretariat would carry out a literature search to update the

evidence base. It was agreed that the results of the literature search should be tabulated. It was noted that since publication of the IOM report, numerous papers on vitamin D have been published, and that the publication rate of papers on Vitamin D continues to increase. A cut-off date for consideration of the evidence was suggested; however, Members thought it would be important to include any large RCTs even if they were published after the cut-off date and it was agreed that a watching brief should be kept on databases of ongoing research projects.

23. Members discussed the criteria that should be used to judge the evidence. It was agreed to have some flexibility in the type of evidence considered but, as a guideline, the preference would be for RCTs, then prospective cohort studies. Animal studies and other types of human studies (e.g., case-control, cross-sectional) might be useful for mechanistic plausibility; however, any recommendations would need to be based largely on RCTs.

*Important factors to consider in assessment of evidence/biases and confounding*

24. Members considered the paper '*Potential sources of biases and confounding in studies of vitamin D and health outcomes*' (SACNvitD/11/12). It was noted that the list did not include some of the general confounders in studies of diet and disease such as smoking, alcohol, physical activity, medical treatment, social class and that some of the bullets were not actually confounders. The secretariat clarified that the paper included various factors (not just confounders) that would need to be considered in the assessment of studies on vitamin D and health outcomes and that general confounders would be considered as a matter of course.
25. It was agreed to change the heading to '*Factors/areas for consideration in studies of vitamin D and health outcomes*'. Under the list of factors affecting cutaneous synthesis of vitamin D, it was agreed to separate skin pigmentation from ethnicity (since skin pigmentation is just one of many factors related to ethnicity). Under the list of factors affecting vitamin D status, it was agreed to add '*activity of key enzymes and cytochromes*'.

**Agenda Item 7: Responses received to call for evidence (SACNvitD/11/05)**

26. The *Call for Evidence* had requested notification of new evidence on vitamin D (i.e., data not already identified by the IOM), data on blood vitamin D status at different life stages/certain subsets of the UK population (particularly minority ethnic groups) and ongoing research due for completion in the next 1-2 years.
27. Ten responses had been received. A summary of the responses and the actions agreed by the WG are summarised in the attached table.

### **Agenda Item 6: Proposed work plan**

#### *Relationship to other committees*

28. The Chair explained that since the WG does not have expertise relating to toxicology or the risks of UV exposure, the SACN secretariat has been in discussions with the secretariat of the Committee on Toxicity (COT) (based at the Food Standards Agency) and the Committee on Medical Aspects of Radiation (COMARE) (whose secretariat is provided by the Health Protection Agency [HPA] on behalf of DH) regarding collaboration. Members were informed that additional expertise (e.g. a dermatologist) could be co-opted on to the WG at a future date, if required.
29. Dr Tedstone informed Members that the secretariat had met with the COT secretariat in February and agreed that evidence for effects of high vitamin D intakes would initially be reviewed by COT and its findings/conclusions would then be considered by the WG. It was agreed that Cath Mulholland from the COT secretariat would attend WG meetings to provide a link between the WG and COT.
30. The secretariat had also attended a COMARE meeting in March and subsequently met with the COMARE secretariat. It was agreed that COMARE would commission the HPA to assess the risks of UV exposure since it had the relevant expertise. The findings would then be considered by a small COMARE working group before consideration by the WG. It was also agreed that Dr John O'Hagan from the HPA would attend WG meetings to provide a link between COMARE/HPA/SACN.

31. Members were informed by the Chair that that work of COMARE and COT will run parallel to that of the WG and that she and/or the secretariat would attend the relevant COT/COMARE meetings.

32. The Chair then invited Dr O'Hagan from the HPA to provide a brief summary of the current knowledge on the risks associated with UV exposure. Dr O'Hagan presented data covering the following areas: the sun's ultra-violet (UV) radiation, global variation in UV radiation, concept of the sun index, UK measurements and adverse health effects. These are summarised below:

- There are three types of UV radiation: UVA (315-400nm), UVB (280-315nm) and UVC (100-280nm). In terms of public health, concerns historically focused on UVB but this may be changing since an important consideration is how the different UV wavelengths interact.
- The Solar UV Index (1-20) is used to advise the public of the strength of the sun's UV rays. It is intended to protect against sunburn, not cancer. UV radiation varies depending on time of day, season, and atmospheric condition; e.g., shade blocks about 50% of UV radiation and cloud blocks about 20%. While the equator has a UV index of about 16, it is unlikely to be higher than 8 in the UK.
- UV radiation can cause damage to the eye: photokeratitis, cataract, and age related macular degeneration.
- Health effects of UV radiation on skin include ageing and skin cancer. Although UVC is a carcinogen, it does not penetrate as far as UVA and UVB in human skin. For skin ageing, UVA is main risk; for basal cell carcinoma, UVB is main risk. Lifetime UV exposure increases the risk of skin ageing and non-melanoma skin cancers. Malignant melanoma has a genetic link and risk factors include large numbers of moles. It also occurs on little exposed areas and appears to be linked to sudden bursts of exposure (e.g., beach holidays) suggesting it may be promoted or triggered by sun exposure. Squamous-cell carcinoma of the skin is probably linked to UVB.

33. The Chair thanked Dr O'Hagan for a very informative presentation and invited questions from Members. The following points were noted in response to questions:

- Differential ratio between daily UVA and UVB - the amount of UVA and UVB depends on atmospheric conditions. The path length of sunlight through atmosphere shortens as the sun rises, causing the UVA to UVB ratio to change through the year and day. UVA appears to break down vitamin D in the skin. This suggests that winter sunshine, which contains only UVA, will reduce vitamin D in skin.
- Intensity of sunshine exposure – the UK adopted Australian advice re staying out of the sun; however, this may not be appropriate as the solar index in the UK is much lower (8) than the solar index in Australia (16). The UV index is lower in Scotland (e.g., Lerwick, 5-6) than England (e.g., Camborne, 8), so to receive the same amount of UVB light would require about 50% longer sunshine exposure in Scotland.
- Artificial light – UVB levels are much lower in artificial light, which contains more UVA. The contribution of indoor lighting to UVB exposure is currently negligible in the UK.

34. The Chair noted that Dr O’Hagan’s presentation had highlighted the complexity of the task ahead and a number of difficult issues that would need to be considered.

35. The Chair then invited Ms Cath Mulholland from COT to summarise the toxicological data on high intakes of vitamin D.

36. Ms Mulholland informed Members that in 2003, the *Expert Group on Vitamins and Minerals* had reported on the safety of vitamin and mineral supplements. *Safe Upper Levels* (SUL) were established when supported by sufficient data and *Guidance Levels* (GL) were set when there was not enough evidence to establish an SUL. A GL of 25 µg/day was set for vitamin D supplementation, based on data from human volunteer studies. A GL was set only for supplementation as exposure from sunlight was unclear so that it was not possible to assess total exposure. It is likely that COT will take a similar approach as in their previous assessment.

37. The Chair thanked Ms Mulholland for her presentation and noted that she would be providing feedback of the WG meeting to COT at their next meeting in June in addition to an introductory paper setting out the scope of the work.

Draft work schedule (SACNvitD/11/04)

38. The Chair informed Members that the draft work schedule was a flexible working document and would be regularly updated. The aim is to complete the report by June 2014. The WG agreed to consider the work in the following order: vitamin D biology, relationship between exposure and vitamin D status, appropriate biochemical markers of vitamin D status, measurement of vitamin D status, relationship between vitamin D status and health outcomes, adverse effects of high intakes, adverse effects of UV exposure, vitamin D status of the UK population/relative contributions made by dietary vitamin D and cutaneous vitamin D synthesis to vitamin D status

**Agenda Item 8: Vitamin D2 and D3 biology**

39. The Chair noted that the WG had been sent a selection of papers on vitamin D biology. Members were invited to discuss elements they felt should be included in this section and to comment on any gaps in coverage of the biology.
40. It was suggested that the starting point should be identification of the sections that needed updating in the COMA<sup>1</sup> reports and the IOM report.
41. It was noted that useful information could be found in an AJCN supplement (2008) that had published proceedings of a symposium on vitamin D held in the USA by the National Institutes of Health (*Vitamin D and Health in the 21<sup>st</sup> century: an Update*).
42. It was noted that some reviews presented certain facts as if they had been substantiated when this is not the case. There are some longstanding knowledge gaps that have not been addressed. Members agreed that it was important to identify and clearly highlight areas where there is lack of understanding and uncertainty.

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<sup>1</sup> Committee on Medical Aspects of Food Policy.

43. The following areas were identified for inclusion in this section:

- Sources of vitamin D2 and D3.
- Absorption of vitamin D2 and D3.
- Metabolism (D2; D3; 25OHD; 1,25D etc.): metabolic pathways of D3 from intestine, D3 from skin, D2 from intestine; different metabolites, enzymes and cytochromes; effect of physiological state (e.g., pregnancy, lactation); effect of life stage (including fetus and role of placenta); effect of adiposity; the point at which 25OHD becomes limiting in the production of 1,25 dihydroxyvitamin D; distinction between tissues (e.g. 1,25 OHD produced in kidney or other tissues).
- Vitamin D binding protein.
- Vitamin D receptors (site specific receptors; role of receptors).
- Storage (where stored, concentrated, released under physiological regulation); storage vs. sequestration; mobilisation from stores.
- Regulation.
- Mechanism of action.
- Biological activity of D2 versus D3.
- Excretion.
- Polymorphisms in vitamin D binding hydroxylases, vitamin D receptors and in all areas of metabolic flux (including transport and turnover).

44. A member of the WG agreed to liaise with the secretariat in drafting this section.

45. It was noted that results of a meta-analysis of studies comparing the biological activity of vitamin D2 and D3 was due for publication in the near future and details of this would be made available to the Secretariat.

46. Members discussed whether there are tracking data on vitamin D status across the lifespan, i.e., if individuals who start with low vitamin D status continue with low status; however, it was noted that obtaining this type of data is problematic since vitamin D blood measurements would need to be made in the same season over many decades.

**Agenda Item 9: Potential health outcomes for consideration in relation to vitamin D status**

47. The Chair informed Members that they would need to agree on the health outcomes for consideration in the vitamin D review. She reminded Members that these should be of public health importance. Members considered the table of health outcomes assessed by the IOM and those suggested at the SACN meeting in October 2010 (SACNvitD/11/10).

It was agreed to consider the following health outcomes:

- All cause mortality (*decision will be made after consideration of the type of evidence available*)
- Cancer (*all cancers, update those in IOM & IARC, plus other cancers where data available*)
- Cardiovascular disease and hypertension
- Immune related disease
  - Asthma
  - Autoimmune disease
    - Diabetes (type 1)
    - Inflammatory bowel disease
    - Multiple sclerosis
    - Rheumatoid arthritis
    - Systemic lupus erythematosus
    - Asthma
    - Atopic disease
    - Other autoimmune disease
- Infectious diseases
  - Tuberculosis
  - Influenza/upper respiratory infections
  - Chronic obstructive pulmonary disease
  - Susceptibility to infectious diseases
- Neuropsychological functioning
  - Cognitive function
  - Dementia
  - Autism
  - Depression
  - schizophrenia
- Non-skeletal reproductive health outcomes (including pre-eclampsia and birth weight)
- Musculo-skeletal health outcomes
  - Bone health
  - Fracture risk
  - Rickets/osteomalacia
  - Muscle function
  - Physical performance
  - Frailty
  - Falls and postural sway (balance/gait)
- Development in infants
- Macular degeneration
- Periodontal disease

## **Agenda Item 10: AOB**

48. The Chair invited Professor Susan Lanham New, Professor Roger Francis and Dr Sheela Reddy to provide feedback on a Workshop they had attended the previous week on vitamin D, organised by the National Institute for Clinical Excellence (NICE) at the NICE HQ's in Manchester . Dr Reddy also provided feedback from a meeting she had attended in London on vitamin D and obstetrics organised by the Vitamin D Association.
  
49. The Chair thanked Members for their attendance and reminded them of the date of the next meeting: 8 September 2011.

**Meeting close**

## Actions agreed to responses received to *Call for Evidence*

Organisation/ Individual	Evidence submitted	Action agreed by Working Group
<b>Dr Margaret Ashwell</b>  Ashwell Associates	Attached following papers: 1. Ashwell et al (2010). UK Food Standards Agency Workshop Report: an investigation of the relative contributions of diet and sunlight to vitamin D status. 2. Wallace et al (2010). Measurement of 25-hydroxyvitamin D in the clinical laboratory: Current procedures, performance characteristics and limitations. 3. de La Hunty et al (2010).UK Food Standards Agency Workshop Consensus Report: the choice of method for measuring 25-hydroxyvitamin D to estimate vitamin D status for the UK National Diet and Nutrition Survey.	Already aware of this evidence. Will be considered as part of the evidence base.
<b>Mrs Belinda Barnes</b>  Foresight	Sent copies of pages (about vitamin D) from pamphlets they have written by doctors and nutritional therapists: 1. Preparation for pregnancy (SG Bradley with N Bennett). 2. Let's have healthy children (A Davis). 3. Daylight robbery (Dr D Dowling). 4. Mental and elemental nutrients (C Pfeiffer). 5. Nutrition and physical degeneration (WA Price). 6. Better babies (F Naish and J Roberts). 7. Prescription for nutritional healing (Balch and Balch). 8. Growing up healthy (J Lunden and M Winick).	This is not primary evidence.
<b>Dr Barbara Boucher</b>  Bart's and the London School of Medicine and Dentistry	Highlighted following studies: 1. Soon to be published RCT of vitamin D and pregnancy (Wagner C and Hollis BW) - large study with various doses up to 100µg/day (UL set by IOM). Outcomes presented to the 14 <sup>th</sup> Vit D workshop in 2010 would also be of relevance. 2. Small RCT (Timms <i>et al</i> , 2002) that showed significant reductions in inflammatory markers [serum CRP by 23% and plasma MMP9 by 67%] in South Asians. 3. Papers she has co-authored on associations of maternal vitamin D status with childhood outcomes, for bone strength age 9-10 years (Javaid <i>et al</i> , 2006), for asthma risk from data on PAH study in Southampton [with adverse effects in contrast to all other published work on this] and on insulin resistance and muscle size in Indian children aged 9-10 years from the Mysore Parthenon study (Krishnaveni <i>et al</i> , 2011).	Will consider study by Wagner & Hollis when published.  Timms <i>et al</i> (2002) in IOM report and (Javaid <i>et al</i> , 2006) in IOM report but will be considered as part of the evidence base. Will consider Krishnaveni <i>et al</i> (2011).
<b>Dr Gail Goldberg</b>  MRC Human Nutrition Research	1. Requests that literature searches be expanded to include data relevant to muscle function and 'bone muscle unit' as a whole and not just on falls (as appears to be the case in IOM report). Could suggest search terms and key papers in this field. 2. Although data from RCTs on sun exposure in the UK may be very limited, could suggest other papers that might be useful for 'modelling' purposes. 3. Since HNR is involved in the National Diet and Nutrition Survey (NDNS) and the Diet and Nutrition Survey of Infants and Young Children (DNSIYC), staff can offer specific expertise and data interpretation if it would be helpful. 4. Would be prepared to share (as yet) unpublished dietary data from a number of studies in ~6000 infants, children and adolescents. These include data collected by food diaries and 24 hour recall from children of white European, South Asian and black African-Caribbean origin living in England. 5. Prepared to keep secretariat updated of ongoing research by HNR scientists on pilot studies of vitamin D turnover and of ongoing/soon to commence RCTs on vitamin D supplementation (in pregnant women, adolescents, older people) in which HNR are collaborating.	Agreed.  Will keep in mind.  Will keep in mind.  Could be explored.  Useful to know but can only consider published data.

<p><b>Mr Rufus Greenbaum</b></p>	<p>Suggests establishing the following new target levels:  Vitamin D deficiency &lt;100 nmol/L  Normal levels 100-200 nmol/L  Normal levels for pregnant women 120-200 nmol/L</p> <p>Suggests that any trials not measuring or achieving levels above 80 nmol/L should be considered “Null” and be disregarded.</p> <p>Suggestions based on following evidence:  <u>Biomarkers of vitamin D sufficiency</u>  1. Hollis (2005). Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D.  2. Zitterman (2003). Vitamin D in preventive medicine – are we ignoring the evidence?  <u>Vitamin D levels in the UK</u>  3. Hypponen &amp; Power (2007). Hypovitaminosis D in British adults at age 45y: nationwide cohort study of dietary and lifestyle predictors.  <u>25-Hydroxy D and health outcomes</u>  4. Venning G (2005). Recent developments in vitamin D deficiency and muscle weakness among elderly people.  5. Compston J (1998). Vitamin D deficiency: time for action. Evidence supports routine supplementation for elderly people and others at risk.  6. Pearce &amp; Cheetham (2010). Diagnosis and management of vitamin D deficiency.  7. Bischoff-Ferrari <i>et al</i> (2006). Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes.  8. Garland <i>et al</i> (2009). Vitamin D for Cancer Prevention: Global Perspective.  <u>Treatment of low 25-hydroxyvitamin D</u>  9. Heaney <i>et al</i> (2003). Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol.</p>	<p>This will be part of the considerations of the Working Group.</p> <p>Will consider all trials.</p> <p>These studies will be considered as part of the evidence base.</p>
<p><b>Dr Nick Harvey</b></p> <p>MRC Lifecourse Epidemiology Unit  University of Southampton</p>	<p>Attached following papers:  1. Javaid <i>et al</i> (2006). Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study.  2. Harvey <i>et al</i> (2008). Paternal skeletal size predicts intrauterine bone mineral accrual.  3. Sayers <i>et al</i> (2009). Estimated maternal ultraviolet B exposure levels in pregnancy influence skeletal development of the child.  4. Mahon <i>et al</i> (2010). Low maternal vitamin D status and fetal bone development: cohort study.</p>	<p>All these studies are included in IOM report and will be considered as part of the evidence base.</p>
<p><b>Dr Adrian Martineau</b></p> <p>Bart’s and The London School of Medicine and Dentistry</p>	<p>Attached following article published after IOM report:  1. Martineau <i>et al</i> (2011). High-dose vitamin D3 during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial</p> <p>Also PI in three ongoing clinical trials due for completion in 2013:  1. Trial of vitamin D supplementation for the prevention of influenza and other respiratory infections (<a href="http://clinicaltrials.gov/ct2/show/NCT01069874">http://clinicaltrials.gov/ct2/show/NCT01069874</a>)  2. Trial of vitamin D supplementation in asthma (<a href="http://clinicaltrials.gov/ct2/show/NCT00978315">http://clinicaltrials.gov/ct2/show/NCT00978315</a>)  3. Trial of vitamin D supplementation in chronic obstructive pulmonary disease (<a href="http://clinicaltrials.gov/ct2/show/NCT00977873">http://clinicaltrials.gov/ct2/show/NCT00977873</a>)</p>	<p>Will consider this study.</p> <p>Results of these trials might be published too late for inclusion in the Working Group’s considerations.</p>

<p><b>Dr Cajé Moniz</b></p> <p>King's College Hospital NHS Foundation Trust</p>	<ol style="list-style-type: none"> <li>1. Has recent data in preparation and/or shortly for submission for peer review on methodology and problems encountered with measurements of vitamin D in clinical samples, baseline and after high dose supplementation of cholecalciferol; studies on inadequacy of supplementation with conventional doses of calcium and vitamin D (Elnenaei <i>et al</i>, 2011. Genomic and metabolomic patterns segregate with responses to calcium and vitamin D supplementation).</li> <li>2. Organising national workshop for clinical scientists in November 2011 to discuss, debate and formulate guidance for clinical scientists.</li> <li>3. Requests that methodology is specifically examined since researchers often do not mention methods used and, if they do, inter and assay CVs not quoted. If assay used, it is usually done once according to manufacturers' recommendation and for cost purposes. With CVs in the order of 12-15%, this could make the result normal or abnormal in one assay. Unless methodology improves, results may remain meaningless.</li> </ol>	<p>Will be considered on publication.</p> <p>Would be interested to learn of the outcome.</p> <p>Intention is to examine methodology.</p>
<p><b>Professor Peter Weber</b></p> <p>DSM Nutritional Products Ltd</p>	<p>Highlighted following articles:</p> <ol style="list-style-type: none"> <li>1. Preece <i>et al</i> (1973). Vitamin-D deficiency among Asian immigrants to Britain.</li> <li>2. Lips <i>et al</i> (2001). A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial.</li> <li>3. Brock <i>et al</i> (2004). Associations with vitamin D deficiency in "at risk" Australians.</li> <li>4. Lips <i>et al</i> (2006). The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation.</li> <li>5. Roddam <i>et al</i> (2007). Association between plasma 25-hydroxyvitamin D levels and fracture risk: the EPIC-Oxford study.</li> <li>6. Nnoaham <i>et al</i> (2008). Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis.</li> <li>7. Ward <i>et al</i> (2009). Vitamin D status and muscle function in post-menarchal adolescent girls.</li> <li>8. Hirani <i>et al</i> (2010). Urgent action needed to improve vitamin D status among older people in England!</li> <li>9. Lowe <i>et al</i> (2010). Vitamin D status and markers of bone turnover in Caucasian and South Asian postmenopausal women living in the UK.</li> <li>10. Mahon <i>et al</i> (2010). Low maternal vitamin D status and fetal bone development: cohort study.</li> <li>11. Mavroeidi (2010). Seasonal 25-hydroxyvitamin D changes in British postmenopausal women at 57 degrees N and 51 degrees N: a longitudinal study.</li> </ol> <p>Currently conducting global systematic review on vitamin D status (based on 25-OH vitamin D serum levels) and offered additional information from that review if required.</p>	<p>These studies will be considered as part of the evidence base.</p> <p>Will be useful addition to evidence.</p>
<p><b>Ed Yong</b></p> <p>Cancer Research UK</p>	<p>Attached number of papers on general outcomes and cancer outcomes published between 2009-2011.</p>	<p>Very useful for the literature update process.</p>