Scientific Advisory Committee on Nutrition

Responses to Consultation Comments

Responses by the Scientific Advisory Committee on Nutrition (SACN)
to comments received during public consultation (22 July – 23 September 2015) on
the draft Vitamin D and Health report

The final report can be accessed on SACN's website

DRAFT VITAMIN D & HEALTH REPORT: SUMMARY OF COMMENTS RECEIVED DURING SCIENTIFIC CONSULTATION

Comments were received from the following organisations & individuals

1) Alliance for Natural Health International (ANHI)
2) Association for Nutrition (AfN)
3) Aziz, M
4) Birmingham Vitamin D Steering Group
5) Bone Research Society
6) British Dietetic Association (BDA)
7) British Nutrition Foundation (BNF)
8) British Retail Consortium (BRC)
9) Children's Food Trust
10) Collins, Dr S (CChem MRSC)
11) Council for Responsible Nutrition UK (CRN UK)
12) Fischer, M (Systems Biology Laboratory, Vitamin D Association)
13) Food & Drink Federation (FDF)
14) Greenbaum R (A & B)
15) Harvey N (Professor of Rheumatology & Clinical Epidemiology) & C Cooper (Professor of Rheumatology & Director) (Southampton University)
16) Health Food Manufacturers' Association (HFMA)
17) Hewison, M (Professor of Molecular Endocrinology, Birmingham University)
18) Hogler, Dr W (Global consensus recommendations for prevention & management of rickets)
19) Huish, S (Specialist Dietitian, Coventry & Warwickshire NHS Trust)
20) Internis Pharmaceuticals Ltd.
21) Jacobs, Dr B (Consultant Paediatrician, Royal National Orthopaedic Hospital)
22) Macdonald, Professor H (University of Aberdeen)
23) Marshall, A (Paediatric trainee)
24) Martineau, A (Professor of Respiratory Infection & Immunity, Barts & The London School of Medicine & Dentistry)
25) Mawjes, Ms Sile
26) MRC Human Nutrition Research (MRC HNR)
27) National Osteoporosis Society (NOS)
28) Newton-Bishop, J (Professor of Dermatology, Leeds Institute of Cancer & Pathology)
29) NHS Health Scotland
30) Northern Ireland Centre for Food & Health (NICHE), Ulster University
31) Norval, M (Professor Emeritus, University of Edinburgh Medical School)
32) Oliver, T (Professor Emeritus in Oncology, Bart's Cancer Institute)
33) Proprietary Association of Great Britain (PAGB)
34) Rayner, J (Paediatric Dietitian, Bedford Hospital NHS Trust)
35) Rhein, H (General Practitioner, Edinburgh)
36) Rhodes, L (Professor of Experimental Dermatology, University of Manchester)
37) Royal College of Physicians (RCP)
38) Sexton, S (Specialist Medicines Management Dietitian, Bristol CCG)
39) Tagliaferri S, De Guiseppe R, Cena H; University of Palma & University of Pavia
40) Taylor, H (Clinical Effectiveness Pharmacist, NHS Sheffield CCG)
41) Thompson, P
42) Waitrose
43) Wales Dietetic Leadership Advisory Group (WDLAG) & Public Health Dietitians in Wales (PHDiW)
44) Watson, I

Table 1: General comments supportive of report

Comments	Organisation/Individual	Action agreed by SACN
Congratulates SACN WG on producing sound & thorough scientific review of the evidence on vitamin D and health.	AfN	All comments were welcomed.
Congratulate committee in producing a comprehensive review of the current status of the evidence for vitamin D and health. Particularly note and welcome the inclusion of muscle health in the guidelines.	Bone Research Society	
Very detailed & comprehensive review. BDA congratulates SACN on such a clear & thorough review.	BDA	
Report very comprehensive and clearly written.	BNF	
Welcome this through review of the scientific evidence on the health outcomes of vitamin D exposure. Report provides objective & independent evidence which can guide future policy & company specific decisions.	BRC	
Congratulates SACN on its thorough review.	FDF	
Congratulate committee on an excellent & extremely comprehensive review of relationships between vitamin D & wide range of health outcomes across life course. Applaud impartial & detailed analysis of the available data and agree with conclusions.	Professor NC Harvey & Professor C Cooper	
Report very thoroughly researched & logically presented.	HFMA	
Depth & scope of draft report is impressive and a credit to the working group's efforts.	S Huish	
Congratulate Secretariat on producing such an extensive & well researched report.	Internis Pharmaceuticals	
Enjoyed reading this excellent report	Professor H Macdonald	
Many thanks for this very thorough report.	A Marshall	
Congratulate Chair & working group on production of comprehensive report.	Professor A Martineau	
The draft report provides very comprehensive review. Builds on IOM report & is an important & authoritative reference work.	MRC HNR	
The SACN report on vitamin D is overall excellent with extremely thorough reviews and as a report is of value to many trying to get a grip on the role of vitamin D.	Professor J Newton-Bishop	
Read draft report with interest & congratulate the co-authors on their comprehensive account of this challenging, controversial and rapidly evolving subject.	Professor M Norval	
Extensive & comprehensive review takes inclusive approach to formulating recommendations aimed at improving population and individual's health related to vitamin D & muscular skeletal health needs.	Wales Dietetic Board	

Table 2 – Specific comments for discussion

Chapter	Comments	Organisation/ Individual	Action agreed by SACN (References to chapters and paragraphs are to those in the draft report)
	Introduction		
Background	Paragraph 1 Concerned at statement "*it was assumed that, for most people, the amount of vitamin D produced by exposure to summer sunlight would produce enough vitamin D for their needs during winter*". This erroneous assumption has resulted in current public health concerns relating to a vitamin D deficit across UK.	PAGB	This sentence describes the existing COMA recommendations and is referenced as such (DH, 1991). Agreed to check this is clear.
	Paragraph 2 Lack of comment in reviewing current Government recommendations on people of African descent also needing extra sun exposure. This lack repeated throughout the text and in conclusions.	Professor T Oliver	This issue is considered in chapters 3, 8, 9, 10 and 11
	Who defines what is "normal lifestyle"? Most prevalent (therefore "normal") lifestyle within UK is lived predominantly indoors & therefore unlikely to benefit from significant vitamin D synthesis generated by sunlight. Where time spent outdoors bodies are covered with clothes or sun cream as fear of skin cancer outweighs understanding of the need to expose skin to sunlight to facilitate vitamin D synthesis.	PAGB	This refers to existing advice. This wording is not included in SACN's draft recommendations.
Terms of Reference	Paragraphs 6-8 Concerned that within *Terms of Reference* there is no remit to set or recommend intake levels or sources from which this intake may be obtained.	PAGB	Terms of reference were to "*review the Dietary Reference Values for vitamin D and make recommendations*".
Methodology	Paragraph 9 Were Mendelian randomisation (MR) studies included in review? These studies can provide strong evidence for/against causality as they are much less subject to confounding than other observational studies. May have particular value in guiding recommendations where clinical trials may be impractical, e.g. in prevention of MS (Mokry *et al,* 2015). Urge WG to make explicit commitment to considering such evidence in final report.	Professor A Martineau	It was agreed that MR studies useful for indicating plausibility but also have limitations. Agreed that inclusion of MR studies in future risk assessments & whether SACN framework for risk assessment should be revised to include consideration of such studies should be discussed at future SACN meeting.
	Evidence lacking on causal relationship between health & interventions at doses which would reproduce natural UVB exposure of unprotected skin (about 4000 IU/d). Evidence only s for interventions up to 400 IU/d with much less evidence at doses 400-1000 IU/d. 2 main approaches were to look at intervention data & disease-specific 25(OH)D3 concentrations. Intervention analysis fails to recognise that data only cover fraction of natural dose, therefore impossible to come to valid scientific conclusion. The 25(OH)D3 analysis does not recognise that populations are grossly deficient as fails to include any reference group with lifetime natural-exposure vitamin D status.	M Fischer	Agreed that there is lack of evidence at vitamin D supplementation doses over 10 µg/d (400 IU). However, recommendations need to be based on the available published evidence.
	Approach was not to determine intake which ensures 'needs are met' which is required for an RNI. Instead determined 25(OH)D3 concentration & vitamin D intake below which the (grossly limited) dataset demonstrates a proven increase in risk of ill health ('proof-of-illness' level). Vitamin D supplementation is oral intake of a hormone precursor to compensate for deficit in endogenous synthesis. WG should have recognised that application of standard approaches for determining intakes of dietary substances not appropriate in forming recommendations for vitamin D.		Rationale and methodology are well explained in the report.
	Correct scientific approach would be to review biochemical evidence showing direct relationship between 25(OH)D & immunological cytokine responses,1,25(OH)2D3 concentration during pregnancy & several indicators of Ca metabolism & bone development. These indicate human physiology abnormal at 25(OH)D < circa 80nmol/L. Consistent with studies showing 80nmol/L bottom of range of 25(OH)D3 from natural levels of UVB exposure of unprotected skin. Fit-for-purpose approach includes precautionary element with safe level of intake which bridges gap between 25nmol/L 'proof-of-illness' threshold & 80nmol/L biochemical normalization threshold. A review which fails to seriously evaluate this precautionary approach is not fit for purpose.		Use of intermediate markers is limited by the inability to determine whether observed changes are normal physiological response. This is why identifiable health outputs were considered by SACN.

	Failure to extend analysis may have been due to gaps in WG expertise. Using narrow criteria described, not surprising that 'insufficient evidence' to draw conclusions in areas of cancer, type 1 diabetes, MS, cognitive degeneration. Report reads as if approach taken has determined adequate intake. Seriously misleading & unethical for final report to represent adult intakes chosen as RNIs & doing so may be subject to legal challenge. Only recommendation which is likely to meet the requirements of RNI is for infants.	M Fischer	Disagree. The WG was selected to cover extensive and relevant expertise. The risk assessment process was open and transparent and the terms of reference were wide-ranging and comprehensive. The review process also included a call for evidence to request notification of any new evidence on vitamin D.
	<u>Biology</u>		
Sources	Rice *et al* (2015) show that many adults can maintain adequate serum 25(OH)D levels despite negligible exposure to solar UVR for several months. Further work required to account for this important finding.	Professor M Norval	Agreed to consider this reference.
	"*Dermis*" or "*dermal*" shouldn't be used as substitute for "*skin*" because dermal layer of skin comprises 2 skin compartments, being the (upper) epidermis and (lower) dermis. Vitamin D synthesis actually occurs predominantly in epidermal layer of the skin not the dermal layer. "*Cutaneous*" or "*skin*" could be used.	Professor L Rhodes	Agreed to correct text.
	<u>Paragraph 20</u> Vitamin D3 (not D2 as stated) is form found in some plants, such as in leaves of Solanaceae family (e.g. see Jäpelt & Jakobsen, 2013). Vitamin D2 is form found in fungi and yeasts & plants containing endophytic fungi or with fungal infections.	Professor M Norval	Agreed to correct text.
	<u>Paragraph 22</u> 7DHC is found predominantly in lower layers of epidermis. Previtamin D is produced from 7DHC in these same layers following UVB irradiation, not in the dermis as stated consistently throughout report.	Professor M Norval	Agreed to correct text.
	<u>Paragraph 27</u> More recent data on vitamin D/25(OH)D content of food than in Ovesen *et al* (2003). Meat can contain substantial quantities of 25(OH)D & consumers of meat have higher 25(OH)D status than non-consumers. As vitamin D3 & 25(OH)D are added to some commercial animal feed, the concentration of these substances in meat could be increasing. Potency factor for 25(OH)D 5x higher than for vitamin D. Thus further consideration of contribution of these metabolites in food is required: e.g. Taylor *et al* (2014) & Heaney & Armas (2014).	Professor M Norval	UK databases already include 25(OH)D content of meat and take account of the 5X potency factor. More recent references noted.
	<u>Paragraph 27</u> Although 100g egg yolk may contain 5µg vitamin D, McCance & Widdowson indicates single egg yolk contains about 1.8 µg. About 3 eggs/d would need to be consumed to achieve intake of 5µg, which is unlikely scenario for majority of population. Consumption of eggs has declined significantly over last 3 decades. Consumption of offal & animal fats also declined all of which have impacted on vitamin D intakes.	PAGB	Agreed to check vitamin D content of egg yolk in most recent edition of McCance & Widdowson's '*Composition of foods*'.[1]
	<u>Paragraph 28</u> UK populations do not consume wild mushrooms to any great extent. Seems disingenuous to have included this as potential source.	PAGB	Wild mushrooms were included as a potential source of vitamin D in contrast to cultivated mushrooms which are grown in the dark.
Physiological regulation	<u>Paragraph 51</u> Concept that 25(OH)D decreases in response to inflammation is very important & merits more explanation and discussion, particularly with regard to the studies on cancer, autoimmunity and infectious diseases.	Professor M Norval	Agreed to include cross-reference to later chapter where it is discussed in more detail.
Storage	<u>Paragraph 59-61</u> Given prevalence of obesity in UK, this is surely another "at risk" population. Advice on risks associated with vitamin D deficiency in obese individuals should be provided.	PAGB	Consideration of obese individuals is included in the report.
Mechanism of action	<u>Paragraph 63</u> To state that the VDR on macrophages & lymphocytes is not target for vitamin D action is wrong & is stated correctly in para 438.	Professor M Norval	Agreed to replace '*not considered targets for vitamin D action*' with '*but its function in these tissues is not fully understood*'.

[1] McCance and Widdowson's composition of foods integrated dataset (March 2015) indicates vitamin D content of egg yolk is approximately 13 µg/100g.

	Paragraph 63 VDRs are present in cells with purpose of recognising & utilising vitamin D & can therefore be assumed to have a function, even if not yet determined. The Committee should have noted that VDRs are present in all of these tissues; however its function in relation to these tissues is not yet fully understood.	PAGB	Agreed to replace '*not considered targets for vitamin D action*' with '*but its function in these tissues is not fully understood*'.
	Paragraph 66 No mention of cathelicidin.	Professor T Oliver	Cathelicidin is mentioned later in the report (under consideration of vitamin D & infectious disease).
Genetic influences	Paragraph 70 (& 740) Report considers over 20 studies that include effects on polymorphisms affecting DBP or VDR genes. However, it ignores their impact suggesting, contrary to findings of several studies, that "*the functional relevance of these polymorphisms is not clear*".	ANHI	Agreed to change last sentence of paragraph 71 to '*the functional relevance of these associations is not clear*'.
Toxicity	Paragraph 78 No mention that sun exposure has no risk of vitamin D poisoning whereas exuberant use of vitamin D in patients with borderline hypercalcaemia might. 25(OH)D >375 nmol/L toxic from hypercalcaemia in drug overdose studies but UVB production switches off long before oral dose effects.	Professor T Oliver	This point is explained in the previous paragraph (77).
Physiological reqmts	Paragraph 86 Infants need vitamin D and Ca, preferably from the mother[2].	R Greenbaum	Considered in chapter 6.
	Paragraph 86 No mention of lasting deformities, e.g. knock knees, bow legs & pigeon toes which are endemic sign in areas of London with high concentration of Asian, African & poor people of all races without access to regular sunshine.	Professor T Oliver	Considered in chapter 6.
	Paragraph 87 Children & adolescents need higher levels of vitamin D & Ca for more than bone development. Having good level of vitamin D cuts in half amount of asthma, chronic illness, doctor visits, allergies, inner ear infection, respiratory tract infection, growing pains, bed wetting[3]	R Greenbaum	Considered in chapter 6.
	Paragraph 87 Fail to mention muscle weakness and lethargy with bone pain as symptom in adolescents.	Professor T Oliver	Considered in chapter 6.
	Paragraph 88 Adults need higher levels of vitamin D for more than bone development[4] Paragraph 90 Women should boost their vitamin D level at least 3m before conception to improve chances of becoming pregnant. Trial evidence that higher vitamin D leads to easier pregnancy with less bacterial vaginosis, gestational diabetes, pre-eclampsia, dental problems, emergency C-sections & fewer pre-term births. Children of women with higher vitamin D levels during pregnancy have fewer seizures and less rickets, diabetes & asthma. Development of child generally improved, with 1 trial showing fewer language problems at age 5y[5] If mother has higher levels of vitamin D after birth, her breast milk will have adequate levels of vitamin D for her baby & reduced risk of post-natal depression. Strong evidence that boosting woman's 25(OH)D to 100 nmol/L will reduce pre-term births to half normal level, across different groups of ethnicity and skin colour[6].	R Greenbaum R Greenbaum	Considered in chapter 6. Fertility was not considered as a health outcome. Other outcomes are considered in chapter 6.
Photobiology			
UVR	Paragraph 96 UVB only 5% of UV exposure. Paragraph 98 70% daily solar UVB between 10.30 & 14.30	Professor T Oliver	Paragraph 95 states *'UVB accounts for about 5% of terrestrial UVR'.* Paragraph 98 correctly states 70% of global UVR exposure *'is delivered during the four hours centred around noon'.*

[2] http://www.vitamindwiki.com/Overview+of+Rickets+and+Vitamin+D & http://www.vitamindcouncil.org/health-conditions/rickets/
[3] http://www.vitamindwiki.com/Infant-Child
[4] http://www.vitamindcouncil.org/health-conditions/; http://www.vitamindwiki.com/Proof+that+Vitamin+D+Works; http://grassrootshealth.net/media/download/dip_with_numbers_8-24-12.pdf
[5] http://www.vitamindwiki.com/Overview+Pregnancy+and+vitamin+D
[6] https://www.youtube.com/watch?v=5jUU4rAQ8lE

	Paragraph 99 States *'synthesis of vitamin D is the only established benefit of solar UV exposure'.* No discussion of nitric oxide and BP.		Currently insufficient evidence on nitric oxide and BP.
Erythema/ skin cancer	Paragraph 104 Incomprehensible. Paragraph 105 No mention of DNA repair time and reduced melanoma with 2 days of outdoor activity.	Professor T Oliver	Agreed to clarify. Insufficient evidence.
	The conflict between advice on prevention of skin cancer & on health benefits of sunlight is still discouraging people from sun exposure. Report should emphasise that intermittent sun exposure and sunburn increase risk of melanoma whereas high continuous patterns of sun exposure can be protective.	CRN UK	No reference provided to support this.
Effect of skin pigmentation on dermal synthesis	Paragraphs 115-117 As stated, not clear whether skin pigmentation influences production of vitamin D following UVR but several key references missing. 12 published studies on this topic, of which 7 indicate vitamin D photosynthesis is reduced in dark-skinned compared with fair-skinned individuals[7] but in remaining 5[8], skin colour made no difference. Possible that spectrum emitted by UV sources may explain contradictory findings as a higher proportion of short-wave radiation in lamps used in latter compared with former group. This could lead to production of previtamin D in superficial layers of epidermis above the melanocyte layer, and therefore not be affected by skin pigmentation (Bjorn, 2010).	Professor M Norval	The additional references were noted but it was agreed that their inclusion would not change SACN's position regarding influence of skin pigmentation on vitamin D production.
	Paragraph 115 Current text *"darker skin has same capacity to synthesise vitamin D if dose of radiation is adjusted for the protective effect of melanin (Farrar et al, 2013)".* The Farrar reference is not the most suitable to refer to in this context.	Professor L Rhodes	Agreed to check suitability of citing study by Farrar *et al* (2013).
	Paragraph 116 The Farrar *et al* (2013) dose-ranging data would be beneficial to present after this paragraph (wording for new paragraph summarising study suggested).	Professor L Rhodes	Agreed to consider suggested text.
Effect of sunscreen on skin synthesis	Paragraph 122 Need to add that vast majority of people do not use sunscreens at appropriate concentration & do not apply to all exposed areas of skin. Review of all available studies (to 2009) in Norval & Wulf (2009).	Professor M Norval	Agreed to include Norval & Wulf (2009) review.
Current recs on sun exposure	Paragraphs 125-126 This advice might be wise when on holiday in hot climate but totally inappropriate when over 1/3 of native & over 75% of immigrant population with darker skin are vitamin D deficient for > half of year. Since people who disregard this advice & take outdoor activity on 2 d/wk have significant protection from melanoma, this para must be rewritten to say it applies particularly when sun is so hot to give burning feeling in skin after short period or person knows they are sensitive to sun. Ideally it should promote 30 mins sun exposure twice/wk between 11.00-15.00 & educate people that given our new knowledge about DNA repair time from work with radiation when 90% of a single dose is repaired within 3 hours, it is likely that this explains the reduced melanoma occurring in people who do so. In fact, NHS consensus (2010) recommends regular short exposure around midday. The time required to make sufficient vitamin D is typically short & less than time needed for skin to redden and burn. Regularly going outside for matter of minutes around middle of day without sunscreen should be enough.	Professor T Oliver	Paragraphs 125-126 state current advice regarding sun exposure.
	Paragraph 126 Recommendation of WHO INTERSUN Programme re "safe" sun exposure should be added which includes use of local UV Index forecast. States no protection needed when UV Index <3 but, above this, should seek shade during midday hours, wear protective clothing, hat & sunscreen.	Professor M Norval	Agreed to include.
	Paragraph 126 Sunscreen also blocks synthesis of vitamin D. Instances where overuse of sunscreen has played role in development of rickets. Evidence from Australia shows there are increasing concerns about vitamin D levels in populations there, largely due to success of "Slip Slap Slop" campaign which has run successfully for over 2 decades.	PAGB	No reference provided to support this.

[7] Clemens *et al* 1982, Matsuoka *et al* 1991, Chen *et al* 2007, Armas *et a*l 2007, Farrar *et al* 2011, Farrar *et al* 2013, Libon *et al* 2013).
[8] Stamp 1975, Lo *et al* 1986, Brazerol *et al* 1988, Matsuoka *et al* 1990, Bogh *et al* 2010.

Measuring exposure			
	There is a need to develop official standard method(s) of measuring levels of vitamin D to ensure better reproducibly / consistency between measurements (although recognising that any analytical test will have some variation between different analysis centres).	Dr S Collins	This issue is considered in the report.
	Initiatives to progress efforts to overcome the stated methodological limitations would be welcomed.	CRN UK	This is an ongoing issue and efforts to overcome the methodological limitations are described in chapter 4.
Biochemical markers of vit D exposure	Paragraph 128 Given data from Kenyan muscle studies showing much higher vitamin D content than UK residents, veterinary studies should be requested to show vitamin D content of meat sold in the UK, whether reared indoors or out and whether slaughtered in summer or winter.	Professor T Oliver	Such studies were not considered to be of relevance.
	Paragraph 131-132 Evidence discussed here underlines unreliability of vitamin D blood assay. Could committee make a recommendation for further research into a more effective and reliable biochemical assay to determine vitamin D status?	PAGB	This is an ongoing issue which is discussed in detail in chapter 4.
	Paragraph 133-135 Issue of reverse causality is excuse to downgrade issue of vitamin D. Inflammation is almost certainly consumed when the cathelicidin system of macrophages & other repair cells are activated. Idea of vitamin D being biomarker of sun exposure is already established through studies on melatonin in nurses on night duty and nitric oxide synthetase and BP (Liu et al, 2014). These observations in association with comments in para 106 are needed to begin undoing harm done over last 20y with obsession that sun avoidance & excessive sun-cream use was good. Particularly relevant now that traffic fumes & chromium have been identified as co-carcinogens with UVB in causation of melanoma (Meyskens & Yang, 2011) .	Professor T Oliver	Discussion about inflammation is included in the report.
	Paragraph 135 Study cited here (Reid *et al* 2011) raises important question about reverse causality and strongly implies that vitamin D has role in inflammation which would benefit from a recommendation by the Committee for further study in this area.	PAGB	Discussion about role in inflammation is included in the report. Research recommendations are included in the final report.
	Paragraph 142 Consumption of foods containing "rich" levels of vitamin D has declined significantly over last few decades and, in relation to recommended intakes, these foods generally contain relatively low levels. If such consumption is not being captured by dietary assessment methods then it is surely safe to make the assumption that intakes from diet are inadequate.	PAGB	Relevance of this comment not clear since this paragraph relates to difficulties in accurate assessment of habitual vitamin D intake.
	Paragraph 142 Estimations of vitamin D in food will always be imprecise as they will also depend on how much sunshine or vitamin D supplements in the diet the animals have been exposed to and whether they have been killed at end of winter indoors or end of summer outdoors.	Professor T Oliver	Noted.
Measurement of 25(OH)D concentration	Paragraph 150 Concept that more biologically relevant to assess free rather than total 25(OH)D in serum requires consideration because unbound form can freely cross cell membrane to exert its intracellular effects while form bound to DBP & other proteins cannot. It is possible currently to measure free 25(OH)D accurately (e.g. as described in Schwartz *et al,* 2014).	Professor M Norval	The biological relevance of free 25(OH)D is currently unknown.
Assessment of vitamin D exposure	A recently validated vitamin D food frequency questionnaire (Weir *et al*, 2015) may be useful for future research on contribution of natural dietary sources, fortified foods & supplements to total vitamin D intake & status. This is of growing importance in vitamin D research given reliance on such exogenous sources that will be required to achieve the revised RNI/Safe Intake.	NICHE	Noted.
Relationship between exposure & 25(OH)D			
	Paragraph 164-171 Evidence discussed here indicates that the blanket 10µg recommendation made by SACN for majority of the population may be inadequate for some cohorts, particularly those of African / Afro Caribbean descent who appear to have requirements ranging from 20-40µg/day.	PAGB	This is considered later in the report.

	Paragraphs 172-181 Longitudinal studies in adults have been performed at mid-UK latitude (Gtr Manchester) examining personal sunlight UVR exposure dose throughout year & relationship to 25(OH)D. Suggest that the main data from 2 studies (Webb *et al*, 2010 & Kift *et al*, 2013) are inserted in this section with elements as appropriate appearing in chapter 8 (under serum 25(OH)D concentration by season, region, ethnicity).	Professor L Rhodes	Agreed to include data from these studies.
	Paragraph 179 States *" A UK group (University of Manchester) has examined & reported 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)."* The Manchester *in vivo* data are substantive human datasets examining relationships between sunlight & simulated sunlight UVR with 25(OH)D outcomes, under realistic conditions. These data require presentation. They are not in the DRV chapter as specific scenarios are addressed there. Also, UK white skin adult study is Rhodes *et al* (2010), & a dose-range study hasn't been performed in white adults. Amended text suggested for use.	Professor L Rhodes.	Agreed to include these data.
	Health outcomes		
	Reviews by Autier *et al* (2014) & Theodoratou *et al* (2014) should be included as most comprehensive, authoritative & balanced meta-analyses of field.	Professor M Norval	Agreed to include these reviews but noted that the findings were in agreement with those of the draft report and that they did not alter SACN's conclusions.
	Vitamin D intake studies - IOM & other authorities established that comparing vitamin D intake estimates from foods & supplements to 25(OH)D concentrations is problematic. Reasons include: comparisons made on group means as opposed to individuals, while skin colour, age, amount & quality of sun exposure & genetic polymorphisms affecting DBP & VDR affect serum 25(OH)D status. Caution also needed re older data that may not fully take into account increased adiposity of contemporary populations, another factor that decreases vitamin D status.	ANHI	Studies comparing vitamin D intake estimates against serum 25(OH)D concentration were not considered.
	Since vitamin D is fat soluble and different people absorb different amounts, medical focus should be the measured blood level rather than the input or nutritional amount.	R Greenbaum	Studies considered by SACN were those that measured serum 25(OH) D concentration rather than input estimates.
	Report only deals with disease prevention. NICE Guidance should consider whether vitamin D should be used for treatment.	R Greenbaum	Noted.

Missing data	Key positive systematic reviews/meta-analyses or studies entirely missing from report: *Hypocalcemia due to hypoparathyroidism:* Systematic review & meta-analysis - Concluded reduced incidence of hypocalcemia (Pisaniello *et al*, 2005; Roh & Park, 2006). *Psoriasis:* Systematic review & meta-analysis - Vitamin D as effective as topical corticosteroids for overall evidence of benefit (Mason *et al,* 2009; Meeuwis *et al*, 2011; Naldi & Rzany, 2009; Ashcroft *et al*, 2000). *Fall prevention*: Meta-analysis - Vitamin D more effective at preventing falling (Richy *et al*, 2008). *Osteoporosis:* Systematic review - Vitamin D effective in osteoporosis treatment in combination with calcium (Vallecillo *et al,* 2000). *Autoimmune diseases:* Systematic review & meta-analysis - Potential benefit for autoimmune diabetes (Li X *et al*, 2009). *Bone density (paediatric):* Systematic review - Monotherapy with vitamin D (alfacarcidol) effective for secondary osteoporosis in children, but combination with riserdronate more effective in improving BMD (Iwasaki *et al,* 2008). *Bone diseases (kidney disease or kidney transplant):* Systematic review - Treatment with a biophosphonate, vitamin D sterol, or calcitonin after kidney transplant may prevent bone disease (Palmer *et al,* 2005). *Cancer prevention (breast, colorectal, prostate, other):* Meta-analysis - Incidence of cancer reduced only when used in combination with Ca (Chung *et al,* 2011). *Corticosteroid induced osteoporosis:* Meta-analysis -Vitamin D analogs prevented bone loss in corticosteroid & non-corticosteroid users (Richy *et al* 2004). *Skin condition:* Systematic review - Calcipotriol may be effective for skin diseases other than psoriasis (Holm & Jemer, 2002).	ANHI	Study by Richy *et al* (2008) predates IOM report. Chung *et al* (2011) concluded evidence not sufficiently robust to draw conclusions regarding benefits or harms of vitamin D supplementation for prevention of cancer. All other studies were conducted in patient groups and are therefore not relevant to the generally healthy UK population.
	Major omission by not making a significant review of type 2 diabetes[9]. Omitted reference to number of other significant health conditions: Acne, anaphylaxis, anaemia, back pain, fibromyalgia, HIV & AIDS, melanoma, myeloma, Parkinson's, psoriasis, sepsis, thyroid conditions & trauma[10].	R Greenbaum	Recent meta-analyses of RCTs have not found a protective effect of vitamin D on type 2 diabetes / glucose homeostasis (Mitri *et al, 2011;* Seida *et al,* 2014). It was agreed that these findings did not, therefore, alter SACN's recommendations Melanoma was considered. Other conditions listed were not considered either because they were not of public health significance or because of insufficient evidence.
Potential sources of bias & confounding	Paragraph 192 Acknowledges that observational studies show individuals with higher serum 25(OH)D tend to be healthier largely due to greater exposure from sunlight, diet and, most telling, "*prophylactic use of supplements*". Despite this SACN does not acknowledge any health benefits other than musculoskeletal, nor any specific recommendation to take food supplements even though it is clear that dietary intakes from food alone are inadequate and sunlight exposure is insufficient, to supply adequate levels in UK populations.	PAGB	Considered in Chapter 6.
Rickets	The '*Global Consensus Recommendations for the Prevention and Management of Rickets'* has been accepted for joint publication. Authored by 33 experts & endorsed by 10 international societies. Consensus strictly evidenced-based using GRADE criteria. In interest of public health, would be favourable if main messages from SACN report were not conflicting with this report.	W Hogler	SACN's recommendations are based on the Committee's own judgements and interpretation of the evidence.

[9] http://www.vitamindwiki.com/Overview+Diabetes+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions/
[10] http://www.vitamindwiki.com/VitaminDWiki; http://www.vitamindcouncil.org/health-conditions/

	Does Committee plan to consider inclusion of *European Society for Paediatric Endocrinology Global Consensus for Guidance on thePrevention & Management of Rickets*? To avoid confusion, important to include reference to these guidelines if published within timeframe of SACN report.	Bone Research Society	Agreed to include reference to *Guidance* if published within timeframe of SACN report.
Osteomalacia	Report refers to osteomalacia as a disorder in adults. Symptoms & disease also occur in teenagers, particularly in girls (Das *et al,* 2006; Ward *et al*, 2005). Important to acknowledge this for public health & prevention of future disease.	Bone Research Society	Noted.
	Paragraph 199-212: Lifelong improvement in bone health more likely if 25(OH)D > 75nmol/L. Priemel *et al* (2010) measured bone health from 675 people who had recently died & interpretation of their data by Dr Heaney suggests values < 75-80nmol/L "*cannot be considered as adequate*".	R Greenbaum	A detailed analysis of this study is included in the report.
Assessment of bone health	Paragraphs 205, 210-212 Should mention osteomalacia in teenagers due to vitamin D deficiency and/or low Ca intake e.g., Das *et al* (2006), Ward *et al* (2009). Paragraph 206 Should add comment that low BMD may be due to osteoporosis or osteomalacia & distinction cannot be made between the two with DXA measurement e.g. Bishop *et al* (2014); Crabtree *et al* (2014). Paragraph 208 Recently published ISCD guidelines for clinical assessment of bone in children should be included (Bishop *et al*, 2014).	MRC HNR	Noted.
	Comprehensive review of assessment of bone health. However, report does not mention that a low BMD can indicate osteoporosis (quantitative loss of bone) or osteomalacia (qualitative disorder of bone). Not possible to distinguish the two using BMD & important to note in context of report. Reference also made to pitfalls of assessment of bone in children. Reference to *International Society for Clinical Densitometry Guidelines for Children* would be relevant here (Bishop *et al*, 2014; Crabtree *et al,* 2014).	Bone Research Society	Noted.
Bone health indices (pregnancy)	Paragraph 247 Javaid *et al* (2006) & Mahon *et al* (2010) both present relationships with 25(OH)D as a continuous variable, so associations are not simply presented above & below a notional deficiency threshold. Additional publications that might be considered: Moon *et al* (2014; 2015); Harvey *et al* (2008); Thacher *et al* (2014a & 2014b).	N Harvey & C Cooper	Noted.
Stress fractures	Paragraphs 282-289 Many reports from the military where stress fractures are reduced when 25(OH)D is higher. They are an ideal group where controlled experiments have and can be done[11].	R Greenbaum	Stress fractures are considered in the report.
Fracture prevention	Surprised report states there is absence of any positive effect on bone strength. Additionally, full report points out that some meta-analyses state there is evidence for fracture reduction for vitamin D & Ca, whereas executive summary states there is no evidence of fracture reduction for vitamin D. Having two inconsistent messages about vitamin D and fracture reduction is unhelpful and could be confusing.	NOS	Agreed to clarify that vitamin D plus calcium is more effective in reducing fracture risk than vitamin D alone.
Falls	Paragraph 328-34: A Cochrane Review shows that falls in the elderly are reduced when vitamin D serum and Ca levels higher. This results from stronger bones and muscles[12] .	R Greenbaum	This is covered in chapter 6.

[11] http://www.vitamindwiki.com/VitaminDWiki; http://www.vitamindcouncil.org/health-conditions/
[12] http://www.vitamindwiki.com/Overview+Fractures+and+Falls+and+Vitamin+D

Pregnancy & lactation (non-musculo-skeletal)	Paragraph 356-391 Women should boost their vitamin D level at least 3 m before conception to improve their chances of becoming pregnant. In 1 trial women given 100 µg/d vitamin D3 during pregnancy. From this & other trials there is evidence that higher vitamin D leads to an easier pregnancy with less bacterial vaginosis, gestational diabetes, pre-eclampsia, dental problems, emergency C-sections and fewer pre-term births. If pregnant woman has higher vitamin D levels their children have less rickets, fewer seizures, less diabetes, less asthma. Development of child is generally improved, with 1 trial showing fewer language problems at age 5[13]. If mother has higher vitamin D levels after birth then breast milk will have adequate levels of vitamin D for baby. She will also have a reduced risk of post-natal depression. Strong evidence that boosting woman's 25(OH)D to 100 nmol/L will reduce pre-term births to half normal level & reduce current disparities between many different groups of ethnicity and skin colour[14].	R Greenbaum	Primary source for this evidence not cited.
	Paragraphs 363-379 No mention of link between suggestion of a role of sun deficiency during pregnancy in MS and schizophrenia.	T Oliver	No references provided.
Later growth & development	Paragraphs 379, 382-383 Gale *et al* (2008) uses earlier & smaller Princess Anne Hospital Cohort (in which associations between maternal 25(OH)D status in pregnancy & offspring bone mass at 9y were observed by Javaid *et al* (2006), and not in the later, larger Southampton Women's Survey.	Profs N Harvey & C Cooper	Agreed to correct.
Cancers	Paragraph 392-404 Evidence that levels of vitamin D > 100 nmol/L help to prevent and treat many cancers. There is good evidence for cancers of the breast, cervix, colorectal, esophagus, stomach, lung, ovaries, pancreas & prostate[15].	R Greenbaum	Insufficient evidence to support this statement. Evidence on cancer considered in chapter 6.
	Paragraph 401 High vitamin D & increased pancreas cancer in 1 study is posted without comment. Is it due to over indulgence in supplements in the particular population or living in high sun environment. Paragraphs 402-404 Show lack of effect of vitamin D supplements on cancer but high vitamin D prevents colon cancer without discussion of life-long ambient sunshine data reducing colonisation of scar tissue by anaerobic microbiome hypothesis in prostate, breast, colon & pancreas (see attached unpublished paper). The data on exercise after diagnosis and confounding effect of exercise and vitamin D while not class 1 data provides more meaningful data when considering a life-long sub-clinical vitamin D hypothesis.	Professor T Oliver	Reason for this association is unclear. Cannot include unpublished data.
	SACN does not recognize generalised relationships between vitamin D status & certain cancers despite copious evidence to contrary (Garland *et al,* 2006).	ANHI	Evidence on cancer considered in chapter 6 including more recent data.
CVD & Hypertension	Key finding in VICtORy study (Wood *et al,* 2012), with all participants starting Jan-Feb, was that BP decreased in summer & went back up again in winter; pattern identical for 2 vitamin D treatment groups & placebo. Suggests other factors besides vitamin D are influencing BP & explains why associations with vitamin D difficult to separate from sunlight exposure/season unless study designed appropriately.	Prof H Macdonald	Noted.
	Paragraph 405-418 Evidence that vitamin D levels between 100-150nmol/L help reduce and treat CVD[16]. Paragraph 419-428 Evidence that levels of vitamin D levels between 100-150 nmol/L help to reduce hypertension by typically 5-10 mm Hg and should be used as part of a range of treatments[17].	R Greenbaum	Insufficient evidence to support these statements.
	Paragraphs 424-8 The above arguments (re cancer) apply equally to most CVD & most relevant in chronic cardiac failure and particularly many years of sub-clinical vitamin D deficiency.	Professor T Oliver	Comment unclear.

[13] http://www.vitamindwiki.com/Overview+Pregnancy+and+vitamin+D
[14] https://www.youtube.com/watch?v=5jUU4rAQ8l
[15] http://www.vitamindwiki.com/Overview+Cancer+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions
[16] http://www.vitamindwiki.com/Overview+Cardiovascular+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions
[17] http://www.vitamindwiki.com/Hypertension+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions

	Given the data on Kenyan runners and Woods et al [?) recovery of heart muscle could take time to build vitamin D stores and there could be non-vitamin D effects of sunshine.	Professor T Oliver	Reference not provided.
All-cause mortality	Paragraph 429-436 Evidence that levels of vitamin D levels between 100-150 nmol/L help to reduce death from all causes[18] .	R Greenbaum	Insufficient evidence to support this statement.
Autoimmune disease	Paragraph 437 '*Autoimmune disease is characterised by production of antibodies against the body's own tissues'*. Not all autoimmune disease is antibody-mediated – just a sub-set. Many of the autoimmune diseases cited in the report are T cell-mediated.	Professor A Martineau	Noted.
	Paragraph 438 Asthma is not an autoimmune disease; it is an allergic / atopic disorder.		Noted.
	Paragraphs 457-60 Multiple sclerosis: here & elsewhere report does not seem to have taken account of mendelian randomisation studies. Highlight 1 study published since Draft Report issued (Mokry *et al,* 2015).		See earlier response in relation to mendelian randomisation studies (page 3)
	Paragraph 437-470 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat many autoimmune diseases[19]. Paragraph 441-450 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat asthma[20]. Paragraph 451-454 Evidence that vitamin D levels between 100-150 nmol/L help reduce & treat both types 1 & 2 diabetes. Draft report only mentions type 1 diabetes. Pity that type 2 diabetes was not reviewed, as there is significant benefit from increased levels of vitamin D[21]. Paragraph 455-456 Evidence that vitamin D levels between 100-150 nmol/L help reduce and treat all forms of Inflammatory Bowel Disease and Crohn's disease. Number of gastroenterologists regularly treat these diseases by boosting level of vitamin D – with good results[22]. Paragraph 457-460 Evidence that vitamin D levels between 100-150 nmol/L help to reduce & treat MS[23]. Paragraph 461-462 Evidence that vitamin D levels between 100-150 nmol/L help to reduce & treat rheumatoid arthritis [24]. Paragraph 463-464 Evidence that vitamin D levels between 100-150nmol/l help to reduce and treat lupus[25] .	R Greenbaum	Insufficient evidence to support these statements.
	Paragraph 470 "*Data on Autoimmune disease are lacking*". The most convincing contrary observation relates to anecdote from Hafstong & Hallegren on Swedish patients getting 6m rehab in either Israel or Tenerife. This observation, taken with Tirwana *et al*'s observation on P.mirabilis in RA & US Nurse study on sun exposure & rheumatoid by Arkema suggest more attention required in this area.	Professor T Oliver	References not provided.
Infectious disease	Paragraph 471 Liu *et al* (& other investigators, including myself) have not demonstrated that cathelicidin kills Mycobacterium tuberculosis; rather, it restricts growth of the bacillus (Martineau *et al,* 2007).	Professor A Martineau	Noted.
	Paragraph 475 '*Evidence is lacking on whether vitamin D supplementation can influence risk of developing infectious disease.*' Would question this statement; e.g. 22 RCTs (n=10,717) have now investigated whether vitamin D can prevent acute respiratory infection (ARI) (see annex). We have recently conducted an individual patient data meta-analysis of these trials & found vitamin D protective against ARI in all	Professor A Martineau	Agreed to change this sentence to "*there is some evidence to suggest vitamin D supplementation can influence risk of developing infectious disease'.* 16 of the 22 RCTs cited were in healthy populations. Out of

[18] http://www.vitamindwiki.com/tiki-index.php?page=Mortality
[19] http://www.vitamindwiki.com/Autoimmune
[20] http://www.vitamindwiki.com/Overview+Asthma+and+Vitamin+D ; http://www.vitamindcouncil.org/health-conditions/
[21] http://www.vitamindwiki.com/Overview+Diabetes+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions/
[22] http://www.vitamindwiki.com/Inflammation; http://www.vitamindcouncil.org/health-conditions/
[23] http://www.vitamindwiki.com/Overview+MS+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions/
[24] http://www.vitamindwiki.com/Overview+Rheumatoid+Arthritis+and+vitamin+D
[25] http://www.vitamindwiki.com/Lupus; http://www.vitamindcouncil.org/health-conditions/

	participants (OR 0.88; 95% CI, 0.80-0.95, p=0.003) & that protective efficacy is greater among those with baseline 25(OH)D <25 nmol/L (OR 0.56; 95% CI, 0.41- 0.76, p<0.001) & on those who receive daily/weekly dosing vs less frequent dosing (OR for daily/weekly dosing sub-group 0.81; 95% CI, 0.72-0.91, p<0.001). Preparation of manuscript underway but hope results can be cited (at least in abstract form) in report.		these 16, only 4 showed a protective effect of vitamin D supplementation. It was agreed that these findings did not alter recommendations.
	Paragraph 476 Findings from Reid *et al* (2011) study have questionable relevance (if any) for field of infectious diseases. Studies in infectious disease have suggested that 25(OH)D levels do not fluctuate in response to infection. Paragraph 477 '*A person exposed to TB will not necessarily develop the disease as the immune system is usually able to destroy the bacteria*'. Evidence supporting this statement very limited. More accurate to say '*a minority of individuals may be able to resist infection*'. Paragraph 478 '*No RCTs of vitamin D supplementation for the prevention of active TB in those with a latent infection could be identified*'. 1 such trial in progress[26]; 1 trial has been conducted to determine whether vitamin D can prevent LTBI (Ganm *et al,* 2012); 1 (n=8,020) phase 3 RCT testing this hypothesis is currently recruiting[27]. Paragraph 481 Cited study (Arnedo-Pena *et al,* 2015) investigated acquisition of latent TB infection, not incidence of TB (universally understood to mean active TB disease as opposed to latent TB infection); wording here needs correction. At least 2 prospective studies have examined association between vitamin D status & subsequent active TB risk which could be cited (Talat *et al*, 2010; Sudfeld *et al*, 2013). Paragraph 482 Appropriate place to cite study by Arnedo-Pena *et al* (2015), currently mentioned in para 481. Paragraph 488 Not clear why Rees (2013) study is cited here – 22 published trials in this field, some positive, some null and some negative (see above). Paragraph 495 At least 2 observational studies investigate whether vitamin D status associates with risk of COPD. Paragraph 496 Does not acknowledge large volume of RCTs of vitamin D for prevention of ARI in general population (see above). Paragraph 498 Does not acknowledge existence of RCT by Ganmaa *et al* (2012). Paragraph 500 Observational studies have investigated whether vitamin D status associated with COPD risk. Not clear why COPD included in the infectious diseases section since it is non-communicable disease caused primarily by exposure to smoke.	Professor A Martineau	Agreed to review wording for this paragraph. Noted. Noted. Study by Arnedo-Peno cited in the report is different reference[28] and does examine incidence of TB. References for the 2 prospective studies noted. See above. Agreed to mention other RCTs in this paragraph. Noted. See comments above. RCT does not examine TB prevention. Agreed to remove COPD.
	Paragraph 471-500 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat many forms of Infectious diseases[29]. Paragraph 477-484 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat tuberculosis[30]. Paragraph 485- 494 Evidence that vitamin D levels between 100-150 nmol/L help to reduce & treat respiratory tract infections[31] . Paragraph 495: Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat COPD[32].	R Greenbaum	Insufficient evidence to support these statements.

[26] https://clinicaltrials.gov/ct2/show/NCT01798680
[27] https://clinicaltrials.gov/ct2/show/NCT02276755
[28] Arnedo-Pena A *et al*. *Vitamin D status and incidence of tuberculosis among contacts of pulmonary tuberculosis patients. Int J Tuberc Lung Dis*. 2015;19(1):65-9. doi: 10.5588/ijtld.14.0348.
[29] http://www.vitamindwiki.com/VitaminDWiki; http://www.vitamindcouncil.org/health-conditions
[30] http://www.vitamindwiki.com/Overview+Tuberculosis+and+Vitamin+D; http://www.vitamindcouncil.org/health-conditions/
[31] http://vitamindwiki.com/tiki-index.php?page_id=3873; http://www.vitamindcouncil.org/health-conditions/

	Paragraphs 496-500 Same situation could apply to this area as in heart & autoimmune disease. Moreover given government's campaign against antibiotic use & coughs/colds being basically a problem of winter, could be a case for a large scale placebo controlled study of vitamin D as an alternate to antibiotics in patients with borderline need for antibiotics.	Professor T Oliver	Outside SACN's remit.
	Wish to highlight effect of vitamin D on diseases involving T cell function. These include TB, sarcoidosis, MS, Crohn's disease, ulcerative colitis, and psoriasis. Note that the epidemiology suggests that latitude, hence vitamin D lack, has causal role.	RCP	These outcomes have been considered in the report. Epidemiological studies can only demonstrate an association, not causality.
Neuro-psychological	Paragraph 501-519 Evidence that vitamin D levels between 100-150 nmol/L help reduce and treat many forms of neuropsychological functioning[33] . Paragraph 503-506 Evidence that vitamin D levels between 100-150 nmol/L help reduce & treat many health problems with cognition and dementia[34] . Paragraph 507-511 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat many forms of depression[35]. Paragraph 512 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat many forms of autism[36]. Paragraph 513-516 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat many forms of schizophrenia[37]	R Greenbaum	Insufficient evidence to support these statements.
	Paragraphs 508-19 Lack of appreciation that exercise & vitamin D are confounding variables in all data on depression, makes it highly likely that it is long-term deficiency as in cancer that is playing a role. Given animal data showing profound effects in brain protein synthesis in offspring born to mothers deliberately made vitamin D deficient mean more attention needs to be paid to observed association between MS & schizophrenia and neurodevelopment during winter.	Professor T Oliver	SACN does not base recommendations on animal data.
Oral health	Paragraph 520-528 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat many forms of oral health[38].	R Greenbaum	Insufficient evidence to support this statement.
	Paragraphs 526-9 Rightly emphasise that vitamin D deficiency association with periodontal disease is due to its relevance to host immunity more than Ca metabolism. However as there are few dentists who acknowledge this ''early'' manifestation of ''chronic'', i.e. 5-20 y subclinical sun-deficiency has relevance to need of alteration of life style rather than more regular attendance for hygienist attention & they could play an important public health role in this respect.	Professor T Oliver	Outside SACN's remit.
AMD	Paragraph 530-537 Evidence that vitamin D levels between 100-150 nmol/L help to reduce and treat Age Related Macular Degeneration[39] .	R Greenbaum	Insufficient evidence to support this statement.
Selection of health outcomes to inform DRVs	Evidence for benefits of vitamin D should be accepted for other than bone health outcomes. Causality has been proven in number of publications with application of Bradford-Hill's criteria, e.g. in breast cancer. RCTs might be 'gold standard' but are not only acceptable wisdom. Other widely accepted public health measures	Dr H Rhein	Insufficient evidence to support beneficial effects of vitamin D on non-musculoskeletal health outcomes.

[32] http://www.vitamindwiki.com/COPD+helped+by+weekly+50%2C000+IU+Vitamin+D+%E2%80%93+several+trials; http://www.vitamindcouncil.org/health-conditions/
[33] http://www.vitamindwiki.com
[34] http://www.vitamindwiki.com/Alzheimers-Cognition+-+Overview; http://www.vitamindcouncil.org/health-conditions/
[35] http://www.vitamindwiki.com/Depression; http://www.vitamindcouncil.org/health-conditions/
[36] http://www.vitamindwiki.com/Overview+Autism+and+vitamin+D; http://www.vitamindcouncil.org/health-conditions/
[37] http://www.vitamindwiki.com/tiki-index.php?page_id=2985
[38] http://www.vitamindwiki.com/Dental; http://www.vitamindcouncil.org/health-conditions/
[39] http://www.vitamindwiki.com/Vision

	have also not been proven by RCTs, e.g. discouragement of smoking, wearing seat belts.		
	Paragraph 548-606 Having devoted most of previous pages to asserting there is no grade 1 evidence i.e. randomised trial data to consistently prove benefit for any other condition, the review ends by concluding that the only issue they wish to inform the public about is musculoskeletal health and what should be RNI.	Professor T Oliver	The outcomes selected to inform the basis of the recommendations are based on the available published evidence.
	Paragraphs 552-556 Rickets present in majority of studies at 25(OH)D concentrations <25nmol/L & para 555 states risk appears to increase at 25(OH)D <20-30nmol/L. Advisable to set 30mnol/L as red flag below which it is likely disease state/s may manifest. In areas of public health, where there is no evidence of risk from levels at 30 nmol/L, setting the bar higher may help prevent or reduce incidence of disease.	PAGB	Report makes it clear that serum 25(OH)D concentration of 25 nmol/L is not a diagnostic threshold for rickets; i.e. not everyone below this threshold will develop rickets.
	Paragraph 559 Population protective cut-off indicates that below this level there is risk of deficiency for everyone and this would seem to be more of an LRNI than RNI. Para 704 indicates that a population mean vitamin D intake of 10ug/d means that 97.5% will be >25 nmol/L. This is confusing especially as report states 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 correct word as it is clearly not 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 combination).	Professor H Macdonald	Agreed to review this chapter for clarity.
25(OH)D threshold	Disturbed that arbitrary definition of vitamin D deficiency, of 25 nmol/L, was set very early in work whereas IOM set it at 50 nmol/L. In my submission to SACN I pointed out that there is good evidence that a level of at least 75 nmol/L is required for good bone health & that a group of experts have recommended a target level between 100-150nmol/L. Please explain why UK should set target of 25nmol/L. A brief review of following websites will show that there are health benefits from maintaining vitamin D blood levels higher than your arbitrary level of 25nmol/L: www.vitamindcouncil.org - 44 health conditions reviewed; www.vitamindwiki.com - 60 health conditions prevented or treated; www.grassrootshealth.net - Blood serum level of 100-150nmol/L to prevent illness.	R Greenbaum	A serum 25(OH)D concentration of 25 nmol/L to define increased risk of musculoskeletal health was not set arbitrarily or early in the process but followed an in-depth review of the evidence base. The basis for the selection of this threshold is explained in the report.
	Report does not suggest what "optimum" level of 25(OH)D might be, but only addresses minimum. Table 17 (Appendix 1) reports studies pointing to better bone health in the elderly at 25(OH)D 3 times proposed minimum. Table 13 reports increased body strength at supplementation 10 times proposed RNI & so on. Should SACN not be recommending optimum as well as a minimum, or at least alluding to potential presence of one?	P Thompson	SACN's remit was to review the DRVs for the UK population. The available evidence did not allow selection of an 'optimum' serum 25(OH)D concentration.
	Maintaining lower limit of 25 nmol/L as indicative of increased risk of vitamin D deficiency & as basis for establishing RNI, seems highly conservative. Lower limit should be based on risk of inadequacy. Particularly for adults over 50y, adequate scientific justification for 30 nmol/L to be used as basis of RNI. Evidence cited in report shows beneficial effects of vitamin D in reducing fall risk (range 23-82 nmol/L) & improving muscle function (range 24-66 nmol/L). Not clear that 25 nmol/L is sufficiently protective for adults over 50y as this concentration at lower end of ranges quoted. Report states it is not possible to distinguish between 20 & 30 nmol/L, reflecting element of subjectivity in chosen value.	HFMA	Although beneficial effects were seen at these ranges, the majority of the evidence indicated that risk increased at serum 25(OH)D concentrations < 25 nmol/L. Report explains that current threshold serum 25(OH)D concentration of 25 nmol/L was retained because the data do not allow differentiation between a serum 25(OH)D concentration of 20 vs 25 vs 30 nmol/L.

	Threshold concentration for inadequacy should not be based on an average for all outcomes & all age groups considered, or set at lower end of ranges as this may not give adequate protection to most vulnerable groups. For adults >50y, it should reflect evidence that a wider range of 25(OH)D concentrations were observed to be protective against falls & muscle strength/function. Threshold of at least 30 nmol/L, equating to dietary intake of about 12 µg/d, would be more protective. Hence, higher RNI should also be set for adults aged > 50y. This would give greater protection to this vulnerable group. The EU disease risk reduction health claim that *"vitamin D helps reduce the risk of falling associated with postural instability and muscle weakness*" requires consumer to be informed that beneficial effect is obtained with 20 µg/d - twice RNI that SACN proposing.	HFMA	The serum 25(OH)D concentration of 25 nmol/L was selected as the threshold for increased *risk* of poor musculoskeletal health. It was not based on an average for all outcomes and all age groups. The basis for the selection of this threshold is detailed in the report.
	25 nmol/L cut-off appears to have been: (i) adopted from 1998 recommendations because lack of strong enough new evidence to change it; (ii) selected on precautionary basis; (iii) chosen because risk of poor musculoskeletal health increased. Report identifies evidence of osteomalacia & rickets with 25(OH)D <30 & <50nmol/L respectively, yet <25 nmol/L chosen because there is a further increased risk? Understand you consider evidence insufficient to define new optimal cut off; however there is insufficient evidence to justify readopting 25 nmol/L level which appears to have been chosen based on case reports & cross-sectional studies, yet (as highlighted) vitamin D levels are lower in case reports because presentation to hospital occurs in later stages of disease. Evidence summaries within report read with bias towards re-adoption of 25 nmol/L cut off which is described as '*population protective'*; does evidence really exist to support a vitamin D level of 26nmol/L as being protective? IOM proposed optimal 25(OH)D of 50 nmol/L. I was unable to identify any risks associated with 25(OH)D >50nmol/L, only potential benefits. Evidence may be inconclusive but does not suggest 25(OH)D >25nmol/L is more protective & safe than >50nmol/L & it has potential to be detrimental. Many patients that present with symptomatic bone disease have vitamin D levels > 25nmol/L. This recommendation, when read alone, without depth report provides, could leave clinicians interpreting 25nmol/L level as sufficient for optimal health. RNIs taken very seriously by health professionals. Our duty is to ensure recommendations are not open for misinterpretation. Report summarised by ambiguous evidence summaries & misleading final recommendations. Hope current recommendations can be modified to better treat problem of vitamin D deficiency in UK. A 50nmol/L cut-off, along with increased RNI, would increase likelihood of actually achieving 'population protection' in terms of osteomalacia & rickets prevention, as well as being consistent with recommendations made by our international partners.	S Huish	Explained in report that there was wide variability in mean & individual serum 25(OH)D concentrations associated with increased risk of poor musculoskeletal health together with many uncertainties in the data including use of predefined cut-offs & high inter-assay & inter-laboratory variation in serum 25(OH)D measurements. The evidence suggests risk of poor musculoskeletal health increased at 25(OH)D between 20-30 nmol/L. However, current threshold of 25 nmol/L retained because data do not allow differentiation between 20 vs 25 vs 30 nmol/L. Purpose of report was to review the vitamin D DRVs for the UK general population. It is outside of SACN's remit to provide diagnostic criteria for clinical use.
	SACN has ignored expert evidence. Such evidence is crucially important given limitations of RCTs, especially for vitamin D, with complications & confounding linked to factors such as UVB sunlight exposure (& use of sunscreen), ethnicity, dietary intake (food sources) & genetic polymorphisms. In such circumstances, observational evidence & decades of clinical experience offers invaluable information about pharmacokinetics of vitamin D supplementation, alongside benefits (& risks). Such expert evidence, recognized even by scientists at US FDA and College of Pharmacy and Nutrition, University of Saskatchewan, Canada, suggests that optimal 25(OH)D at least 3 times greater than that proposed.	ANHI	SACN used its own judgement to carry out a thorough review of the evidence base and make recommendations based on its considerations.
	<u>Paragraph 556</u> For consistency with other countries, and most clinicians & IOM, would have been preferable if 30 nmol/L chosen as cut-off, rather than what was used in past. Clear that cut-off is not diagnostic of disease but indicative of poor musculoskeletal health; therefore higher cut-off preferable.	Professor H Macdonald	SACN used its own judgement to carry out a thorough review of the evidence base and make recommendations based on its considerations

	No universal consensus on biochemical definition of vitamin D deficiency. Report recommends that in order to protect musculoskeletal health, the 25(OH)D of individuals should not fall < 25 nmol/L at any time of year. A measurement of <25 nmol/L would therefore be considered deficient. However, a definition of deficiency for measurements of <30 nmol/L has already been widely adopted in the UK & reflects the IOM guidelines. As difference between these measurements in practical terms is so small, in comparison to variability of assays used for measurements, it may be pragmatic to use <30 nmol/L as threshold.	NOS	SACN used its own judgement to carry out a thorough review of the evidence base and make recommendations based on its considerations
	IOM report was used extensively to update review on vitamin D as well as evidence published since then. However, unclear why cut-off for deficiency set at <25 nmol/L rather than <30 nmol/L as suggested by IOM. Clarification of this within report would be useful, especially as setting this at a lower concentration will have implications for how data is interpreted within UK studies and compared to that from elsewhere.	NICHE	SACN used its own judgement to carry out a thorough review of the evidence base and make recommendations based on its considerations
	Chosen to retain the very conservative 25(OH)D threshold of 25nmol/L to define "population protective level" for musculoskeletal health in 97.5% of population. Previous SACN report (2007) had already observed that this low level had been questioned as inadequate & is in strong contrast with thresholds defined by IOM for 97.5%tile figure of 50nmol/L (which was described as conservative) i.e. double proposed SACN figure.	BDA	SACN used its own judgement to carry out a thorough review of the evidence base and make recommendations based on its considerations
	Definition of sufficiency of serum 25(OH)D of 25 nmol/l is no longer adequate. At least IOM's recommendation of 50 nmol/l should be accepted. Many other vitamin D experts would go even further & say sufficiency should be defined as 25(OH)D >75 nmol/l (Holick *et al,* 2011). Evidence also available that different serum levels are required for non-skeletal disease (Spedding *et al*, 2013).	Dr H Rhein	SACN used its own judgement to carry out a thorough review of the evidence base and make recommendations based on its considerations
	Paragraph 43 states "*little correlation between serum concentrations of 25(OH)D and 1,25(OH)2D*". WG has missed/omitted to report that there is a very important time when 1,25(OH)2D concentrations are variable & strongly correlated with 25(OH)D concentration. In pregnancy, one of first changes is that serum 1,25(OH)D concentration typically doubles or triples to concentration which would be lethal in non-pregnant subject. Assumption has to be that this change has functional importance. The pregnancy 1,25(OH)D concentration only becomes independent of 25(OH)D at concentrations > 80nmol/L. Therefore, unless & until proven otherwise, there is a material risk to 25(OH)D < 80 nmol/L from pre-conception to delivery. At the minimum 25(OH)D concentration of 25nmol/L, the median 1,25(OH)2D concentration during pregnancy is about half its 'plateau level' at serum 25(OH)D of about 80 nmol/L. Thus there can be no scientific conclusion that 25(OH)D3 of 25nmol/L is demonstrably sufficient from conception to delivery, either for the mother or fetus.	M Fischer	No references provided to support this. It was noted that ongoing RCTs may answer some of these questions.
<u>Dietary vitamin D intakes & 25(OH)D concentrations of UK population</u>			
	<u>Paragraph 620-688</u> This is most significant part of report that public needs to be educated about. Absence of discussions about liver as source of vitamin D in diet which is known to make a major contribution to lack of deficiency illnesses in Northern Norway Eskimo populations that should be corrected. Could also explain why African populations in the UK have a higher vitamin D level than Asians. Lack of any discussions of vitamin D content in meat, eggs and milk taken from modern indoor reared animals compared to those reared outdoors and slaughtered at end of summer. If these points accepted, might be reasonable to circulate table 1 (para 620) to every household, modified to include liver as a separate meat item.	Professor T Oliver	Agreed to mention liver as a dietary source of vitamin D.
	Paragraphs 649-656 Data from a longitudinal study by Rhodes *et al* (2014) on photosensitive patients should be included in these paragraphs on 25(OH)D concentration by season and by region (and in chapter 9 under section on *at risk* groups)	Professor L Rhodes	SACN's advice applies to the UK general healthy population and not to patient groups.

	Paragraph 661 No discussion about extraordinary comment that black adults have higher vitamin D level than Asian adults despite having darker skins. From personal experience, with educating African & Asian parents in E London, possible that different intake of liver in diets could be a factor as liver more frequently eaten by African-Caribbean community than Asian. Perhaps education needed for Curry house cooks to look at using liver in menus.	Professor T Oliver	Outside SACN's remit.
	Quantitative information on dietary intakes and nutritional status should be highlighted in executive summary.	CRN UK	Agreed to include this information in executive summary.
	Review of DRVs		
	Important to protect musculoskeletal health through avoiding vitamin D deficiency. If year round supplementation required & an RNI is set at 10 µg/d (400 IU), need to clarify that this includes dietary intakes. If supplementation required it is likely that 400 IU will be given, so population intakes would be 500-600 IU/d.		The RNI refers to total intakes – agreed to check this is clear in the report.
	SACN has not provided different intake thresholds for vitamin D2 & D3 despite recognising a substantial body of evidence suggesting that vitamin D2 has an inferior capacity to raise serum levels compared to vitamin D3.	ANHI	There is insufficient evidence to be able to do this.
Comparison with IOM	Detailed comparisons are made between approaches used by SACN & IOM. This critique very useful in understanding reasoning behind the different approaches. The German Nutrition Society & NORDEN have also recently established new vitamin D recommendations. Would be helpful if final report includes more discussion about any points of consistency and difference in approaches used.	BNF	Noted.
Modelling summer sun exposure	Paragraph 681-691 This section addresses specific projections requested by SACN regarding regular sunlight exposures over 6 (spring to autumn) and 3 months (Jun-Aug) and a target of 95% population achieving 25(OH)D ≥25 nmol/L in winter. The *in vivo* data on which this was modelled isn't included here & requires a separate mention earlier in the document (such as paragraph 179).	Professor L Rhodes	The data used as basis of modelling summer sunshine exposure required to maintain a winter serum 25(OH)D ≥ 25 nmol/L are clearly referenced in the report. Point noted regarding data requiring mention earlier in the report.
	Paragraph 688 As pointed out by B Diffey, these timings do not take account of fact that only one side of body gets exposed to the sun at any one time. Therefore they need to be doubled. Many of the British population have "sun" holidays, sometimes more than 1 per year. ONS data show there were 37.1 million holidays abroad in 2013, (more than 20% in Spain). Being in environments with significantly higher solar UVB than in the UK contributes significantly, estimated as 30% (Diffey, 2002), to annual exposure of individuals to solar UVB & therefore to raising 25(OH)D status. Such a factor has not been taken into consideration in model described in report.	Professor M Norval	Noted.
	Paragraph 688 Needs dissemination to each household in UK with 3 minor adjustments: 1) calculation should be made for darkest African skin as used by Clemens et al (1982) for his estimate that Africans need 16 X more sun than Caucasians; 2) instead of daily/in addition to daily need calculations, the figures 2 days should also be given to address Newton-Bishop's observation that 2 days outdoor activity significantly reduces melanoma risk possibly due to 5 days DNA repair time; 3) calculation should be remade based on adding into diet a portion of outdoor/end of summer slaughtered liver every 2 or 4 weeks. In addition it might make a greater impact if it coincided with NICE sunlight exposure guidance.	Professor T Oliver	Insufficient evidence to make separate recommendations for people with darker skin colour and insufficient evidence that 2 days' sun exposure reduces melanoma risk.
	The clear comment that it is not possible to recommend amount of sunshine exposure required in summer to ensure levels in winter do not fall < 25nmol/L is welcome. SACN has therefore suggested that a minimum daily intake of 10µg/d should be taken by all. Have no problem with this in general terms as it is supported by data. Unfortunate that the NICE report on sunlight currently out for stakeholder review appears to suggest something else. Hope SACN can find way to liaise with NICE GDG working on sunlight to avoid inconsistency.	Professor J Newton-Bishop	SACN has been liaising with NICE.

	Newton-Bishop's unconfirmed observation that 2 days outdoor activity significantly reduces risk of melanoma suggests some UVR damage repairable with time away from exposure & it could be <5 days implied by her research & closer to the 90% repair within 3 hours for therapeutic radiation. If this is case, report's recommendations about sun exposure completely wrong & should not be used in this document but replaced by 2010 Consensus statement & hopefully reinforced by the NICE guidance on sunlight exposure due shortly.	Professor T Oliver	The report does not make recommendations about sun exposure.
At risk groups	To continue to justify 10µg/d limit for adults, SACN has chosen to ignore rash of data showing benefits at intake levels well above this (over 25X greater). SACN considers 25(OH)D of 25nmol/L as adequate which is half that considered adequate by IOM (50nmol/L). It has failed to provide sufficient flexibility to deal with requirements of individuals outside norms in relation to factors such as genetic polymorphisms or adiposity. Insufficient evidence provided that 10µg/d can lead to 25(OH)D levels of 25nmol/L in at risk individuals in a given population, let alone twice this.	ANHI	Insufficient evidence to make separate recommendations for different population groups.
	Evidence discussed (paras 164-171) seems to indicate that some populations may require higher intakes to maintain health. What is SACN's rationale for setting one-size-fits-all blanket level for majority of population?	PAGB	Insufficient evidence to make separate recommendations for different population groups.
	Report concerns the whole of UK. Although I applaud universal recommendation for all UK citizens to take a vitamin D supplement, latitude and climate play an important role in obtaining cutaneously produced vitamin D & recommendations should therefore be more differentiated; e.g. some sections of Scottish population have 25(OH)D < 25 nmol/l at a rate of 47%[40]. Therefore not acceptable to simply recommend a 'one-size-fits-all' vitamin D supplement, when there are obviously quite different regional needs.	Dr H Rhein, GP	The RNI covers 97.5% of the UK population which includes people living in Scotland.
	Report states that the proposed RNI of 10µg/d will help to maintain a serum 25(OH)D concentration >25 nmol/L. In some health boards in Wales this level considered to be deficient enough to generally treat with 80µg/d vitamin D for 12 wks followed by maintenance dose of 20-40µg/d. Reference to recommendations for treatment for those with serum 25(OH)D concentration <25nmol/L would be welcome.	WDLAG & PHDiW	Outside SACN's remit as this relates to treatment.
	I am male patient (54y) who corrected a vitamin D "insufficiency" from 37.3 to 83.7 nmol/L by supplementing at 100-125 µg/d (4000-5000 IU) for 3m. To correct my low level of vitamin D I took a high strength supplement daily, in line with evidence of Diamond *et al* (2013) & Bacon *et al* (2009). Suggest SACN report should be clearer on level of supplementation that may be required to correct an insufficiency, as proposed RNI may be inadequate to bring about a correction.	P Thompson	Outside SACN's remit as this relates to treatment.
	Report has not fully addressed needs of specific groups, particularly > 65 y. Evidence supports need for higher vitamin D intakes in older adults who are at increased risk of poor vitamin D status due to reduced sunlight exposure, decreased skin synthesis, reduced dietary intake, impaired intestinal absorption, & impaired hydroxylation in liver & kidneys (Brouwer-Brolsma *et al,* 2013, Janssen *et al*, 2002). 70y-old exposed to same amount of sunlight makes about 25% of vitamin D made by 20y-old (Holick, 2004). Evidence that supplementation with 700-1000 IU/d beneficial for older adults (Zhu *et al*, 2010, Bischoff-Ferrari *et al*, 2009, Broe *et al*, 2007). Impact of poor vitamin D status in older people includes increased risk of falls & fractures (Venning, 2005) & nursing home admissions (Visser *et al*, 2006). In hip fracture patients ≥65y, 80% with 25(OH)D < 50 nmol/l; <5% with levels of 75 nmol/l. Vitamin D deficiency also associated with poor muscle strength (Venning, 2005), greater decline in physical performance (Wicherts *et al*, 2007) & increased risk of mortality (Visser *et al,* 2006). Vitamin D supplementation shown to improve muscle strength, functional ability & fewer falls & fractures (Janssen *et al,* 2002). Beneficial effects in reducing falls & fractures appears to be dose-related – fall risk significantly reduced with 700-1000 IU/d (Bischoff-Ferrari HA et al, 2009) &fracture risk reduced in those receiving 482–770 IU/d (Bischoff-Ferrari *et al*, 2009).	I Watson	Evidence in this age group was considered in great detail including more up to date evidence than the studies cited here.

[40] Food Standards Agency, Scotland. Vitamin D status of Scottish adults. Results form 2010 & 2011 Scottish Health Surveys. Purdon G, Comrie F, Rutherford L, Marcinkiewicz A. 2013.

	In community-dwelling women (n=302; 70-90y) with 25(OH)D<60 nmol/L, Zhu *et al* (2010) reported vit D improved muscle strength & mobility by 17.5% in experimental group in those with baseline 25(OHD) in lowest tertile. A review (Janssen *et al*, 2002) concluded that vit D supplementation in vit D deficient older people can improve muscle strength, walking distance and reduce falls & nonvertebral fractures. A meta-analysis of RCTs found 700-1000 IU/d vitamin D reduced falls by 19% in those aged ≥ 65y (Bischoff-Ferrari *et al*, 2009) & a randomised study found nursing home residents receiving vitamin D (800 IU/d) for 5 m had 72% lower falls rate than control group (Broe *et al*, 2007). A Meta-analysis (Bischoff-Ferrari *et al,* 2009). found 482–770 IU/d vitamin D reduced non-vertebral fractures by 20% & hip fractures by 18% in ≥65y.		
	There is scarce data examining responses to & 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 examination is warranted particularly considering the UK's demographic changes.	Professor L Rhodes	An improved understanding of the effect of ageing on cutaneous synthesis is included as a research recommendation.
	Evidence on which RNI of 400 IU/d for adults is based is largely limited to interventions at this level. From review of meta-analyses in report, doses of 700-1000 IU/d showed greater benefit than 400 IU/d. WG should have carried out/commissioned meta-analyses in older people on falls & breaks which specifically compared supplementation at 400 IU/d with 700-1000 IU/d. Communication & medication costs of supplementing whole population at 400 IU/d is near borderline of futility for older age groups. Supplementation at 1000 IU/d could be done at identical cost& likely to produce greater benefit. The data also challenge adoption of 25(OH)D target of 25 nmol/L. Unlikely that a material number of subjects supplemented at 400 IU/d in the test groups covered by meta-analyses would have serum 25(OH)D <25 nmol/L. If 25 nmol/L was cut off for benefit, there would be no differential between outcomes at 400 IU/d & those at 700-1000 IU/d. WG is perhaps only body in last 5y to set target minimum 25(OH)D low as 25nmol/L. Above meta-analyses are evidence that WG may be in error in setting such a low target.	M Fischer	Proposed RNIs are based on a thorough review and consideration of existing evidence.
	Different levels have not been given for different racial groups. No variation in dark-skinned individuals despite extensive evidence that circulating 25(OH)D levels are around half that of whites given similar UVB exposure.	ANHI	Recommendations were not made for UVB exposure.
	Report determines vitamin D deficiency rickets is one of main identifiable & avoidable pathologies in UK. Does not recognise that >90% rickets cases are in non-white population. Study from Glasgow (Ahmed, 2011) consistent with incident about 100X higher in non-white population. Needs of non-white population should have been given rigorous attention with recognition of larger risks of setting too low intakes, & therefore greater need for precaution. Key scientific premise on which report claims to have addressed needs of more at risk groups is fundamentally flawed (para 796). Approach based on 2 trials of white subjects (Cashman e.a.). Key premise was that, as measurements were made at end of winter, there was minimal benefit from sunshine exposure. *This interpretation fundamentally flawed*. The distribution of end-of winter concentrations of white population in regions covered by trials had large dependency on end-of summer sunshine-generated stores; e.g. median winter 25(OH)D of post-menopausal Caucasian women in Surrey was circa 44nmol/L, about 10 nmol/L higher than in Aberdeen. Median winter 25(OH)D of Asian women in Surrey was circa 23nmol/L. The % of each group with 25(OH)D <25nmol/L in winter is 9%, 40% & 64% respectively. End of winter vitamin D status white cohorts in Cashman e.a. studies have benefitted significantly from sunshine & to conclude otherwise is serious flaw. Assuming determinations made for white group were valid, such that supplementation at RNI would result in 97.5% achieving 25(OH)D3 of ≥ 25nmol/L, then fraction of non-white population, even in southern England, with 25(OH)D3 of ≥25noml/L at recommended intake will be significantly < 97.5% target considered acceptable for white population. Thus detailed basis for calculating intakes is invalid for non-white population & for any sub-group of UK white population living in regions with substantially lower UVB availability than that represented by reference studies.	M Fischer	Insufficient evidence to set differential RNIs for ethnic groups with darker skin.

	2nd methodological flaw is not taking account of the circa 2X higher incidence of pathological vitamin D deficiency in non-white groups. Appropriate approach would be to set target 25(OH)D & RNIs for non-white group with larger precautionary component on basis that risk up to 100X higher in this group. If rickets incidence in white southern UK population were 100X higher, highly likely that target 25(OH)D would have been set with a precautionary increment well above 25nmol/L, and similarly for recommended daily intake. One of most serious consequences of inadequate adult intake will be deficiency from conception through gestation, birth & increased incidence of deficiency where infant supplementation not started soon after delivery. On best available UK data (Cockburn 1980) supplementation at recommended intake will result in mean umbilical cord 25(OH)D <*20 nmol/L* for winter births of white mothers in Edinburgh. Cockburn (1980) most relevant study available. Large trial size & substantial degree of reported deficiency supports conclusion that it is likely that with supplementation at recommended intake, an unacceptable fraction of non-white mothers & progeny will have 25(OH)D below target level during conception, gestation & at birth for pregnancies anywhere in UK, at any time of year. WG failed to address needs of most at risk groups. Should have proposed conservative intake with precautionary element or determined it was not in position to make recommendation for these groups without additional studies. Approach & resulting recommendations irresponsible & discriminatory.		The available evidence (including the study by Cockburn *et al,* 1980) suggests that an RNI of 10 µg/d is sufficient to achieve serum 25(OH)D concentrations of 25nmol/L in most pregnant women. Disagree. At-risk groups were considered but there was insufficient evidence to make separate recommendations for at risk groups.
	Report should mention people who avoid sunlight & are advised to photoprotect for medical reasons, i.e. photosensitive patients & those prone to skin cancer (especially organ transplant patients). Photosensitive patients usually do not take vitamin D supplementation (Stafford *et al*, 2010) and they and their physicians may not recognise that "*at-risk group*" applies to them.	Professor L Rhodes	SACN's advice applies to the UK general population and includes at risk groups. It does not apply to patient groups.
Pregnancy & lactation	RNI proposed for general population includes pregnant & lactating women. Human milk contains very little vitamin D & NDNS data show large numbers of breastfed infants are not meeting requirements. SACN should consider how much vitamin D is needed by mother to ensure adequate amount in her milk. This could be best way to meet needs of both mother & child. If recommendation is 10µg/d for nursing mothers & 8.5-10µg/d for baby, there appears to be a disconnect between physiological facts & proposed recommendations. SACN is urged to reconsider appropriateness of its recommendation for the RNI for pregnant & lactating women.	CRN UK	Insufficient evidence to make separate recommendations for pregnant & lactating women. A safe intake (8.5-10µg/d) is proposed for breast fed infants to take account of the low levels of vitamin D in breast milk.
Safe intake	Concerned about 'safe intake' recommendation of 8.5-10 µg/d for infants. So much simpler and clearer to just say 10 µg/d. Range has always led to confusion in the past & data supports 10 µg/d as safe for whole population.	Dr B Jacobs	Agreed to retain the *Safe Intake* range of 8.5-10 µg/d since it accommodates current practice determined by concentrations of vitamin D in infant formula.
	ESPGHAN[41] recommends oral supplement of 10µg/d for all infants during 1st year of life to prevent vitamin D deficiency-associated diseases. SACN proposal for range of safe intakes from 8.5-10 µg/d cannot be justified on basis of scientific evidence, taking into account the factors that could affect endogenous synthesis, storage and utilisation. Proposal for range is likely to create confusion among doctors, healthcare professionals & parents. From practical point of view, it is difficult to give baby a drop of supplement that contains 8.5 µg/d. Urge SACN to reconsider recommended level for infants during 1st year of life as well as infants > 12 months and all children & adolescents aged 2-18 y. Could table 2 include '*neonatal hypocalcaemia*' as one of the factors to set DRV?	CRN UK Dr B Jacobs	Proposed RNIs/Safe Intakes are based on a review and consideration of existing evidence. Agreed to retain *Safe Intake* range of 8.5-10 µg/d since it accommodates current practice determined by concentrations of vitamin D in infant formula. Data insufficient to relate clearly, occurrence of hypocalcaemia to maternal or neonatal serum 25(OH)D concentrations.

[41] European Society for Pediatric Gastroenterology, Hepatology and Nutrition.

	Use of new term "*Safe Intake*" for those under 4y may cause alarm & confusion. Intakes far above 10µg have been shown to be "safe", and there is already a "Safe Upper Limit" for vitamin D. Since "safe intake" seems to mean "safe" in sense of "sufficient to prevent deficiency" suggest calling it "sufficient intake" instead. Since babies taking large volumes of formula would exceed the 8.5 -10 µg/d, by up to 40%, feel further clarification needed that this does not constitute a risk and, by extrapolation, that our local policy that vitamin D supplements should start from soon after birth rather than at 6 months is also safe. Given number of cases of hypocalcaemic fits in infants < 6m, many of which are receiving formula milk, urge committee to consider making clear recommendations about vitamin supplements starting soon after birth.	Birmingham Vit D Steering Group	Agreed to retain the term *Safe Intake* which was used in a previous COMA report[42] (DH 1991) and is clearly defined in the draft report. Agreed to clarify that this refers to the total vitamin D intake. The *Safe Intake* range of 8.5-10 µg/d is proposed for all infants 0-11m including those exclusively breast fed.
Summary & conclusions	Paragraph 722 Recommend this sentence is re-worded as quantification of sunlight exposure can be performed, though not in standard nutritional terms; could be amended to: "Sunlight UVB exposure could not be taken into account in setting RNI because it is not possible to quantify contribution it made to serum 25(OH)D concentrations within the general population *with the standard assessment methodology used for oral nutrients.*	Professor L Rhodes	Agreed not to make the suggested amendment to this sentence because the reason why sunlight exposure could not be taken into account was because of a number of limitations in the model which are discussed in the report.
	Recommendations		
RNI	With the contradictory results published thus far, even for some of the positive effects of vitamin D on bone health, together with points outlined previously, I am not confident there is sufficient evidence currently to recommend that the general UK population, living "normal" lifestyles, should ingest 10 µg/d vitamin D.	Professor M Norval	Opinion noted.
	Agree recommendations are reflective of most recent evidence which should inform future policy and public health. Note that determining clinical cut-offs for vitamin D deficiency is beyond scope of the SACN report and this may be a consideration for managing dissemination of the report.	MRC HNR	Noted.
	Support RNI of 10µg/d (400 IU). Following observations submitted for consideration in final report: Consensus among influential bodies (British Geriatric Society, American Geriatric Society & National Osteoporosis Society) is that 20 µg/d necessary for most at risk groups. Assume that SACN recommendation of 10µg/d is intended for general public who fall outside of at risk groups identified by DH? Recommend that clear distinction is made between 10µg/d RNI for prevention of deficiency in the *general population* & existing, widely accepted[43] [44] recommendations for prevention of deficiency in most at-risk groups, which is 20 µg/d. Can be best achieved through use of an MHRA licensed product & an MHRA licensed prescription product in most vulnerable at-risk groups (i.e. pregnant & breast-feeding women, babies & children aged 6m-5y & >65y).	Internis Pharmaceuti-cals	The proposed RNI is for the UK general population and includes at risk groups. The RNI does not apply to patient groups.
	High risk groups -Some consideration needed on how to ensure public remains clear about differences between correct 25(OH)D concentrations for general well-being & concentrations which may be required to treat vitamin D insufficiency/deficiency, or where a higher dose is required for improvements to bone health; e.g. standard care to recommend 800 IU/day in treatment of osteoporosis.	NOS	The proposed RNI is for the UK general population and includes at risk groups. The RNI does not apply to patient groups.
	Concerned about limited nature of some of the evidence to inform the recommendations. In particular, about insufficient data to advise on a safe upper limit & adverse effects of a higher than recommended intake.	NHS Scotland	Research recommendations will be included in the final report.

[42] *Dietary reference values for food energy & nutrients for the United Kingdom.*

[43] American Geriatric Society / British Geriatric Society Clinical Practice Guidelines for Prevention of Falls in Older Persons http://www.bgs.org.uk/index.php?option=com_content&view=article&id=320:bgsagsfalls2010&catid=47:fallsandbones&Itemid=307

[44] National Osteoporosis Society (NOS) Guidelines published April 2013, Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management http://www.nos.org.uk/document.doc?id=1352

	Impact of sunlight on vitamin D status should be clear. If this hasn't been considered already, modelling should be undertaken to identify impact on vitamin D status of adequate exposure to sunlight combined with a regular intake of foods containing vitamin D and addition / omission of supplement. This will give clarity as to whether supplementation is required for the whole population.	NHS Scotland	Impact of sunlight exposure was considered in detail but it was decided not to give advice on sunlight exposure due to the number of factors that affect cutaneous synthesis.
	Extremely cautious nature of final recommendations is disappointing. RNI of 10 µg/d is lower than IOM's RDA (15 µg/d) which was itself considered to be conservative. Whilst IOM proposed optimal 25(OH)D of 50 nmol/L, SACN set their sights much lower (25 nmol/L). This may be sufficient to improve some bone parameters & reduce incidence of rickets/osteomalacia, but unlikely to improve much else. Many extra-skeletal effects of vitamin D remain unproven in clinical trials but clearly this may take many years and huge funding to address. Current SACN recommendations are a missed opportunity for a country where vitamin D levels are alarmingly low. Would have been prudent to adopt similar strategy to IOM. An RNI raised modestly to 15 µg/d to target 50 nmol/L would increase likelihood of lowering rickets/osteomalacia rates & would be consistent with strategies in N America. Nutrient recommendation reviews are not trivial undertakings & it is hoped that current SACN advice can be modified in final version to provide lasting value to the UK public.	Professor M Hewison	The recommendations were based on the protective effective of vitamin D on musculoskeletal health. Evidence of vitamin D and any non-musculoskeletal health outcomes were considered to be insufficient at this time to inform the setting of DRVs for vitamin D. SACN drew conclusions and made judgements based on the evidence considered. See Chapter 6.
	Report recommends "*that the serum 25(OH)D concentration of individuals in the UK should not fall below 25 nmol/L at any time of the year*" This is too low. Number of reasons why it should be higher: 1. People out in the sun such as life guards have levels higher than 250 nmol/L 2. Unclear what the maximum level of vitamin D should be, but parathyroid levels have been reported to plateau ~78nmol/L (Heaney, 2005) 3. Melanoma experts consider range to be aimed for to be 60-85 nmol/L (Field *et al,* 2013). 4. Clinical review in BMJ advised that an adequate level of serum 25(OH)D is 50-75 nmol/L (Pearce & Cheetham, 2010) Consequently the recommended RNI needs to be revised up if health of country is to be properly protected.	Dr S Collins	SACN drew conclusions and made judgements based on the evidence considered. See Chapter 6.
	My reading of the literature suggests we should be aiming to elevate 25(OH)D >50 nmol/L (threshold for adequate vitamin D status more broadly accepted internationally) rather than the more modest 25 nmol/L threshold proposed. My preference would be RNI of 15µg or more in adult population, to bring UK recommendations into line with those in US. However, welcome SACN's recommendation as significant move in right direction.	Professor A Martineau	SACN drew conclusions and made judgements based on the evidence considered. See Chapter 6.
	Welcome introduction of RNIs for vitamin D in the UK. However, recommended intake is significantly lower than RNIs around the world which tend to be in range of 15-20 µg/d (600-800 IU).	NOS	SACN drew conclusions and made judgements based on the evidence considered. See Chapter 6.
	If a doctor measures a patient's blood level because of clinical concerns about their bone health and then on reading the SACN report latches on to level of 25 nmol/L as key level, the recommendations do not remind him/her that there is on average 20 nmol/L difference in levels between winter and summer, so a level of 45nmol/L might be key if measured in August.	Professor J Newton-Bishop	Clinical diagnosis is outside SACN's remit.
	Report describes concerns about U or J-shaped survival curves but discusses the evidence suggesting lack of concern about high doses of vitamin D. The recommendation that a general population intake of 10µg is presumably based on lack of evidence that high levels are not deleterious in any way. In my role as doctor I am anxious not to do harm & would like to ensure I am not recommending extra vitamin D intake where patients already have highish levels. I have therefore measured levels & given advice on this basis. SACN quite reasonably argues the difficulties in interpreting blood levels and I assume this is why blood level measurement plays no part in recommendations. Yet this leaves doctors even more unclear about what to do.	Professor J Newton-Bishop	SACN is recommending that that in order to protect musculoskeletal health, serum 25(OH)D concentration of individuals in the UK should not fall below 25 nmol/L at any time of the year. The RNI of 10 µg/d is the average amount of vitamin D intake required to ensure serum 25(OH)D concentrations are ≥ 25 nmol/L in 97.5% of the population.

	Can the guidance make clear that Committee is not mandating that everyone takes 400IU/d as a supplement? Realise document is a risk assessment & not guidance of how to implement advice, however this is not widely appreciated & the guidelines as they stand may be interpreted as so.	Bone Research Society	Agreed to make it clear that recommendation does not refer just to supplements but all dietary sources.
	Effects of increased body weight & use of sunscreens have not been adequately considered in terms of the public health recommendation and RNI proposal of 10µg/d.	ANHI	Both factors were considered and taken account of in setting the DRVs for vitamin D.
<4 years	Would welcome clarification regarding rationale for both mother and baby to take vitamin D supplements during breastfeeding since this is a common query we've encountered.	WDLAG & PHDiW	Agreed to check rationale is clearly explained in the report. Proposed recommendation of 8.5-10µg/d for breast fed infants based on evidence that suggests 25(OH)D of an exclusively breast fed infant unlikely to be maintained > 25 nmol/L during winter without vitamin D supplementation.
	Welcome recommendation that exclusively breast fed infants should achieve same RNI as non-breast fed infants. Report removes recommendation that there is no need for vitamin D supplements for babies taking more than 500ml of infant formula. While this provides a simpler message, there is the potential that the recommendation of an RNI of 8.5ug/d from birth could be interpreted as meaning no additional supplements are required by formula fed infants. Would welcome clarification on this point.	NOS	The *Safe Intake* of 8.5-10 µg/d of vitamin D for all infants 0-11 months refers to total intake. Agreed to clarify in the report.
At risk groups	Methodology of determining needs of the groups at greater risk is flawed and if not corrected the resulting recommendations are discriminatory and irresponsible. The working group should have made a rigorously-determined recommendation specific to these groups, or no recommendation at all.	M Fisher	Evidence insufficient to make separate recommendations for at risk groups.
	Report describes how levels may be lower in the obese, which is an increasingly common occurrence in the UK. What would the SACN suggest GPs do there in terms of advice?	Prof Newton-Bishop	Evidence insufficient to make separate recommendations for obese individuals. Clinical advice outside SACN's remit.
	Recent scientific impact paper by RCOG recommends: *High-risk women are advised to take at least 1000 units a day (women with increased skin pigmentation, reduced exposure to sunlight, or those who are socially excluded or obese). The RCOG has highlighted the importance of addressing suitable advice to these women. Women at high risk of pre-eclampsia are advised to take at least 800 units a day combined with calcium*. Has/will this be considered? Currently SACN draft vitamin D advice implies pregnant women with increased skin pigmentation, reduced exposure to sunlight or those who are socially excluded or obese take 10µg/d.	H Taylor	Clinical advice to high risk women is outside SACN's remit. Insufficient evidence to make separate recommendations for women with darker skin, reduced exposure to sunlight or obese women.
	Should be guidance on impact of supplementation during pregnancy & effect on the infant's vitamin D status. Such guidance could inform the recommended intakes discussed as 'safe intake' during infancy.	NHS Scotland	This point was considered in the report.
	Evidence should be provided for impact on infant of breastfeeding woman taking vitamin D supplement. 10µg not enough to transfer vitamin D to infant via breast milk so should they take higher dose? Or should breastfed infant receive a supplement from birth?	NHS Scotland	The report recommends a *Safe Intake* of 8.5-10 µg/d from birth for exclusively breast fed infants.
	'Safe intakes' for <3 y – how confident is SACN that evidence to support amount added to formula is based on best available evidence? Sources of evidence that support the vitamin D content of infant formula should be reviewed again if this hasn't been done already.	NHS Scotland	There is a paucity of data for infants; however, data from DNSIYC[45] show that none of the infants with 25(OH)D < 25 nmol/L were receiving infant formula.
	Recommendations should be made for women who are formula feeding. Assumption that they would have same requirements as general adult female population but this should be clear.	NHS Scotland	Women who are formula feeding are included in the UK general population.

[45] Diet and Nutrition Survey of Infants and Young Children (Lennox *et al,* 2013)

	Scientific points that could inform strategies for vitamin D nutrition include fact that appearance of vitamin D in plasma is short lived & effects of ageing on skin synthesis. SACN is requested to consider a sufficient amount of daily vitamin D to ensure stable circulating concentrations & how amounts can be affected by the short-circulating half-life. Report needs to highlight that effective strategies must take into account the need to sustain constant circulating vitamin D concentrations by daily supplements and/or chronic UVB exposure.	CRN UK	SACN drew conclusions and made judgements based on the evidence considered. See Chapter 6.
	Should clarify whether we no longer need to provide specific messages for specific population groups.	NHS Scotland	Agreed to clarify.
	Object to your recommendation for mass fortification of food supply with vitamin D on following grounds: Your conclusion (para 783) that data reviewed was insufficient to establish clear threshold to support musculo-skeletal outcomes. Paras 756-757 stated benefit to bone health from supplementation was inconclusive. I was prescribed vitamin D. 25µg caused hypercalcaemia, hyperparathyroidism, permanent parathyroid hyperplasia & calcification of calf muscle. Transpired I have genetic variant to the VDR. Report acknowledges those with propensity for hyperparathyroidism/hypercalcaemia but does not identify proportion of population with such genetic variations or parathyroid polymorphisms.	Ms S Mawjes	Report does not make a recommendation for mass food fortification with vitamin D.
Example of outline recommend-ations	Agree with WG conclusion that threshold for 'proof-of-illness' is serum 25(OH)D3 of circa 25 nmol/L. Totality of evidence demonstrates threshold 25(OH)D3 concentration for normalization of biochemistry at circa 80nmol/L - same as bottom end of natural-exposure range. Associative & scientific evidence establishes possibility of substantial ill-health due to low vitamin D status. Together with absence of proof-of-non-causality this leads to conclusion that correct strategy is one which includes significant precautionary element. On this basis recommended daily intake for white UK adults should be 1000 IU/d.	M Fischer	Evidence not provided to support these statements.
	Target 25(OH)D3 in majority of any significant sub-group should be ≥ 50nmol/L. Expect that with adult supplementation of white sub-group, this target will be met by about 80% of group at end of winter. This is below '97.5%' number used for dietary recommendations, but there is as yet no scientific basis to support the proposition that the 97.5% target is a rational target for minimum vitamin D status. Recommendations should be properly explained. 50nmol/L is not 'RNI-like' & 1000 IU/d is not RNI level. On current best evidence the 'RNI' 25(OH)D3 concentration is circa 80nmol/L & RNI intake for adults is circa 4000IU/d. However, in absence of direct proof of benefit, the 50nmol/L concentration is chosen as a common sense interim target, providing a significant safety factor above the 25nmol/L threshold for proof-of-illness.		References not provided to support this.
	Should make clear that vitamin D supplementation is not 'magic bullet'. Supplementation > 'proof-of-illness' level is risk-free precaution which will help to normalise immunological, Ca & bone pathway biochemical indicators & serum 1,25(OH)D3 during pregnancy & go some way to protect population against evident risk arising from associations and scientific studies in which a causative role for vitamin D deficiency is plausible.		Report makes it clear that the proposed RNI of 10µg/d is to protect the UK population against risk of poor musculoskeletal health.
	For non-white adult population, recommended intake should be 2000 IU/d. This dose s estimated to bring distribution of 25(OH)D3 more into line with expected distribution of white population. This recommendation also recognises that there is a greater imperative for a precautionary increment in this group given the estimated 2 times higher incidence of rickets relative to white population.		Insufficient evidence to make separate recommendations for ethnic groups with darker skin.
	Recommendations should be presented as interim guidelines to be reviewed after 5y or earlier if mandated by new evidence. In interim, should commission studies to determine actual 25(OH)D response at these intakes & dosing trials in non-white & southern & northern white UK population to establish distribution of 25(OH)D3 response at higher doses, e.g. 2000IU/d in white & 4000IU/d in the non-white populations. Separate small dosing trials also needed to properly inform revision of intakes for each of these sub-groups in age range 3-18y.		Outside of SACN's remit to commission studies. Research recommendations will be included in final report.

Other			
	Should be published as work in progress with recommendations for areas where urgent need for further work because of analysis highlighting apparent lack of reproducible grade 1 data in multiple areas of health in face of apparent significant observational studies suggesting association.	Professor T Oliver	Research recommendations will be included in final report.
	Report fails to review evolutionary development of vitamin D synthesis. Data (from 1930s) show sizeable proportion of plankton produce vitamin D. Holick (1992) reviewed synthesis in non-vertebrate kingdom[46]. These data suggest it may have evolved from photosynthetic pathways in plants. If so, duplication of genetic system could explain why it is involved in neuronal, muscle cell & phagocytic/immune cell development of invertebrates long before involved in bone formation. If so modern urban 24/7 living for 10-40 y on borders of "sun-deficiency" could account for wide range of pathologies & lack of gain from relatively short term trials of vitamin D.	Professor T Oliver	Outside SACN's remit.
	Would like to offer information that would be of use when formulating recommendations. I am an independent investigative author who has followed vitamin D for nearly a decade. I produced a book in 2012 titled *Prescribing Sunshine: Why vitamin D should be flying off shelves* (www.prescsun.com) which details my findings & experiences and has interviews with 3 renowned experts. Book quite controversial but supported by evidence and logic, and presents interesting arguments in favour of higher supplementation.	Mohammed Aziz	SACN's recommendations are based on published evidence and not on expert opinion.
	Primary concern is that vitamin D should be considered as a medical & health concern rather than being based on nutrition. For this reason individual health topics should also be considered by NICE.	R Greenbaum	SACN's remit is to consider nutritional requirements for the UK population in relation to disease prevention.
	Report provides a plethora of scientific data & info but does little to point risk managers towards effective strategies to improve vitamin D intake and nutritional status		SACN's remit is risk assessment and not risk management.
Balance with other nutrients	Is it assumed that calcium adequate? Interaction with other nutrients has not been considered. Vitamin A is also present In foods that naturally contain vitamin D3 & there may be an optimal balance which will be altered if vitamin D only is given in foods/supplements. This may affect some 'at risk' groups more than general population.	Professor H Macdonald	The report states that the DRVs proposed for vitamin D assume that calcium intake is adequate. Agreed to check this point is also included in the overall summary and conclusions (chapter 10).
	Report does not adequately address co-supplementation of vitamin D &calcium for elderly institutionalised individuals and use of targeted supplementation to reduce risk of fracture.	CRN UK	The report states that the DRVs proposed for vitamin D assume that calcium intake is adequate.
Nutrient-drug interactions	Report fails to include vitamin D recommendations for individuals taking drugs that can induce vitamin D deficiency, e.g. antiepileptic drug therapy & osteomalacia (anticonvulsant osteomalacia), corticoids, tuberculostatic & antiretroviral drugs. Drug-induced interactions may manifest as hyperparathyroidism & bone mineralisation disorders.	CRN UK	SACN's dietary recommendations apply to the UK general healthy population and not to patient groups.
Body weight:	The need for further research on understanding influence of body weight/composition on 25(OH)D response to vitamin D intake could be given greater emphasis.	BDA, WDLAG & PHDiW	Noted.

[46] see http://www.ncbi.nlm.nih.gov/pubmed/1297827

	With respect to maternal obesity, the recent publication of the RCOG (2014) scientific impact paper on vitamin D makes specific recommendations for supplementation for cohorts of pregnant women (those with increased skin pigmentation, reduced exposure to sunlight, socially excluded or obese – to take 25µg/d vitamin D & women at high risk of pre-eclampsia are advised to take 20µg/d vitamin D combined with Ca). Would be interested to know committee's views on these recommendations.		Insufficient evidence to make specific recommendations for those with darker skin, reduced exposure to sunlight, socially excluded or obese. Outside of SACN's remit to make recommendations for women requiring medical treatment during pregnancy.
	Report acknowledges that 25(OH)D may be confounded by BMI. In Wales, 1 in 5 (22%) of adult population classified as obese[47] & 26% children aged 4-5y are either overweight/obese[48]. Significant proportion of UK population may therefore be at increased risk of vitamin D deficiency including children from most deprived areas of Wales. Greater emphasis could be given in report that further research needed to understanding influence of body weight/composition on serum concentration response to vitamin D intake/exposure.	WDLAG & PHDiW	Agreed further research required in this area and will be included in research recommendations.
	To investigate possible association between vitamin D & different measures of body fatness, analysed 3 recent meta-analyses, performed for BMI (Kg/m^2), Fat Mass (FM, Kg) and Free Fat Mass (FFM, Kg) % FM and % FFM. Pathak *et al* (2014) 12 RCTs. Small non-significant effect of vitamin D supplementation on BMI reduction & FM. Authors concluded that, in absence of caloric restriction, vitamin D supplementation did not reduce obesity. Saneei *et al* (2013) 34 cross-sectional studies. Significant inverse, but weak, correlation between 25(OH)D & BMI. Pereira-Santos *et al* (2015) 23 observational studies (cohort, case-control, cross-sectional). Positive association between BMI & 25(OH)D. Conclude that even if some evidence suggests inverse association between vit & body fatness measures, not sufficient to support causal relationship. Studies considered were heterogeneous & several confounding factors were not taken into account in papers included in meta-analysis.	S Tagliaferri, R De Giuseppe, H Cena	Agreed to make reference to these studies in the report.
Overlap risk & benefits	Should be recognition that highest intake among those populations most in need of a given nutrient may overlap with those most susceptible to mildest adverse effect.	ANHI	Risk assessment included consideration of adverse effects and those with high intakes.
Daily dosing	Why daily dosing is important for all non-bone health matters (from Dr Bruce Hollis). Vitamin D functions within 2 systems in human body: 1. Endocrine system - maintains Ca homeostasis & bone health. This system uses 25(OH)D. By time it is turned into 1,25(OH)2D, it has a half-life of 3 wks. All studies on bone health have been successful based on dosage, not frequency, because of this long half-life. 2. Autocrine/paracrine system - vitamin D delivered to non-skeletal systems such as breast, colon, and prostate tissues & helps affect autoimmune disorders, cancer, CVD, infections. In this system, vitamin D goes into a cell & helps regulate cell growth. After this process vitamin D has half-life of 24h, meaning frequency of dosing matters when testing for disease reduction and immune control.	R Greenbaum	Details on half-life and biology of vitamin D are provided in Chapter 2. Dosing regimens for treatment and immune control are outside SACN's remit.
Sun exposure	Regarding amount of sunlight exposure, as sunlight on skin is the most effective way of producing vitamin D a suggested safe time for exposure to sunlight would be a sensible population approach. Benefits of outdoor activity for all ages, especially during summer, need to be part of public health policy.	BDA, WDLAG & PHDiW	Did not make any recommendations about sunlight exposure because of the number of factors that affect cutaneous synthesis.
	Clearer message about benefit of sunlight exposure required. There are months where no vitamin D synthesis occurs at the UK's latitude (Dec, Jan, Feb) & other months when very little occurs. Should PHE be advocating appropriate exposure tactics for the summer months where vitamin D is synthesised in order to counter the prevailing phobia of sun exposure and use of excessive sun protection factor creams.	P Thompson	Did not make any recommendations about sunlight exposure because of the number of factors that affect cutaneous synthesis. NICE guidance on *Sunlight exposure – risks & benefits* is due for publication in early 2016.

[47] Welsh Government, 2014.
[48] Public Health Wales, 2015.

	Possibility that exposure to UVR likely to have many more effects than cutaneous production of previtamin D is not addressed. These could be either protective or detrimental for a range of diseases. This aspect reviewed by Hart *et al* (2011). Therefore limited exposure to solar UVR could result in loss of several positive aspects for health which would not be compensated for by administering vitamin D supplements.	Professor M Norval	SACN's remit did not include looking at other benefits of sunlight exposure. NICE report (see above) covers positive effects of sunlight exposure.

Table 3 – Comments relating to risk management (For information - risk management is outside SACN's remit)

Dietitians will be pivotal in the intense communication that will be required to support the public's understanding & motivation for this recommendation. Particular issue will be clear support for vitamin D supplementation as a routine health action by the entire population beyond previously defined risk groups, as levels of 10ug are well beyond the food-only intake of 97.5%tile intakes. Dietitians will also need to work with the UK food industry advising on issues around vitamin D fortification practices.	BDA
Would welcome clarity regarding advice for breastfed infants. Suggested that all exclusively breastfed infants will need supplementing with vitamin D from birth. Important to consider the fit with current public health recommendations & impact of this message for women choosing to breastfeed exclusively i.e. do not want women to perceive breast milk is inferior to infant formula. Already find some mothers are reluctant to accept that breast-fed infants need supplements.	BDA & WDLAG and PHDiW
Concerned no recommendations on how to implement these recommendations in practice, which may lead to inaction, or delays in policy change, particularly with reference to the age, or volume of formula intake, at which supplements should be introduced in babies.	Birmingham Vit D Steering Group
Recommendation that consideration should be given to strategies for UK population to achieve RNIs/safe intakes is too vague& does not address issues raised by the scientific evidence & specific at risk groups. SACN needs to highlight subsets of UK population at real risk of deficiency (e.g. consider focus on institutional care & pregnant & nursing mothers).	CRN UK
In view of limited resources, the evidence base could inform better, effective strategies, including selective testing of at-risk groups (in the winter), benefits of vitamin D with respect to reducing risk of falling and fracture , relative contribution to vitamin D intake of certain foods and food supplements and from cutaneous synthesis.	CRN UK
Report very useful in understanding current intakes & levels of vitamin D & effectiveness of food fortification & supplementation. We will be asking DH for their view on current levels of vitamin D used in fortified products & supplements and their advice on how businesses can enable improved uptake of vitamin D.	BRC
If fortification considered, important to consider whether fortification alone would be: sufficient to raise dietary vitamin D intakes to level to minimise risk of poor musculoskeletal health, whether it should be on a mandatory/voluntary basis & which foods should be fortified. If advice revised to state vitamin D supplementation is recommended for all population groups, there are a number of considerations: <u>Infants and young children</u>: would need to ensure supplementation was readily available & appropriately communicated to families via health professionals & that supplements would provide safe levels of vitamin D for infants. Clear advice would be needed about vitamin D content of infant formula, & what point vitamin D supplementation would be necessary as volume of infant formula is reduced. Currently recommended that infants should be given daily supplement of 7-8.5 µg/d. If safe intake for children 1-3y is increased to 10µg/d, available supplements may need to be reformulated to provide appropriate levels. <u>Children aged ≥ 4y & adults</u>: clear info needed to ensure as many people as possible aware of new recommendations & encouraged to follow them. <u>Support to encourage people to follow recommendations</u>: • Consider whether eligibility for Healthy Start scheme would need to be extended to support children/adults from low income groups. • Guidance on new recommendations in relation to vitamin D supplementation would need to be effectively cascaded to health professionals supporting families (including GPs, midwives, health visitors, school nurses). Irrespective of whether strategies to support UK population to achieve the RNI are based on supplementation or fortification, the population should still be encouraged to eat a diet which provides good sources of vitamin D.	Children's Food Trust
If the draft recommendation is finalised and accepted by Government, we would welcome being involved in developing strategies to help increase dietary vitamin D levels. Draft report highlights that there are few naturally rich sources of vitamin D. NDNS (2008/9–2011/2) shows fortified foods can play significant role in helping population achieve RNI: fat spreads contributed around 20% of vitamin D across all age groups, & fortified breakfast cereals provide 6 -9%. Manufacturers fortify these products on voluntary basis, alongside range of other products. Helpful if report could reflect valuable role fortified foods can play in helping people achieve vitamin D recommendation.	FDF
Internis is aware of instances of British children who have been (possibly permanently) damaged by ultra-high doses of vitamin D. Anyone could purchase product which claims to contain 30,000iu (750µg) vitamin D, 75X recommended maximum paediatric dose & 15 X EFSA upper safe limit for children 1-10y. To date all Ca/ vitamin D combined therapies have included 800iu (20µg) vitamin D in each daily dose. Internis recommends: Vitamin D supplementation doses > 400iu/10µg are provided only on prescription. Particularly important as a public health & safety issue because of current regulatory	Internis Pharmaceuticals

inconsistency in the regulator (MHRA) demanding fully supported package of data to demonstrate adequate quality, safety & efficacy for a licensed product while at same time allowing distribution & supply of highly variable, potentially dangerous, unregulated products. Vitamin D supplementation should be available in a 'mono' formulation, rather than being combined with variety of other vitamins to ensure that most appropriate dose of vitamin D (& other supplements) can be delivered. Mono formulations are vital where dose titration is required to establish the most effective dose for an individual patient.	
25(OH)D < 25 nmol/L in summer is much more of an issue than in winter. No evidence that bone turnover changes from season to season. The concern is reaching those with low vitamin D status year round because of low sunlight exposure in summer. Also not known whether giving vitamin D year round could potentially interfere with any natural adaptation to low vitamin D status. ANSAViD study measured 25(OH)D in spring for 3 years (2006, 2007, 2008). Despite poor summer in 2007, no difference found in end of winter values (Mavroeidi, 2013) suggesting adaptation or that 25(OH)D has to be much lower than 25 nmol/L to affect bone turnover. Not possible to determine who is at risk from lack of sunlight exposure; however, as none of UK population can make vitamin D in winter, only summer behaviour determines who will 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 route taken – then taking vitamin D in the summer might be answer. If there is adaptation to low vitamin D in winter, supplementation could interfere with this process. A campaign of taking supplements if at work/ putting on sunscreen may be an option rather than year round supplementation. Although this would differ from RNI approach it would be advantageous as interim approach; if it effectively reduced risk of vitamin D deficiency, there may be no need to supplement year-round. Alternative approach would be to supplement everyone in winter but that would not reach the groups most at risk of deficiency, who do not go out in summer or cover up. They should continue to take vitamin D year-round as currently recommended.	Professor H Macdonald
While the dose from the sunlight/skin source clearly doesn't sit well within standard methods of nutrient assessment and recommendation, it is recognised that sunlight remains the major source of vitamin D for most people. It would be good to consider pragmatic ways that the cutaneous source is viewed to produce recommendations benefiting UK health and avoiding potential harm to human health of giving no guidance (for example white skinned people taking more sunlight to satisfy their vitamin D than is needed, increasing the risk of skin cancer, and brown skinned 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 could benefit most UK people.	Professor L Rhodes
Should recommendations be more specific /prescriptive, or is that role of another body? For example, NHS already recommends multivitamin drops for children aged 6m-5y, but this is not widely offered or taken up. Would be very useful to have national guidance on the importance of this and how best to implement it, including from 0 months. Starting from birth may actually improve uptake.	A Marshall
The casual reader of the SACN guideline recommendations may be unaware that very few UK diets include 10µg of vitamin D and therefore that supplementation is currently the easiest means of accomplishing this intake in the absence of increased fortification of foods.	Professor J Newton-Bishop
Important to review evidence for effective interventions for promoting uptake of vitamin D supplements, particularly for population groups who find it difficult to engage with statutory services or are not in position to purchase supplements. If this is not the role of SACN this should this be included as a recommendation for future research. Review should be clear about the impact of fortification on vitamin D status within a population. This would inform future debate at a national level. If the review of such evidence is not the role of SACN then a recommendation for future research should be made. Lessons could be learned from other countries who have implemented this approach. If fortification is route of preference the inequalities impact should be considered. Latest Infant Feeding Survey shows increasing number of infants are fed mixture of breast & formula milk. Important SACN considers evidence for this population group & provides specific recommendations for this group. Should be clear guidance on when to start supplementation in formula fed infants. Is 500 ml cut off still valid? Has evidence for this been reconsidered? Infants should be introduced to solid food at 6m but are often introduced well before then. Recommendations should be made for impact of timing of introduction of solid foods on vitamin D status. Should be clear guidance on how to safely achieve adequate vitamin D by natural means, encompassing dietary choice & outdoor exposure. Presumption remains that whole population requires medication rather than providing balanced view about how to do it by natural means.	NHS Scotland
Welcome & fully support Committee's acknowledgement that "*it is difficult to achieve the RNI/Safe Intake from natural food sources alone*" and recommendation "*that consideration is given to strategies for the UK population*" to help achieve the RNI/Safe Intake. This is also an area of ongoing research within our department, where we are specifically investigating efficacy of cow's milk as a vehicle for vitamin D fortification or enrichment to help improve the vitamin D intake & status of the population. Such a fortification strategy would not only have an impact on milk consumers, but also for those consuming other dairy products that are produced from fortified/enriched milks.	NICHE

No concrete recommendations to supplement with vitamin D drops – just statement at very end that won't get enough from dietary sources & strategies needed. Helpful if 'strategies' could be stated as simply to recommend supplementation to all (except the indicated infants).	J Rayner
Given that 10µg/d intake will be almost impossible to achieve through diet alone, will SACN recommend everyone take a food supplement? Our interpretation is that SACN proposing safe intake for '*exclusively breast fed infants'*. How will this work in practice? Is recommendation that exclusively breast fed babies receive a vitamin D supplement? If so, will there be recommendations for administering this and which supplements are suitable (for example liquid preparation/dose)? Will relevant health care professionals be supported in the advice/message? Same questions apply for children aged 1 to <4years.	PAGB S Sexton
Who will consider strategies? Will there be further national guidance about practical delivery of this recommendation at local level? Or will local CCGs & public heath teams be left to interpret & implement this? Ultimately such strategies will involve supplementation & if there is expectation that this is prescribed rather than over the counter products this will have huge impact on prescribing costs across the NHS. Advice on how to deliver recommendation at a local level would be appreciated.	
Current cost to NHS of vitamin D supplements is about £80m & is 12th/13th highest number/cost prescription item. How will SACN's recommendations affect this? Would a population health strategy reduce NHS expenditure or do we expect to see more prescribing and testing to maintain minimum blood levels proposed?	P Thompson
Waitrose are in favour of RNI of 10µg/d vitamin D for UK population aged > 4y. Request further clarification on following points: 1. How will SACN communicate new recommendation to public? 2. Bearing new recommendation in mind, would SACN like amount of vitamin D already added to fortified foods to increase further? 3. How do SACN propose to explain disparity between the new recommended level of 10µg/d vs current RNI on food/supplement packaging (i.e. European level of 5µg/d) to general public? Is overall objective to change the European RNI to reflect the new recommendation? 4. Would SACN like amount of vitamin D in supplements increased, considering that current RNI is 5µg/d, and any increase would make the % RNI greater than 100?	Waitrose
Without wider discussion on policy and strategy needed to enable people to achieve RNI, including food fortification & vitamin D supplementation, setting an RNI is likely to have little impact. Current advice is not for all at risk people to take a supplement – if we advise that all at risk people take a supplement this is new advice and needs to be carefully considered. A summary of supplements and fortification policies in selected European countries is available (Spiro & Buttriss, 2014) and could be discussed within report. Food fortification should be considered over range of foods, particularly now that mandatory fortification of spreadable fats has been removed. Chicken feed may be supplemented to increase vitamin D in egg yolk. Aware that formulation of Healthy Start children's vitamins would need to change (currently contain 7.5 µg falling short of recommended 8.5-10 µg/d Safe Intake). This would also require a strategy to ensure that a national supplement is easily & cheaply available and promoted widely, as current availability and uptake is known to be low. Future policy & strategy should be informed by outcomes of the EU-funded, Food-based solutions for optimal vitamin D nutrition and health throughout the life cycle (ODIN) project, as consideration of a food solution is likely to be more effective on a population wide basis. NICE have developed public health guidance which aims to increase supplement use to prevent vitamin D deficiency amongst at risk groups. Consideration of this guidance could be encouraged. Helpful to have one RNI for vitamin D for general UK population over 4 y & not to differentiate between summer & winter intake. In Wales a national nutrition training programme, Nutrition Skills for Life ^{TM}, provides mechanism to raise awareness amongst health, social care and community workers of the importance of vitamin D & key health messages i.e. following a healthy lifestyle associated with a healthy BMI, including a varied diet with vitamin D containing foods & adequate outdoor activities with adequate sun exposure. Further discussion towards potential strategies that may assist population to achieve RNI is needed, particularly for those at increased risk of vitamin D deficiency. Policy and strategy should continue to focus on reducing diet related inequalities in health.	WDLAG & PHDiW
Public health messages highlight that children < 4-5y & pregnant/ breastfeeding women are also at risk of vitamin D deficiency and, in view of supporting evidence, these populations groups could be considered at risk of low vitamin D status. Request that committee considers incorporating a statement advocating need to prioritise work with these important population groups.	WDLAG & PHDiW & BDA
Report states *'high doses of oral vitamin D supplements have[ ] been shown to have toxic effects'. N*o mention of huge difference between levels in supplements & amount causing adverse effects. If strategies are to be considered to achieve proposed RNIs, risk managers need to be reassured of safety of levels in supplements. Currently, report emphasises risks & does not provide either assurances of safety of levels used in food supplements or public health benefits for general population & at-risk groups.	CRN UK
Points that could be highlighted for risk managers to re-evaluate sun protection strategies vs vitamin D status include fact that vitamin D production may be completely abolished when amount of sunscreen & SPF advised by WHO is used, that dietary sources are scarce and that determination of the average %of vitamin D production from skin compared with vitamin D provided in food & supplements is still an open question.	CRN UK

The evidence that limited exposure to sunlight is not sufficient needs to be communicated to public more effectively. Case for use of vitamin D supplements at intakes above 10 µg/d, at least in winter, in addition to careful sunbathing in summer, should form basis of public health advice, especially for pregnant/nursing mothers & babies. Fatty fish & fish oil supplements can provide the vitamin D to achieve optimal levels of 25(OH)D in both summer & winter. Special attention should be given to careful sun exposure, greater use of supplements, fortification & provision of new vitamin D containing products. This may prove difficult if additives for such products for infants & young children are not permitted in proposed new category for this target population under additives regulation 1333/2008. Issue under discussion at Commission level & current proposals by Commission could lead to majority of vitamin D containing food products for infants & young children being removed from UK market.	CRN UK

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ANNEX

Studies on vitamin D & acute respiratory infection (cited by A Martineau)

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