Author's response to reviews

Title: Vitamin D in health and disease: Current perspectives

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Author's response to reviews: see over
Dear Editor,

Firstly, thank you and the reviewers for your comments on the manuscript. I have addressed these as outlined below. I hope that the review is now suitable for publication.

Kind regards
Declan

**Editor's comments**
Thus, you should include some other meta-analyses in the text or tables. Table 3 may be enhanced by adding those meta-analyses about osteoporosis.

I have added every meta-analysis (search for “Vitamin D and supplementation” on pubmed) that was published during the past 20 years. These are in Table 3 with a discussion on page 8 under “4. Disease management”

The headings for some subsections should be carefully revised by using appropriate numbers and italic or gothic. There are several confusions in p4-8. I have added numbers to the titles for clarity.

**Referee 1**

Major compulsory revisions:
p.11 Disease prevention - rickets should be discussed and is not.

**This has been added – page 11.**

p12. Diabetes - type 1 and type 2 diabetes should be differentiated and handled separately as they are quite different problems in terms of aetiology etc.

**Only Type 1 has been the subject of a meta-analysis and this has been specified in Table 3.**

Minor Essential Revisions: **Now Corrected**
Spelling mistakes: p.4 line 9 ‘researches’, p.9 line 13 ‘can leads’, ‘the incidences of falls’, p.9 line ‘in recent year suggests’
Sentences that don't make sense: p.7 line 21 ‘the more difficulty it is for the skin of getting burned’, p.9 lines 6-8 ‘Therefore, whether ... further investigated’, p.10 ‘vitamin D supplementation is required to boost vitamin D’.

‘Choice of wavelength’ p7. - an additional major concern of using UVB to boost vitamin D that is not discussed, but perhaps should be, is skin cancer. **This has been added on page 6.**
‘Vitamin D intake in different conditions’ p.8 - add references for 'role of vitamin D in reducing risks of ... cancer etc. A linking sentence has been added to table 3 which details the meta-analyses.

p.10 ‘Malabsorption’ chapter talks mainly about bone mineral density and so would be better placed either under 'causes of vit D deficiency' or under ‘osteoporosis’ **This has been located below the new section on rickets**

Discretionary revisions:
Consider discussing in greater depth policies to prevent vitamin D deficiency through fortification of food, given the given the widespread nature of the problem and the
potential benefit of such policies. **This would be very useful and I would like to reserve it for a future report as I am watching the overall page and reference section length.**

**Referee 2.**

Major Compulsory Revisions

- Globally, this manuscript suffers from a lack of clear methodological approach. I would suggest to include the search methodology. **This has been added to the end of the introduction on page 3.**

- Since the literature on this topic is very exhaustive, the selection of paper needs to be explained. For example, and in the case of osteoporosis for which I am more familiar, the selection of paper seems very biased. As a matter of fact, the authors only report one meta-analysis (out of more than 5 or 6). **This has been added to the end of the introduction (p3) and on p8 under “4. Disease management”**

  All meta-analyses published in the past 20 years have been included in Table 3 (as per pubmed)

Moreover, the authors also report the result of single randomised controlled trials already included in the meta-analysis. I presume, but I do not know the whole literature on this subject, that such biased literature research has also been conducted in the other sections of the paper. Please see answers above – we now have a full coverage of meta-analysis over 20 yrs and a justification for selecting promising trials as well.

- From a general point of view, the analysis of the literature must be more critical. **This has been added via the meta-analyses.**

- The authors state that sufficient vitamin D should reach a level of 30ng per ml or greater. Is it truth for all ages or for all diseases preventions? **See below**

- The authors state that children and adults require approximately 800 to 1000 IU per day. The rationale for such statement need to be exhaustively developed. **A section on doses for infants has been added along with the meta-analyses doses where available.**

- I do not understand why a long part of the paper is devoted to UVB exposure. At least, a benefice-risk analysis must be performed. **An explanation for this has been added.**

- Statement such as “increasing vitamin D level is vital in the management of several diseases” should be deleted or must have appropriate references. **these have been added via Table 3.**

- A lot of trials (e.g. in the muscles weakness section) also relate to vitamin D and calcium supplementation. Moreover, this section only deals with fall prevention and muscles weakness is only one of the risk factors of fall. **Again see Table 3**

- Where possible, I would suggest, from a general comment, to include meta-analysis instead of individual randomized controlled trial. In cases where no meta-analysis is available, then, randomized controlled trial could be included. **All in Table 3 along with a justification for picking trials that show promise in the text**

- A lot of sentences need references. **There are 179 references (including meta-analyses) – one of the longest lists in the target journal**

- Across the whole manuscript, a clear definition of doses and duration of vitamin D supplementation or exposure needs to be exhaustively reported. **Doses have been added to table 3 for meta-analyses, where they available**
- The authors need to be more systematic and report clearly the clinical interest of vitamin D supplementation, sun exposure or UVB exposure, in each disease. **We have added the meta-analyses for this reason**

- Some references are not cited appropriately (see, for example, reference 71 in the conclusion). **This has been removed**

- I would suggest to be much more exhaustive in the literature research regarding vitamin D. On the other hand, I would suggest to reduce the number of references regarding definition or physiopathology of diseases. **We have added all meta-analyses on “Vitamin D and supplementation” appearing on pubmed in the past 20 years.**