Author’s response to reviews

Title: Vitamin D levels and deficiency with different occupations: a systematic review

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Author’s response to reviews:

Dear Editor,

We would once again like to thank you and the peer-reviewers for the very helpful comments on the revised version of our manuscript. We feel the paper has improved substantially as a result of the peer-reviews.

We include a point-by-point response to the peer-reviewers’ comments below.

As you had asked, we will submit a clean version of our manuscript only and will not include track changes or highlighting with this submission.

KATHRYN HART (Reviewer 1): Vitamin D levels and deficiency with different occupations: a systematic review.
From previous comments:

The abstract gives no indication of how the potential confounding by factors such as gender and body composition (which would be expected to differ significantly between occupational groups) may have been accounted for. Could this be added?

- I thank the authors for their response to this point and would again suggest some indication of this limitation is added to the abstract to reflect what is in the main discussion.

Author’s response: We have added this limitation to the abstract (page 3, just preceding the ‘conclusions’ part of the abstract).

I still have reservations about the potential overlap of occupation categories since you are reliant on the primary authors' descriptions and therefore have to assume that if they do not state their population are shift workers (for example) then they are not (as opposed to this just not being reported) and the appropriateness of recommending widespread screening and therefore, presumably supplementation. However the majority of my concerns have been addressed and certainly the revised manuscript is more streamlined and focused and I thank the authors for their attention to the previous comments and suggestions.

Author’s response: We agree that this is a concern but in our systematic review we are limited to what has and has not been described in the primary studies. To give this issue due prominence, we have also included this limitation in the abstract now (page 3, just preceding the ‘conclusions’ part of the abstract).

Additional minor queries/ corrections:

Pg 12, line 24 - Data the on average serum 25-(OH)D levels - word order error

Author’s response: Thanks for spotting this. Addressed (page 12, first sentence of ‘Statistical Analysis’ subsection).
Pg 13, line 11(approx.) - before stating the proportion who were women can you also include the total number of subjects covered by the included studies and the range of sample sizes?

Author’s response: We have now done this (page 12, third full sentence on that page).

Pg 14, 33 - 77.7% of indoor workers - report all % as either whole numbers or 1 decimal place but not a mixture

Author’s response: Addressed – we now report all percentages rounded to integers (page 14 and elsewhere throughout the document).

pg 16, line 54 ‘Additionally, approximately 65% and 72%’ - why approximately?

Author’s response: ‘Approximately’ has been removed from the sentence (page 16, last full sentence on that page).

pg 17, line 12 - physicians and; - remove 'and'

Author’s response: Thank you. Addressed (page 17, first sentence of second paragraph).

pg 19, line 12 'Additionally, the 25-(OH)D levels in summer and autumn in outdoor workers were significantly different relative to levels found in winter (p<0.0001) and spring (p<0.0001).' - suggest moving this to previous page where you present data from outdoor workers.

Author’s response: Addressed – this sentence has been moved page 18.

pg 20, line 51 'Additionally, we observed a higher prevalence of vitamin D deficiency in all occupational groups examined than the reported population burden of vitamin D deficiency in multiple populations, suggesting that workers may be particularly vulnerable to vitamin D deficiency [25, 43].' - could you perhaps give an example, e.g. the prevalence in one of your working populations compared to the prevalence in the same country's general population

Author’s response: Thank you. We have done that (page 21, lines 2-8).
pg 22, line 27 - compounding factor - do you mean confounding?

Author’s response: The word ‘compounding’ has been deleted (page 22, 3rd sentence from the bottom on that page)

References - minor formatting errors - please check all, e.g. 2 and 12

Author’s response: Addressed – we have checked all references (page 36 and following pages).

Table 2. First line - is this an inter-assay CV? Others are specified as such

Author’s response: Although this may be inferred from the original study authors’ description of the assay, the authors only reported CV and did not explicitly specify whether it was inter- or intra-assay CV. Hence, we only report it as such (page 59 and following).

Table 3 - requires footnote to give reference for deficiency cut off - this is in main text but tables should 'stand alone'

Author’s response: Addressed (page 63).

Table 4 - as for table 3

Author’s response: Addressed (page 64).
Figure 1 'Error bars represent pooled standard error of means computed as shown in the method section' - assuming journal policy is for figures to stand alone more detail is required of methods used

Author’s response: Addressed – we have added a formula for the calculation (page 65).

Figure 2. % vitamin D deficiency in different occupational groups - % in words

Figure 3 - as for figure 2

Could figure 2 and 3 be combined? - 2 bars per group - would be a more efficient use of space and allow direct comparison of deficiency and insufficiency rates

Author’s response: Addressed as suggested. Thanks for the suggestion. The previous Figs. 2 and 3 are now combined in the new Fig. 2.

Mark Farrar (Reviewer 2): This manuscript is greatly improved. I just have one further comment - The authors have clarified that ES definitions of vitamin D sufficiency/deficiency have been used. However, these are not widely accepted and have been criticised by the IOM. This is a significant point that the authors should address as it has implications for interpretation of their paper.

Author’s response: We would like to thank the reviewer for pointing out a very significant point, which indeed has implications for our paper. We are aware that there is some controversy in the scientific and medical community regarding the definitions of vitamin D sufficiency, insufficiency and deficiency. We would argue that the ES criteria are actually widely used. Out of our 71 included studies, 28 studies used the ES definitions, 10 used the IOM definitions, 2 used both, 7 used definitions other than the ES and IOM, and 24 did not use any definitions as those studies only measured serum 25(OH)D levels. This we feel provides a justification to base our definitions on the ES cutoff's values. We do acknowledge that there is a lack of consensus in the field regarding the level of 25-(OH)D that constitutes vitamin D deficiency (page 11, last paragraph) and that using the IOM definitions would have been an alternative (page 30).
We would once again like to thank you and the peer-reviewers for their comments. We hope that we have addressed the issues raised to your satisfaction.

With best wishes,

The authors.