Author’s response to reviews

Title: Screening for vitamin D deficiency in a tropical area: results of a sun exposure questionnaire

Authors:
Fernanda Bittar (ferbarrosbittar@yahoo.com.br)
Charlles Castro (cheldan@uol.com.br)
Vera Szejnfeld (vera@cura.com.br)

Version: 1 Date: 15 Feb 2018

Author’s response to reviews:

To the Editor

BMC Endocrine Disorders
São Paulo, February 15th, 2018

Dear Editor,

We are submitting a revision to the manuscript entitled “Screening for vitamin D deficiency in a tropical area: results of a sun exposure questionnaire” for possible publication in BMC Endocrine Disorders.

All the comments and suggestions raised by the reviewers have been properly addressed. We hope that the changes listed below can thoroughly and satisfactorily address each point raised by the reviewers and that the manuscript may now be suitable for publication.

Thank you for your kind attention.

Yours sincerely,
Fernanda Barros Bittar, Charlles Heldan de Moura Castro, and Vera Lúcia Szejnfeld.

1. Rheumatology Division, Universidade Federal de São Paulo/Escola Paulista de Medicina (Unifesp/ EPM), São Paulo – Brazil
Answer to the reviewers

Rachel Crowley (Reviewer 1): The authors have described use of a sun exposure questionnaire in both young and old populations, in both winter and summer (different patients) living in Brazil, in an attempt to identify patients with vitamin D deficiency.

As a general comment, there is no indication to start population screening in otherwise healthy individuals, regardless of the definitions of deficiency used and of the expected prevalence of the risk factor for bone disease, therefore the benefit of wide application of a questionnaire is unclear.

Answer: We thank the reviewer for her comments, which will certainly add to the final manuscript. We could not agree more that any diagnostic tool should be tested in the very clinical scenario where the tool is supposed to be applied. As vitamin D deficiency is quite common and increasingly prevalent among otherwise healthy individuals, the present study was conducted in healthy individuals. Applying the questionnaire in a population with significantly higher rate of vitamin D deficiency (such as the elderly or patients with osteoporosis) would eventually increase the rate of false-positive results. This limitation is now acknowledged in the revised manuscript (pages 10-11)

Major points

1 - Given the findings of this study and the Canadian study, and the caveats regarding time of day of exposure and environmental pollution, the authors should comment on the validity of the questionnaire itself as a tool for measurement of exposure and whether this is satisfactory.

Answer: The reviewer is correct and the manuscript has been modified accordingly to acknowledge that the questionnaire did not correlate with serum vitamin D measurements at least in part due to its poor performance to measure sun exposure (page 9 line 14).

2 - The authors commented in the introduction that there is a need for more accurate measurement of vitamin D status in non-white individuals (p4 line 16); a) this is not a study of vitamin D status assessment and b) the authors should comment on the study design - the participants were Fitzpatrick skin type I-III, thus paler-skinned than the population most likely to benefit from optimal vitamin D status.

Answer: The sentence referring to vitamin D deficiency screening in non-white populations has been taken out in the revised manuscript since that was not evaluated in the present study. Since darker skin phototypes are associated with lower vitamin D UVB radiation induced synthesis in the skin, we have chosen to evaluate paler-skinned individuals as a way to control for that variable. The study could have also been conducted with all skin phototypes but we would need a higher number of subjects to address the question.
3 - The authors should standardize use of the IOM criteria in the manuscript (insufficiency / deficiency).

Answer: In the revised manuscript the regard nomenclature has been standardized as “deficiency”.

4 - The authors should expand upon the clinical significance of the mean 25OHD measurements - these are greater than 16ng/ml (with the exception of wintertime in young patients) - the median population requirement as per IOM.

Answer: The reviewer is correct. According to the IOM, serum 25OHD levels of 16 ng/ml cover the requirements of approximately half the population, while levels of 20 ng/ml cover the requirements of at least 97.5% of the population, the later being used a cut off value for deficiency. A new paragraph in the revised manuscript addresses this point and discusses the prevalence of vitamin D deficiency in Brazil (page 8, last paragraph).

5 - What is the potential impact of the high female subject representation in the cohorts? Was there equal distribution in the summer and winter cohorts?

Answer: There was no statistically significant difference in the proportion of men/women in both young and old groups during either summer (p=0.190) or winter (p=0.053).

6 - How was BMI correlation with 25OHD analysed? - it is reported as an odds ratio.

Answer: BMI was inversely associated with serum 25OHD concentration and vitamin D deficiency in both multiple linear and logistic regression analyses. This is better presented as tables 2 and 3 in the revised manuscript.

7 - The conclusion should be written - clearly this questionnaire cannot be used in this population to identify patients with insufficient 25OHD.

Answer: The manuscript has been revised and the conclusion now clearly states that the questionnaire has very low accuracy to estimate serum 25OHD concentration.” and does not allow discriminating between vitamin D sufficient and deficient individuals…” (Conclusion on page 9).

8 Figure 1&2 should be combined and superimposed, with TSES plotted vs 25OHD and sensitivity and specificity curves overlaid, so that readers can appreciate the performance of the questionnaire at different measurement points - figure 2 does not make statistical sense.
Answer: Figures have been revised as suggested. Figure 1 show the linear correlation between TSES and serum 25OHD measurements. The ROC curve analysis showing that TSES is not a good predictor of serum 25OHD concentration is now shown as a supplemental material (Supplemental figure 1).

Minor corrections

1 - status does not require italicization

Answer: The text has been corrected as suggested.

2 - Figure 1 should include units

Answer: ok

3 - Figure 2 y axis sensitivity

Answer: ok corrected.

4 - the questionnaire items should be included in the methods

Answer: The items ‘daily time in sun’ and ‘skin exposure’ were included.

Neil Gittoes (Reviewer 2): Manuscript could be written more succinctly as data content is small.

Answer: The manuscript has been revised as suggested.

In some areas the 'potential' role of vitamin D to health beyond bone and calcium is over stated - this should be moderated.

Answer: We agree with the referee and the text has been modified accordingly.

Recall of subjects is problematic in this type of study - this needs to be made clearer.

Answer: This is probably the major pitfall for the use of the questionnaire. The revised manuscript now acknowledges that.

Do the authors believe the questionnaire is actually fit for purpose?
Answer: Clinical practice in a developing country is quite challenging in the sense that resources available are limited and should then be used rationally. We first thought that the questionnaire could help identifying individual at a higher risk of vitamin D deficiency. As we started using the questionnaire it became clear that it would not be of significant help since patients had difficulty recalling sun exposure in the previous week.