Author's response to reviews

Title: Determinants of serum levels of vitamin D: A study of lifestyle, menopausal status, dietary intake, serum calcium, and PTH

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Dear Reviewers,

We are grateful for your valuable comments regarding our manuscript “Determinants of serum levels of vitamin D: A study of reproductive history, lifestyle, dietary intake, serum calcium, and PTH” which we have taken into account and consequently adjusted the article.

The following paragraphs have been modified according to your comments and instructions:

Reviewer: Tamar Gur

1. The question posed by the authors is well defined, and he authors do a good job delineating lifestyle and biochemical factors that are related to vitamin D levels. Furthermore, this cohort has already been characterized, and results presented in the literature, reflecting the appropriate and well defined methods. In addition, their samples are well characterized, their data cleanly and clearly presented, and their interpretations are sound. The authors largely do a good job discussing each finding, providing relevant citations, and addressing limitations and contradictions with the literature. The title and abstract are an accurate reflection of the findings within the paper. Finally the paper is well written and easy to follow.

- Thanks for your comment.
2. However, I would like them to comment on any recommendations that could be made based on their findings. i.e- should one conclude that OC and moderate alcohol intake would be recommended based on their findings? Age is not modifiable, neither is the status of being born outside of Sweden, but some of the other factors are modifiable (weight, etc). It would be important to broaden their discussion to include any health or diet recommendations that can (or cannot) be made based on their findings.

Revised: The study may have implications e.g. for dietary recommendations. However, the analysis is a cross-sectional study and it is difficult to suggest lifestyle recommendations as cause-effect relationships are not clear. We have added this in the conclusions section.

3. It would be useful for the authors to further discuss the findings of an association of moderate alcohol use and vitamin D, as they do with their other findings.

Revised: Differences with regard to dietary intake may be an explanation behind the low vitamin D levels in zero-consumers, for example vegetarians may have a relatively low intake of vitamin D [45] and it is possible to hypothesize that they consume less alcohol as compared to other groups. In general, the concentration of vitamin D has shown to be reduced among high consumers of alcohol. This could be due to a variation in the dietary intake of vitamin D during different drinking periods with marked reduction during hard-drinking weeks [46]. This has been added to the discussion section along with two more references.

4. Sub-optimal should be spelled: Suboptimal (Page 2 and elsewhere in document).

Revised: Thanks for pointing out this. The text has been changed accordingly.

Reviewer: Briana Rudick

1. Is the question posed by the authors well defined?
   a. Yes. They clearly state that despite the fact that vitamin D insufficiency is associated with a multitude of chronic diseases; few studies have examined the impact of lifestyle, reproductive, dietary, and biochemical factors on vitamin D status. They also state the magnitude of the problem especially in northern countries. Authors should be aware that not only may reproductive history affect vitamin D levels, but low vitamin D levels are also implicated in fertility and female reproduction. Would have been interesting to see gravidity and parity assessed since this is what we typically think of when one considers “reproductive history.”

Revised: The term “reproductive history” has been replaced with “menopausal status”.

b. Race also would have been very important to consider, since multiple studies
have shown that vitamin D levels do vary by race. This could have been considered in context with the variable “born in Sweden.” If the two main sources of vitamin D are through diet and sunlight, then skin pigmentation should play a very large role in mean vitamin D levels.

Revised: Race and skin pigmentation are important factors according to many studies which we have referred to in the introduction part of the article. However, in this study the majority of data population are either Swedish or from other Nordic countries. Therefore, this specific factor has not been possible to investigate further in our study. This has been pointed out in the first paragraph of the material and methods section.

2. Are the methods appropriate and well described?
   a. Yes. They review the Malmo Diet and Cancer study including that study’s main aim, and the study dropout rate. They go into detail about how they collected baseline info and dietary data. The only thing that would have been helpful to me, but only because I don’t look at alcohol consumption all that frequently, would be a more user friendly definition of alcohol intake (i.e., what is one glass of wine equivalent to?)

Revised: Alcohol consumption was recorded as gram alcohol / day. We have added an example of what one glass of wine contains.

3. Are the data sound?
   a. Yes, the data are sound. The authors describe in great detail how the demographic data was obtained and how blood samples were run.

   - Thank you for your comment.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   a. Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   a. Yes. There is a reference missing on page 11 when the authors state that multiple other studies in Sweden have shown that older women in this cohort consume relatively more vitamin D. Which studies are they referring to?

Revised: No article has been referred to but we have clarified this in the text. There has been a possible explanation that in our study could vitamin D consumption be a possible reason to this trend among women.

   b. They provide physiologic explanations as to why the variables seen may or may not be associated with higher vitamin D levels. What would be the reason for the association with moderate alcohol intake as opposed to none or heavy alcohol intake?
Revised: Please see comment above on alcohol consumption.

6. Are the limitations of the work clearly stated?
   a. Yes the authors state this clearly in the discussion

b. I think they chose the correct study population if they wanted to identify groups with low versus high vitamin D levels, but I do think it would have also been interesting to see which factors affected vitamin D levels the most.

Revised: It may be inappropriate to include all factors into same statistical model as they are correlated. Moreover, we prefer to use a descriptive approach as there was no à priori hypothesis on which factors to be the strongest determinant.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   a. Yes, they go into detail about previous work in both the discussion and the introduction.

8. Do the title and abstract accurately convey what has been found?
   a. My only issue is with the words “reproductive history.” They do define what they mean by this, but reproductive history means gravidity and parity which is not something that they evaluated.

Revised: “Reproductive history” has been replaced with “menopausal status”.

9. Is the writing acceptable?
   a. Yes, this is a well written paper.

In addition to the above changes, we have also added EW in the “authors contributions” section as this had been overlooked in the first version.

Thank you for your time and consideration.

Yours sincerely,
Leila Shirazi