Author's response to reviews

Title: Physical performance and 25-OH D vitamin. A cross-sectional study of pregnant and newly pregnant Swedish and Somali women

Authors:

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Version: 5 Date: 22 August 2013

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

According to Your request for a detailed point by point response to reviewers we hereby resubmit our previous reviewer response sent on June 28th 2013. We enclose a new cover letter in a fuller version and hope that you will find this easier to read and follow. Since there are some major corrections of sections we have marked the corrections and new sentences covering the notions of the two reviewers with colors in a PDF file of the revised manuscript.

Once again we sincerely thank both reviewers for their thorough work and valuable comments on our previous manuscript MS 20288709245907280. As suggested by the first reviewer, our manuscript has been given a new title: Muscular performance and 25-OH D vitamin. A cross-sectional study of pregnant and newly pregnant Swedish and Somali women (formerly: Weak grip strength unveils vitamin D. A cross-sectional study of pregnant and newly pregnant Swedish and Somali women)

We have tried our best to correct our text according to the reviewer’s suggestions. The three major changes are additional references suggested by both reviewers and the statistics section is slightly revised for clarity as suggested by reviewer 2. Furthermore, the text about the sampling procedure is reorganized in order to make it easier for the reader to follow the procedure.

Below we have listed our responses to the reviewers’ comments in more detail.

Sincerely,

On behalf of the authors

Paul Kalliokoski
Author’s response to reviews

Title: Weak grip strength unveils vitamin D deficiency. A cross-sectional study of pregnant and newly pregnant women in Sweden

Authors:

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Version: 2 Date: 13 August 2013

Reviewers’ comments and authors responses point by point

Title: Weak grip strength unveils vitamin D deficiency. Across-sectional study of pregnant and newly pregnant women in Sweden (the title is now changed).

Version: 1 Date: 7 May 2013

Reviewer I: Michael Holick

Reviewer’s report:
1. It is perplexing recording the conclusion drawn from this study. It is well documented in the literature that time from sitting to standing position and walking 8 feet is markedly increased in men and women who are vitamin D deficient as reported by Bischoff-Ferrari et al AJCN 2006; 84:18. It is also well documented that vitamin D deficiency is associated with proximal muscle weakness. Indeed these investigators observed that the women who were most vitamin D deficient could not stand up without assistance. Thus to suggest that only grip strength was associated with vitamin D deficiency is inconsistent with both the literature and their observations.

- We are sorry if our conclusion seemed inconsistent with both literature and our own findings. We have reformulated the text to alter that impression. Our hypothesis and findings were consistent with the mentioned literature and a positive correlation between 25-OH D levels and strength. The women with low levels of 25-OH D were very weak compared to those with good levels as seen in the results in text and tables. The Somalian women were much weaker than the
Swedish group also in upper leg tests but only hand grip strength showed statistical significance in this study. We seem to have pointed out this statistical finding too strongly and thus given rise to uncertainty. We hope that our revised conclusions in the abstract and the main manuscript is more satisfying now.

- 1a. Sorry about this, the reference to Bishoff-Ferraris article on leg tests and vitamin D had been eradicated by mistake in our previous revised text. It is now in its place in the introduction and again in the discussion part, p 3. The introduction is reorganized and sun exposure etc. is now first in the section.
- 1b. Also, Houston DK, Tooze JA, Neiberg RH et al, Am J Epidemiology. The health, aging and body com 25-Hydroxivitamin D status and change in physical performance and strength in older adults position study 2012;176:1025-1034 is now added to the reference list (published after our first draft). p. 3.

2. To suggest a handshake can help identify severe vitamin D deficiency is without merit since they provide no evidence for this. They would need to do a study blinded and shaking hands of women and relating this to their blood level of 25-hydroxyvitamin D. The title should be changed.

   - We agree. We have removed this statement and changed the title, see above, p 1 and also the conclusion in the abstract, p 2. and the main text, p. 11.

3. Sunlight converts 7-dehydrocholesterol to vitamin D3. It is not 7-deoxy Cholesterol
   - Done

4. The manuscript is poorly referenced especially regarding vitamin D and muscle strength. Also it is poorly referenced regarding the effect of latitude and clothing on cutaneous production of vitamin D.

   - We have added more references especially regarding vitamin D and muscle strength (n=2 Houston and Girgis) p. 3 but also regarding clothing (Cannel) and latitude (Webb), p 3. Also on p. 13.

All changes according to comments by reviewer one (Michael Holick) are found in the new manuscript marked in green color. Please see the PDF file.

Reviewer II (CL. Wagner)

Reviewer's report
Title: Weak grip strength unveils vitamin D deficiency. A cross-sectional study of pregnant and newly pregnant women in Sweden
Version: 1 Date: 2 June 2013
Reviewer II: Carol C.L. Wagner
Reviewer's report:
This report is an important first step in deciphering the effects of vitamin D
deficiency on daily living tasks that involve muscular strength. The authors' inclusion of pregnant women adds to the mounting evidence that vitamin D deficiency has adverse effects on the health outcomes of both the mother and her developing fetus. The inclusion of two groups of women at latitude 60 degrees with such dichotomy in vitamin D status improved the ability to detect differences between the two groups of women.

Given the need to control for season, the study design and sample size calculations appear appropriate for the scientific question posed--does 25(OH)D status influence muscle strength in two groups of women living at latitude 60o. The methodology for measuring grip strength and overall muscle strength seems appropriate. One issue is the higher rate of continued breastfeeding during pregnancy in the Somali women compared to the Swedish women. This potential confounded must be controlled for in a regression analysis because the changes that occur during lactation that seemingly follows a recent pregnancy could impact on muscle strength as the woman has a different hormonal profile and may have depleted certain other nutrients during her recent pregnancy, lactation and now new pregnancy. Likewise, because women were recruited at different gestational ages, gestational age at time of strength measurement should be included in the model.

- Continuing breastfeeding during pregnancy was a minor issue and concerned only one Somali woman. see p. 9. Furthermore, there was no relationship between lactation and physical performance, see page.9. Also anemia and glucose was checked for, please see page. 8, and also pp. 6-7.

Other comments:
(1) the following sentences needs to be rewritten for clarity: "Thus, anything preventing UV light from reaching the skin will reduce the production of vitamin D3 exemplified by long transportation in air of sun rays, dark skin pigmentation or veiling clothes [11]." The phrase "long transportation in air of sun rays" is not easily understandable in its present form.

- This sentence has been removed and the content is now moved to the first part in the introduction section, p. 3.

(2) Page 4, sentence "From other countries it is reported that dark-pigmented women tend to have adverse fetus growth and delivery outcome [19, 23, 24]", please elaborate more on these aspects--what are the specific growth and delivery outcomes. There are two additional studies to include by Hollis and Wagner (2012) and Wagner et al (2013) on the adverse outcomes of pregnancy associated with vitamin D deficiency that will strengthen your position.

- One more sentence is added on this aspect of adverse events in pregnancy, see p 4. We have also added the suggested references, page 3 and p. 13.

(3) It is not clear when the strength tests were performed and how the blood samples were obtained if ..."A list was provided by the antenatal clinic containing the names of 118 Somali women (21 months backwards) and 309 Swedish women (9 months backwards)." Please rewrite this section as later it is stated the
women had their strength testing performed within two weeks of their 25(OH)D measurements.

- The whole text about the procedures is reorganized and hopefully the sequences of the tests are easier to follow now. Please, see p. 5.

(4) the statistical analysis section needs to be expanded to include how potential confounded such as breastfeeding, gestational age at time of evaluation, and parity were controlled. Specifically, it is not sufficient to state "Multiple linear regression models with stepwise exclusion in main effect models were used to examine the effect of 25-OH D on physical grip strength." What was included in these models needs to be specified.

- The text regarding statistics has been revised and so has the text to the table legend.pp. 7 and 19.

(5) another potential confounded is whether or not the woman was postpartum and had recently undergone a cesarean section--this could significantly affect strength results, particularly if the woman had undergone cesarean section, had significant blood loss, and was on narcotics. These factors need to be addressed.

- Only one woman had had a caesarean section two weeks before and this is noted on p 8... The questions about blood loss and analgesics are addressed. see p. 8. Only mild analgesics were used by these women (not narcotics).

(6) on page 8, “The Somali women with low categories of 25-OH D had particularly high PTH levels indicating long-standing skeletal depletion." please provide references for this statement and expand--how long does it take for the PTH to rise during pregnancy? What effect does concurrent lactation or recent delivery have on PTH, if any?

- 6 a. The sentence about long-standing depletion is now removed because it was not in focus here and PTH was not associated to concurrent lactation, gestational age or recent delivery, noted now on p. 8.

(6) Page 10, paragraph 2: please expand on what sociocultural factors might have accounted for the difference.

- 6.b. Socio-cultural factors have been exemplified, please see page 9.

(7) in the Discussion, this section needs to be rewritten or omitted because it seems subjective: “Another consequence of low 25-OH D in plasma might be poor intrauterine contractions [18, 20]. Overall, the Somali women in our county more often had an emergency section compared to the Swedish women, but this was because their fetus was small for gestational age (personal information). Here, two of the 23 Somali women had had, or later had, emergency sections." SGA does not automatically necessitate an emergent C/S.

- This part has been removed as suggested by the reviewer, please see page 10.
(8) Discussion, page 11, next to last paragraph, "This paper adds information that vitamin D deficiency is a frequent and a long-standing condition with metabolic and target organ consequences in this high-risk population." We really do not know how long-standing the deficiency was because the women were not followed over time. You can infer that the condition existed for a certain period in those with elevated PTH but the duration is truly unknown.

- We agree, we have removed this part of the discussion, p. 11.

(9) the following needs to be modified in the last part of the Discussion: "...winter and a wash-out effect of inter-individual variations of exposure to UV light by also including dark-pigmented study persons wearing veiled clothing." It is unclear what is meant by a "wash-out effect of individual variations..."

- The question about the wash out effect is now removed, p. 11.

All changes according to comments by reviewer II (CL. Wagner) are found in the new manuscript marked in lilac color.