Author's response to reviews

Title: Vitamin D status and dental caries in healthy Swedish children

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Response of the review to the academic editor and reviewers of the manuscript

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"Vitamin D status and dental caries in healthy Swedish children"

The authors would like to thank the reviewers for their assessment of the revised version of the manuscript "Vitamin D status and dental caries in healthy Swedish children". We have changed the manuscript according to the additional comments.

Please, find our responses to the comments raised by Reviewer 1 and 3 below. A new version of the revised manuscript with revisions highlighted in yellow is enclosed.
Reviewer #1:

Background: line 60-63 - these were historical studies conducted in the early 1900s. It might be good to mention that they are historical clinical trials of vitamin D "supplementation", not actual vitamin D status.

Response: The word "supplementation" is now included in the sentence (line 61).

Also, I think the authors haven't really correctly interpreted what the Hujoel reported in his paper. Each form of supplementation, including irradiation produced similar outcomes and overall supplementation was associated with lower risk of caries.

Response: The text has been edited to increase clarity (line 62).

Results: Watch the tense being used.

Line 175 - suggest adding the word "adjusted" before odds ratios.

Response: We have edited to past tense in line 214, and the word “adjusted” was included in the sentence as suggested (line 175).

Table 3 - please show all of the covariates and their associated adjusted odds ratios for the final models. Simply just reporting the odds ratio for vitamin D status is not sufficient. The readers want to see more details and this could be achieved.

Response: We acknowledge the comment but would prefer to leave the Table as it is since (1) we have added additionally corrected OR in response to reviewer 3 and these data would expand the table very much, and (2) the other variables are confounders in the models and it is not uncommon not to include specific results for confounders. We are of course willing to reconsider our opinion if the reviewer and editor mean we should add the data.

Page 18, line 263-275 - can this be shortened? It doesn't flow and the average reader may not understand this section. The same applies to lines 284-286.
Response: We have deleted the text related to PCA in relation to a comment by reviewer 3, which have also simplified the text (lines 263-269.) We have also simplified the text in the previous lines 284-286. The new text reads “PLS modeling only identified intake of a vitamin D supplement at 8 years of age as associated with having defects, which likely reflects reversed causality.” Line 281.

Discussion: instead of saying "negative" association, perhaps rephrase as and "inverse" association between vitamin D status and caries experience. There are two instances in the discussion when this is referred to as a negative association (some may mistake this to mean no association).

Response: The word negative is now changed to "inverse” as suggested (lines 295 and 360).

Figure 2A and 2B are a bit difficult to follow as there is no heading or legend.

Response: Fig. 2A has been deleted as the PCA results were removed. The new figure is Fig. 2 and the revised figure legend is found in lines 270 to 272.

Reviewer #3:

The reviewer thanks the authors for providing details regarding the two-step method for PCA and PLS. However, to avoid confusion in Lines 188, 265, and 270, the reviewer suggests choosing another wording for "clustering of subjects" (Line 188), "clustering of the children" (Line 265), and "clustering of subjects" (Line 270) as the "clustering" wording typically refers to another type of data-driven technique (cluster analysis) and is a very different technique than PCA or PLS.

Response: We have changed the word clustering to grouping (line 190), changes in the text followed suggestions from Reviewer 1 did erase the two other sections with the word.

In addition, if the objective of using PCA and PLS is to select independent variables that are important in explaining the variations in y, then the reviewer suggests removing results from PCA: PCA, unlike PLS, chooses the scores t1 and t2 without regard to the dependent variable (e.g., caries status).
Response: We have restricted the multivariate modelling to the PLS analysis (lines 263-269).

Table 3: The reviewer apologizes for not being clear in the previous comment regarding Table 3. The reviewer understands that this table is now restricted to all 85 children as recommended by reviewer 1. Since 37 children had caries (according to Table 2), and that Model 1 includes 6 covariates; Model 2 includes 8 covariates and Model 3 includes 9 covariates; this leads to low EPVs (events per variable) of 6, 5, 4, for Models 1, 2, 3, respectively. Consequently, there is likely an issue of estimating inaccurate logit coefficients when using the traditional (maximum likelihood) logistic regression in small samples. The reviewer suggests applying a method, such as the Firth's correction, to improve the accuracy of the logit coefficients in this study.

Response: Thanks for the clarification. We have done the adjustment using SAS and have added results in table 3. As seen the OR remained virtually the same but statistical significances were lost for models 2 and 3. Since we had a very conservative interpretation already we do not see that this impacts other sections of the text. New text is found in lines 186-188 and 256, 259.