Author's response to reviews

Title: Vitamin B12 and folate levels in healthy Swiss senior citizens

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To the Editors of
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Liebefeld, 07 january 2015

VITAMIN B 12 AND FOLATE LEVELS IN HEALTHY SWISS SENIOR CITIZENS
MS7058833321453348

Dear Ms Jose and Bombales
Thank you for your mail message of December 8, 2014 and for the two reviewers comments.
To follow a list of major amendments, on the basis of these comments.
Reviewer: Johan Frederik Bern Arendt
Shortening. We agree with the suggestions made in points 1,3,4,5,7 and 8, all of which allude to text-relevance to the original data of the study, the revised
version is now shorter and now counts 3253 words

2. Coherence of the abstract is improved with the addition of the last sentence of the ‘methods’ part as well as re-wording in the conclusion section.

6. Folate fortification in Switzerland. We have now consulted the experts of the Federal Food Safety & Veterinary Office FSVO and their answer has been used to re-formulate the text – folate fortification is not mandatory, but widely used for grain-based dietary supplement; vitamin B12 fortification is much less applied.

9. The second part of the last paragraph is newly written such that we comply with reviewers request.

10. The 2nd paragraph of Methods now mentions those who took metformin and PPI. Separate calculation of their vitamin B12/folate levels are included in the last 5 lines of the Results section Subjects taking metformin and OTC PPI were separately analysed. The use of these drugs is now referred to in the study population description, as well as in the results and in the discussion section.

11. Haematological parameters and cystatin C measurements are now delineated.

12. see added: last sentence of the middle paragraph as accuracy and precision of our assays complying with the Swiss accreditation license.

13. “normalized” is a term coined by Fedosov (see ref 25) resulting from the formula of the Fedosov quotient

14. We agree that setting cut-offs is controversial but within the combined B12/folate metabolic folic acid deficiency, the value of < 35 pmol/L for holo-TC is generally accepted (Clarke R et al, ref 45)

15. The statistical evaluation of the data include reference to small numerical differences.

16. We propose to leave the ROC analysis (former figure 3, now Figure 2) since it also answers also to the concern of the reviewers point 12.

17 and 18. Figure 5 is now additional file 1 and additional file 2 is now illustrating the relationship of Vitamin B12, folate, MMA and Hcy with kidney function as measured using CKD-EPI version involving creatinine and corrected cystatin C level # cystatin measurement procedure is now included in the section entitled: Materials and Methods, biochemical measurements.

19. it is now explained in the text why we combined the two lower age groups 60 years up to 79.

20. We now explain in the materials and methods section, why methylmalonic acid was analysed in a partial sample number only

21. new wording

22. new wording

23. we feel, by using literature references from which the origin of the completely different populations can be seen, would explain global differences.

24. After consulting the FSVO and after introducing the vegetarian-issue in the
Background section this major issue of the revised version is now explained

25. We agree that absence of cognitive deficiency in our study population is speculative – at least there was no overt evidence while we interrogated and talked to all the individuals taking part.

26. paragraph omitted

27. Number of references: reduced from 67 to 60.

The minor essential revisions have all been answered by text modifications. The part on alcohol has been deleted, letters to panels in prior figure 4, now figure 3, are added. Since we had also participants from outside the Berne Canton, we propose that Swiss midlands is appropriate.

Reviewer: Johnny McHugh

The writing has been thoroughly improved by consulting a linguistic professional, Mr. N. Lindup (see acknowledgments)

The folate deficiency across the three age groups are mentioned.

The metabolic folate deficiency as well as the combined vitamin B12/folate deficiency have been calculated. Assuming B12 < 200 pmol/L, holo-TC < 35 pmol/L and folate < 7 nmol and Hcy > 20 μmol/L extremely few of the subjects hat a combined deficiency and we propose that Table 1 lets the reader recognize this fact. However, the metabolic vitamin B12 deficiency was around 10% in the whole population, which is why we write this in the 1st paragraph of the results section.

Word count text: 3253
Word count abstract: 272

We thank the editors and the reviewers for their constructive expertise. We are looking forward to the editorial decision and are ready to answer further questions.

Sincerely,

Urs E. Nydegger, M.D.