Reviewer's report

Title: Short term micronutrient-antioxidant supplementation has no impact on gastric atrophy in Zambian adults: retrospective analysis of a randomised controlled trial

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Reviewer: Jan Bornschein

Reviewer's report:

The authors present valuable data on the clinically highly interesting issue if antioxidant supplementation has an influence on present premalignant conditions in the stomach, mainly glandular atrophy. However, there are some essential flaws in the study design and presentation of the data, probably due to the retrospective character of the study. I am not entirely convinced that the results truly support the conclusions drawn. Some aspects have to be considered before this article can be considered for publication.

Major points:

- Abstract, methods and results: please be careful with using the PG-ratio as an equivalent of gastric atrophy since there is an inverse association between the ratio and the degree of atrophic changes. So if you state that gastric pH correlates with atrophy and you state an negative Spearman's rho, this is just wrong. In these cases you should always just refer to the PG-ratio as surrogate since you don't have data on the actual atrophy scores, and discuss this thoroughly. (The same accounts for table 4, where it looks like age over 40 years would be protective against atrophy as stated here.)

- You should furthermore discuss very thoroughly the assumption that due to a "random allocation" the distribution of atrophy at baseline should be similar in both groups. It is very difficult to make assumptions on that fact without baseline values. I have several questions concerning that issue.

First, you state that there have been baseline blood tests at inclusion and then "annually". Why are these not included in the study but just the "final outcome" values. To make hypothetical assumptions on the baseline values is very dangerous in my point of view.

Second, you only refer to "presence of atrophy" but not to the degree (as you would in case of available histological data). As far as stated in the results there is no difference in overall presence, but you don't show the absolute data. Often there is no complete but partial regression of atrophy score, as shown e.g. after H. pylori eradication.

Third, I miss information on prevalence of H. pylori infection in this population as a major confounder.

- "gastric pH was measured in fasting participants by endoscopic aspiration...".
When was the endoscopy performed and isn't there any basic histology available?

- Alcohol is not an accepted risk factor for gastric cancer. There is no convincing data as there is for tobacco smoking. Please rephrase the respecting sentences.

- Discussion: The first paragraph is mainly a repetition of the introduction section and should be deleted from here. This is followed by information highly redundant top the results section. Please focus more on critical discussion of your data instead of repeating your results in different phrasing.

- Please discuss more meticulously the discrepancy between a 3-years study with respective follow-up and the discrepancy to the 18-19 months "follow-up" here.

Minor points:

Abstract:

- Please split the sentence in the methods section "Atrophy was determined..." into two sentences, starting the second at "HIV serology...". Otherwise content would be misleading.

- In general throughout manuscript, please give the confidence interval as (example): HR 1.07; 95% CI 0.37-3.2;P=0.89

- please change "advancing" age into "advanced" age, since you didn't really study a time series.

Background:

- Please delete the second sentence. Gastric adenocarcinoma is the most common type of gastric cancer all over the world.

- "Pre cancerous" etc. should always be "precancerous".

- Please change "precancerous lesions" into "premalignant" conditions according to current consensus, since the definite malignant potential of intestinal metaplasia and gastric glandular atrophy have not been confirmed yet. Thus also rephrase the sentence "as it is within metaplastic mucosa...". This has never been proven by a study!

- Please change into "...was as high as 32% (30/94) with 23% (7/30) of these being less than 45 years.

Results:

- "(Kelly 2008)" should be stated as proper reference.

- "signifying hypochlorhydria" should be "significant".

- Why do you put the data on correlation and nutritional status under the "pH" paragraph?

Tables and figures:

- Table 1: please introduce abbreviations.

- Table 2: a) please state if mean or median is given (including SD, range etc.). Why are population figures ("n") given for some features and for some not.
Please state numbers rather as "1.8" instead of "2" (e.g. Cannabis.
- Figure 1: Please carefully review this figure since it is not really straightforward (e.g. samples that are stated as "total available before cross over" were excluded further down for the reason of being taken "after crossover")

General:
- Minor revision of language and style would be recommended.
- Please introduce any abbreviation with first use, including HR, CI, H. pylori (in italics please), RNI, IQR etc.
- Please give at least one decimal for any outcome number/figure presented.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

There is no financial or in any other way competing interest related to this article and the presented work.