Author’s response to reviews

Title: Omega-3 fatty acids to prevent preterm birth: Australian pregnant women’s preterm birth awareness and intentions to increase omega-3 fatty acid intake

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Author’s response to reviews:

Associate Editor
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Dear Dr. Ameer Taha

Minor Revisions of Manuscript for Submission
Thank you for this opportunity to revise our manuscript entitled “Omega-3 fatty acids to prevent preterm birth: Australian pregnant women’s preterm birth awareness and intentions to increase omega-3 fatty acid intake” to be considered for publication in Nutrition Journal. We would like to extend our gratitude to the reviewers and associate editor for their assessment of our manuscript and their valuable feedback. Changes in the revised manuscript addressing your comments have been highlighted in yellow and a detailed point-by-point response to the reviewers’ comments follows below. We hope that the revised manuscript and corresponding responses will be to the satisfaction of the reviewers and associate editor.

Yours Sincerely,

Jamie de Seymour on behalf of all authors
Massey University, Auckland
New Zealand
Reviewer #1:

Dr. de Seymour and colleagues present a survey among Australian mothers, investigating three different areas: knowledge on preterm birth, knowledge about pregnancy nutrition and nutritional supplementation, potential willingness to increase omega-3 intake during pregnancy.

The issue is interesting and of clinical relevance, with a high potential for clinical care as well as a high potential to impact a high number of children. The study design is adequate. However, information on how the instrument was developed, tested and evaluated should be provided. Was the instrument validated? Was it at least pilot tested?

Response: The survey was developed, tested and revised by all the authors. The items were developed to provide insight for translation and implementation. The initial survey was tested and evaluated by health professionals and women who had given birth. The survey was subsequently pilot tested by 100 participants for feasibility.

Revision to the manuscript: “…and evaluated by health professionals and women who had given birth to assess the knowledge, attitudes, behaviours, and intentions of pregnant women…The survey was subsequently pilot tested by 100 participants for feasibility.”

The English quality is good. However, the current manuscript is too long and should be shortened by about 10-20%.
Response: As per the reviewer’s suggestion, the manuscript length (excluding abstract) has been shortened by ~10%.

Furthermore, the Discussion uses too much space to re-summarize the results and fails to interpret some interesting and/or surprising results (these are listed below, in the "specific comments" section)
Response: A detailed response to this comment can be found in the responses to the related comments in the “specific comments” section.

As a consequence of the identified gap, authors propose the "implementation of behavioural change interventions". However, especially considering the high adherence to the already recommended vitamins and their finding of health professionals being the main information source, I feel that simply updating the recommendations, asking health professionals to recommend (or prescribe) omega-3 rich diet (or supplementations) might likely be a sufficient and very easy first step. Stressing this very simple and straightforward consequence of your study would emphasize the usefulness and applicability of your research! (Please also see specific comments below.)
Response: A detailed response to this comment can be found in the responses to the related comments in the “specific comments” section.
Specific comments:

Line 28: please eliminate "substantial" and write "42%" instead.
Response: This has been changed in the revised manuscript.

Line 41: "81.9%" --&gt; "82%"
Response: This has been changed in the revised manuscript.

Line 45: "89.5%" --&gt; "90%"
Response: This has been changed in the revised manuscript.

Line 48: "... through supplementation increased." --&gt; "... through supplementation increased from 54% to 79%.
Response: This has been changed in the revised manuscript.

Line 54: "implementation of behavioural change interventions to increase": see also comments to the body of the manuscript. This is a possibility (above all if dietary intake is preferred), but, also considering the high adherence to the already recommended vitamins and your finding of health professionals being the main information source, the simple recommendation (and/or prescription) from health professionals might be a sufficient and very easy first step, without the need of developing (already as a first step) behavioural change interventions.

Response: The authors agree with the reviewer’s suggestion. The sentence in Line 54 has been altered to reflect that general implementation strategies to increase the intake of omega-3 fatty acids during pregnancy should be the next stage of translation, without restriction to ‘behaviour change interventions’.

Revision to the manuscript: “…the next stage of translation of the Cochrane review findings – the design of implementation strategies to increase the intake of omega-3 fatty acids during pregnancy.”

Line 62: delete "(birth &lt; 37 weeks' completed gestation)"
Response: This has been changed in the revised manuscript.

Line 63: delete "devastating"
Response: This has been changed in the revised manuscript.

Line 63: delete "for the infant"
Response: This has been changed in the revised manuscript.

Lines 66-67: "as many preterm births are unexpected, women may miss out on effective treatments...": sorry, but I do not really understand the causal relationship between the fact that several preterm births are unexpected and the missing of prevention interventions, which, for their nature, are directed to all (and not only to the future preterm) pregnant mothers (probably, these measures are even more effective in unexpected than in expected preterm births. I mean, probably the supplementation will not be as much effective in twin pregnancies or severe IUGR or twin-twin transfusion syndrome or lupus erythematosus induced AV-block and bradycardia, ..., as in otherwise healthy pregnancies). Could you please explain a little better the causal link?

Response: The authors thank the reviewer for their comment. A large number of preterm birth prevention strategies occur after women have been identified as ‘at-risk’ i.e. progesterone, pessaries, and cerclage. However, as many preterm births are spontaneous and universal
screening is not offered in all settings, these options may not be presented. As such, this means that many women may miss out on effective treatments. However, we realise this isn’t clear in the manuscript and have removed this sentence in the revised manuscript during the requested reduction in manuscript length.

Line 103: "A cross-sectional research design was used to survey pregnant women." --&gt; "A cross-sectional survey was performed among pregnant women."
Response: This has been changed in the revised manuscript.

Line 103: 73-items! This is a lot and appears to contradict recommendations on survey research, which recommend to prefer short, simple, "user-friendly" surveys. Obviously, a long survey might be justified in special circumstances. Please refer to such recommendations and argument your choice (references: - Boynton PM, Greenhalgh T. Selecting, designing, and developing your questionnaire. BMJ. 2004;328(7451):1312-5. - Boynton PM. Administering, analysing, and reporting your questionnaire. BMJ. 2004;328(7452):1372-5.). (In any case, the impressive number of participants seems to provide some proofs that your survey was not that long that nobody was interested in participating.)
Response: The authors thank the reviewers for pointing this out. We apologise for the error in our reporting, the survey actually contained 43 items (please see the response below for details). This has now been rectified in the manuscript. Our survey took participants an average of 9.2 (6.6-12.8) minutes to complete. As the reviewer kindly points out, the number of questions did not appear to be a deterrent from survey completion.

Lines 105-106: please also add (either at the beginning: "In addition to demographic characteristics, ..." or at the end ("...; (4) demographic data") the fact, that you also assessed demographic, "baseline" information.
Response: This has been changed in the revised manuscript.
It would be good to provide the instrument you developed and used, at best as a table (your future Table 1). As an example/model, you might refer to following recently published paper: Santi M, et al. Prescription of vitamin D among Swiss pediatricians. Eur J Pediatr. 2019;178(7):1119-1123.). In this way, it is clear to the readership which questions were asked, and also in which form (which can impact the results/answers received).
Response: The survey items have now been included as Online Supplementary Material. Please see the response below for details about the numbering of items.

Revision to the manuscript: “A 43-item survey was developed based on best practice principles (Bonython and Greenhalgh 2004) and evaluated by health professionals and women who had given birth to assess the knowledge, attitudes, behaviours, and intentions of pregnant women to assess the knowledge, attitudes, behaviours, and intentions of pregnant women (survey items listed in the Online Supplementary Material).”
Lines 112-115: please simply write "The survey contained n=... demographic questions (Table 1)". (see comment here above in relation to such "Table 1")
Response: The section referred to has now been removed and the following has been altered in the manuscript to reflect the number of demographic questions. “In addition to demographic data (15 items), information was collected across three domains: (1) preterm birth; (2) nutrition and
supplementation during pregnancy; and (3) omega-3 fatty acid consumption to prevent preterm birth (28 items).”

Line 118: was really possible to answer n=73 questions within 10 minutes? Was this checked before the survey was launched? Was this checked during the survey? Was there a difference between the pilot-test phase and the actual survey performed among the participants?

Response: Thank you for querying the possibility of completing all of the questions in the specified timeframe. This alerted us to the fact that we had erroneously stated the number of items (n=73) based on numbering for analysis, which included screening questions, follow-on questions based on a specified answer (sometimes up to 3 different possibilities depending on the participant’s initial response), as well as “Other (please specify)” questions in the total number of items. In the revised manuscript, we now include the number of items (n=43) reflecting the number of questions that every participant completes (which gives a better indication of how the median time for participants completing the survey was 9.2 minutes). Survey sampling International provided data on the time taken by each participant to complete the survey. We can confirm that the survey was completed in less than 10 minutes, on average. The median (interquartile range) for time to complete the survey was 9.2 minutes (6.6-12.8) . There were no substantial changes to the time to completion between the pilot-phase and actual survey performed.

General comment on Methods: See also general comments in the introduction. How was the instrument developed? How (and by which researchers’ group: all authors, only a part, ...) were the questions generated, selected, checked, corrected, evaluated? Was internal and external reliability assessed? Was the instrument pilot-tested? Was it evaluated? Was it validated? How? Please also refer to recommendations on survey research (see also above: Boynton PM, Br Med J, 2004)

Response: Please see the response to the first comment.

Line 129: delete "recently"
Response: This has been changed in the revised manuscript.

Line 130: "birth (within the last six months),..." --&gt; "birth within the last six months,..." 
Response: This has been changed in the revised manuscript.

Lines 131-135: this means that there were some screening questions. Please state this already before (initial part of the Methods section) and also identify these questions as such (as screening questions). The insertion of the suggested "Table 1" would allow to elegantly solve this "problem".

Response: Supplementary Table 1 in the revised manuscript includes all of the survey items, including the screening questions. We have also moved information about the screening questions to the initial part of the Methods section, as suggested.

Lines 146-147: delete ", due to differences in knowledge and attitudes expected for women who have not given birth."
Response: This has been changed in the revised manuscript.

Line 151: "Over 700 women..." --&gt; "Seven-hundred sixty-three (n=763) women..."
Response: This has been changed in the revised manuscript.

Lines 152-153:
"...survey (total respondents N=763). Respondent demographic characteristics..." --&gt; "...survey. Demographic characteristics..."

Response: This has been changed in the revised manuscript.

Line 154: please report ranges separated by "-" instead of ",", it means: "30 (26, 34)" --&gt; "30 (26-34)", and so on.

Response: This has been changed in the revised manuscript.

Lines 154-156: are these high % of high school representative of the overall population or were participants a particular group ("intellectual elite")? If yes, this might well insert a selection bias... Could you insert a comparison (also rough) with the overall population?

Response: The latest Australian Bureau of Statistics report “4221.0 – Schools, Australia, 2018” shows that 89.0% of females in Australia completed high school (https://www.abs.gov.au/AUSSTATS/abs@.nsf/Latestproducts/4221.0Media%20Release502018?opendocument&amp;tabname=Summary&amp;prodno=4221.0&amp;issue=2018&amp;num=&amp;view=). Therefore, the % of high school completers (87.9%) in our study is comparative to the overall population.

Lines 156-158: it is curious, surprising and interesting that nulliparous mothers, although younger (which is expected), also were more likely to have completed high-school. Do you have any explanation / hypothesis of interpretation for that? "Secular trend" with younger generations having access to "more" education? Please briefly address this point in your (revised) Discussion section.

Response: The authors agree with the reviewer’s suggestions of the “secular trend” explanation whereby younger generations have greater access to education. However, due to the recommendation to reduce the manuscript length, we are unable to cover this in the Discussion as changes in access to education is not a primary objective of this manuscript.

Line 160: "While" --&gt; "Although"

Response: This has been changed in the revised manuscript.

Line 161: "this study had similar demographic" --&gt; "this study globally had similar demographic"

Response: This has been changed in the revised manuscript.

Lines 169-170: please merge the respondents who had heard "preterm birth" and "premature birth" in a single category with a global percentage (mothers who already had heard either "preterm birth" or "premature birth"). Your following sentence (line 171-172) should, instead, not be modified.

Response: The authors thank the reviewer for the suggestion. However, we believe it is important to retain the information in the manuscript covering the percentage of women who had heard of preterm birth when compared to the percentage who had heard of premature birth as it is common for health professionals to use the term “preterm birth”. This finding demonstrates that women are more familiar with premature birth and combined with the findings from subsequent questions, emphasises that they may not understand what preterm birth is when it is referred
to/mentioned. This is important for future research in the area and has potential clinical implications.

Lines 191-192 (nulliparous women more likely to consume a dietary supplement than multiparous women): this is interesting. Why? Do you have any explanation / hypothesis? Please address this issue in your (revised) Discussion.

Response: The authors wish to thank the reviewer for raising this interesting point. From responses collected in the survey, we can confirm that there were a few statistically significant differences between the nulliparous and multiparous women in the main reasons they decided to take a nutrient supplement during their pregnancy. These findings have been added to the revised manuscript.

Revision to the manuscript: “This finding may be partially explained by the differences between the two groups in reasons for supplementing during pregnancy. Nulliparous women were significantly more likely to cite their main reason for supplementing was due to advice given to them or because they had seen/heard of other pregnant women taking them.”

Lines 295-297 (nulliparous mothers were more likely to have changed their diet and to take dietary supplements): why? Do you have any data explaining this difference? Do you have any hypothesis of explanation? Please discuss this in your Discussion section!

Response: This comment is partially addressed in the response above and the corresponding addition to the manuscript. We also hypothesise that with the addition of a dependent child/children in the household that the following could also be potential barriers to supplementation or dietary change for multiparous women: cost of supplementation and time available to make dietary changes. However, we do not have the data to support these hypotheses and as such have just included in the manuscript the data we obtained in the survey. We are also conscious of word count and Reviewer #1’s request to reduce the manuscript by 10-20% so have prioritised the inclusion of hypotheses/explanations supported by our findings.

Line 272: this was even more unexpected considering the high level instruction the participants received (88% high-school)! Please state this in your revised manuscript.

Response: This consideration has been added to the revised manuscript. Revision to the manuscript: “This was an unexpected finding in a cohort of well-educated pregnant women”.

Line 286: "...birth indicate that..." --&gt; "...birth suggests that..."

Response: This has been changed in the revised manuscript.

Lines 299-300 ("despite it not being routinely recommended or prescribed in Australian antenatal care."): please also see comment on the Abstract. This is probably the key of the problem! And this is probably the first thing that should be addressed. Even more considering the good adherence to the already existing recommendations, and the fact that health professionals are the number 1 source of information. Please explicitly state it. I am not practicing in Australia, but basing on your data I feel that it is likely that, by integrating this new recommendation on omega-3 fatty acids, the problem will already be solved, without the need to develop behavioural interventions (which is more complicated and more costly than simply updating the
recommendations). Updating the recommendations would be very easy, cheap and, probably, effective. This would be a simple and logical consequence of your study and your result (stressing the usefulness and relevance of your study!). This same comment also applies to lines 305-308: please add there that updating the recommendations and prescribing either an omega-3 rich diet or a supplement would probably work very well and effectively!
Furthermore, on lines 310-311, you might refer to that: exactly because of this, your survey "will contribute towards the design and implementation of strategies to increase the intake of omega-3 fatty acids in pregnant women"! Finally, this same comment also applies to lines 326-327. Please revise them accordingly.
Response: The authors have revised this section in the discussion and made the suggested changes.

Revision to the manuscript: “This strong link with health professionals in antenatal care as a trusted source of information and guidance highlights antenatal visits as a promising avenue to deliver information on preterm birth and evidence-based strategies to reduce the risk of preterm birth. An effective implementation strategy might include updating the clinical practice guidelines and educating health professionals in antenatal care to encourage an increase in omega-3 fatty acid consumption during pregnancy.”

Lines 300-301 ("These findings suggest that..." until "...omega-3 fatty acid intake."): are you sure that the fact that about 1/3 took omega-3 supplements on a voluntary basis suggests that they are well tolerated? I mean, chemotherapy is not always good tolerated, but I know several patients, who would ask for it also without a specific physician recommendation... Maybe were these 30% women well-informed, or convinced of the benefit of this supplementation, and took it irrespective of the tolerance... Although this is improbable, and your interpretation might applies, I find this interpretation a "logical fallacy". If you do not have data on tolerability (did you ask questions on that?), simply delete this sentence.
Response: This sentence has been deleted in the revised manuscript.

Line 323 ("barriers and enablers"): which barriers and which enablers did you identify? Sorry, but in the Result section I do not find them...
Response: The authors thank the reviewer for bringing this point to our attention. We acknowledge that this is the first time we have referred to the factors affecting supplement use during pregnancy and awareness of preterm birth as “barriers and enablers”. For clarity, we have changed “barriers and enablers” in the manuscript to “important factors that could be addressed”.

Table 1: - How is it possible that "total in household" was 2 (2,3) in nulliparous (how is it possible that the upper quartile arrives at n=3)? Patchwork families?

Response: It is possible to have three in a household if the household includes flatmates/housemates, boarders, international students, a parent of either of the partners, or an extended family member, for example.
- State: please directly write the complete state names into the table, instead of using abbreviations and then explaining them at the bottom of the table.
Response: This has been changed in the revised manuscript.
- Statistical comparisons: which columns did you compare? Nulliparous vs multiparous? Please state it in the legend of the Table. To compare these 2 columns with the "Australian pregnant
women" would probably not be possible/correct, unless you dispose about the whole dataset (and not only on the mean). However, for proportions it would be possible...
Response: Yes, nulliparous and multiparous groups were compared. This is now stated in the table legend of the revised manuscript.
Table 2:
- Please merge the two categories "Advice given to me" and "The supplements were given to me" in an unique category (differential understanding from different respondents might have confounded these 2 categories, rendering them not so easy to interpret / compare one to another).
Response: We thank the reviewer for this suggestion. However, we believe that it is inappropriate to merge these two categories as they have different meanings and appeal to different people. For example, when compared to simply being given advice, being given a supplement helps to address barriers around cost, accessibility, convenience etc and therefore can often make someone more likely to consume a supplement/product than simply receiving advice. There is evidence that advice/knowledge alone doesn’t always translate into action.

- "I took supplements in my other pregnancies": is the % calculated on the total of participants or on the multiparous mothers? The second would be the correct way to calculate this value... at best, this should be noted with a symbol (e.g. "\*\") and acknowledged/explained in a footnote of the Table.
Response: This has been changed in the revised manuscript.

Table 4
- Line 263: please provide the full legend for the "intention grading": 1 = highly unlikely, 5= highly likely, but what did 2=..., 3=... and 4=... stay for? Since the formulation might have an impact on the answers, please state the full range of corresponding expressions. Thank you!
Response: The “intention grading” was only used for 1 and 5 in the question, to clarify the direction of the grading. The response options were presented as simply the numbers 1, 2, 3, 4, 5.

Figure 1:
- please merge the categories "Blogs" and "Internet" in a single category.
Response: Online blogs as a source of information is a very different information source to the general internet (excluding blogs). For example, in regards to dietary information during pregnancy, in many countries government resources/dietary guidelines are accessed on the internet and these may contain substantially different types of information than information from blogs, which may include personal opinions of the blogger (who is not necessarily reflecting the current guidelines and/or may have vested interests). Also, there are notable differences in the percentage of respondents who indicated that blogs influenced their decision to take nutrient supplements, compared to information from the internet, despite both having similar numbers of respondents indicating that they were key sources used to obtain information. Therefore we deem it inappropriate to treat these two groups as a single category.
The literature is globally well-done. However, there are n=4 citations, which are not peer-reviewed publications. Please either substitute them with peer-reviewed literature or eliminate them:

- lines 383-384 (but I understand that maybe you need to cite the official source... this would be the only exception allowed for a non-peer-reviewed reference); - lines 387-388; - lines 415-416.

Please insert the references suggested above at the corresponding places of the manuscript:
- Boynton PM, Greenhalgh T. Selecting, designing, and developing your questionnaire. BMJ. 2004;328(7451):1312-5.

Response: The citation on lines 383-384 is an official Australian Government report and cannot be substituted. The thesis cited and corresponding information included in the manuscript has now been removed, and the book citation has been replaced by peer-reviewed literature. Although there was not sufficient space in the revised manuscript to incorporate all suggested citations, the suggested citation of Bonython and Greenhalgh 2004 has been incorporated into the revised manuscript.

Reviewer #2:

This paper describes a questionnaire assessing knowledge and intentions around pregnant women's knowledge of omega-3 in preventing preterm birth. The paper describes the results of short online questionnaire completed by pregnant or recently birthed women in Australia. The information is timely, given the recently published Cochrane review on the effect of omega-3 PUFAs on pre term birth. The sample size is sufficient. The study is justified, well described by the authors, and provides important information on knowledge of omega-3 polyunsaturated fatty acids from pregnant women in Australia.

Minor comments:

Suggest the authors check that all units have been included (e.g. line 154)
Response: The authors thank Reviewer #2 for their review of our manuscript. The units throughout the manuscript have been checked and corrections have been made to the revised manuscript.