PEER REVIEW HISTORY

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ARTICLE DETAILS

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<th>Fruit and vegetable consumption and psychological distress: cross-sectional and longitudinal analyses based on a large Australian sample</th>
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<td>AUTHORS</td>
<td>Nguyen, Binh; Ding, Ding; Mihrshahi, Seema</td>
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VERSION 1 - REVIEW

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GENERAL COMMENTS

Comments to the authors:

This manuscript assesses the cross-sectional and also prospective associations between fruit and vegetable consumption and psychological distress in a large cohort of Australians. The results seem to suggest that there are sex differences in the data, and that medium, but not high, levels of fruit and vegetable intake are associated with lower levels of psychological distress.

There are several major problems with this manuscript as it now stands in my opinion, as I attempt to describe hereafter.

First of all, a recent publication on a sample of more than 20 000 Swiss adults on the same topic has not been cited and needs to be integrated as it is highly relevant to the current manuscript. The results of these two manuscripts need to be compared, and in particular the authors need to state what the cross-sectional analysis of their study adds to the cross-sectional analysis previously published by the Swiss authors.


Second, the authors seemed to find sex differences for some of the cross-sectional analyses (combined fruit and vegetable consumption and sex p<0.049) but not for the prospective analyses (p=0.08). Their cut-off of p<0.1 as a threshold for significance for the sex interaction analysis hardly seems justifiable. The authors need to decide for which analyses there are sex differences or not, and for that they could go deeper into their data. For e.g. are there sex differences without the imputations? For which associations exactly do the sex differences hold? If there are meaningful sex differences,
which could also be tested by computing males against females for each statistical analysis, then only the results by sex should be presented and not the results of the overall sample. I would then suggest to present the unadjusted ORs, perhaps the age adjusted ORs and the fully-adjusted ORs separately by sex, and not the overall analyses which should be removed from the paper for these respective analyses. If the authors conclude on an absence of sex differences, then only the overall analyses should be presented and not the specific analyses by sex. They should only mention that this was tested and revealed non significant results. It should be one or the other, right now they present a hybrid of the two types of results which is confusing.

Third, the authors seem to find different associations for 1-2 serves of fruit per day (or for 4-7 serves of combined fruit and vegetables a day) and not for more serves a day. First, they need to justify this cut-off. Then, the fact that a moderate consumption, and not a higher consumption, is associated with lower psychological distress should be interpreted. The authors fail to comment on this fact at all, and the data are not exploited in the discussion section. The readers are basically left to guess as to why this is the case, no explanation being advanced as to what these findings really represent.

Other small comments: The variables “current smoker” and “history of chronic disease” should be defined.

Overall, the analyses require more work and justification, and a clear interpretation of the findings needs to be made before this manuscript can be considered ready for publication.

REVIEWER
Mila Kingsbury
University of Ottawa, Canada

REVIEW RETURNED
26-Sep-2016

GENERAL COMMENTS
This study assessed the cross-sectional and longitudinal associations between fruit and vegetable consumption and psychological distress among middle-aged and older adults.

Overall, this is a nice study. The measure of psychological distress is well-validated, and the authors adjust for several important covariates, including BMI, physical activity, and smoking. The conclusions are not overstated based on the results, and the study replicates previous work while providing new longitudinal evidence of the association between fruit and vegetable intake and mental health, as well as new evidence of gender differences in this association.

A few points for consideration:
- why was p<.10 selected as the cutoff for interaction analyses (whereas p<.05 was used for other analyses)?
- given the observed interaction with gender, I would be interested in seeing if sample characteristics (including fruit and vegetable consumption and covariates) were different among men and women.
- The authors briefly mention the reverse-causation hypothesis (the impact of psychological distress on fruit and vegetable
consumption), but do not test this. Though they do attempt to address this limitation by excluding participants in severe distress at baseline, I would be interested to see either a formal test of this in their sample (e.g., time 1 distress predicting time 2 consumption). At the least the authors should include a more balanced discussion of this issue (for example, in a recent paper using data from a prospective cohort study, we did find evidence supporting reverse causation; Kingsbury et al., 2015. J Epidemiol Community Health doi:10.1136/jech-2015-205858)

- on a related note, was a measure of history of depression available? History of depression is an important confounder as it may be related to the incidence of psychological distress as well as to dietary quality.

REVIEWER
Allison Hodge
Cancer Council Victoria
Australia

REVIEW RETURNED
28-Sep-2016

GENERAL COMMENTS
Fruit, vegetables and psychological distress. This is a generally well written paper on a relevant topic and including a large number of people.
It is not clear in the Abstract methods section whether K10 or diet questions were administered at both times and whether the cross-sectional analysis was based on follow-up or baseline data.
Given what we know about other foods and nutrients which have been associated with psychological distress the lack of data on dietary intake of other items is a limitation.
Reverse causation is particularly relevant for this work so should be addressed in the introduction as a major limitation of existing cross-sectional studies.
Methods section could perhaps be restructured to make it easier to follow. While reading the section 'Study population' the reader is not clear that both K10 and fruit/veg questions were completed at both occasions. Maybe stop the study pop section after ‘… complete the SEEF questionnaire (60.4% response rate) around line 20. Then describe measurement of outcome and exposure and then describe how many people were included in the analysis.
Although the ethical approval is noted there is no mention of the consent process.
Is the cross-sectional analysis done on follow-up data? This appears to be the case as n=60,404 which seems to match the 60.4% response at FUP. If so are baseline covariates such as age up-dated for the time when follow-up was completed?
Table 1 is baseline characteristics according to K10 classification at FUP, ie prospective study. Why not start with cross sectional analysis. Why do the two groups in Table 1 not add up to the total?
Table 2 is looking at prevalence of psychological distress according to description on page 9, ie the cross-sectional association. It is confusing when the heading for this table states ‘…baseline association between fruit and vegetable consumption…’. Why not show raw data for this as you did for prospective in table 1. Give numbers in fruit and veg intake categories in table 2.
Table 3 shows both the cross-sectional and prospective sex-specific associations between fruit and veg intakes and psychological distress. This is odd as the results in Table 4 incidence of psychological distress is described before the sex-specific results in
Table 3 as would be expected. Give numbers in fruit and veg intake categories in Table 4.

The first paragraph of the discussion could be modified to more clearly contrast the findings of cross-sectional and prospective analyses. Not clear what “…remained mostly significant at medium levels…” means.

Page 16, line 20 is. What is meant by three separate data sets in relation to the 80,000 randomly selected British adults?

Page 16, the study on 12,385 Australian adults appears to be an intervention but is not clearly described. The following comment that differences between studies could be due to several factors is not useful unless such differences between the studies mentioned are identified.

In relation to the sex differences mentioned at the bottom of page 16 it would be helpful if the number of men and women in each consumption category and with elevated K10 was shown. Some of the difference could be explained by there being more women, more of whom develop psychological distress and possibly more of whom consume fruit and veg at higher levels.

In the second paragraph on page 17 nutrients such as vitamin B12, calcium and iron are discussed as possibly being important in relation to depression or mood but these nutrients are not at high levels in fruit and vegetables. B12 is only in animal foods. Thus this is completely irrelevant to your findings and rather misleading as it reads as if these could be part of the mechanism for the association.

While reverse causation is not an issue for the prospective analysis it could be important for the cross-sectional analysis and could contribute to the stronger results here.

Funding - Should ref number 1072223 go after “…NHMRC of Australia”? Spell NHMRC out in full?

In flowchart clarify that the exclude participants were excluded on the basis of baseline data.

VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1’s comments

General comments: This manuscript assesses the cross-sectional and also prospective associations between fruit and vegetable consumption and psychological distress in a large cohort of Australians. The results seem to suggest that there are sex differences in the data, and that medium, but not high, levels of fruit and vegetable intake are associated with lower levels of psychological distress.

There are several major problems with this manuscript as it now stands in my opinion, as I attempt to describe hereafter.

Response: Thank you for your valuable comments. The authors have responded to specific comments below. Please note that all changes are marked as tracked changes in the revised manuscript. Page and line numbers that are referred to in this response relate to the marked copy of the manuscript.

Comment 1: First of all, a recent publication on a sample of more than 20 000 Swiss adults on the same topic has not been cited and needs to be integrated as it is highly relevant to the current manuscript. The results of these two manuscripts need to be compared, and in particular the authors need to state what the cross-sectional analysis of their study adds to the cross-sectional analysis previously published by the Swiss authors.

Response: Thank you for your suggestion. The authors cited other relevant studies in the original manuscript and will incorporate this recent publication in the revised manuscript (reference #14 in the revised manuscript).

We made changes accordingly in the introduction (reference added on page 5, line 17) and discussion (page 19, lines 17-20). The results of these two manuscripts have been compared in the discussion (page 19, lines 17-20).

Comment 2: Second, the authors seemed to find sex differences for some of the cross-sectional analyses (combined fruit and vegetable consumption and sex p<0.049) but not for the prospective analyses (p=0.08). Their cut-off of p<0.1 as a threshold for significance for the sex interaction analysis hardly seems justifiable. The authors need to decide for which analyses there are sex differences or not, and for that they could go deeper into their data. For e.g. are there sex differences without the imputations? For which associations exactly do the sex differences hold? If there are meaningful sex differences, which could also be tested by computing males against females for each statistical analysis, then only the results by sex should be presented and not the results of the overall sample. I would then suggest to present the unadjusted ORs, perhaps the age adjusted ORs and the fully-adjusted ORs separately by sex, and not the overall analyses which should be removed from the paper for these respective analyses. If the authors conclude on an absence of sex differences, then only the overall analyses should be presented and not the specific analyses by sex. They should only mention that this was tested and revealed non significant results. It should be one or the other, right now they present a hybrid of the two types of results which is confusing.

Response: The cut-off of p<0.1 was originally selected as a more lenient p-value, as often used in epidemiological research, to detect statistically significant interactions. However, to avoid confusion, and considering the relatively large sample size, we have decided to use a cut-off of p<0.05 as for other statistical analyses in the paper.

In the statistical analysis section, we have removed the sentence indicating that the cut-off for statistically significant interactions is p<0.1 (original manuscript: page 8, lines 22-24). The second-to-last sentence in this paragraph, stating that p-values <0.05 were considered statistically significant, remains unchanged (revised manuscript: page 8, lines 30-32).

As per your suggestion, we have also computed unadjusted and age-adjusted ORs separately for each sex (now Table 4, pages 16-17). All unadjusted, age-adjusted, and fully-adjusted cross-sectional and longitudinal associations were significant for females. For males, the cross-sectional associations were largely significant for unadjusted and age-adjusted associations. However, most of these associations did not remain statistically significant in the fully-adjusted models. In unadjusted and adjusted models, there were no clear longitudinal associations in males. Based on these results, it appears that there could be sex differences for cross-sectional analyses and possibly prospective analyses (p for the interaction between combined fruit and vegetable consumption and sex is trending significant, which is worth noting).

In Table 4 (pages 16-17) of the revised manuscript, we now present the unadjusted, age-adjusted and fully-adjusted ORs separately in each sex. The results in the overall sample are also presented as we believe that these are relevant findings. To avoid confusion, we have changed the order of the tables and present the overall findings in Tables 2 and 3 (pages 14-15), and the last table (Table 4) only includes results by sex.
Comment 3: Third, the authors seem to find different associations for 1-2 serves of fruit per day (or for 4-7 serves of combined fruit and vegetables a day) and not for more serves a day. First, they need to justify this cut-off.

Response: In this study, the authors chose to use fruit and vegetable consumption tertiles rather than using cut-offs based on recommended dietary guidelines to better explore variations in exposure in the study cohort. Using tertiles ensures that the range in exposure is captured evenly across distribution categories in a selected sample of participants and also facilitates comparison between different levels of fruit and vegetable consumption among the cohort. Quantiles have been used in a previous large study examining the effect of dietary variables (including fruit and vegetable consumption) on incident depression (Gangwisch et al., 2015; reference #16 in the revised manuscript).

A sentence justifying the use of tertiles has been added in the methods section (page 7, lines 26-29).

Comment 4: Then, the fact that a moderate consumption, and not a higher consumption, is associated with lower psychological distress should be interpreted. The authors fail to comment on this fact at all, and the data are not exploited in the discussion section. The readers are basically left to guess as to why this is the case, no explanation being advanced as to what these findings really represent.

Response: We agree that these findings could be interpreted further. Although tertiles of consumption were used, it is possible that longitudinal associations between higher consumption and psychological distress did not remain statistically significant in fully-adjusted models due to a relatively smaller sample of individuals with high-to-very high levels of distress in higher consumption compared with lower consumption categories.

A sentence has been added in the discussion (page 20, lines 1-5).

Comment 5: Other small comments: The variables “current smoker” and “history of chronic disease” should be defined.

Response: A “current smoker” was defined as a self-reported current “regular” smoker. A “history of chronic disease” included a self-reported history of cancer other than non-melanoma skin cancer, cardiovascular disease (heart disease, stroke or blood clot), diabetes and/or hypertension as indicated in the original manuscript (page 8, lines 3-5).

We have defined “current smoker” further in the methods section, on page 8, line 9.

Comment 6: Overall, the analyses require more work and justification, and a clear interpretation of the findings needs to be made before this manuscript can be considered ready for publication.

Response: Thank you. We have tried to address these suggestions in our revisions to the manuscript as described throughout this response.

Briefly, we made changes to: justify the use of consumption tertiles (page 7, lines 26-29), present more detailed findings relating to sex-specific analyses (Table 4, pages 16-17), and further interpret our longitudinal findings (page 20, lines 1-5).

Response to Reviewer 2’s comments
General comments: This study assessed the cross-sectional and longitudinal associations between fruit and vegetable consumption and psychological distress among middle-aged and older adults. Overall, this is a nice study. The measure of psychological distress is well-validated, and the authors adjust for several important covariates, including BMI, physical activity, and smoking. The conclusions are not overstated based on the results, and the study replicates previous work while providing new longitudinal evidence of the association between fruit and vegetable intake and mental health, as well as new evidence of gender differences in this association.

Response: We are appreciative of your positive comments and suggestions to help improve the manuscript.

Comment 1: A few points for consideration:
- why was $p < .10$ selected as the cutoff for interaction analyses (whereas $p < .05$ was used for other analyses)?

Response: Please refer to our response to Reviewer 1’s specific comment #2.

Comment 2: Given the observed interaction with gender, I would be interested in seeing if sample characteristics (including fruit and vegetable consumption and covariates) were different among men and women.

Response: Thank you for your suggestion. When examining baseline sample characteristics, most sample characteristics were significantly different between men and women. Women were more likely younger, less educated, single/widowed/divorced/separated, to report a lower household annual income, to have a lower BMI, and to consume more fruit and vegetables and less alcohol.

Table 1 (page 11) has been modified accordingly and sample characteristics for men and women are now presented in this table. A sentence summarising differences between men and women has been added in the results section (page 9, lines 9-11).

Comment 3: The authors briefly mention the reverse-causation hypothesis (the impact of psychological distress on fruit and vegetable consumption), but do not test this. Though they do attempt to address this limitation by excluding participants in severe distress at baseline, I would be interested to see either a formal test of this in their sample (e.g., time 1 distress predicting time 2 consumption). At the least the authors should include a more balanced discussion of this issue (for example, in a recent paper using data from a prospective cohort study, we did find evidence supporting reverse causation; Kingsbury et al., 2015. J Epidemiol Community Health doi:10.1136/jech-2015-205858).

Response: Thank you for your suggestions. We agree that reverse causation could be discussed at greater length in the manuscript and we now also refer to the mentioned study.

We made changes accordingly under Strengths and Limitations, in the discussion (page 21, lines 17-20) and have added the suggested reference (reference #33 in the manuscript).

Comment 4: On a related note, was a measure of history of depression available? History of depression is an important confounder as it may be related to the incidence of psychological distress as well as to dietary quality.

Response: In the questionnaires, participants were asked whether they had ever been told by a doctor that they have depression. However, we did not include this variable as its reliability was uncertain.
Response to Reviewer 3’s comments

General comments: This is a generally well written paper on a relevant topic and including a large number of people.

Response: Thank you for your comments.

Comment 1: It is not clear in the Abstract methods section whether K10 or diet questions were administered at both times and whether the cross-sectional analysis was based on follow-up or baseline data.

Response: In the abstract, we have now clarified that K10 was assessed at both time points. Although fruit and vegetable consumption was also assessed at both times, we only use baseline fruit and vegetable consumptions in our analyses. Cross-sectional analysis was based on baseline data. The abstract (page 3; lines 8, 12, 16, 19) has been modified accordingly.

Comment 2: Given what we know about other foods and nutrients which have been associated with psychological distress the lack of data on dietary intake of other items is a limitation.

Response: We have acknowledged this limitation in the “Strengths and limitations” section of the discussion in the original manuscript (page 17, lines 46-56). No changes made.

Comment 3: Reverse causation is particularly relevant for this work so should be addressed in the introduction as a major limitation of existing cross-sectional studies.

Response: Thank you for this suggestion. We agree that reverse causation is an important limitation and we have addressed this issue in the discussion. Please refer to our response to Reviewer 2’s specific comment #3. We made changes accordingly under Strengths and Limitations, in the discussion (page 21, lines 17-20).

Comment 4: Methods section could perhaps be restructured to make it easier to follow. While reading the section ‘Study population’ the reader is not clear that both K10 and fruit/veg questions were completed at both occasions. Maybe stop the study pop section after ‘… complete the SEEF questionnaire (60.4% response rate) around line 20. Then describe measurement of outcome and exposure and then describe how many people were included in the analysis.

Response: Thank you for these suggestions. To avoid confusion, we have slightly restructured the “Study population” section (page 6). We have decided to keep the description of the number of people included in the analysis under “Study population” as it made more sense for this description to follow the flow chart.

No changes were made in the “Outcome” section as we already state that K10 was assessed at both baseline and follow-up (page 6, line 27). Although fruit and vegetable consumption was assessed at both time points, we only use baseline fruit and vegetable consumption for the purpose of this study. We have now clarified this in the “Exposure” (page 7, line 16) and “Statistical analysis” sections (page 8, line 13) by adding the word “baseline” in relevant places.
We made changes to the methods section (page 6, lines 11-18; page 7, line 16; page 8, line 13).

Comment 5: Although the ethical approval is noted there is no mention of the consent process.

Response: In the original manuscript, we have briefly described the consent process under “Study population” (original manuscript: page 6, lines 11-14) and have also provided a more detailed reference for the 45 and Up Study (original manuscript: page 6, lines 15-16; reference #22).

No changes made.

Comment 6: Is the cross-sectional analysis done on follow-up data? This appears to be the case as n=60,404 which seems to match the 60.4% response at FUP. If so are baseline covariates such as age up-dated for the time when follow-up was completed?

Response: Apologies for the confusion. The cross-sectional analysis was performed on baseline data. As we wanted to conduct both cross-sectional and longitudinal analyses on the same sample, we used n=60,404 as these were the participants that also had follow-up data.

We have restructured the “Study population” section which presents the participant flow chart followed by a description of the number of people included in the analysis. To avoid confusion, we have added “baseline” next to “cross-sectional” analyses.

We made changes to the “Study population” section (page 6, lines 11-18).

Comment 7: Table 1 is baseline characteristics according to K10 classification at FUP, ie prospective study. Why not start with cross sectional analysis. Why do the two groups in Table 1 not add up to the total?

Response: We agree that Table 1 could be modified to present sample characteristics based on K10 classification at baseline.

In the original manuscript, the two groups in Table 1 did not add up to the total as K10 data was missing for some of the participants (highlighted in the footnotes of the original manuscript on page 11, lines 31-32). Similarly, in revised Table 1 the two K10 groups do not add up as K10 data is missing for n=5,981 as highlighted in footnote b.

Table 1 has been modified accordingly (pages 11-13).

Comment 8: Table 2 is looking at prevalence of psychological distress according to description on page 9, ie the cross-sectional association. It is confusing when the heading for this table states ‘…baseline association between fruit and vegetable consumption…’. Why not show raw data for this as you did for prospective in table 1. Give numbers in fruit and veg intake categories in table 2.

Response: We have re-worded the title in Table 2. Raw data was not shown as we use tertiles of consumption.

The word “prevalence” has been added in the title of Table 2 (page 14).

Comment 9: Table 3 shows both the cross-sectional and prospective sex-specific associations between fruit and veg intakes and psychological distress. This is odd as the results in Table 4 incidence of psychological distress is described before the sex-specific results in table 3 as would be...
expected. Give numbers in fruit and veg intake categories in table 4.

Response: In the original manuscript, as sex-specific prevalence results were presented after Table 2 (original manuscript: page 9, lines 43-45) before the results relating to incidence (original manuscript: Table 4, page 9, lines 56-57), we thought that this table should be named Table 3, in order of appearance.

However, it would also make sense and be less confusing to have the incidence results presented in Table 3 followed by the sex-specific results.

Tables 3 and 4 have now been interchanged (revised manuscript: pages 13 and 14).

Comment 10: The first para of the discussion could be modified to more clearly contrast the findings of cross-sectional and prospective analyses. Not clear what ‘…remained mostly significant at medium levels…’ means.

Response: In this paragraph, we have attempted to more clearly contrast findings from cross-sectional and prospective analyses by adding a sentence and making other changes.

For the sentence that is unclear, please refer to our response to Reviewer 1’s specific comment #4, including changes that were made. This will help clarify the meaning of this sentence.

We made changes to the first paragraph in the discussion (page 10, lines 25-32).

Comment 11: Page 16, line 20 is. What is meant by three separate data sets in relation to the 80,000 randomly selected British adults?

Response: Three individual data sets (from three separate health surveys) together involved 80,000 randomly selected British adults.

This sentence has been re-worded (page 19, lines 11-14).

Comment 12: Page 16, the study on 12,385 Australian adults appears to be an intervention but is not clearly described. The following comment that differences between studies could be due to several factors is not useful unless such differences between the studies mentioned are identified.

Response: The study was not an intervention but investigated longitudinal linkages between fruit and vegetable consumption and mental well-being in Australians surveyed at three different time points.

That study has been described more clearly (page 19, lines 28-29). The sentence relating to differences between studies has been removed (page 19, lines 31-33 and page 20, line 1).

Comment 13: In relation to the sex differences mentioned at the bottom of page 16 it would be helpful if the number of men and women in each consumption category and with elevated K10 was shown. Some of the difference could be explained by there being more women, more of whom develop psychological distress and possibly more of whom consume fruit and veg at higher levels.

Response: Thank you for your comments. In Table 4 of the revised manuscript, we have used tertiles of consumption and therefore did not include the number of participants in each consumption category. Adding sample size to this now very detailed table would also make it too busy.

No changes made.
Comment 14: In the second paragraph on page 17 nutrients such as vitamin B12, calcium and iron are discussed as possibly being important in relation to depression or mood but these nutrients are not at high levels in fruit and vegetables. B12 is only in animal foods. Thus this is completely irrelevant to your findings and rather misleading as it reads as if these could be part of the mechanism for the association.

Response: Thank you for pointing this out. We agree that these three nutrients are not present in high amounts in fruit and vegetables, and are not pertinent to this part of the discussion. Sentences mentioning these three nutrients have been deleted or changed accordingly (page 20, lines 24-27).

Comment 15: While reverse causation is not an issue for the prospective analysis it could be important for the cross-sectional analysis and could contribute to the stronger results here.

Response: Please refer to our earlier response to Reviewer 3’s specific comment #3.

Comment 16: Funding - Should ref number 1072223 go after “…NHMRC of Australia”? Spell NHNRC out in full?

Response: Thank you for pointing this out. The reference number has now been placed after “NHMRC of Australia” (page 24, lines 4-6) and NHMRC has been spelled out in full.

Comment 17: In flow chart clarify that the exclude participants were excluded on the basis of baseline data.

Response: The flow chart now includes this additional data.

We made changes to the flow chart (Figure 1).

Other revisions made by the authors

Other revision 1: Introduction: we rectified a mistake made in the description of one of the studies cited.

Changes made: “Australian” was changed to “American” for reference #16 in the revised manuscript (on page 5, line 21).

Other revision 2: Discussion: We inadvertently gave the wrong reference number for one of the cited studies.

Changes made: Reference #13 was changed to #12 on page 17, line 12.

Other revision 3: References: seven references were re-formatted as per BMJ reference style, presenting only the first three authors’ names and initials followed by “et al.”.

Changes made: Seven references (#6, 10, 16-18, 20, 25) were re-formatted in the References section.
Other revision 4: The heading “Discussion” was re-formatted.

Changes made: The heading "Discussion" was changed to capital letters (on page 10, lines 24).

Other revision 5: The Figure title was added at the end of the manuscript. This Figure does not require a legend as its title is self-explanatory.

Changes made: The Figure title was added at the end of the manuscript (page 30).

**GENERAL COMMENTS**

The revision has led to a much improved manuscript overall, with clearer methodology and easier interpretable findings. There is however one point with which I still don’t agree, and this concerns the interpretation of the moderate and higher consumption of fruit and vegetables. My initial comment was the following: “Third, the authors seem to find different associations for 1-2 serves of fruit per day (or for 4-7 serves of combined fruit and vegetables a day) and not for more serves a day. First, they need to justify this cut-off. Then, the fact that a moderate consumption, and not a higher consumption, is associated with lower psychological distress should be interpreted. The authors fail to comment on this fact at all, and the data are not exploited in the discussion section. The readers are basically left to guess as to why this is the case, no explanation being advanced as to what these findings really represent.”

In the revision, the authors disregard their findings by merely attributing the lack of associations between psychological distress and the highest levels of consumption to “a lack of power”. I disagree with this completely. When you compare the effect sizes of the odd’s ratios (OR) in the fully-adjusted models, it becomes apparent that the non significant p-values are not attributable to a lack of power but to the effect sizes as such. Indeed for instance, in the cross-sectional analyses in males, a fully-adjusted OR of 0.78 is significant for 1-2 serves a day, whereas the OR for >2 serves a day is 0.99 and n.s. This is not a problem of power, but due to the effect size of the OR. Another example is the effect sizes in the longitudinal analyses for females. The fully-adjusted OR for 4-7 serves of fruit and vegetable consumption is 0.77 (p=0.002) whereas that for > 7 serves a day is 0.86 (n.s.). If you compare this to other effect sizes of =.85 for instance in other categories, the latter are also non significant, so clearly this is not a problem of power. Besides, given the overall huge sample size, I doubt whether we have a problem of power here, even in the smallest group.

What I see in these results is clearly the suggestion of a threshold between moderate and high consumption. In males, the cross-sectional analyses (fully-adjusted models) seem to suggest that a too high consumption of fruit and vegetables (each taken individually) is not associated with less psychological distress, whereas a moderate consumption is. However, this does not seem to be the case in females in the cross-sectional analysis. In females, the longitudinal analysis also suggests a threshold. For me this...
suggests that a too high consumption of fruit and / or vegetables is no longer protective against psychological distress, cross-sectionally in males and longitudinally in females, indicating that too much fruit and / or vegetable is in fact not beneficial for mental health. The question remains as to why the authors found this cross-sectionally in males only, and longitudinally in females only.

In females, one limitation of the longitudinal analysis is that fruit and vegetable consumption were not assessed at follow-up so the associations could still be attributable to differential consumption patterns at follow-up. Moreover, in the cross-sectional analysis in males and the follow-up analysis in females, the OR were not adjusted for other food intake, and it is possible that individuals who eat (too) large quantities of fruit and / or vegetables also eat larger quantities of other foods as well, which could lead to a higher BMI in these individuals. It is true that the analyses were controlled for BMI, but the use of categories of BMI may not have fully captured the fact that these individuals might have had a larger BMI within each of the categories (for e.g. the authors grouped together overweight and obese: BMI > 25, so individuals of BMI 26 are in the same category as those with a BMI of 40). One way to find out more about this hypothesis would be to leave BMI as a continuous variable in the adjusted models. Other confounders may have included the presence of a series of other cardio-metabolic risk components which this study did not control for (this study controlled for diabetes, hypertension and a history of other chronic diseases) which should be mentioned in the limitation section.

These are some ideas regarding these differences which the authors should explore more. In any case, the authors need to interpret the differences between moderate and high consumption of fruit and / or vegetables and their association with psychological distress, and not simply attribute these differences to a lack of statistical power which they are clearly not. The discussion section should be revised accordingly and the limitations section should also be expanded (some of the elements I mentioned are already stated, but this section could be completed).

REVIEWER  
Mila Kingsbury  
University of Ottawa, Canada  
REVIEW RETURNED  
07-Nov-2016

GENERAL COMMENTS  
Thank you for thoughtfully addressing my original comments. Though I agree with the authors' decision not to include the available measure of physician diagnosis of depression, the absence of a measure of history of mental illness should be mentioned in the discussion as a limitation. I am also still curious about the reverse causation hypothesis, since you have the data to test this... but if the editor is satisfied without this then I am also satisfied with your discussion in the limitations section.

REVIEWER  
Allison Hodge  
Cancer Council Victoria, Australia  
REVIEW RETURNED  
09-Nov-2016

GENERAL COMMENTS  
The manuscript has been much improved in response to comments
but there are still a few things that need to be clarified/corrected. 
Page3 line 13. Should be ‘after’ rather than ‘during’
Page 8, line 20 p<0.05 is significant but on page 10, line 17 says interaction with sex is significant p=0.08.
Table 1 needs to be carefully checked. The sample size for K10>22 is 551,393 which is larger than the whole study population. The ages of the two lo/hi K10 groups are over 600 years. 468% of people with hi K10 have < 10 years education and people with lo K10 have 43.9 serves of veg per day.
In Tables 2 and 3 it would be good to include the total number of people in the heading and then give numbers in the tertiles and number of incident cases. This would also help with the arguments that perhaps fewer cases in the top tertiles of intake resulted in non-significant ORs.
Table 4 is very busy. Perhaps it would be better just to show the fully adjusted model if that is the results we should focus on. Can describe in text what other models showed.

VERSION 2 – AUTHOR RESPONSE

Response to Reviewer 1’s comments

General comments: The revision has led to a much improved manuscript overall, with clearer methodology and easier interpretable findings. There is however one point with which I still do not agree, and this concerns the interpretation of the moderate and higher consumption of fruit and vegetables.

Response: Thank you for your constructive comments, which helped us improve our manuscript. We have responded to specific comments below. Please note that all changes are marked as tracked changes in the revised manuscript. Page and line numbers that are referred to in this response relate to the marked copy of the manuscript.

Comment 1: My initial comment was the following:
“Third, the authors seem to find different associations for 1-2 serves of fruit per day (or for 4-7 serves of combined fruit and vegetables a day) and not for more serves a day. First, they need to justify this cut-off. Then, the fact that a moderate consumption, and not a higher consumption, is associated with lower psychological distress should be interpreted. The authors fail to comment on this fact at all, and the data are not exploited in the discussion section. The readers are basically left to guess as to why this is the case, no explanation being advanced as to what these findings really represent.”

In the revision, the authors disregard their findings by merely attributing the lack of associations between psychological distress and the highest levels of consumption to “a lack of power”. I disagree with this completely. When you compare the effect sizes of the odd’s ratios (OR) in the fully-adjusted models, it becomes apparent that the non significant p-values are not attributable to a lack of power but to the effect sizes as such. Indeed for instance, in the cross-sectional analyses in males, a fully-adjusted OR of 0.78 is significant for 1-2 serves a day, whereas the OR for >2 serves a day is 0.99 and n.s. This is not a problem of power, but due to the effect size of the OR. Another example is the effect sizes in the longitudinal analyses for females. The fully-adjusted OR for 4-7 serves of fruit and vegetable consumption is 0.77 (p=0.002) whereas that for > 7 serves a day is 0.86 (n.s.). If you compare this to other effect sizes of =.85 for instance in other categories, the latter are also non significant, so clearly this is not a problem of power. Besides, given the overall huge sample size, I doubt whether we have a problem of power here, even in the smallest group.

Response: We appreciate your input and interpretation. We now provide a different interpretation of
these findings (please refer to our responses below to your other comments) and have removed sentences relating to “a lack of power” in the Discussion section.

Changes made: The following sentence has been removed from the Discussion (page 19, lines 1-4): “In our study, it is possible that longitudinal associations between higher fruit and vegetable consumption and psychological distress did not remain statistically significant in fully-adjusted models due to a relatively smaller sample of individuals with high-to-very high levels of distress in higher consumption compared with lower consumption categories, despite the use of tertiles.”

Comment 2: What I see in these results is clearly the suggestion of a threshold between moderate and high consumption. In males, the cross-sectional analyses (fully-adjusted models) seem to suggest that a too high consumption of fruit and vegetables (each taken individually) is not associated with less psychological distress, whereas a moderate consumption is. However, this does not seem to be the case in females in the cross-sectional analysis. In females, the longitudinal analysis also suggests a threshold. For me this suggests that a too high consumption of fruit and / or vegetables is no longer protective against psychological distress, cross-sectionally in males and longitudinally in females, indicating that too much fruit and / or vegetable is in fact not beneficial for mental health. The question remains as to why the authors found this cross-sectionnally in males only, and longitudinally in females only.

Response: Thank you for your helpful comment. We agree that this interpretation makes sense in light of our results, and discuss this further in the revised manuscript. As to the question relating to different results in men and women, please refer to our response to comment #3 and corresponding changes below.

Changes made: The following paragraph was added in the Discussion (page 19, lines 14-32): “Future investigations should also explore the possibility of a threshold between medium and higher consumption levels. In our study, fruit and vegetable consumption at the highest levels was not protective against psychological distress in fully-adjusted models, suggesting a potential threshold effect. This was also evident in the fully-adjusted models in the cross-sectional analysis in men, and the longitudinal analysis in women. The reason for this observation is unknown. It is possible that consuming more fruits and vegetables beyond the potential threshold is no longer beneficial. However, the observed pattern of association could also be a result of residual confounding. For example, participants consuming higher amounts of fruit and vegetables may also have been consuming larger quantities of other foods which could lead to psychological distress. However, despite adjusting for BMI in our analyses, this study did not measure other potential dietary confounders. The study’s findings also did not change when adjusting for BMI as a continuous variable rather than a categorical variable. Participants with very high fruit and vegetable consumption may have other unmeasured characteristics that could have offset the beneficial effects of fruit and vegetable consumption. Finally, it is important to acknowledge that fruit and vegetable consumption was based on a one-time measure only, which could not take into account long-term consumption patterns. However, as compared with the baseline, we found a similar pattern of consumption at follow-up (93% of participants remained in the same consumption categories between baseline and follow-up). Some of these limitations should be addressed in future studies.”

Comment 3: In females, one limitation of the longitudinal analysis is that fruit and vegetable consumption were not assessed at follow-up so the associations could still be attributable to differential consumption patterns at follow-up. Moreover, in the cross-sectional analysis in males and the follow-up analysis in females, the OR were not adjusted for other food intake, and it is possible that individuals who eat (too) large quantities of fruit and / or vegetables also eat larger quantities of other foods as well, which could lead to a higher BMI in these individuals. It is true that the analyses were controlled for BMI, but the use of categories of BMI may not have fully captured the fact that
these individuals might have had a larger BMI within each of the categories (for e.g. the authors
grouped together overweight and obese: BMI > 25, so individuals of BMI 26 are in the same category
as those with a BMI of 40). One way to find out more about this hypothesis would be to leave BMI as
a continuous variable in the adjusted models. Other confounders may have included the presence of
a series of other cardio-metabolic risk components which this study did not control for (this study
controlled for diabetes, hypertension and a history of other chronic diseases) which should be
mentioned in the limitation section.

Response: Thank you for your constructive suggestions. We acknowledge that differential
consumption patterns at follow-up could explain some of the longitudinal findings. To explore this
further, we have computed the consumption of fruit and vegetables at follow-up in the overall sample
and by sex, based on the same cut-off points used for baseline categories. We found that
consumption patterns at follow-up for fruit and vegetables (considered separately or combined), were
similar to those at baseline in the overall sample and by sex. For example, in the overall sample, on
average about 93% of participants remained in the same consumption categories between baseline
and follow-up.

There is also the possibility that high levels of fruit and vegetable consumption were accompanied by
high intakes of other foods and overall caloric intake which we were unable to account for. Based on
your suggestion, we ran all of the cross-sectional and longitudinal analyses again using BMI as a
continuous variable but the results remained essentially similar. For example, the odds ratio (95%
confidence interval) for the prevalence of psychological distress by combined fruit and vegetable
consumption was similar between baseline (cross-sectional analyses: highest tertile vs lowest tertile:
OR=0.82 [0.74, 0.92], p=0.001) and follow-up (cross-sectional analyses: highest tertile vs lowest
tertile: OR=0.82 [0.73, 0.92], p<0.001). Similarly, the odds ratio (95% confidence interval) for the
incidence of psychological distress by combined fruit and vegetable consumption was comparable
between baseline (longitudinal analyses: highest tertile vs lowest tertile: OR=0.90 [0.79, 1.03],
p=0.12) and follow-up (longitudinal analyses: highest tertile vs lowest tertile: OR=0.90 [0.79, 1.02],
p=0.11). Given similar findings, BMI was left as a categorical variable in our analyses.

Changes made: We have acknowledged that fruit and vegetable consumption was based on a one-
time measure only (Discussion, page 19, lines 28-29) and have added a sentence about finding
similar fruit and vegetable consumption patterns at baseline and follow-up (Discussion, page 19, lines
30-32), and similar findings when using BMI either as a categorical or continuous variable
(Discussion, page 19, lines 24-25). As high intakes of other foods have been discussed as limitations
of this study in the Discussion (page 19, lines 21-24) and the lack of dietary information was also
highlighted in the Strengths and Limitations section (page 20, lines 19-22), we have added other
cardio-metabolic risk components as other potential limitations of this study (Strengths and
Limitations, page 20, line 23).

Comment 4: These are some ideas regarding these differences which the authors should explore
more. In any case, the authors need to interpret the differences between moderate and high
consumption of fruit and / or vegetables and their association with psychological distress, and not
simply attribute these differences to a lack of statistical power which they are clearly not. The
discussion section should be revised accordingly and the limitations section should also be expanded
(some of the elements I mentioned are already stated, but this section could be completed).

Response: Thank you. In response to your suggestions, we have revised our interpretation of these
findings and made changes accordingly. We have also incorporated further limitations in the
Discussion section.

Changes made: Please refer to our responses to comments #1-3.
Response to Reviewer 2’s comments

General comments: Thank you for thoughtfully addressing my original comments. Though I agree with the authors’ decision not to include the available measure of physician diagnosis of depression, the absence of a measure of history of mental illness should be mentioned in the discussion as a limitation. I am also still curious about the reverse causation hypothesis, since you have the data to test this... but if the editor is satisfied without this then I am also satisfied with your discussion in the limitations section.

Response: Thank you for your suggestions. We have added the absence of a measure of history of mental illness as a limitation in the discussion. We initially attempted to address the possibility of reverse causation by excluding participants with high/very high levels of psychological distress at baseline and have also discussed reverse causation as an important limitation of this study (page 20, lines 27-33 and page 21, lines 1-4). Per the reviewer’s request, we have also tested the possibility for reverse causation in an additional exploratory analysis. We found that baseline psychological distress was not predictive of fruit and vegetable intake at follow-up (p>0.05). Altogether, we believe that our consideration of reverse causation was sufficient.

Changes made: The absence of a measure of history of mental illness has been added as a limitation of this study (Strengths and Limitations section, page 20, line 23).

Response to Reviewer 3’s comments

General comments: The manuscript has been much improved in response to comments but there are still a few things that need to be clarified/corrected.

Response: Thank you for your valuable comments.

Comment 1: Page 3 line 13. Should be ‘after’ rather than ‘during’

Changes made: We have changed ‘during’ to ‘after’ in two places in the manuscript (page 3, line 15 and page 10, line 1).

Comment 2: Page 8, line 20 p<0.05 is significant but on page 10, line 17 says interaction with sex is significant p=0.08.

Response: Thank you for noting this.

Changes made: We have rectified this sentence which now states that the interaction “approached significance” (page 10, line 17).

Comment 3: Table 1 needs to be carefully checked. The sample size for K10>22 is 551,393 which is larger than the whole study population. The ages of the two lo/hi K10 groups are over 600 years. 468% of people with hi K10 have < 10 years education and people with lo K10 have 43.9 serves of veg per day.

Response: Thank you for informing us of these typos which occurred to our inadvertence.

Changes made: We have now corrected all of these figures in Table 1 (pages 11-12).

Comment 4: In Tables 2 and 3 it would be good to include the total number of people in the heading
and then give numbers in the tertiles and number of incident cases. This would also help with the arguments that perhaps fewer cases in the top tertiles of intake resulted in non-significant ORs.

Response: Thank you for these suggestions.

Changes made: We have added the total number of people in the titles of Tables 2 and 3 (pages 14-15). The sample size and number of incident cases in each tertile have also been added in both tables (pages 14-15).

Comment 5: Table 4 is very busy. Perhaps it would be better just to show the fully adjusted model if that is the results we should focus on. Can describe in text what other models showed.

Response: In the original manuscript, Table 4 only presented full-adjusted models. However, we added unadjusted and minimally-adjusted models in response to Reviewer 1’s initial comment #2 in the previous round of revision.

Other revisions made by the authors

Other revision 1: We have further clarified our results in relation to the longitudinal findings presented in Table 4.

Changes made: We have added “and combined fruit and vegetable tertiles (p=0.09) in the fully-adjusted models” in the Results (page 10, lines 21-22).

Other revision 2: We have clarified that BMI is a categorical variable by defining BMI categories in the Methods.

Changes made: BMI categories were added in the Methods (page 8, lines 6-7).

VERSION 3 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Caroline Vandeleur</th>
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<td></td>
<td>Lausanne University Hospital, Department of Psychiatry, Prilly, Switzerland</td>
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| REVIEW RETURNED          | 06-Dec-2016                        |

| GENERAL COMMENTS         | Nguyen, Binh et al. Fruit and vegetable consumption and psychological distress: cross-sectional and longitudinal analyses based on a large Australian sample – revision 2 |

Comments to the authors:

1) Table 2, does the second column have an incorrect heading? Should Incident/total number of cases” read "prevalence/total number of cases”?
2) I had another careful look at the tables last night, and realized that there is now a confusion regarding the interpretation of the findings. It seems that I went over the sex-specific results too quickly and made an error in my interpretation. It's difficult to appreciate the findings because I don’t have access to the study data, my apologies, it is in fact more complicated than I initially thought. The authors need to correctly interpret their data if they want to publish this manuscript. Here is what I further suggest, I know this now seems never-ending but we need to eventually try and get there. My problem is with the sex-specific findings:
Cross-sectional analyses: In females, associations with moderate and high consumption remain statistically significant in all models, even in the fully adjusted model. So it seems that even high consumption is beneficial for psychological health in females cross-sectionally. Likewise, moderate fruit or vegetable consumption is associated with less psychological distress in males throughout all models. However, in males, moderate combined consumption is significantly associated with less distress until the final model. The previous association between moderate consumption and less distress appears to be cancelled out due to one or more of the adjustments. Which one(s)? Concerning high consumption (fruit and combined) in males, the associations with psychological distress disappear after the full adjustment(s). The authors should find out which one(s) cancel out the associations with psychological health; this variable / these variables are potentially mediators in the relationship between high consumption and psychological health. The authors could conduct a mediation analysis here (for e.g. using Baron and Kenny criteria). In any case, this needs to be discussed. There may be other confounders too here, but essentially the authors are capturing something in their data which seems to cancel out the association between high consumption and lower distress, and they should find out what that is. The hypothesis of “residual confounding” does not hold here because the association becomes non significant and so the previous association is explained by something the authors have indeed measured.

Prospective analyses: There appear to be no association between any consumption and psychological health in males, in either adjusted or non adjusted models. Hence, fruit and/or vegetable consumption is not linked to psychological health in males longitudinally. In females, moderate consumption stays linked to psychological health in all models (including the fully adjusted models) and appears therefore to be beneficial for psychological health. In contrast, high consumption (fruit/vegetables/combined) is not associated with psychological health ONLY in the fully-adjusted models and therefore one or more of the adjustments is/are potentially mediators in the associations which were shown in the previous models. Again, which one(s)? The authors could find this out using mediation analyses and discuss this. What is mediating the association between high consumption and psychological health in females?

The fully-adjusted models for moderate consumption also need to be controlled for BMI as a continuous variable as BMI categories are perhaps not potentially mediating the association for reasons which I explained in my previous review. Is it possible that BMI may mediate the associations between moderate consumption and less distress in females if it is kept continuous? If not, then there may be other confounders which are uncontrolled for in the analyses and which might have mediated the associations if they had been assessed.

3) The conclusion paragraph seems to be based on the authors’ beliefs that fruit and vegetable consumption is beneficial for psychological health, and not on their findings. This is not what their data are telling us. The authors should already account for the threshold findings. The authors have already shown this in this manuscript and need to show this even more, even if it still needs to be further investigated in future studies. This should be specified by saying something like (for females for example): “Moderate and high fruit and vegetable consumption may help reduce psychological distress among middle-aged and older females in the short-term, but not potentially at the highest levels of intake in females over time. In fact, high levels of fruit and vegetable consumption and low distress
in females over time were mediated by XXX”.
4) The concluding sentences of the abstract should also be changed according to the findings.

**REVIEWER**
Mila Kingsbury
University of Ottawa, Canada

**REVIEW RETURNED**
05-Dec-2016

**GENERAL COMMENTS**
Thank you for thoughtfully addressing my remaining comments.

**VERSION 3 – AUTHOR RESPONSE**

Response to Reviewer 1’s comments

Comment 1: Table 2, does the second column have an incorrect heading? Should Incident/total number of cases” read ”prevalence/total number of cases”?

Response: Thank you for noting this.

Changes made: We have changed the heading to “prevalence/total number of cases” (Table 2, page 14, second column).

Comment 2: I had another careful look at the tables last night, and realized that there is now a confusion regarding the interpretation of the findings. It seems that I went over the sex-specific results too quickly and made an error in my interpretation. It’s difficult to appreciate the findings because I don’t have access to the study data, my apologies, it is in fact more complicated than I initially thought. The authors need to correctly interpret their data if they want to publish this manuscript. Here is what I further suggest, I know this now seems never-ending but we need to eventually try and get there.

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Cross-sectional analyses: In females, associations with moderate and high consumption remain statistically significant in all models, even in the fully adjusted model. So it seems that even high consumption is beneficial for psychological health in females cross-sectionally. Likewise, moderate fruit or vegetable consumption is associated with less psychological distress in males throughout all models. However, in males, moderate combined consumption is significantly associated with less distress until the final model. The previous association between moderate consumption and less distress appears to be cancelled out due to one or more of the adjustments. Which one(s)? Concerning high consumption (fruit and combined) in males, the associations with psychological distress disappear after the full adjustment(s). The authors should find out which one(s) cancel out the associations with psychological health; this variable / these variables are potentially mediators in the relationship between high consumption and psychological health. The authors could conduct a mediation analysis here (for e.g. using Baron and Kenny criteria). In any case, this needs to be discussed. There may be other confounders too here, but essentially the authors are capturing something in their data which seems to cancel out the association between high consumption and lower distress, and they shouid find out what that is. The hypothesis of “residual confounding” does not hold here because the association becomes non significant and so the previous association is explained by something the authors have indeed measured.

Prospective analyses: There appear to be no association between any consumption and psychological health in males, in either adjusted or non adjusted models. Hence, fruit and/or vegetable consumption is not linked to psychological health in males longitudinally. In females, moderate consumption stays linked to psychological health in all models (including the fully adjusted
models) and appears therefore to be beneficial for psychological health. In contrast, high consumption (fruit/vegetables/combined) is not associated with psychological health ONLY in the fully-adjusted models and therefore one or more of the adjustments is/are potentially mediators in the associations which were shown in the previous models. Again, which one(s)? The authors could find this out using mediation analyses and discuss this. What is mediating the association between high consumption and psychological health in females?

The fully-adjusted models for moderate consumption also need to be controlled for BMI as a continuous variable as BMI categories are perhaps not potentially mediating the association for reasons which I explained in my previous review. Is it possible that BMI may mediate the associations between moderate consumption and less distress in females if it is kept continuous? If not, then there may be other confounders which are uncontrolled for in the analyses and which might have mediated the associations if they had been assessed.

Response: Thank you for these additional reflections. The authors believe that what Reviewer 1 is describing as “mediation analysis” is in fact an analysis of whether any of the covariates act as confounding variables in the association between fruit and/or vegetable consumption and psychological distress. Specifically, mediation analysis implies testing an intermediate outcome in the causal pathway, which is not the case in our current analysis (for example socioeconomic status may act as a confounder and attenuate the association between fruit and vegetable intake and psychological distress when included in the model, but it is not a mediator because fruit and vegetable intake does not lead to socioeconomic status). Based on Reviewer 1’s suggestions, we carefully investigated whether any covariate(s) cancel(s) out the associations with psychological distress in the overall prospective analyses with fruit and/or vegetable consumption, and in the sex-specific analyses detailed in Reviewer 1’s comment #2, by manually entering each variable in a step-by-step fashion into the models. In each analysis that was conducted (with BMI used as a continuous variable), all potential confounders alone changed the magnitude of the association minimally (<10% change in odds ratio), and no variable alone independently cancelled the significance of the association. We therefore conclude that the association between fruit and vegetable consumption and psychological distress was attenuated by the collection of covariates adjusted for in the full model, namely, socioeconomic status and other lifestyle risk factors. Again, this should not be interpreted as an indirect effect in mediation analysis, but rather, those who consumed healthy amounts of fruit and vegetables are also more likely to be of higher socioeconomic status and to engage in other health-promoting lifestyle behaviours (such as physical activity and not smoking), and they are also more likely to have lower distress.

Although we used BMI as a continuous variable in the above analyses, we had noted in our response to Comment #3 in the previous round of comments that the study’s results remained essentially similar when BMI was included as a continuous variable and had therefore, decided to leave BMI as a categorical variable in the analyses. We had also added a sentence in relation to this issue in the Discussion (current manuscript, page 19, lines 23-24).

Changes made: We have added two sentences in the Discussion (page 18, lines 31-33 and page 19, lines 1-3) about the possibility of confounding:

“In the case of our study, the longitudinal association between fruit and vegetable consumption and psychological distress was attenuated the most between the age and sex-adjusted model and the fully-adjusted model, suggesting confounding. This may indicate that those who consume healthy amounts of fruit and vegetables are more likely to have favourable socioeconomic status and other lifestyle risk factors (e.g., physical activity), which together contributed to lower psychological distress.”

Comment 3: The conclusion paragraph seems to be based on the authors’ beliefs that fruit and
vegetable consumption is beneficial for psychological health, and not on their findings. This is not what their data are telling us. The authors should already account for the threshold findings. The authors have already shown this in this manuscript and need to show this even more, even if it still needs to be further investigated in future studies. This should be specified by saying something like (for females for example): "Moderate and high fruit and vegetable consumption may help reduce psychological distress among middle-aged and older females in the short-term, but not potentially at the highest levels of intake in females over time. In fact, high levels of fruit and vegetable consumption and low distress in females over time were mediated by XXX".

Response: Thank you for your comment. We have made changes to the concluding paragraph.

Changes made: Several sentences (Conclusions, page 21, lines 8-12 and line 15) have been added and the concluding paragraph now reads as follows:

"Fruit and vegetable consumption may help reduce the prevalence of psychological distress among middle-aged and older adults. However, the association between fruit and vegetable consumption and the incidence of psychological distress requires further investigation and possibly, a longer follow-up time. Fruit and vegetable consumption may help reduce psychological distress among middle-aged and older females in a cross-sectional context, but not potentially at the highest levels of intake in females over time. Consumption at medium levels of intake may help lower psychological distress in men in a cross-sectional context; however, longitudinal associations remain unclear. Although findings from this study lend support to existing public health guidelines which encourage fruit and vegetable consumption as part of a healthy diet and add evidence to support the benefits of fruit and vegetables for mental health, further research is clearly needed."

Comment 4: The concluding sentences of the abstract should also be changed according to the findings.

Response: Thank you for this suggestion. We have made changes to the concluding sentences of the abstract in relation to the threshold findings. Due to space constraint, we have not added specific sentences relating to findings based on sex.

Changes made: The following words have been added to the concluding sentence of the abstract (page 3, lines 25-26): "including the possibility of a threshold effect between medium and higher consumption levels."

Response to Reviewer 2’s comments

General comments: Thank you for thoughtfully addressing my remaining comments.

Response: Thank you for all of your comments.

Other revisions made by the authors

Other revision 1: We have inserted a comma in one of the sentences in the Discussion.

Changes made: We have added a comma after “drug use” (Discussion, page 20, line 22).

Other revision 2: We have added one word to one of the paragraphs in the Discussion.

Changes made: We have added the word “generally” in line 3, on page 18 of the Discussion.
Other revision 3: We have updated the Acknowledgements section.

Changes made: We have made changes to the Acknowledgements section (page 22, line 3 and lines 6-7).

VERSION 4 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Caroline Vandeleur</th>
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<tr>
<td>Lausanne University Hospital, Department of Psychiatry, Lausanne, Switzerland</td>
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| REVIEW RETURNED  | 30-Jan-2017 |

| GENERAL COMMENTS | Thank-you to the authors for their efforts in responding to my questions. I think this manuscript should be published now, and further analyses could be conducted in a subsequent paper. |
Fruit and vegetable consumption and psychological distress: cross-sectional and longitudinal analyses based on a large Australian sample

Binh Nguyen, Ding Ding and Seema Mihrshahi

*BMJ Open* 2017 7:
doi: 10.1136/bmjopen-2016-014201

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