Subject: BMJ - Decision on Manuscript ID BMJ.2014.023070

Body: 12-Jan-2015

Dear Dr. Imamura

Manuscript ID BMJ.2014.023070 entitled “Consumption of sweet beverages and incidence of type 2 diabetes: a systematic review, meta-analysis, and estimation of population attributable fraction”

Thank you for sending us this paper, which we were pleased to have the chance to consider, enjoyed reading and have discussed in our manuscript committee meeting.

We recognise its potential importance and relevance to general medical readers, but we have not yet been able to reach a final decision on it. This is because several important aspects of the work still need clarifying.

We hope very much that you will be willing and able to revise your paper as explained below in the report from the manuscript committee meeting, so that we will be in a better position to understand your study and to decide whether The BMJ is the right journal for it.

I include below the comments from our our meeting along with the reviewer comments. In addition to any revision to the manuscript please respond to these comments with point-by-point response.

**THE REPORT FROM THE MANUSCRIPT COMMITTEE MEETING, REVIEWERS’ REPORTS, AND THE BMJ’S GENERAL REQUIREMENTS FOR RESEARCH PAPERS ARE AVAILABLE AT THE END OF THIS LETTER.**

First, however, please read these four important points about sending your revised paper back to us:

1. Deadline: Your revised manuscript should be returned within one month.

2. Online and print publication: All original research in The BMJ is published with open access. The full text online version of your article, if accepted after revision, will be the indexed citable version (full details are at http://resources.bmj.com/bmj/about-bmj/the-bmjs-publishing-model). While the print and iPad BMJ will carry an abridged version of your article, usually a few weeks after. This abridged version of the article is essentially an evidence abstract called BMJ pico, which we would like you to write using a template and then email it to papersadmin@bmj.com (there are more details below on how to write this using a template). Publication of research on bmj.com is definitive and is not simply interim “epublication ahead of print”, so if you do not wish to abridge your article using BMJ pico, you will be able to opt for online only publication. Please let us know if you would prefer this option.

If/when your article is accepted we will invite you to submit a video abstract, lasting no longer than 4 minutes , and based on the information in your paper’s BMJ pico evidence abstract. The content and focus of the video must relate directly to the study that has been accepted for publication by The BMJ, and should not stray beyond the data.

3. Open access publication fee: The BMJ is committed to keeping research articles Open Access (with Creative Commons licences and deposit of the full text content in PubMedCentral as well as fully Open Access on bmj.com). To support this we are now asking all authors to pay an Open Access fee of £3000 on acceptance of their paper. If we accept your article we will ask you to pay the Open Access publication fee; we do have a waiver policy for authors who cannot pay. Consideration of your paper is not related to whether you can or cannot pay the fee (the editors will be unaware of this), and you need do nothing now.

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You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center. When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) and Committee in the space provided. You can use this space to document any changes you make to the original manuscript and to explain your responses. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

**IMPORTANT:** Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Many thanks again. We look forward to seeing your revised article within a month and, we hope, to reaching a decision. Please do not hesitate to contact me if you have any queries, quoting your manuscript ID.

Yours sincerely
As well as submitting your revised manuscript, we also require a copy of the manuscript with changes highlighted. Please upload this as a supplemental file with file designation ‘Revised Manuscript Marked copy’.

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

INFORMATION ON REVISING THE CONTENT AND FORMAT OF YOUR ARTICLE

**Report from The BMJ's manuscript committee meeting**

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript. Members of the committee were: Elizabeth Loder (chair), Jon Deeks (statistician), Emma Parish, Tiago Villanueva, Rebecca Burch, Wim Weber and Georg Roggla. Kristina Fister abstained from comment.

Decision: Request revisions

Detailed comments from the meeting:
First and foremost, please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below.

Please also respond to these additional comments by the committee:

*Editors feel the title of the paper could be improved to make clearer the different beverage types included in this review.*

*Explanation of findings could be clearer throughout the manuscript. There is a very large number of supplementary files, tables and diagrams. It would be helpful if these could be reduced to the most important and essential supplementary items.*

*Our statistician team have advised they would encourage more documentation of confounders and how these were dealt with. They have advised to include these as part of the quality assessment (Cochrane has a new tool for assessing quality of non-randomised intervention studies which could help).*

*While the conclusions drawn from statistical analysis seem appropriate, the methods as described are overly-complicated and would benefit from clearer explanation and less supplementary material.*

*We do not want fixed effect analyses and feel the graphs on page 18 of the material give the wrong impression about the precision of estimates at the lowest category.*

*Observational and reverse causality was a concern and the editors would like the authors to discuss this in more detail in the limitations of the study.*

*It would also be helpful to explain more clearly the clinical application of the findings in the discussion.*

*Please address reviewer concerns as included at the end of this letter.*

IMPORTANT

When you revise and return your manuscript, please take note of all the following points about revising your article. Even if an item, such as a competing interests statement, was present and correct in the original draft of your paper, please check that it has not slipped out during revision.

a. In your response to the reviewers and committee please provide, point by point, your replies to the comments made by the reviewers and the editors, and please explain how you have dealt with them in the paper. It may not be possible to respond in detail to all these points in the paper itself, so please do so in the box provided.

b. If your article is accepted it will then be edited, proofed, and - after your approval - published on bmj.com with open access. This open access Online First article will not be a pre-print. It will represent the full, citable, publication of that article. The citation will be year, volume, elocator (a unique identifier for that article): eg BMJ 2008;337:a145 — and this is what will appear immediately in Medline, PubMed, and other bibliographical indexes. We will give this citation in print and online, and you will need to use it when you cite your article.

c. Please write an abridged version of the article for the print and iPad BMJ using the appropriate BMJ pico template for your study’s design. Please be reassured that it doesn’t take long to complete this. When your BMJ pico is ready please email it to papersadmin@bmjgroup.com. The templates for you to download are at http://resources.bmj.com/bmj/authors/bmj-pico

d. Please include these items in the revised manuscript to comply with BMJ style:

Title: this should include the study design eg “systematic review and meta-analysis”
Abstract
structured abstract including key summary statistics, as explained below (also see http://resources.bmj.com/bmj/authors/types-of-article/research) for every clinical trial - and for any other registered study - the study registration number and name of register – in the last line of the structured abstract.

Introduction
this should cover no more than three paragraphs, focusing on the research question and your reasons for asking it now

Methods:
for an intervention study the manuscript should include enough information about the intervention(s) and comparator(s) (even if this was usual care) for reviewers and readers to understand fully what happened in the study. To enable readers to replicate your work or implement the interventions in their own practice please also provide (uploaded as one or more supplemental files, including video and audio files where appropriate) any relevant detailed descriptions and materials. Alternatively, please provide in the manuscript urls to openly accessible websites where these materials can be found

Results
please report statistical aspects of the study in line with the Statistical Analyses and Methods in the Published Literature (SAMPL) guidelines http://www.equator-network.org/reporting-guidelines/sampl/

summary statistics to clarify your message. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:

For a clinical trial:
• Absolute event rates among experimental and control groups
• RRR (relative risk reduction)
• NNT or NNH (number needed to treat or harm) and its 95% confidence interval (or, if the trial is of a public health intervention, number helped per 1000 or 100,000)

For a cohort study:
• Absolute event rates over time (e.g. 10 years) among exposed and non-exposed groups
• RRR (relative risk reduction)

For a case control study:
• OR (odds ratio) for strength of association between exposure and outcome

For a study of a diagnostic test:
• Sensitivity and specificity
• PPV and NPV (positive and negative predictive values)

one or more references for the statistical package(s) used to analyse the data, e.g. RevMan for a systematic review. There is no need to provide a formal reference for a very widely used package that will be very familiar to general readers e.g. STATA, but please say in the text which version you used for articles that include explicit statements of the quality of evidence and strength of recommendations, we prefer reporting using the GRADE system

Discussion
please write the discussion section of your paper in a structured way, to minimise the risk of careful explanation giving way to polemic. Please follow this structure: statement of principal findings of the study strengths and weaknesses of the study strengths and weaknesses in relation to other studies, discussing important differences in results and what your study adds. Whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses (e.g. Cochrane reviews) meaning of the study: possible explanations and implications for clinicians and policymakers and other researchers; how your study could promote better decisions unanswered questions and future research

Footnotes and statements
What this paper adds/what is already known box (as described at http://resources.bmj.com/bmj/authors/types-of-article/research)

ID of ethics committee approval and name of the ethics committee/IRB; or a statement that approval was not required (see http://resources.bmj.com/bmj/authors/editorial-policies/guidelines) and a statement that participants gave informed consent before taking part

a statement that any identifiable patients have provided their signed consent to publication. Please submit, as a supplemental file, the signed BMJ patient consent form giving consent to publication in The BMJ of any information about identifiable individual patients. Publication of any personal information about a patient in The BMJ, for example in a case report or clinical photograph, will normally require the signed consent of the patient.

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a data sharing statement declaring what further information and data you are willing to make available, over and above the results reported in the paper. Suggested wording: "Data sharing: technical appendix, statistical code, and dataset [state whether any patient level data have been anonymised] are available at this repository or website OR from the corresponding author at ". If there are no such further data available, please use this wording: "Data sharing: no additional data available". For papers reporting the main results of trials of drugs or devices we require that the authors state, at a minimum, that the relevant anonymised patient level data are available on reasonable request from the authors.
The BMJ has partnered with the Dryad Digital Repository datadryad.org to make open deposition easy and to allow direct linkage by doi from the dataset to the BMJ article and back - we encourage authors to use this option.

Patient centred research

for studies that are relevant to patients we expect authors to report in their articles the extent of their study’s patient-centredness, as highlighted by these questions:
did you involve patients/service users/carers/lay people in the design of this study? Please state whether you did, and give details (Methods section)
was the development and/or selection of outcome measures informed by patients’ priorities and experiences? Please give details (Methods section)
were patients/service users/carers/lay people involved in developing plans for participant recruitment and study conduct? If so, please specify how (Methods section)

have you planned to disseminate the results of the study to participants? If so how will this be done? (Describe in brief footnote)
are patients thanked in the contributorship statement or acknowledgements?

for articles reporting randomised controlled trials: did you assess the burden of the intervention on patients’ quality of life and health? If so, what evaluation method did you use, and what did you find? (Methods and Results sections)

REFEREES COMMENTS

Reviewer: 1

Recommendation:

Comments:
This is a rigorously conducted systematic review and meta-analysis that examined the role of sweet beverage consumption in the incidence of type 2 diabetes. Several earlier meta-analyses have summarized observational studies that examined sugar-sweetened beverage consumption and type 2 diabetes (e.g., Greenwood et al. Br J Nutr. 2014; Malik et al. Diabetes Care 2010). However, the paper adds important policy-relevant measures such as population attributable fraction. The main strengths include a range of sensitivity analyses to examine the robustness of their findings as well as an estimation of population attributable fraction. Major limitations include high heterogeneity in estimates across studies and potentially a high risk of bias because of the nature of observational studies. There are points that should be better addressed:

Major points:
Introduction
1. (Page 4, lines 21 to 35) The authors considered adiposity as a potential confounder between sweet beverage consumption and type 2 diabetes risk. However, as sweet beverage consumption can elevate the risk of obesity/overweight, adiposity could also be a mediator between sweet beverage consumption and
type 2 diabetes risk. The authors should explicitly state that adjustment for adiposity may control confounding, but also remove the mediation effect and potentially bias the estimate.

2. (Page 4, lines 27-35) The authors stated that no review has quantified population attributable fraction due to sugar-sweetened beverages for type 2 diabetes. A recently published modelling study reported the population preventable fraction for type 2 diabetes by taxing sugar-sweetened beverages in India (PLoS Med 11(1): e1001582. doi:10.1371/journal.pmed.1001582).

As the paper published in PLoS Med provides relevant information, I suggest the authors mention the findings in the manuscript.

Methods:

1. The authors stated that they followed the PRISMA guidelines but they did not state whether the protocol of the systematic review was registered in database(s) such as the PROSPERO database.

2. Eligibility criteria included follow-up of at least two years. Two years of follow-up may be too short to examine the risk of type 2 diabetes. Please provide relevant information to support this criterion.

3. In the estimation of population attributable fraction, the authors modelled if the sugar-sweetened beverage consumption would become zero. It might be difficult to eliminate sugar-sweetened beverage consumption from the UK or US. Alternatively, it may be practical to reduce the contribution of sugar-sweetened beverages to <5% of total energy intake (or tax sugar-sweetened beverages). Thus, I would suggest the authors examine the fraction under different scenarios.

4. (Page 33, lines 15 to 18) In the supplemental text, the authors provided procedures to estimate population attributable fraction in the UK and US. They stated that (3) estimated separate ideal 10-year risk (Ri) if all adults reduced their SSB consumption to zero. Please describe a more detailed explanation to derive Ri.

Results

1. (Page 9, lines 13 to 25) According to Table S6, many studies, including CARDIA, EPIC-Inter Act, SCHS, and MESA, did not control for a family history of diabetes. Because a family history of diabetes is a strong risk factor for type 2 diabetes, risk of bias is potentially high in these studies. Moreover, age was not listed as a covariate in studies, including NHS I, NHS II, HPFS, EPIC-InterAct, E3N; I believe these studies controlled for age. Thus, please check whether covariates are accurately listed. If such important covariates were not controlled in the included studies, the risk of bias of this meta-analysis is high; I suggest that the authors conduct additional sensitivity analysis (or bias analysis) to examine the impact of residual confounding due to these factors.

2. (Page 10, lines 3 to 4) A possible non-linear association was assessed using a cubic spline model. However, only 13 studies were included in this analysis because category-specific estimates of the other four studies were not available. Did the authors contact the authors of those studies to request the category-specific estimates? In addition, because the evaluation of the dose-response relationship is quite important in the meta-analysis of nutritional epidemiologic studies, it may be more informative to show the spaghetti plots proposed by Dr. Eric Ding to graphically illustrate the shape and direction of the dose-response relationship of individual study.

3. (Page 11, lines 9 to 11) The authors described the results of examining potential influence of residual confounding by measured adiposity with a focus on "statistical significance". As the degree of bias (or confounding) matters, we should focus instead on the magnitude and direction of the corrected estimates. Based on the displayed results, the magnitude of the estimate was attenuated after incorporating residual confounding by measured adiposity.

Discussion

1. The population attributable fraction is a useful measure but we need to assume that all other lifestyle factors remain constant after eliminating sugar-sweetened beverages. From a public health perspective, the possible impact of eliminating sugar-sweetened beverages on other lifestyle factors such as added sugar consumption (not from beverages) or fat consumption may deserve discussion. What are the authors' expectations?

Minor point:

1. (Page 7, lines 11 to 12) Should two-sided α=0.1 be revised to two-sided α=0.2?

Additional Questions:
Please enter your name: Atsushi Goto

Job Title: Assistant Professor

Institution: Department of Public Health, Tokyo Women's Medical University

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No
Reviewer: 2

Recommendation:

Comments:
Thank you for giving me the opportunity to review this interesting article. The review which examines the association between consumption of sugar sweetened beverages, artificially sweetened beverages, fruit juice and incidence T2DM has been conducted and reported to a high standard. I believe the report will be of interest to the BMJ readership, and comes at a time when interest in this topic is growing. I would recommend a statistician review the methods.

Abstract
The conclusion should be reworded to make it clearer that the estimation of 2 million events in the USA and 80 thousand events in the UK of T2DM are based on assumptions. In addition the phrase "but still support not consuming ASB or fruit juice as alternatives to SSB" is confusing to the reader, please re-phrase.

Introduction
Some re-wording of sentences is required, please check the introduction, and the whole document for grammar and sentence structure. For example, page 4, line 11: "T2DM have not be well established"

Methods
Please make it clearer what volume your definition of "serving/day" is equivalent to. It is unclear what confounders have been adjusted for; I would prefer to see an unadjusted RR presented, followed by the adjusted RR (with a clearer presentation of what confounders have been included) and then the adiposity adjusted RR. RR and OR are not the same, although converted this should be noted as a limitation in the discussion.

Results
On page 10, line 31, it states after stratification none of the beverages were significantly associated with T2DM. Please can you provide more information on this.

Discussion
The discussion is nicely presented, however please note a number of limitations; the data is from observational studies, interventions would be of interest and add to the findings. Have you adjusted for lifestyle factors? As stated earlier, this is unclear. Those who drink SSB may have other behaviours which are detrimental to their health.

Table S1; a number of studies were excluded but the table does not make it clear if they were excluded because they were ineligible due to study design or ineligible because the authors did not respond to your contact? If this is the case this is unfortunate.

Additional Questions:
Please enter your name: Patrice Carter
Job Title: Diabetes, Nutrition and Lifestyle Research Associate
Institution: The University of Leicester

Reimbursement for attending a symposium?: No
A fee for speaking?: No
A fee for organising education?: No
Funds for research?: No
Funds for a member of staff?: No
Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No
Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here:

Reviewer: 3
Recommendation:

Comments:
TO EDITOR:
This is a manuscript on a very interesting topic: the relationship between consumption of sweet beverages and incidence of type 2 diabetes, one of the epidemics of the XXI century. No previous review or It is especially relevant the estimation of the population attribute fraction for type 2 diabetes due to sweet beverages. However, in addition to adiposity, I think that the authors should take into account in the statistical analysis the consumption of other foods that have been related to protection against diabetes (whole-grain cereals, coffee, tea, skimmed milk, fruit, vegetables, legumes, nuts and moderate alcohol intake) or induction of diabetes (red meat, processed meat products, eggs and high alcohol intake). Other lifestyle factor related to diabetes is physical activity. In addition, these dietary and lifestyle factors should be included in the discussion.

TO THE AUTHORS:
This is a very interesting systematic review and meta-analysis on the relationship between consumption of sweet beverages and incidence of type 2 diabetes. It is especially relevant the estimation of the population attributable fraction (PAF) for type 2 diabetes due to sweet beverage intake. No previous review or individual study has evaluated PAF. They concluded that habitual consumption of sweet beverages is associated with a greater type 2 diabetes incidence, independently of adiposity. However, the authors should take into account the following in order to improve the quality of the manuscript:
1. According to the conclusions of a landmark study (Nurses') on key factors that may influence the appearance of diabetes mellitus in 84,941 nurses followed up a mean of 16 years (N Engl J Med 2001;345:790), the main factors that induced diabetes were: body weight, physical activity, smoking, moderate consumption of alcohol and four dietary factors (intake of fiber, PUFAs/SFAs, trans fatty acids and low glycemic load foods). In addition to adiposity, these other factors should be taken into account in the statistical analysis and also included in the discussion.
2. Diabetes has also been related to high consumption of several foods such as red meat, processed meat products and eggs. On the other hand, consumption of other foods may protect against the development of diabetes such as whole-grain cereals, coffee, tea, skimmed milk, fruit, vegetables, legumes and moderate consumption of alcohol. These other key foods should be included in the analysis.

Additional Questions:
Please enter your name: Ramon Estruch
Job Title: Associate Professor - Senior Consultant
Institution: Hospital Clinic - University of Barcelona, Spain
Reimbursement for attending a symposium?: No
A fee for speaking?: No
A fee for organising education?: No
Funds for research?: No
Funds for a member of staff?: No
Fees for consulting?: No
Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No
Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No
If you have any competing interests (please see BMJ policy) please declare them here: NO

Reviewer: 4
Recommendation:
Comments:
This meta-analysis used standard methodology and was thoroughly conducted. My only comment is about presentation of the ASB and fruit juice results as the authors have mentioned the issues of heterogeneity and potential reverse causation. I can see that authors tried to be careful about this by mentioning multiple times the caveats and caution needed for interpreting the ASB and fruit juice results, but this study has the potential to see a lot of media attention, so one can't be too careful (throughout the entire manuscript). In particular, the first sentence of the discussion lumps all three beverages together. Although the authors did specify that it was about the summary estimates, it is confusing then to see another sentence later saying that the estimates for ASB and fruit juice could be questionable, I think it is better not to mention ASB and fruit juice in the same sentence as SSB, and maybe use something like "Although ASB and fruit juice also shown......, however, .......(caveats, potential bias).....".

Regarding the reverse causation, could the authors check the "table 1" of the original papers to see if those consumed high amounts of ASB were also at high risk (e.g. obesity, physical activity, etc) than those with
Additional Questions:
Please enter your name: Teresa Fung
Job Title: Professor
Institution: Simmons College
Reimbursement for attending a symposium?: No
A fee for speaking?: No
A fee for organising education?: No
Funds for research?: No
Funds for a member of staff?: No
Fees for consulting?: No
Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No
Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No
If you have any competing interests (please see BMJ policy) please declare them here:

Date Sent: 12-Jan-2015