Dear Dr. Imamura

Manuscript ID BMJ.2014.023070.R1 entitled “Consumption of sugar-sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: a systematic review, meta-analysis, and estimation of population attributable fraction”

Thank you for sending us this revised paper, which we have read again with interest. We have not yet been able to reach a decision as there are still some points raised by reviewers which we very much hope you will be willing and able to respond to.

The comments from the reviewers can be found at the end of this letter. Please respond to each point made, as well as with any amendments you may make to the manuscript itself.

We appreciate your efforts to clarify these points and look forward to seeing your revised article within one month and, we hope, to reaching a decision.

Yours sincerely

Emma Parish
Editorial Registrar - The BMJ
eparish@bmj.com,
https://mc.manuscriptcentral.com/bmj?URL_MASK=256e9871b2ea45a9a7f3bbf454290c7

** THE 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:

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INFORMATION ON REVISING THE CONTENT AND FORMAT OF YOUR ARTICLE

a. In your response to the reviewers please provide, point by point, your replies to the comments made, 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.

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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:
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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:
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• RRR (relative risk reduction)

For a case control study:
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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, eg 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 eg 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 (eg Cochrane reviews)

meaning of the study: possible explanations and implications for clinicians and policymakers
and other researchers; how your study could promote better decisions

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Footnotes and statements

What this paper adds/what is already known box (as described at
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to submit the article for publication

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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)

Reviewer: 1
Recommendation:
Comments:
Thank you again for giving me the opportunity to review this revised paper. I think that the authors have made substantial efforts to improve the paper and I agree with most of their responses; however, there are several points that I believe still need to be addressed.

3. GRADE system: I am pleased to see that the authors have adopted the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to rate the quality of evidence. However, I am not sure whether the authors have followed the principles of the GRADE system appropriately. According to the GRADE handbook (Schünemann H et al. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from www.guidelinedevelopment.org/handbook), the quality of evidence from observational studies is initially classified as low. Factors for downgrading the evidence include study limitations, indirectness of evidence, inconsistency of results (i.e., unexplained heterogeneity of results), publication bias, and imprecision. Factors for upgrading the evidence include a dose-response relation, a large effect, or the existence of plausible confounders that would result in the underestimation of the true effects. Of note, the 5 factors for downgrading quality of evidence must be rated prior to the 3 factors for upgrading it and the decision to upgrade should only be made when serious limitations in any of the 5 factors reducing it are absent.
Please provide an explicit explanation for your evaluation. I also suggest that the authors specify the investigators who assessed the quality.

Additional Questions:
Please enter your name: Atsushi Goto
Job Title: Assistant Professor
Institution: Department of Public Health, Tokyo Women’s Medical University

If you have any competing interests (please see BMJ policy) please declare them here: I have
received lecture fees from Boehringer Ingelheim and Takeda Pharmaceutical Co. Ltd.

Reviewer: 2
Recommendation:
Comments: Thank you for providing me with an opportunity to re-read this manuscript. As initially noted this is a rigorously conducted meta-analysis, on an interesting topic which is gaining interest from both researcher and the public alike.

The manuscript now demonstrates much more clarity; the methods have greater transparency and the results are well presented. The additional information regarding confounding variables and acknowledgement of limitations provides a well-balanced and comprehensive article. The accuracy and attention to detail has been greatly improved, making the manuscript a pleasure to review. I believe the research will be of interest to the BMJ readership.

Additional Questions:
Please enter your name: Dr Patrice Carter
Job Title: 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
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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
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Reviewer: 3
Recommendation:
Comments: Statistical Review BMJ.2014.023070.R1

Consumption of sugar-sweetened beverages, artificially sweetened beverages and fruit juice and incidence of type 2 diabetes

The authors have submitted a revised manuscript.

The authors have now included a quality assessment process for the included studies which is based around the Cochrane ACROBAT-NSRI tool for assessing risk of bias in non-randomised intervention studies. I am not completely clear from the manuscript how they have undertaken this process or that the results of it have been appropriately presented.

1. Page 6 – they do not describe whether the ACROBAT-NSRI assessment was undertaken by a single observer, checked by a second or done independently in duplicate.

2. Page 6 - it also state here that sensitivity analysis was undertaken for each of the seven quality domains in the ACROBAT-NSRI tool, but no results of these are mentioned in the text or presented in any table.

3. Page 9 – a key aspect of the ACROBAT-NSRI tool is documenting which confounders are balanced/matched/adjusted for in each study. There is no list of the confounders reported – the best description is given in the middle of page 9 as "socio-demographic variables, clinical factors (family history of diabetes or prevalent diseases) and lifestyle factors including a diet". However, the adjustments used in Table 2 are noted in the footer as being only for "demographic and lifestyle covariates" which isn't the same. The legend for Figure 1 doesn't
mention adjustment for these factors at all, which I presume is an oversight. I would have expected, particularly given the extension supplementary material provided, to have a tabulation of the actual adjustments made study-by-study. Table S4 gives the results of unadjusted and adjusted analyses and does not fully state what was adjusted for.

4. It is also not clear what criteria were used to rate the risk of confounding. In Table S2 it is noted that only one study was rated as being at high risk of bias due to confounding. Table S4 lists four studies of omitting adjustment for "diet and clinical factors" so it is not clear why these are also not flagged as being at risk of bias from confounding. Other studies may omit other key variables, but given that no list of variables is presented we cannot tell.

5. There is no mention whether the analyses of the drink types are mutually adjusted for each other (for example, is the SSB analysis adjusted for ASB and fruit juice?) It is hard to think that consumption of each drink is independent.

6. Table S2 and Supplementary material on page 17. Overall quality assessment has to make a leap from the ratings of the individual domains to obtaining an overall assessment of likelihood of bias. It is not clear what rule the authors used to achieve this. The text on page 17 does not describe a consistent system for doing this. For example, studies 25 and 48 are stated as being at high risk of bias because their classification of diet was wrong, but the other seven studies marked as having high risk of bias on the dietary measures domain are not classified as being at high risk of bias overall. The same problem appears across multiple domains in the tool.

7. Page 13 – the authors indicate that publication bias created a false positive effect for ASB. However, the degree of publication bias seems rather small (not really visible at all in the funnel plot) and adjustment for it did not substantially change the magnitude of the effect.

8. Page 11 - The authors make GRADE assessment and place two outcomes (ASB and fruit juice) as being of low quality and one (SSB) as being of moderate quality. There is no strong argument why SSB is argued to be of moderate quality. It is hard to see why one outcome would differ from the others given that they are all reported in the same studies which were done using the same methods and adjusted for the same confounders. Given that the estimates for both SSB and ASB shift considerably between the analyses adjusting for measurement error, confounders and publication bias, it is hard to attribute moderate or high credibility to any of them. The estimate for fruit juice seems to be close to a null effect in all analyses – the authors seem distracted by it moving either side of the null effect value, but it seems consistently close to it in all analyses.

9. The population attributable fraction computations are based on assumptions of causality, and on reducing consumption of the three types of drink to zero. Given that the estimates of effect vary considerably between the sensitivity analyses, they perhaps should investigate how much the estimates varies. The authors do state the assumptions behind this, and indicate that causality is a concern, but are keen to promote intense public health interventions based on this evidence. Would not trials of SSB reduction be justified now rather than public health interventions? Also I wonder whether the illustration would be more helpful if it were based on the sort of magnitude of reduction in SSB that was achievable by a public health intervention and not an unachievable reduction to zero.

Additional Questions:
Please enter your name: Jon Deeks
Job Title: Professor of Biostatistics
Institution: University of Birmingham
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
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If you have any competing interests (please see BMJ policy) please declare them here:
Reviewer: 4

Recommendation:

Comments:
The authors have answered all queries appropriately. The manuscript has been improved. No more concerns on the manuscript. Congratulations to the authors.

Additional Questions:
Please enter your name: Ramon Estruch

Job Title: Assistant Professor of Medicine

Institution: Hospital Clinic, School of Medicine, University of Barcelona

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: Yes

Funds for a member of staff?: No

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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: I have received funds from the Spanish Government to study the effects of Mediterranean diet on cardiovascular system. The Mediterranean Diet, as dietary pattern, does not include the consumption of sugar-sweetened beverages or artificially sweetened beverages, but it includes consumption of fruit juice.

(Document not available)

Date Sent: 19-Apr-2015