

8-Jan-2016

Dear Dr. Borgi,

Manuscript ID BMJ.2015.030374 entitled "Long-term Potato Intake and the Incidence of Hypertension in Three Prospective Cohort Studies"

Thank you for sending us your paper. We sent it for external peer review and discussed it at our manuscript committee meeting. We are very interested in proceeding with it, but request that you revise the paper in accordance with reviewer and editorial comments before we make a final decision about it.

We are looking forward to reading the revised version and making a final decision.

Very truly yours,

Elizabeth Loder, MD, MPH
BMJ Editorial Team

https://mc.manuscriptcentral.com/bmj?URL_MASK=b8720d71f71e48df90b935bed78fc03a

****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.

Present: Present: Wim Weber (chair); Angela Wade (statistician); Tiago Villanueva; Jessamy Bagenal; Jose Merino; Georg Roeggla; Rubin Minhas; Elizabeth Loder

Decision: Request revisions before final decision

* We wondered if some of the findings might be driven by sodium content rather than potatoes themselves. Could you discuss this more thoroughly?

* Please include a full statement on patient involvement. Typically we ask that the statement be worded as follows (if this accurately reflects the extent of patient involvement):

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

* Our statistician had a number of comments. She will be reviewing the revised version of the paper and will be looking for responses to the following:

- For all analyses the pooled HR are presented using fixed effects models whereas random effect models would be better to generalise from (Wang mentions this too). The random effects models should be presented.

- It does seem that sex may be a major factor and this is alluded to in the discussion. The HPFS (male) cohort appear to have a different relationship than the other 2 (female) cohorts. We think there should be more discussion of this, although since sex and cohort are confounded there is no way to separate the potential effects.

-Information for 3 potato groups was collected in 9 categories. These categories were collapsed for the analysis into 4 for each potato group and 5 categories for all 3 groups combined. It is not clear how cumulative averages over time were calculated for the analyses. Does this mean the modal category recorded at that time?

-The substitution analyses use the HRs for the alternatives to represent the 'effect' of replacing one portion of potatoes. Whilst these HR will give the difference associated with a unit increase, why is a unit decrease in potatoes (and the associated fall in HR) also incorporated into the calculation?

-Only one HR from table 6 (substitution analyses) is discussed in the text and this is highlighted as significant. The other values should also be discussed to reach a conclusion from the findings here. Why is the NHS II value only given in the results section? (The more appropriate combined value is given in the abstract.)

-The results in table 5 require more discussion. A significant association becomes non-significant after adjustment for a variety of factors. What is the adjustment that is making a difference?

-Hypertension was self-reported and presumably the participants gave a date of onset which was used in the cox models. We should clarify this and that it would not be better to have used interval censored models (ie. if it was only recorded as present/absent at each of the 4 year assessments).

-It should also be clarified that the cox models incorporated the updated BMI, smoking etc. information as time-varying

covariate.

* We wonder whether it is appropriate to use the phrase "long term" in the title. Do we know that participants continued these dietary patterns long term?

First, 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:

In your response please provide, point by point, your replies to the comments made by the reviewers and the editors, explaining how you have dealt with them in the paper.

Comments from Reviewers

Reviewer: 1

Recommendation:

Comments:

This is an interesting study examining the association between potato consumption and diagnosed hypertension in three cohorts – the Nurses' Health Study I and II and the Health Professionals Follow-up study in the US. Appropriate adjustment is made in the analysis for confounding by factors such as BMI and change in weight.

The introduction is too US centric for an international audience. It would be useful to refer to international recommendations (eg WHO recommendations about portions of fruit and vegetables state "Potatoes, sweet potatoes, cassava and other starchy roots are not classified as fruits or vegetables" <http://www.who.int/mediacentre/factsheets/fs394/en/> although FAO guidelines do not.

The major limitation of the study is that the determination of hypertension based on self-report. While validation studies have confirmed the positive predictive value of this against samples of measured blood pressure in the cohorts, they have not confirmed the negative predictive value of this. Other studies have suggested an 89% NPV (Okura Y 2004). It should be discussed that false negative individuals may have had lower educational background or income and this may have been correlated diet.

The findings that participants who consumed 4 or more servings of potato chips per week had a lower risk of developing hypertension in men in the HPFS and no association in the other two cohorts is puzzling. This is discussed. However the most likely explanation is residual confounding. It is possible that sodium intake was poorly assessed in the food frequency questionnaire (high variances from urinary sodium and potassium have been reported from FFQ especially in men who may have been less familiar with food preparation in the last century – eg Day N, McKeown N et al Int J Epidemiology 2001).

Additional Questions:

Please enter your name: Mark Harris

Job Title: Professor

Institution: University of New South Wales

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: 2

Recommendation:

Comments:

The authors investigated the associations between potato consumption and risk of hypertension in 3 large cohort studies of US health professionals. It was found that total potato consumption, as well as intakes of baked, boiled or mashed potatoes, and French fries, but not potato chips are positively associated with hypertension risk.

As recently limitations on potato products of several health promoting programs such as WIC were lifted, due to a lack of evidence on potato's negative effects on chronic diseases, this study provides timely evidence which suggests a potential harmful effects of potato consumption on developing hypertension, an established risk factor of cardiovascular diseases. This study is well designed and written.

I only have one minor suggestion:

The associations in table 2, 3, and 5 seem heterogeneous among 3 cohort studies, with non-significant or inverse associations observed in HPFS. Please provide a P value for heterogeneity for these associations. If P for heterogeneity is statistically significant, a random effect model should be used for the pooled analyses. If not, please mention the results in the text.

Additional Questions:

Please enter your name: Ying Wang

Job Title: Senior Epidemiologist

Institution: American Cancer Society

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 competing interests.

Reviewer: 3

Recommendation:

Comments:

Good paper presented by an excellent team with a worldwide visibility. The paper uses existing data from three US population-based cohorts to explore the long-term effects of the intake of various potatoes preparation. Perhaps the most interesting aspect of this paper is its direct relevance for a current public health issue in the US, namely the change allowing potatoes replacing vegetables in food packages of nutrition programs for women and children.

Overall, few remarks on the scope, the methods, the results and the discussion as presented in the paper. A couple of thoughts though:

- the most embarrassing part of the paper is the absence of effect of potato chips on blood pressure, including a depressing effect in one of the cohorts under study (participants consuming ≥ 4 servings/week of potato chips have a lower risk of developing hypertension). If the association between boiled potatoes and French fries is taken as granted, thus the association with chips is expected to be stronger. Could it be that the consumption of chips is associated with healthier meals (e.g., more crude vegetables and fruits ?) Or, conversely, the consumption of French fries could be associated to high meat consumption ? I understand from the paper that the statistical methods that the effect of potatoes have been isolated, but only up to a certain point. And I do not believe that the recent changes in oil composition (less transfat) is a good explanation.

- the large size of the database (3 millions persons-years) explains that the modest relative risks related to two potatoes processings are strongly significant.

- there is nothing on the cost of including or excluding potato vs. vegetables. This should be briefly addressed within the context of the current US debate.

However, this paper is worth to be published, also as an example of a timely analyse of existing database to intervene in a public health decision.

Additional Questions:

Please enter your name: fred paccaud

Job Title: director and chairman

Institution: IUMSP, Lausanne, Switzerland

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

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:

****Information for submitting a revision****

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

How to submit your revised article: Log into <http://mc.manuscriptcentral.com/bmj> and enter your Author Center, where you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision.

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

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. Please include these items in the revised manuscript to comply with BMJ style (see: <http://www.bmj.com/about-bmj/resources-authors/article-submission/article-requirements> and <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists>).

Items to include with your revision (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>):

1. What this paper adds/what is already known box (as described at <http://resources.bmj.com/bmj/authors/types-of-article/research>)
2. Name of the ethics committee or IRB, ID# of the approval, and a statement that participants gave informed consent before taking part. If ethics committee approval was not required, please state so clearly and explain the reasons why (see <http://resources.bmj.com/bmj/authors/editorial-policies/guidelines>.)

3. Patient confidentiality forms when appropriate (see http://resources.bmj.com/bmj/authors/editorial-policies/copy_of_patient-confidentiality).
4. Competing interests statement (see <http://resources.bmj.com/bmj/authors/editorial-policies/competing-interests>)
5. Contributorship statement+ guarantor (see <http://resources.bmj.com/bmj/authors/article-submission/authorship-contributorship>)
6. Transparency statement: (see <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/transparency-policy>)
7. Copyright statement/licence for publication (see <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse>)
8. Data sharing statement (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>)
9. Funding statement and statement of the independence of researchers from funders (see <http://resources.bmj.com/bmj/authors/article-submission/article-requirements>).
10. Patient involvement statement (see <http://www.bmj.com/about-bmj/resources-authors/article-types/research>).
11. Please ensure the paper complies with The BMJ's style, as detailed below:
 - a. Title: this should include the study design eg "systematic review and meta-analysis."
 - b. Abstract: Please include a structured abstract with 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 last line of the abstract must list the study registration number and the name of the register.
 - c. Introduction: This should cover no more than three paragraphs, focusing on the research question and your reasons for asking it now.
 - d. 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.
 - e. 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/>. Please include in the results section of your structured abstract (and, of course, in the article's results section) the following terms, as appropriate:
 - i. 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.)
 - ii. For a cohort study: Absolute event rates over time (eg 10 years) among exposed and non-exposed groups; RRR (relative risk reduction.)
 - iii. For a case control study:OR (odds ratio) for strength of association between exposure and outcome.
 - iv. For a study of a diagnostic test: Sensitivity and specificity; PPV and NPV (positive and negative predictive values.)
 - v. For a systematic review and/or meta-analysis: Point estimates and confidence intervals for the main results; 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.
 - f. Discussion: To minimise the risk of careful explanation giving way to polemic, please write the discussion section of your paper in a structured way. Please follow this structure: i) statement of principal findings of the study; ii) strengths and weaknesses of the study; iii) strengths and weaknesses in relation to other studies, discussing important differences in results; iv) what your study adds (whenever possible please discuss your study in the light of relevant systematic reviews and meta-analyses); v) meaning of the study, including possible explanations and implications for clinicians and policymakers and other researchers; vi) how your study could promote better decisions; vi) unanswered questions and future research
 - g. Footnotes and statements

Online and print publication: All original research in The BMJ is published with open access. Our open access policy is detailed here: <http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse>. 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>). The print and iPad BMJ will carry an abridged version of your article. This abridged version of the article is essentially an evidence abstract called BMJ pico, which

we would like you to write using the template downloadable at <http://resources.bmj.com/bmj/authors/bmj-pico>. 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 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.