

BMJ - Decision on
Manuscript ID
BMJ.2017.042924.R
1

Body:

30-Jun-2018

Dear Dr. Merriman

Manuscript ID BMJ.2017.042924.R1 entitled "An evaluation by meta-analysis of the diet-wide contribution to serum urate levels"

Thank you for sending us your paper. We sent it for external peer review again. We recognise its potential importance and relevance to general medical readers, but I am afraid that we have not yet been able to reach a final decision on it 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 reviewer's comments, so that we will be in a better position to understand your study and decide whether the BMJ is the right journal for it. We are looking forward to reading the revised version and, we hope, reaching a decision.

Yours sincerely,

Tiago Villanueva
Associate Editor
tvillanueva@bmj.com

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** Comments from the external peer reviewers**

Reviewer: 1

Recommendation:

Comments:

I would like to thank the authors for addressing my initial comments. This article considers sophisticated methods to generate data from the 5 cohorts and to convert the data into analysable scores for analysis.

The methods section is quite long and I wonder also if some of this detail could be placed in supplementary material, for example, the computation of each of the dietary scores. Perhaps an overview of each score is all that is required in the main text.

In the main text I would like to see more detail on how the grouping and combining of questions was done across the dietary assessment questionnaires to come to the list of 63 food items with comparable questions, e.g. was this done by one person, multiple persons independently etc.. This is important for validation and replication.

The language in the methods and in places in the results may still be beyond the average BMJ reader. For example in the DWAS section, the authors refer to 'Regression beta-values'. In lay terms, what does the beta-value represent? I would refer to this specifically in the text as the pooled effect estimate representing the 'change in ...'

You use $p < 0.01$ to denote the presence of heterogeneity - do you not mean < 0.1 ? This is evident throughout and table footnotes (in one instance you did not change this from the original $p < 0.05$.)

Results - the study power section is hard to comprehend for an average BMJ reader - what does '>80% power to detect and effect size corresponding to an R² of approx. 1%' mean exactly. Why is this even important and is this a post-hoc calculation?

I think the rest of the results tables are clear. One of the main statements made in the paper is the estimation of diet quality explaining less variability $< 0.3\%$ than hereditary factors 23.9% in serum urate. It's not clear in the results where this came from - should I be seeing this result in either of Tables 1 or 2 - this needs bringing to the forefront if this is the main message.

Discussion - Paragraph 2 in the methods discusses QC procedures which resulted in a number of exclusions. In the limitations, it might be useful to explain the potential impact of these exclusions on the results.

Additional Questions:

Please enter your name: Jamie Kirkham

Job Title: Senior Lecturer in Medical Statistics

Institution: University of Liverpool

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 have answered to all my concerns.

I still have one minor point, I am not clear why the authors have removed precise p-values and just have indicated <math><0.001</math>. In my opinion it would be best to keep the precise p-values.

Additional Questions:

Please enter your name: Nicola Pirastu

Job Title: Chacellor's Fellow

Institution: Usher Institute PHSI - University of Edinburgh

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: 3

Recommendation:

Comments:

Revised Title An evaluation by meta-analysis of the diet-wide contribution to serum urate levels

Reviewer Nithya Neelakantan
National University of Singapore

Review comments:

This manuscript has been extensively revised to address the comments raised by the reviewers. However, I have a few queries that require further clarification.

Abstract:

1. Data-driven methods ('a Posteriori' approach) empirically derive underlying dietary patterns using statistical methods such as PCA/factor analysis. Whereas, Indices of overall diet quality ('a Priori' approach) are typically constructed based on dietary recommendations or International dietary guidelines for the general population. "Data-driven diet quality score" is a confusing terminology (abstract results: line 48).
2. Since the authors have used both data-driven and hypothesis-driven methods in this manuscript, it is recommended to mention 'dietary pattern' instead of 'diet quality' (abstract objective: line 10).
3. Please correct the typo error in line 50. This should have been "raised" serum urate.

Materials and Methods:

1. Page 30 of 52; Line 44 (sub-section: diet quality scores): indicating higher adherence to the DASH diet.
2. Page 31 of 52; lines 12-17 (sub-section: diet quality scores): Please clarify whether sex-specific categories of alcohol consumption were considered in the construction of Mediterranean diet score. What is the definition of moderate alcohol intake (in servings per day or week), and how did you assign the scores for moderate, heavy and no intake?
3. Page 31 of 52; line 21 (sub-section: diet quality scores): delete repetitive words (i.e., a larger number number indicating...)
4. line 21: indicating higher adherence to the Mediterranean diet.
5. Page 31 of 52; line 51: Is there a specific name for the derived dietary pattern (ie., healthy or unhealthy dietary pattern)? What does the maximum value ('71') indicate?

Tables:

Table 1: Please simplify (especially the description of partial R-square analyses) the footnote of table 1. What is the comparison group for beer and liquor; skim milk?

Table S4: CARDIA study

- 1) Please verify the median and maximum values for coffee and tea! (for example, mean \pm SD of coffee intake: 12.79 \pm 20.97; whereas, the maximum value is 0)
- 2) Maximum value of diet soft drink is 184 serv/week in the female cohort. Extreme values are observed for non-citrus juice, white bread (among males), butter and etc. Are they outliers or typo error?

Additional Questions:

Please enter your name: Nithya Neelakantan

Job Title: Postdoctoral fellow

Institution: National University of Singapore

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

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