

Dr. Elizabeth Loder, MD
Editorial Team
BMJ

Dear Dr. Loder,

On behalf of myself and all of the co-authors, I wanted to thank you for giving me the opportunity to re-submit our manuscript. The reviewers' comments are greatly appreciated and by responding to their critical assessment, we believe that our manuscript is significantly improved.

We have addressed all comments in the following pages; the comments are repeated verbatim, and our responses to those comments are displayed in **bold print**. Where applicable, we have indicated the location within the manuscript that the revision can be found. In addition, changes made to the manuscript are marked clearly in yellow highlighting.

We hope you find this revision suitable for publication in *BMJ*.

Lea Borgi, MD, MMSc

Reviewer's comments:

1. Of particular importance is the coding of potato intake as this is fundamental to the whole question/ interpretation of findings. It is still unclear how this was done and incorporated into the models.

It seems that at baseline and approximately every 4 years thereafter participants recorded how often on average over the preceding year they had consumed each of the potato categories in a standard portion size. For each potato type they were asked to give this information as one of 9 categories ranging from "never or less than once a month" to "6 or more a day".

This data was then re-grouped into 4 categories ranging from " ≤ 1 serving /month" to " ≥ 4 servings a week". Additionally for all except potato chips a 5 category combined grouping was used ranging from " < 1 serving a month" to " ≥ 1 serving/day".

- Why the changing categories? – Were some levels of the original 9-category not used or very small and hence combined? – More information/justification should be given.

Why 5 then 4 categories for any collapsing of the full range?

We agree with the reviewer that more information needs to be given. Indeed, participants recorded how often on average a specific food was consumed from 9 different categories ranging from "never or less than once a month to "6 or more a day". Because the number of individuals in some of these 9 categories was frequently low (for example, consuming a food 6 times a day was a rare event), we therefore collapsed the smaller categories into larger ones out of necessity. As a result, three potato variables, specifically French fries, potato chips, and the combination of baked, boiled or mashed potatoes (which were ascertained as a group on the questionnaire with a single question) were collapsed into 4 categories for the purpose of analysis. When we analyzed baked, boiled, or mashed potatoes together with French fries, the number of participants in each response category was larger, permitting us to examine a broader range of intake (ie, 5 rather than 4 categories). We did not alter the manuscript to include this detailed description (because it is long and perhaps out of the scope of a standard methods section); however, we would be happy to do so at the discretion of the editor.

- The paper subsequently refers to the baseline category for the 4 category response as " < 1 serving/month" rather than " ≤ 1 serving/month". – Presumably this is a typo in the analysis section?

The category (and the question on the food frequency questionnaire was "none or less than one serving a month". Thus, the wording is correct as is.

- Although baked, boiled and mashed have information collected separately, they are combined in all analyses. Why is this? Why collect separately if the combined is only of interest? What are the individual associations?

We apologize if this was not clear in our manuscript and previous letter. The food frequency questionnaire contained three questions about potato intake (rather than five questions).

Intake of French fries and potato chips was ascertained as two separate questions. However, the food frequency questionnaire contained one (rather than three questions) to ascertain intake of baked, boiled, or mashed potatoes. Thus, these three methods of preparing potatoes were analyzed together out of necessity.

We did update our manuscript to clarify the ascertainment of potatoes:

Page 5, paragraph 2: Three questions on the FFQ ascertained potatoes: baked, boiled potatoes (1) or mashed (1 cup), which were ascertained as a group on the FFQ as a single question,

- Additional to these issues remains the question of how “cumulative average” (or “cumulative weighted average” as suggested in the author response) is calculated for each participant. If for example, someone records “< 1 serving/ month” at the baseline and then “1-3 per week” at the next assessment, followed by “>= 4 per week” and then “1-3 per week”, what values are used for them throughout the modelling process?

All 9 categories were used to calculate intake of a given food for a give participant during a given FFQ cycle. The 9 categories included: “Never or less than once/month”; “1-3/month”; “1/week”; “2-4/week”; “5-6/week”; “1/day”; “2-3/day”; “4-5/day”; and “6+/day”. As an example, if a participant reported eating French fries 2-4 times per week, we assigned that person a value of 3 servings of French fries per week (or 0.43 servings per day) for that cycle. If, however, the response was 2-3 times per day, we assigned an intake of 2.5 servings per day. At the subsequent questionnaire cycle, we went through the same process and computed a cumulative average using these values. This is the standard way in which food data using the FFQ from our cohorts are used for longitudinal analyses. Although there is measurement error inherent with this method (which we mention), there is measurement error with all types of food intake tools (such as 24 hour recall), and FFQ is potentially the best method for measuring longitudinal dietary intake in large cohort studies. We believe that this detailed description of how intake was averaged is beyond the scope of the methods section of the paper. However, we can include it at the discretion of the editor.

2. Although the authors state that the random effects models did not materially change the pooled HRs apart from widening confidence intervals, and give one example in the response, I think that these should be the primary analyses with the fixed effects secondary. The p-values for heterogeneity as requested by reviewer 2 have not been given.

We agree with the reviewer and have updated our manuscript accordingly. The tables now include both the random and fixed effects. P for heterogeneity is also included.

3. There was a typo in the substitution analysis query – apologies for this. My question was why NOT include a unit decrease in potato consumption when calculating the effect of substitution. It seems that the authors have fitted a model with all predictors (including potato) and then interpreted the coefficient of the non-starchy vegetable as the effect of replacing one portion of potato with this which it is not. The coefficient for the non-starchy vegetable gives the average change associated with an increase in one serving of that vegetable, all else (including

potato consumption) kept constant ie. not replacing/substitution but additional to the current consumption.

We created several variables (all as continuous, in servings per day):

- The first variable included Total potatoes= boiled, baked and mashed potatoes *plus* French fries (*without* potato chips)
- The second variable was starchy vegetables *without* potatoes
- The third variable was non-starchy vegetables
- The fourth variable we labeled “Allvegot” (*without* potato chips), which was starchy vegetables *plus* non-starchy vegetables *plus* total potatoes.

We then used a model that included “Allvegot”, starchy vegetables *without* potatoes, non-starchy vegetables, and French fries. The hazard ratio for French fries, therefore, was the “effect” of replacing one serving of baked, boiled, or mashed potatoes with one serving of French fries, since “Allvegot” is held constant, as are starchy vegetables (without potatoes) and non-starchy vegetables. The interpretation of the hazard ratios for starchy vegetables and non-starchy vegetables is similar. Thus, the hazard ratio for starchy vegetables is interpreted as the increased risk (if above 1.0) or decreased risk (if below 1.0) of developing hypertension if one serving of baked, boiled, or mashed potato is replaced with one serving of starchy vegetable.

4. The authors have verified that time-varying covariates have been used. Given the interval censored nature of the outcome, at what point are they assumed to have changed?

Exposure status was calculated using time-varying covariates that were updated every four years for participants who did not report a diagnosis of hypertension or who were otherwise censored. This exposure status was used to categorize person-time for the subsequent four years of follow-up.