Author's response to reviews

Title: Race and region have independent and synergistic effects on dietary intakes in black and white women

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Author’s response to reviews: see over
Thank you so much for providing us with the opportunity (and extra time) to revise our manuscript. We have carefully considered each of the reviewer’s comments and have made conducted additional analyses to address the reviewers’ comments, below. Our responses appear below each of the comments, and all changes to the manuscript are highlighted in yellow. We believe the comments have greatly strengthened the paper and appreciate the reviewers’ and editors’ additional consideration of our work.

Comments from Reviewer 1

Race and region have independent and synergistic effects on dietary intakes in black and white women, by Newby et al.

The authors describe a cross-sectional analysis of dietary patterns in a large study population of women, and how nutrient intake may vary by race, region, or both. Strengths of the study include its large size, the use of a well-established food frequency questionnaire for dietary assessment, and the availability of measurement-based data on covariates. My suggestions are as follows:

Major compulsory revisions:

1. The income and education differences between blacks and whites in this study are so large, and the nutrient differences between blacks and whites found are so small, it is possible that the black/white differences are a result of residual confounding by income or education. Socioeconomic status has a strong influence on diet. The authors should discuss the potential implications to their findings. Further, they should attempt to explore this issue using the data, to either confirm or alter their statements regarding race effects. For example, as one step, they could perform a sub-analysis among the group with income <$25,000 per year and see whether black/white differences disappear that were there previously.

Response: We conducted a sub-analysis among women with an income <$25,000 per year, as the reviewer suggested, and have included the table below. Results show that the effects for race and region for nutrient intakes in the sub-group of women with an income of <$25,000 were almost identical to the analyses in the full sample. We have included
the following sentence at the end of the results section: “We repeated multivariable analyses in a sub-sample of women with an income <$25,000 per year to further assess potential residual confounding by income. Results for women with an income <$25,000 per year were similar to those in the full sample (data not shown).” (lines 195-197) We also added a sentence to the discussion when we discuss our study’s adjustment for multiple confounders, as follows: “As well, we performed an additional analysis among women with incomes <$25,000 and results were similar to those in the full sample, thus it is unlikely that the observed differences are a result of residual confounding by socioeconomic status.” (lines 275-278)

Table. The effects of race and region for nutrient intakes for women with an income level <$25,000.

<table>
<thead>
<tr>
<th>Nutrient outcome</th>
<th>B (SE)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber (g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-0.36 (0.12)</td>
<td>0.003</td>
</tr>
<tr>
<td>Saturated fat (% energy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-1.05 (0.05)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Trans fat (% energy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke Buckle: Black</td>
<td>-0.07 (0.05)</td>
<td>0.19</td>
</tr>
<tr>
<td>Stroke Belt: Black</td>
<td>-0.17 (0.04)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Other: Black</td>
<td>-0.008 (0.04)</td>
<td>0.81</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-84.6 (9.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Potassium (g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-227.9 (13.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-22.62 (16.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke Buckle: Black</td>
<td>-96.9 (11.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stroke Belt: Black</td>
<td>-97.1 (9.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other: Black</td>
<td>-135.2 (8.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke Buckle: Black</td>
<td>-1.3 (3.8)</td>
<td>0.73</td>
</tr>
<tr>
<td>Stroke Belt: Black</td>
<td>-1.8 (3.1)</td>
<td>0.56</td>
</tr>
<tr>
<td>Other: Black</td>
<td>-9.7 (2.76)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>
2. Page 10, line 147. What proportion of the study population would have been dropped from the models had dummy variables for the covariates not been used? This statement raises concern that missing data was common.

Response: Less than 2% of covariates had missing data with the exception of income, which had 14% with missing data. We and others working on the REGARDS study have done extensive checks and have determined that these data are missing at random and therefore do not believe missing values bias our results. Our goal in using dummy variables was to retain as many participants as possible in our analyses. We have added the following sentence to clarify this point: “The proportion of missing data in this study was low (<2% for all covariates with the exception of income, which was <14%), and dummy variables were used to include those with missing covariate information.” (lines 143-145)

3. Did the authors use any formal statistical testing (e.g., likelihood ratio test) of the race*region interaction? Also, was any consideration given to using a different cutoff for statistical significance (i.e., other than 0.05) to adjust for the multiple comparisons being made?

Response: We stratified analyses by race and region based on a priori hypotheses that there would be differences in anthropometric measures and dietary intakes based on race and region. This is noted in the statistical analyses section, as follows: “For all descriptive analyses, we stratified our sample by region and by race within region a priori, as our study objective was to examine differences across these population sub-groups.” (lines 122-123) We formally tested for interactions by including interaction terms in a final, multivariable-adjusted model, and interactions with $p<0.05$ were considered significant, in which case stratified analyses were performed. The reviewer makes a good point that we should have used a more stringent cut point due to multiple testing. We are happy to change the text/criterion to a lower cut point if the reviewer or editor prefers, but it seems a bit odd to do this after the fact. As well, all interactions would remain significant even at the $p<0.01$ level, a function of our large sample size; we address this issue in the discussion. If the reviewer still prefers we change alpha we will do so.

Minor essential revisions:

4. Page 10, lines 137-140. Actually, the number of nutrients examined is substantially larger than the few presented here. This should be changed to either list them all, or refer to the tables.

Response: We conducted descriptive analyses for a range of nutrients including energy, macronutrients and micronutrients and performed linear regression analyses (hypothesis testing) on a subset of nutrients that have been associated with chronic disease risk factors and outcomes. We have clarified the text, as follows: “Descriptive analyses of
dietary intakes included energy, macronutrient and micronutrient intakes. We then performed linear regression analyses to examine whether race and region were associated with selected nutrients that have been associated with health promotion and disease prevention, as follows: fiber (g), saturated fat (percent energy), trans fat (percent energy), sodium (mg), potassium (mg), magnesium (mg), calcium (mg), and dietary cholesterol (mg).” (lines 132-136)

5. It is unclear from the text why some (i.e., few) nutrients are presented in Table 5 and not others.

Response: We believe we have addressed this point above and have clarified the text accordingly.

6. Page 14, lines 227-229. The authors are probably aware the FFQs can provide a means of determining the RELATIVE intake of nutrients between groups, but are usually not an appropriate means of accurately determining ABSOLUTE intake. Therefore, their statement about overall fiber intake has dubious validity.

Response: We agree with the reviewer, which is why in our discussion section we mention that FFQs do not provide estimates of absolute intakes as a limitation of our study, as follows: “FFQs were not designed to measure absolute intakes, and estimates for some of our micronutrients were lower than expected.” (lines 292-293) That said, even though FFQs do not provide accurate estimates of absolute intakes, that fiber intakes were so far below the recommendations on average across all racial/geographic groups is nonetheless notable, in our view, and is consistent with other reports. To address this reviewer’s comment, we have also added the following sentence to the above section to further underscore this point where the fiber results are presented: “Although FFQs are not able to provide accurate measures of absolute nutrient intakes, our results of low fiber intakes are consistent with Champagne et al [8], who examined both race and regional effects in a representative sample of adults in the United States and the Mississippi Delta.” (lines 231-233)

Discretionary revisions:

7. Page 4, lines 21-22: “The evidence on racial and regional disparities in diet among women is thus equivocal and limited.” I do not believe a case is made for this statement. The authors describe a number of studies, and indeed there are many more, that have examined either racial or regional differences in diet. The fact that the results of these studies vary has largely to do with their coverage of different decades, different geographical areas/states, different age groups, etc. The authors’ current study certainly adds to this existing literature, but again only as a reflection of their particular study.
Response: We have removed this portion of the sentence, as the reviewer requested, and have modified the sentence as follows: “While differences in findings may reflect cohort effects and other differences in study design and samples…” (lines 21-23)

8. Page 5, line 32: The authors should define or clarify “elsewhere”.

Response: We revised this sentence as follows: “Our objective was to examine dietary intakes of women currently enrolled in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study and determine whether there were race and regional differences in intakes among black and white women living in the Stroke Belt (non-coastal regions of North Carolina, South Carolina, and Georgia, as well as Alabama, Arkansas, Georgia, Louisiana, Mississippi, and Tennessee) and Stroke Buckle (coastal plain regions of North Carolina, South Carolina, and Georgia) compared to those living in the Other regions of the United States.” (line 32)

9. Page 5, line 40: The authors should clarify the breakdown of black and white among the 30,000.

Response: We clarified the breakdown of black and white participants among the total study population, as follows: “Participants come from REGARDS, a national longitudinal cohort study which enrolled approximately 30,000 black (~41%) and white (~59%) individuals aged 45 years and older between 2003 and 2007; this paper examines dietary intakes at baseline.” (lines 40-42)

10. In this Reviewer’s opinion, the paragraph on page 9, lines 119-124, is not necessary. First, the proportion of those who completed the FFQ (81%) is high enough to not warrant strong concern about analyzing a very selected group. Second, those who completed vs. did not complete the FFQ actually seem to be quite similar for many of the factors (e.g., mean BMI= 29.6 vs. 30 kg/m$^2$), but the size of the study sample is driving the statistical significance, and so the fact that these are being called out as significant differences can be misleading to the reader. Finally, even acknowledging some real differences (e.g., there are clear differences for education and income), your analyses are internal to the (large) cohort subset who completed the FFQ and so does have internal validity.

Response: This paragraph has been removed from the manuscript.

Comments from Reviewer 2

Major compulsory revisions:

1. Abstract. Black women in the belt consumed 2.9% of energy from trans fat where in other regions it was 2.8 or 2.9; therefore, there seems to be an error in the last sentence of the results.
Response: We are uncertain as to what the reviewer is referring. We believe the reviewer may be looking at the unadjusted nutrient intakes in Table 4. Our results in the abstract refer to the multivariable adjusted results of the linear regression models in Table 5.

2. The conclusions are too general to be of any take home importance. They do not indicate the nutrients.

Response: We added the nutrients with interactions to the section to be clearer. We also and revised the concluding sentence of the abstract (in part in response to comment 8, below), as follows: “Race and region thus interact to impact dietary intakes, and their effects may be mediated by such factors as the broader food environment and food availability as well as food customs and culture when influencing what people eat. Race, region, and their correlates should therefore be considered together when examining diet and disease associations and planning dietary advice for population sub-groups.” We hope this change addresses the reviewer’s comment.

3. Consider the wording- race and region were associated with- why not intake varies with race and by region or differs by as stated in the objective paragraph.

Response: We appreciate the reviewer’s comment but prefer to use the word “association” throughout the paper, which we do later in the same paragraph and find less cumbersome. If the reviewer and editor still prefer we will change the verbiage we will do so but, with all due respect, we are not sure why this wording is a compulsory revision.

4. line 173-174. This statement is not true. Trans fat was not different between blacks and whites in the stroke buckle. Alcohol consumption differences were at most 0.3% of energy.

Response: We are uncertain as to what the reviewer is referring; we apologize if we are in error. We do not refer to trans fat in the above paragraph. Our statements that do refer to trans fat (lines 188-189) reflect findings from multivariable analyses (see responses to comment 1). While alcohol differences were small, they were significant, which is why it was listed in this sentence to be complete. We agree that the alcohol differences are not meaningful, which is why we do not highlight them and refer to the issue of statistical significance versus clinical significance in the limitations section of the discussion. We would prefer to leave alcohol in this sentence to be complete, since in this paragraph we are simply reporting the results from the table and it would look like an omission. However, if the reviewer prefers we can certainly remove the word alcohol from this sentence.

5. line 181-183. Black women in the buckle region also had higher cholesterol intake than whites in the buckle region.
Response: We have added the following sentence: “Black women in the Buckle region also had higher cholesterol intakes compared to white women (161 mg/d vs. 155 mg/d, \( p=0.13 \)).” (lines 181-182)

6. Table 5 is difficult for the reader to digest as is- beta weights vs. lsmeans for regions/races. Providing adjusted means for the different areas would allow the reader to judge better whether there is any clinical significance to the differences.

Response: In addition to the regression coefficients, we have added the adjusted means for race/region differences in Table 5 to address the reviewer’s comment.

7. Line 184 suggests that race was a significant predictor of all nutrients, but table 5 indicates no significance between races for the 2 of the regions for both saturated and trans fats.

Response: Region is a categorical variable. We found an interaction between race and region (as stated in our next sentence), which is why not all levels of the race/region variable are significant, as the reviewer notes. We omitted the opening sentence of the paragraph to remove any ambiguity.

8. The way the discussion is written it implies that race itself and region itself are the reasons for differences in diet. Whereas other factors such as food availability, culture and custom may be associated with race and region and therefore we see associations…

Response: We agree with the reviewer wholeheartedly and have several sentences in the paper throughout to allude to this point, as follows: “Therefore, race and region have both independent and synergistic effects on diet and their effects may be mediated by diverse cultural influences as well as environmental factors influencing food availability, accessibility, and eating behaviors.” (lines 210-213) Of note, we continue in this same paragraph to give an example of how these factors may operate. As well, we have modified our conclusion statement in the abstract and conclusions to make these important points clearer, as follows: “Race and region thus interact to impact dietary intakes, and their effects may be mediated by such factors as the broader food environment and food availability as well as food customs and culture when influencing what people eat. Race, region, and their correlates should therefore be considered together when examining diet and disease associations and planning dietary advice for population sub-groups.” (abstract, concluding sentences) Thank you for this excellent suggestion, which greatly improved the paper and its interpretations.

9. Line 222. This reviewer is not convinced that the adjusted mean differences in intakes between whites and blacks are clinically significant. Statistical significance is not interesting and is misleading. Adjusted means should be presented. The unadjusted means were 1.5 different between whites and blacks.
Response: We have included the adjusted means in Table 5, as requested. (Please also see our response to comment 13.)

10. Line 229- this must be an adjusted mean as in table 3 blacks had 12.8 g fiber per day??

Response: Thank you for finding this error. As part of addressing the below comment, we have omitted this sentence and its concurrent result from this paragraph.

11. Line 231 and 232- this reviewer is not sure of the clinical significance of 1 g fiber difference between whites and blacks in table 3.

Response: We agree that the differences across groups are not meaningful, which is why this paragraph is focused on comparing our results with other studies and we elected to omit the previous result noted above. Rather, our point in this paragraph is to highlight the low fiber intakes across all groups. We have also added text to this paragraph to address reviewer 1, comment 6, as follows: “In our study, fiber intakes were much lower than the recommended 14 g/1000 kcal [20] across all race/region groups, with no clinically meaningful differences across strata. Although FFQs are not able to provide accurate measures of absolute nutrient intakes, our results of low fiber intakes are consistent with Champagne et al [8], who studied a representative sample of adults in the United States and the Mississippi Delta.” (lines 229-233) We hope both reviewers find our edits acceptable.

12. The authors suggest that there is little risk of reverse causality. While this reviewer agrees that there would not be reverse causality related directly to race or region, reverse causality related to higher rates of disease by race or region and the resulting dietary advice is still possible. Is it not?

Response: We edited the sentences in the discussion to note this as a potential limitation, as follows: “First, this study is a cross-sectional analysis, although the potential for reverse causality is unlikely for our main exposures and outcomes (i.e., nutrient intake can not predict race or region). It is possible that disease status may have impacted our results, although we adjusted for baseline disease to reduce this potential bias.” (lines 282-285)

13. Finally, on line 292 clinical importance is mentioned. However, statistical difference is not the important difference here. Focusing on statistical differences is not only not interesting but potentially misleading.

Response: We agree with the reviewer that this point has not been adequately made and have added the text and added another sentence to underscore its importance, as follows: “It is also important to remember that while our large sample allowed us to detect (highly) statistically significant differences in nutrient intakes, likely due to our large sample, many of these differences are quite small. Relying upon statistical
significance can be misleading and some of our findings are likely of limited clinical importance.” (lines 299-302)

Discretionary revisions:

14. Introduction: Differences in published reports of diet in blacks and whites may also reflect temporal differences.

Response: Thanks for this comment. We have added a clause to the sentence to this effect, as follows: “While differences in findings may reflect cohort effect and other differences in study design and samples…” (line 21-23)

15. The last two sentences of the introduction are redundant- suggest removing the first more generic sentence.

Response: We have clarified the text in this paragraph to remove the redundancies the reviewer noted. Although the first sentence is more generic, it describes a major part of our objective in this study, which is to describe overall macro and micronutrient intakes across groups. Our additional goal (the second sentence) states our hypothesis testing for key nutrients. We hope our edits to this paragraph clarify the objectives of the study and the reviewer finds it acceptable to leave both of these revised sentences in the introduction. (various words added in lines 26-34)

16. Line 55, does the author mean that data from 12,111 was available?

Response: We have clarified the sentence as follows: “After all exclusions, data from 12,105 women were available for the analysis.”

17. Line 256-258 are confusing—“In another study the REGARDS cohort, Cushman et al [19] also showed smaller regional differences in stroke risk factors such as blood pressure and hypertension compared to the effect of race”—are the authors trying to suggest that the differences are genetic related to race?!

Response: Thank you for this observation. Our comparison with Cushman was to corroborate our own findings of stronger effects for race than for region. We are not suggesting genetic differences due to race and have added a final sentence to the paragraph to clarify this point: “It is not clear why stronger effects for race/ethnicity were observed compared to region in this study and ours, but results suggest that perhaps innate and/or learned preferences for dietary intakes and food behaviors among blacks transcend the effect of geographic region.” (lines 260-262)

18. Conclusions-again please consider wording- as worded effect of region was modified by race is obtuse to the reader.
Response: We do keep the above words in the manuscript with regards to effect modification: as this is standard nutritional epidemiologic language we believe it is important to do so. However, we understand not all readers are epidemiologists and have added additional sentences to the paper that we hope the reviewer and readers find more comprehensible, as follows: “Race and region thus interact to impact dietary intakes, and their effects may be mediated by such factors as the broader food environment and food availability as well as food customs and culture when influencing what people eat. Race, region, and their correlates should therefore be considered together when examining diet and disease associations and planning dietary advice for population sub-groups.” (lines 312-316) (Note that these modifications were also made in response to comments 2 and 8.)