Author’s response to reviews

Title: Rural-Urban and Racial-Ethnic Differences in Awareness of Direct-to-Consumer Genetic Testing

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Version: 2 Date: 12 Feb 2018

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February 12, 2018

Dear editor,

Thank you for the opportunity to revise our manuscript. Changes in the accompanying manuscript are highlighted in yellow. Below we list each comment along with our response. Please do not hesitate to be in touch if we can clarify anything further. We look forward to hearing from you.

Sincerely,

Ramzi Salloum, PhD
1. The authors correctly indicate that genetic services typically require multiple office visits; however, no mention is made of recent developments related to the provision of genetic counseling by telephone. Two prior trials have demonstrated the equivalence of the provision of genetic counseling by telephone, a modality that is likely of use for rural populations. The authors are encouraged to update the introduction to include this information.

Response: The existence of telephone modality for genetic counseling has now been acknowledged in the Discussion section (4th paragraph).

2. Another key barrier to accessing genetic counseling and testing is language; this should be noted.

Response: We have noted language as another key barrier in the Background section (1st paragraph).

3. The primary outcome based on the question noted on page 4 is awareness of direct-to-consumer tests and may or may not have captured awareness of genetic testing through clinical providers. The authors appropriately note this distinction on the bottom of page 6. Although a nuanced difference, the authors are encouraged to also make this clear in both the introduction and in the discussion (e.g. First sentence on page 6).

Response: We have now made this clarification throughout the manuscript, by adding the ‘DTC’ descriptor where applicable.

4. Were all HINTS surveys completed in English? If so, then the caveat about the results not being generalizable to Spanish-speaking Hispanics should be noted in the discussion.

Response: HINTS surveys were available in Spanish, and 3.6% of responses in the current study were completed in Spanish.
5. Was family history of disease assessed (e.g., cancer)? If so, this may influence awareness of genetic testing and could be an important covariate. If not, this could be noted as an unmeasured factor that may have influenced awareness of genetic testing.

Response: We found ‘family history of cancer’ not to be a significant predictor of awareness of DTC genetic testing, and as such, it was not included in final models. We also now acknowledge this point in the Results section (2nd paragraph).

6. It is not clear why for the primary outcome the results are reported as (OR = 0.74, 95% CI = 0.63-0.87; results not shown). Which results are not shown? The mean response for this question by geography residence?

Response: This statement was referring to the fact that the regression results were not presented in a Table. We have now present the regression results in Table 3.

7. This reviewer agrees with the authors for the need for greater awareness about genetic services; however, there is a distinction between greater awareness of appropriate use of genetic services among high risk populations or for use as 'precision medicine' within clinical care and the utility of information obtained from DTC genetic tests. The authors are encouraged to provide greater distinction in the conclusion about level of awareness, appropriate use of recommended genetic services and the currently limited evidence regarding health benefits following DTC testing.

Response: Revisions have been made in the Introduction section (3rd paragraph) and Discussion section (4th paragraph and Conclusions) to acknowledge this important distinction.

(Reviewer 2):

1. I suggest that the title of the paper is potentially misleading, as many readers would take it to refer to awareness of genetic testing health services. It is not technically incorrect, but the terms 'direct-to-consumer' genetic tests, or 'consumer genetic services' would be more informative. I have further comments on the focus in my comments section below.
Response: The title has been revised to the following: “Rural-Urban and Racial-Ethnic Differences in Awareness of Direct-to-Consumer Genetic Testing.”

2. I liked that the authors presented predicted marginals rather than just p-values but I would suggest that the y-axis in Figure 1 be reworded to be more informative to readers unaware of this approach - indicating that these are meant to indicate adjusted awareness rates in the defined population groups would facilitate comprehension for some readers.

Response: We added ‘adjusted awareness rate’ to the y-axis label in Figure 1, as recommended.

3. I also found myself wondering about interactions within the dataset - were any of the variables for which the data were adjusted in fact possible effect modifiers? (I don't think this is handled within the analysis strategy used.) Might there be a potential interaction between urban/rural residence, race/ethnicity and gender? It may be beyond the scope of the work, or perhaps there are space limitations in what can be reported.

Response: We tested for potential interactions between urban/rural residence and other sociodemographic characteristics, but none of the interactions were significant. This point is now clarified in the Results section (2nd paragraph).

4. For Table 1, a minor style point is that the "%" symbol should not appear in every cell if it is indicated in the column heading ("n (%)"). Table 2 needs the heading to be better specified - the cells under "information sources" are percentages but this is not directly indicated.

Response: The “%” symbols have been removed from the individual cells in Table 1, as recommended. In Table 2, we now specify that the cells under “information sources” are %s.

5. However, my most important comment is that the paper needs to be clearer about how awareness of DTC genetic tests is linked into a larger argument about precision medicine, underserved populations, and health disparities. A DTC genetic test in itself is not a substitute for a precision medicine approach to risk assessment, prevention, diagnosis, or disease management. The authors themselves state in the
introduction: "...the rapid growth of direct-to-consumer (DTC) genetic tests has led to important concerns related to knowledge gaps in their clinical validity and utility, the potential for consumer misrepresentation of results .... and the possibility of widening health-related disparities." I don't see that they can then argue that DTC tests (at present, at least) represent potentially "[m]ore inclusive approaches for measuring disease and susceptibility" or "better assessment of population health" (Conclusions). I would suggest that the paper would be greatly improved by reconsidering the relationship between awareness of DTC genetic tests, the goals of precision medicine, and population health goals of improving healthcare access and reducing health disparities. No new analyses would be required.

Response: We have made clarifications in the Introduction section (3rd paragraph) and Discussion section (4th paragraph and Conclusions) to disentangle the issue of DTC testing awareness from the broader argument about the benefits of precision medicine.