Reviewer’s report

Title: Diet and exercise changes following direct-to-consumer personal genomic testing

Version: 0 Date: 13 Sep 2016

Reviewer: Laura M. Koehly

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With the advent of Precision Medicine and publically available DTC genomic testing, this paper a sneak peak into the potential for genetic information to change health behaviors. The results presented are not surprising; however, as I was reading, I developed several follow-up questions that, if addressed, would significantly improve the manuscript. Below, I outline several points for the authors to consider upon revision:

1. The Introduction ends with the authors' hypotheses related to diet and physical activity from pre- to post-PGT. Given the potential realization of Precision Medicine, it might be helpful if the authors provide more rationale for their hypotheses. One might expect, for example, changes to occur specifically for those receiving increased risk assessments, who are currently not following dietary and exercise guidelines, and whose perceptions of risk are appropriately increased based on such results. My suggestion is to add more rationale for specific hypotheses, and provide a figure that illustrates the moderators (self-rated health) and mediators (appropriate change in risk perception; motivation to change behavior) on outcome. In particular, why is there expectation that the cardiometabolic genetic risk score might impact such behavioral outcomes? or, the total genetic risk score when diet and physical activity are not risk factors related to many of the diseases in question?

2. The seasonal change variable was confusing, as its impact may depend on participants' location. One might imagine an expected increase in physical activity in the Winter months for those living in Gulf coast regions and a decrease in Winter months for those living in the Northeast. A bit more justification, in light of regional variability, is needed for this variable.

3. Given the differences in how risk assessments were provided to participants, it would be helpful to have more information regarding the impact on changes in risk perception and behavior due to testing company. For example, consumers' numeracy may be important in understanding the RR values provided by 23andMe, whereas Pathway provided the qualitative measure. Did the authors see appropriate changes in risk perception for the cardiometabolic conditions? And, did testing company modify this change?

4. The last time that I looked at the 23andMe reports, there were multiple SNPs presented for some of the conditions. For example, coronary heart disease presents 15 SNPs with associated adjusted odds ratios, type 2 diabetes 11 SNPs, and obesity 2 SNPs. How did the
authors integrate this information to arrive at their genetic risk score? How might offsetting odds ratios play into consumers' understanding of their risk? The cited paper (Carere, VanderWeele, Moreno, et al., 2015) does not seem address this issue.

5. Motivation to change behaviors seems a particularly important process variable based on the results presented in Table 3. Similar to the point made above, did the authors find that motivation was associated with test results? And, did testing company modify this association?

6. Are the parameter estimates presented in the text standardized betas? Or, are these raw coefficients? Similarly for the estimates presented in Table 5.

7. For Table 5, I wanted to see more results, particularly with respect to some of the covariates, modifiers, and mediating variables. Ideally, the structure of the table and presented results would map to the figure suggested in comment 1. In other words, did SRH modify the impact of genetic risk score on outcome? Did risk assessment result in appropriately adjusted risk perceptions, which in turn impacted outcome? Did risk assessment and/or risk perceptions impact motivation to change behavior? Finally, did testing company modify these associations?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
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Yes

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