Reviewer’s report

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

Version: 0 Date: 23 Aug 2016

Reviewer: Nathan Wineinger

Reviewer's report:

Dr. Nielson and colleagues examine changes in exercise and diet behaviors in roughly 1,000 direct-to-consumer customers, 6 months after receiving their test results. Study participants were invited to complete a baseline and follow-up survey assessing these outcomes, and they received the earlier versions of DTC-PGT a more informative, though controversially so, genomic test result than what 23andMe me currently offers.

Overall, the design is similar to the Bloss et al. paper referenced. The most interesting, or troubling, point is the result that DTC-PGT improved diet and exercise whereas this previous work did not. What is strange is that this result also contradicts some of Dr. Green's own work examining diet and exercise after giving patients information on their genetic risk for CHD (Kullo et al., Circulation 2016), in which they found in a randomized trial that providing patients their CHD genetic risk did not affect diet or exercise (though it did affect statin use). The authors acknowledge many of the limitations of this study, but given the contradictory result I am left questioning if returning genetic risk results to people will modify health behavior, or if the study participants were simply already planning on modifying their health behavior in the first place?

In this light, it seems a little more appropriate to focus the question around "are DTC-PGT customers modifying health behavior" rather than "is DTC-PGT resulting in a health behavior modification" - the latter which seems like the paper is instead focusing on.

I did like how the authors stratified by baseline health. I am assuming "low SRH" is poor health and "high SRH" is good health? I would appreciate it if the authors go into a little more detail on how these are defined as they form a major component of the result and remain a little unclear. Was it just based on one survey question? I am also curious if there were there other ways the authors considered splitting the data.

The results 23andMe now provides to customers is quite different than the genomic test results study participants received here. I would like to see included - maybe as a supplement - some information on what results participants received, and what is currently being offered by 23andMe as well as Pathway (not sure if/how Pathway has changed since 2012).

Given this and the authors' expertise in this field, an interesting discussion point would be the future of returning genetic risk information to individuals. Some examples of discussion questions: does the FDA ruling limit the health benefit 23andMe customers receive? What issues
need to be resolved so that customers can get more detailed genetic risk information, like they could in 2012? Is the future not DTC at all, but through academic medical facilities like in some of Dr. Green's other work? I think we can all acknowledge that returning genetic risk information to people in 2016 is not perfect, but there certainly are some benefits - like some shown in this manuscript. What issues need to be resolved so we can get patients that health benefit?

**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?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.