Reviewer’s report

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

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Reviewer: Roger Vaughan

Reviewer's report:

The report by Nielsen et al. entitled "Diet and exercise changes following direct-to-consumer personal genomic testing" under consideration within BMC Medical Genetics describes the relationship between personal genomic testing (PGT) on self-reported changes in fruit and vegetable consumption as well as physical activity. The report identified subtle relationships between PGT and favorable changes in diet and exercise in those with lower self-reported health (SHR), however the meaningfulness of these self-reported changes in behavior are unclear. In general the manuscript is well-written, however given the seemingly small changes in behavior within a large sample size, the implications of these findings are questionable. The authors should consider the following points.

Within the discussion, the authors do not adequately address the fact that high SRH exhibited reduced physical activity, which if interpreted with the same magnitude as observations within lower SRH could be seen as an undesirable relationship (especially when coupled with the findings within table 5). It should also be noted that it is unclear if any of the self-reported changes in behavior are clinically meaningful, and that significant findings may be large part due to the large sample size. For example, the increase of light exercise in the lower SRH group (which exhibited the greatest change) equates to a mean increase of approximately 13 days that include light exercise per year or roughly 7 additional days per year of strength exercise in all subjects (without detail of how exercise intensity was distinguished or and without consideration for exercise duration). The authors should include a statement about the uncertainty of the significance of these observations as they relate to health outcomes given the self-reported nature and lack of distinctions regarding variable factors (i.e. exercise duration, type of fruit or vegetable).

The authors include broad statements of article limitations line 290 and line 305, however because of the design, virtually ALL extraneous variables that could have contributed to behavioral changes in diet and exercise/physical activity were not controlled for. The authors should include a statement highlighting that although a pre/post design was used, the design of this study did not allow for the control of many extraneous variables that could have contributed to their findings (unlike in line 305-306 which states the authors "may not have accounted for all factors that could have influenced our outcome variables on interest.").
The authors describe how participants were directly asked about the role of their PGT test/results in their behavior change(s) which, in this reviewer's mind seems like a highly leading question. Was the question posed along with additional questions regarding other potential contributors such as interaction(s) with healthcare professional (physical exam), recently ailment(s), or newly diagnosed disease (or newly diagnosed loved one/relative)? The authors should comment on this point as this approach may have influenced the level to which subjects identified PGT as a contributing factor.

The authors state a desire to extend their findings exclusively to users of PGT. While the potential associations identified may be of interest to those that are using the resource, this statement seems to reduce the application of the project given that such consumers may use the resource regardless of documented efficacy. Moreover, currently PGT-naïve subjects that are possible future users of PGT may have an interest in these findings (and may choose to use PGT (or not) based on these findings). It seems like the dynamic of the discussion would be improved if the authors point out that this study was based on a convenient sample of PGT purchasers, therefore the results cannot be extended beyond this population. Then it would be ideal for the authors to highlight a need of future studies to investigate (or highlight findings of existing studies) the effects of PGT on a mixed population of current users and non-users (obviously the non-users would need to be recruited, and the services ultimately provided at no charge to either population).

Page 8 lines 201-207- This paragraph and description of findings seems opposite of the authors conclusions. As it reads (and is displayed in Table 5) high risk scores were inversely associated with change in fruit consumption and vigorous exercise (once adjusting for perceived risk). In other words, the higher the risk the lower the increase of fruit intake and engagement in vigorous exercise. Is this correct? If so, the authors describe this potentially negative association between PGT and the two variables in greater detail within the discussion.

Table 5- Within the table, "B" should be replaced with "β". It would also be ideal to include either the R or R2 value for each of the relationships.

Page 8 lines 211-213- The authors state that "These changes appear to have been driven primarily by participants of lower self-reported health - this subgroup also demonstrated a significant in fruit consumption and frequency of light and vigorous exercise." however given the data, the authors cannot speculate as to what the changes are "driven" by. They can only state that there appears to be a difference when participants are separated in this fashion. This is very important as the designation of groups by SRH could have been distributed differently (i.e. low, moderate, and high SRH) which may have altered the conclusion(s) of identical data. The sentence should be revised accordingly.

Page 9 lines 211-213- When referring to differences between groups of vigorous exercise, the authors state that "we cannot rule out the possibility that this finding arose due to chance." This
seems like an unusual statement that implies that this is the only finding for which the authors were unable to exclude the possibility of chance (when in fact, the possibility of chance exists within all data). This phrase should be removed.

Page 10 line 263-264- the authors should re-write this sentence to state that heterogeneity may contribute to some varied observations and effects….

Page 10 line 265-266- the authors should re-write this sentence to reflect that their results supports the position that DTC-PGT has potential to motivate health behavior changes in users that self-identify as lower SRH.

**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.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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