Reviewer's report

Title: Genotype-Driven Recruitment: A strategy whose time has come?

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Reviewer: Zubin Master

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Review of “Genotype-Driven Recruitment: A strategy whose time has come?” by Soye et al. for BMC Medical Genomics

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The paper aims to review and critically analyze the ethics literature on Genotype-Driven Recruitment (GDR) and argues that the existing ethical recommendations are not sufficient if GDR was more broadly used to include individuals who did not participate in research e.g., individuals who had genetic information available about them through direct-to-consumer genetic testing services, as part of their healthcare diagnosis or treatment, or because their relatives have participated in research. The paper discusses additional challenges and proposed recommendations if GDR was more broadly used. Overall, I think the paper present a new way of thinking about the ethics of GDR, but I have several points I would like the authors to address.

The comments are separated into Major Compulsory Revisions and Minor Essential Revisions and are in the order they appear in the manuscript.

Major Compulsory Revisions

1) The background section would benefit from an explanation distinguishing GDR and phenotype driven recruitment. Not all of the readers will know about this difference.

2) The Potential future uses of GDR section can benefit from further discussion on how genetic information from individuals through DTC genetic testing or from medical diagnosis will be obtained by researchers who will then contact individuals. The entire premise of the arguments put forward by the authors hinges upon this scenario being a reality. Yet there is limited discussion on whether this actually could or would be done. For example, is it common practice for DTC genetic testing companies to share private customer information with other researchers or pool it in common databases? Similarly, if whole populations would be screened, “both healthy and sick individuals,” why would this information be so freely available to researchers? If someone receives a genetic test for medical reasons, how would this information be available or shared with researchers? I think this discussion needs to talk about the feasibility that
genotypic information will be available to researchers. Is this being currently done? What are the privacy measures in place? Without a thorough discussion, I am not likely to believe that the scenario the authors propose will be a reality and if so, the arguments they put after do not rest on solid footing.

3) This research begins by systematically identifying the available literature on GDR by performing keyword searches on PubMed prior to performing a conceptual analysis of the ethical issues and the recommendations written in the articles they collected. Although I have recommended four additional aspects to include in their search methods below, I do not think the authors need to be so specific in their search methods for a conceptual paper as it is currently written. The paper is about analyzing recommendations on GDR and arguing that they do not adequately cover cases when GDR research may be performed in cases where individuals are recruited as non-research subjects. The purpose of the paper is not to conduct a systematic review of the arguments (e.g., see the methods proposed for such activities in papers by Daniel Strech Neema Sofaer in the J Med Ethics 2012 and Bioethics 2012). My suggestion is to either address the four points below, or write the search methodology more generally saying that a literature search on the topic was performed. If however the authors wish to indicate the details of their search strategy, I feel it is missing several parts and recommend addressing the following four points:

First, I assume that the authors have captured all the relevant literature as there are a limited number of articles on this topic, but I think it would be best to demonstrate this beyond doing a PubMed search. PubMed does not contain every type of journal in its database that bioethicists publish in. Perhaps additional search engines would demonstrate a wider search. I indicate in the fourth point that I found a paper using Google Scholars that wasn’t cited and I did not do an exhaustive search.

Second, due to a limited number of articles obtained, have the authors identified and analyzed the reference sections within the 14 articles to ensure they are capturing all of the literature. If so, please indicate this in the methods.

Third, it seems from their search criteria that having the word “OR [genotype]” or “OR [ethics]” would generate hundreds of articles. Their search string needs to be clarified. I think the authors meant only to write “AND” in PubMed not “and/or”. I would write the string as you would in PubMed. Please note that AND and OR statements are capitalized when using them in PubMed and square brackets can be used for things like [ti] – title searches or [au] searches or MeSH subject headings etc.

Fourth, what are the inclusion/exclusion criteria for including or excluding GDR ethics studies? Just on a keyword search of “GDR” in Google Scholar I found one by Jill Oliver and Amy McGuire published in Genome Medicine in 2011. This particular article really didn’t go into much discussion about the ethics of GDR, but I didn’t see this paper included in their reference section. Thus I figured there must have been some reason to exclude it, most likely based on topic relevance or the depth of analysis of the topic in the paper. I think the authors should
describe the inclusion/exclusion criteria used in selecting articles for analysis in this study.

4) The first argument made in the Discussion section (pages 6-7) needs further substantiation. I am not convinced that because there is no informed consent previously obtained will amplify ethical concerns of “unnecessary distress and anxiety among individuals.” From my understanding, there is very little empirical evidence suggesting that consumer knowledge of the results of genetic testing causes distress and anxiety. Empirical research on this should be referenced. If this is the case, then why would the authors believe that this low level of distress and anxiety would be “amplified” in their proposed scenario? Although this point is somewhat mentioned in the second argument at the end of page 7-beginning page 8, I would like to see the authors further flesh out this argument by discussing what evidence is out there, and perhaps despite the lack of evidence of distress and anxiety caused by an individual’s knowledge of their genetic information, why the authors believe this concern will be amplified if informed consent was never obtained.

5) The third argument made in the Discussion section (page 8) does not add any really new insight beyond the point that greater integration and coordination is needed if an independent body is to manage data access requests. The same model can be used, but it now has to possibly consider data and information about individuals collected from population wide genomic screening, DTC information, and other sources. Stating that a greater degree of integration and coordination is needed is minimal and does not really deepen our understanding of the problem presented. Can the authors comment on how this could be handled, would it be feasible for an independent body to handle such additional information, what policy mechanism might be needed e.g., legislation requiring DTC and other private companies or medical organizations to provide information to the independent body.

Minor Essential Revisions

6) The Results written on page 5 only partially correspond to Table 1. Not all the results summarized in Table 1 are written in the text, only a few highlights seem to be included. Perhaps the last sentence explaining that an overview of ethical concerns in Table 1 should be the first sentence in the paragraph along with a sentence explaining that the authors are only highlighting some of the concerns in the text.

7) On page 9, the word “an” should be placed before “individual” in issue number 3.

I would accept the manuscript after the major compulsory revisions have been made or are adequately addressed in a response from the authors.

Level of interest: An article whose findings are important to those with closely
related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.