Author’s response to reviews

Title: Structural Racism in Precision Medicine: Leaving no one behind

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Author’s response to reviews:

Dear Dr Pradeep M. Muragundi (reviewer 1) and Prof. Leslie Francis (reviewer 2),
We thank you for your efforts and time put in the ensuring that this manuscript makes significant contribution to the field of medical ethics. We are very pleased that Dr. Muragundi is satisfied with the changes that we made previously based on his comments.

In this version, we have sought to further improve our manuscript with Prof. Francis’ suggestions to the previously reviewed and revised version. We thank you for your constructive comments, which we have carefully considered and have made point-by-point changes. Changes to the manuscript are indicated by the line numbers in the revised manuscript. We certainly hope that you will also be pleased with our corrections and look forward to seeing this manuscript published in BMC Medical Ethics.

Best regards,
Lester Geneviève

Reviewer 1’s comments:
I am happy to review a revised version of the manuscript "Structural Racism in Precision Medicine: all patients are equal but some patients are more equal than others". I am very thankful to the editorial
office of BMC Medical Ethics for choosing me to review the same. My comments are as below.

* Authors have taken care to include the suggested revisions and made subtle modifications in the manuscript wherever necessary.
* I am also satisfied by the authors' comments on the modifications suggested by me and on the revisions made therein.
* I am also very pleased and satisfied at the modifications made in figure 1, which appears more informative now.
* I can also see that there no change in the flow of the content and objective after the inclusion of suggested revisions.
* I recommend this manuscript for future actions without any suggested revisions form my side.

RESPONSE:
We thank the reviewer for the positive feedback on the manuscript and for approving its publication.

Reviewer 2’s comments:
This article presents a discussion of structural racism in precision medicine. It emphasizes three "nodes": initial bias in data collection, integration of biased data into PM initiatives, and influence of structural racism in the deliverables of PM initiatives for minority groups. As a general matter, the influence of structural racism on health care is a critically important topic. More specifically, awareness of the actual impact of structural racism in PM is also critically important. Any assessment of this article must begin with these points. In what follows, my goal is to evaluate the article on its own terms: does it raise awareness of how structural racism influences PM initiatives? To do this, the article would need (1) to bring to light important and under-recognized information about the impact of structural racism on PM and (2) to do so in a manner that will catch readers' attention. The argument of the article as presented really amounts to this: because structural racism has had major impacts on clinical care and research to date, in the US particularly but also in Europe, we need to take care to ensure that it does not also infect PM. This is a useful caution, but one that many involved in PM are trying to address; for example, the "all of us" initiative in the US is seeking to collect data directly from individuals and to oversample individuals in underrepresented groups. My concerns relating to these points are discussed below.

RESPONSE:
The “all of us” initiative and others are highlighted in the paper to underpin the growing awareness of including minority in PM.

Regarding (1).
L. 90. That most genetic databases contain primarily Euro-ancestry data is not an illustration of how the research field has been characterized by exploitation and abuse, although it does indicate how research has disproportionately yielded information about those of Euro-ancestry.

RESPONSE:
We thank the reviewer for pointing out this issue, which indeed needed more clarification. The manuscript was modified to point out that the resulting distrust from the exploitation and abuse is not necessarily the sole and direct cause of the relatively lower participation rate of minority groups in health research. Indeed, underrepresentation is often linked to other factors than willingness (or unwillingness, due to – for example distrust) to participate, such as issues of accessibility or the design of the single studies as demonstrated in a study by Wendler and colleagues.

Modifications to the manuscript are at lines 84-92, lines 126-134, and lines 134-142.
Please kindly see below the two references added to support our claim:

L. 106 ff. This information is well known and terrible. Its relevance to the specific conduct of precision medicine is less clear, however. The article would be far better served to focus on precision medicine, rather than structural racism in health care generally. Otherwise, it's a speculative caution, leaving open the possibility that PM might serve as a counter to the structural problems with contemporary health care.

RESPONSE:
We thank the reviewer for this important comment. For this section, we believe it is critical for the readers to understand how minority groups are being discriminated in their current healthcare system. This forms the baseline to anticipate some spill over in the era of PM. Since PM is a product of our current healthcare system and health research, it would be naïve to assume that PM would be totally immune to the problems of the context of where it originated. For this reason, it is still important to highlight that there are systemic factors (e.g. implicit provider bias) influencing the delivery of care and negatively impacting the trust minority groups have for healthcare professionals, researchers and the healthcare system in general. In the era of PM, where data play an even more central role, it is vital that this endeavour is based on trusted relationships between patients and their doctors/researchers. Otherwise, as rightly pointed out by Kraft and colleagues, PM initiatives are unlikely to succeed in their research objectives as representative collection and integration of data will be compromised. We have thus emphasized the importance of not forgetting the context where PM originated and of safeguarding the trust of minority groups for the proper collection and integration of health data in PM initiatives.

Modifications to the manuscript are at Lines 134-142.

L. 201 ff. There's an important difference between the bias exhibited by health care personnel in treating patients (e.g. all the material in the Unequal Treatment 2002 report in the US) and "biased data" in the form of data that disproportionately represent people of Euro ancestry. This first section is largely a critique of the former; however, it's important to also emphasize the latter: even if people get similar treatment when they get into the system, if fewer people of color get into the system, there will be less informative data about them. This section needs to bring out this difference more sharply than it does. Discussing how structural racism affects each of these ways in which data might be biased would be a very helpful contribution but right now, this section risks just re-iterating important concerns about bias in health care generally.

RESPONSE:
We thank the reviewer for this clarification to highlight our main point in this paragraph. Modifications were made accordingly to the manuscript (Lines 208-219; 221-222; 224 and 267).

The discussion of the second node again is about general problems with AI in clinical medicine and research. It does not explain how these issues with AI are appearing specifically in PM. L. 305-308 raise the central point, but only in speculation. Also, l. 318 ff. it would be great to have an example
of this in action in PM.

RESPONSE:
AI is a defining feature of many PM initiatives. The big data sources (e.g. genomics, other omic-es, mobile data etc.) have exceeded the analytical capabilities of clinicians and researchers, and AI is the tool, which will facilitate the interpretation of these massive sources of health data. We have made modifications to the manuscript (Lines 306-308) to highlight that AI is an integral component of the PM endeavour. Additionally, the flaws of AI discovered in other domains (e.g. the judicial sector) are also likely to occur in PM initiatives. Regarding the last point raised, we provided two additional examples of how biased AI used in the healthcare system can lead to racially discriminatory actions against minority groups (Lines 348-359). The negative repercussions can also result from the improper selection of labels in datasets used for training AI or from the use of postal codes (e.g. residential segregation, a known consequence of structural racism).

The discussion of the third node is much better—it sends a direct and informative caution about current outcomes of the PM initiative. Correspondingly, the discussion of correctives at this node is also directly aimed at PM. For the first node, it would be great to see discussion of whether the "all of us" initiative is addressing the problems of limited data in populations not of Euro ancestry, along with whether private sector initiatives such as Ancestry.com or the biobanks mentioned in the discussion of node 3 are doing so. It would also be useful to consider whether there are any promising initiatives to deal with correcting data arising from bias in treatment. Right now, this discussion aims to correct health care more generally.

RESPONSE:
We thank the reviewer for the positive feedback on the third node. Regarding the first node, modifications were made accordingly to the manuscript (Lines 440-460), where we discussed the All of Us Research Program and the UK biobank, which adopted different approaches to solving the data representativeness issue in their datasets. To the best of our knowledge, we did not find any initiatives, dedicated to PM initiatives that aim to correct data arising from bias in treatment. However, our proposed solutions/actions also aim to correct bias in treatment in PM (e.g. through (i) implicit bias training, (ii) targeted recruitment of minority groups, (iii) solutions to fight algorithmic discrimination (datasheets for datasets or algorithmic impact assessments), (iv) community-based research and (v) biobanks targeted for and led by minority groups). Additionally, we added an important promising initiative by IBM called “AI Fairness 360”, which not only aims to correct bias in the training datasets but also in setting up of fair classifiers and predictions used in AI tools.

Modifications were made accordingly to the manuscript (Lines 528-539) and to Figure 1.

Regarding (2).
Starting with Animal Farm introduces a confusion between metaphysics and social structures. Orwell's novel is a scathing critique of a metaphysical view: that some have lesser moral status than others. Social structures perpetuating racism may have originated in such views as they reflect the heritage of slavery. However, today the primary aim of the critique is not assumptions about differential moral status. Rather, the primary aim is to have us notice how social structures have different effects on people who are agreed to be equal in moral status, effects that are correlated with a difference, race, that is utterly irrelevant to moral status. There's some recognition of this difference beginning at p. 156.

RESPONSE:
We have removed references to the novel in the manuscript and changed the title as well from “Structural racism in Precision Medicine: All patients are equal but some are more equal than others” to “Structural racism in Precision Medicine: Leaving no one behind” (referring to the United Nations SDG).

To the extent that this article attacks bias in health care more generally, it is unlikely to raise awareness among the PM crowd. PM folks might argue that their efforts—at collecting new data, for example—are aimed to counter the background problems with structural racism and health care. The discussion of the third node comes closest to raising awareness of PM—I would encourage the authors to be far more targeted in their consideration of the other nodes. Otherwise, this article will read as a general critique of health care and research, rather than as a specific concern about PM as it is currently practiced.

RESPONSE:
We have made changes accordingly throughout the manuscript to target more specifically PM initiatives (Lines 126-130; 134-142; 208-219; 306-308; 408-421; 440-460; 528-539).