Author's response to reviews

Title: Use of Next Generation Sequencing Technologies in Research and Beyond: Are Participants with Mental Health Disorders Fully Protected?

Authors:

Iris Jaitovich Groisman (iris.jaitovich.groisman@umontreal.ca)
Ghislaine Mathieu (ghislaine.mathieu@umontreal.ca)
Beatrice Godard (beatrice.godard@umontreal.ca)

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Author's response to reviews: see over
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BMC Medical Ethics  
Prof. Akira Akabayashi, Editor

Re: Editorial submission “Use of Next Generation Sequencing Technologies in Research and Beyond: are participants with mental health disorders fully protected?” MS: 4554642747182471

Dear Professor Akabayashi,

We considered Reviewers 1’s and 2’s comments received last July 19, 2012 and made changes accordingly in the manuscript. These new changes are listed on a point-by-point format in the pages that follow this letter.

Attached please find our revised manuscript.

We hope that our response and amendments we have brought to our previous version meet with your approval and that you find the revised manuscript acceptable for publication.

Thanking you in advance for your consideration, we look forward to hearing from you.

With kind regards,

Béatrice Godard, PhD  
Professor  
Department of Preventive and Social Medicine  
Faculty of Medicine, University of Montreal  
C.P. 6128, succ. centre-ville  
Montreal, Québec, Canada H3C 3J7  
Email: beatrice.godard@umontreal.ca
Reviewer 1’s

Major Compulsory Revision
Add references 40-44 to the list of references. In the version available to me, the text refers to references 1-44, while the list of references ends with reference 39.

Authors’ response:
The references were corrected.

Minor Essential Revisions
The language of the manuscript is improved. I have a couple of suggestions:
(a) Proper use of prepositions. Examples: Abstract, Conclusions, page 3: "...suffering from BD..." Methods, page 5: "...were relevant to our project..."

Authors’ response:
The Abstract, Conclusions section has changed. However, a similar sentence in Abstract, Results has been corrected as requested.
Under Methods, it now reads “to our project” instead of “for our project”.

(b) Feedback, Return of Results and Incidental Findings, page 14, last paragraph. Correct the sentence "This becomes particularly true due when including the costs of associated genetic counselling."

Authors’ response:
The sentence was corrected and it reads now: "This becomes particularly true when including the costs of associated genetic counselling."

Discretionary Revisions
The manuscript presents a thorough overview of a complicated and evolving ethical issue. What I would like to see in some critical areas is the position of the authors. I will use the example which impressed me most: The three options for protecting participants in genetic research presented in page 12 have huge philosophical, and practical, differences and provide greatly varying, potentially, degrees of "protection". I would like to know the authors preference and their
reasons for it.

Authors’ response:

We understand Dr. Tzamaloukas is referring to the following paragraph:

“While protective measures as to future use are being established, it is possible to seek a broad consent implying permission for eventual applications, an option already in use in oncology settings [32]. Two other options, keeping genetic research closer to the subject of the original consent, or obtaining a new, updated consent from research participants [33], are also legitimate.”

We have stated our position at different points of our discussion, for instance: “We agree with other commentators” (Protecting participants); “we believe the process of”, “we infer that” (Clinically relevant ethical challenges). However, we consider that protective measures regarding return of results is in fact an open subject because it depends on many variables: the type of project (i.e., local versus multicenter), subject matter, goals of study, review boards involved, project budget and applicable (local and international) regulations. Thus, we decided to only enumerate the different possibilities found in the literature instead of siding towards some of them, leaving this subject as we consider it should be: an issue to be resolved almost on a case-by case-basis.
Reviewer 2’
The manuscript has improved ... Anyway, some small comments are remaining:

- The "results" and "conclusion" sections in the abstract are almost similar.
  Please change one of the paragraphs.

Authors’ response:
The Abstract has been corrected. The Results and Conclusion sections now read as follows:

“Results
The amount of information generated by NGS renders individuals suffering from BD particularly vulnerable, and increases the need for educational support throughout the consent process, and, subsequently, of genetic counselling, when communicating individual research results and incidental findings to them. Our results highlight the importance and difficulty of respecting participants’ autonomy while avoiding any therapeutic misconceptions. We also analysed the need for specific regulations on the use and communication of incidental findings, as well as the increasing influence of NGS in health care.”

“Conclusions
Shared efforts on the part of researchers and their institutions, Research Ethics Boards as well as participants’ representatives are needed to delineate a tailored consent process so as to better protect research participants. However, health care professionals involved in BD care and treatment need to first determine the scientific validity and clinical utility of NGS-generated findings, and thereafter their prevention and treatment significance.”

- Key words: I would not prefer to use very broad concepts such as 'clinical ethical challenges' and 'autonomy' as key words here

Authors’ response:
These two key words were removed and a new one was added: return of results.

- The manuscript is quite lengthy and elaborate. Some sections show overlap,
e.g., the paragraph on feedback with the one on consent. If necessary I see plenty of possibilities for making the manuscript shorter.

Authors’ response:
The following paragraph on “Feedback” was removed:
“The use of NGS in research generates an enormous amount of data identifying... or even derived from the study design itself, and the above factors can complicate the interpretation of results.”
This section now starts: “The question of how to determine...”

Another (longer) paragraph on “Clinically relevant ethical challenges” was removed:
“The use of NGS technology would modify clinical practice by providing information helpful in recognizing a greater number of conditions. Thus, tackling more diseases... Health care systems may not be ready to take on the challenge of direct clinical applications of NGS.”
We decided to remove it because, even if in our view it included a rich discussion of the subject matter, it made the section longer and probably less well focused on mental health proper.

- p. 19 what is ‘biohype’?

Authors’ response:
The term biohype has been used in reference to high expectations new biomedical technologies or new applications of known procedures can generate at different levels of society, triggering the need to analyse, in many instances, the ethical aspects of their implementation and their social impact.
This word has been previously used in relation to genomic research1.
We have used this term in our work on nutrigenomics (please, see reference below2 as an example), and consider it can also be applied when describing the impact of the use of NGS technologies in the context of mental health disorders at the clinical level.


- some references are missing in the list (as of ref 39)

Authors’ response:
The references were added.