Author's response to reviews

Title: Technology assessment and resource allocation for predictive genetic testing: A pilot study of the perspectives of Canadian genetic health care providers

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Author's response to reviews: see over
We would like to thank-you for the opportunity to resubmit. The reviewer’s comments were most helpful and have served to strengthen our article. Our responses to the reviewer’s comments are summarized below. The comments from the reviewers are provided in the numbered bolded text below, which are followed by our responses on a point by point basis. These changes are also noted in the revised manuscript.

**Reviewer #1:**

**ABSTRACT**

1. It would be useful to see the N of participants in the methods or results of the abstract.
   - The N of participants has been included in the methods section of the abstract.

2. The results section needs to be a little more detailed, and include the main findings from the study, or highlights of the main findings. Ideally, the results should directly inform the conclusions.
   - The results section has been flushed out, highlighting the main findings from the study:
     - *Surveyed lab directors and clinicians indicated that predictive genetic tests were funded provincially by one of two predominant funding models, but they themselves played a significant role in how these funds were allocated for specific tests and services. They also rated and identified several factors that influenced allocation decisions and patients’ decisions regarding testing. Lastly, participants provided recommendations regarding changes to existing allocation models and showed support for a national evaluation process for predictive testing.*
BACKGROUND
3. Page 3, para 1: It is not clear what is meant by ‘genetic health providers.’
   - The following sentence has been included in the paper.
     - Assessment for genetic technologies raises questions with regard to legal and ethical duties of care owed by health care providers involved in the provision of genetic services [3-5].

4. Page 3, para 1: This paragraph and the introduction more generally needs to make clearer what is meant by ‘predictive genetic testing.’ A definition is needed. Additionally, predictive testing covers a broad range of tests from completely predictive (e.g. Huntington’s) through BRCA1/2, to the emerging predictive tests with Odds Ratios of only 1.2 or so being provided commercially by companies. The introduction therefore also needs to include a description of the range of tests covered in this study, i.e. its scope, and some examples of tests/diseases tested for.
   - Predictive genetic testing has been defined and examples of the types of tests covered in this study have been given.
     - The number of facilities and individuals providing predictive genetic testing – or tests that help determine an individual’s predisposition to a particular health condition or disease -- is a relatively small community in Canada, and those interviewed were identified by their community as leaders in this context. The interviews specifically focused on predictive genetic testing for adult onset hereditary diseases, such as breast and colon cancer, and Huntington’s disease.

5. Page 3, para 2: It would be helpful to have ‘genetic medicine’ defined.
   - A definition for genetic medicine has been provided.
     - For the purposes of this paper genetic medicine has been defined as “the study of genetic mechanisms including the genetic basis for human diseases, and the development of genetically based tests and therapies” [30].

6. The Background is lacking clear research questions and study aims.
   - This point has been addressed and included in this section.
     - These interviewers were designed to provide key information regarding the allocation of resources for predictive genetic testing and associated ethical, legal and social issues. More specifically, they explored existing provincial funding structures, criteria and factors that influence resource allocation decisions, relationships between primary health providers and government representatives, the role the media plays in influencing patients requests for genetic tests, and the strengths and weaknesses of the current regulatory framework within which these facilities operate. Policy recommendations regarding changes to resource allocation models and
the viability of a national evaluation process for predictive genetic tests were also examined. Information obtained from these interviews have been used to inform ongoing research investigating resource allocation of emerging genomic technologies, the end goal of which is to formulate a list of funding criteria to assist in resource allocation decisions.

METHODS
7. Page 4, para 2: The statement that this paper “presents the results of a pilot study of predictive genetic testing” is inaccurate. It could be made clearer by stating for example that the paper presents the results of a pilot study exploring key players’ attitudes towards allocation of resources for predictive genetic testing and associated ethical, legal and social issues.
   • The sentence similar to the one suggested has been incorporated.
     o This paper presents the results of a pilot study exploring senior lab directors and clinicians perspectives on resource allocation for predictive genetic testing in Canada and associated ethical, legal and social issues.

8. Page 5: The measures section in general needs considerably more detail, particularly for the quantitative measures. These are mentioned later in the results, but could be inserted and described here in a ‘Measures’ subsection.
   • The method section has been considerably flushed out. In relation to this specific point the following has been incorporated.
     o The semi-structured interview instrument was developed in consultation with project collaborators and senior geneticists. In total 13 questions were included, and data was collected through a series of both open and closed ended questions. All participants received a copy of the survey instrument in advance of their scheduled telephone interview and all interviews were conducted by the same individuals. They were tape-recorded and open ended responses were transcribed at the time the interviews were conducted. For those that participated via telephone, consent to participate was obtained before the survey commenced, and was recorded on tape. For those participants that completed the survey via email, consent to participate was explained to be implicit in their completion of the survey. Given the small sample size results are descriptive and have no transferrable statistical significance. Open ended questions were transcribed and general themes were simply identified. For closed ended questions, responses were simply counted on a question by question basis and compared to the total sum of responses given for each corresponding question. Participants were also given the opportunity to discuss any additional topics or issues.

9. Page 5: A fuller description of the quantitative analyses is needed (e.g. were these chi-squares? ANOVAs? Linear regressions?) Ideally, there should be a ‘Statistical Analysis’ subsection.
Due to the small sample size, quantitative analyses such as those listed above were not performed. The results presented can not be generalized, rather they are simply meant to describe the findings of a pilot study.

RESULTS
10. Page 5, para 3: The first paragraph of the results section should be set up in the Background and moved to the Methods.
   • This sentence has been set up in the Background section and move to the Methods section.

11. Page 5, para 4: Similarly, The paragraph starting “Funding for genetic testing varies widely in Canada… each province approaches funding in a slightly different manner” should be moved to the Introduction.
   • This sentence was not moved. The authors felt that the sentence best fit the results section.

12. Page 6: The last sentence on this page (beginning “In all provinces surveyed…”) appears to be body text but is currently presented as part of the quote.
   • This formatting error has been corrected.

13. Page 8, para 1: It would be very interesting to know what the tests were that participants wanted to provide but which were not funded. If this was asked, the results could be included here. If not, the authors may wish to mention this in the discussion as a limitation or pointer for future research.
   • Several examples were given, however not all participants gave examples. Given this, the authors do not believe the responses given would add much to the discussion.

14. Figure 1: The error bars are unusually wide. The authors may wish to double-check these, and re-do them if necessary (are they currently standard errors? 95% confidence intervals? They are so wide they look like they could encompass the whole range of responses. A fuller explanation of analyses done in the methods section would also help here).
   • Due to the small sample size and comments from reviewers, the figures have been removed from the paper.

15. Page 11, para 3: ‘Figure X’ should read ‘Figure 2’. See also comments for Figure 1.
   • Please see above response.

16. Page 12: The questions asked of respondents here about the media come as a surprise. Why these questions were of interest (which they clearly are) should be set up in the introduction generally, as well as in the research questions, and described in the methods.
A sentence referring to the role of the media and how it influences participants’ requests for genetic tests has been included in the Background section of the paper. As it is one of many factors explored the authors do not feel that it should receive greater emphasis than the others.

- These interviewers were designed to provide key information regarding the allocation of resources for predictive genetic testing and associated ethical, legal and social issues. More specifically, they explored existing provincial funding structures, criteria and factors that influence resource allocation decisions, relationships between primary health providers and government representatives, the role the media plays in influencing patients requests for genetic tests, and the strengths and weaknesses of the current regulatory framework within which these facilities operate. Policy recommendations regarding changes to resource allocation models and the viability of a national evaluation process for predictive genetic tests were also examined. Information obtained from these interviews have been used to inform ongoing research investigating resource allocation of emerging genomic technologies, the end goal of which is to formulate a list of funding policy recommendations to assist in resource allocation decisions.

17. Page 12, para 2: The authors may wish to put the last sentence of the Results into the Discussion
- This sentence was not moved. The authors felt that the sentence best fit the results section.

DISCUSSION
18. Page 13: ‘RESULTS AND DISCUSSION’ may be replaced with ‘DISCUSSION’.
- The title for this section has been changed to reflect the reviewer’s suggestion.

19. Page 13, para 1: The manuscript would generally benefit from a greater consistency in terminology. For example, here, what is meant by ‘genetic professionals’ is not clear.
- Genetic professionals has been replaced by the following sentence:
  - The pilot study also focused on the relationship between resource allocation and the legal and ethical duties of care owed by health care providers involved in the provision of genetic services in the context of resource allocation policies [4,6,16].

20. Page 14, para 2: It looks as though the references might be out of sync – refs 8,9 are described as referring to current UK frameworks, but one is from 1992 and the other is clearly referring to Canada.
- The references have been corrected.

21. Page 14: Generally, I like the Discussion and Conclusion sections. A
‘limitations’ section is needed though.

- This point has been addressed at the end of the discussion section of the paper.
  - The study has a number of limitations. In addition to a small sample size, and therefore limited generalizability of results, telephone and email surveys have the potential to yield different results as they are each distinct modes of data collection. Despite these limitations the findings provide baseline data on key players’ perspective on factors and criteria that influence and shape the allocation of resources for publically funded predictive genetic testing in Canada.

22. Page 15: In the ‘Author’s Contributions’ section should ‘improved’ read ‘approved’?

- Improved has been replaced with approved.

Reviewer #2:

Minor essential revisions

1) Sample: it is not clear how “key” or “best member” is defined and therefore the criteria that are used for recommending and choosing potential informants.
- The methods section has been significantly flushed out noting that both purposive and snowball sampling have been utilized. Both methodologies are used when select individuals within a community need to be identified. The term key member has been removed and replaced with project collaborators and senior lab directors or project collaborators and senior clinicians as indicated below.

- … As the study was a pilot study and the community sampled was identified as being relatively small and challenging to access, purposive sampling coupled with snowball sampling methodologies were utilized [28,29].

A preliminary list of potential interview participants was created through consultation with project collaborators and senior lab directors, with reference to the Canadian College of Medical Geneticists membership directory. A total of 45 individuals were invited by email to gauge interest in completing the interviews, and were subsequently contacted by telephone. Of the original sample of 45, the authors were able to speak with 31 potential participants. During the initial discussions with these individuals, the authors asked them to identify the best member within their local genetic testing community to interview. Eleven individuals referred the authors to other genetic community members -- all of whom were on the original contact list - three declined to participate, and scheduling conflicts preventing the participation of one, resulting in a final sample of 16. Between January-March 2007, semi-structured interviews were conducted with individuals from the final sample either
by telephone (14) or be email (2) according to the respondent’s preferences, with the average telephone interview lasting approximately 40 minutes. Participants were drawn from British Columbia, Alberta, Manitoba, Ontario, Quebec, and Nova Scotia, and, the final sample was composed of eight lab directors and eight clinicians.

The semi-structured interview instrument was developed in consultation with project collaborators and senior clinicians.

2) The sample contacted – lab directors and clinicians, these are potentially very different groups with a very different role to play in terms of the allocation of genetic testing, and I think it is important to involve both groups in this study. However, it is not clear how many in the final sample come from these groups and thus, how many are involved in patient care. It would be helpful to have this information indeed, information about the final sample is very sparse.

- The following sentence has been included in the methods section.
  - Participants were drawn from British Columbia, Alberta, Manitoba, Ontario, Quebec, and Nova Scotia, and, the final sample was composed of eight lab directors and eight clinicians.

3) I found the figures difficult to read and, given the tiny sample in the study, am not really sure how much work they are doing. It may be better to have a discursive summary of these findings.

- Based on reviewers’ comments all figures have been removed.

4) Data collection: the study is described as using in-depth methods, but then the method of data collection, analysis and presentation, suggests that actually these were semi-structured rather than in-depth.

- The methods section has been flushed out and this point has been addressed. The terms in-depth interviews has been replaced by semi-structured interviews.

5) I also wondered whether the authors would like to reflect on the differences in using telephone and email interviews and the different types of data they may generate.

- This point has been addressed at the end of the discussion section of the paper.

  - The study has a number of limitations. In addition to a small sample size, and therefore limited generalizablity of results, telephone and email surveys have the potential to yield different results as they are each distinct modes of data collection. Despite these limitations the findings provide baseline data on key players’ perspective on factors and criteria that influence and shape the allocation of resources for publically funded predictive genetic testing in Canada.

6) Some of the conclusions are actually discussion and therefore, the latter sections of this paper could do with being reorganized.
• The latter sections of the paper have been reviewed and reorganized and discussion points have been removed from the conclusion.

7) Typos etc.

P12 line 2 insert of - a couple of
P10 sentence containing (figX) not sure where fig X is and the sentence does not correspond to either of the figs that are included.
Bottom p6 sentence starting In all provinces….- Is not a part of the quote is it?
P4 l 21 eleven WERE unavailable.
• All typos have been corrected

Reviewer #3:

1) The authors should clearly state whether they had hypothesis, expectations etc.
• This comment has been addressed in the Background section of the paper.
  o These interviewers were designed to provide key information regarding the allocation of resources for predictive genetic testing and associated ethical, legal and social issues. More specifically, they explored existing provincial funding structures, criteria and factors that influence resource allocation decisions, relationships between primary health providers and government representatives, the role the media plays in influencing patients requests for genetic tests, and the strengths and weaknesses of the current regulatory framework within which these facilities operate. Policy recommendations regarding changes to resource allocation models and the viability of a national evaluation process for predictive genetic tests were also examined. Information obtained from these interviews have been used to inform ongoing research investigating resource allocation of emerging genomic technologies, the end goal of which is to formulate a list of funding policy recommendations to assist in resource allocation decisions.

2) The interview guideline is introduced step by step in the result section. This makes it quite hard to understand what is really the goal of the study. A more top down approach coming from topics to results would be much more informative. The method section does mainly contain information about recruitment which seems quite difficult. At the end 16 interviews were done. This self selection could be a problem but the confusing description of the selection process is the larger problem. Is there any information why the 15 other participants were not interviewed? Moreover the strategy of analysis is not described sufficiently. How did the authors deal with open questions? Have there been a code book? Was there a training of the coder?
• The methods section has been significantly flushed out and has addressed the comments raised above.
- Of the original sample of forty-five, researchers were able to speak with thirty-one potential participants. During the initial discussions with these individuals, the authors asked them to identify the best member within their local genetic testing community to interview. Eleven individuals referred the authors to other genetic community members, all of whom were on the original contact list, three declined to participate, and scheduling conflicts preventing the participation of one. Between January-March 2007, sixteen semi-structured interviews were conducted either by telephone (14) or by email (2) according to the respondent’s preferences, with the average telephone interview lasting approximately 40 minutes. Participants were drawn from British Columbia, Alberta, Manitoba, Ontario, Quebec, and Nova Scotia, and the final sample was composed of eight lab directors and eight clinicians.

- The semi-structured interview instrument was developed in consultation with project collaborators and senior clinicians. In total 13 questions were included, and data was collected through a series of both open and closed ended questions. All participants received a copy of the survey instrument in advance of their scheduled telephone interview and all interviews were conducted by the same individuals. They were tape-recorded and open ended responses were transcribed at the time the interviews were conducted. For those that participated via telephone, consent to participate was obtained before the survey commenced, and was recorded on tape. For those participants that completed the survey via email, consent to participate was explained to be implicit in their completion of the survey. Given the small sample size results are descriptive and have no transferrable statistical significance. Open ended questions were transcribed and general themes were simply identified. For closed ended questions, responses were simply counted on a question by question basis and compared to the total sum of responses given for each corresponding question. Participants were also given the opportunity to discuss any additional topics or issues.

2) The abstract is written very uninformative. The number of participants of the study should be added. It remains unclear whether this is only a pilot study or not. The results sections describes only the dimensions analyzed without giving any concrete result. The conclusions “a national approach to allocation decisions in this context may be appropriate” is very broad. I was asking myself whether there are any health issues where a national approach is not appropriate.
   - The abstract has been flushed out addressing concerns raised above. The number of participants has been included and it is has been made clear that the study is a pilot study. As well the results section highlights the main findings of the study.

Minor comments
3) Is this paper specifically written for the Canadian audience or are there any results with international perspective. What conclusions can be drawn for other
countries?

- As all participants interviewed were Canadian, this paper was written mainly for a Canadian audience. However, we believe these are themes relevant to all countries struggling with resource allocation policy issues – a point we imply in the discussion and conclusions sections of the paper.

4) I am not sure whether the figures are really required.
- Based on reviewers’ comments all figures have been removed.

5) Are there any limitations of this “study”?
- This point has been addressed at the end of the discussion section of the paper.
  - The study has a number of limitations. In addition to a small sample size, and therefore limited generalizability of results, telephone and email surveys have the potential to yield different results as they are each distinct modes of data collection. Despite these limitations the findings provide baseline data on key players’ perspective on factors and criteria that influence and shape the allocation of resources for publically funded predictive genetic testing in Canada.

6) Assuming this is a pilot study it would be interesting to get information about the conclusions for the main study. Or was this study just the preparation for the workshop. It would be helpful to get an idea about the overlap of participants of the study and the workshop. This could be a major threat for internal validity of the results.
- Information obtained from the interviews was used to inform both the workshop and ongoing research investigating resource allocation of emerging genomics technologies. The main study, which is still underway, is to formulate a list of funding criteria to assist in resource allocation decisions.
- There was no overlap of participants interviewed and those individuals that attended the workshop.

7) The first sentence in the conclusions is not clear as genetic test are internationally not just a over the counter product (“commercially available”) like nicotine replacement of others.
- The word commercially has simply been removed to make the sentence more clear.

8) Why where additional results presented in the conclusions?
- The latter parts of the paper have been slightly reorganized, and discussion points have been removed from the conclusion.