Author's response to reviews

Title: Public's attitudes on participation in a biobank for research: An Italian survey.

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Author's response to reviews: see over
Dear Editor,

Please find enclosed the revised version of the paper *Public’s attitudes on participation in a biobank for research: An Italian survey* to be submitted to *BMC Medical Ethics*.

We have answered all the comments of the referee.

The changes in the text are in bold.

We are available for any further clarifications or information, and we hope that the work will now be suitable for publication.

Best regards.

Corinna Porteri

Brescia, 17 September 2014
Please, find below our answers to the reviewers’ comments:

**Reviewer:** Conrad Fernandez

**Reviewer's report:**

1. Page 5 line 12. In reading the discussion it appears that all the participants are exclusively family members but it is unclear in the way this section is worded as to whether or not those approached to take part in the questionnaires were the patients themselves, a family member of a patient or both. Please clarify. If both, Table 1 should indicate the demographics of each group of participants and the authors should consider analyzing the responses between groups to see if these were different. If only family members, please clarify if they were interviewed alone or in the presence of a patient and if this might have influenced responses (and the later strong voiced support for research in dementia).

   *Only family members were invited to participate in the survey. Patients could not hear or interfere with the interview. We clarified the point in the test (p 5, lines 17-21).*

2. Page 5 line 13. Why were previous participants in biobanks excluded from this study. How many met this category of exclusion. They would seem to offer a unique perspective.

   *At the time of planning the project, we decided to exclude subjects who had previously taken part in the constitution of biobank knowing that only few subjects, if any, could meet that criterion, and therefore it would have been impossible to compare people with and without experience in biobank. At the same time it would have been confounding to put all data together. In the reality, none of the approached subjects had previously participate in a biobank. We modified the point in the text (p 5, lines 19-20).*

3. Page 5 line 21 The authors state: “The study was favourably reviewed by the IRCCS Fatebenefratelli ethics committee.” Please clarify that this means the study received formal approval.

   *The study received formal approval by the ethics committee. We modified the point in the text (p 6, line 5).*

4. Page 6 Questionnaires. Only one of the questionnaires has been previously published. The authors should describe more about how all of these were developed, whether these were pilot tested and whether or not there was any attempt at validation for any of the questionnaires. If it is the case that these steps were not taken then lack of validation should be described as a limitation. Access to these questionnaires should be offered.

   *The section Questionnaires has been completed with supplementary information (p 6 line 11- p 7 line14). The questionnaires are in Italian: we specified that a copy of the questionnaires is available on request contacting the corresponding author (p 20 line 22- p 21 line 2).*

5. Page 6 Questionnaires. More detail should be provided. How many questions in each, how long did they take to complete.

   *We added the suggested information in the section Questionnaires (p 7 lines 11-14).*

6. Page 6 line 18-page 7 line 12. It is not clear to me if this analysis refers to previous analysis of a different study that informs this one or of the current study.

   *If it is of the current study, then this section describes a result not a method and should be in the results section.*
The analysis refers to the current study. We clarified the point (p 7 line 15) and, as suggested, we moved the lines in the section Results. (p8 lines 3-18).

7. Page 7 line 5. It is not clear to me what the concept “freedom of research” is meant to convey. More detail is needed to understand this element. The questions grouped under the concept “freedom of research” are detailed in the text (“positive view on research”, “need to devote more resources to research” and (inversely) “research needs to be regulated by government”). May be a better name for the concept is “boost of research”. We modified the point in the text (p 8 line 12).

8. Page 7 line 15. The authors should be more precise in their reporting. Exactly how many were approached to make 80% response rates. How many were patients and how many family members? How many of the respondents came from one family unit? Only family members were approached and only one member for each family unit (p 5 lines 20-21). We are sorry to say that we cannot be more precise in reporting the number of the approached family members as, unfortunately, some data are missing. The reported percentage of 80% has been calculated on a subsample of 47 subjects and can therefore be considered sufficiently reliable (Standard Error=6%) for our purpose.

9. Page 14 line 13. Promotion of research as described does not seem to me linked to the previous statement. Please clarify or modify. We meant to say that the active promotion of research by patients and family members’ associations, in the field of dementia too, confirms that personal proximity to a disease makes people more aware and sensitive to the need for research. We deleted the reference to Alzheimer’s Association and made reference to a paper written by the Bioethics group of the Italian society of neurology on patients’ associations (p 15 lines 15-16)

10. Page 14 line 22- page 15 line 2. While this statement about discrimination makes sense, the authors should be clear if this is their opinion or that reflected by the participants in this survey. This is our opinion. We made this clear in the text (p 15 line 22)

11. Page 16 The authors should explore briefly other reasons for a difference in the response by the Eurobarometer study, the ECs and this study. For example = a key variable not discussed is the formulation and validation of understanding of the question about this issue. How different were the questions in the different studies examining this issue? We added elements regarding the formulation of the question in the Eurobarometer, and regarding the relation between willingness to participate in biobank and broad consent. (p 17 lines 7-11; 15-17; 20-21)

12. Discussion could be shorter given that much of what is said repeats the results. We shorted the discussion, as suggested.

13. Discussion should include a specific section on limitations of the study. We added a section on Limitations, as suggested (p 19 line 9 – p20 line 4)

14. Table 3 would be more accessible if organized in a hierarchical way – for example by highest percentage of required elements by the public (or by the ECs) and then where there are significant differences that they be highlighted in some way eg bold type. As presented it seems random.
Table 3 reflected the order in which the options were submitted to the participants. We thought this was a meaningful order to present information in an informed consent form. Nevertheless, we revised the table, as suggested by both the reviewers, and listed the information from the most to the less important in the view of participants. We also highlighted the statistical significance (p 29).

15. Table 3. Unclear what “information on samples property” means. Similarly - what does “solidarity” in the context of voluntary consent mean.

*With the expression “Information on samples property” we meant information on who is entitled to the property of the samples (i.e. the subjects or the sponsor of research/biobank). We changed the formulation in “information on the property of samples”. We changed the expression “Solidarity and voluntary character of participation” in “Solidarity character of the participation” that was in fact the meaning of the Italian version of the questionnaire (p 29)*

16. Table 3. Surprising that benefit sharing has a significant p value given the small difference in numbers. Please confirm this is correct.

*We checked the result and we confirm it is correct.*

17. Table 5. The title of the table should be self-explanatory including if this is the respondents opinions or the ECs.

*The table refer to respondents. We modified the title of the table (p 31).*

18. Figure 1 does not add substantially to the paper. Suggest delete.

*Even though the figure may be regarded as not essential, we believe it is not redundant as the mean values are not reported in other parts of the paper. For this reason we preferred to maintain the figure and we added a descriptive caption.*

19. References: There have been quite a few publications in this area in the last year. The references cited could be more comprehensive (but I realize that there may be a journal described limit in number of references). If allowable, suggest increase these.

*Literature on the topic is in fact quite large and we selected references. Instruction for authors ask to “avoid excessive referencing”. In any case, we added a couple of papers published in the last year, as suggested. (references n 5 and 20)*
Reviewer: Kyle Brothers

Reviewer's report:

Major Compulsory Revisions

1. You refer repeatedly to the "availability" of respondents to donate biosamples or participate in a biobank. This is ambiguous: Does this refer to willingness to participate? Or perhaps availability to donate biosample? You could consider using a different word (willingness?) or define explicitly what you mean when you refer to "availability".

   We changed “availability” with “willingness” in the text.

2. You make comparisons between survey of the public and survey of EC members. Therefore, you should state in the methods section whether the questionnaires used in this study and your earlier study with ECs was identical, or how this earlier study was different. You should state the sample size of the earlier study. Also, you should explicitly reference your earlier work in the methods section.

   Except for the questions specifically related to ECs activities, that were omitted, the questions used in this survey were the same questions used in the previous study. Forty eight ethics committees (ECs) took part in the study. We revised the section Method that has been completed with additional information on the previous study, as suggested (p 6 line 19 – p7 line 5)

3. Papers of this sort typically have a section immediately before the Conclusion section with the title "Limitations". I believe this study does have a few limitations, and it would be helpful to discuss them explicitly.

   We added a section on Limitations, as suggested (p 19 line 9 – p 20 line 4)

Minor Essential Revisions

1. Introduction section of the paper: You refer frequently to "people". This is ambiguous because, of course, others involved in biobanks, such as healthcare providers and members of ethics committees, are "people". I think you want to speak here of "Laypersons" or, perhaps, "research subjects."

   We revised the section as suggested.

2. Introduction section, Line 19: The phrase "Existing in our institute a biobank for research on dementia and psychiatric disorders..." is awkward and unclear. Revision recommended here.

   We modified the sentence (p 5 line 1-2).

3. Methods section, Page 5: There are a few statements here that are confusing or ambiguous. Please consider revising the following phrases:

   Line 12: "Consecutive family members were invited to participate..."

   We modified the point, making clear that we invited to participate family members of patients consecutively referring to the department (p 5 line 17-18).

   Lin2 15: "Three questionnaires were submitted to the participants by an independent researcher"

   What does it mean that the research "submitted" three questionnaires to the participants? Perhaps you mean "administered"? In what way was the research independent?

   We changed the text, explaining that the researcher who administered the three questionnaires was not involved in the patients’ care or in the management of the local biobank (p 5 line 22-23).
4. Methods section: Were their patients at these clinics who were not suffering from cognitive impairment? How did you assess whether they were or were not?
Our institute is exclusively for research and cure in the field of dementia and psychiatric disorders. Our research subjects were family members of patients attending a geriatric or neurological visit to monitor their cognitive status because they have dementia or mild cognitive impairment or at minimum they experienced something wrong with their cognitive performance. We did not check for their cognitive status because this was not in the aim of the study. Please also consider that patients were not asked to take part in the survey. Family members of patients with psychiatric disorders were not involved in the survey. We reformulated the sentence (p 5 line 16 and p 20 line 8)

5. Perhaps the information on the performance of the first questionnaire found in the methods section should instead be moved to the results section? Also, Since you indicate this questionnaire came from another source, it would be helpful to state explicitly whether principal component analysis was performed in the original study from which this questionnaire was derived.
The principal component analysis has been performed within the present study. We clarified the point in the text (p 7 line 15) and moved information regarding the first questionnaire to the section Results, as suggested (p 8 lines 3-18).

6. Page 9, Line 7: You refer to "the three types of genetic research" here, but it is not clear what those three types are or their order, and therefore it is impossible to interpret the 77%, 75%, and 77% that are listed immediately afterwards.
We referred to genetic research in general, genetic research related to psychiatric disorders, and related to dementia. We clarified the point in the text (p 10 lines 7-8).

7. Page 10, Lines 8-9: "The full questionnaire was completed by 122/125 subjects: from point 2 “Protection of confidentiality”, the percentage of answers is calculated based on those subjects.” This sentence is confusing and should be revised.
We modified the sentence as follow: […] the reported percentage refer to 122 subjects (p 11 line 9).

8. Page 11, Line 4: Earlier you stated that more than one option could be selected, but here you say that "(although public participants chose only one answer)". Does this mean that respondents only provided one response even though they were allowed to provide multiple answers? If so, perhaps this indicates that they did not understand the question?
Yes, family members only provided one response even though they were allowed to provide multiple answers. We think they understood but preferred to choose only one option.

9. Page 13, Line 10: I would be more precise with the statement "It also assures that our sample’s opinion is representative of the target population." If by "target population" you mean the general public, then this is not the case, since this is a very specific population (i.e. family members of a loved one with dementia). I think you mean that your sample is representative of those who have a loved one with dementia. If that is the case, you should state it this way.
The clarified the point (p 14 lines 11-12).

10. Table 5: Although the text provides more information, Table 5 is confusing. What do the percentages represent? Are these the conditions that participants think client studies should meet in order to access data and samples stored in a biobank, or are they conditions that participants would
consider important when deciding whether to allow their own samples and data to be included in a biobank?

*These are the conditions that participants think for profit and not for profit organizations should meet in order to access data and samples stored in a biobank. We clarified the point in the text (p 13 lines 10-11) and we modified the title of table 5 (p 31).*

11. Figure 1: I believe you mean "Utilitarianism" rather than "Utitlarism". Also, this figure should have a more detailed caption. Even though the text of the manuscript provides some information about this, the figure should have a descriptive caption.

"Utilitarism" is a misprint: we meant "utility". *We revised the figure and added a descriptive caption (p 26).*

**Discretionary Revisions**

1. The conclusions section of the abstract should be revised to reflect the implications of the empirical findings of this study. For example, you could say something about the fact that the views of lay persons are quite different from those of ECs. As it is, the conclusion section states, essentially, that people should pay attention to results from studies like yours. I wouldn't consider this a conclusion of the findings from the current study.

*We revised the section Conclusion in the abstract (p 3 lines 7-10).*

2. Introduction section of the paper: You have several sentences here that state how "biobanks should be regarded" and that people's perceptions "need to count". However, you provide no justification for these statements. I think it is OK not to provide a detailed justification, but it would be helpful to give reasons rather than simple stating "this is the way it should be".

*We took into consideration the reviewer’s suggestion in the text (p 4 lines 9-18).*

3. Page 12, Lines 3-5: "Forty-three subjects (35%) want the research results of value for themselves as donors to also be communicated to family members; 34 (79%) of them ask for communication to family members in any case." This is just a little confusing. What is the difference between these two categories?

*The difference is between every kind of individual result and result relevant for health. We reformulated the sentence to clarify (p 13 lines 4-5).*

4. Page 12, Lines 20-22: "Regarding donors’ remuneration to take part in a biobank, the large majority (87%) think this should not be the case; the others agree with remuneration, but exclusively as a flat refund and refund for documented expenses." Just two comments on this sentence:

(1) What does "this should not be the case" mean? I suspect you mean to say, "The large majority (87%) think donors should not be remunerated for taking part in a biobank."

*Yes, we modified in the text (p13 lines 20-21)*

(2) "Refund" refers to the circumstance when a person pays for something and then gets some of that money back. In this case I think it would be more accurate to say "as a flat payment plus reimbursement for documented expenses"

*We are strictly speaking of refund, i.e. the person pay for something and has money back (on the basis of an approximate calculation of the expenses [flat refund]; or on the basis of documented expenses).*
5. Page 15, Line 7: "Our work was also finalised to collect lay subjects’ opinion..." I think you mean "Our work was designed to...

We modified the point (p 16 line 7).

6. Table 3: There are a large number of items on this table, so it would be helpful if they were organized in some way. For example, they could be listed in order from most important to least important based on the responses of the public. Alternatively, they could be grouped by domain. Table 3 reflected the order in which the options were submitted to the participants. We thought this was a meaningful order to present information in an informed consent form. Nevertheless, we revised the table, as suggested by both the reviewers, and listed the information from the most to the less important in the view of participants. We also highlighted the statistical significance (p 29).