Author’s response to reviews

Title: Psychosocial impact of prognostic genetic testing in uveal melanoma patients: A controlled prospective clinical observational study

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Author’s response to reviews:

Dear Ladies and Gentlemen,

Thank you once again for considering our research article for publication in your scientific journal and your second review on this matter. As requested, we made the following alterations:

Technical Comments

1. Editor Comment:
The first objective would be better conceptualised as “the USE of interventions over time” rather than the “need”, since need was not explicitly assessed. This should be rephrased in the abstract, methods and throughout.

1. Authors’ Adjustments:
As suggested, we changed the phrase “need for interventions” to “use of interventions”, in the abstract (line 20) as well as in the section ‘Designs and Methods: Objectives of the Study’ (line 95).

2. Editor Comment:
Some of the language used indicates causality when this could not be established through this
observational study e.g., “prognostic testing does not result in…”; “the psychosocial impact of prognostic testing”. Such statements should be tempered.

2. Authors’ Adjustments:
We kindly considered this recommendation and made the following changes to temper expressions in which causality could be implied:
- Abstract: ”Prognostic testing does not impair psychological well-being” (line 35)
- Results: “Result announcement did not have a significant effect […] (line 198)
- Discussion: “significant immediate effect” (line 284)
- Discussion: “Prognostication in UM seems to influence […]” (line 290)
- Summary: “genetic testing does not influence psychological well-being” (line 333)

3. Editor Comment:
I agree with Elizabeth Bancroft’s review that the comparison with germline genetic testing is not appropriate in this context and that the second and third paragraphs in the Introduction can be removed. At the very least, studies investigating the psychosocial impact of prognostic testing should be presented first and only then related to the wider genetic counselling literature (whilst highlighting why hereditary testing is very different). Corresponding changes should be made in the Discussion.

3. Authors’ Adjustments:
We removed the paragraphs on BRCA1/2 cancer from the introduction as recommended and only left literature on uveal melanoma. We also discarded part of the 5th paragraph where we mentioned which patients opt for genetic testing in breast cancer (“In case of breast cancer, personal history of cancer, perceiving more benefits than barriers regarding testing, having greater family hardiness, and associating a cancer diagnosis with fewer negative consequences were related with the decision for genetic testing […]. Another study revealed that the opportunity of more screening offers, reassurance, and taking care of oneself were associated with the decision for prognostication”, former line 87-91).

In the Discussion we removed the note on how prognostic testing affects patients with breast cancer: “In breast cancer it even reduces adverse emotional states” (former line 296).
In the section ”Risk”, we added that there are no comparable studies in UM patients and highlighted that there is a difference in testing of patients with breast cancer (“No studies on factors predicting prolonged psychological distress in UM patients could be identified. Although prognostic testing in breast cancer is not exactly applicable to uveal melanoma, there are similarities in the emotional response of these cancer patients”, line 319-321).

We left two references of other types of cancer in which the dynamics of behavior and psychological responses are likely to be transferable to UM patients. For example:
1) ‘It appears that psychological impact of genetic testing is not only the result of the communicated cancer risk but can be mediated by the patients’ interpretation and perception of this risk (introduction, lines 69/70)
2) […] suggests an improved accuracy of risk perception (discussion, line 292); here we added: “similar to hereditary testing in other cancer types” to point out the difference in testing of different cancer types.

4. Editor Comment:
There is some unnecessary repetition e.g., re the number of patients who opted for genetic testing (lines 155 and 162).
4. Authors’ Adjustments:
Thank you for this comment. We discarded the following sentences to avoid repetition: “As outlined above (in figure 2), 74 participants decided to undergo genetic testing (IG) at the beginning of the study, whereas only 63 patients remained in the study until result announcement (t2)”. We added the phrase “result announcement at t2” in the second sentence (lines 147/148) for clarification.

5. Editor Comment:
In table 2, the column indicating n (%) or M (SD) could be removed and these could be incorporated in the column headings for TG and OG, with the % sign included after the relevant percentage figures to indicate categorical variables in these columns. This would allow space for a column with the results of the statistical tests (in addition to the p value column that is already included), and would mean that this information could be removed from the text itself.

5. Authors’ Adjustments:
As requested, we removed the column with n (%) and M (SD) in table 2 (line 153). For better understanding we added it to the column of the variable names, instead of incorporating it in the column headings for Test Group and Observational Group. According to the recommendations, we added another column that depicts the results of the respective (significant) statistical tests while removing this information from the text.

6. Editor Comment:
While the manuscript is generally well written, I think some language proofing would help improve some of the phrasing used. For example, rather than “both scoring higher in TG” (page 13 line 176), it would be clearer to say “Participants in the treatment group had higher general distress and perceived a greater risk of metastases than those in the observational group”. Additionally, saying that patients “agreed to testing” or “refused” implies that patients were pressured or advised to be tested. Instead, it may be more accurate to state that patients “availed of” or “opted for” genetic testing and others “did not avail of” or “opted out of”. Such terms are already used in places in the manuscript; the same term should be used consistently throughout. I also still think that using the TG and OG abbreviations is unnecessary and overly complicates things for reader while doing little to shorten the text. If these were just written out throughout, the reminders to the reader as to what these stand for (e.g. p8, line193) would not be necessary.

Other examples of minor typos and phrasing suggestions include:
- Line 45 – “a” instead of as
- Line 55 – 56 “anxiety was found to significantly decline”
- Line 93 – “declining prognostic testing”
- Line 95 – “either the test or the result”

6. Authors’ Adjustments:
Thank you for your language-related suggestions. In the lines 160/161 we changed the Phrase “both scoring higher” to “Participants in the treatment group had higher general distress and perceived a greater risk of metastases than those in the observational group” as recommended.

We further altered the above mentioned phrases (“avail of”, “opt for” etc.) accordingly in the following sections:
- Abstract: line 22, 23
- Design and Methods, Study Design and Allocation to groups: line 110
- Results, Decision Making [...] lines 149, 157, 158, 168

We further discarded the abbreviations for Test Group (TG) and Observational Group (OG) throughout the whole manuscript. Those alterations where made in the following sections/lines:
- Design and Methods, Study Design and Allocation to Groups: lines 110, 111
- Design and Methods, Measurement Points and instruments: line 114 (figure 1)
- Design and Methods, Statistical Analysis: lines 127, 128, 130
- Results: lines 140, 141
- Results, Decision-making: lines 148, 150, 151, 153 (table 2), 154 (table 2), 157, 160, 161, 162
- Results, Psychological Distress [...] line 175
- Results, Psychological Distress [...], Perceived Risk of Metastases: lines 179, 180, 183, 188 (table 4), 190 (table 4)
- Results, Psychological Distress [...], Fear of Progression: line 195
- Results, Psychological Distress [...], General Distress: line 200
- Results, Psychological Distress [...], Depression: line 206
- Results, Psychological Distress [...]. Anxiety: line 212
- Results, Psychological Distress [...], Quality of Life Mental: line 217
- Results, Psychological Distress [...], Quality of Life Physical: lines 221, 222, 223
- Results, Utilization of psycho-oncological interventions: line 236
- Discussion, Psychological Distress [...]: lines 281, 288, 289, 297

To save on word count in figural graphs and to standardize the depiction of groups (M3, D3, OG, TG), we kept the abbreviations in the respective figures and noted the meaning in the corresponding legends. Equally, we left the abbreviation OG in table 5, 6 and 7.

We also altered the above mentioned typing errors in line 45 and 95 (now line 79). Since we discarded the section on BRCA1/2 breast cancer, we did not correct these errors. We did not make an alteration in former line 93 (declining prognostic testing), since in fact it was not declined but opted for. So we changed the expression to ‘a more recent treatment increased the likelihood of opting for prognostic testing’ (line 77).

Further Adjustments:
- We made a correction of one author’s name (line 3)
- We corrected the affiliation of two co-authors (lines 9, 12)
- In the abstract we changed the word “detected” to “estimated” since we considered it more appropriate (line 17)
- In the introduction we changed “choroidal melanoma” to “uveal melanoma” for unification within the text (line 62)
- In the section Availability of data and material we added another author (line 378)
- In the acknowledgements we added another note of thanks (line 390)
- We changed two author’s information (lines 400, 402)

If you consider further alterations appropriate, please let us know.

Sincerely,
Marietta Lieb