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 third review on this matter. As requested, we made the following alterations:

Technical Comments
1. Editor Comment:
Changes made in response to Comment 2 still imply causality e.g. Impair, effect and influence. For example, “Prognostic testing does not IMPAIR psychological well-being” would be better written as “Availing of prognostic testing is not associated with poorer subsequent psychological well-being; rather, it may help to alleviate distress and promote a more realistic risk perception.” Similarly, in the Discussion: “In our study, we found a significant immediate EFFECT of genetic testing for perceived risk of metastases, fear of progression and depression. Receiving test results LEADS TO an instant decline of depressive symptoms and fear of progression on both patients with good and fatal prognosis. On the other hand, the perceived risk of metastases significantly increased in patients diagnosed with M3 while it decreased in patients with until it reached the same level as the Observational Group.” would be more appropriately written as: “In our study, genetic testing was associated with an immediate reduction in fear of progression and depressive symptoms irrespective of whether patients
were informed they had a good or a poor prognosis. While perceived risk of metastases increased following prognostication in those with a poor prognosis, it declined to the level observed among the observation group among those with a good prognosis.” On that note, it may also be preferable to say a "poor prognosis" throughout, rather than a "bad/fatal prognosis"

Authors’ Adjustments:
Thank you very much for your recommendations. We eliminated all language implying causality and used the suggested phrases as follows:
- Abstract line 35/36: We changed the two sentences as recommended (“Availing of prognostic testing is not associated with poorer subsequent psychological well-being. It rather may help to alleviate distress and promote a more realistic risk perception”)
- Results line 198: we changed the sentence which included the word “effect” and changed it as follows: Result announcement was not associated with a significant change in general distress, neither for patients with the good prognosis (D3) (.17 [.32], p = .60), nor for those with the poor one (M3) (-.08 [.31], p = .80).
- Results line 234: we changed the sentence which included the word “effect” and changed it as follows: “Prognostication, however, was not associated with a change in utilization, independent of diagnosis (M3: -.55 [.39], p = .16; D3: -.76 [.40], p = .06).”
- Discussion line 287f.: “In our study, genetic testing was associated with an immediate reduction in fear of progression and depressive symptoms irrespective of whether patients were informed they had a good or a poor prognosis. While perceived risk of metastases increased following prognostication in those with a poor prognosis, it declined to the same level as in the observation group among those with a good prognosis.”
- Discussion line 292: we changed the word “influence” with “be associated with”
- Summary line 337: we changed the sentence “overall, we found that genetic testing does not influence psychological well-being in a negative way” to “Overall, we found that genetic testing is not associated with poorer subsequent psychological well-being”

As far as the expression “impact” is concerned, we left the wording of the title in conformity with Elizabeth Bancroft’s paper (“Psychosocial impact of undergoing prostate cancer [..]”) where a similar formulation was used.

As suggested we also exchanged the expression “bad/fatal diagnosis” with “poor diagnosis” throughout the whole manuscript (lines 50, 199, 221).

2. Editor Comment:
Abstract results section: last line – should this read psycho-oncological interventions? Maybe rephrase to “The use of psycho-oncological interventions increased significantly after prognostication; however, this was equivalent in the test and observation groups. Female sex, higher general distress and higher anxiety predicted greater use of psycho-oncological interventions.”

Authors’ Adjustments:
We changed the last sentences in the abstract results section (lines 32-34) accordingly.

3. Editor Comment:
The addition of the following in the Discussion is good: “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”. However, it would be helpful to briefly clarify for the reader why they are not equivalent (just one line).
Authors’ Adjustments:
Thank you for your suggestion. Considering your comment that this statement could be confusing to an external reader without having further information, we decided to completely eliminate the phrase that breast cancer patients are not equivalent to uveal melanoma patients.

As recommended in the first review, we discarded all literature on prognostic testing in breast cancer patients. Since this specific research question has nothing to do with prognostic testing (in this case it indeed would be quite different in other types of cancer), but with psychological adjustment over time (irrespective of testing, groups were not significant see table 7), the dynamics of coping with cancer might be similar in all cancer patients. The cited literature does not deal with prognostic testing but with the course of adjustment in cancer patients in general. So in fact there are no differences that need to be mentioned.

We left the sentence as follows: “We chose to relate to literature on other types of cancer, since we assume similarities in the psychological adjustment of cancer patients over time”(line 324). We added the information that the respective groups (M3, D3, Observational Group) had no significant influence on any psychological outcome (line 322).

We hope that this solution is in your interest. In case of any other change requests, please let us know.

4. Editor Comment:
I still think adding a % after the relevant figures in the Test group and Observational group columns would aid interpretation; however, I am happy to leave these as is if preferred.

Authors’ Adjustments:
We made the alterations in table 2 as suggested. We incorporated the % sign into the respective columns for better interpretation. We further inserted a ± sign in front of each standard deviation in order to emphasize the difference between categorical and continuous data. We also added a little description below the table as follows: “Except as indicated, categorical data are presented as count (percentage), continuous data are presented as mean (±standard deviations)” (line 154).

Further Adjustments:
- In table 1 we added “and” between utilization of and satisfaction with
- We further changed the affiliation of one author (line 8, line 402)
- In the result section (line 223) on “Quality of Life”, we provided more elaborated information on the interpretation of our results to improve comprehensibility; we changed two sentence in the discussion (line 290f., 296f., 316f.) accordingly.

We hope our changes are in your interest. If further adjustments are necessary, please do not hesitate to let us know.

Sincerely,
Marietta Lieb