Author’s response to reviews

Title: Screening for Distress, the 6th Vital Sign: Common Problems in Cancer Outpatients Over One Year in Usual Care: Associations with Marital Status, Sex, and Age

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Author’s response to reviews: see over
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Dear Dr Chap,

Thank you for recently reviewing our manuscript entitled: Screening for Distress, the 6th Vital Sign: Common Problems in Cancer Outpatients Over One Year in Usual Care: Associations with Marital Status, Sex, and Age. Enclosed is an extensively revised version of our manuscript. We have addressed the points identified by the Reviewers as outlined below. We have quoted each of the Reviewers’ comments in boxes, addressed the concerns below each comment, and included relevant excerpts from the text in italics.

Peer Review 1

There is no justification for the proposed hypotheses. For instance, it is unclear how the proposed interaction between age, marital status, and gender on needs in practical and psychosocial problems was derived. Please justify (1) why being in a relationship will buffer reports of practical and psychosocial problems, but lead to less awareness of and utilization of psychosocial services, (2) why there is an interaction between age, marital status and gender on needs in practical and psychosocial problems, as well as on awareness and utilization of services, but not on reports of problems.

- Our hypotheses are based on the literature reviewed in the introduction indicating that practical and psychosocial problems/unmet needs have in the past been correlated with age, gender, or marital status as individual variables. One of the new aspects for this study is that instead of just considering these three main effects, we consider all interactions among those variables on the level of problems identified throughout the course of 1 year. We believe it is important to consider all possible interactions because a main goal of the paper is to provide some information to people making decisions about specific services to offer in psychosocial oncology units. Interactions allow us to see where need might be greatest (e.g. young single women might have a higher specific need and planners could use that information to add programs to address these needs). We have modified the introduction to be clearer that our goal is to provide this clinical insight and to further clarify the justification for our hypotheses.
- 1. In a number of papers cited in the introduction, being in a married or committed relationship does buffer reports of unmet needs and distress in cancer patients (paragraph beginning at the bottom of page 4). We predicted that if marriage provides a buffer then it also may mean that married people, who do not need services as badly, might be less aware of the services offered. This is a secondary hypothesis rather than a primary analysis. We have modified the introduction to be clear about the reason for testing this hypothesis.
• 2. I am not sure I understand the second point here, so it is difficult to address.
• As this is the first paper to investigate these complex three-way interactions, the interpretation of the results is not always straightforward. In many cases these results may serve to stimulate further research investigating the potential underlying reasons for these sometimes unexpected results, such as the interaction noted by the reviewer.

More information should be given regarding the measure “psychological screen for cancer”. Information regarding the validity and internal consistency of each of the measures should be given.

• We have added the following to the manuscript.

\[ p. 8 \ \text{Cronbach alphas range from .79 to .89 and test-retest stabilities ranged from .49 to .87 [47, 48].} \]

\[ p. 8 \ \text{The Distress Thermometer has been validated against the HADS, BSI, CES-D and clinical diagnosis in patients with mixed diagnoses and stages of disease [45]. A review of diagnostic validity studies reported a pooled sensitivity of 77.1% and specificity of 66.1% [46].} \]

Please clarify whether hierarchical linear model was referred as Linear mixed effects model. Suggest using the terms consistently to minimize confusion.

Thank you for pointing out this inconsistency. The terms all now say “hierarchical linear model” or HLM

It is unclear whether the multivariate analyses adjusted for the effect of distress measured by distress thermometer, depression, and anxiety. Since the measures of distress were significantly associated with practical problems and psychosocial problems, their effect should be adjusted in the multivariate analyses.

• We present the zero-order correlations with distress as a check to see whether in fact these problems are associated with distress. We have changed the introduction to reflect this intention. We did not conceptualize this check as an aspect of our main analysis, simply as documentation that problems can contribute to distress.

• The question we addressed in this study did not involve whether common problems adjusted for distress were associated with age, marital status, and gender. Rather simply whether common problems were associated with age, marital status, and gender to inform clinical services. A number of other research papers have analyzed associations between distress, depression, anxiety and common problems where it has been noted that people with higher distress also identify more common problems. In this paper our intention was to focus on the less-studied list of common psychosocial and practical problems in order to better understand their associations with a number of demographic risk factors.

For the secondary analysis, 95% CI should be included when reporting OR.

• Thanks, we added confidence intervals.
Possible explanations should be given on why younger, single patients endorsed the most practical problems throughout the study whereas younger, female patients endorsed the most psychosocial problems throughout the study.

- We have revised the manuscript so that we convey a consistent message about both issues. For instance, here is a section from the discussion about these issues:

  This study is the first longitudinal investigation of common problems in patients new to the TBCC. The large sample size and longer follow-up period have enabled us to refine previous knowledge in this area. Similar to others, we found that common practical problems include finances and drug coverage [21, 27, 29, 35], with work/school only a concern for younger people [27]. At baseline older people had considerably fewer problems, as did married people, resulting in the highest prevalence of practical problems in young, single people, particularly women. Marital status findings are consistent with other reports in the literature [21, 21, 27, 33, 53], but we add interactions with age to extend this literature. Younger and single people may have lower incomes, less financial stability if they need to leave work for long periods of time, and greater responsibility for young children. Cancer may disrupt their ability to handle all of these competing demands, so practical help might lead to the most positive improvements.

  For psychosocial problems, younger patients reported greater psychosocial problems than older patients, while women reported greater psychosocial problems than men at baseline. Few psychosocial resources target specifically young men and women with support groups or counseling interventions [54, 55], and anecdotally young patients often report that they feel they have nothing in common with older people with cancer in support groups. Again, other reports have consistently shown more psychosocial problems in women [24, 26, 37], perhaps due to an under-reporting bias in males [34, 56] or due to a greater tendency in women to focus on processing emotions [57].

- It is surprising to see young single men were more likely to use psychosocial resources than young single women as studies often showed female patients were more likely to use psychosocial resources. Further elaboration should be given to explain the study findings.

- Yes, we were also surprised. We have elaborated in this paragraph in the discussion

  p.16 Lastly, report of use of the Psychosocial Resources Department at baseline reflected some of these findings. More young single men than young single women reported using Psychosocial Resources, whereas the reverse was true in older participants. This is an unusual finding, perhaps reflecting the prominent erectile dysfunction services offered, and further investigation could document which services young men accessed throughout the year. More young and single men and women reported interest in future use. These results mimic their reports of greater problems. However, older patients may not access services due to experiencing greater barriers in transportation or low caregiver help [58]. Apparently, being married reduces rates of reported current and future interest in the use of services, reflecting some of the buffering seen in the low endorsements of practical problems in married people. Future research could also examine the tumour type of the younger people endorsing use of psychosocial resources which is beyond the scope of this paper. Additionally, future research could examine whether older patients perceived greater barriers to access.

Moreover, did the study identify the types of psychosocial resources being used by the participants? It would be interesting to see what types of psychosocial resources being used by participants who are stratified by gender x marital status x age.

- Yes, we agree with you that it would be interesting. We feel that this question is beyond the scope of this particular paper because it would involve many more analyses, tables, and figures, but if the editor feels strongly that we ought to include this information in this paper we do have these data and are willing to accommodate.
Peer review 2

The authors have previously reported cross-sectional findings from this data and focus here on the longitudinal data. The size of the sample is a strength of the present study. However, conclusions that from this study regarding persistence of distress and practical problems in relation to age, gender, and marital status are difficult to draw because the sample includes some cancers that are gendered, some which are associated with enormous practical problems related to the cancer and its treatment and all with widely differing clinical courses. The longitudinal course of patients in remission or who have had curative treatment appears to be grouped here with that of patients with progressive and terminal disease. In that regard, 7.8% had died by the time of the 3-month follow-up and 15.3% by the 6-month follow-up. It has not been possible in this study to take into account the stage and course of disease and the nature of treatments received during the time period of the study.

- We regret that we had not considered whether stage and treatment were proxies for our findings in the first submission; however, we have considered this in our revision. With the advice of our biostatistician, Helena C. Kraemer, Ph.D., we have conducted the appropriate analysis to rule in or out whether our variables (age, gender, or marital status) are simply proxies for these prognostic variables. We found that they were not, and therefore these variables do not explain our results. We have added a section in the analysis and results sections, and a comment in the discussion about these analyses.

...from the analysis section...... *Lastly, we examined whether stage of disease (primary vs. metastatic) and type of treatment (surgery, chemotherapy, radiation, hormone therapy) could explain our results. In order for our results to be proxies for these underlying prognostic variables, we would have to find significant correlations between the prognostic variables and both hypothesized independent (IVs) and dependent (DV) variables. We tested these associations using Spearman Correlations. Any prognostic variable significantly correlated with both IVs and DVs would then be included in adjusted HLM and logistic regression models.*

.....from the results section......

**Are Age, Gender, and Marital Status Proxies for Prognostic Variables?**

*Stage and Treatment did not simultaneously correlate significantly with IVs and DVs for any of our analyses. Because this condition was not met, and they could not be considered proxies, we did not adjust our HLM analyses.*

- We have also in part quoted Dr. Kraemer to address the issues of gender and age correlated cancers in the discussion:

p.19 *Lastly, because this is a mixed cancer sample in a usual-care cancer centre setting, the frequency of cancer types varied. Our goals were to provide evidence for a general cancer population and services offered in a general cancer setting. Certain cancers (testicular, prostate, breast) are gender-specific. It is not possible to adjust for this in an analysis examining gender. However, a larger number of participants in the current study had cancers that are not gender-specific (747 of 1196). Some cancers are age-correlated, and again, it is not possible to adjust for this in an analysis examining age. Other cancers are too rare in this sample for adjustment. As such, age effects may in part reflect the influence of those types of cancers that are age-dependent, and gender effects may in part reflect the influence of*
those types of cancers that are gender-specific. Further research could investigate larger samples of non-gender- and age-specific cancers.

Further, the authors suggest that the higher use of psychosocial services in young people reflects greater need but have not considered the possibility – which has been reported – that lesser usage of services by older patients may reflect greater barriers to access in the older population than those in younger patients.

- We have added this explanation in the discussion as quoted above.

- **Peer review 3**

Since the patients in the research group concern a mixed group with very different forms of cancer, possibly different phases of cancer (I cannot find information on this subjects: were patients in the phase of diagnosis, primary treatment, after care?), different severity of the cancer, and different treatments prior to the baseline measurement (and possibly also following the baseline measurement), these differences are likely to influence the results of the study.

- (copied from above)
- We regret that we had not considered whether stage and treatment were proxies for our findings in the first submission; however, we have considered this in our revision. With the advice of our biostatistician, Helena C. Kraemer, Ph.D., we have conducted the appropriate analysis to rule in or out whether our variables (age, gender, or marital status) are simply proxies for these prognostic variables. We found that they were not, and therefore these variables do not explain our results. We have added a section in the analysis and results sections, and a comment in the discussion about these analyses.
- We have also in part quoted Helena to address the issues of gender and age correlated cancers in the discussion:

  p. 19 Lastly, because this is a mixed cancer sample in a usual-care cancer centre setting, the frequency of cancer types varied. Our goals were to provide evidence for a general cancer population and services offered in a general cancer setting. Certain cancers (testicular, prostate, breast) are gender-specific. It is not possible to adjust for this in an analysis examining gender. However, a larger number of participants in the current study had cancers that are not gender-specific (747 of 1196). Some cancers are age-correlated, and again, it is not possible to adjust for this in an analysis examining age. Other cancers are too rare in this sample for adjustment. As such, age effects may in part reflect the influence of those types of cancers that are age-dependent, and gender effects may in part reflect the influence of those types of cancers that are gender-specific. Further research could investigate larger samples of non-gender- and age-specific cancers.

The influence of type of cancer, severity of the cancer, phase of the treatment, and actual treatment was not taken into account in the analyses of the relations of demographics with distress or experienced problems. However, this seems very relevant, as it can be expected that some of the differences in distress and experienced problems in for example age and gender could be the result of differences in the severity of the disease, the treatment, the phase of the disease, et cetera between different
demographic groups. In other words: could the relations now presented in the study be really the result of confounder effects, and could differences between for instance age groups, marital status or gender in reality be the result of the fact that the characteristics of the disease were different between these different groups (if the disease, the treatment and the consequences are more severe in certain demographic groups, than that could be the logical reason for experiencing more distress, more experienced problems and more awareness and use of psychosocial sources). To give a real valid conclusion of relations between demographics and experienced distress or problems these differences in characteristics of the disease should be taken into account (and corrected for), which was not done now. This comment concerns all analyses done in the results section.

Moreover, in the discussion there is no mentioning concerning this possible severe bias of the results. The least the researchers could do is to provide both analyses (with and without correction for these possible biases), in order to get a thorough insight in whether it is really demographic groups that view their cancer experience differently (do certain demographic groups cope differently with their disease), or that these differences are the result of different characteristics of the disease between the group (which would mean that they do not differ in the way they cope with the disease, but that they have different (more severe) situations to cope with).

We understand entirely your concern about the stages and types of cancer associated with these results. We have responded to this in the paper and in this revision letter (above).

**Editorial requests**

Please include a 'Competing interests' section between the Conclusions and Authors' contributions. If there are none to declare, please write 'The authors declare that they have no competing interests'.

- We have added this to the end of the manuscript.

Please include an Authors' contributions section before the Acknowledgements and Reference list. For the Authors’ contributions we suggest the following kind of format (please use initials to refer to each author's contribution): AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination. All authors read and approved the final manuscript.

- We have added author contributions to the manuscript.

We hope that these changes have adequately addressed the concerns of the reviewers, and look forward to hearing back from you soon regarding the status of this manuscript.

Sincerely,
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