Author's response to reviews

Title: Differences in the symptom experience of older versus younger oncology outpatients: a cross-sectional study

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RESPONSE TO REVIEWERS’ COMMENTS

Manuscript #8105022047431189 - Differences in the symptom experience of older versus younger oncology outpatients: a cross-sectional study

We would like to thank the reviewers for their thoughtful comments on the above referenced manuscript. All of the positive comments were removed from the responses. Our response to each of the comments is below the comment in italics. The suggested revisions have strengthened the manuscript.

Reviewer: Gary Rodin

The findings from this study are interesting but its methodological limitations make them difficult to interpret. No analyses are presented regarding age differences in each of the studies and global distress ratings on the MSAS are not reported. It is not clear that grouping samples from 3 disparate studies in which there is no control for cancer type, treatments, gender, stage of disease etc allows for meaningful conclusions to be drawn about differences related purely to age. Although the authors indicate that they plan to include these factors in subsequent publications, their lack of consideration here limits the value of the present findings. The age cut-off of 60 is arbitrary and analyses should be presented using age as a continuous variable or with other cut-offs. Finally, the inverse relationship of both physical and psychological distress to age has been previously reported in cancer populations.

Major Compulsory Revisions

1. Presentation of age differences in each the 3 individual studies and using the global distress rating on the MSAS.

Response – In the original submission, on Table 1, we showed that no differences were found among the three studies in the proportion of younger as compared to older patients. In addition, no differences in mean age were found among the three studies. Unadjusted and adjusted values for age differences in all of the MSAS subscales scores (i.e., Physical, Psychological, and Global Distress), were added to the revised manuscript. Of note, younger patients reported significantly higher MSAS subscale and total scores than older patients.

2. Control for factors listed above in comparing age groups.

Response – All of the tables were revised and include unadjusted and adjusted values for each symptom x each symptom dimension. It is interesting to note that, across all of the symptom dimensions, for the majority of the symptoms, age-related differences in various aspects of the symptom experience did not change after the covariates were included in the analyses.

3. The analyses should be repeated with age as a continuous variable since age 60 is an arbitrary cut-off even if commonly used.

Response – While we agree with the reviewer’s comment that an age cutoff of 60 is somewhat arbitrary, a rationale for this cutoff was included in the original submission. An analysis of the effect of age, used as a continuous variable, is included in the revised Table 2 for the occurrence of symptoms. However, the remainder of the analyses used age as a dichotomous variable to answer the primary research question in this study.

4. More complete review of previous literature-including in the palliative care literature- on age differences in physical and psychological distress

Response – The main purpose of this paper was to evaluate for differences in multiple dimensions of the symptom experience (i.e., occurrence, frequency, severity, and distress) between younger and older patients. In addition, for the majority (~70%) of the patients in both age groups, their performance status was either fully active or ambulatory with light work. Therefore, comparisons with the palliative care literature are not entirely
appropriate for this sample. If the reviewer has specific references that warrant inclusion in this paper, he can provide them to us for consideration.

Reviewer: Lucia Gagliese

This manuscript addresses the important, understudied issue of age-related variation in cancer symptoms. It is well written and easy to follow. However, there are some methodological issues which make it difficult to interpret the results or draw firm conclusions.

Major Compulsory Revisions

1. The analyses presented in this manuscript are based on the pooling of samples from three independent studies. The descriptions of the studies suggest that they may be quite different in terms of patient characteristics. Therefore, prior to pooling the data, the authors should determine whether there are any significant differences between the three samples on demographic and biomedical factors and MSAS scores. They should also consider looking at sample by age group interactions.

Response – The primary analysis for this study is to evaluate for differences in various aspects of the symptom experience between younger and older patients. As noted in the response to comment #1 from Dr. Rodin, in the original submission, on Table 1, we showed that no differences were found among the three studies in the proportion of younger as compared to older patients or in the mean age of the patients across the three studies. In addition, in the current revision, all of the potential covariates that differed between the two age groups were controlled for in the analyses. It is not clear what purpose the other analyses that the Dr. Gagliese suggested would serve in relationship to answering the primary aims of this study.

2. More information should be provided on the age-distribution of the participants. Given the fairly young mean age (61.3 ± 12.1 years), the range and distribution by decade would be informative.

Response – The age distribution by decade was added to the results section of the revised manuscript.

3. The authors state that “because the initial goal of this analysis is to report the complete data on unadjusted age-related differences in all four symptom dimensions for all 32 MSAS symptoms, covariates were not included in these analyses” (paragraph 2, page 13) and that these will be reported in subsequent publications. The rationale for this decision is not clear. It would be better to report the unadjusted and covariate analyses in one manuscript. This would give a richer understanding of age-related variation, including potential interactions and would make a more significant contribution to the literature. As it stands, it is very difficult to interpret the findings because they may simply reflect age-related differences on any of the covariates. For instance, the finding that older people are more likely than younger people to report difficulties with urination (page 11), may reflect the age group differences in cancer diagnosis (older participants are more likely have prostate cancer, Table 1) than an effect of age per se. To aid in interpretation, the authors also should report age differences in comorbidities, length of illness, and any symptom management strategies used at time of assessment and examine each as covariates when appropriate.

Response – See response to comment #2 from Dr. Rodin.

In addition, we agree with the reviewer that additional analyses that include age differences in comorbidities, length of illness and symptom management strategies are extremely important. However, these variables are not available in all three data sets. We plan to include all of these variables in future studies.

4. In assessing age differences on a standardized measure, it is important that the measure’s psychometric properties have been established across age groups. Is there evidence that the MSAS’s validity and reliability are invariant across age groups? If not, the authors could perform some psychometric analyses by age group to determine if it is valid to proceed with assessing age differences on scale scores.
Response – The MSAS is one of the most valid and reliable measures to evaluate multiple dimensions of the symptom experience in oncology patients. It has been used in a large number of studies with oncology patients of varying age groups. In the original study [5], the patient’s ranged in age from 23 to 86 years. In other studies [1-4] the age range has been equally as large. In addition, in the methods section of the revised manuscript, the Cronbach's alphas for each of the subscales and total MSAS scores for the total sample and the two age groups are reported.

5. Related to the issue of psychometrics and cross-sample differences, I note that the mode of administration of the MSAS differed across studies (Australia: face-to-face interview, FPS: pen and paper, self-completion at study site (not entirely clear), Symptom Prevalence: completed at home and mailed back). Has the MSAS been validated for each of these modes of administration? Has equivalence of outcomes across administration mode been demonstrated? What response biases might be important to consider in each one?

Response – Across the numerous studies that used the MSAS, the instrument was administered in inpatient and outpatient settings. One study was found that specifically stated that the MSAS was administered in a face-to-face interview.[1] We do not know of any formal comparisons of the psychometric properties of the MSAS based on method of administration.

6. The authors also should consider the clinical relevance of the differences because many seem quite small.

Response – The discussion section of the manuscript was revised to reflect the reviewer's comment.

7. It is difficult to comment on the Discussion until the data are reanalyzed to account for potential subsample differences and covariates.

Response – This comment should be resolved with the inclusion of the covariate analyses.