Author's response to reviews

Title: The Australia-modified Karnofsky Performance Status (AKPS) scale: a revised scale for contemporary palliative care clinical practice. ISRCTN 81117481

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Author's response to reviews: see over
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Editorial Board
BioMed Central Palliative Care
http://www.biomedcentral.com/manuscript/login/man.asp?txt_nav=chk&txt_jou_id=2044

Dear Editorial Board of BioMed Central Palliative Care:

Please find our revised manuscript titled “Assessing performance status in palliative care: a version of the Karnofsky Performance Status Scale for the twenty-first century”. We appreciate the reviewers’ supportive and thoughtful comments and have carefully attended to all of them, with improvements in the manuscript.

A detailed list of all responses and changes is below. A version of the revised manuscript with track changes marked has been posted with the revised manuscript. A supplemental file with our methodology manuscript for the Palliative Care Trial (accepted for publication) is also included.

We have reviewed the formatting checklist carefully to ensure that our manuscript conforms to all of the points.

We are prepared to pay the processing charge if this paper is accepted. Dr. Abernethy has previously reviewed an article for BMC Cancer and has a letter regarding a £130 discount on BMC article processing charges.

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Thank you for reconsidering our manuscript. We look forward to your comments.

Yours sincerely,

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General response:

In the editorial letter there is a request for the ISRCTN to be added to the title and text. This has been done.

Overall, the response from reviewers was generally positive with 1 reviewer recommending to accept the manuscript, 2 recommending revisions and 1 recommending to reject the manuscript. The primary area of dispute was around the significance of the investigation. According to Reviewer 1: “I find it difficult to understand the rationale for an elaborate evaluation of a modified scale that is completely identical to the original scale in 7 of the 11 categories.” Reviewer 3 reflects that “I do not find that the differences in these items among the scales do matter.” And Reviewer 4 requests: “Please emphasize more why the AKPS is really an innovation in palliative care in the new century... Is it relevant to clinical care.”
The original KPS was developed in the 1940’s, a time when hospitalization was an expected response when progressive life-threatening illness was evident. The Thorne modification developed in the 1990’s was an important update, making the scale useful for contemporary palliative homecare settings, especially hospice. The TKPS concentrated on the community setting though, limiting the scales utility in the varied clinical settings encountered in palliative care including inpatient hospice, acute inpatient care, and nursing home care. The Australia-modified version (AKPS) is an important amalgam of the original KPS and the TKPS applicable to both inpatient and community palliative care. Its categories are less directive of the expected location of care, but as much of the original KPS and TKPS language as possible has been maintained in order to reduce confusion and the need for extensive retraining for clinicians already familiar with the earlier versions.

As pointed out by Reviewer 4, the AKPS more accurately reflects the current palliative care population and provides better correlation with survival for patients at the lower ranges of the scale. The better performance of the AKPS will assist with better decision-making in palliative care. Clinical nurses reflect that it is easier to use the AKPS because the categories reflect the varied clinical settings. It is more relevant to contemporary clinical practice. Consistent with Review 1’s suggestion, we have added more detail about the clinical nurses who participated in the study.

We agree that the high level of agreement among the three versions is as expected, given how similar that are. However, before a new scale is adopted for day-to-day clinical practice it is important that it is carefully and prospectively evaluated to ensure that the results reflect what the user expects to be measuring. Further, as we planned to use performance status as a primary outcome in a major clinical trial in palliative care it was vital for us to verify the validity of the AKPS as an outcome measure within the palliative care setting before limiting all of our data collection to this single measure.

The need for formal validation is evident in Table 4 and Figure 2. As Reviewer 1 insightfully indicates, some participants were assessed as a KPS of 20 and an AKPS of 50 even when the KPS 50 and AKPS 50 had exactly the same phrasing. This was done by the same nurse assessing the patient using each of the scales sequentially at the same evaluation visit. This difference in scoring is reflective of the difference in phrasing at other levels on the scales. For an individual palliative care patient a score of KPS 20 (“very sick; hospitalization necessary; active supportive treatment necessary”) may be the best option on that scale, however when reviewing the AKPS scale the score of 50 (“requires considerable assistance and frequent medical care”) is more appropriate in relation to all other levels on the scale. Importantly, this shift to the AKPS instrument with more palliative care appropriate language did not alter the scales’ expected overall correlation with survival, was more correlated with survival at lower levels of the scale, and was more acceptable to the clinical nurses. (Note: Reviewer 1 later suggested that we delete Table 4 and Figure 2, as well as other figures and tables. As this discussion highlights these are important tables and figures for a validation study of a scale such as this. Similar tables and figures were generated for the validation study of the TKPS.)

As highlighted by Reviewer 4, the AKPS may be more appropriate than the other performance status scales in settings outside of cancer. Ninety-two percent of participants in this study had cancer, so evaluation of the AKPS in non-cancer diagnoses was limited. Future studies will focus on further evaluation of the validity outside of the cancer setting.

We have added a significant portion of this explanation to the discussion to ensure that the implications of our findings are more clear for readers. The text added is indicated in the tracked changes version of the manuscript.

In addition, we have individually addressed each reviewer comment, as described below.

Reviewer 1
Most assessments are in the upper range, showing that only a minority of patients were bedridden. The evaluation might have been biased by this, and an evaluation on a palliative care unit with more severely
disabled patients might show other results. The missing correlation of KPS and TKPS with survival in the lower range of the scale may have been biased by small patient numbers in these clusters.

This is an important point and has been added to the limitations section of the manuscript.

The main advantage of the AKPS seems to be the preference of that scale by the nurses doing the assessment. However only very few details on the nurse preference are provided.

We have added further information about the nurses including their credentials and years in practice.

Reading the paper I become confused at how many patients were included. In the abstract assessment of 275 patients are mentioned. In the results section assessment from 306 patients are recorded

We have amended the abstract to 306 patients.

In the methods section the authors state that assessment of the first 120 patients was planned a priori, later on in the methods section collection of the first 200 patients was mentioned. If the sample size was much larger than originally planned, what were the reasons? Did the authors increase the study size because the initial assessment did not show significant differences?

The sample size was not increased. The methodology stated the first 120 participants to exit the trial. In order to have 120 complete data sets, we had to collect all three scales from the first 300 participants recruited into the study. We have added the following statement to page 9 to clarify this point.

“…for the first 300 participants randomized into the trial. Based on our sample size assumptions, this would provide data for 120 exited participants.”

I wondered why the authors did not choose a more divergent scale such as the ECOG scale?

We agree that ECOG is an important scale for assessment of performance status in both oncology and palliative care. Historically KPS has been more widely used, however. We were looking for a scale that had a greater number of levels and greater ability to discriminate between our interventions in our planned clinical trial. As such, we considered the three versions of the KPS.

We have updated the manuscript to reflect the use of ECOG in some trials in palliative care and have noted the lack of use of ECOG in the limitations section.

The manuscript should be shortened considerably. Table 3 and 4 as well as figures 2 and 3 should be deleted.

These tables and figures are important to the paper and are used consistently across other validation papers of performance scales. For example, similar tables and figures were presented in the validation paper of the TKPS and it is useful to be able to compare across the two studies when assessing the scale. In fact, use of Table 4 and Figure 2 was important to address Reviewer 1’s own comment as noted above. Only 1 of the 4 reviewers suggested removing these tables and figures.

The plots in Figures 2 and 3 can be compressed in size so that they fit in a smaller area on a page. This has not been done, but may be done at the discretion of the editors.
Page 10: actuarial survival
No change needed

Page 13: Phases of palliative is predictive
Changed to palliative care phase

Page 13: Nurses preferred the AKPS, but this seems to be related to burden more than to face validity. This section has been expanded to explore issues surrounding face validity.

Page 12: Spearman correlation coefficients below 0.3 between performance scales and survival show that correlation between these items are not relevant for clinical practice.

While low, these correlation coefficients do demonstrate a significant correlation with survival with p < 0.001. In many disease, KPS is considered a predictor of survival (e.g. lung cancer) albeit not the only predictor and the correlations can be low. As noted in the introduction, in an evaluation of predictive validity, Mor et al found significant correlation between KPS at initial interview and survival time (r=0.30, P<0.001). Our findings are consistent with that which is seen with other KPS studies. We have not changed the manuscript regarding this issue.

Reviewer 2
There were no revisions to be addressed

Reviewer 3
I do not find that the differences in terms of these scales matter.

Selection of patients with pain is of concern, because it is not representative of the entire population.

We agree that to purposely select patients with pain would produce a non-representative study population. The eligibility criteria stated that the patient must have experience pain in the preceding 3 months. This definition was very broadly applied and could refer to any type of pain. This pain could have been temporary and not related to the predominate illness. For example, a patient could have stubbed their toe and been eligible for the trial; they just need to have the reference point of what pain felt like some time in the preceding three months. Using this definition of pain we found that all patients screened were able to meet the pain eligibility requirement.

Further, pain is a common finding in palliative care with over 70% of patients reporting some pain on presentation to our palliative care service in South Australia. Limitation of this study to people with some pain at the time of the study or in the preceding three months should be broadly generalizable to palliative care.

We have amended the manuscript to make this point clearer and added baseline pain to Table 2. As can be seen, the standard deviation for baseline present and usual pain indicates that a substantial portion of patients did not have pain on entry into the trial.

A MMSE score <24 as inclusion criteria does not include most patients with low level of performance score for the purposes of the study.
A MMSE of <24 does not exclude people from being eligible in the trial due to a proxy consent procedure approved by all relevant Ethics Committees. Fourteen patients had a MMSE score of <24, of those 10 had an AKPS of <60. We have amended the manuscript to make this point clearer.

How predetermined was the number and timing of assessments per individuals?
As stated on page 7 of the manuscript, it was decided a priori that the 3 scales were to be collected from the first 120 patients who exited the trial. This figure allowed for 6 months data collection using the projected recruitment estimate of 20 participants per month. In addition, as described on page 9 of the manuscript, data was to be collected at every clinical encounter and data collection time point until death. Minimally this was fortnightly for the first 3 months from referral to the palliative care service and then monthly until death or withdrawal from the study. These data collection time points were specified during the planning phase of the study in consultation with the clinical team. We have amended the manuscript to make this point clearer.

A median score of 60 means that most patients were requiring occasional assistance or professional visits, for what palliative care referrals do not seem to be a strict indication.

As stated on page 7, referrals to the local palliative care service could come from heath professionals, family, and patients. In South Australia there are no requirements about patient or caregiver need in order to be referred to palliative care services. The median of AKPS 60 merely reflects the referral patterns of the region and not guided indications for referral to palliative care services.

This embedded substudy does not clear how patients were randomized and for what in the palliative care trial (I did not find data in the literature yet)

We agree that this manuscript does not contain the detailed methodology of the trial. The full methodology of the trial will be published in Contemporary Clinical Trials, likely in late 2005. We have included a copy of the methodology paper as a supplemental file for your review.

Reviewer 4

More careful wording of the title, running title, discussion, and conclusion related to the reason why the AKPS is innovative.

We have addressed the significance of the AKPS to palliative care as indicated at the beginning of this response to reviewers. We have tried to more carefully weave this theme into the discussion and conclusion. Further, we have amended the title and running title.

Please shorten the presentation of statistical analysis considerably (too many data, while lacking issues as discussed above. Please use less precise numbers after the semi-colon).

We have focused our discussion and conclusions as per above. We believe that the presentation of the statistical data and the tables and figures are important for validation of this scale. As per the discussion above, the statistical data, tables and figures mirror other important validation work in the field. Unfortunately, without these it will be difficult to ascertain that the AKPS indeed does perform as well as the KPS and TKPS, and better at the lower ends of the scale.

To abbreviate the manuscript we have removed statements in the results section that clearly repeats data in the tables.

We have limited all p values to three places (numbers) after the decimal point, coefficients to two places (numbers), and all presentations of percentages to one place (number) or less.
The first sentence states an important development, but the reference is a self-reference and from a manuscript honestly declared as still in review processes.

We have instead referenced two important preceding papers demonstrating the importance of performance status evaluation in palliative care, and then included a reference to our Palliative Care Trial where performance status is being used as an outcome measure. The full methodology of the Palliative Care Trial has been accepted for publication in *Contemporary Clinical Trials*. We have included a copy of the methodology paper as a supplemental file for your review.

*The expected goals should be written more precise: 1. Predictive value for what in the settings mentioned? I suspect for survival, then it is prognostic value, of really predictive then maybe for the decision to care for the patients in a certain setting, see major issue.*

These changes have been made.

*In the study setting the word supportive care is mentioned, what does it mean in this context?*  
This has been changed to “multi-disciplinary”.

*Ethics approval: trial registration is already mentioned, duplicate information.*

Trial registration has been deleted from the methods section.