Author’s response to reviews

Title: Determining the prevalence of palliative needs and exploring screening accuracy of depression and anxiety items of the Integrated Palliative care Outcome Scale – a multi-centre study

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Author’s response to reviews:

Chong Guan Ng, PhD (Reviewer 1): It is a psychometric properties assessment of a Portuguese Translated version of IPOS. It is not clearly stated in the Title. The causes the title to be misleading.

This present study aims to explore the screening accuracy of two items of the Portuguese IPOS. The psychometric properties assessment study of the Portuguese IPOS has been submitted elsewhere. IPOS is a Patient Reported Outcome Measure, so we feel the title is not misleading. Nevertheless we have changed it to: Determining the prevalence of palliative needs and exploring screening accuracy of depression and anxiety items of the Integrated Palliative care Outcome Scale – Page 1, lines 1-4 and Page 3, lines 84-87

There is no clear description of IPOS in the whole article. The reader has no clue at all what is IPOS and what is the scale measuring about. The methods session is poorly written. There is no description of the scale. Results were included into the Methods session.

The manuscript contains one and a half pages dedicated to explaining what the Integrated Palliative care Outcome Scale is, with details of each item and how the scale is constructed. This includes the specific psychometric properties of this scale, not results of the present study. We believe readers will have a clear description of this measure. Please see Pages 6 and 7, lines 163-200. Regarding the methods section, we feel it is well structured, with sub headings clearly indicating what the reader will be presented with in each section.

The sampling method is unclear. How could it be the mean reason for exclusion is "Healthy". What is the sample size calculation? There are centres with 1 or 3 subjects included into the study. How could it be? Was the sampling frame selected appropriately?

This is a multi-centre study. There were 9 centres collecting data distributed across the country, from primary to tertiary health care providers. It is expected that in the primary care facilities most patients are healthy, given that our national health system provides medical appointments for all citizens to have periodical health check-ups. We also know that patients
with palliative needs are present in health providers across the sector, so we expect to find them from primary to tertiary healthcare providers. Hence, it is only natural that most screened eligible people in primary care facilities did not fulfill the inclusion criteria of having an advanced disease, as most are healthy. On the other hand, in the tertiary providers, it is expected that most screened eligible people are not healthy, given that these facilities are to care for acute problems, as well as, follow-up of these problems, which in most cases will be chronic and eventually advanced and terminal.

Regarding the numbers of patients per centre, it makes sense that the number of included patients is different, because rural providers will have less patients in the same time frame as urban providers. Additionally, they will have less resources than the urban and have to travel longer distances when providing community and home care, hence will see less patients per the same time frame. Moreover, we cannot assume that the sub populations cared by different providers are exactly the same and the same numbers would appear in different centres. We had a specific time frame to collect data and each centre had the patients that appeared in that time frame, as this study used convenience sampling. See Page 6, lines 149-160.

We did not perform a sample size calculation because there is only one similar study published and it does not use the IPOS, it uses the POS (Antunes B, Murtagh F, Bausewein C, Harding R, Higginson IJ. Screening for Depression in Advanced Disease: Psychometric Properties, Sensitivity and Specificity of Two Items of the Palliative care Outcome Scale (POS), . J Pain Symptom Manage. 2014, doi: 10.1016/j.jpainsymman.2014.06.014.) Additionally, it used several independent data sets combined, so the methodology was a secondary analysis of those data sets.

The analysis and finding description are poorly written. How was the ROC determined? What was the criteria used for cut off?

We previously tested all possible cut-offs but don’t present these results. We determined that the cut-off 2/3 was the most appropriate. We have added this information in the manuscript. See Page 8, lines 212,213.

The criteria used for cut-off of the HADS are the one determined by the authors of that scale, as mentioned in page 8, lines 203, 204.

Why was IPOS used to determined the sensitivity and specificity for depression and anxiety? What was IPOS has to do with anxiety and depression?

On page 7, line 187 of the manuscript it reads: IPOS It is a brief, 19-item, multidimensional scale that captures core concerns in palliative care. This is the reason why IPOS was used in this study. What IPOS has to do with anxiety and depression is stated in the manuscript, page 7, lines 193, 194: item 3 pertains to anxiety, (…) , item 5 is on depression. IPOS asks about anxiety and asks about depression in a quick, clear way. If we can show that these items screen patients for these problems, then, it is much quicker and simpler to do so, rather than having to ask advanced care patients to fill one measure with several items to screen for depression and another measure with several items to screen for anxiety. Patients with advanced diseases often do not have the stamina to fill long measures or a lot of measures. This causes the occurrence of missing data. Moreover, clinically, and for pragmatic purposes in clinical practice it is best to use as few items as possible. So, it is a clear advantage to use a short, multidimensional scale to screen for several issues.
The study objectives, design, methods are unclear. The results and findings are questionable.

We feel the manuscript has clear, well described objectives. The study design is appropriate to meet those objectives and the methods describe the full process of data analysis.

Lisa Jane Mackenzie (Reviewer 2): Thanks to the authors for submitting their revisions to interesting manuscript, reporting on a cross-sectional study of Portuguese patients diagnosed with an incurable and potentially life threatening illness. Distress and concerns relating to symptoms, supportive care and spirituality were assessed using reliable and valid scales (Portuguese versions of the Integrated Palliative care Outcome Scale; Hospital Anxiety and Depression Scale).

The data reporting on the prevalence of palliative care needs is useful new information.

Thank you for your assessment.

I have some concerns about the statistical approach to assessing screening accuracy of the IPOS psychological needs items. This relates to a) the small sample size;

Because there is only one similar study published which uses HADS but not IPOS, it uses the POS measure (Antunes B, Murtagh F, Bausewein C, Harding R, Higginson IJ. Screening for Depression in Advanced Disease: Psychometric Properties, Sensitivity and Specificity of Two Items of the Palliative care Outcome Scale (POS), . J Pain Symptom Manage. 2014, doi: 10.1016/j.jpainsymman.2014.06.014.), we did not perform a sample size calculation. However, our results are somewhat similar to that study, which perhaps is a reasonable sign that the sample size could be appropriate for the analysis plan.

b) use of HADS in place of a gold standard psychiatric interview to detect true positive "cases" - the authors should describe HADS as a measure of symptoms of anxiety and depression, rather than a measure of anxiety and depression disorders;

Due to low resources, it was not possible to use a mental health specialist to provide the gold standard psychiatric interview to ascertain the diagnostic criteria for depression and anxiety. This is one of the main limitations mentioned in page 13, lines 310-315. We used the “next best thing”, the HADS. In Page 8, line201, of the manuscript it reads: The Portuguese Hospital Anxiety and Depression Scale (HADS) is a 14 item screening measure. We feel this is an appropriate description of the measure.

and c) use of sensitivity/specific analysis. I recommend a statistical review of whether this approach is appropriate, or whether an assessment of agreement (kappa) between measures might be more appropriate. If sensitivity/specific analysis, then 95% CIs of these estimates should be included.

In our study we use two different measurement instruments to measure the same variable in patients (anxiety and depression) in one single moment in time. If it was appropriate to treat IPOS items as continuous variables, we would have used the Bland-Altman plots to estimate agreement between the measures. However, IPOS items are on an ordinal scale. For this, Cohen’s kappa and its variations are used. The issue here is that we only use one rater, i.e., the patient, in one single measurement moment. Hence, it is not appropriate to use kappa agreement, as these measurements always assume at least two independent raters.

This is what led us to conduct a sensitivity and specificity analysis using ROC curves and estimating AUC. This is why the title and aims mention screening accuracy (screening properties and we never mention assessment of agreement).

The 95% CIs for this analysis are provided in Table 4.

Minor comments: Figure 1 not required. Please report this information and the overall consent rate among eligible patients should also be reported in text and the abstract.

Thank you for this suggestion. We have removed Figure one and report the information in page 9, lines 232, 233.

Figure 2 should be edited so item descriptions on the y axis to describe item focus rather than question number. These descriptions should align with equivalent item descriptions in Figure 3.

Thank you for this suggestion. We have edited the item descriptions in Figure 2 (which is now Figure 1) to focus on the issue rather than its number and both descriptions match on both figures.

Figures 4 and 5 need to provide key (reference line vs depression/anxiety).

Thank you. This has been done.

Reference list formatting needs review for consistency.

Thank you. We have reviewed and corrected the reference list.

Riccardo Torta (Reviewer 3): The paper is interesting, well structured and easy to understand.

Thank you for your assessment.

Some considerations arise from the text:

Line 60
Why Patient in distress have to be excluded? How the distressed status was evaluated? The explanation of patient in distress is actually reported at page 6 line 155 ("unable to maintain a conversation during a period of time"). It is better to anticipate such statement

Thank you. We have added this to the abstract. Page 2, lines 60, 61

Line 195
Patient version. There are other versions, for example for caregivers?

Yes, this measure has proxy versions, namely healthcare professional and informal caregiver. The Portuguese IPOS has the healthcare professional version validated. We have added this information to the text. Please see Page 7, lines 196, 197.

Line 202
Why the 11 cut-off threshold of HADS was proposed? In literature other cut-off are presented and discussed in comorbid pathologies

The HADS authors propose a cut-off threshold of 11 for clinical use, as stated in page 8, lines 203, 204. This is why we use it in this study.
I think that the following concepts have to be more explained: feeling at peace and share feelings.

Thank you. The discussion of each item content, i.e., cultural adaptation, has been published elsewhere, as mentioned in the text, page 6, line 164 (Antunes B, Ferreira PL. Integrated palliative care outcome scale: Protocol Validation for the Portuguese population. Revista Cuidados Paliativos 2017 Vol 4-N.º1-julho 2017 http://www.apcp.com.pt/revista-cuidados-paliativos/revista-cuidados-paliativos-volume-4-n.-1-julho-2017.html; Antunes B, Rodrigues PP, Higginson IJ, Ferreira PL. “Validation and Cultural Adaptation of the Integrated Palliative Care Outcome Scale (IPOS) for the Portuguese Population” poster at 5th World Congress of the European Association for Palliative Care in Madrid, Spain on 18-20 May 2017). Also, the cultural adaptation for the original english measure and the german measure have been published. These studies contain indepth explanations as to why the items are described in that manner (Schildmann EK, Groeneveld EI, Denzel J, et al. Discovering the hidden benefits of cognitive interviewing in two languages: the first phase of a validation study of the Integrated Palliative care Outcome Scale. Palliat Med 2016; 30(6): 599–610.). Therefore we feel that the discussion of item content is not relevant for the present study.

The evaluation for anxiety and depression is only concerning the item 3 and 5 of IPOS? Are also data from HADS considered? Did the Authors a comparison between IPOS and HADS results?

Yes. We only study screening properties for the IPOS anxiety item and for the IPOS depression item. We use these items dichotomised using a cut-off on 2/3 and cross them with the also dichotomised HADS subscales results with the cut-off 10/11.

In the dignity approach by Chochinov one of the most relevant worries is to be a burden for the family. Is the IPOS item concerning family anxiety and worry also related to this aspect?

Yes, it can be. Being a burden for the family seems to have a cultural nature. The IPOS has an item relating to the family anxiety, however the information the measure gives is rather vague in terms of why the respondent chooses a particular response. This needs to be discussed with the patient in order to understand what family anxiety means to them. This is how the IPOS is used in clinical practice. It is a multidimensional scale to rapidly identify the main palliative needs of patients and families, by using one item per need. What they mean for each patient must be assessed during the therapeutic encounter(s) between patient, family and healthcare professionals.

Did the Authors considered the relationship between pain and depression? Are Patients free of psychopharmacological and/or psychological interventions?

This is a valid point. Due to the heterogeneity of palliative care provision within centres (mental health specialist are scarce in the portuguese NHS and as part of multidisciplinary palliative care teams), its absence in some centres and low resources to conduct this study, it was not possible to go through the patient records and see whether interventions had been prescribed. However, because evidence shows that psychological and emotional diagnoses are frequently overlooked in this population, one could assume that most patients would not
have been diagnosed with these issues, hence, would not be medicated for them. We recognise that the only way to be sure would be to go through the patients’ records.