Author’s response to reviews

Title: Specialist palliative care support is associated with improved pain relief at home during the last 3 months of life in patients with advanced disease: analysis of 5-year data from the national survey of bereaved people (VOICES)

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Author’s response to reviews:

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Dear editorial board,

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Manuscript title: Palliative care support is associated with improved pain relief at home during the last 3 months of life in patients with advanced disease: analysis of 5-year data from the national survey of bereaved people (VOICES).

Thank you for allowing us to respond to the concerns raised by reviewers to our manuscript. We’ve detailed our responses below to each point and highlighted changes in the manuscript.

Please do not hesitate to contact me if you have any questions or require further clarification to our responses.
Yours sincerely

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Reviewer reports:

Reviewer #1: Thank you very much for the possibility to review this manuscript that I read with great interest. The data presented is impressive, the methodology is sound, and the conclusions drawn are reproducible. The issue fits into the scope of BMC Medicine. The manuscript contains very important data for Medicine in general and Palliative Care in particular. Hence, I can fully recommend to publish it. There are only very minor remarks that can easily be solved by the authors.

Content:
It may not be fully clear to an international readership whether the named institution are part of what we would call specialist or generlist palliative care. In most times the paper just names it palliative care. For me a carification would help.

Response: We have specified “specialist palliative care” and defined it in methods section, lines 146-146, page 6. The term “palliative care” has been replaced throughout the manuscript with the term “specialist palliative care”.
Reviewer #2: This is a potentially important report of a very large representative sample. However, the quality of writing lets it down somewhat, in that the narrative is sometimes poorly structured and there are numerous grammatical errors. I have identified several specific issues below but recommend that the whole manuscript be properly edited.

Response: The manuscript has been revised and edited.

The title and Methods both in the Abstract and manuscript should make it clear that this was a cross-sectional survey requiring family members to summarise experience over the last 3 months of life on one occasion rather than a longitudinal survey conducted at different time points over 3 months.

Response: We had stated that the survey’s results are based on a relative’s perspective in methods, lines 109 to 110, page 5. We have clarified that the survey was cross sectional within the abstract (line 34, page2) and methods (lines 105 to 106, page 5).

The definition of palliative care also needs to be given both in the Abstract and Methods to make it clear this does not refer only to specialist palliative care services. The Result that people with cancer were more likely to receive palliative care needs to be presented within the context that one of the providers was cancer specific. This also influences the conclusion that increased receipt of palliative care by people with non-malignant diagnoses is likely to result in better pain relief - i.e. would Macmillan nurse care be as appropriate for people with other diseases? My
understanding from the Results is that people with cancer were significantly more likely to receive good pain relief even after controlling for receipt of palliative care? What proportions of people received care from each of the palliative care providers? And will distribution allow the researchers to compare the relationship with pain relief and the different services?

Response: We have clarified that we have analysed contact with specialist palliative care (professionals and services that are trained in palliative care and provide this care as their core activity) by constructing a proxy indicator as described in the Methods (methods section, lines 139 to 149, page 6). Although Macmillan and Marie Curie nurses have in the past been associated with cancer, in practice both types of nurses see all palliative care patients. The term ‘Macmillan’ nurse is often used interchangeably (as with this survey questionnaire) with the more correct Clinical Nurse Specialist in palliative care. We have also clarified that these services do not differentiate between patients with cancer or non-cancer diseases (methods section, lines 143 to 144, page 6).

I would strongly recommend replacing reference to 'advance care planning' with 'documentation of preferred place of death' throughout to show how limited the measure was.

Response: We have now amended this to “recorded preference for place of death”. The term 'advance care planning' has been replaced throughout the manuscript with the term “Recorded preference for place of death”.

More specific suggestions are as follows.

Abstract

Change verb tense in the first sentence from 'reported pain' to 'report'

Suggest replacing 'expressed' with 'preferred' in the following: 'most commonly expressed place of death'

Insert 'were' into 'who cared for at home'.

Use 'who' instead of 'that' for people (i.e. 'decedents', 'patients' etc) here and throughout.
Results - final sentence; and therefore to experience better pain relief, as the rest of the Results might suggest?

Response: We thanks the reviewer for pointing them to us. We have corrected them and the rewritten the abstract. The term 'that' has been replaced throughout the manuscript with the term “who” for people.

Introduction

First para - There is an update to reference #1 that should be included

Are the sentences on access to opioids relevant?

Second para first sentence - needs to end with a statement that most people die in hospital.

Third para - The first two sentences don't lead at all logically to the aim of the study; I suggest they are moved to the Discussion to be explored in more detail. I also don't understand why the second sentence starts with 'In routine care, however'? I suggest leaving off the final sentence of this paragraph because, in fact, the analysis looked at a whole range of factors associated with pain relief.

Response: We thank the reviewer for their suggestions which we have incorporated. The introduction has been revised and edited.

Methods

A rationale is needed for the choice and definitions of independent variables, especially for palliative care and ACP.

Response: We have clarified the definitions of the independent variables, particularly specialist palliative care (in methods section, lines 146 -147, page 6). We have now replaced the term ‘advance care planning’ with the term “recorded preference for place of death”. We have also used the term “specialist palliative care” instead of “palliative care”.

'Did he/she get any help from any of the services' requires a question mark. Conversely, no question mark is needed after 'preferred place of death'.

Response: We thank the reviewer for pointing it to us. We have corrected it.
Analysis

The sentence 'the differences in the decedents' characteristics were compared using χ2 test' doesn't quite make sense.

Response: This sentence has been amended to improve clarity (methods section, lines 162-163, page 7).

'Multivariate' is much more widely used than 'multivariable' to describe logistic regression.

Response: We have not changed the term used. The terms multivariate and multivariable are often used interchangeably in the public health literature. However, these terms actually represent 2 very distinct types of analyses. Multivariate is more appropriate when you have more than one dependent variable, while multivariable is used when you have one outcome with multiple independent variables – which is the case in our paper.

Was any attempt made to find the most parsimonious model, or were independent variables always left in if they improved fit according to the likelihood-ratio test?

I recommend review by a statistician.

Response: As the aim of the analysis was to identify factors associated with good pain relief, a parsimonious model was not the priority. This strategy was developed before analysis in consultation with the statistician on the team (TF). We have outlined the model development strategy and justification in the statistical methods section, lines 163-171, page 7.

Results

Figure 1 - should be 'respond' rather than 'response'.

Response: We thank the reviewer for pointing it to us. We have corrected them in Figure 1.

I thought Tables 1 and 2 could be combined; indeed, Table 2 looks a bit odd being separate.

Response: Tables 1 and 2 describe different data and we don’t see how they can be combined. Table 1 describes the characteristics of the decedents and respondents, while Table 2 shows the relationships between specialist palliative care and preferred place of death against different causes of death.
Line 174 - no bracket before 'Over'.
Response: We thank the reviewer for pointing it to us. We have corrected it.

What amount of variance in pain relief was explained by the multivariate model?
Response: In logistic regression models there is not an equivalent statistic to R2, although several pseudo R2 have been developed. It is not possible to use these to calculate the variance explained and are only valid in evaluating multiple logistic models predicting the same outcome on the same dataset.

Is there a reason ORs and CIs are given for some but not all variables in the Results? Arguably, some of this text could be removed as it repeats information in the table.
Response: Certain ORs and CIs were provided in the text so as to help the reader interpret all the results in each table and provide key messages from each table.

Discussion
The first paragraph should be focused on pain relief rather than access to palliative care, given this was the main focus of the analysis. The reference to inequity of access should be clarified to indicate this refers only to cancer versus non-cancer (with the caveats suggested earlier) rather than inequity based on other social determinants as has been found by other studies.
Response: We thank the reviewer for this suggestion which we have incorporated (discussion section, lines 235 to 246, page 10)

I am less concerned about the risk of bias from retrospective reporting than the authors are. Bereaved relatives' memory of the quality of care is an important outcome in its own right. Also, the multivariate analysis is still valid given recall bias should have affected all people equally.

What possible explanations could there be for other findings from the multivariate analysis - for example, differences in pain relief reporting according to relationship to patient, the limited difference as a factor of urgent help seeking, or the surprising finding (in the context of other literature) SES was not strongly associated with outcomes? I think the authors could offer much more exploration of these results, especially where there were changes in the strength of associations from univariate to multivariate results.
Response: We wanted to be cautious in our interpretation of the data and analyses and so have highlighted potential limitations. We stated that we cannot exclude the possibility of uncontrolled confounding by factors that were not measured within the survey. We had stated in the results that good pain relief was more likely among decedents who lived in the least deprived areas in comparison with decedents from the most deprived areas, although this was not a strong influence. We have added further discussion about the influence of respondent within the discussion (discussion section, lines 283 to 289, page 12).

The authors make a valid point that 'eligibility criteria for referral to palliative care services include symptoms that are uncontrolled or complicated' but don't follow this with the logical conclusion that, if anything, we might have expected those referred to palliative care to have higher baseline pain and therefore the likelihood for estimates of pain relief associated with palliative care to be an underestimate.

Response: We thank the reviewer for highlighting this and have added a sentence that makes this point (discussion section, lines 277 to 283, page 11).

Reviewer #3: can you answer the following questions /remarks?

126 : no pain ....and without chronic treatment with analgesics ? add these last 6 words
Response: We have used the categories of questions as used in the survey which did not ask about chronic pain treated with analgesics and so have not changed these exclusion categories.

147 Having a preference recorded 148 for place of death: is that enough to evaluate the patient as somebody who did advance care planning?
Is does say nothing about needs and effective symptom con troll, to stop or to withhold some treatments!
This is an a minima advance care plan up to my opinion
Response: We have now amended this to recorded preference for place of death rather than advance care planning. The term “palliative care” has been replaced throughout the manuscript with the term “specialist palliative care”.

Figure 2: why is the sum of % of patients with and without palliative care not 100%?

Idemditto for the (non-)engagement for advance care planning cohort

Response: Figure 2 illustrates the proportions of decedents with good pain relief at home not all decedents (it compares only the decedents with good pain by cause of death and service characteristics during last three months of life).

Reviewer #4: Thank you for asking me to review this paper. The authors have used data from the VOICES survey, a nationally representative post bereavement survey, to investigate the association between receipt of palliative care and pain relief. It’s a useful addition to the literature. My comments are mainly points of clarity, though I do think an additional sensitivity analysis would be useful.

Methods

It is unclear in the methods section where the data came from. I assume the authors had access to individual level data for this study, rather than aggregate data. It would be useful to clarify this in the methods for ease of reading.

Response: we have clarified that we used individual-level data in both the methods (line 162, page 7) and the abstract (line 37, page 2).

Exclusion criteria - Please justify exclusion of people who did not have any pain - could this be because they were very well palliated? I think it would be useful to include this group as a sensitivity analysis.

Response: Our outcome was the success of pain relief at home and we assessed it according to the response to the survey question: “During the last three months of life, while he/she was at home, how well was pain relieved?”

We excluded people who did not have any pain as our outcome was the success of pain relief not the degree of pain at baseline.
Exclusion criteria - please justify exclusion of people who did not spend time at home in last 3 months. Presumably most of this cohort lived in care homes - would hypotheses about pain relief and palliative care not hold for care home residents?

Response: we included people who spent time at home in last 3 months as the information about access to specialist palliative care was only available for this population. Unfortunately, VOICES survey does not contain information about palliative care in a care home or hospital.

Please clarify timescale for 'receiving palliative care at home' - was this for duration of last 3 months?

Response: Yes, we have now clarified the time scale methods part (in line 137 and line 149, page6)

The 'advance care planning' variable seems to encompass only having a preference for place of death recorded, which is a little misleading. Suggest re-name as 'preference for PPD recorded'.

Response: We have amended this description. We have now replaced the term ‘advance care planning’ with the term “recorded preference for place of death”.

Analysis - Multivariable model - clarity needed on how model was built - I am assuming that variables were included in forced manner? Rather than stepwise?

Response: We used a backward selection technique but forgot to report it. We have now rewritten the Statistical analysis part and added a paragraph to explain the variable selection technique.

Results

The sentence beginning 'All characteristics remained in the multivariable model…' does not make sense grammatically.

Response: This sentence had been rewritten (results part, line 202, page 9).

Line 204 (3%) - can't interpret Odds Ratios as % increase, especially when outcome is common (as it is in this study). Needs rewording.
Response: This sentence had been rewritten (results part, line 211, page 9).

Line 212/213 - Good pain relief was more likely in least deprived areas? This is not what the results of the MV model show.

Response: This sentence had been rewritten (results part, line 223-line 226, page 9).

Table 4 - big swing in ORs for age from unadjusted to multivariate analyses - how interpret?

Response: There are two potential reasons for a difference between the adjusted OR (AOR) and the unadjusted (UOR).

Firstly, which is not the case here, if the UOR is conducted on a different number of patients than the AOR, due to case wise deletion.

The second reason for differences is confounding with other variables in the final multivariable model. While we checked and found no evidence of a high degree of multicollinearity, associations between both the outcome and age and another variable(s) are likely to be present. The AOR accounts for confounder(s).

Discussion

First 2 sentences do not relate to aims or main analysis. Suggest re-write. Also advance/advanced spelling error.

Response: This section had been rewritten (discussion part, line 235-line 246, page 10).

More discussion of why 'ACP' variable might be associated with better pain outcomes needed - does not seem logical that discussing PPD would be causally associated with better pain, as suggested in first para.

Response: We have offered an explanation for this relationship within the discussion, line 279-line 283, page 11-12.

Discussion of association with who filled in the survey (child or spouse) would be useful addition to discussion.

Response: We have added discussion of this point (discussion part, line 283-line 289, page 12).
Line 259, would be useful to give suggestions of additional confounders not measured.

Response: We have added examples of potential confounders (discussion part, line 291-line 293, page 12).

General

Occasional confusion of 'advanced' and 'advance' (see abstract, discussion). Misspelling 'relived'.

The thread from aims to methods to results and discussion feels a little disjointed - eg see comment about discussion first para.

Response: We have corrected them. We hope our amendments have improved the flow of the paper.