Author's response to reviews

Title: Symptom experience and subsequent mortality: results from the West of Scotland Twenty-07 Study

Authors:

Alison M Elliott (a.m.elliott@abdn.ac.uk)
Philip C Hannaford (p.hannaford@abdn.ac.uk)
Blair H Smith (blairsmith@abdn.ac.uk)
Sally Wyke (sally.wyke@stir.ac.uk)
Kate Hunt (kate@msoc.mrc.gla.ac.uk)

Version: 2 Date: 9 November 2006

Author's response to reviews: see over
Dear Sir,

Symptom experience, self-assessed health and mortality: results from the West of Scotland Twenty-07 study.

Many thanks for your e-mail of 2nd October requesting a revised version of the above manuscript. My colleagues and I have now had a chance to revise the paper in light of the referees’ comments and have pleasure in enclosing a revised manuscript.

I shall discuss each of the points raised by the reviewers in turn.

**Reviewer One: Anu Molarius**

**Major compulsory revisions**

1. **Why examine number of symptoms?**
   When deciding how to examine the relationship between symptoms and mortality we considered a number of approaches. We decided to examine number of symptoms for two main reasons.  1) We were interested in investigating symptom burden and examining whether there was a dose effect relationship with mortality i.e. as the number of symptoms increased did the association with mortality become stronger.  2) The only previous paper¹ to examine the relationship between symptom burden and mortality had found a relationship between a simple count of the number of symptoms and mortality and we were interested in investigating whether these findings were replicated in our cohort.

   We accept that a simple count of the number of symptoms experienced by individuals is a crude measure that has a number of limitations as highlighted by the reviewer. In order to try to overcome the limitations of this simple count of symptoms and improve our understanding of the relationship between number of symptoms and mortality seen in the previous paper¹, we decided to also look at the impact of these symptoms. We therefore examined the number of symptoms within 5 different symptom summary measures, which take into account the impact of the symptoms in terms of the tendency to have the symptoms, their effect on usual activities, and whether they led to a consultation with a GP. We hypothesised that summary measures of symptom experience that took into account not only the number of symptoms
experienced but also the tendency to have symptoms or their impact on functioning would be a better predictor of mortality than a simple count of symptoms.

We have rewritten the Background of the paper clarifying why we are interested in looking at the relationship between symptom burden and mortality and why we have chosen to look at the number of symptoms within a range of impact groups in the way we have. We have also amended the Discussion to acknowledge the limitations of this approach i.e. that the findings are dependent on the number of symptoms asked about and which symptoms are listed. We have also undertaken some additional research (as suggested by this reviewer) to address the question in a different way (see point two below).

2. Why not look at what kind of symptoms are related to mortality?
The reviewer felt that a more relevant and interesting way to address our research question would be to look at what symptoms are related to mortality and whether these relationships are independent or explained by chronic conditions or self-assessed health. We thank the reviewer for this suggestion and agree that looking at types of symptoms is also interesting. We have therefore undertaken some additional analysis of our cohort to address this question. The revised paper includes a new table (Table 3) showing the relationships between types of symptoms (respiratory/ENT, musculoskeletal, gastro-intestinal, mental health, neurological, and systemic) and mortality. Since our main aim was to look at symptom burden and mortality we have included this new data in addition to the previous analyses (using number and impact of symptoms) since we (and other reviewers) feel that our original approach looking at symptom burden is also important and useful (see point 1 above).

3. Adjustments for chronic conditions
On reflection, we agree with the reviewer that the variable ‘presence of any chronic condition’ is unspecific and too simplified. We have therefore excluded it from the paper and not used it for adjustments in the analyses. In the original paper we had created a separate dichotomous variable for each chronic condition. As suggested by the reviewer we have used these for adjusting for chronic conditions. Rather than adjusting for one variable including three conditions (musculoskeletal, digestive and mental health) which are not related to mortality and two that are (respiratory and cardiovascular) we now simply adjust for the presence of cardiovascular conditions and the presence of respiratory conditions i.e. those conditions shown to be related to 13-year all cause mortality in Table 2, and therefore potential confounding factors.

4. Use of symptom categories
As highlighted in point 1 above, we feel that investigating different groups of symptom impact is important. Since our main hypothesis is that summary measures of symptom experience, which take into account the number of symptoms experienced, any tendency to have the symptoms and any impact on functioning, may be better predictors of mortality than simple counts of symptoms we feel it is important to show the findings for each of the 5 groups examined in a table. However, since (as the reviewer points out) few differences in the groups exist (particularly after the new adjustments requested have been made) we have substantially shortened the description of these results in the text of the paper. Adjustments for these different groups are no longer included in subsequent tables as requested.
Other comments

Background
In rewriting our Background (to address comments from each of the reviewers) we have removed sweeping references as requested.

Methods
We have expanded the paragraph describing the cohort to provide additional details on how the cohort was selected and to highlight the participation rate for the part of the cohort used in the study.

We have provided further description of the personal and social information collected and added a reference when referring to the Carstairs deprivation category.

We present several measures of socio-economic status (social class, housing tenure, car ownership and deprivation category) in the paper. We have retained these in Table 1 to show the relationships between individual variables and mortality. However, as highlighted by the reviewer many of these variables are intercorrelated, making it inappropriate to adjust for each of these in the Cox regression as collinearity may result. We chose to retain housing tenure as the single socio-economic status variable adjusted for. We have expanded the data analysis section of the paper to clarify this.

Discussion
We have removed the reference to gender when discussing the strengths of the study. Examining differences between men and women was not an aim of this paper and so we agree that this is not relevant to highlight in the strengths section.

Abstract
We have amended the conclusion of the Abstract to remove the generalisation, since our findings may only apply to the age group and follow-up period studied and the variables used.

Minor essential revisions
We have deleted “two-sided p-values” from the text on page 6.

We have removed the odds ratios and confidence intervals for the results in reference 29 (now ref 11) in the Discussion and described the findings with words as requested.

Reviewer Two: Bo Burstrom

We thank the reviewer for his positive comments about the study.

Minor essential revisions
We have undertaken an additional review of the literature to address the reviewers concerns about having a number of older studies in the paper and missing more recent studies. We have removed the older studies from the paper and added more recent references where relevant. As requested by one of the other reviewers (Reviewer 4) we have changed the main focus of our paper (in particular our Background) to concentrate on the relationship between symptoms and mortality rather than self-
assessed health, symptoms and mortality. Additional papers focussing on the relationship between self-assessed health or chronic conditions and mortality have therefore not been included.

**Reviewer Three: Peter Bath**

We thank the reviewer for his positive comments about the study.

*Minor essential revisions*

We agree with the reviewer that the use of the word ‘linear’ is not appropriate here and we have omitted the word as requested.

We have changed the wording of the sentence requested by the reviewer. This now reads “there was no clear trend in any of these symptom summary measures with increasing number of symptoms”. We have chosen to refer to symptom summary measures rather than use the word ‘categories’ or ‘variables’ to make our meaning as clear as possible for the reader as we refer to symptom summary measures throughout the paper.

**Reviewer Four: Ellen Idler**

*Major compulsory revisions*

1. **Motivation for the paper**

   We accept the reviewer’s criticism that the Background did not clearly establish the motivation for the paper. The primary aim of the paper was to look at the ability of symptoms to predict mortality and the structure for the analysis followed this aim (with symptoms and symptom counts as the primary independent variable). As a secondary aim of the paper we had also looked at whether the relationship between self-assessed health and mortality was mediated through symptoms (with self-assessed health as the primary independent variable; originally Table 4). By focussing on our understanding of self-assessed health and its relationship with mortality at the start of the paper we appreciate the main aim and motivation for the paper may have been lost. We have restructured the paper and rewritten the Background so that our main aim of the paper (examining the ability of symptoms to predict mortality) is much clearer. We have said less about our secondary aim looking at the relationship between self-assessed health and mortality) and the original Table 4 has been deleted. We believe the motivation of the paper is now much clearer.

2. **Symptoms examined**

   We agree with the reviewer that the symptoms included in this study are largely symptoms of minor, transient, self-limiting conditions and that symptoms of more serious conditions are not included. This was a result of the way in which the cohort was originally established and could not be controlled in the present analysis. We acknowledge the limitations of this and the effect it could have had on our findings in the Discussion.
This reviewer was also concerned that the symptoms measured had simply been counted and no combination of symptoms had been undertaken. We have now included a new analysis showing the relationship between different types of symptoms and mortality as suggested by another reviewer (see Reviewer 1, point 2).

3. Measures of self-assessed health and symptoms

We have added a sentence into the Discussion to acknowledge the fact that symptoms and self-assessed health were measured over different time periods. Although there is no known association between self-assessed health and non-chronic conditions and so no reason to expect a relationship between them we did find a clear relationship between self-assessed health and the symptoms measured in this study, with 31 percent of those with 0 symptoms in the last month and only 5 percent of those with ≥6 symptoms in the last month reporting excellent health. Restructuring of the paper has meant we no longer allude to such a relationship.

4. Measure of chronic conditions

We agree with the reviewer that our measure of chronic conditions was limited by lumping different conditions together, both in terms of having “any condition” or a count of conditions experienced. We accept that different conditions show different relationships with mortality. In order to address this we have now used different types of conditions (musculoskeletal, respiratory, digestive, cardiovascular and mental) in our new analyses, as suggested by another reviewer (see Reviewer 1, point 3).

Minor essential revisions

We have tried to make the variants of the symptom variables clearer in the description of each category in the Methods section of the paper. We have also amended the wording used in the Tables to make this clearer.

Discretionary revisions

We have gone through the paper carefully to ensure we do not use the terms “self-perceived health”, “self-rated health” and “self-assessed health” interchangeably. We are now consistent in the use of the term “self-assessed health” throughout.

We hope this letter clarifies our work and answers all the reviewers’ questions and comments adequately. We believe our revised paper is much improved by the changes suggested by the reviewers and we thank them for their input. We will be happy to respond to any further queries you or the reviewers may have.

We look forward to hearing from you in due course.

Yours sincerely,

Dr. Alison M. Elliott

Senior Research Fellow and Wellcome Trust Research Career Development Fellow
On behalf of all authors