Author's response to reviews

Title: COPD Uncovered: An International survey on the impact of chronic obstructive pulmonary disease (COPD) on a working age population

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Version: 2 Date: 8 June 2011

Author's response to reviews: see over
Dr A Bourdin
BMC Public Health

8 June 2011

Dear Dr Bourdin

I am delighted to send you a revised copy of our manuscript. We would like to thank the two reviewers for their very helpful suggestions and comments.

We believe that we have addressed the points that have been raised. In order to assist the editorial process we have itemised each point overleaf. We have also placed comment boxes alongside the manuscript where changes have been made. The comment boxes are coded according to the comment numbers.

On behalf of the team of authors I thank you for your kind attention. We look forward to seeing this important work published in BMC Public Health.

Yours sincerely

Monica Fletcher
Chief Executive

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Reviewer's report and comments

Reviewer 1

METHODS:

R1- 1.1 Comment: The inclusion criteria must be more clearly defined.

Response: The methods section now includes complete information with regard to inclusion criteria.

R1- 1.2 What is the target population in each country, as they come from different origins? For example, in Brazil COPD patient associations, in front of major hospitals, in parks and squares; but it is not indicated how many patients come from each one of these places. In China it says “random sample of household”, but what is the sample unit: single family homes, a block of flats (in this case is a flat or the whole building selected?)…do all the inhabitants have the same probability of being included?

Response: We aimed to recruit 400 people from each country and to obtain a broad spectrum of respondents with a range of demographics, including age and disease severity in the cohort as a whole, which we have succeeding in doing. In order to achieve this we used a mixed method of recruitment which accounted for country specific differences. We have described in more detail the recruitment methods in Table 1. The data was collected by a contract research organisation in July 2009 and specific information regarding exact numbers of people recruited in each place is no longer available.

R1- 1.3 Comment: The very different patient inclusion criteria probably generate a selection bias. Members of patient associations are usually very different from the general population, less motivated and less informed about the disease.

Response: We gained a broad mixture of people in the final cohort, representing the rich diversity of people with the disease in terms of severity, age, and number of comorbidities.

R1-1.4 Comment: What comorbidities are included? It mentions an article, and “adapted from a predetermined list”, but it does not specify whether these are included (all or some) or others similar. The face to face or by telephone survey probably modifies the response.

Response: the full list of comorbidities included in our survey is now listed within the Methods section in order to clarify the scope of comorbidity information requested from respondents.

R1- 1.5 Comment: It is not clearly specified during what time the impact on work was evaluated, or on the use of hospital resources. In the last month? In the last year? In Figure 2 it says “last month”. If only one month is analysed, in a disease like COPD, where the exacerbations have an important seasonal component, the inclusion of a time period with different seasons (summer, winter,...) would probably change the impact of the disease.

Response: Healthcare utilisation is now clear within the Methods section in terms of the time measurement (within the last month). As a result, the measurement of healthcare utilisation is clarified prior to the reader reaching the Results section. This will allow for a more accessible read. The WPAl questions relate to experience in the previous week because of the unreliability of recall over long periods.

The seasonality point is correct, if indeed the exacerbations follow a seasonal pattern, as all countries except Brazil are in the northern hemisphere. We have acknowledged the possibility of underestimation in the discussion.

R1- 1.6 Comment: The included age also implies differences between countries. If patients up to 68 years are included in a country where the retirement age may be 58 years makes it difficult to analyse the impact on work at that age, and even in age groups near retirement age.

The survey is focused on the working aged age group, not those purely in work. We would certainly agree that the earlier the retirement age in a country, the less the expected impact of the disease on work or retirement decisions within that age group for that specific country. The objective was not only to assess the impact on early retirement in each country. If it had been then a different age sample in each country might have been necessary. We have noted in the text the country specific retirement ages and that they differ for the interest of the reader.
It is our intention to further analyse and publish country specific data and explore country specific issues such as retirement ages (which have indeed increased in some countries already since the survey was undertaken). We have now added an objectives section early in the manuscript for the reader to keep these in mind when reading the article in its entirety.

R1- 1.7 The analysis on the impact on the carers is not well explained. It says “we made the following assumptions about carers’ ability to participate in the workforce”, but it does not explain the basis on which these assumptions were made.

There is no formal basis for the assumptions other than application of logic, as there was no space in the questionnaire to explore the full details of each carer’s personal circumstances. Sensitivity analysis indicated that this was not a major element in the societal costs for this age group so further work might not be worthwhile.

STATISTICAL ANALYSIS:

R1- 1.8 Comment: It is not described how it was done. Confidence intervals are mentioned, but not which (95%, 99%??)

Response: This has been added within the Statistical Analysis section, the confidence interval of 95% has now been included.

R1- 1.9 Comment: It does not specify which variables are analysed as independent variables and which are dependent variables.

Response: We have now outlined the objectives of the study (see ‘Objectives’ section). We would explore the statistical significances in future research studies. COPD Uncovered thus far has been a hypothesis generating study rather than a hypothesis confirmation study. As a result, we did not set out to test hypotheses. As a result, significance tests are mostly not included with the exception of one independent samples t-test.

R1- 1.10 Comment: It is not analysed whether the increase or decrease in the severity of the disease, quality of life, comorbidity… is significant or not.

Our response to R1-1.9 is also relevant here. We did not aim to test relationships between variables in terms of statistical significance. Productivity, healthcare utilisation, severity and quality of life as you rightly elude to, represent our key variables, in order to measure the personal ,social and economic burden of COPD, and we discuss our results for these key factors in relation to age and severity.

R1- 2.1 Comment: Perhaps a study in which the dependent variables were those defined as the outcome of the study, and the other available ones as independent variables, performing a univariate and multivariate analysis, including the statistical significance would be more enlightening.

We reiterate the response to R1-1.10 here. As we did not conduct statistical significance tests, and we did not test hypotheses but instead generated hypotheses from this study, we have not listed variables in terms of being either independent or dependent variables.

ETHICS

R1- 2.2 Comment: We see no information on whether the study was submitted for the approval of the Research Ethics Committee.

Response: We have included the standards adhered to by the contract research organisation. This clarifies the ethical standards which were incorporated in the survey.

RESULTS:

R1- 2.3 Comment: The refusal to participate by 58% of patients might be a selection bias in the study.

It is acknowledged in the study limitations that surveys may lead to some bias, but we attempted to mitigate against this by the wide methods of recruitment methods. We did not want all participants to come from one setting: for example being recruited in a hospital out- patients department as this
would have led a potential bias in that we may only have recruited subjects with moderate to severe disease..

In Table 2 we observe that the majority are women, in some countries very much in the majority. This appears to contradict known prevalence data (Han, Am J Respir Crit Care Med 2007). Could it be that some selection bias has influenced these results?

We did not set quotas for the number of men and women. It is recognised that women on the whole are more likely to participate in surveys (either face to face or by telephone). The total cohort is evenly balanced and we have made reference to this in the paper now.

R1- 2.4 Comment: The results are not clearly expressed. A systematic presentation is not followed. For example, in Table 3, EQ-5D is analysed according to age and severity of the COPD; but in Table 5, productivity only according to age.

Response: We have incorporated productivity analysed by severity in order to produce the systematic presentation of results between the variables age, severity and productivity.

R1- 2.5 Comment: Comorbidity in accordance with severity was not an objective of the study (Table 4). This adds confusion to the reading of the results, distracting attention from the primary objectives.

We would prefer to keep this in the paper and will be explored in more detail in subsequent publications/abstracts, as comorbidities may contribute to early retirement. Thank you. We have changed the format so easier to read.

R1- 2.6 Comment: The results are presented in some age ranges in Table 2. Other different age ranges are used in Tables 3 and 5.

Response: For consistency the age bands have been changed in table 1 to reflect EQ-5D figures in Table 3 and 5. The age bands for EQ5D are the population norm data and therefore cannot be changed. This provides continuity in the age ranges presented throughout the paper.

R1- 2.7 Comment: The data are expressed simultaneously in dollars, euros, pounds. This leads to confusion and makes reading the article difficult.

Response: Our Health economist advises us that this is standard practice, but the journal may have a policy on this? We have removed the Euro equivalents in order to make the article easier to read. We have therefore removed the Euros.

R1- 2.8 Comment: Page 8: Work productivity. It shows that loss of productivity was more marked with advancing years, but we do not know if the difference is significant (as we point out in “Statistical Analysis”)

We have now outlined the objectives of the study (see ‘Objectives’ section). We would explore the statistical significances in future research studies as an aspect of hypothesis testing. COPD Uncovered thus far has been a hypothesis generating study rather than a hypothesis confirmation study, and therefore we did not set out to test hypotheses. As a result, just two significance tests are included related to EQ-5D.

R1- 2.9 Comment: Page 9: “impairment of regular activities outside work is greater than overall work impairment”. Perhaps this may be due the most severe cases already do not work but have difficulties in regular activities. This analysis adjusted for severity may be of interest.

Response: We have now included a table presenting productivity analysed by severity. This helps explain the possible effect of severity on work capacity.

R1- 2.10 Comment: The influence of gender on the results is not analysed. It would be interesting to include this as an independent variable.

Response: we have the significance value within the EQ-5D results section in order to clarify the possible influence of gender.

DISCUSSION:
R1- 3.1 Comment: It must focus on the significant aspects of the study. With the current analysis we do not know whether the results are significant or not, and whether they justify discussion.

Response: we have re-written small sections of the Discussion, and given more attention to the factors which may have influenced the results, including cultural aspects.

MINOR REVISION:
R1- 3.2 Comment: Abbreviations defined in the text where first used.

Response: All abbreviations have been checked and now are defined in the text where they first appear.

R1- 3.3 Comment: Page 5, first paragraph:

The average values for the respondents were compared to age- adjusted population values for those countries where normative data were available. Here we need the reference.

Response: Thank you we have now added into the manuscript the Szende reference for this.

R1- 3.4 Comment: Page 5, third paragraph: “An alternative would have been to have used the friction…. On wages and employment caused by COPD”. I think is not necessary.

Response: This explanation has been removed. As possibly superfluous,

R1- 3.5 Comment: Page 7, last paragraph. Table 2. I seems to be mistake, we can’t see EQ-5D in table 2.

Response: This has been changed to Table 3 to rectify the above.

R1- 3.6 Comment: TABLES. There are two different table 4. Check.

Response: This has been altered to clarify Tables 4 and 5. All table numbering has been altered.

REFERENCES:
R1- 3.7 Comment: Some references are not adapted to the format of the journal. They must be revised. There seems a lot. To focus the discussion on the significant results would help to reduce the number of references.

Response: This has been re-checked and references have been revised in order to provide

GRAMMAR AND STYLE:
R1- 3.8 Comment: On page 12, "summise" perhaps is "surmise".

Response: That you for highlighting this typing error. This alteration has been made.

ABSTRACT:
R1- 3.9 Comment: Well structured. It must be re-written in line with the new analysis and discussion.

We have re-written small sections of the Discussion where we have included more cultural context, in particular with regard to Chinese culture. The sections within the Discussion have been re-ordered to maximise the flow of text.

Reviewer 2:
R2-2.1 Reviewer Comment: Given the scope of the study it is a little disappointing that more data is not available when comparing COPD patients from different Countries.

Response: The analyses by country will be covered in forthcoming articles. This initial paper provides the overall data from the study, and therefore does contain specific analyses related to country.

R2-2.2 Reviewer Comment: A more in depth questioning may have more accurately identified some of the reasons for the differences between illness behaviour and resource utilization that is seen. A breakdown of the data by age may be worth the effort as this will further inform the conclusions.
Response: Thank you for this comment and we accept the comment made here. The objectives however clarify the aim of the present study. Future research derived from this initial COPD Uncovered study will explore the relationship between age and healthcare utilisation.

Comments R2-2.3 to R2-2.8

R2-2.3 Comment: Minor:p8 para 2 this would be worth rewriting to improve syntax and clarify understanding.
R2-2.4 p8 para 3 line 2 2nd sentence does not make sense. Hospital inpatient Thank you the missing word is ……inpatient STAYS represented 68%……..

R2-2.5 p8 para 3 line 6 “These estimates exclude…” this sentence could be rewritten to improve clarity
R2-2.6 p8 para 3 last sentence; need to add that the utilisation occurred in the preceding month.
R2-2.7 Figure 3: why were there no subjects with severe COPD in China?

Response: we have now discussed the possible cultural effects within the Discussion section and this is labelled.

R2-2.8 p12, para 5 line 4: missing objec in sentence. Add "studies" after "some of the studies..."

Response: All of the minor issues above (R2-2.3 to R2-2.8) have been addressed in order to improve grammar and syntax.