Author's response to reviews

Title: Causes of death in asthma, COPD and non-respiratory hospitalized patients. A multicentric study

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Author's response to reviews: see over
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BMC Pulmonary Medicine (Section: Asthma and allergic disorders).

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Author’s response to reviews: see over
Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your reviewer’s comments. We have included the recommendations of the editorial team with the inclusion of sections of 'Authors' contributions' and Acknowledgements. The changes suggested by the reviewers have been included in the manuscript and the statistical analysis has been revised.

Reviewer's report
Title: Causes of death in asthma, COPD and non-respiratory hospitalized patients. A multicentric study

Version: 3 Date: 29 January 2013

Reviewer 1: Mark Weatherall

Reviewer's report:

The authors present a cross-sectional study of a set of deaths from a number of hospitals for four months of the year examining the association between respiratory diagnoses and deaths from cardiovascular disease.

Major compulsory revisions

The study is not a case-control study as the source of the patients was those who died in hospital and not a group with a disease and a group without the disease.

- According to the reviewer is a observational, retrospective, cross-sectional, multi-centre study. Is not a case-control study. We have changed this in the text.

The sample is limited in a number of ways, not discussed by the authors. It was unclear how the cause of death was determined or how many patients had post-mortems to confirm diagnostic accuracy. Although the authors have used reasonable criteria to assign diagnoses of asthma and COPD it was unclear what happened to those without clear diagnoses (excluded from the analysis), for example how many were there and why were each excluded? It was also unclear how certain the authors were that those who did not have asthma/COPD actually did not have these disorders. This sample is of those dying in hospital. What proportion of deaths in Spain do not occur in hospital?

- In our study, we included deaths in different Spanish hospitals in four months representing different seasons. The cause of death was determined according to certification that existed in medical history signed by the doctor who treated the patient, no death was excluded. In Spain about 68% of deaths occur in hospitals with certain regional geographic variation. We believe that the information collected is representative because most of the Spanish population deaths occur in hospitals. It may be that some deaths not reach the hospital: secondary to traffic accidents, violent deaths, sudden deaths and some terminally ill.
There are a number of weaknesses in the presentation of the data summaries and the analyses. The authors should consistently present numerators and denominators and not just proportions in all of the tables and the text. P values cannot = 0.000; the usual practice is to present very small P values as <0.001 (or whatever the journal style is)

- Done

In the statistical analysis section it is not that variables have normal distributions but that normality assumptions (e.g. distribution of residuals) are not met.

- We check the normality or otherwise of the sample using the Kolmogorov Smirnov. In statistical analysis

In Table 1: I was unclear about contingency table analysis it looks like the authors have compared each row separately rather than a proper Chi-square analysis of the complete contingency tables? In ANOVA have presented P values for individual contrasts and not overall and there are no point estimates and CI and probably no pre-specified contrasts

- The overall intergroup comparison was performed using ANOVA test (comment entered in results). The overall comparison of the three groups usin ANOVA showed significativs differences in gender (p< 0.001), smoking (p< 0.001), obesity (p = 0.002) and BMI (p < 0.001). The results are shown in the results section. We kept the comparisons between groups (2-2) in the table 1 and 2, to consider providing more information. We have introduced a confidence interval of 95% in the tables.

Table 2: Similar problems for this table

- The overall intergroup comparison was performed using ANOVA test (comment entered in results). The comparison of the causes of mortality among the three groups usin ANOVA showed significativs differences in solid malignancies (p < 0.001), respiratory insufficiency (p < 0.001) and other causes (p = 0.008). The results are shown in the results section. We kept the comparisons between groups (2-2) in the table 1 and 2, to consider providing more information.

Table 3: Although have N’s not presenting P values and unclear what hypotheses were being tested.

- In table 3 we try to reflect the homogeneity of the populations considered as asthmatics. It represented previous clinical and functional respiratory characteristics of all patients with asthma who died, by the degree of certainty of the diagnosis of asthma. Differences between asthma high certainty and asthma lower certainty.
Table 4: Unclear is the Odds ratio for association between death from CVS disease versus from other, in which case need appropriate N/N’s to accompany ‘crude’ OR

- Done

Table 5: Need the other N/N but also probably not a sensible analysis as have divided up CVS system deaths

- We have changed the table 5 by another more appropriate. We performed multivariate analysis using as dependent variable the causes of cardiovascular death with different parameters including previous diagnosis of asthma, as reflected in Table 5. We found that prior diagnostic asthma was not significantly associated with these causes of death, with a high odds ratio was obtained for heart failure (see Table 5)

**Minor compulsory revisions**

There has been no control of type I error rate and many statistical tests have been performed, with no comment on this as a weakness.

- As for the type I error, we penalized or adjusted p values for multiple comparisons. The method used is the Bonferroni. Thus, only be significant after adjustment, those differences which were approximately original p less than 0.005

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare I have no competing interests
Reviewer's report

Title: Causes of death in asthma, COPD and non-respiratory hospitalized patients. A multicentric study

Version: 3 Date: 19 February 2013

Reviewer 2: David Mannino

Reviewer's report:
The authors have responded to my prior concerns

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'