Author's response to reviews

Title: Correcting Misdiagnoses of Asthma: A Cost Effectiveness Analysis

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Author's response to reviews: see over
Reply to Reviewers’ comments:

Thank you for a thorough review and comments on our paper. We have replied to all the comments below. The reviewers’ comments are given in italics:

1) Page 4, introduction, paragraph 2, lines 7 – 10: The statement describing the diagnostic algorithm is misleading. According to figure 1 and Luks et al. (ERJ 2010) the first diagnostic steps were lung function and bronchial challenge testing, to be followed by tapering off of asthma medication.

The sentence has been edited to reflect the diagnostic algorithm.

2) Page 12, discussion, paragraph 2, lines 2-3: It does not bother me that I do not understand the specifics of the statistical analyses described on page 8. However, I am sure that the sentence “The non-parametric bootstrapping used … sample size” can be phased differently so that the average reader of the BMC represented by me understands what is meant.

We have now provided a simplified version of this in the manuscript.

3) Table 1: The information in this table is not critical for the message of the paper and could easily be presented in an online repository. This is even more so since drug prices in different countries differ, and the authors do not tell us which patients were on which drugs.

Though the costs are Canadian, we think the table 1 is important to understand the contents of the paper. It is also a good reference for readers from different countries to compare the drug costs since drug cost is a major expense in asthma care in all countries.

4) Figures 2 and 3 should be changed in a way that the lines representing any medication and daily medication can be distinguished even on a black and white copy.

We have now edited the figures using different styles of the lines rather than just color shades.

5) The study objectives are to show the cost-effectiveness of screening, but only costs are considered. The authors should make clear the effectiveness assumptions that are being made.

The assumptions made in estimating the effectiveness are stated in the manuscript. We have now edited the manuscript to clarify that we assumed that the subjects lived a maximum of 50 years since the time of first diagnosis of asthma. Moreover, we have performed three sensitivity analyses. The first, restricting analysis to 25 years, the second with the assumption that only a general physician rather than a specialist sees the patient; and the third, with the assumption that low vs. high inhalations of the daily short acting bronchodilators.
6) Patients were supposed to live 50 years from the time of first diagnosis. This assumption should be justified and tested in the sensitivity analysis.

We have edited the manuscript to make it clear that the subjects were presumed to live a maximum of 50 years from the time of first diagnosis of asthma. We have added sensitivity analysis restricting the maximum to only 25 years.

7) It would also be helpful to know for how many patients the year of diagnosis was imputed, whether other methods of imputation were considered and the effects of the imputation on results compared to a complete case analysis.

We had imputed data for only 20 (3.7%); thus, we think complete case analysis will have negligible effect. Imputation was done using the average years since diagnosis for each group. Manuscript has been edited to reflect the above.

8) The authors mention that drug costs collected from patients are subject to recall bias. What is the expected effect? Don't patients overestimate their prescription adherence? How will this affect your results? The expected effect of other limitations should also be stated.

We agree with the reviewer. Measurement errors, uncertainties in the estimates, and recall bias may affect data obtained from such studies – although the direction of such bias is unknown. This information is in the discussion section of the manuscript.

9) Need to provide estimated resource use for each unit cost provided.

We agree with the reviewer. We have provided further information on the proportion of patients who were shown not to have asthma that were receiving asthma medications.

Minor points
10) The authors state the asthma treatments in the US are more expensive and therefore screening would be expected to generate even greater savings. Is screening not also more expensive, making the difference in savings ambiguous? Are you certain that it would generate greater savings?

We agree with the reviewer. This is obviously a speculation. We do not know for sure if it will generate greater savings in USA. We definitely will need similar cost-effective study in USA to answer that question.

Discretionary revisions
11) It is not clear from the methods how the authors calculated the probability that an asthmatic was on medication. Does figure 2 represent the survival function?

We first estimated, from the longitudinal study, the probability that non asthmatics would be on medication in the year after the diagnosis of asthma. This was performed using
methodology congruent to survival analysis. This is given on the page 8, paragraph 2 in lines 7-10 of the manuscript.

12) It would be informative to present the 95% CI around the average cost per patient of the asthma screening algorithm.

This has now been added to the manuscript in table 2.

13) Is there a concern that by recommending screening more physicians will rely on screening rather than judgment and overall costs will go up?

We do not think judgment only should be used in making the diagnosis of asthma. Physiological testing should be performed if diagnosis of asthma is clinically considered since asthma is a label that patient carries for rest of their lives.