Reviewer's report

Title: The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases

Version: 0 Date: 11 Apr 2016

Reviewer: Mohsen Sadatsafavi

Reviewer's report:

This is peer review of the manuscript entitled "The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases" submitted to BMC Medicine.

This is a nationwide study of the epidemiological and economic burden of asthma in the UK (Britain, Scotland, Wales, and Northern Ireland). The study capitalizes on multiple (27) different databases and uses a variety of data linkage and mapping to fill the identified data gaps.

This is quite a comprehensive study of the burden of asthma. It showcases the power of using a variety of public health, government, and administrative databases to estimate the burden of a chronic disease. The efforts in undertaking this study is likely to leave a legacy in terms of the data linkage and data collection generated. The fact that the study protocol has previously been peer-reviewed published (and it seems the authors have largely adhered to their proposed methods) is also a positive aspect.

Nevertheless, I have found the described methodology not to be quite clear and comprehensive enough. Specific details are lacking in several places, as detailed in major comment #1. This is not a threat against the validity of the methods rather a request to provide additional information to facilitate peer-review and improve the quality of the paper.

Major comments:

- There is missing information in the methods section of the manuscript. The separately published protocol and the additional files do not cover the gaps. It is understandable that the complex methodology of the paper makes it impossible to present everything in the main text, but some important elements must appear there and not relegated to a published protocol. These include more detailed description of all included databases and their information content, and how they were used to estimate the reported metrics. It would be great if the authors could provide the relevant Read codes and list of asthma medications used in relevant data sets. It will
help the review process and can also help future investigators to replicate the results using the same methodology in different jurisdictions.

- The authors have used two different definitions for incidence and seven for prevalence. These definitions must have affected, in substantial ways, the calculation of costs. Lack of detailed description has made it difficult to reconcile all the permutation of incidence/prevalence and the reported cost values. The reader would expect different estimates of costs per different definitions of prevalence. The relation between cost calculations and estimates of incidence/prevalence is a major gap in the methodology that should become clear in a revised version.

Minor comments:

- Abstract, second paragraph: 'costs were estimated for' should be corrected.

- Abstract: no date range provided so the reader cannot understand to which time periods these numbers apply.

- Cost currency (year) should be provided in the abstract

- Background, line 53: 'report' should be 'reported'

- Study outcomes, lines 39-43: this paragraph is out of place. Why suddenly talking about absenteeism where you just described the data?

- Study outcomes, paragraph starting at line 46: the narrative starts from prevalence, then switches to incidence, and back to prevalence. Suggest rewriting the paragraph. In general, given the many study outcomes, this section could have subheadings.

- It will help if a table is put in the main text that describes all the 27 databases and the essential information therein (what they contain, what date range, how many records/individuals, and why they were used). This information is an integral part of the methods and should not be relegated to the Appendix.

- Early on please explain what the four countries are. For readers not familiar with the UK context it might not be clear.

- The paper should more deeply discuss the situation with COPD. Asthma-COPD overlap syndrome (ACOS) is a recognized disease phenotype and the paper should at least discuss the implications of censoring patients who had coexisting COPD. Ideally a sensitivity analysis should be done that includes these patients otherwise the authors should acknowledge that the reported results are underestimates of the true burden of asthma.
- Seven different definitions for prevalence were used, but the results section in the text does not provide the results of such prevalence estimates. Table 2 does but textual description is also required for clarity.

- Discussion: It might be worth mentioning that the calculated costs and health resource use are 'attributable' to asthma and they do not incorporate the burden of coexisting and comorbid conditions. It is known that asthma is associated with a potentially wide spectrum of comorbid conditions and the true burden of asthma also includes the excess burden of such conditions (Gershon et. al. Thorax. 2010 Jul;6)

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Unable to assess

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable
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