Reviewer’s report

Title: The economic burden of bronchiectasis - known and unknown: a systematic review

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Reviewer: Catherine Ann Byrnes

Reviewer's report:

This is an important area of work and needed to determine potential impact and cost saving for future interventions or early diagnosis and instigation of management.

The review is thorough, the systematic approach clearly outlined, with a good review of papers and points made.

Overall:

The flow of the manuscript is not right - mostly in results section - with paper reviews being repeated in different parts of the manuscript so as a reader you feel you are jumping around. For example, the second paragraph in results page 6 details how the cost analyses are going to be presented. Then the next three paragraphs on pages 6, 7, 8 details results specifically in USA, Spain, and then USA again, also noting effect on severity and pseudomonas. Then the paragraphs start following the headings signposted in the 'Resource composition and cost drivers' which means that the material covered in the studies already reported are covered again as they fall into 'Hospital resource use' costs and length of stay (page 8, 9), 'Total annual costs' (page 10, 11), less so in 'incremental resource use' page 11. So one reads everything twice. It would be clearer to follow the results as the authors say they are going to present them in the second paragraph, and if needed also have a heading between to note the differential costs associated with severity and/or pseudomonas following the headed sections for these and any other studies.

Points:

1. Page 4 paragraph 3 - slightly tired of the 'orphan disease' label
2. Page 5 paragraph 1 - 'similar' or the 'same'
3. Methods thoroughly laid out and easy to follow.
4. Results Page 6 paragraph 2 - the resource use and composition drivers are broken into sensible costing brackets - the only criticism here is I think what is include in diagnostics should be mentioned - so possibly initial chest CT scan, blood tests, immune work-up, lung function testing?
5. Page 6 & 7 all the inpatient days given to 2 decimal points seems unnecessary - 1 decimal point realistic.
6. Page 7 paragraph 2 - annual costs in six Spanish hospitals - was this hospital costs, hospital and community costs, all medication costs?
7. Page 7 paragraph 2 - the fact that the largest costs was in the bronchodilators, corticosteroids, and anticholiniergics is important as these are not confirmed
medications for those with bronchiectasis - rather for co-morbidities and may be being overused - check this is covered in discussion

8. Page 11 paragraph 2 - define controls healthy? Disease controls?
9. The discussion is a much better distillation of what was in results.
10. Discussion page 12 end of first paragraph - also future interventions or improved management may decrease hospitalisations but likely to decrease other outpatient or community costs as well and the bigger saving may be in the latter.
11. Discussion page 12/13 paragraph 2 - "the major driver of healthcare costs - and worse quality of life" while probably true - there has been no reporting of quality of life to the article to date, no data presented and this is not referenced. Page 14 - these two large paragraphs on QoL could be shortened and combined. The QoL is not the purpose of this paper - and this has not been reviewed as part of this systematic review - only costs have. Also there are no references here to any study that has looked at absenteeism, inability to work, time needed for clinic review etc - they may not have been costed - but can the authors check that there are truly no papers noting community and societal costs of bronchiectasis as a chronic respiratory illness.
12. Conclusions page 15 - I think that the opening sentence should say something about the costs of bronchiectasis being substantial rather than starting with under recognised. The authors have presented data to show while it is likely under captures - what has been reported remains substantial. Also that an idea of true costs would be useful to evaluate success and cost-effectiveness of new interventions.

13. Some shortening of discussion can be achieved:
Page 12, paragraph 2 - "with the severity of disease and those with Pseudomonas were also higher." (combine sentences).
Page 13 paragraph 1 "Taken together the increased costs observed with disease severity and P aeruginosa serve to emphasize the importance to the healthcare system of improving management of these patients" to "The increased costs of P aeruginosa and disease severity emphasize ..."
Page 13 paragraph 1 "as provided by this manuscript" superfluous - can be dropped. Page 13, paragraph 3 - "a further consideration is that.." to just "These retrospective.."And last 2 sentences of this paragraph could be combined and shortened.
14. Should 'highfieId: communication' etc all be in lowercase?
15. Reference 35 article title misspelt
16. Table 1 good - note that 'mean annual number of admissions' and 'mean 12-month hospital admission frequency' is the same thing and should be said the same way
17. Table 2 also good. Don't understand the 2 columns for Joish et al both saying 'incremental cost of bronchiectasis' with different figures - what denotes the difference? And Joish et al further below could have 'annual cost bronchiectasis with exacerbation, annual bronchiectasis without etc
18. Figure 2 if published in black and white the 2 lighter greys are too similar to pick difference.

Thanks

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

Yes

**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.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Acceptable

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