Author’s response to reviews

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

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Author’s response to reviews:

General

1) The PRISMA checklist has been completed and systematic has been added to the title of the paper
2) The author contributions have been revised as requested and initials added for greater clarity
3) The statement has been added that all authors reviewed the manuscript and approved the final version
4) in terms of availability of data the following has been added: All data included within this manuscript have been published in peer review publications.
Reviewer 1

5) The methods now clarify that all studies were in adults and that most studies reported as full papers reported on the presence of comorbidities. Some adjusted for comorbidities but many do not report this level of detail

6) The results have been reworked to make it clearer how the authors differentiated between cost of management of bronchiectasis, cost associated with exacerbations and hospitalisation cost for management of exacerbations

7) The text "exacerbations accounted for the greatest proportion (34%) of the total costs" has been revised and clarified (line 273-276)

8) the text on "Total annual costs were higher in patients experiencing >2 exacerbations per year compared with no exacerbations" has been clarified to make it clear that the comparison was ≤2 or >2 exacerbations per year and with and without COPD (line 282-284)

Reviewer 3

9) The flow of the manuscript is not right: The results section has been reordered so that each study is only described once. The section includes the following subsections: a) Incremental resource use and cost due to bronchiectasis b) Hospitalization and other resource use c) Costs and cost drivers

10) Orphan disease has been changed to neglected disease (line 91)

11) The update was similar to the original literature review

12) Methods thoroughly laid out and easy to follow - this section has been revised

13) Results: details of diagnostics have been added (one 149)

14) Values for inpatient days has been changed to 1 decimal place (line 196)

15) Clarified that the six Spanish studies data were for hospital and primary care costs including medication (line 254)

16) The Results section includes the following statement: However, as these agents are not recommended for bronchiectasis, these costs may relate to the management of comorbidities such as chronic obstructive pulmonary disease (COPD), or inappropriate use in patients with bronchiectasis (line 270) The discussion focusses on more general points rather than the individual studies so we have kept this point in the Results rather than move to the Discussion.

17) Controls were individuals included in the claims data base, without a diagnosis of bronchiectasis and matched for age, sex, geographic region, and selected comorbid conditions. This is clarified in the text. (line 167)

18) We hope that the changes to the results have helped with the clarity

19) The following has been added to the end of the 1st paragraph of the Discussion:
"Furthermore, the introduction of new treatments that improve the management of bronchiectasis may reduce not only the need for hospitalization but also care in outpatient and primary care settings." (line 315-316)

20) Only a brief mention of HRQoL is now included. Our review of the literature indicates there are no publications on productivity or absenteeism (line 345-360)
21) Initial statement revised to state that costs are substantial (line 297)

Statement added regarding the need for an understanding of costs to allow the accurate assessment of the cost-effectiveness of new interventions. (line 315)

22) The discussion has been shortened as requested
23) highfield:communication is in lower case
24) Reference 35 (now reference 33) is correct as it is
25) Table 1 has been amended in line with comment
26) Clarified the Joish entry so that one is overall costs and the other is respiratory-related costs
27) Figure 2 has been amended to make it more appropriate for black and white printing