

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Healthcare costs of asthma comorbidities: a systematic review protocol
<b>AUTHORS</b>	El Ferkh, Karim; Nwaru, Bright; Griffiths, Chris; Patel, Anita; Sheikh, Aziz

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Rachael Hunter UCL, UK
<b>REVIEW RETURNED</b>	29-Nov-2016

<b>GENERAL COMMENTS</b>	This protocol for a systematic review of healthcare costs in asthma comorbidities looks excellent. I have no additional comments.
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<b>REVIEWER</b>	Komal Singh Bristol-Myers Squibb, United States
<b>REVIEW RETURNED</b>	14-Dec-2016

<b>GENERAL COMMENTS</b>	The review protocol discusses the methodology of the review clearly. Please pre-specify and elaborate on all outcomes that would be assessed in the review.
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<b>REVIEWER</b>	Solmaz Ehteshami Afshar the University of British Columbia (UBC), Vancouver, Canada
<b>REVIEW RETURNED</b>	03-Jan-2017

<b>GENERAL COMMENTS</b>	<p>This is a peer-review of manuscript bmjopen-2016-015102 entitled "Healthcare costs of asthma comorbidities: a systematic review protocol " by Ferkh et. al.</p> <p>This is a well-designed, comprehensive protocol to conduct a systematic review, investigating the impact of comorbidities on the cost of asthma. The result of this systematic review is very important and will add to the scant knowledge of this aspect of economic burden of asthma. I have no major comments, but have some minor ones and have offered suggestions.</p> <p>Major comments: - none</p> <p>Minor comments: 1) I recommend considering wider range of comorbidities as there are not much studies regarding this matter and by restricting the search you may loose some of them. In Self-administered Comorbidity Questionnaire (SCQ) 13 general comorbidities are</p>
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	<p>included: heart disease, hypertension, diabetes mellitus, pulmonary disease, ulcer or stomach disease, kidney disease, liver disease, anemia or other blood disease, cancer, depression, osteoarthritis or degenerative arthritis, back pain, and rheumatoid arthritis. Also I suggest adding Charlson comorbidity index to your search strategy.</p> <p>2) It has been demonstrated that the indirect costs of asthma accounted for the greater proportion of the costs than direct cost (Ehteshami-Afshar S, et al. Int J Tuberc Lung Dis. 2016 Jan) Thus it should also be considered as one of the outcomes and be included in search key words.</p> <p>3) For subgroup analysis the studies can be divided and interpreted based on the type of costs they report (indirect, direct or total) to investigate the impact of comorbidities on different aspects of economic burden of disease.</p> <p>4) Page 5, first paragraph: cardiovascular disease been repeated twice.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Rachael Hunter

Institution and Country: UCL, UK

Please state any competing interests: None declared

Please leave your comments for the authors below

This protocol for a systematic review of healthcare costs in asthma comorbidities looks excellent. I have no additional comments.

R: Thank you

Reviewer: 2

Reviewer Name: Komal Singh

Institution and Country: Bristol-Myers Squibb, United States

Please state any competing interests: None declared

Please leave your comments for the authors below

The review protocol discusses the methodology of the review clearly.

Please pre-specify and elaborate on all outcomes that would be assessed in the review.

R: Thank you for your comment. Our sole outcome of interest is healthcare costs (i.e. direct costs) and this is specified as our main outcome in the Outcome heading (Page5 L15) and elaborated in Data extraction heading (Page6 L25).

Reviewer: 3

Reviewer Name: Solmaz Ehteshami Afshar

Institution and Country: The University of British Columbia (UBC), Vancouver, Canada

Please state any competing interests: None declared

Please leave your comments for the authors below

This is a peer-review of manuscript bmjopen-2016-015102 entitled "Healthcare costs of asthma comorbidities: a systematic review protocol " by Ferkh et. al.

This is a well-designed, comprehensive protocol to conduct a systematic review, investigating the impact of comorbidities on the cost of asthma. The result of this systematic review is very important and will add to the scant knowledge of this aspect of economic burden of asthma. I have no major comments, but have some minor ones and have offered suggestions.

Major comments:

- none

Minor comments:

1) I recommend considering wider range of comorbidities as there are not much studies regarding this matter and by restricting the search you may loose some of them. In Self-administered Comorbidity Questionnaire (SCQ) 13 general comorbidities are included: heart disease, hypertension, diabetes mellitus, pulmonary disease, ulcer or stomach disease, kidney disease, liver disease, anemia or other blood disease, cancer, depression, osteoarthritis or degenerative arthritis, back pain, and rheumatoid arthritis. Also I suggest adding Charlson comorbidity index to your search strategy.

R: Thank you for raising this point. The comorbidities we are interested in are those that impact on asthma management and/or prognosis, regardless of whether these conditions develop before or after asthma. This definition has been added to the manuscript under Comorbidities of interest (Page 5 L3). The list of comorbid conditions considered was revealed by our recent scoping review (El Ferkh et al. BMJOpen, 2016).

2) It has been demonstrated that the indirect costs of asthma accounted for the greater proportion of the costs than direct cost (Ehteshami-Afshar S, et al. Int J Tuberc Lung Dis. 2016 Jan) Thus it should also be considered as one of the outcomes and be included in search key words.

R: Thank you for this comment. We agree that indirect costs are important in asthma, however in terms of this particular systematic review, our focus is on the direct healthcare costs of asthma comorbidities. This is in part because our previous work has demonstrated the considerable challenges in obtaining valid estimates of indirect costs Mukherjee M, et al, 2016. We may however in due course extend this work through a follow-on study to also include indirect costs.

3) For subgroup analysis the studies can be divided and interpreted based on the type of costs they report (indirect, direct or total) to investigate the impact of comorbidities on different aspects of economic burden of disease.

R: In terms of our systematic review our sole outcome for this systematic review is direct healthcare costs.

4) Page 5, first paragraph: cardiovascular disease been repeated twice.

R: Thank you; this has now been corrected.

#### EDITORIAL COMMENTS:

- Please ensure the article is correctly formatted as per our guidelines:

<http://bmjopen.bmj.com/pages/authors/#studyprotocols>

R: The article is formatted as per BMJ Open guidelines and PRISMA-P

- Please revise the Strengths and Limitations section (after the abstract) to focus on the

methodological strengths and limitations of your study.

R: The strengths and limitations section has been revised.

- Please ensure the introduction section is fully up to date with a discussion of the relevant literature.

R: The introduction section has been updated with a discussion of the relevant literature.

- Please ensure the details in the protocol registration section at the end of the manuscript are correct.

R: The protocol registration section is now corrected.

We hope these revisions are to your satisfaction and we look forward to your decision in due course.

#### **VERSION 2 – REVIEW**

<b>REVIEWER</b>	Solmaz Ehteshami-Afshar University of British Columbia
<b>REVIEW RETURNED</b>	10-Feb-2017

<b>GENERAL COMMENTS</b>	I have no additional comments.
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