

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

TITLE (PROVISIONAL)	Treatment persistence and exacerbations in asthmatic patients initiating treatment with inhaled corticosteroids and beta-adrenergic agonists: retrospective cohort study
AUTHORS	Sicras-Mainar, Antoni; Gómez Rodríguez, Belén; Traseira-Lugilde, Susana; Fernández-Sánchez, Toni; Velasco Garrido, José Luis

VERSION 1 – REVIEW

REVIEWER	Amin, Suvina AstraZeneca Pharmaceuticals LP, Oncology
REVIEW RETURNED	09-Sep-2021

GENERAL COMMENTS	<p>The authors determined treatment persistence and exacerbations in asthma patients who sought care and initiated inhaler treatment with combinations of ICS/LABA at various primary care centers in Spain between 2015 and 2016. The data presented is interesting. However, the results pertain to a limited sample size and cannot be generalized to a broader population outside the select primary care centers in Spain. I recommend addressing the following points below:</p> <ol style="list-style-type: none">1. Provide additional context in the patients and methods section on the data source as many readers may be unfamiliar with the Health services Research network. Which primary care centers were enrolled in this network, and how were they chosen (i.e. geographical representation)?2. Were there other inclusion/exclusion criteria used to identify the cohort? Were patients with other co-morbidities included or excluded in the analysis?3. Provide additional details on previous exacerbation history in the pre-index period. The results section states that in the multivariate model, the number of exacerbations during follow-up was associated with previous exacerbation history, FEV and persistence. However, was the previous exacerbation history adjusted for during the creation of the five study groups?4. Exacerbations in the text are identified in line 43 as based on clinician's discretion and use of resources, which is a proxy and can potentially result in incomplete capture of data. Please elaborate further on this within the limitations section since healthcare resource information was not captured as part of this study.5. In Line 14, which states 'it is estimated that 36% of patients with asthma have exacerbations of varying intensity.' Recommend including a more recent reference from the literature or recent systematic review.6. Recommend stating in the limitations section that capturing patient behavior through treatment persistence cannot be directly
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	assessed through structured data available in electronic databases. Time to discontinuation are assumed to be proxies to estimate patient persistence.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comments to the Author:

The authors determined treatment persistence and exacerbations in asthma patients who sought care and initiated inhaler treatment with combinations of ICS/LABA at various primary care centers in Spain between 2015 and 2016. The data presented is interesting. However, the results pertain to a limited sample size and cannot be generalized to a broader population outside the select primary care centers in Spain. I recommend addressing the following points below:

Reply:

Thanks for your comments.

1. Provide additional context in the patients and methods section on the data source as many readers may be unfamiliar with the Health services Research network. Which primary care centers were enrolled in this network, and how were they chosen (i.e. geographical representation)?

Reply:

We have modified this section: “We performed a retrospective observational analysis of electronic medical records (EMR) obtained from the administrative database of the RediSS Foundation (Health services research network; www.rediss.es), a source of secondary data. The primary data came from various primary care centers in Catalonia (Spain), which are computerized with the OMIAPWIN (EMR). Before export to RediSS Foundation, data are rigorously anonymized and it is not possible to identify the territory, health care provider, treating physician, or patient or access any other information that would permit individual identification. This procedure ensures adherence to current law governing the protection of personal data”.

2. Were there other inclusion/exclusion criteria used to identify the cohort? Were patients with other co-morbidities included or excluded in the analysis?

Reply:

The inclusion and exclusion criteria were those described on page 8.

Correct comment. The identification of the patients was based on the diagnosis, and at the discretion of the specialist doctor. Asthmatic patients with the comorbidities described above (page 8) were excluded.

3. Provide additional details on previous exacerbation history in the pre-index period. The results section states that in the multivariate model, the number of exacerbations during follow-up was associated with previous exacerbation history, FEV and persistence. However, was the previous exacerbation history adjusted for during the creation of the five study groups?

Reply:

Please see table 3. Thank you.

There was no need to perform a propensity score matching due to the comparability of the groups at baseline. Thanks for the comment.

4. Exacerbations in the text are identified in line 43 as based on clinician’s discretion and use of resources, which is a proxy and can potentially result in incomplete capture of data. Please elaborate

further on this within the limitations section since healthcare resource information was not captured as part of this study.

Reply:

Correct comment.

Please see study limitations section. Page 13.

5. In Line 14, which states 'it is estimated that 36% of patients with asthma have exacerbations of varying intensity.' Recommend including a more recent reference from the literature or recent systematic review.

Reply:

We have updated reference 6. Page 15

6. Recommend stating in the limitations section that capturing patient behavior through treatment persistence cannot be directly assessed through structured data available in electronic databases. Time to discontinuation are assumed to be proxies to estimate patient persistence.

Reply:

Thanks a lot.

See limitations section. Page 13.

VERSION 2 – REVIEW

REVIEWER	Amin, Suvina AstraZeneca Pharmaceuticals LP, Oncology
REVIEW RETURNED	28-Feb-2022

GENERAL COMMENTS	Thank you for addressing all comments.
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