

Peer Review File

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Reviewer A	
<p>1. If the authors have access to it, please provide the average eosinophil count in the year prior to the day of admission. The absence of this data severely limits the interpretation of your primary outcome.</p>	<p>We thank the reviewer for this comment; however, these data were not captured during this study.</p>
<p>2. If the authors have access to the first outpatient follow up with the doctor that managed their COPD, the data on inhaler modification should be collected from there. That would give a better estimation of how well the guidelines were followed</p>	<p>We thank the reviewer for their comment; however, data regarding the first outpatient follow-up are unavailable.</p> <p>A 2021 study found that hospitalization for an exacerbation presents an opportunity to help reduce the patient’s risk of experiencing an exacerbation in the future. This study also found that follow-up by a physician after the patient has been discharged is also important, as it provides an opportunity to make any treatment changes and improve patient’s health outcomes (Singh et al, 2021). As a result of fragmentation of care in many health systems, some patients may be lost to follow-up, or some physicians may forget to change a patient’s treatment during follow-up. By capturing both prescriptions at the time of admission and discharge, we are capturing whether changes to treatment were implemented during the period of exacerbation.</p> <p>Singh D, Holmes S, Adams C, Bafadhel M, Hurst JR. Overcoming Therapeutic Inertia to Reduce the</p>

	<p>Risk of COPD Exacerbations: Four Action Points for Healthcare Professionals. <i>Int J Chron Obstruct Pulmon Dis.</i> 2021 Nov 1;16:3009-3016. doi: 10.2147/COPD.S329316.</p>
<p>3. The percentage of patients that were lost to follow up in the outpatient would also be excellent to look at as a high rate would provide more support to making the inhaler regimen modifications in the outpatient.</p>	<p>The percentages of patients that were lost to follow-up were not captured during this study.</p>
<b>Reviewer B</b>	
<p>1. This study aimed to evaluate the proportion of additional patients who would have had treatment escalations if the GOLD 2019 updated strategy had been available and adhered to. Patients included from October 2018 to April 2020. In fact, the GOLD document revised annual and LABA+ICS has been deleted from the management of follow-up pharmacological treatment in GOLD 2023. In addition, this is a single center study and the sample size is so small.</p>	<p>Thank you for your comment. We have added a point in the study limitations regarding the removal of ICS+LABA as a treatment option for stable COPD (please see lines 391–4).</p> <p><i>“Furthermore, ICS+LABA is not encouraged as a treatment option for patients with stable COPD in the updated GOLD 2023 strategy. This may further affect the generalizability of findings in current real-world practice”.</i></p> <p>The reviewer is correct that this study was limited by its small sample size and by being a single-center study. These points are included in the limitations section (lines 388–91).</p> <p><i>“Limitations of this study include its single-center design with a small sample size, which may limit the generalizability of the findings. The small sample size also precluded further subgroup analyses (comparison of patient characteristics between escalation and non-escalation groups according to initial therapy).”</i></p>

<p>2. Furthermore, this study included the patients at their hospital visit and collect the initial inhalation therapy regimen. Then, the inhalation therapy regimen adjustment was defined as from “Admission” to “Discharge”. The design of this study is unreasonable.</p>	<p>In our study, therapy received by the patients at admission does not represent a change in therapy at this timepoint, rather the existing maintenance therapy the patients were receiving at the time of their admission (please see lines 149–50 of the manuscript for this definition).</p> <p>A 2021 study found that hospitalization for an exacerbation presents an opportunity to help reduce the patient’s risk of experiencing an exacerbation in the future. This study also found that follow-up by a physician after the patient has been discharged is also important, as it provides an opportunity to make any treatment changes and improve patient’s health outcomes (Singh et al, 2021). As a result of fragmentation of care in many health systems, some patients may be lost to follow-up, or some physicians may forget to change a patient’s treatment during follow-up. By capturing both prescriptions at the time of admission and discharge, we are capturing whether changes to treatment were implemented during the period of exacerbation.</p> <p>Singh D, Holmes S, Adams C, Bafadhel M, Hurst JR. Overcoming Therapeutic Inertia to Reduce the Risk of COPD Exacerbations: Four Action Points for Healthcare Professionals. <i>Int J Chron Obstruct Pulmon Dis.</i> 2021 Nov 1;16:3009-3016. doi: 10.2147/COPD.S329316.</p>
<p>3. Table 1 and 3, the number of patients in BMI, pulmonary function, CAT and smoke history does not match the total patients. I don't understand the reasons</p>	<p>BMI, CAT score, pulmonary function and smoking history data were not available in the</p>

<p>for this results. In general, the results of are not representative and credible.</p>	<p>CGH data warehouse for every patient included in this study.</p> <p>A point regarding the missing data for some variables in this study was included in the limitations section (lines 409–14).</p> <p><i>“There were also missing data for some key variables. Although this is reflective of the variation observed in clinical documentation in real-world practice, this may have affected the data analysis).”</i></p> <p>We have now expanded on this limitation (lines 410–12).</p> <p><i>“Missing data is a common limitation of retrospective studies, as they rely on the accurate reporting and recording of results by clinicians (19).”</i></p> <p>We have added in a footnote underneath tables 1 and 3 to acknowledge the missing data for certain variables.</p> <p><i>“<sup>1</sup>Data were not available for all patients included in this study.”</i></p>
<p>4. P values is needed among LAMA, LABA+LAMA and LABA+ ICS group in table 1.</p>	<p>Available P values have now been added to Table 1.</p>
<p>5. The conclusion of the abstract needed rephrase.</p>	<p>The conclusion has now been rephrased (lines 60–62):</p> <p><i>“Compared with real-world clinical practice, a significantly higher proportion of patients may be eligible for treatment escalation under the GOLD 2019 and 2023 eosinophil-directed algorithms”.</i></p>

<p>6. Abstract: “Retrospective analysis of the COPD *****MASKED BY EDITOR*****data”. Please adjust the format of the paper.</p>	<p>This was a retrospective cohort study which used data from the COPD Changi General Hospital data warehouse.</p> <p>Please could the reviewer provide more specific comments about how they would like the format of the manuscript to be adjusted?</p>
<p>7. Methods: “This was a retrospective analysis of data that were prospectively collected...”. Is this a retrospective or cohort study?</p>	<p>This study is a retrospective cohort study. “Cohort” has been added in the text for clarification (lines 43, 128, 465): <i>“Retrospective cohort analysis”</i>.</p>