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Reply to Chen *et al.*: Reexamining COPD in Bronchiectasis: Elucidating Overdiagnosis and Outcomes from EMBARC's ROSE Criteria

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From the Authors:

We thank Chen and colleagues for their letter regarding our recent report from the EMBARC registry[1]. First, Chen et al, wonder what the clinical implications of severe bronchiectasis with airflow obstruction without a smoking history may be. It is well established that patients with lower lung function have worse outcomes, as illustrated in the original derivation and validation of Bronchiectasis Severity Index where forced expiratory volume (FEV1) is a major predictor of future mortality.[2] We agree, it is important in future research to understand why certain patients with bronchiectasis experience a rapid decline in FEV1and others do not. FEV1 has proven a less useful clinical tool in bronchiectasis than in other diseases such as cystic fibrosis largely because it does not consistently change with exacerbation or respond to treatments such as antibiotics. Understanding the mechanisms that lead to airflow obstruction in around 35% of bronchiectasis patients is important.[3]

Second Chen et al, query the patients who carry a COPD diagnosis but do not have airflow obstruction or a smoking history (COPD+ROSE- in our paper) and patients with no diagnosis of COPD who have both airflow obstruction and a greater than 10 pack year smoking history (COPD-ROSE+ in our paper). We agree the finding that these labels are inconsistently applied in clinical practice is important, not least because labels such as COPD are often used to exclude patients from randomized controlled trials[4], and inappropriate disease labels may lead to inappropriate treatment. The available data within the EMBARC registry does not allow us to definitively explain why clinicians labelled the patients in the way that they did. We agree that the label of COPD may be applied to patients with asthma who go on to fixed airflow obstruction. We would argue that clinically giving a patient a label of bronchiectasis-asthma-COPD overlap is likely to be unhelpful. Bronchiectasis has diverse aetiologies and can cause airflow obstruction through progressive lung damage. We feel labelling such patients in the absence of a relevant environmental exposure as COPD is inappropriate.

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Finally, Chen et al, raise the question of why patients with the COPD label, despite not having true COPD (COPD+ROSE-) had poor outcomes. We are unable to provide biomarker or microbiome data in this group as it was not collected in the EMBARC registry during the study period, but would point the authors to a parallel work that investigated the proteomic and microbiomic characteristics of COPD, bronchiectasis and the overlap syndrome and found that patients with both diagnoses had more neutrophilic disease and over-representation of proteobacteria in the microbiome.[5] This does not directly address the question of why these patients with an apparent mis-diagnosis had worse outcomes. We did observe possible evidence that more severe patients may be labelled with COPD as they had lower FEV1, higher MRC dyspnoea score and other markers of more severe bronchiectasis. This may suggest that clinicians apply the label of COPD to patients who are more severe, or that more frequent contacts with healthcare reflected by the higher hospitalization and exacerbation rate we observed, increase the potential for a misdiagnosis or misapplication of the label.

We agree with Chen et al, about the need for further dialogue on this issue. Standardising terminology internationally will be important going forward to ensure patients with bronchiectasis and COPD receive the right treatment, and are appropriately included in studies, ideally based on objective criteria for each disease.[6]

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