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References

1. Polverino E, De Soyza A, Dimakou K, Traversi L, Bossios A, Crichton ML, *et al.* The Association between bronchiectasis and chronic obstructive pulmonary disease: data from the European Bronchiectasis Registry (EMBARC). *Am J Respir Crit Care Med* 2024;209:119–127.
2. Traversi L, Miravittles M, Martinez-Garcia MA, Shteinberg M, Bossios A, Dimakou K, *et al.* ROSE: radiology, obstruction, symptoms and exposure – a Delphi consensus definition of the association of COPD and bronchiectasis by the EMBARC Airways Working Group. *ERJ Open Res* 2021;7:00399.
3. Flume PA, Chalmers JD, Olivier KNJ. Advances in bronchiectasis: endotyping, genetics, microbiome, and disease heterogeneity. *Lancet* 2018;392:880–890.
4. Chandrasekaran R, Mac Aogáin M, Chalmers JD, Elborn SJ, Chotimall SH. Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis. *BMC Pulm Med* 2018;18:83.
5. Keir HR, Contoli M, Chalmers JD. Inhaled corticosteroids and the lung microbiome in COPD. *Biomedicines* 2021;9:1312.
6. Choi H, Chalmers JD. Bronchiectasis exacerbation: a narrative review of causes, risk factors, management and prevention. *Ann Transl Med* 2023;11:25.

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

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To the Editor:

We thank Chen and colleagues for their letter regarding our recent report from the European Bronchiectasis Registry (EMBARC) (1). First, Chen and colleagues 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 the Bronchiectasis Severity Index, whereby FEV₁ is a major predictor of future mortality (2). We agree that it is important in future research to understand why certain patients with bronchiectasis experience a rapid decrease in FEV₁ and 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 antibiotic therapy. Understanding the mechanisms that lead to airflow obstruction in approximately 35% of patients with bronchiectasis is important (3).

Second, Chen and colleagues wonder about the differentiation of patients who carry a COPD diagnosis but do not have airflow obstruction or a smoking history (i.e., do not meet the ROSE criteria of radiological bronchiectasis [R], obstruction defined by an FEV₁/FVC ratio <0.7 [O], symptoms [S], and exposure to a ≥10-pack-year smoking history [E]) and patients with no diagnosis of COPD who have airflow obstruction and a ≥10-pack-year smoking history (i.e., met the ROSE criteria). We agree that the inconsistent application of these labels 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 EMBARC do not allow us to definitively explain why clinicians labeled the patients the way they did. We agree that the label of COPD may be applied to patients with asthma who go on to exhibit fixed airflow obstruction. We would argue that clinically labeling a patient as having a bronchiectasis–asthma–COPD overlap is likely to be unhelpful. Bronchiectasis has diverse etiologies and can cause airflow obstruction through progressive lung damage. We believe it inappropriate to label such patients as having COPD in the absence of a relevant environmental exposure.

Finally, Chen and colleagues raise the question of why patients with the COPD label despite not having true COPD (i.e., not meeting the ROSE criteria) had poor outcomes. We are unable to provide biomarker or microbiome data in this group because they were not collected in EMBARC 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 an overrepresentation of proteobacteria in the microbiome (5). This does not directly address the question of why these patients with an apparent misdiagnosis had worse outcomes. We did observe possible evidence that patients with more severe disease may be labeled with COPD because they had a lower FEV₁, a higher Medical Research Council dyspnea score, and other markers of more severe bronchiectasis. This may suggest that clinicians apply the label of COPD to patients with more severe disease, or that the more frequent contacts with healthcare services reflected by the higher hospitalization and exacerbation rates we observed increase the potential for a misdiagnosis or misapplication of the label.

We agree with Chen and colleagues about the need for further dialogue on this issue. Standardizing terminology internationally will be important going forward to ensure that 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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References

1. Polverino E, De Soya A, Dimakou K, Traversi L, Bossios A, Crichton ML, *et al*. The association between bronchiectasis and chronic obstructive pulmonary disease: data from the European Bronchiectasis Registry (EMBARC). *Am J Respir Crit Care Med* 2024;209:119–127.
2. Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, *et al*. The bronchiectasis severity index. An international derivation and validation study. *Am J Respir Crit Care Med* 2014;189:576–585.
3. Chalmers JD, Polverino E, Crichton ML, Ringshausen FC, De Soya A, Vendrell M, *et al*. EMBARC Registry Investigators. Bronchiectasis in Europe: data on disease characteristics from the European Bronchiectasis Registry (EMBARC). *Lancet Respir Med* 2023;11:637–649.
4. Haworth CS, Bilton D, Chalmers JD, Davis AM, Froehlich J, Gonda I, *et al*. Inhaled liposomal ciprofloxacin in patients with non-cystic fibrosis bronchiectasis and chronic lung infection with *Pseudomonas aeruginosa* (ORBIT-3 and ORBIT-4): two phase 3, randomised controlled trials. *Lancet Respir Med* 2019;7:213–226.
5. Huang JTJ, Cant E, Keir HR, Barton AK, Kuzmanova E, Shuttleworth M, *et al*. Endotyping chronic obstructive pulmonary disease, bronchiectasis, and the “chronic obstructive pulmonary disease–bronchiectasis association”. *Am J Respir Crit Care Med* 2022;206:417–426.
6. Traversi L, Miravittles M, Martinez-Garcia MA, Shteinberg M, Bossios A, Dimakou K, *et al*. ROSE: radiology, obstruction, symptoms and exposure – a Delphi consensus definition of the association of COPD and bronchiectasis by the EMBARC Airways Working Group. *ERJ Open Res* 2021;7:00399-2021.

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Erratum: Inflammatory Activity of Epithelial Stem Cell Variants from Cystic Fibrosis Lungs Is Not Resolved by CFTR Modulators

There are errors in the article by Wang and colleagues (1), published in the November 1, 2023 issue of the *Journal*. In Figure 4E, the authors inadvertently duplicated one of the panels. A copy of the middle right panel (the CFv3 variant) was accidentally used in place of

the correct CFv5 variant image on the lower right. The *Journal* is replacing the online version of the article with a version in which the duplicated panel has been replaced with the correct image. There are no changes to the Figure 4 legend or labels.

In addition, in Figure 6B, the same image was used twice as part of a schematic diagram to indicate two different types of transplanted cells. To avoid confusion, this panel has been replaced with a version that eliminates the repeated image. The authors state that these corrections and changes do not affect the interpretation of the data or the conclusions of the paper; they apologize for any inconvenience that was caused. ■

Reference

1. Wang S, Niroula S, Hoffman A, Khorrami M, Khorrami M, Yuan F, Gasser GN, Choi S, Liu B, Li J, Metersky ML, Vincent M, Crum CP, Boucher RC, Karmouty-Quintana H, Huang HJ, Sheshadri A, Dickey BF, Parekh KR, Engelhardt JF, McKeon FD, Xian W. Inflammatory activity of epithelial stem cell variants from cystic fibrosis lungs is not resolved by CFTR modulators. *Am J Respir Crit Care Med* 2023;208:930–943.

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Erratum: Structural Predictors of Lung Function Decline in Young Smokers with Normal Spirometry

There is an error in the article by Ritchie and colleagues (1), published in the May 15, 2024 issue of the *Journal*. In the second sentence in the Figure 3 legend, the midcoronal section from the nonsmoking subject is incorrectly identified as the panel on the right; that image is in fact on the left. For the convenience of our readers, the *Journal* is replacing the online version of the article with a corrected version. ■

Reference

1. Ritchie AI, Donaldson GC, Hoffman EA, Allinson JP, Bloom CI, Bolton CE, Choudhury G, Gerard SE, Guo J, Alves-Moreira L, McGarvey L, Sapey E, Stockley RA, Yip KP, Singh D, Wilkinson T, Fageras M, Ostridge K, Jöns O, Bucchioni E, Compton CH, Jones P, Mezzi K, Vestbo J, Calverley PMA, Wedzicha JA; British Early COPD Network (BEACON) Cohort Investigators. Structural predictors of lung function decline in young smokers with normal spirometry. *Am J Respir Crit Care Med* 2024;209:1208–1218.

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