ORIGINAL ARTICLE
COPD

SHAREABLE PDF

Should the number of acute exacerbations in the previous year be used to guide treatments in COPD?

Mohsen Sadatsafavi[1,2,3], James McCormack[2], John Petkau[4], Larry D. Lynd[2,5], Tae Yoon Lee[1,2] and Don D. Sin[3]

Affiliations: [1]Respiratory Evaluation Sciences Program, Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada. [2]Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada. [3]UBC Centre for Heart Lung Innovation and Dept of Medicine (Respirology), University of British Columbia, Vancouver, BC, Canada. [4]Dept of Statistics, University of British Columbia, Vancouver, BC, Canada. [5]Centre for Health Evaluation and Outcome Sciences, Providence Healthcare Research Institute, Vancouver, BC, Canada.

Correspondence: Mohsen Sadatsafavi, UBC Centre for Heart Lung Innovation and Dept of Medicine (Respirology), Faculty of Pharmaceutical Sciences, University of British Columbia, 7th Floor, 828 West 10th Avenue, Research Pavilion, Vancouver, BC, V5Z 1M9, Canada. E-mail: msafavi@mail.ubc.ca

@ERSpublications
Dichotomisation of COPD exacerbation frequencies based on observed number of events in the previous year results in phenotypes that are inherently unstable, so much so that their suitability for informing treatment decisions should be seriously questioned https://bit.ly/34nFClc

Cite this article as: Sadatsafavi M, McCormack J, Petkau J, *et al*. Should the number of acute exacerbations in the previous year be used to guide treatments in COPD? *Eur Respir J* 2021; 57: 2002122 [https://doi.org/10.1183/13993003.02122-2020].

ABSTRACT

Background: In contemporary management of chronic obstructive pulmonary disease (COPD), the frequent exacerbator phenotype, based on a 12-month history of acute exacerbation of COPD (AECOPD), is a major determinant of therapeutic recommendations. However, there is considerable debate as to the stability of this phenotype over time.

Methods: We used fundamental principles in time-to-event analysis to demonstrate that variation in the frequent exacerbator phenotype has two major sources: variability in the underlying AECOPD rate and randomness in the occurrence of individual AECOPDs. We re-analysed data from two large cohorts, the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study and the SubPopulations and InteRmediate OutcoMes In COPD Study (SPIROMICS), using a Bayesian model that separated these sources of variability. We then evaluated the stability of the frequent exacerbator phenotype based on these results.

Results: In both cohorts, the pattern of AECOPDs strongly supported the presence of an individual-specific underlying AECOPD rate which is stable over time (Bayes Factor less than 0.001). Despite this, the observed AECOPD rate can vary markedly year-to-year within individual patients. For those with an underlying rate of 0.8–3.1 events·year^{-1}, the frequent exacerbator classification, based on the observed rate, changes more than 30% of the time over two consecutive years due to chance alone. This value increases to more than 45% for those with an underlying rate of 1.2–2.2 events·year^{-1}.

Conclusions: While the underlying AECOPD rate is a stable trait, the frequent exacerbator phenotype based on observed AECOPD patterns is unstable, so much so that its suitability for informing treatment decisions should be questioned. Whether evaluating AECOPD history over longer durations or using multivariate prediction models can result in more stable phenotyping needs to be evaluated.