

## Long-Acting Bronchodilators in Patients With Chronic Obstructive Pulmonary Disease: Still More to Know

To the Editor:

Lindenauer and colleagues recently published the results of a retrospective cohort study comparing patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) treated with long-acting bronchodilators (LABDs) with those not receiving this treatment. The primary composite measure was the risk for treatment failure, and secondary measures evaluated length of stay and hospital costs (1). We read this timely study and have several comments.

Given the large clinical spectrum of AECOPD and the high degree of misdiagnosis (2), we feel the broad inclusion criteria used by the authors may confound the study results. More strict criteria would have undoubtedly diminished the sample size but would have selected a cohort closer to the true chronic obstructive pulmonary disease (COPD) population that we aim to estimate. It may have been more telling to only include patients with spirometry-documented obstructive disease. In addition, congestive heart failure, which has a prevalence of 25–30% in patients with AECOPD, is an independent risk factor for mortality (3). Conducting separate analyses for patients with coexisting heart disease would also be more useful from a clinical standpoint.

Although it is more difficult to accomplish, the use of a staging system such as the Winnipeg criteria to stratify the study population would have strengthened the data obtained. We raise concerns of construct validity resulting from the use of discharge codes in the inclusion criteria to define AECOPD, which has been previously shown to underestimate the number of true AECOPD admissions and is associated with significant misclassification when compared with physician chart review (4).

In their analysis, the authors used propensity scoring. Of patients treated with LABD on hospital Day 2, 81% were successfully matched to a nontreated patient with similar propensity scores. Given the fact that propensity scoring was used to mitigate the differences in LABD-treated and nontreated patients, it would be of interest to know why 19% of patients were not matched and whether outcomes differed in that subset of patients. With a significant number of unmatched patients in the treatment group, it is difficult to know exactly which population is being studied, and therefore we raise concerns about external validity for the findings.

We appreciate that the authors showed minimally increased cost with no perceived effect on length of stay with inpatient LABD use. This finding, that LABDs may have little to no benefit in reversing the acute process of an AECOPD when administered within the first 2 days of a hospital stay, is interesting, but in our opinion, it is not definitive evidence to warrant cessation of inpatient use. LABAs are an important part of maintenance regimen in COPD (5), and their use in a hospitalized setting may

have other advantages. Improper inhaler technique is a common finding among patients with COPD, and reinforcing proper inhaler technique under the supervision of a respiratory therapist in the hospital may help facilitate better long-term control of a chronic disease. Indeed, Press and colleagues showed that a targeted inhaler education intervention for the inpatient with COPD was associated with fewer subsequent hospitalizations and death (6). It is also possible that inpatient use may subsequently ensure inhaler prescription or renewal at time of discharge, leading to better access to medications for COPD control.

One interesting observation is that although there were no differences in the composite primary outcome, inpatient LABA use appeared to be associated with less use of late invasive mechanical ventilation and fewer readmissions resulting from AECOPD. These intriguing findings warrant further investigation.

We applaud this extensive undertaking but do not feel that the full value of LABD use for AECOPD during the inpatient setting was entirely explored in this study.

**Author disclosures** are available with the text of this letter at [www.atsjournals.org](http://www.atsjournals.org).

Tina Shah, M.D., M.P.H.  
University of Chicago  
Chicago, Illinois

Sugeet Jagpal, M.D.  
Rutgers Robert Wood Johnson Medical School  
New Brunswick, New Jersey

Rosemarie Beckford, M.D.  
University of Michigan Health System  
Ann Arbor, Michigan

## References

- 1 Lindenauer PK, Shieh MS, Pekow PS, Stefan MS. Use and outcomes associated with long-acting bronchodilators among patients hospitalized for chronic obstructive pulmonary disease. *Ann Am Thorac Soc* 2014;11:1186–1194.
- 2 Pellicer Císcar C, Soler Cataluña JJ, Andreu Rodríguez AL, Bueso Fabra J; en representación del Grupo EPOC de Sociedad Valenciana de Neumología. Diagnosis of COPD in hospitalised patients. *Arch Bronconeumol* 2010;46:64–69.
- 3 MacIntyre N, Huang YC. Acute exacerbations and respiratory failure in chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2008;5: 530–535.
- 4 Stein BD, Bautista A, Schumock GT, Lee TA, Charbeneau JT, Lauderdale DS, Naureckas ET, Meltzer DO, Krishnan JA. The validity of International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis codes for identifying patients hospitalized for COPD exacerbations. *Chest* 2012;141:87–93.
- 5 Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2013;187:347–365.
- 6 Press VG, Arora VM, Shah LM, Lewis SL, Charbeneau J, Naureckas ET, Krishnan JA. Teaching the use of respiratory inhalers to hospitalized patients with asthma or COPD: a randomized trial. *J Gen Intern Med* 2012;27:1317–1325.

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