Reply

From the Authors:

Shah and colleagues express concern with a number of aspects of our study, including the use of *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), diagnosis codes rather than spirometry or Winnipeg criteria to identify and classify study participants, the potential for confounding by concomitant heart failure, and incomplete propensity matching. In addition, they describe a number of potential benefits associated with continuation of long-acting bronchodilators (LABDs), including the opportunity to reinforce teaching and to ensure patients are discharged with appropriate prescriptions.

Although we acknowledge the limitations of ICD-9 codes, this study was conducted using claims data from more than 400 US hospitals, and therefore neither the results of spirometry testing nor physician admission notes were available to us. Nevertheless, as Stein and colleagues showed at two academic centers in Chicago, Illinois (1), although sensitivity is low, the specificity of ICD-9-based algorithms is approximately 99%, with positive predictive values ranging from 81% to 97%. Therefore, to the extent that Stein's findings are generalizable, they suggest that the large majority of patients included in our analysis did have exacerbation of chronic obstructive pulmonary disease (COPD). Moreover, as described in our Methods, because we remained concerned about the validity of ICD-9 codes, we took advantage of information about medication dispensing to further limit the analysis to patients receiving treatment doses of systemic corticosteroids, thereby strengthening the internal validity of our results. Although we undoubtedly missed some patients with COPD, there is little reason to believe the association we observed between treatment with LABD and outcomes would differ in those patients.

Shah and colleagues are also concerned that the presence of heart failure could confound the relationship between LABD and outcomes. Because we shared this concern, we included heart failure (along with other patient demographic and comorbidity variables) in our standard regression and propensity models, even though the difference in prevalence of heart failure between treatment groups was quite modest. We sought to estimate the association between LABD treatment and outcomes independent of these other factors. In the absence of a mechanistic reason to expect an interaction between heart failure and this association, we did not consider stratified analyses.

Shah and colleagues also note that we were only able to match 81% of LABD-treated patients with nontreated patients with similar propensity. This occurred for two reasons: First, although there was substantial overlap in the distribution of propensity for receipt of long-acting agents among the LABD-treated and nontreated participants, the distributions clearly differ. Second, the proportion of LABD-treated participants in the full cohort was large (41%), so that at the upper end of the propensity range, we quickly ran out of eligible matches among the untreated patients. This does indeed "raise concerns about external validity" of the matched analysis: It is difficult to understand the population of patients for whom the results are applicable. To address this concern, we performed two additional analyses that include the full sample, using propensity score weighting. As described in our Methods section, inverse probability of treatment weighting gives estimates that can be generalized to the entire population of patients, providing a population-average treatment effect estimate. Standardized mortality ratio weighting provides an estimate of the average treatment effect among the treated patients (2). These results are included in our figure 2 and are in line with propensity-matched and propensity-adjusted estimates, indicating there is unlikely to be great treatment effect heterogeneity related to propensity for treatment.

Finally, Shah and colleagues offer a number of potential reasons that physicians may wish to continue LABD during an acute care admission. Although we do not disagree that hospitalization can offer an opportunity for patient education, there is currently no evidence that such programs lead to better patient outcomes. Contrary to the comment by Shah and colleagues, if anything, our propensity-matched analyses suggested slightly higher rates of COPD-related readmission and late use of noninvasive ventilation. However, given that more patients are hospitalized each year for exacerbations of COPD than for myocardial infarction, we see no reason these hypotheses should not be tested in clinical trials.

Author disclosures are available with the text of this letter at www.atsjournals.org.

Peter K. Lindenauer, M.D., M.Sc.
Baystate Medical Center
Springfield Massachusetts
and
Tufts Clinical and Translational Science Institute and Tufts University School of Medicine
Boston, Massachusetts

Meng-Shiou Shieh, Ph.D.
Baystate Medical Center
Springfield Massachusetts

Penny Pekow, Ph.D.
Baystate Medical Center
Springfield Massachusetts
and
University of Massachusetts Amherst School of Public Health and Health Sciences
Amherst, Massachusetts

Mihaela S. Stefan, M.D.
Baystate Medical Center
Springfield Massachusetts
and
Tufts Clinical and Translational Science Institute and Tufts University School of Medicine
Boston, Massachusetts

References

1 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.
2 Brookhart MA, Wyss R, Layton JB, Stürmer T. Propensity score methods for confounding control in nonexperimental research. *Circ Cardiovasc Qual Outcomes* 2013;6:604–611.

Author Contributions: All authors have participated in the preparation of this letter.