In Reply In their response to our Original Investigation, Cho and Jun raise interesting points about the reach and limitations of state drug product selection laws. While many biologic medications bypass pharmacist dispensing and are administered by physicians in an outpatient setting, many that account for substantial spending do not. The 2 examples that Cho and Jun mention, adalimumab and etanercept, accounted for approximately $3.2 billion and $1.9 billion in reported Medicare Part D spending, respectively, in 2018. Several other top-selling biologics, such as the interleukin (IL)-12/IL-23 antagonist ustekinumab, the IL-17 inhibitor secukinumab, and insulin products—which were reclassified as biologics in March 2020—and alone account for many billions of dollars in annual expenditures in the US—are also primarily pharmacy dispensed. Therefore, meaningful health system savings can result from optimizing state drug product selection laws to facilitate interchangeable biosimilar use.

The study highlighted by Cho and Jun, an analysis of 3 classes of drugs—statins, antidepressants, and proton-pump inhibitors—did not find an association between changes in mandatory substitution policies and generic use between 2006 and 2011. The authors of that study attributed this null finding to higher pharmacy gross profit margins from generic compared with brand-name drugs. However, it is not clear that the disparity in gross profit margins between originator and interchangeable biologics will follow this model given the increased complexity of manufacturing biologic medications and the likelihood of fewer competitors. The study also found that “presumed consent” policies were associated with a 3.2% reduction in the probability of purchasing brand-name drugs. These findings underscore our message of the importance of evaluating the effect of variation in state drug product selection laws, particularly for additional variables such as pharmacist liability protection and patient notice independent of consent.

Insurance management tools such as tiering and prior authorization can have substantial effect on generic and bio-similar use. As we noted in our article, optimization of state drug product selection laws to facilitate generic and interchangeable biologic use should be coupled with other policy levers, which can include educational outreach to prescribers and patients and closer oversight of pharmacy benefits management practices.

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Many administrative databases include only calendar days, not times for admission, discharge, and medication administration. This leads to the use of potentially confusing “hospital day” terminology, in which a day does not mean 24 hours. For example, the article by Stefan et al states, “A total of 6833 patients treated with antibiotics during the first 2 hospital days were successfully matched to patients with a similar propensity score who did not receive antibiotics by hospital day 2.” If hospital day 1 is the day of admission, does this mean that patients could be included in the unexposed group if they were discharged on hospital day 2? This would not be possible for patients who initiated antibiotic therapy on hospital day 2, because the definition of exposure required that antibiotics be prescribed for a minimum of 2 days.

The authors could address this concern by clarifying how they defined hospital days, by providing the range of length of stay in exposed and unexposed groups and the proportion of the exposed group that initiated antibiotic therapy after the first day, and by presenting the results of their instrumental variable analysis for length of stay, which should not be susceptible to this bias. To avoid a bias that leads to a higher minimum length of stay in at least some of the exposed group, the authors should define exposure to antibiotics as antibiotic therapy started on the day of admission and not require any minimum duration of treatment in the exposed group.

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In Reply On behalf of our coauthors, we thank Dr Newman for raising concern that our study reported in the article, “Association of Antibiotic Treatment With Outcomes in Patients Hospitalized for an Asthma Exacerbation Treated With Systemic Corticosteroids,” published in the March 2019 issue of JAMA Internal Medicine, was susceptible to immortal time bias because of how we had determined the timing of antibiotic exposure and length of stay in our original analysis.

As originally reported, we had conducted a retrospective cohort study of data collected from 542 US acute care hospitals that participate in Premier Inpatient Database (an inpatient administrative database developed for measuring healthcare quality and use). We identified 19,811 patients hospitalized for an asthma exacerbation treated with corticosteroids and included an analysis of 87,888 (44.4%) patients who received antibiotics during the first 2 days of hospitalization and were prescribed antibiotics for a minimum of 2 days. The primary outcome was hospital length of stay measured in days. Secondary outcomes included a composite measure of treatment failure (initiation of invasive or noninvasive mechanical ventilation, transfer to the intensive care unit after hospital day 2, in-hospital mortality, or readmission for asthma exacerbation within 30 days of discharge), hospital cost, and antibiotic-associated diarrhea. In our original propensity score-matched analysis that compared patients who were not started on antibiotic therapy during the first 2 days or who were started on antibiotic therapy after day 2 with those who were started on antibiotic therapy during that time frame and treated for at least 2 days, we found that treated patients had a significantly longer hospital stay, similar rate of treatment failure, higher hospitalization cost, and nonsignificant increased risk of antibiotic-related diarrhea.

However, when we repeated the analysis to address concerns about immortal time bias with the treatment cohort defined as patients who started antibiotics during the first day of hospitalization compared with a group of patients who were not treated or who started treatment after day 1 of hospitalization and eliminated the requirement that antibiotics be prescribed for at least 2 days, our findings changed. The number of eligible patients included increased to 21,628; the number of hospitals decreased to 540; and the number of patients who received antibiotics decreased to 8927 (41.3%). The corrected findings of the propensity score-matched analysis now show that receipt of antibiotics on day 1 was associated with a marginally longer but not clinically meaningful length of hospital stay (unadjusted mean [SD], 2.81 [2.27] vs 2.57 [2.45] days; difference, 0.11; 95% CI, 0.03 to 0.19); length-of-stay ratio, 1.06; 95% CI, 1.04 to 1.09) and higher cost of hospitalization (median [IQR] cost, $4320 [$2754-$6716] vs $3861 [$2479-$6236]; mean [SD], $5662 [$5855] vs $5302 [$6959]; difference, $360; 95% CI, $155 to $566; odds ratio [OR], 1.10; 95% CI, 1.08 to 1.12). The risk for antibiotic-related diarrhea was higher in the antibiotic-treated patients (adjusted OR, 1.34; 95% CI, 1.05 to 2.17), but the association became nonsignificant in the propensity score-matched cohort (adjusted OR, 1.19; 95% CI, 0.90 to 1.57). In addition, in the corrected analyses, we found a lower risk of treatment failure in the antibiotic-treated patients (7.1% vs 8.2%; difference, −1.08%; 95% CI, −1.93% to −0.24%; OR, 0.86; 95% CI, 0.77 to 0.97).

Corrections for these new findings affected the Abstract, Key Points, Text, Tables, Figure, and Supplement. Thus, we have requested that our originally published article be retracted and replaced with the corrected version. We regret this oversight and apologize to the readers and editors for any confusion. We appreciate the opportunity to publish the corrected article and confirm that there are no other errors. With this corrected version, a copy of the original article with the errors highlighted and a copy with the corrections highlighted are included as new Supplements 2 and 3, respectively.
Letters

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CORRECTION

Error in Quiz Answer Option: In the CME Online Quiz Questions for the Original Investigation titled “Association of Antibiotic Treatment With Outcomes in Patients Hospitalized for an Asthma Exacerbation Treated With Systemic Corticosteroids,” published online in the March 2019 issue of JAMA Internal Medicine, a quiz answer option has been updated. In Question 4, option C has been changed to “Lower risk of treatment failure.” The quiz has been updated online.


Incorrect Answer in CME Online Quiz Questions: In the CME Online Quiz Questions for the Original Investigation titled Effects of Time-Restricted Eating on Weight Loss and Other Metabolic Parameters in Women and Men With Overweight and Obesity: The TREAT Randomized Clinical Trial,” published in the November 2020 issue, there was an omission in an answer choice for question 1. The correct text is “Noncaloric beverages (only water and black coffee or tea) were permitted outside of the eating window for the TRE group.” This quiz was corrected online.


Errors in Degree Symbols and Descriptors: In the Original Investigation entitled “Filtration Efficiency of Face Masks Used by the Public During the COVID-19 Pandemic,” Dr Steinbrook’s surname was incorrectly written as “Steinbeck.” This article was corrected online.


Error in Author Surname: In the Editor’s Note entitled “Filtration Efficiency of Face Masks Used by the Public During the COVID-19 Pandemic,” Dr Steinbrook’s surname was incorrectly written as “Steinbeck.” This article was corrected online.


Replacement of Nonauthor Collaborator Names: In the Original Investigation titled “Association Between Early Treatment With Tocilizumab and Mortality Among Critically Ill Patients With COVID-19” that printed on January 4, 2021, the nonauthor collaborator names were omitted from the PubMed listing. The article has been corrected by adding Supplement 3 containing all names.


Errors in Data Presentation in Text, Table, and Supplement: In the article by Rooney et al titled “Risk of Progression to Diabetes Among Older Adults With Prediabetes,” published online February 8, 2021, and also in the April 2021 print issue of JAMA Internal Medicine, because of a calculation error, the incidence rates in Results, Table 2, and Table 3 in the Supplement were incorrectly reported and have been replaced with corrected values. In addition, text was omitted from the first sentence in the findings portion of the Key Points. The corrected sentence now reads, “In this cohort study of 3412 older adults, the prevalence of prediabetes (mean [SD] age, 75.6 [5.2] years) was high and differed substantially depending on the definition used, with estimates ranging from 29% for glycated hemoglobin levels of 5.7% to 6.4% and fasting glucose levels of 100 to 125 mg/dL to 73% for either glycated hemoglobin levels of 5.7% to 6.4% or fasting glucose levels of 100 to 125 mg/dL.” The overall interpretation and implications of the study still stand.


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