

Letters

COMMENT & RESPONSE

Possible Immortal Time Bias in Study of Antibiotic Treatment and Outcomes in Patients Hospitalized for Asthma

To the Editor In their Original Investigation published in the March 2019 issue of *JAMA Internal Medicine*, Stefan et al¹ reported a 1-day higher median length of stay among patients admitted for acute asthma who were treated with antibiotics for at least 2 days starting in the first 2 days of their hospitalization, compared with propensity score-matched controls not so treated. The authors should clarify how the timing of antibiotic exposure and length of stay were determined because it seems like the study might be susceptible to immortal time bias,² in which there is a period in the exposed group during which they are not at risk of the outcome (which in this case is discharge from the hospital).

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 al¹ 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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Published Online: January 19, 2021. doi:[10.1001/jamainternmed.2020.7602](https://doi.org/10.1001/jamainternmed.2020.7602)

Conflict of Interest Disclosures: None reported.

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