

Community-Acquired Pneumonia and Proton Pump Inhibitors

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To the Editors:—We read with interest the article by Jena and colleagues regarding the possibility of residual confounding in the association of proton pump inhibitors (PPIs) and community-acquired pneumonia (CAP).¹ Specifically, we appreciated the argument for “falsification analysis,” which Jena has discussed elsewhere.²

The notion that a hypothesized causal relationship between an exposure and one outcome can be weakened or strengthened by observing whether the exposure is associated with various other “implausible” outcomes has previously been described as the “specificity” criterion for causality. Notably, this criterion has a long and debated history of use in epidemiological research.³ We agree with the authors that it deserves further attention in causal interpretations of observational data.

However, this method cannot replace other standard considerations in observational data analysis. For example, in this study, the authors base their conclusions about confounding on an association between quarterly claims for PPIs and disease diagnoses without determining when the events occurred in relationship to each other. They do not address the most fundamental feature of any causal relationship—that exposure precedes disease.⁴ This leaves numerous possible explanations for why PPI claims may be associated with the “implausible” outcomes under consideration. The analysis here may merely show that pre-

scriptions for PPIs are more likely to appear after a healthcare encounter.

Other observational studies evaluating the relationship between PPIs and CAP accounted for temporality and drug dose and differentiated incident from prevalent PPI use, finding important differences related to these factors.⁵ Accounting for these factors in the current study would allow a more valid comparison with existing evidence.

We agree with the authors that the criterion of specificity may be a useful tool to evaluate causal relationships in observational studies.¹ However, we submit that it should not distract from other important considerations in determining causality.

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