Clinical Infectious Diseases

CORRESPONDENCE

Reducing Diagnostic Bias Through Multiplex Polymerase Chain Reaction (PCR) Testing for SARS-CoV-2, Influenza A/B, and RSV

To the Editor—We thank the authors for their comments on our study of outcomes in adults attending the emergency department (ED) with infections caused by Omicron, seasonal influenza, or respiratory syncytial virus (RSV) [1].

First, the authors raise concerns about potential diagnostic bias and confounding by indication. During the pandemic period, 98% of the study participants were tested for all 3 viruses by multiplex polymerase chain reaction (PCR) testing, thus reducing potential differential diagnostic test bias. Furthermore, multiplex PCR testing for influenza and RSV was employed during the pre-pandemic study period. The numbers of RSV patients in relation to Omicron and influenza patients in our study are in line with previous studies of hospitalized patients [2, 3]. Our study focused on adults seeking the ED due to a respiratory virus infection, and the source population would thus not include milder infections in the community [4]. We do not agree that including test-negative patients is very informative because it consists of a heterogenous group of patients with many different infections and diagnoses.

Second, the authors mentions that we had access to time-to-event data but used logistic regression for statistical modelling purposes. The cumulative incidence was included in the article to present the temporality of mortality among study participants. However, our main objective was not to model time to mortality, but rather to evaluate mortality as a binary outcome at 30 and 90 days after the ED visit. If using Cox regression, the adjusted hazard ratio (95% confidence interval [CI]) for 30-day mortality would be 2.21 (1.50–3.25) for Omicron versus influenza and 1.36 (.92–2.01) for Omicron versus RSV, that is, similar findings to those from the logistic regression models.

Third, the authors bring up a sentence in the discussion where it is mentioned that "*around 14 times more deaths occurred in the Omicron cohort compared to the influenza 2021/2022 cohort and the RSV 2021/2022 cohort…*." It is correct that these figures stem from dividing the number of deaths in the Omicron cohort with the number of deaths in the influenza and RSV cohorts, respectively. As mentioned in the article, this calculation assumes that all deaths were related to the respiratory infection and the length of the infection seasons were similar. The purpose of this calculation is to emphasize that during the 14-month study period, Omicron was both more prevalent and associated with more severe outcomes, a "double whammy," compared with influenza and RSV infections.

Finally, the authors point out that almost all cases of influenza in our study were influenza A (1082/1099), and thus we did not have sufficient power to compare patients infected with Omicron to patients infected with influenza B. This is mentioned as a limitation in the discussion, and we do agree with the authors that further investigations into this could provide important insights into the comparative severity of these respiratory viruses. It is important to emphasize that the severity of influenza epidemics varies widely [5] and continued assessments of the comparative severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and influenza and RSV infections are warranted as described in our article.

Notes

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