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Dear Taissa Vila, PhD
Editor-in-Chief, *The Lancet Regional Health Americas*

We wish to submit the Article entitled “Uncovering the Post-Pandemic Timing of Influenza, RSV, and COVID-19 Driving Seasonal Influenza-like Illness in the United States” for full consideration by *The Lancet Regional Health Americas*.

The landscape of respiratory epidemics that drive seasonal Influenza-like Illness (ILI) in the US experienced a momentous shift after the introduction of COVID-19. The emergence of this new infection adds to existing misconceptions about ILI (such as attributing surges in ILI to only outbreaks of influenza A and influenza B) which circulate among healthcare workers and public health authorities, hinder the timely administration of vaccinations and therapeutics, and inhibit messaging about the different timings of seasonal respiratory outbreaks. Acknowledging the signals that precede respiratory epidemics is especially important for proper prevention. For example, while most health facilities and staff are well prepared to supply influenza vaccinations and treatment, prophylaxis for RSV, which is associated with more severe symptoms such as lower respiratory infections in young children and the elderly, involves time-sensitive and more financially burdensome administration. Our findings thus have direct implications for RSV prophylaxis administration using nirsevimab. While current ACIP guidance recommends a fixed October-March window for nirsevimab nationwide, we demonstrate substantial state-level variability in RSV epidemic timing. Our work suggests that data-informed, state-specific administration windows could better align prophylaxis with local RSV seasons, enabling more precise public health guidance and optimal resource allocation.

To clear some of these misconceptions, we used newly released emergency department visit data from the CDC’s National Syndromic Surveillance Program to show the timings of onsets and peaks of Influenza, RSV, and COVID-19 epidemics. We additionally use stacked regression methods to show the contribution of each of these diseases to the overall volume of seasonal ILI. Our analyses show that RSV epidemics peak before Influenza epidemics in most states, with about a one to three week difference separating the epidemic peaks. Our study provides a framework to be used with respiratory epidemic data collected in the future and serves as a test case for the effectiveness of early warning systems as applied to forecasting infectious disease epidemics in the United States.

Your consideration of this manuscript is greatly appreciated. Please address any correspondence to the corresponding author, Mauricio Santillana (msantill@g.harvard.edu).

Sincerely,

George Dewey