Systematic Testing for Influenza and Coronavirus Disease 2019 Among Patients With Respiratory Illness

To the Editor—A recent report by Rosenberg and colleagues highlights the importance of multiple sources of information for monitoring trends in the coronavirus disease 2019 (COVID-19) pandemic [1]. The authors used influenza-like illness (ILI) surveillance data and laboratory-confirmed influenza and COVID-19 cases to estimate population-based rates of illness during the beginning of the pandemic in New York state. Because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing was rapidly increasing during this period in many areas of the United States, numbers of COVID-19 cases were likely underestimated. This raises the question of whether COVID-19 contributed to ILI trends prior to widespread testing.

We recently examined the timing and extent of COVID-19 among patients with acute respiratory illness (ARI) enrolled in 2 US influenza vaccine effectiveness networks [2, 3]. We retrospectively tested specimens collected between late January 2020 and mid-March 2020, a time period during which genomic analyses of SARS-CoV-2 isolates suggested silent community spread in several US locations [4–6]. In the influenza networks, outpatients aged ≥6 months and inpatients aged ≥18 years with ARI (defined as cough or respiratory symptoms with onset ≤10 days earlier) were enrolled during the influenza season at healthcare facilities associated with study sites in 6 states (Michigan, Pennsylvania, Tennessee, Texas, Washington, and Wisconsin) [7]. During the influenza season, respiratory specimens, including nasal, throat, or nasopharyngeal swabs, were prospectively tested for influenza using reverse-transcription polymerase chain reaction (RT-PCR). We retrospectively tested a subset of stored specimens or extracted RNA at study sites for SARS-CoV-2 using RT-PCR designed to detect the SARS-CoV-2 nucleocapsid gene.

Although the number of confirmed influenza cases decreased after mid-February, influenza positivity among participants remained above 30% through early March when enrollment was interrupted due to the COVID-19 pandemic (Figure 1). Of 4961 specimens tested retrospectively, 5 (0.1%) specimens from patients at 3 study sites tested positive for SARS-CoV-2, all from patients enrolled within 1 week of the first COVID-19 cases reported in surveillance counties (Table 1). None of the patients had been previously identified as having COVID-19. Although few SARS-CoV-2–positive patients were identified before facility-based enrollment was halted, the timing of initial reports of COVID-19 cases in these surveillance areas coincided with detection of SARS-CoV-2–positive cases among outpatients and inpatients with respiratory symptoms.

Rapid increases in COVID-19 cases may have contributed to peaks in ILI activity observed in many states near the end of the influenza season, as

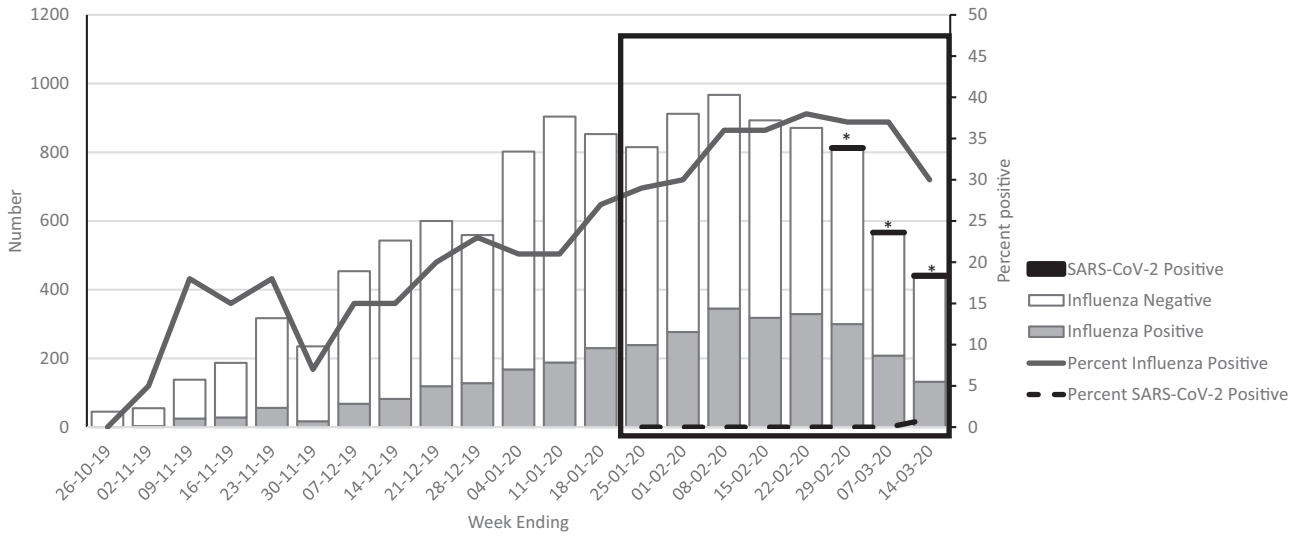

Figure 1. Number and percent of specimens from ambulatory patients and hospitalized adults with acute respiratory illness who tested positive for influenza or SARS-CoV-2, October 2019–March 2020. Box indicates weeks included in retrospective testing for SARS-CoV-2. *Week of first reported coronavirus disease 2019 case associated with community transmission in surveillance counties. Abbreviation: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1. Number of Enrolled Patients With Acute Respiratory Illness Tested, Positive Tests and Enrollment Dates for Severe Acute Respiratory Syndrome Coronavirus 2–Positive Patients, and Date of First Reported Nontravel-related Coronavirus Disease 2019 by Study Population, January 2020–March 2020

Study Site	Surveillance Counties	Time Period	No. Enrolled[a]	Severe Acute Respiratory Syndrome Coronavirus 2			Date of First Reported Coronavirus Disease 2019 Case[b]
				No. Tested	No. Positive (%)	Date of Enrollment	
Ann Arbor and Detroit, Michigan	10 counties in southeast Michigan	23 January–13 March	1026	848	2 (0.2)	9 March, 11 March	10 March
Pittsburgh, Pennsylvania	Allegheny	27 January–22 March	1294	1260	2 (0.2)	3 March, 11 March	7 March
Nashville, Tennessee	7 counties in central Tennessee	1 February–21 March	226	226	0 (0)	NA	5 March
Temple, Texas	8 counties in central Texas	25 January–5 March	875	584	0 (0)	NA	13 March
Seattle, Washington	King, Pierce, and Snohomish	31 January–29 February	1619	1214	1 (0.1)	25 February	21 February
Marshfield, Wisconsin	Clark, Marathon, and Wood	5 February–13 March	1367	660	0 (0)	NA	16 March
All sites		23 January–22 March	6407	4792	5 (0.1)		

Abbreviation: NA, not applicable.

[a]Includes ambulatory patients aged ≥6 months and hospitalized adults aged ≥18 years who presented to healthcare facilities with acute respiratory illness.

[b]Date of first reported COVID-19 case associated with community transmission in surveillance county.

suggested by computer modeling [8], but changes in ambulatory care utilization may have also contributed. Given overlap between ARI/ILI and symptoms of mild/moderate COVID-19 [9], systematic testing for SARS-CoV-2 and influenza will be needed during the upcoming influenza season to interpret trends in ILI surveillance and determine contributions of each viral illness to the burden of respiratory disease. Testing for both pathogens (and other respiratory viruses) may become routine for inpatients with respiratory illness but will depend on availability and access to testing among patients with mild illness. Facility-based surveillance for ILI and research studies will have to adapt. We agree with Rosenberg et al that alternatives to facility-based specimen collection, including home-based nasal swabs or saliva collection, will be needed.

Notes

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References

1. Rosenberg ES, Hall EW, Rosenthal EM, et al. Monitoring COVID-19 through trends in influenza-like illness and laboratory-confirmed influenza and COVID-19—New York State, excluding New York City, January 1–April 12, 2020. Clin Infect Dis **2021**; 72:144–7.
2. Jorden MA, Rudman SL, Villarino E, et al; CDC COVID-19 Response Team. Evidence for limited early spread of COVID-19 within the United States, January-February 2020. MMWR Morb Mortal Wkly Rep **2020**; 69:680–4.
3. Rha B, Lively JY, Englund JA, et al. SARS-CoV-2 infections in children—multi-center surveillance, United States, January-March 2020. J Pediatric Infect Dis Soc **2020**:piaa075. doi: 10.1093/jpids/piaa075.
4. Chu HY, Englund JA, Starita LM, et al; Seattle Flu Study Investigators. Early detection of Covid-19

through a citywide pandemic surveillance platform. N Engl J Med **2020**; 383:185–7.
5. Gonzalez-Reiche AS, Hernandez MM, Sullivan MJ, et al. Introductions and early spread of SARS-CoV-2 in the New York City area. Science **2020**; 369:297–301.
6. Deng X, Gu W, Federman S, et al. A genomic survey of SARS-CoV-2 reveals multiple introductions into northern California without a predominant lineage. medRxiv. **2020**. doi: 10.1101/2020.03.27.20044925.
7. Dawood FS, Chung JR, Kim SS, et al. Interim estimates of 2019-20 seasonal influenza vaccine effectiveness—United States, February 2020. MMWR Morb Mortal Wkly Rep **2020**; 69:177–82.
8. Silverman JD, Hupert N, Washburne AD. Using influenza surveillance networks to estimate state-specific case detection rates and forecast SARS-CoV-2 spread in the United States. medRxiv. doi: 10.1101/2020.04.01.20050542.
9. Kong W, Li Y, Peng M, et al. SARS-CoV-2 detection in patients with influenza-like illness. Nat Microbiol **2020**. doi: 10.1038/s41564-020-0713-1.

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