We conducted a rapid sentinel surveillance study to determine what proportion of mild, outpatient influenzalike illnesses were caused by SARS-CoV-2.

Methods | Between March 12-13 and 15-16, 2020, the Los Angeles County + University of Southern California Medical Center conducted testing among patients presenting with mild influenzalike illness to the emergency department or urgent care. Patients who had nasopharyngeal swabs tested with polymerase chain reaction assays for influenza and respiratory syncytial virus (GeneXpert Flu, Cepheid) were automatically tested for SARS-CoV-2 (Quest Diagnostics).

Only the influenza tests conducted during the day shift were automatically tested for SARS-CoV-2 because the process was manual. Patients were excluded if they had specific risk factors for SARS-CoV-2 (eg, travel exposure or known contact with a traveler, severely ill patients admitted for respiratory tract infections). Positive test results were followed up by Department of Public Health experts to assess clinical factors and demographics.

The number of influenza tests ordered by physicians at the Los Angeles County + University of Southern California Medical Center between March 2 and March 18, 2020, and the proportion testing positive for influenza were also assessed. In addition, the rate of influenzalike illnesses obtained from weekly surveys of emergency departments over the past 5 years were summarized, as well as the percentage of respiratory specimens testing positive for influenza from ongoing public health sentinel surveillance conducted at 7 clinical laboratories across Los Angeles County, California.

This study was approved as expedited with a waiver of informed consent by the University of Southern California health sciences campus institutional review board.

Results | One hundred thirty-one tests for SARS-CoV-2 were obtained and 7 were positive (5.3%; 95% CI, 2.2%-10.7%). The median age of patients who tested positive was 38 years (range, 34-44 years), 3 were male (43%), and the median duration of symptoms was 4 days (range, 2-4 days) at presentation. Six of 7 patients presented with fever, 5 with myalgias, and only 1 with cough. Only 1 patient had a travel history (returned from Miami, Florida). All patients had mild illnesses, and all tested negative for influenza and respiratory syncytial virus.

At the Los Angeles County + University of Southern California Medical Center, the number of influenza tests ordered by physicians was relatively stable, but the percentage of positive test results for influenza declined around the time of the study (**Figure 1**). Across the county, sentinel testing revealed a third seasonal spike in influenzalike illnesses during the weeks before the study; no third seasonal spike was seen during the prior 4 years, and the third spike occurred later than any spike during those years (**Figure 2**A). This late, third seasonal influenzalike illness spike occurred even as the percentage of respiratory specimens that tested positive for influenza steadily declined (Figure 2B).

Discussion | The 5% rate of SARS-CoV-2 among patients with mild influenzalike illness without risk factors is concerning. These patients had sufficiently mild illness to be active in the community throughout their illness, increasing the possibility of transmission. Such transmission is consistent with the unusual, third countywide influenzalike illness spike that occurred late in the season and with declining rates of influenza positivity.

The primary limitations of the study were the sampling for a brief period at 1 medical center and SARS-CoV-2 testing only being conducted during the day. Nevertheless, the results suggested that containment efforts were unlikely to succeed and helped inform the Los Angeles County Department of Public Health to adopt a more aggressive mitigation strategy to reduce COVID-19 morbidity and mortality. Similar efforts may be needed in other jurisdictions.

Brad Spellberg, MD
Meredith Haddix, MPH
Rebecca Lee, MPH
Susan Butler-Wu, PhD
Paul Holtom, MD
Hal Yee, MD, PhD
Prabhu Gounder, MD

Author Affiliations: Los Angeles County + University of Southern California Medical Center, Los Angeles (Spellberg, Butler-Wu, Holtom); Los Angeles County Department of Public Health, Los Angeles, California (Haddix, Lee, Gounder); Los Angeles County Department of Health Services, Los Angeles, California (Yee).

Corresponding Author: Brad Spellberg, MD, Los Angeles County + University of Southern California Medical Center, 2051 Marengo St, Los Angeles, CA 90033 (bspellberg@dhs.lacounty.gov).

Published Online: March 31, 2020. doi:10.1001/jama.2020.4958

Author Contributions: Dr Spellberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Spellberg, Haddix, Holtom, Yee, Gounder.
Acquisition, analysis, or interpretation of data: Spellberg, Haddix, Lee, Butler-Wu, Holtom, Gounder.
Drafting of the manuscript: Spellberg, Gounder.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Gounder.
Administrative, technical, or material support: All authors.
Supervision: Spellberg, Holtom, Yee, Gounder.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We acknowledge the tireless surveillance efforts of Bessie Hwang, MD, MPH, and Emily Kajita, MS, MPH (both with the Department of Public Health Acute Communicable Disease Control Syndromic Surveillance Unit), and Elizabeth Traub, MPH (with the Department of Public Health Acute Communicable Disease Control Syndromic Respiratory Diseases Unit). None received additional compensation beyond salary.

1. Del Rio C, Malani PN. 2019 novel coronavirus—important information for clinicians. *JAMA*. 2020;323(11):1039-1040. doi:10.1001/jama.2020.1490

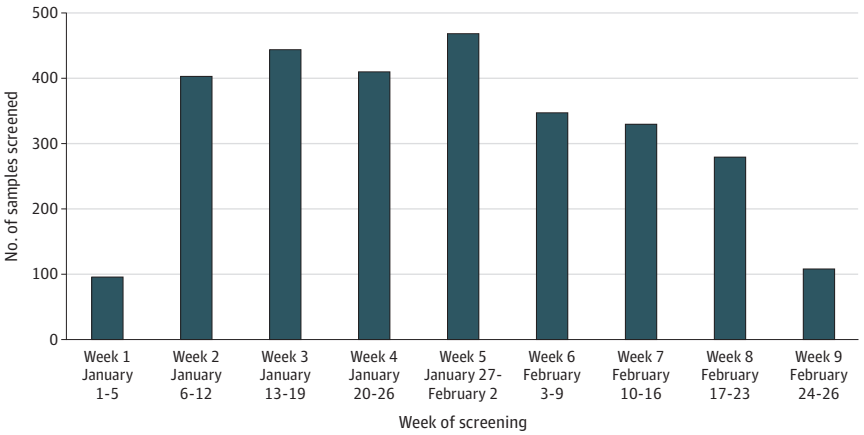
2. Del Rio C, Malani PN. COVID-19—new insights on a rapidly changing epidemic. *JAMA*. Published online February 28, 2020. doi:10.1001/jama.2020.3072

3. Paules CI, Marston HD, Fauci AS. Coronavirus infections—more than just the common cold. *JAMA*. 2020;323(8):707-708. doi:10.1001/jama.2020.0757

Sample Pooling as a Strategy to Detect Community Transmission of SARS-CoV-2

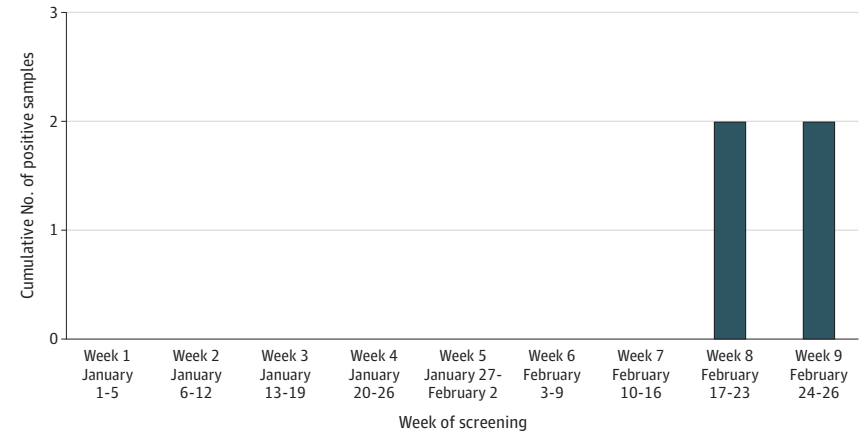
The coronavirus disease 2019 (COVID-19) pandemic has revealed the global importance of robust diagnostic testing to differentiate severe acute respiratory syndrome coronavirus 2

Figure 1. Number of Samples Screened for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)



Testing was performed by pooled sample screening at the Stanford Health Care Clinical Virology Laboratory over a 9-week period (January 1, 2020-February 26, 2020). Each pool included 9 to 10 individual samples that tested negative for other respiratory viruses. The number of SARS-CoV-2 samples, listed for weeks 1 through 9, were 96, 404, 444, 410, 469, 347, 330, 280, and 108. A total of 292 pools composed of 2888 individual samples were screened.

Figure 2. Cumulative Number of Positive Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Samples



Two positive samples were identified through pooled screening during week 8. Week 9 indicates the cumulative number for the screening period. See Figure 1 caption for testing details.

(SARS-CoV-2) from other routine respiratory infections and guide appropriate clinical management. Given the limited testing capacity available in the United States early in the pandemic, individuals with a clinical syndrome consistent with COVID-19, but without travel or exposure history, were not tested.[1] Therefore, it remains uncertain whether there may have been community circulation of SARS-CoV-2 prior to the identification of individuals with positive results through standard public health surveillance. Sample pooling, a strategy used for community monitoring of other infectious diseases such as trachoma, has not, to our knowledge, been deployed for the early comprehensive screening of SARS-CoV-2 in the United States.[2]

Methods | The Stanford Health Care Clinical Virology Laboratory serves adult and pediatric tertiary care hospitals and affiliated primary care and specialty clinics in the San Francisco Bay Area in California. We performed a retrospective study that evaluated all nasopharyngeal and bronchoalveolar lavage samples collected between January 1, 2020, and February 26, 2020, from inpatients and outpatients who had negative results by routine respiratory virus testing (respiratory pathogen or respiratory viral panels [GenMark Diagnostics] or Xpert Xpress Flu/RSV [Cepheid]) and had not been tested for SARS-CoV-2. After February 26, 2020, clinical testing for SARS-CoV-2 on individual samples was begun, as recommended by institutional policy. Nine or 10 individual samples were pooled, and screening was performed using reverse transcriptase–polymerase chain reaction targeting the envelope (*E*) gene.[3] Positive pools were deconvoluted and individual samples tested for both *E* and the RNA-dependent RNA polymerase (*RdRp*) gene for confirmation.[3] This study was approved by the Stanford institutional review board. Given the deidentified nature of testing, individual patient consent was not required, as determined by the institutional review board, for this study.

Results | A total of 292 pools were screened, corresponding with 2740 nasopharyngeal samples and 148 bronchoalveolar lavage samples (**Figure 1**). The confirmed positivity rate for SARS-CoV-2 was 0.07% (2/2888) (**Figure 2**). The positive results were from nasopharyngeal samples collected on

February 21, 2020, and on February 23, 2020. The 2 positive samples showed detection of *E* and *RdRp*. Sanger sequencing revealed 100% identity with the SARS-CoV-2 *E* gene. Only 1 pool showed a positive *E* signal that was not reproducible with testing of the individual samples of that pool.

Discussion | Results from this screening strategy support that the burden of disease in the San Francisco Bay Area early in the pandemic was low; less than 1% of all symptomatic individuals with negative routine testing had SARS-CoV-2 infection. The timing of the positive pools overlapped with the first 3 individuals with positive results reported from Santa Clara County, tested using criteria established by the Centers for Disease Control and Prevention.[4,5] Thus, public health counts of individuals with SARS-CoV-2 infection indicated a reasonable estimate of overall disease burden among symptomatic individuals in this area.[6] Nevertheless, the individuals identified with positive results via this screening strategy would not have met the existing testing criteria.

A pooled screening strategy was pursued to increase testing throughput, limit use of reagents, and increase overall testing efficiency at an expected slight loss of sensitivity. With only 1 false-positive reading, the strategy was specific. Due to the challenges of restricted access to diagnostic tests and kit supplies across the United States, early testing has largely been limited to symptomatic individuals fulfilling testing criteria.[4] Although this approach facilitates rational use of resources, it may miss individuals in whom COVID-19 risk has not been identified.[4] This study is limited in that it was performed in a single laboratory in a restricted geographical area; additional data are thus required to validate this approach on a larger scale. Furthermore, this screening strategy does not obviate the need for individual diagnostic testing, particularly as community transmission intensifies.

Strategies such as pooled screening may facilitate detection of early community transmission of SARS-CoV-2 and enable timely implementation of appropriate infection control measures to reduce spread.

Catherine A. Hogan, MD, MSc
Malaya K. Sahoo, PhD
Benjamin A. Pinsky, MD, PhD

Author Affiliations: Department of Pathology, Stanford University School of Medicine, Stanford, California.

Corresponding Author: Benjamin A. Pinsky, MD, PhD, Department of Pathology, Stanford University School of Medicine, 3375 Hillview, Room 2913, Palo Alto, CA 94304 (bpinsky@stanford.edu).

Published Online: April 6, 2020. doi:10.1001/jama.2020.5445

Author Contributions: Drs Hogan and Pinsky had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Hogan, Pinsky.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Hogan, Sahoo.
Administrative, technical, or material support: Pinsky.
Supervision: Pinsky.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank ChunHong Huang, PhD, Department of Pathology, Stanford University, for her contribution in generating the data for this study, without compensation.

1. Sharfstein JM, Becker SJ, Mello MM. Diagnostic testing for the novel coronavirus. *JAMA*. Published online March 9, 2020. doi:10.1001/jama.2020.3864

2. Ray KJ, Zhou Z, Cevallos V, et al. Estimating community prevalence of ocular Chlamydia trachomatis infection using pooled polymerase chain reaction testing. *Ophthalmic Epidemiol*. 2014;21(2):86-91. doi:10.3109/09286586.2014.884600

3. Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill*. 2020;25(3):1-8. doi:10.2807/1560-7917.ES.2020.25.3.2000045

4. Centers for Disease Control and Prevention. Evaluating and testing persons for coronavirus disease 2019 (COVID-19). Updated March 24, 2020. Accessed March 25 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html

5. Santa Clara County Public Health. Healthy Santa Clara County: novel coronavirus (COVID-19) data dashboard. Accessed March 25, 2020. https://www.sccgov.org/sites/phd/DiseaseInformation/novel-coronavirus/Pages/dashboard.aspx

6. Lipsitch M, Swerdlow DL, Finelli L. Defining the epidemiology of COVID-19—studies needed. *N Engl J Med*. 2020;382(13):1194-1196. Published online March 26, 2020. doi:10.1056/NEJMp2002125

Seasonal Influenza Activity During the SARS-CoV-2 Outbreak in Japan

Since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak began, measures for avoiding disease transmission have been widely promoted in Japan, such as use of masks and handwashing, remote work, and cancellation of large events. If effective, these measures may also reduce the spread of other infectious diseases, such as seasonal influenza. We compared the weekly influenza activity in the 2019/2020 season vs 5 previous seasons.

Related article page 1966

Audio

Methods | We used data from 2014 to 2020 from the National Institute of Infectious Diseases Japan, which gathers the number of cases of seasonal influenza weekly, diagnosed by physicians based on clinical symptoms or laboratory findings, from approximately 5000 sentinel centers, including hospitals and clinics (60% pediatrics and 40% internal or general medicine clinics).[1,2] We grouped the weekly reports into seasons (week 40 of the year through week 11 of the following year [September 30, 2019, through March 15, 2020, for the 2019/2020 season]; the season was truncated after week 11 because this was the latest available data for 2020). In each season we assessed the weekly influenza activity, presented as a crude standardized estimate of influenza activity nationally, calculated by multiplying the mean number of reported cases per sentinel center with a constant number (n = 72 201) representing the number of outpatient visits to hospitals and clinics in the country in 2019[3] vs the health care institutions in the surveillance system.[1,4] We estimated the change in influenza activity after the SARS-CoV-2 outbreak using a "difference-in-difference" regression model that included a variable for each week, a variable representing the average difference in influenza activity per week for the 2019/2020 season vs the 2014 to