Figure 1. Influenza Vaccination and Diagnosis in Children 2 to 5 Years of Age, According to Birth Month.

Shown are the percentages of children who had insurance claims for receipt of an influenza vaccine (Panel A) or an encounter during which they received a diagnosis of influenza (Panel B). The center of each box represents the point estimate of the adjusted event rate, and I bars represent 95% confidence intervals (which may be very small).

preventive visit with vaccination because their birthday is outside the September-December window when the influenza vaccine is typically available; returning to the doctor's office for a separate vaccination visit may be difficult. Vaccinations for young children outside the doctor's office - such as at preschools, pharmacies, or community centers — may have public health benefits.

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1. Recommended child and adolescent immunization schedule for ages 18 years or younger. Atlanta: Centers for Disease Control and Prevention, 2020 (https://www.cdc.gov/vaccines/schedules/ downloads/child/0-18yrs-child-combined-schedule.pdf).

2. Committee on Practice and Ambulatory Medicine, Bright Futures Periodicity Schedule Workgroup. 2017 Recommendations for preventive pediatric health care. Pediatrics 2017;139(4): e20170254.

3. Reichert TA, Sugaya N, Fedson DS, Glezen WP, Simonsen L, Tashiro M. The Japanese experience with vaccinating schoolchildren against influenza. N Engl J Med 2001;344:889-96.

4. King JC Jr, Stoddard JJ, Gaglani MJ, et al. Effectiveness of schoolbased influenza vaccination. N Engl J Med 2006;355:2523-32. 5. Layton TJ, Barnett ML, Hicks TR, Jena AB. Attention deficithyperactivity disorder and month of school enrollment. N Engl J Med 2018;379:2122-30.

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Early Detection of Covid-19 through a Citywide Pandemic Surveillance Platform

ratory virus surveillance may not identify novel for testing to identify influenza and other respipathogens in time to implement crucial public ratory pathogens (see the Supplementary Appenhealth interventions.¹ The Seattle Flu Study is a dix, available with the full text of this letter at multi-institutional, community-wide pandemic NEJM.org). In one study group, persons enrolled surveillance platform that was established in online and were sent kits, by rapid-delivery ser-November 2018.² Persons reporting symptoms vices, for home collection of a midnasal swab;

TO THE EDITOR: Traditional approaches to respi- of respiratory illness provided informed consent

N ENGL J MED 383;2 NEJM.ORG JULY 9, 2020

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Figure 1. Covid-19 Case Detection through the Seattle Flu Study.

Panel A shows SARS-CoV-2 tests over time, further stratified according to age group; detection of positive SARS-CoV-2 test results over time and as a percentage of the total number of tests run; and Covid-19-positive case counts over time. Panel B shows cycle threshold values from a laboratory-developed multiplex quantitative reverse-transcriptase polymerase-chain-reaction (qRT-PCR) assay as a function of days elapsed from swab collection to freezing or nucleic acid extraction for virus detection, shown separately for SARS-CoV-2, other respiratory viruses, and RNase P, a human cellular marker. The horizontal line in each box represents the median, the lower and upper boundaries of the boxes the interquartile range, and the ends of the vertical lines 1.5 times the interquartile range. Individual points represent outliers (>1.5 times the interquartile range).

samples were returned by mail. After identification of the first case of Covid-19 in Washington State, the samples that were collected were also tested for SARS-CoV-2. After March 4, 2020, a human subjects institutional review board determined that results could be reported to public health authorities and to participants, who were notified under a public health surveillance exemption.

From January 1 through March 9, 2020, a total of 3524 participants provided specimens after online enrollment. Of these, 2353 (66.8%) completed all the study procedures, including testing; SARS-CoV-2 was detected in 25 (1.1%), of whom 2 were children (Fig. 1A). Enrollment increased markedly in late February, most likely motivated by public concern about Covid-19 (Fig. 1A). Some of the collection kits (1316 of 2353 [55.9%]) were sent to participants for same-day delivery, with a median delivery time of 2.3 hours (interquartile range, 1.7 to 3.1). The median number of days from swab collection to receipt of the specimen by the laboratory was 2 days (interquartile range, 2 to 4). Semiquantitative viral loads from home-collected midnasal swabs were stable over time for SARS-CoV-2, other respiratory viruses, and RNase P, a human cellular marker (Fig. 1B).

In this early phase of the pandemic, only 7 of the 25 persons with Covid-19 (28%) reported seeking clinical care. The most common reported symptoms were fatigue, myalgia, fever, cough, and chills. The median duration of symptoms before swab collection was 4 days; 9 participants (36%) had had symptoms for less than 2 days at

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time of swab collection. Coinfection with another respiratory virus was present in 4 cases (16%).

The first Covid-19 case detected through the Seattle Flu Study, in a specimen collected on February 24, 2020, was the first documented U.S. case of community transmission at the time.³ These results initiated assessment of the spread of the virus in the Seattle region, which in turn accelerated public health efforts to mitigate the emerging pandemic.⁴ As the Covid-19 pandemic progresses, widespread implementation of simple methods that are scalable and require minimal interaction for collection of samples from persons who may not seek clinical care is critical for early detection of community cases. Looking beyond the current crisis, we envision ubiquitous, community-based sampling for respiratory illnesses as essential infrastructure for early detection and mitigation of future pandemics.

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1. Fink S, Baker M. "It's just everywhere already": how delays in testing set back the U.S. coronavirus response. New York Times. March 10, 2020 (https://www.nytimes.com/2020/03/10/us/coronavirus-testing-delays.html).

2. Chu HY, Boeckh M, Englund JA, et al. The Seattle Flu Study: a multi-arm community-based prospective study protocol for assessing influenza prevalence, transmission, and genomic epidemiology. March 6, 2020 (https://www.medrxiv.org/content/ 10.1101/2020.03.02.20029595v1). preprint.

3. Bedford T, Greninger AL, Roychoudhury P, et al. Cryptic transmission of SARS-CoV-2 in Washington State. April 16, 2020 (https://www.medrxiv.org/content/10.1101/2020.04.02 .20051417v1). preprint.

4. Klein D, Hagedorn B, Kerr C, Hu H, Bedford T, Famulare M. Working paper — model-based estimates of COVID-19 burden in King and Snohomish counties through April 7, 2020. March 10, 2020 (https://institutefordiseasemodeling.github.io/COVID -public/reports/Working%20paper%20%E2%80%93%20model -based%20estimates%20of%20COVID-19%20burden%20in%20 King%20and%20Snohomish%20counties%20through%20April %207.pdf).

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