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Assessment of 135 794 Pediatric Patients Tested for Severe Acute Respiratory Syndrome Coronavirus 2 Across the United States

L. Charles Bailey, MD, PhD; Hanieh Razzaghi, MPH; Evanette K. Burrows, MPH; H. Timothy Bunnell, PhD; Peter E. F. Camacho, MS; Dimitri A. Christakis, MD, MPH; Daniel Eckrich, MLIS; Melody Kitzmiller, BS; Simon M. Lin, MD, MBA; Brianna C. Magnusen, MD; Jason Newland, MD; Nathan M. Pajor, MD, MS; Daksha Ranade, MPH, MBA; Suchitra Rao, MD, MSCS; Olamiji Sofela, MBChB, MMCi; Janet Zahner, BS; Cortney Bruno, MSW; Christopher B. Forrest, MD, PhD

IMPORTANCE There is limited information on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing and infection among pediatric patients across the United States.

OBJECTIVE To describe testing for SARS-CoV-2 and the epidemiology of infected patients.

DESIGN, SETTING, AND PARTICIPANTS A retrospective cohort study was conducted using electronic health record data from 135 794 patients younger than 25 years who were tested for SARS-CoV-2 from January 1 through September 8, 2020. Data were from PEDSnet, a network of 7 US pediatric health systems, comprising 6.5 million patients primarily from 11 states. Data analysis was performed from September 8 to 24, 2020.

EXPOSURE Testing for SARS-CoV-2.

MAIN OUTCOMES AND MEASURES SARS-CoV-2 infection and coronavirus disease 2019 (COVID-19) illness.

RESULTS A total of 135 794 pediatric patients (53% male; mean [SD] age, 8.8 [6.7] years; 3% Asian patients, 15% Black patients, 11% Hispanic patients, and 59% White patients; 290 per 10 000 population [range, 155-395 per 10 000 population across health systems]) were tested for SARS-CoV-2, and 5374 (4%) were infected with the virus (12 per 10 000 population [range, 7-16 per 10 000 population]). Compared with White patients, those of Black, Hispanic, and Asian race/ethnicity had lower rates of testing (Black: odds ratio [OR], 0.70 [95% CI, 0.68-0.72]; Hispanic: OR, 0.65 [95% CI, 0.63-0.67]; Asian: OR, 0.60 [95% CI, 0.57-0.63]); however, they were significantly more likely to have positive test results (Black: OR, 2.66 [95% CI, 2.43-2.90]; Hispanic: OR, 3.75 [95% CI, 3.39-4.15]; Asian: OR, 2.04 [95% CI, 1.69-2.48]). Older age (5-11 years: OR, 1.25 [95% CI, 1.13-1.38]; 12-17 years: OR, 1.92 [95% CI, 1.73-2.12]; 18-24 years: OR, 3.51 [95% CI, 3.11-3.97]), public payer (OR, 1.43 [95% CI, 1.31-1.57]), outpatient testing (OR, 2.13 [1.86-2.44]), and emergency department testing (OR, 3.16 [95% CI, 2.72-3.67]) were also associated with increased risk of infection. In univariate analyses, nonmalignant chronic disease was associated with lower likelihood of testing, and preexisting respiratory conditions were associated with lower risk of positive test results (standardized ratio [SR], 0.78 [95% CI, 0.73-0.84]). However, several other diagnosis groups were associated with a higher risk of positive test results: malignant disorders (SR, 1.54 [95% CI, 1.19-1.93]), cardiac disorders (SR, 1.18 [95% CI, 1.05-1.32]), endocrinologic disorders (SR, 1.52 [95% CI, 1.31-1.75]), gastrointestinal disorders (SR, 2.00 [95% CI, 1.04-1.38]), genetic disorders (SR, 1.19 [95% CI, 1.00-1.40]), hematologic disorders (SR, 1.26 [95% CI, 1.06-1.47]), musculoskeletal disorders (SR, 1.18 [95% CI, 1.07-1.30]), mental health disorders (SR, 1.20 [95% CI, 1.10-1.30]), and metabolic disorders (SR, 1.42 [95% CI, 1.24-1.61]). Among the 5374 patients with positive test results, 359 (7%) were hospitalized for respiratory, hypotensive, or COVID-19–specific illness. Of these, 99 (28%) required intensive care unit services, and 33 (9%) required mechanical ventilation. The case fatality rate was 0.2% (8 of 5374). The number of patients with a diagnosis of Kawasaki disease in early 2020 was 40% lower (259 vs 433 and 430) than in 2018 or 2019.

CONCLUSIONS AND RELEVANCE In this large cohort study of US pediatric patients, SARS-CoV-2 infection rates were low, and clinical manifestations were typically mild. Black, Hispanic, and Asian race/ethnicity; adolescence and young adulthood; and nonrespiratory chronic medical conditions were associated with identified infection. Kawasaki disease diagnosis is not an effective proxy for multisystem inflammatory syndrome of childhood.

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Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: L. Charles Bailey, MD, PhD, Department of Pediatrics, Children's Hospital of Philadelphia, 2716 South St, 11th Floor, Philadelphia, PA 19146 (baileyc@chop.edu).

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in November 2019 and by March 2020 was pandemic.[1] Reported cases of coronavirus disease 2019 (COVID-19) have exceeded 8.5 million in the United States[2] and are declining in some regions and rising in others.[3] Although several syndromic presentations have been reported, there is a lack of systematic information documenting the effects of SARS-CoV-2 on children, adolescents, and young adults.

Pediatric patients account for a disproportionately small number of reported cases of COVID-19.[4-6] The Centers for Disease Control and Prevention noted that, although 23% of the US population is younger than 18 years, 2% of cases of COVID-19 occurring between February 12 and April 2, 2020, were in the pediatric population.[7] In a series of 2135 pediatric cases in China, 51% were mild.[8] Asymptomatic pediatric cases of COVID-19 have also been documented,[8-10] and because asymptomatic patients are not routinely tested, the full extent of SARS-CoV-2 infection and COVID-19 illness in the pediatric population has been underrepresented in epidemiologic studies.

The role of chronic medical conditions in disease severity remains a major concern. A retrospective study of 177 children found that 63% of those hospitalized with COVID-19 had underlying conditions, compared with 32% of nonhospitalized patients with COVID-19, and 78% of critically ill children with COVID-19 had underlying conditions compared with 57% of hospitalized, non-critically ill patients with COVID-19.[11] In a report on 48 patients with COVID-19 in the pediatric intensive care unit, nearly all (83%) had underlying conditions.[12] The US Centers for Disease Control and Prevention has noted that, in a series of 295 children with COVID-19, a much higher percentage (77%) who were hospitalized had an underlying condition than those who were not hospitalized (12%).[7]

In addition to respiratory illness, concerns have arisen around multisystem inflammatory syndrome in children (MIS-C).[13] An Italian series of 10 cases of Kawasaki-like syndrome included 8 patients with antibodies against SARS-CoV-2.[14] New York state has reported more than 100 cases of Kawasaki-like disease, including 3 deaths, among children with COVID-19.[15] Our evolving knowledge of MIS-C suggests that available evidence may be revealing only a partial picture of the effect of COVID-19 in the pediatric population.

Most information about pediatric COVID-19 arises from single institutions and international studies. We report here the multicenter experience of 7 large pediatric health systems in PEDSnet (https://pedsnet.org), a collaborative learning health network that shares inpatient and outpatient electronic health record data for all patients and conducts research and outcomes improvement, as well as contributes to initiatives such as OHDSI (Observational Health Data Sciences and Informatics [https://www.ohdsi.org]) and PCORnet (the National Patient-Centered Clinical Research Network [https://pcornet.org]).[16,17] PEDSnet institutions provide care for both healthy pediatric patients and those with medically complex conditions. We describe the use of testing for SARS-CoV-2 across the network through September 8, 2020, and describe patient characteristics associated with testing and infection.

Key Points

Question What is the epidemiology across the United States of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among pediatric patients undergoing diagnostic testing for the virus?

Findings In this cohort study using electronic health records for 135 794 US pediatric patients in 7 children's health systems, 96% of patients tested had negative results, and rates of severe cardiorespiratory presentation of coronavirus disease 2019 (COVID-19) illness were low. Minority race/ethnicity, chronic illness, and increasing age were associated with SARS-CoV-2 infection.

Meaning This study suggests that for most pediatric patients, the risk of SARS-CoV-2 infection appears low, but higher concern may be warranted for patients with medically complex conditions or those of minority race/ethnicity.

Methods

Human Participant Research

Extraction and transformation of data for PEDSnet, including removal of direct identifiers, proceeded with oversight of institutional review boards at each institution, which determined that waiver of consent and Health Insurance Portability and Accountability Act authorization were required owing to impractability. The Children's Hospital of Philadelphia institutional review board reviewed the analyses reported here and determined that they did not constitute human participant research. Reporting of study design and results follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for observational research.[18]

Study Setting

PEDSnet institutions participating include Children's Hospital of Philadelphia, Cincinnati Children's Hospital Medical Center (tested patients only), Children's Hospital of Colorado, Nationwide Children's Hospital, Nemours Children's Health System (a Delaware and Florida health system), Seattle Children's Hospital, and St Louis Children's Hospital. Annually, PEDSnet institutions provide services to about 3% of the nation's children (2.5 million patients).

PEDSnet Viral Illness Group

Since March 2020, PEDSnet institutions have implemented rapid data refreshes of data describing patients who were (1) tested for infection using reverse transcriptase-polymerase chain reaction for SARS-CoV-2, (2) assigned a diagnosis code for COVID-19 illness, or (3) assigned a diagnosis code for viral illness, respiratory infection, or fever (collectively referred to as the inclusion diagnosis) (eTable 1 in the Supplement).[19] All historical data were extracted for patients who met inclusion criteria and were standardized to the PEDSnet common data

model, an extension of the OMOP (Observational Medical Outcomes Partnership) common data model, described elsewhere.[16,20,21] Institutions validated the count of tested patients and patients with positive test results with internal registries. This report uses the data extract occurring from January 1 through September 8, 2020.

Within this group, recent patients are those with at least 1 diagnosis between July 1, 2018, and December 31, 2019 (ie, 18 months before the study's observation period), and were used as the denominator for testing rates. Recurring patients had at least 2 visits in the 3 years before the time of inclusion, and are used as the denominator for analyses including chronic medical conditions.

Cohort Formation

Included patients were younger than 25 years prior to March 1, 2020; this age was selected based on institutional policies for the transition of patients to adult care, and reflects national trends extending pediatric care into early adulthood.[22,23] Patient characteristics and health care use were recorded in the electronic health record according to institutional practice. Tested patients were subdivided into those with positive results without severe illness, positive results with severe illness, and negative test results. If a patient had multiple test results, they were classified as positive if any reverse transcriptase–polymerase chain reaction test result was positive or a serologic test result was positive and no negative reverse transcriptase–polymerase chain reaction results were present. Severe illness was defined as hospitalization no earlier than 7 days prior to the testing date and an inpatient diagnosis of pneumonia, sepsis, respiratory failure, or COVID-19 (eTable 2 in the Supplement). Demographic and clinical features were compared across the 3 groups.

Health Care Use

Hospital admission was defined as an inpatient visit extending across 2 calendar days, an emergency department (ED) visit at a site designated by the health system as an ED, and an outpatient visit as any other in-person visit. Intensive care unit admission was defined as the presence of an admission or transfer event to an intensive care unit in the electronic health record. Mechanical ventilation was established by documented use of continuous positive airway pressure, bilevel positive airway pressure, or a mechanical ventilator; 2 or more entries were required.

Health Conditions

We used the taxonomy from the Pediatric Medical Complexity Algorithm (PMCA),[24,25] which uses *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Clinical Modification* (*ICD-10-CM*) codes to aggregate related chronic diagnoses according to body system, with a separate category for malignant neoplasms. A condition is considered progressive if it is associated with deteriorating health and increased risk of shortened life expectancy in adulthood. For our examination of baseline chronic conditions, we considered only diagnoses occurring prior to March 1, 2020, and looking back 3 years from the date of the test (when available) or last recorded diagnosis (for comparison groups), to remove any effect of COVID-19. For these analyses, we required that patients meet the recurring patient criteria to ensure that adequate history was available. Obesity was defined as presence of an age- and sex-standardized body mass index *z* score in the 95th percentile or higher for patients aged 2 to 20 years, or body mass index of more than 30 (calculated as weight in kilograms divided by height in meters squared) for patients aged 21 to 24 years, based on height and weight measured in 2020. Specific conditions (eg, diabetes and asthma) were identified using Systematized Nomenclature of Medicine–Clinical Terms (SNOMED-CT) terms.[26]

Kawasaki Estimation

Multisystem inflammatory syndrome in children lacks a specific diagnostic term or case definition, and it shares several clinical features with Kawasaki disease (KD). We therefore examined diagnoses of KD (eTable 3 in the Supplement) observed in PEDSnet from March 1 to May 15, 2020, in comparison with the same intervals in 2018 and 2019. The at-risk denominator was defined as the mean number of patients seen between these dates in 2018 and 2019. Cases were defined as all patients with a KD diagnosis code during the same intervals.

Statistical Analysis

All statistical analyses were performed from September 8 to 24, 2020, using R, version 3.6.1-4.0.2 (R Foundation for Statistical Computing).[27] We computed standardized ratios (SRs) of chronic disease risk by dividing the observed count of patients with different PMCA body system involvement with an expected count for the number of patients present in each test denominator group. To ascertain the expected count, we computed chronic disease proportions for patients with a visit from March 1 to September 8 in 2018 or 2019 (combined) who also had a viral illness diagnosis during those intervals. These proportions were then multiplied by the sample size for all tested patients or patients with positive test results for each PMCA body system category. The 95% CI was estimated using the method of Vandenbroucke.[28]

Multivariable logistic regression was performed using generalized linear models. The model included age category, race/ethnicity, PEDSnet health system, sex, testing location, and insurance status. We also controlled for presence of PMCA body system diagnostic codes, in one model as a composite indicator and in another as independent variables so that one body system was not overrepresented. One analysis comprised all recurring patients and the outcome was presence of a SARS-CoV-2 test. A second comprised only tested patients and the outcome was a positive SARS-CoV-2 test result. The third analysis examined patients with positive test results and the outcome of severe disease.

Results

SARS-CoV-2 Testing

Through September 8, 2020, a total of 135 794 patients were tested for SARS-CoV-2 virus infection across PEDSnet (eFig-

Table 1. SARS-CoV-2 Testing Patterns by Health System

Characteristic	Overall	Health system[a]							
		A	B	C[b]	D	E	F	G	H
Recent patients, No.[c]	2 425 942	225 762	537 652	198 332	331 408	351 973	311 441	197 848	271 526
Patients tested, No. (%)									
Recurring[d]	111 785 (82)	9872 (93)	25 513 (93)	8657 (61)	22 920 (82)	10 594 (86)	15 684 (82)	11 929 (71)	6616 (95)
Nonrecurring	24 009 (18)	798 (7)	1961 (7)	5555 (39)	5043 (18)	1783 (14)	3539 (18)	4982 (29)	348 (5)
Test result, No. (%)									
Positive	5374 (4)	425 (4)	1152 (4)	952 (7)	1046 (4)	751 (6)	503 (3)	250 (1)	295 (4)
Negative	130 420 (96)	10 245 (96)	26 322 (96)	13 260 (93)	26 917 (96)	11 626 (94)	18 720 (97)	16 661 (99)	6669 (96)
No. tested per 10 000 recent patients	338	314	375	239	555	235	341	426	161
No. of cases of SARS-CoV-2 infection per 10 000 recent patients	13	13	16	11	17	15	10	6	8

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] The Delaware and Florida sites in the Nemours Children's Health System are represented separately.

[b] Patients 18 years or older were removed owing to the presence in this health system's data of test information from adults seen at affiliated institutions.

[c] Patients younger than 25 years with at least 1 physician visit with a recorded diagnosis from July 2018 to December 2019.

[d] Patients with at least 2 in-person visits in the 3 years prior to testing, or to March 1, 2020, if not tested.

ure 1 in the Supplement). A total of 13% of tested patients were younger than 1 year, 25% were 1 to 4 years, 27% were 5 to 11 years, 25% were 12 to 17 years, and 10% were 18 to 24 years. A total of 53% were male, the mean (SD) age was 8.8 (6.7) years, 11% identified as Hispanic, 15% as Black, 3% as Asian or Pacific Islander, 3% as multiracial, and 59% as White, with 9% not categorized (290 per 10 000 population [range, 155-395 per 10 000 population across health systems]). Most patients tested (82%) were recurring patients (**Table 1**). Overall, 5374 patients (4%) had positive test results for the virus (12 per 10 000 population [range, 7-16 per 10 000 population]). The positivity rate for recurring patients was 4%, while for nonrecurring patients it was 6%. The proportions of new and recurring patients who underwent testing as inpatients, outpatients, or ED patients were similar. The number of tests per patient ranged from 1 to 28, with 87% of patients receiving 1 test, 9% receiving 2 tests, 2% receiving 3 tests, and 2% receiving 4 or more tests. The number of tests performed weekly increased sharply from 80 during the first week of March to 11 519 during the third week of July (eFigure 2 in the Supplement); systems with higher overall testing volume reached their peak rate several weeks before those with lower volume. This increase was associated with adoption of preemptive screening of inpatients and patients scheduled to undergo aerosol-generating procedures, such as general anesthesia.

There was substantial variation in the rates of testing and positivity across PEDSnet (Table 1). Among recent patients, the testing rate varied from 161 to 555 per 10 000 population (mean, 338), or 3% of the patient population tested. The overall rate of positive test results ranged from 1% to 6% (eFigure 3 in the Supplement). The cumulative rate of SARS-CoV-2 infection among recent patients ranged from 6 to 17 per 10 000 population, with an overall rate of 13 per 10 000; the rate was 12 per 10 000 when the population was restricted to recurring patients only.

Characteristics of Patients Tested for SARS-CoV-2

A higher proportion of patients with negative test results were young children, had commercial insurance, and underwent testing as inpatients. In contrast, patients with positive results were more likely to be Black, Hispanic, or Asian; undergo testing in the ED; and have been insured by a public insurance program such as Medicaid at some point (**Table 2**). Of the 5374 patients with positive test results, 359 (7%) met our criteria for severe illness, that is, were admitted with respiratory, cardiovascular, or COVID-19–specific diagnosis codes (the most common case). These patients had higher intensive care unit use (99 [28%]) and slightly increased length of stay; 33 patients (9%) required ventilatory support. Overall, 8 patients with positive test results died (case fatality rate of 0.2%), 6 of whom had complex preexisting comorbidities; 1 patient was inevaluable for chronic illness owing to lack of follow-up prior to 2020.

Association of Chronic Conditions With SARS-CoV-2 Infection

Figure 1 shows associations between preexisting conditions, combined into body systems using the PMCA taxonomy, and testing for or proven infection with SARS-CoV-2. We report these as SRs of the number of patients in each category observed in our current data to that expected based on 2018-2019 data. Except for malignant neoplasms, tested patients were less likely to have all types of chronic conditions. However, several groups were associated with increased positive test results: malignant disorders (SR, 1.54 [95% CI, 1.19-1.93]), cardiac disorders (SR, 1.18 [95% CI, 1.05-1.32]), endocrinologic disorders (SR, 1.52 [95% CI, 1.31-1.75]), gastrointestinal disorders (SR, 2.00 [95% CI, 1.04-1.38]), genetic disorders (SR, 1.19 [95% CI, 1.00-1.40]), hematologic disorders (SR, 1.26 [95% CI, 1.06-1.47]), musculoskeletal disorders (SR, 1.18 [95% CI, 1.07-1.30]), mental health disorders (SR,

Table 2. Characteristics of Patients Tested for SARS-CoV-2 Infection

Characteristic	Patients, No. (%)		
		SARS-CoV-2–positive test result	
	SARS-CoV-2–negative test result (n = 130 420)	Asymptomatic or mild illness (n = 5015)	Severe illness[a] (n = 359)
Age, y			
<1	17 431 (13)	494 (10)	72 (20)
1-4	32 619 (25)	808 (16)	40 (11)
5-11	35 617 (27)	1029 (21)	72 (20)
12-17	32 362 (25)	1521 (30)	117 (33)
18-24	12 391 (10)	1163 (23)	58 (16)
Sex			
Female	61 637 (47)	2527 (50)	172 (48)
Male	68 701 (53)	2485 (50)	187 (52)
Other or unknown	82 (0.06)	3 (0.06)	0
Race/ethnicity			
Hispanic	14 156 (11)	918 (18)	108 (30)
Asian or Pacific Islander	4471 (3)	151 (3)	9 (3)
Black or African American	18 646 (14)	1424 (28)	119 (33)
White	77 540 (60)	1988 (40)	97 (27)
Multiple	3883 (3)	126 (3)	5 (1)
Other or unknown	11 724 (9)	408 (8)	21 (6)
Payer			
Commercial	45 219 (35)	1067 (21)	58 (16)
Public	46 363 (36)	2016 (40)	236 (66)
Other or unknown	38 838 (30)	1932 (39)	65 (18)
Testing location[b]			
Outpatient	72 102 (55)	2793 (56)	22 (6)
Emergency department	18 328 (14)	894 (18)	113 (32)
Inpatient	16 750 (13)	102 (2)	213 (59)
Other or unknown	23 240 (18)	1226 (24)	11 (3)
Visit within 7 d of testing			
Admission	20 967 (16)	130 (3)	307 (86)
Outpatient	109 453 (84)	4885 (97)	52 (15)
Among hospitalized patients			
Length of stay, median (IQR)	2 (1-5)	2 (1-4)	3 (2-7.5)
Admitted to ICU	4843 (4)	22 (0.4)	99 (28)
Mechanical ventilation	907 (1.0)	4 (0.08)	33 (9)
Mortality	281 (0.2)	1 (0.02)	7 (2)
Obese			
Yes	23 553 (18)	944 (19)	132 (37)
No	106 867 (82)	4071 (81)	227 (63)
Chronic condition			
None	72 972 (56)	3132 (63)	172 (48)
1 Body system	25 222 (19)	1040 (21)	52 (15)
≥2 Body systems	32 226 (25)	843 (17)	135 (38)

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Severe COVID-19 required a positive SARS-CoV-2 test result, hospitalization starting no earlier than 7 days before testing, and an inpatient diagnosis of pneumonia, sepsis, or COVID-19. All patients with positive test results who did not meet this definition were classified as having asymptomatic or mild illness.

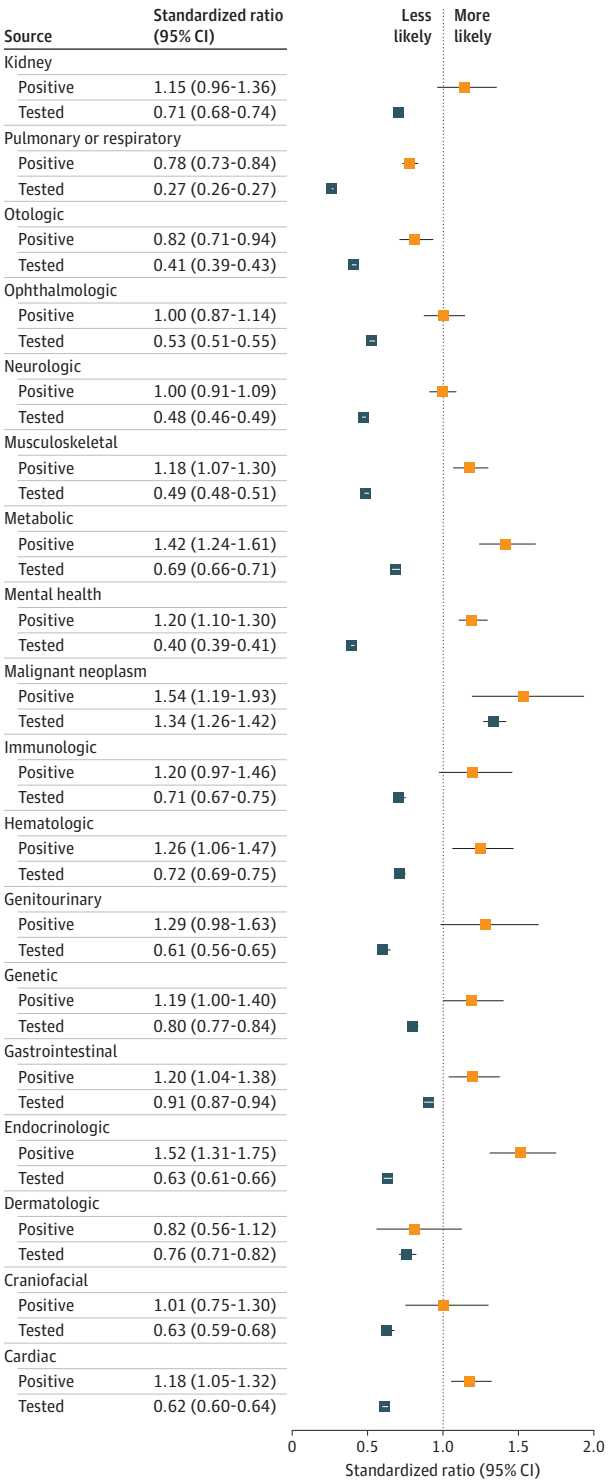
[b] Percentages may not sum to 100%, as a single patient may have tests performed in more than 1 location, and the location for some tests is not known (eg, reference laboratories and community testing sites).

1.20 [95% CI, 1.10-1.30]), and metabolic disorders (SR, 1.42 [95% CI, 1.24-1.61]). Respiratory conditions were not associated with increased positive test results (SR, 0.78 [95% CI, 0.73-0.84]), nor was asthma specifically, which had a significant negative association (SR, 0.86 [95% CI, 0.80-0.91]).

Consistent with the endocrine group, diagnosis of type 2 diabetes was associated with a higher likelihood of undergoing testing (SR, 2.67 [95% CI, 2.46-2.90]) and risk of positive test results (4.10 [95% CI, 2.87-5.55]). We found the same to be true for diagnosis of type 1 diabetes: SR of 2.20 (95% CI, 2.05-2.35) for testing and SR of 3.67 (95% CI, 2.76-4.71) for positive test results.

We also examined several drug categories in the 3 years prior to testing. Children with use of bronchodilators or systemic corticosteroids had evidence of decreased testing and

Figure 1. Standardized Ratios for Chronic Conditions Among Pediatric Patients With Severe Coronavirus Disease 2019 Illness



Ratios were the quotient of observed number of patients with at least 1 condition in body system category and expected number. Expected values were obtained by computing for each chronic condition category the proportion of patients seen from March 1 to May 15 in 2018 and 2019 and having an inclusion diagnosis, and then multiplying these proportions by the total number of patients in the 2020 cohort (testing outcome) or undergoing testing (positive result outcome). A vertical line is placed at 1.0 for reference.

Table 3. Logistic Regression of SARS-CoV-2 Test Use and Positivity for Recurring Patients

Characteristic[a]	Adjusted odds ratio (95% CI)	
	Test performed[b] (n = 218 537)	Positive test result (n = 102 919)
Age, y		
<1	1.54 (1.49-1.59)	1.17 (1.03-1.33)
1-4	1 [Reference]	1 [Reference]
5-11	1.08 (1.05-1.11)	1.25 (1.13-1.38)
12-17	2.20 (2.13-2.26)	1.92 (1.73-2.12)
18-24	3.40 (3.24-3.57)	3.51 (3.11-3.97)
Sex		
Male	1.13(1.11-1.16)	0.97 (0.91-1.04)
Female	1 [Reference]	1 [Reference]
Race/ethnicity		
Hispanic	0.65 (0.63-0.67)	3.75 (3.39-4.15)
Asian or Pacific Islander	0.60 (0.57-0.63)	2.04 (1.69-2.48)
Black or African American	0.70 (0.68-0.72)	2.66 (2.43-2.90)
White	1 [Reference]	1 [Reference]
Payer		
Commercial	1 [Reference]	1 [Reference]
Public	0.95 (0.93-0.97)	1.43 (1.31-1.57)
Testing location	Not applicable	
Outpatient	Not applicable	2.13 (1.86-2.44)
Emergency department	Not applicable	3.16 (2.72-3.67)
Inpatient	Not applicable	1 [Reference]

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Regression models also adjusted for health system and chronic condition body systems as fixed effects. They also included an "other" category for observations with missing data for race/ethnicity, payer, and testing location. The 95% CIs were generated using the profile likelihood method for generalized linear models.

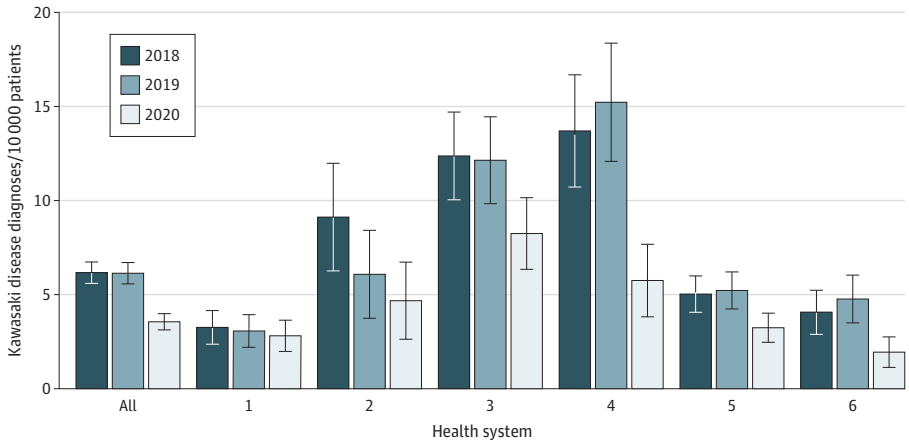
[b] These analyses excluded data from 1 PEDSnet health system because information about recent patients was not available.

test positivity. However, children taking immunomodulators had an increased likelihood of testing (SR, 1.15 [95% CI, 1.08-1.23]) and of positive test results (SR, 2.37 [95% CI, 1.89-2.90]).

Demographic Correlates

To examine demographic factors that may be associated with outcomes of testing, we performed multivariable regression including chronic medical conditions, health system, and location of testing (outpatient, ED, or inpatient) as well as demographic variables. Although Black, Hispanic, and Asian patients were significantly less likely to undergo testing (Black: odds ratio [OR], 0.70 [95% CI, 0.68-0.72]; Hispanic: OR, 0.65 [95% CI, 0.63-0.67]; Asian: OR, 0.60 [95% CI, 0.57-0.63]), these groups had a markedly increased chance of a positive test result (Black: OR, 2.66 [95% CI, 2.43-2.90]; Hispanic: OR, 3.75 [95% CI, 3.39-4.15]; Asian: OR, 2.04 [95% CI, 1.69-2.48]) (**Table 3**). Similarly, patients with a history of public insurance had a slightly lower likelihood of undergoing testing compared with those with only commercial coverage (OR, 0.95 [95% CI, 0.93-0.97]), but the likeli-

Figure 2. Rates of Kawasaki Disease Diagnosis in the PEDSnet Population



The mean number of patients seen between March 1 and May 15 in 2018 and 2019 was used to establish an at-risk denominator. Case counts based on diagnoses assigned during this date interval were taken from PEDSnet data for 2018 and 2019 (for 1 PEDSnet health system, institution-supplied counts were used throughout) and reported separately by each health system (data for Nemours Children's Health System are reported here as a composite total) for 2020 to minimize data latency. Vertical bars indicate 95% CIs.

hood of a positive test result was modestly increSased (OR, 1.43 [95% CI, 1.31-1.57]). Testing performed in the outpatient (OR, 2.13 [1.86-2.44]) or ED setting (OR, 3.16 [95% CI, 2.72-3.67]) was more likely to yield a positive result compared with inpatient settings, as was testing for adolescents and young adults (aged 12-17 years: OR, 1.92 [95% CI, 1.73-2.12]; and age 18-24 years: OR, 3.51 [95% CI, 3.11-3.97]). Grouping all chronic conditions into a single indicator variable yielded a slightly decreased likelihood of positive test results. Significant differences were again observed in testing patterns across health systems.

When investigating severe COVID-19, we first used a single aggregate variable for any progressive condition, with severe illness as the outcome. In this model, Black race/ethnicity (OR, 1.44 [95% CI, 1.02-2.04]), younger than 1 year of age (OR, 2.96 [95% CI, 1.85-4.73]), 12 to 17 years of age (OR, 1.85 [95% CI, 1.22-2.81]), 18 to 24 years of age (OR, 1.63 [95% CI, 1.02-2.61]), history of public insurance (OR, 1.91 [95% CI, 1.27-2.87]), and presence of progressive condition (OR, 5.99 [95% CI, 4.51-7.96]) were significantly associated with severe illness among patients with SARS-CoV-2 infection. In an alternate model using individual body systems, endocrinologic (OR, 2.17 [95% CI, 1.17-4.01]), metabolic (OR, 2.34 [95% CI, 1.27-4.33]), and malignant involvement (OR, 3.38 [95% CI, 1.32-8.63]) were associated with increased risk of severe infection.

Kawasaki Disease

When compared with case counts of KD from March 1 to May 15 in 2018 or 2019, we detected a 40% decrease in 2020 case counts across all health systems (259 vs 430 in 2019 and 433 in 2018). These case counts translate to a decrease in population rates (**Figure 2**), where the denominator is the mean of patients seen in these 2018 and 2019 intervals.

Within the 2020 viral illness cohort, 107 patients with KD (41%) underwent SARS-CoV-2 testing, and 8 of those patients (8%) had positive test results. Six patients in the severe illness cohort received a diagnosis of KD.

Discussion

In response to the SARS-CoV-2 pandemic, we have mobilized PEDSnet to rapidly evaluate the pediatric impact of SARS-CoV-2 infection across the United States. This work reflects the core principles of learning health systems, directly connecting health care delivery to learning about new challenges to child health.[16,29] PEDSnet is able to rapidly establish learning at large scale, to test hypotheses developed in smaller case series, and to detect emerging patterns of disease biology and therapeutic effect across large populations of children, whether as acute or late effects of the virus.

We report here a multicenter study of 135 794 pediatric patients tested for SARS-CoV-2 through September 8, 2020, in which 4% of patients were infected. Overall testing rates are 338 of 10 000 recent patients, and the overall infection rate is 13 of 10 000. Among the 5374 patients with positive test results, the disease burden was low, with 7% of patients meeting a relatively broad definition of severe illness. The case fatality rate was 0.2%.

Among tested patients, risk factors for infection included increasing age, public payer, and Hispanic, Black, or Asian race/ethnicity. The rate of testing for patients from these racial/ethnic groups was below that for White patients. Further work will be needed to evaluate to what extent the higher rate of positive test results reflects different testing strategies across subpopulations, different social determinants of risk (eg, exposure to air pollution, housing density, or likelihood of family continuing to work at in-person essential jobs), or differences in disease biology associated with different rates of symptomatic presentation.

Preexisting chronic disease also appears to be associated with SARS-CoV-2 infection. This finding may result from a greater share of patients with chronic illness seeking testing when symptomatic (ie, higher prior probability of a positive test result) or because certain chronic diseases predispose pediatric patients to infection. The finding that both types 1 and

2 diabetes were associated with positive test results, as was chronic use of immunomodulators, suggests that further work is needed to identify specific patients who may benefit from additional testing and risk reduction.

Our finding that the number of diagnosed cases of KD is reduced in 2020 suggests that patients presenting with MIS-C likely do not receive diagnoses of KD, which should not be used as a proxy for this new entity. Because specific diagnostic coding for MIS-C is not yet available, computable phenotypes incorporating other primary data, such as laboratory test values, vital signs, and medical therapy, will be needed to identify patients with this condition. Although we cannot exclude the possibility that the reduction in KD diagnoses is the result of incomplete ascertainment owing to lower overall health care use during the pandemic, it would be unusual for a syndrome of this severity. The decreased number of cases of KD also raises the possibility that true KD is less prevalent, as measures targeting SARS-CoV-2 prevention also reduce the infection rate of other pathogens.[30]

Limitations

There are several limitations to this study, some inherent in the secondary use of electronic health record data and some arising in the context of the rapidly changing pandemic response. Because our analyses are based on data from clinical care across a large population of patients, our conclusions may be influenced by evolving patterns in clinical decision-making and health care use. We used viral genome detection, given its specificity for SARS-CoV-2 infection. However, this approach excludes patients with COVID-19 when viral testing was not readily available or differentially available across sites and excludes those with asymptomatic or mild cases not reaching current thresholds for testing. We expect this limitation will decrease over time as testing becomes more widely available. In addition, the population tested may reflect shifting of children with more acute illness to pediatric tertiary care centers of the type represented in PEDSnet, which may inflate the observed infection rate. Paradoxically, increasing availability of testing creates a second limitation: because health systems are currently targeting testing to high-risk processes, such as inpatient and surgical care, even when patients may be asymptomatic, there is a potential bias in ascertainment of infection status, and the associations we describe may reflect practice pattern rather than disease biology. We have attempted to address this challenge by examining association with undergoing testing as well as positive test results, but more effective attribution will require broader examination of available data, such as characterization of treatment patterns or other test results more indicative of COVID-19 than underlying illness.

In addition, limitations in the ability of standard terminologies, such as SNOMED-CT and *ICD-10-CM* for diagnoses and RxNorm for medications, to designate COVID-19–specific outcomes complicate identification of emerging phenotypes such as MIS-C. Moreover, significant discordance exists between diagnosis code use and actual illness for complex conditions, such as KD,[31] kidney disease,[32] and leukemia.[33] The breadth of primary data available in networks such as PEDSnet offers opportunities to develop accurate computable phenotypes by integrating multiple factors, but this will require sustained effort. Finally, the recent onset of the pandemic limits our current understanding of rare or longer-term outcomes of coronaviral infection.

Conclusions

Effective response to SARS-CoV-2 will require rapid but robust development of new clinical and public health practices, based on a better understanding of viral and host biology. This knowledge will be critical not only in caring for severely ill patients, but also in constructing sustainable ways to minimize the disease burden caused by SARS-CoV-2. Further work is needed in both traditional medical research paradigms and in rapid and highly collaborative science to provide better care for pediatric patients across the spectrum of health.

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Author Affiliations: Applied Clinical Research Center, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (Bailey, Razzaghi, Burrows, Bruno, Forrest); Department of Biomedical and Health Informatics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (Bailey, Razzaghi, Camacho, Forrest); Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (Bailey, Razzaghi, Burrows, Forrest); Biomedical Research Informatics Center, Nemours Biomedical Research, Alfred I. duPont Hospital for Children, Wilmington, Delaware (Bunnell, Eckrich); Seattle Children's Research Institute, University of Washington, Department of Pediatrics, Seattle (Christakis, Ranade); Editor, *JAMA Pediatrics* (Christakis); Research IT R&D, Abigail Wexner Research Institute, Nationwide Children's Hospital, Columbus, Ohio (Kitzmiller); Department of Research Information Solutions and Innovation, Nationwide Children's Hospital, Columbus, Ohio (Lin); Institute for Informatics, Washington University School of Medicine in St Louis, St Louis, Missouri (Magnusen); Department of Pediatrics, St Louis Children's Hospital, St Louis, Missouri (Newland); Division of Pulmonary Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio (Pajor); Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio (Pajor, Zahner); Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio (Pajor); Department of Pediatrics (Infectious Diseases, Hospital Medicine and Epidemiology), University of Colorado School of Medicine and Children's Hospital Colorado, Aurora (Rao); Research Informatics–Analytics Resource Center, Children's Hospital Colorado, Aurora (Sofela).

Author Contributions: Dr Bailey 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. Dr Bailey and Ms Razzaghi contributed equally to the work reported here.
Concept and design: Bailey, Razzaghi, Christakis, Rao, Sofela, Forrest.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Bailey, Razzaghi, Camacho, Rao, Sofela, Bruno, Forrest.
Critical revision of the manuscript for important intellectual content: Bailey, Razzaghi, Burrows, Bunnell, Christakis, Eckrich, Kitzmiller, Lin, Magnusen, Newland, Pajor, Ranade, Rao, Sofela, Zahner, Bruno.
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