# ARTICLE

## The Impact of COVID-19 on Laboratory Test Utilization at a Pediatric Medical Center

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**Background:** The epidemiology and clinical manifestation of coronavirus disease 2019 (COVID-19) in the pediatric population is different from the adult population. The purpose of this study is to identify effects of the COVID-19 pandemic on laboratory test utilization in a pediatric hospital.

**Methods:** We performed retrospective analysis on test utilization data from Ann & Robert H. Lurie Children's Hospital of Chicago, an academic pediatric medical center. Data between two 100-day periods prior to (prepandemic) and during the pandemic (mid-pandemic) were analyzed to evaluate changes in test volume, lab utilization, and test positivity rate. We also evaluated these metrics based on in- vs outpatient testing and performed modeling to determine what variables significantly impact the test positivity rate.

**Results:** During the pandemic period, there was an expected surge in COVID-19 testing, while over 84% of lab tests studied decreased in ordering volume. The average number of tests ordered per patient was not significantly different during the pandemic for any of the laboratories (adjusted *P* value > 0.05). Thirty-three studied tests showed significant change in positivity rate during the pandemic. Linear modeling revealed test volume and inpatient status as the key variables associated with change in test positivity rate.

**Conclusions:** Excluding severe acute respiratory syndrome coronavirus 2 tests, the COVID-19 pandemic has generally led to decreased test ordering volume and laboratory utilization. However, at this pediatric hospital, the average number of tests performed per patient and test positivity rates were comparable between preand mid-pandemic periods. These results suggest that, overall, clinical test utilization at this site remained consistent during the pandemic.

#### INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has had an enormous impact on the healthcare system. One area that has been no-ticeably impacted is laboratory testing. Since COVID-19 was officially declared a pandemic by the WHO on Wednesday, March 11, 2020,

laboratories have generally reported a drop in non-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related lab test ordering (1–3). This decrease may be partly attributed to lockdown and stay-at-home orders, which started on March 21, 2020 in Illinois, leading to fewer healthcare visits and associated laboratory test orders.

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## **IMPACT STATEMENT**

We analyzed lab test data before and during the coronavirus disease 2019 pandemic to examine how lab utilization, test volume, and positivity rate were affected. We observed (a) overall reduction in test volume and lab utilization during the pandemic; (b) on average, comparable number of tests per patient for each laboratory between pre- and mid-pandemic periods; (c) on average, comparable test positivity rate for each laboratory between pre- and mid-pandemic periods; and (d) higher volume tests and inpatient testing were associated with higher test positivity rate. Our results provide an overview of clinical test utilization changes experienced by a pediatric medical center.

Studies on the impact of COVID-19 on lab test utilization have generally been based on adult hospital data (1, 3) or based on specific tests of interest (2). The epidemiology and clinical manifestation of COVID-19 in the pediatric population appears to be different compared to the adult population for example, COVID-19 appears to be less common and less severe in children (4–6). Therefore, it is not entirely clear whether the effects of COVID-19 on lab test utilization in a pediatric hospital will be similar to those in adult hospitals.

In this study, we took a data-driven approach and analyzed test ordering patterns before and during the COVID-19 pandemic at Ann & Robert H. Lurie Children's Hospital of Chicago, an urban academic pediatric medical tertiary care center with outpatient sites in surrounding communities. Specifically, we wanted to find out whether lab utilization, lab test ordering volumes, and test positivity rates were significantly affected by the pandemic.

We hypothesize that (a) SARS-CoV-2 PCR and antibody test volume increased while most other tests decreased in volume during the pandemic; (b) decrease in lab utilization will be more significant for specialty laboratories, relative to laboratories performing more common, routine tests (e.g., chemistry laboratory); and (c) the mean test positivity rate would be increased during the pandemic for each laboratory.

We suspect the utilization of specialty laboratory may decrease more significantly during the

pandemic, due to possible reasons such as decreased rate of outpatient volume and less reliance on specialty testing results by acute care areas of the hospital during the pandemic (e.g., emergency department, intensive care unit, etc.). We also suspect the mean test positivity rate for each laboratory may increase during the pandemic, due to possible reasons such as more careful lab test selection by healthcare providers in light of decreased resources during the pandemic (e.g., lab staff shortage), as well as difference in patient visits (e.g., fewer patient visits overall or patients requiring more urgent and necessary care are more likely to visit the hospital during the pandemic lockdown).

By answering these questions, we hope to gain insight into changes in laboratory and test utilizations at a pediatric medical center during the COVID-19 pandemic. These results may also facilitate future research on the effect of lab test utilization changes on patient care, elucidating elusive outcome measures often considered in investigations of test over- or underutilization for disease management.

## **MATERIALS AND METHODS**

#### Data

Laboratory test order volume data between 2019 and 2021 were extracted from Epic

Systems and Sunquest integrated laboratory information system. The Institutional Review Board at Ann & Robert H. Lurie Children's Hospital of Chicago determined the use of these data was exempt from Institutional Review Board review (IRB 2022-5294). Data between March 21, 2020 (date when executive stay-at-home order was issued for Illinois) and June 28, 2020 was considered as the mid-pandemic period. The term "midpandemic" used throughout the study should be regarded as during the pandemic, given that the pandemic has lasted >2 years at this point. This timeframe was selected as it was representative of the most significant societal changes due to the initial wave of the pandemic. Data between March 21, 2019 and June 28, 2019 was used as the prepandemic period for comparison. Both of these periods represent a 100-day span, including the end-date. When we use the phrase "lab test," we are referring to the individual orderable lab test that may or may not have multiple components. For example, the comprehensive metabolic panel is considered as a single lab test, although it has multiple components that may be ordered independently (e.g., glucose, sodium, etc.).

Data cleaning and analysis were performed using R, version 3.6.2 (7) in R Studio, version 1.2.1335 (8). R packages used for data clean-up and analysis include tidyverse version 1.3.0 (9), janitor version 2.1.0 (10), and lubridate version 1.7.10 (11).

#### Analysis

*Metric 1: Overall test ordering volume.* We first summarized the total number of times each test was performed during the 100-day periods.

Raw change in test ordering volume was calculated as:

(midpandemic volume – prepandemic volume).

Percentage change in test ordering volume was calculated as:

(midpandemic volume – prepandemic volume) prepandemic volume × 100%.

The raw and percentage changes in test ordering volume were calculated per lab test. To examine lab tests that were used rather regularly before the pandemic—that is, lab tests for which we observed high enough usage rate to make reasonable inference about test utilization changes during the pandemic—we focused on lab tests that were ordered at least 20× during the 100-days prepandemic period. The cutoff of 20 is ad hoc but represents approximately one test per week.

*Metric 2: Daily test order volume.* We also measured daily test ordering volume for each lab test —that is, how many times that particular orderable test was performed on each of the 100 days in the prepandemic period and each of the 100 days in the mid-pandemic period.

 $Mean \ daily \ volume = \frac{[(Test \ volume \ day \ 1) + (day \ 2) + \ldots + (day \ 100)]}{100}$  $= \frac{total \ volume}{100}$ 

We studied the mean daily test volume for each lab for the pre- and mid-pandemic periods. *t*-tests were performed to compare the mean daily ordering volume during pre- vs midpandemic period. The resulting *P* values were adjusted using the Benjamini–Hochberg method with a false discovery rate of 5% to account for multiple testing across the 456 unique lab tests studied.

*Metric 3: Normalized test rate.* Normalized test rate, or the average number of a specific test per patient (i.e., number of unique patients who had that specific type of test performed), was calculated as:

number of tests performed number of patients *Metric 4: Test positivity rate.* Test positivity rate, or simply referred to as positivity rate, was calculated as:

 $\frac{number of 'out of reference interval' or 'positive' test results}{total number of tests} \times 100\%.$ 

In this study, the term "positivity" refers to test results that fall outside of the reference range. For panel tests (e.g., comprehensive metabolic panel), if one of the components tested positive (i.e., abnormal), then the test was considered as positive.

Relative positivity rate was calculated as:

Test positivity rate midpandemic Test positivity rate prepandemic

Fisher's exact test was used to evaluate the proportion of in- and outpatients during the pre- vs mid-pandemic periods. Similar to the rationale described earlier, for analysis involving in- vs outpatient subpopulations, we focused on tests that were ordered at least 10x in inpatients and at least 10x in outpatients during the 100 days pre- and mid-pandemic periods. This is to help focus on lab tests for which we observed sufficiently high usage rates for both in- and outpatients to make reasonable inference about test positivity rate changes during the pandemic. For statistical analysis involving proportions, a sample size of n = 10 per group is a common rule of thumb (12). Genetics and molecular diagnostics lab tests do not have a single, straightforward notion of positive vs negative, or within-range vs out-of-range, results. As such, these tests were not included in the positivity rate analysis.

Wilcoxon signed rank test was used to evaluate whether the overall utilization across test types for each laboratory was significantly different during the mid-pandemic vs prepandemic period (i.e., if the percentage change in test volume for each lab is significantly different from 0). "Send out" lab refers to all tests sent to reference laboratories.

We also fitted a linear regression to evaluate the effect of different variables on test positivity rate. Variables considered were overall test volume, inpatient vs outpatient, pre- vs midpandemic, and interactions between pairs of these variables.

Implementation of all statistical tests and models, as well as P value adjustments, relied on the "stats" package in base R (7). All figures were constructed using the R package ggplot2 version 3.2.1 (13) in RStudio (8).

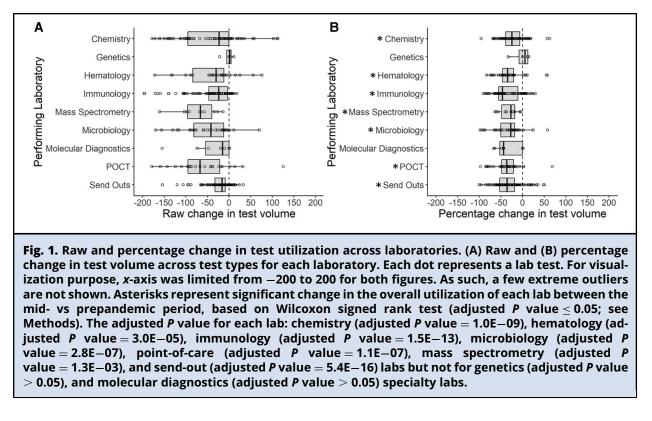
### RESULTS

#### SARS-CoV-2 Test Volume during the Pandemic

As anticipated, we observed high volume of SARS-CoV-2 tests ordered during the midpandemic period (see online Supplemental Table 1) and an overall reduction in lab test volume during the mid-pandemic period, relative to the prepandemic period (Fig. 1).

## Changes in Test Ordering Volume and Laboratory Utilization

The number of inpatients and outpatients during the pre- and mid-pandemic periods is summarized in Supplemental Table 2. During the prepandemic period, 456 tests were ordered at least 20 times. Overall, test ordering volume decreased for most of these tests (approximately 84% of tests; n = 385) during the pandemic period. No change was observed for 6 tests. Test volumes increased for 65 tests. Of these, 6 were statistically significant (adjusted P value < 0.05) based on comparison of the daily average test ordering volume between mid-vs prepandemic. Table 1 shows the 6 lab tests that showed significant increase, and 6 lab tests that showed the most significant decrease. The daily mean test volume for these tests (e.g., average number of methicillin-resistant Staphylococcus aureus [MRSA] screening tests per day) were all significantly different during the mid-pandemic, relative to the prepandemic period (adjusted *P* value < 0.05).



We also analyzed the change in test utilization across laboratories within our department. Figs. 1 and 2 show a general trend of reduction in test volume during the pandemic. The overall utilization pattern across test types (not including SARS-CoV-2 tests) for each laboratory was significantly different (based on Wilcoxon signed rank test; see Methods) between the mid- vs prepandemic period for chemistry (adjusted P value = 1.0E-09), hematology (adjusted P value = 3.0E-05), immunology (adjusted P value = 1.5E-13), microbiology (adjusted *P* value = 2.8E–07), point-of-care (adjusted P value = 1.1E– 07), mass spectrometry (adjusted P value = 1.3E-03), and send-out (adjusted P value = 5.4E-16) labs, but not for genetics (adjusted 1.0E+00) and molecular diagnostics (adjusted P value = 6.7E-02) specialty labs.

In general, for most of the tests studied, we see a significant decrease in volume during the pandemic but also in general, for most these tests we do not see a significant decrease in volume per patient. For each laboratory, Wilcoxon signed rank test was used to evaluate whether the median difference in tests per patient between the pre- and mid-pandemic era was equal to 0. The volume of tests ordered per patient was not significantly different across pre- and mid-pandemic periods for all laboratories (adjusted *P* value > 0.05).

## Changes in Test Positivity Rate during the Pandemic

To further examine the utilization of labs and clinical assays, we also analyzed the positivity rate for the individual tests and compare the positivity rates between the pre- and mid-pandemic periods. Thirty-three out of 456 tests showed a statistically significant change in positivity rate during the pandemic. Table 2 shows the 5 lab tests that showed the most statistically significant increase in test positivity, as well as the 5 lab tests that showed the most statistically significant

Test name	Prepandemic	Mid-pandemic	Raw change	% change	Adjusted <i>P</i> value
Lactate, plasma	166	730	↑ <sup>a</sup> 564	340	1.3E-20
Beta-2-microglobulin, serum	33	135	↑ 102	309	1.6E-08
Methotrexate, plasma	177	288	↑111	63	8.0E-05
BK virus PCR, blood	121	191	↑ 70	58	8.0E-03
Hemoglobin, HemoCue (POC <sup>b</sup> )	182	307	↑ 125	69	4.0E-02
D-dimer, plasma	44	69	↑ 25	57	4.5E-02
MRSA <sup>c</sup> screen, PCR, nasal	2242	45	↓ <sup>d</sup> 2197	-98	3.6E-47
Culture, bacteria, blood	4165	2659	↓ 1506	-36	6.0E-36
Streptococcus group A DNA	976	336	↓ 640	-66	1.7E-29
Urinalysis, POC	6742	4292	↓ 2450	-36	7.3E-28
Sodium, plasma or serum	2012	658	↓ 1354	-67	4.2E-24
Basic metabolic panel	8602	5438	↓ 3164	-37	9.0E-23
↑ = increase by. Point-of-care testing Methicillin-resistant <i>Staphylococcus aureus</i> ↓ = decrease by.	i.				

decrease in test positivity during the midpandemic period (adjusted P value < 0.05).

#### Identifying Factors that Influence the Test Positivity Rate

We also fitted a linear regression to evaluate the effect of different variables on test positivity rate. Variables considered were overall test volume, inpatient vs outpatient, pre- vs mid-pandemic period, and interactions between pairs of these variables.

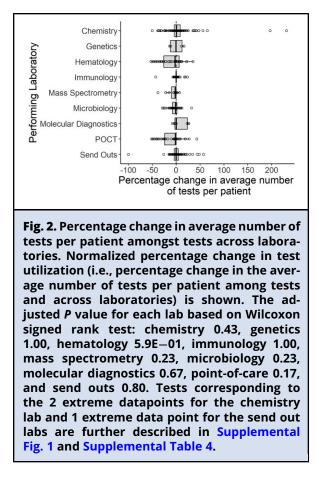
We found a significant relationship between inpatient status and test positivity rate, as well as between test ordering volume and test positivity rate. Specifically, for every 1 unit increase in test order volume, there is an associated 0.01% increase in test positivity rate (P value = 1.3E-05) (Supplemental Table 3).

All else being equal (i.e., when all other variables are held constant), the positivity rate for inpatient testing is, on average, 9% greater than the positivity rate compared to outpatient testing (i.e., positivity rate tends to be higher among the inpatients; P value = 4.8E–03) (Supplemental Table 3). However, this relationship is not significantly different between the pre- vs mid-pandemic data (P value = 0.72) (Supplemental Table 3), when all other variables are held constant. Furthermore, the relationship between test volume and positivity rate was not significantly different when we compare pre- vs mid-pandemic data (P value = 0.31) (Supplemental Table 3).

#### Comparison of Positivity Rate of Tests Between In- and Outpatient Testing, during the Mid- and Prepandemic Periods

We constructed density plots to visualize the distribution of positivity rate across all lab tests and observed higher test positivity rates for inpatient testing (Fig. 3; dotted curve). However, the distribution patterns between the mid- vs prepandemic period appear to be comparable (Fig. 3).

As shown in the boxplots in Fig. 4, which demonstrate aggregation of tests and their positivity rates for each lab, we observed that the distributions of positivity rates were similar between the pre- and



mid-pandemic periods. Moreover, in either time period, the average positivity rate appears to be higher for inpatient testing, relative to outpatient testing.

#### DISCUSSION

The COVID-19 pandemic has had a massive impact on the healthcare system, including laboratory test utilization. Due to factors such as lockdown and stay-at-home-orders, numerous medical centers have reported a general decrease in lab test ordering volumes (1–3).

The epidemiology and clinical manifestation of COVID-19 is undoubtedly different in the pediatric population (4–6). However, it is not entirely clear whether its impact on lab test utilization in a

pediatric hospital setting will be comparable to those reported based on adult hospital data (1,2). Not surprisingly, we also observed a surge of SARS-CoV-2 test volume during the pandemic.

To make better inferences about the test utilization changes during the pandemic, in this study we focus on tests that were used reasonably regularly during the prepandemic period (i.e.,  $\geq$ 20 times during the 100-day prepandemic period). Over 84% of these laboratory tests showed a decrease in test ordering volume. Notably, the MRSA PCR screening tests showed a dramatic decrease in test volume during the mid-pandemic period (approximately 98% decrease; from n = 2242 prepandemic to n = 45 mid-pandemic). This change likely reflects the change in testing policy, as well as the possible effects that social distancing and universal masking have on respiratory infection incidence during the pandemic. Additionally, prior to the pandemic, as mandated by the state of Illinois, MRSA screening is performed to reduce transmission within each hospital (14,15). MRSA-positive patients obtain contact isolation status by the Infections Control and Prevention group at Lurie Children's during the hospitalization and require healthcare providers to use dedicated gowns, gloves, and other personal protective equipment. During the pandemic, as recommended by the Illinois Department of Health, active surveillance for MRSA was suspended, and MRSA screening was discontinued for intensive care unit admission and transfers to preserve personal protective equipment (16).

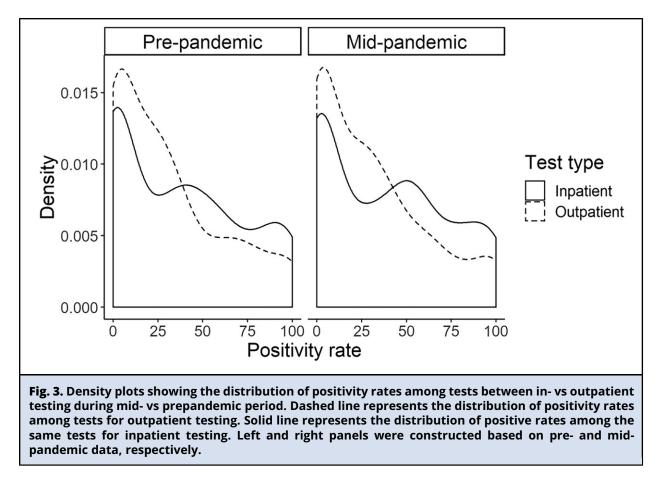
A number of tests showed significant increase in test volume during the mid-pandemic period. For example, lactate was a test that showed significant increase in test volume during the pandemic period. However, this was likely, at least in part, due to discontinuing the use of the i-STAT blood gas cartridge with lactate, which is used in i-STAT point-of-care testing, due to recall from Abbott during the pandemic period. This, in turn, may have led to the increased usage of the non-point-of-care

Test name	Prepandemic		Mid-pandemic		Relative positivity rate	
	Total tests, n	Positive tests, n	Total tests, n	Positive tests, n	(mid-pandemic relative to prepandemic)	Adjusted <i>P</i> value
Glucose, whole blood, POC <sup>a</sup>	8601	4711	7952	4935	1.13	3.2E-19
Comprehensive metabolic panel	9645	8683	7058	6586	1.04	3.5E-12
Renal function panel	8562	8162	8242	8000	1.02	3.0E-07
GGT, <sup>b</sup> plasma or serum	1437	670	1111	646	1.25	4.8E-07
Sodium, plasma or serum	2012	819	658	351	1.31	9.4E-07
Respiratory panel, PCR	1197	564	681	114	0.36	2.3E-39
Calprotectin, feces	198	94	150	1	0.01	3.8E-25
lonized calcium, blood or serum	5947	3228	5409	2497	0.85	7.0E-16
Troponin I, plasma	516	272	377	121	0.61	5.7E-08
Reticulocytes, blood	2474	1395	1799	882	0.87	8.4E-05

## Table 2. Tests that showed substantial and significant change in test positivity rate between mid- and

lactate testing available in-house. Another example of a test that significantly increased in test volume during the pandemic is beta-2-microglobulin. Serum beta-2-microglobulin test may be used for stratification and staging of conditions including multiple myeloma and Waldenstrom macroglobulinemia, as well as other lymphoproliferative disorders. It can also be used in helping to differentiate glomerular and tubular renal disease. The exact clinical cause of this observation is beyond the scope of the current study. Longitudinal plots of plasma lactate and serum beta-2-microglobulin daily test volume over time during the pre- and mid-pandemic periods are also provided in Supplemental Figs. 2 and 3.

We also analyzed the utilization of different tests performed across laboratories (Fig. 1) to gain insight into potential changes that occurred during the pandemic period. There was an overall trend of negative percentage change in test ordering volume for non-SARS-CoV-2 tests during the pandemic. This change on average was statically significant for chemistry, hematology, immunology, microbiology, point-of-care, mass spectrometry, and send-out labs, but not for genetics and molecular diagnostics specialty labs (based on Wilcoxon signed rank test with adjusted P value cutoff of 0.05). A large number of tests performed in the chemistry lab experienced a large raw decrease in test ordering volume (Fig. 1, A), but these changes translate to a less notable percentage decrease (approximately 22%) on average compared to the specialty labs (approximately 4%-40%) (Fig. 1, B). This is not entirely surprising given that chemistry lab tests are among those most frequently ordered. As well, this may suggest less reliance on specialty testing results by acute care areas of the hospital during the pandemic. As a point of reference, Durant et al. reported an overall decrease in lab test volume by approximately

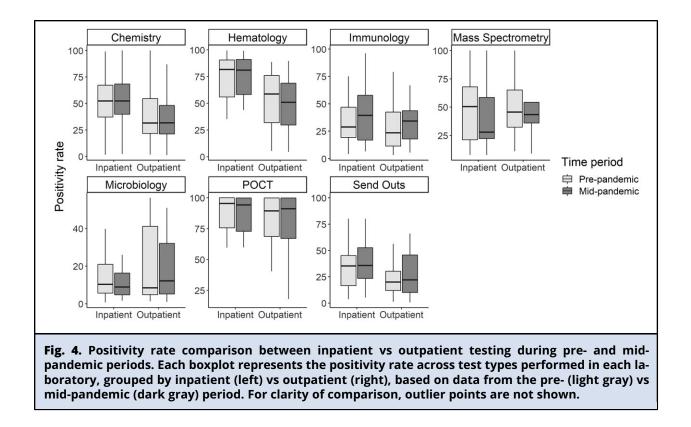


15% in an adult hospital setting during the COVID-19 pandemic (1).

We were also interested in how the normalized test rate (i.e., average number of tests per patient) varied among tests across laboratories. A similar metric has been described in a number of test utilization studies (17–23). We found that the number of tests per patient across test types, on average, was not significantly different for all labs. This may suggest that the test ordering pattern by the care providers remained consistent during the pandemic period (e.g., physicians are not more or less selective in terms of when to order a specific test).

Traditionally, to evaluate lab test utilization, metrics such as those described earlier (e.g., test ordering volumes and ordering rates) are commonly analyzed (24–26). Other metrics such as test positivity rate have also been described as a useful benchmark for examining lab test utilization (27– 30). While research involving this metric is still evolving, low positivity rate has been suggested as a possible signal for test overutilization, while high positivity rate has been suggested as a possible signal for test underutilization (30).

To further examine the utilization of labs and clinical assays, we also analyzed the positivity rate for the individual tests and compared the positivity rates between the pre- and mid-pandemic periods. The relative positivity rate can also be thought of as being analogous to relative risk (i.e., risk ratio). Thirty-three out of 456 tests showed a statistically significant change in positivity rate during the pandemic based on Fisher's exact test (adjusted *P* value  $\leq$  0.05). Interestingly, the fecal calprotectin test showed a significant decrease in relative positivity rate. It is not clear at the time of this study why



the rate of positive test was significantly lower during the pandemic. Overall, however, most tests did not exhibit statistically significant change in positivity rate during the pandemic.

Results from linear regression modeling showed that there was a significant relationship between inpatient status and test positivity rate, as well as between test volume and test positivity rate. Interestingly, the relationship between test volume and positivity rate was not significantly different between the pre-vs mid-pandemic period. This observation was further supported by the density plots of positivity rate among tests between in-vs outpatients during the mid- vs prepandemic period (Fig. 3). The density plots showed a higher positivity rate among inpatient testing but a comparable pattern between pre-vs mid-pandemic periods. A similar pattern was also observed when we examined the positivity rate among tests across labs, as well as between in- vs outpatient and pre- vs mid-pandemic data (Fig. 4).

Together, results from this study highlight the dramatic increase in SARS-CoV-2 test ordering volume and decrease in ordering volume for most tests across labs during the pandemic. However, the average number of tests performed per patient, as well as the positivity rate among non–SARS-CoV-2 tests, was generally comparable during the pre- vs mid-pandemic period. Collectively, these results also provide evidence that despite the test volume changes, clinical test utilization remained largely consistent during the pandemic, as the test positivity rate was significantly associated with the test volume and whether the test is performed for in- or outpatient, rather than when the test was performed (i.e., pre- vs mid-pandemic period).

It is difficult to say how these results may be applied to future pandemics, but we believe that the importance and role for laboratory data analytics that was realized during the COVID-19 pandemic will be sustained. Improved access to laboratory test order data with skills and infrastructure enabling data analytics and visualization should be applied in future pandemics and even today in routine laboratory operational decision-making. Accurate and timely data on test order volumes and relevant factors may be used to guide workforce staffing and process improvement decisions, for example.

There are several caveats and limitations to this study. First, this is a retrospective, observational study conducted at a single institution. Although we have controlled for the date range (e.g., same start and end date on different years), which was relatively larger than several published studies, there are other factors that may have impacted the results. For example, changes to institutional practices and composition of patient population may have occurred during the pandemic period that were unrelated to the pandemic and could confound the results. Although this is an observational study, so no causal claim can be made, our observations are consistent with other published reports on the impacts of COVID-19. This leads us to believe that the conclusions of our study may represent some effects of the COVID-19 pandemic on test utilization.

Additionally, a small change in number of positive tests may translate to large changes in the test positivity rate for tests with low ordering volume. The relative positivity rate, based on the equation described (see Methods), cannot be calculated when the prepandemic test positivity rate is 0, or if the test positivity rate happens to be 0 for both the pre- and mid-pandemic data. However, since both the pre- and the mid-pandemic data were evaluated in the same manner and over 74% of tests studied in the positivity rate analysis had  $\geq$ 1 positive test results during the pre- and/or mid-pandemic period, we believe this limitation is not likely to significantly change the conclusions drawn from the study.

The other major limitation of the study is that test positivity rate was used as an indicator of clinical test utilization between the mid- vs prepandemic period. As described earlier, this metric is still relatively new and warrants future research. Finally, this study did not evaluate patient outcome and focused on test and laboratory utilization instead. Repeat testing pattern is also beyond the scope of this study and may warrant future studies. All factors that may have impacted ordering provider behaviors, due to the pandemic or otherwise, were not investigated.

#### SUPPLEMENTAL MATERIAL

Supplemental material is available at *The Journal* of *Applied Laboratory Medicine* online.

**Nonstandard Abbreviations:** COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; MRSA = methicillin-resistant *Staphylococcus aureus*.

**Author Contributions:** All authors confirmed they have contributed to the intellectual content of this paper and have met the following 4 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; (c) final approval of the published article; and (d) agreement to be accountable for all aspects of the article thus ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.

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