

Title: Mounting a Regional Response to the COVID-19 Pandemic: Another Reason to “Keep”
Your Lab

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ABSTRACT

Context: Declining reimbursement shifts hospital laboratories from system assets to cost centers. This has resulted in increased outsourcing of laboratory services which can jeopardize a hospital systems ability to respond to a health care crisis.

Objectives: To demonstrate investment in a core laboratory serving an academic medical center equipped a regional health system to respond to the pandemic.

Design: COVID-19 diagnostic testing data was analyzed. Volumes were evaluated by result date (3/16/2020 – 5/6/2020) and the average of received to verified turn-around-time (TAT) was calculated and compared for in-house and send-out testing, and different in-house testing methodologies.

Results: Daily viral diagnostic testing capacity increased by greater than 3000 % (from 21 tests per day to 658 tests per day). Total viral diagnostic testing resulted by the core lab increased by 128 times over 22 days of test method validation and 826 times over the analysis period while average turn-around-time per day for send-out testing increased from 3.7 days to 21 days. Decreased overall average TAT was observed at the core laboratory (0.45 days) verses send-out testing (7.63 days) ($P < .001$).

Conclusions: Investment in a core laboratory provided the health system with the necessary expertise and resources to mount a robust response to the pandemic. Local access to testing allowed rapid triage of patients and conservation of scarce personal protective equipment. In addition, the core laboratory was able to support regional health departments and several hospitals outside of the system.

INTRODUCTION

In the current healthcare environment with decreased reimbursements¹ and increased focus on the provision of value-based medical services, many hospitals struggle to keep their doors open and provide local access to care². Outsourcing of non-clinical support work in hospitals has been on the rise for years in the U.S.³ and has now spread to clinical services with laboratory, pharmacy and radiology commonly targeted⁴. Continued downward pressure on reimbursements has shifted laboratories from system assets to cost centers⁵. This increases the burden on hospital based laboratories to provide value to their organizations and invites chief financial officers (CFO's) to outsource some or all of their laboratory services⁴. Others have discussed the importance of regional "sentinel" laboratories in the event of a pandemic or health crisis⁶ as well as the presence of a strong system-wide integrated laboratory service line to maintain laboratory operations in times of crisis⁷. The outsourcing of laboratory services has also been described, most recently as it relates to academic medical centers⁸. Sentinel clinical labs are defined as laboratories that are certified to provide high complexity microbiology testing as part of the laboratory response network to support the public health laboratory system. To the author's knowledge, no one has discussed what the potential effects of outsourcing leading to a lack of sentinel laboratory services would have during a health care crisis such as the current pandemic.

As one of the nation's leading academic medical centers with an expanding hospital network, the regional health system described here consists of six hospitals and covers a 95 mile radius. This includes the flagship hospital at the medical center which is an 886 bed facility that provides high level tertiary care to the region. The remaining hospitals in the enterprise range from a 261 bed inner-city hospital offering some tertiary services to a 15 bed acute care community hospital in a rural setting.

System leadership made the decision to invest in their laboratory infrastructure by building a large core laboratory to support the regional health system clinical enterprise. The core laboratory was completed in June of 2019 and serves the clinical enterprise and surrounding region, including 48 nursing homes. It is a 157,400 square foot state of the art facility providing clinical pathology services with implementation of large scale automation in chemistry, hematology and microbiology. The investment was made with the goals of increased efficiency and standardization while enabling local access to high quality specialized testing⁹.

The Coronavirus Disease 2019 (COVID-19) is the cause of an ongoing global pandemic that was first reported as a disease outbreak in early January 2020¹⁰. The first case diagnosed in the United States presented on January 19, 2020¹¹, and declaration of a public health emergency of international concern was issued on January 30, 2020 by the World Health Organization. The first case in the geographic area covered by the clinical enterprise was diagnosed on March 11, 2020. It quickly became obvious that the virus was spreading rapidly enough to overwhelm the testing capabilities of our state and local health departments speaking to the need for access to prompt diagnostic testing¹². Shortages of personal protective equipment, testing supplies, and semi-private patient rooms made it necessary to cohort patients into different groups based on risk assessment and testing status. This further compounded the demand for access to rapid and accurate diagnostic testing¹³. In coordination with the state department of health, work was begun immediately on the development of Emergency Use Authorized (EUA) approved testing to bring in-house at the core laboratory.

DESIGN

Over the course of 22 days from March 11, 2020 to April 2, 2020 the core laboratory was able to validate and implement testing using 5 different assays (Figure 1). The State Health Department, with permission from the United States Food and Drug Administration (FDA),

designated certain laboratories throughout the state to implement the Centers for Disease Control and Prevention (CDC) EUA 2019-Novel Coronavirus (2019-nCoV) real-time polymerase chain reaction (RT-PCR) diagnostic test. With assistance from the state, the core lab was able to validate and perform this diagnostic test within 5 days of the sentinel case in the region. The protocol utilized three different CDC approved RNA extraction methods and the reverse transcribed cDNA was amplified in the Thermo Fischer Scientific Applied Biosystems 7500 Fast Dx Real-Time PCR instrument. This was followed by validation of the DiaSorin Molecular Simplexa COVID-19 Direct real-time RT-PCR assay performed on the LIAISON MDX instrument for the in vitro qualitative detection of nucleic acid nine days later. Within less than 2 weeks the lab was able to implement high throughput automated testing using the Roche cobas SARS-CoV-2 on the Roche Cobas 8800 System giving us the capability to drastically increase our volumes (to the extent that reagent and supplies were available). These methods were followed by validation of SARS- COV-2 on the Cepheid GeneXpert Xpress platform and BioGx SARs-CoV-2 on the Becton Dickinson BD MAX System.

Average daily turn-around-times (TAT's) were calculated from the time the specimen was received in the core laboratory to the time the final result was verified. The TAT's were then combined and averaged for all in-house testing platforms and for all send-out testing sites respectively. All testing sent out to reference laboratories added 24 hours to the average received to verified TAT. Reference and health department laboratories received to verified TAT was averaged to maintain anonymity between laboratories for the purposes of publication. A *P* - value was calculated by performing a student's T-test. Volumes of verified results by date as well as TAT's for both send-out and in-house testing were graphed to illustrate differences (Figure 2). Average TAT's for the five platforms used at the core lab were also calculated and graphed for illustration (Figure 3).

RESULTS

While implementing multiple testing platforms at the core laboratory, diagnostic testing was sent out to 5 different reference laboratories, as well as the state and local health department labs to keep up with demand. Analysis of testing data demonstrated that reference and health department laboratories average daily TAT's were increasing from a low of 3.7 days to a high of 21 days as they were being overwhelmed with testing demand during this time period. Taking into account the additional 24 hours for transport to the various reference labs the TAT range was 2.7 days to 20 days. In contrast the core lab was able to increase its daily testing capacity by greater than 3000 % with resulted viral diagnostic testing volumes per day going from a low of 21 tests per day to a high of 658 tests per day over the analysis period. Total viral diagnostic testing resulted by the core lab increased by 128 times (from 21 tests resulted to 2694 tests resulted) over the 22 days it took to validate five different platforms and 826 times (from 21 tests resulted to 17359 tests resulted) over the analysis period with a decrease in daily average received to verified TAT's from a high of 1.8 days to a low of 0.14 days (Figure 2). This met the initial demands for testing in our system and by April 2, 2020 when all five different assays were running at the core laboratory the need for reference testing had been eliminated. Statistical analysis of overall average turn-around-time (TAT) data demonstrated a statistically significant decrease in average TAT when testing was performed at the core laboratory as compared to being sent out to a reference or health department lab (0.45 days vs. 7.63 days) ($P < .001$) (Figure 2).

Review of the overall average TAT results by testing platform demonstrated that all testing methodologies performed at the core laboratory had less than an average 24 hour TAT from received to verified with daily average received to verified TAT's ranging from 0.22 days for the Cepheid GeneXpert Xpress platform to 0.97 days for the CDC 2019-Novel Coronavirus (2019-nCoV) real-time polymerase chain reaction (RT-PCR) diagnostic panel.

DISCUSSION

Investment in the Central Laboratory provided the physical space and instrumentation to bring multiple different diagnostic assays into operation to use in parallel. The ability to do this was critical as supply chain for different reagents was unpredictable at best. The presence of a large core laboratory at an academic based health system also enabled attraction and retention of specialized academic faculty who were able to navigate the intricacies of testing on multiple different platforms and provide the highest quality results for our patients. The core laboratory microbiology division is run by a seasoned Ph.D. as well as an M.D. who trained at a leading academic institution. They are assisted by additional postdoctoral students with expertise in microbiology and laboratory science as well as pathology residents and specialized technical staff. This combination of expertise facilitated the validation process and ensured development of assays with appropriate targets and detection rates. Our faculty experts participated in and led a large portion of the daily emergency command center calls for the system. They interacted with clinical leadership and infection control on a daily basis to develop testing protocols and triage strategies that conserved both testing supplies and personal protective equipment to the maximum extent possible. In addition they played a critical role in educating providers about the different assays employed and why they were chosen. This was imperative given the combination of tremendous political pressure and medical necessity with the large number of tests that were issued EUA status by the FDA over a short period of time. Real-time access to faculty experts who were able to interact with clinical leadership to develop testing protocols and provide consultation was invaluable¹⁴. As others^{8,15} have described, outsourcing clinical laboratory services can lead to loss of clinical faculty and the expert knowledge necessary to implement more complex diagnostic testing.

The pandemic strained the global supply chain which led to supply shortages and testing backlogs. This forced laboratories to compete with each other for supplies which led to more

downstream breaks in the supply chain¹⁶. In addition, worldwide demand for personal protective equipment (PPE) led to disruption in that supply chain¹⁷ and shortages that made rapid access to testing even more critical. The ability to utilize multiple testing platforms helped us to mitigate the impacts from shortages of testing reagents and supplies, and facilitated the rapid triage of patients. All emergency room and inpatients were screened for COVID-19 symptoms. Symptomatic patients underwent diagnostic testing. Testing was sorted in microbiology receiving and run using the fastest available method (Figure 3). All employees in the regional health system were screened daily for symptoms. Other symptomatic diagnostic testing, including essential services and healthcare workers were performed on the first available testing platform after the prioritization outlined above. At the time of this analysis asymptomatic testing was not being performed due to shortages in testing supplies, including swabs, media, reagents and other consumables. The practices outlined above aided in patient flows throughout the hospitals in the system by decreasing potential exposures of non-covid patients and staff, and conserving scarce personal protective equipment¹⁸. Access to rapid and accurate diagnostic testing for the system allowed the cohorting of both high and low risk patients and helped to conserve PPE. Many hospitals and geographic areas in the U.S. were not so lucky¹⁹.

CONCLUSIONS

It is the experience of the author that testing capability and access to reagents and testing supplies was directly related to the size of the health system and laboratory infrastructure with smaller non-integrated health systems experiencing much more difficulty in accessing the necessary equipment and supplies. In our experience small to moderate sized hospitals in our geographic area outside of a larger health system had almost no choice but to rely on a remote reference laboratory for testing, with many outside of our system reaching out for help. There are many advantages to having a relationship with reference laboratories, such as the provision of esoteric and low volume testing and the ability to augment testing capacity in times of need.

However, it is our observation that the ability to mount a local response to a health care crisis may not be as easy to manage if divestment in the laboratory has gone too far. Investment in a large core laboratory for our system provided us with the space, instrumentation, and expertise that allowed our clinical enterprise to mount a robust response to the pandemic and care for the regional health system patient population. In addition, we were able to provide support to four additional hospital systems outside of our immediate area who had no or limited access to testing and augment testing for local health departments who could not keep up with demand. There is significant likelihood of future pandemics or natural disasters that will require mounting a coordinated response from health systems. The investment in a laboratory that can perform high complexity testing and rapidly increase capacity in response to demand not only serves the main academic medical center, but supports the regional health system and public health of the region at large⁶. The well-established goals to provide high quality, efficient care with turn-around times that can maximally support clinical operations²⁰ are demonstrated here. This would not have been possible if our institution had not invested in their lab.

Figure Legends

Figure 1: Timeline of diagnostic testing implementation at the core laboratory.

* Centers for Disease Control and Prevention (CDC) Emergency Use Authorization (EUA) laboratory developed test

▫ DiaSorin Molecular Simplexa COVID-19 Direct Kit

◇ Roche cobas SARS-CoV-2 Test

● Cepheid Xpert Xpress SARS-COV-2

† Becton Dickinson BioGX SARS-CoV-2

Figure 2: Combined graph with average turn-around-time (TAT) and result volumes for in-house and send-out testing.

Figure 3: Received to verified turn-around-time (TAT) by in-house platform (days).

[Roche cobas SARS-CoV-2 Test; Cepheid Xpert Xpress SARS-COV-2; Becton Dickinson (BD) BioGX SARS-CoV-2; DiaSorin Molecular Simplexa COVID-19 Direct Kit; Centers for Disease Control and Prevention (CDC) Emergency Use Authorization (EUA) laboratory developed test]

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