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Case Report

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Optimizing COVID-19 testing capabilities and clinical management using pathology informatics

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ABSTRACT

Coronavirus disease 2019, first reported in China in late 2019, has quickly spread across the world. The outbreak was declared a pandemic by the World Health Organization on March 11, 2020. Here, we describe our initial efforts at the University of Florida Health for processing of large numbers of tests, streamlining data collection, and reporting data for optimizing testing capabilities and superior clinical management. Specifically, we discuss clinical and pathology informatics workflows and informatics instruments which we designed to meet the unique challenges of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing. We hope these results benefit institutions preparing to implement SARS-CoV-2 testing.

Key words: COVID-19, medical informatics, pathology, diagnostic tests, clinical laboratory information systems

INTRODUCTION

The Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread rapidly in the United States.[1] All states have reported cases, and community spread is present in a number of states, where the epidemic spread exponentially. By March 29, 2020, the state of Florida had carried out 45 045 tests with a 9.2% positive test rate.[2] In the county of Alachua alone, 1252 tests had been performed by then. As the disease was in its exponential phase of spread, we anticipated that the daily number of tests performed in the state of Florida would continue to increase for the foreseeable future.

In early March 2020, the University of Florida Health (UF Health) did not have on-site capacity for performing SARS-CoV-2 testing, and tests were sent to the Florida Department of Health (DOH). These tests were also concurrently sent to the UF Emerging Pathology Institute (EPI) through a research protocol and informed consent. If these rapid tests were positive, the samples were then sent to the DOH for priority testing. As commercial laboratories developed capacity for SARS-CoV-2 testing, UF Health also started sending tests from outpatient clinics to these labs, but the increase in demand for SARS-CoV-2 testing caused a significant increase in the turnaround time from commercial labs to more than 5 days.[3] To meet the clinical need, we developed on-site testing at UF Health.

To complement on-site testing at UF Health and to deal with the challenge of large anticipated volumes for testing, we developed informatics workflows and technologies to address bottlenecks in testing, reporting, and triaging procedures. We also developed a real-time tracking dashboard for specimen testing within our hospital system. Several teams working in infectious disease, pathology, and

LAY SUMMARY

The rapid spread of the Coronavirus disease 2019 pandemic left many nations unprepared for developing testing capacity. The United States was no expectation of this. As pathology laboratories across the nation started building severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) capabilities, the high demand for testing volumes resulted in a shortage of test reagents. In this article, we describe our experience in using informatics instruments for ordering and triaging of SARS-CoV-2 testing to meet turnaround times for patient care.

informatics worked together to build these informatics solutions. A timeline of major external events (grey)[4,5] and internal events (red) at our institution are presented in Figure 1.

ASSESSING PATHOLOGY INFORMATICS NEEDS ACROSS UF HEALTH

By March, a large volume of COVID-19 cases was expected throughout the state of Florida.[3] The sudden surge in demand for SARS-CoV-2 testing created a global shortage of all testing reagents and platforms.[6] If testing platforms were diversified, then even if one part of the supply chain was blocked, testing could be diverted to other parts and continue uninterrupted. To accomplish this, we set up a coordinated effort between UF Health Pathology Laboratories, UF Health Shands Jacksonville laboratories, UF Health Villages Hospital, UF Health Leesburg Hospital, and UF Health Shands Gainesville laboratories. Representatives from these four organizations met twice daily by zoom meetings to discuss the logistics of coordinated testing. We discussed how testing platforms could be diversified at each of the four organizations and identified our individual as well as joint testing capacities.

For choosing testing platforms, we evaluated the following factors: automated analyzer type (random access vs batch analyzers), required staffing licensure, workload, turnaround time, throughput, availability of supplies and cost, availability of equipment in our facilities, impact on existing testing needs, and specimen collection kits. Preexisting testing platforms within the UF Health system and the availability of testing reagents were the two primary factors that influenced our platform choice. As a group, we decided to first build our SARS-CoV-2 testing capabilities using SARS-CoV-2 Integrated DNA Technologies (IDT) kits on the QuantStudio platform, followed by EliTech's InGenius and Cepheid's GeneXpert platforms.

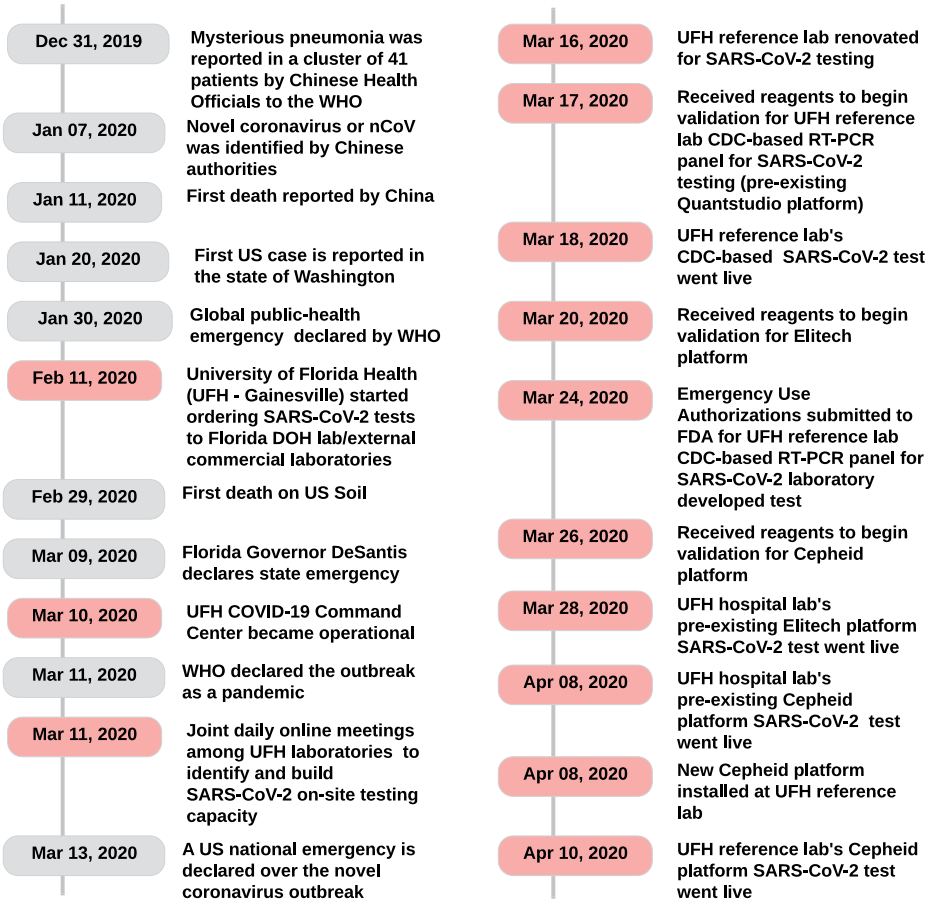

Figure 1. Timeline major external (grey) and internal (red) events of COVID-19 test development.

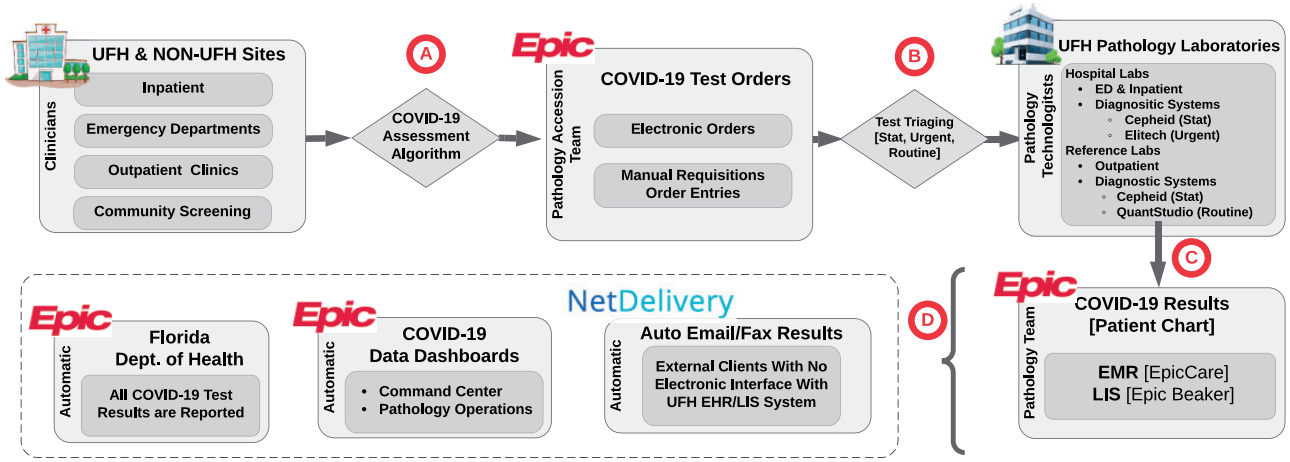

Figure 2. Overall workflow summary of SARS-CoV-2 testing.

For each testing platform, we determined sensitivity and specificity prior to the initiation of testing using control samples. All platforms were fully functional by May 2020. We are now in the final stages of implementing Hologic's Panther platform.

We developed optimal informatics solutions for implementing SARS-CoV-2 testing at UF Health. Specifically, we focused on (1) optimizing electronic health record (EHR)/laboratory information system (LIS) implementation for ordering, capturing, and interfacing results coming from different SARS-CoV-2 testing platforms and clinical facilities, (2) reporting results back to caregivers, patients, researchers, state/national agencies, (3) reducing duplication of work across the UF Health by harmonizing data elements and workflows, (4) rapid implementation of testing, and (5) ongoing improvement of informatics workflows. Another key outcome of our discussion was the development of informatics solutions in anticipation of future workloads, reducing the time needed for validation. We parallelized tasks that significantly expedited the implementation process. An overview of our SARS-CoV-2 testing implementation workflow is depicted in Figure 2.

A COVID-19 INFORMATICS INSTRUMENT FOR ENSURING COMPLIANCE WITH CDC GUIDELINES

Given the large number of anticipated tests, it was critical that tests were ordered with strict adherence to Centers for Disease Control and Prevention (CDC) criteria for recognizing patients at high risk for SARS-CoV-2 infection. Minimizing test wastage was particularly critical as the test capacity across the nation was not sufficient for handling large expected numbers of patients as well as challenges in acquiring reagents to perform the assays. To implement CDC guidelines, our clinicians first defined multiple COVID-19 assessment algorithms for the following patient groups: Health Care Workers, Newborns, Adults, Adults Immunocompromised, Pediatrics, and Pediatrics Immunocompromised. We initially lacked a suitable informatics instrument that could assess the extent to which CDC guidelines for hospital assessment and decision-making in the context of COVID-19 were being implemented before ordering tests (Figure 2, Step A). We therefore developed an informatics instrument (Figure 3) which ensured compliance with the assessment algorithm developed by our clinicians.

The instrument consisted of primarily two questions which allow rapid assessment. First, the clinician is asked about the patient type: emergency department, inpatient, and outpatient (Q1 in Figure 3). Next, the menu provides a series of reasons for testing which are different depending on whether the patient is an emergency department (ED) patient, inpatient, or outpatient (Q2 in Figure 3). The granularity of these questions and options ensures CDC compliance and meets our health care facility COVID-19 testing needs. Only if these two questions are answered in a compliant manner, can SARS-CoV-2 test orders be placed. The remaining questions are for tracking purposes and are not related to triage.

TRIAGING INSTRUMENT FOR COVID-19 TESTING

Because a large number of patients with COVID-19 exposure were anticipated, we next developed an instrument for triaging requests (Figure 2, Step B). The triaging was based on the responses to "Patient type" and "Reason for testing" questions listed in Figure 3 above. These responses were next mapped into specific turnaround times, testing platform, and testing laboratory. The instrument is shown in Table 1.

Some test orders are less time sensitive while others may require faster results due to the acuity of the patient's medical condition. We therefore divided our tests into three categories based on the turnaround times—Stat (<2 h), Urgent (∼<7 h), and Routine (∼24–36 h). An advantage of this categorization was that laboratory staff were already familiar with this terminology and their associated turnaround times expectation. These three categories were matched with testing platforms that can meet the turnaround times—Cepheid's GeneXpert (Stat), EliTech's InGenius (Urgent), and Thermofisher's QuantStudio (Routine). As of May 08, 2020, we have performed 3848 tests on UFH hospital's Elitech, 1403 tests on UFH hospital's Cepheid, 4989 tests on UFH pathology lab's QuantStudio, and 1216 tests on UFH pathology lab's Cepheid platform.

The choice of a particular laboratory was made based on proximity and specimen logistics. COVID-19 tests ordered from emergency and inpatient departments were directed to the hospital laboratory. Orders from outpatient clinics and community screening were directed to our reference laboratory. All testing of patients was performed internally at UF Health as capacity permitted.

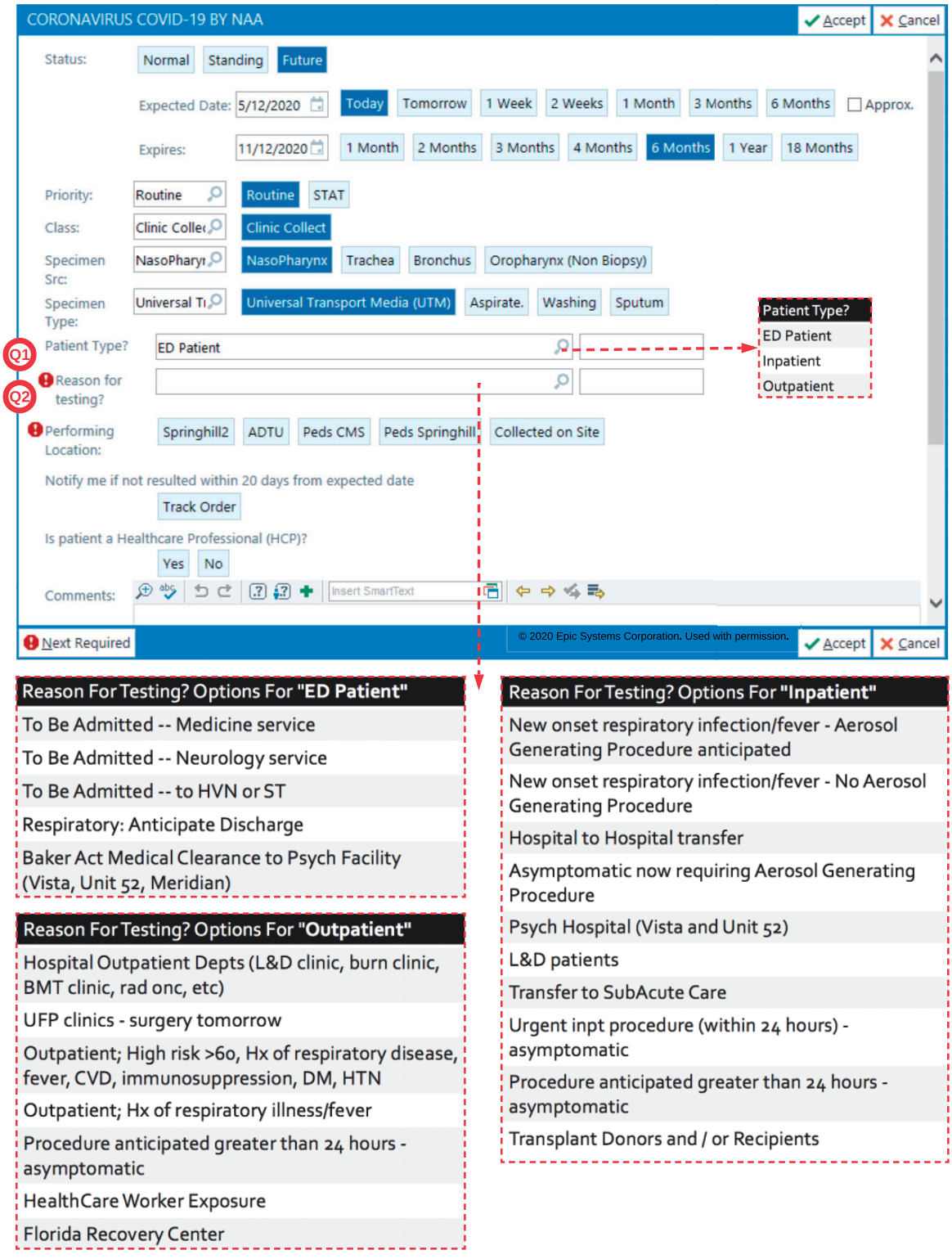

Figure 3. Epic EHR informatics instrument for SARS-CoV-2 test ordering.

If instruments or reagents were not available at a particular laboratory, technologists were allowed to change the laboratory and instrument to minimize turnaround times. When capacity was exceeded, low priority tests were triaged to different UF Health Laboratories or an external commercial laboratory. Currently, each lab testing site reports total reagent usage on a daily basis. We also monitor inventory daily and accordingly shift test reagents to sites with greater needs on a daily basis.

The backend of our Epic EHR system was configured to automatically route to appropriate laboratory and testing platforms (as

Table 1. Triaging instrument for COVID-19 tests at pathology laboratories in the UF Health system

		Hospital lab		Reference lab	
	Reason for testing	Cepheid	Elitech	Cepheid	Quant-Studio
ED patient	To be admitted—medicine service		Urgent[b]		
	To be admitted—neurology service		Urgent		
	To be admitted—to HVN or ST	Stat[a]			
	Respiratory: anticipate discharge		Urgent		
	Baker Act Medical Clearance to Psych Facility (Vista, Unit 52, Meridian)		Urgent		
Inpatient	New onset respiratory infection/fever—aerosol generating procedure anticipated		Urgent		
	New onset respiratory infection/fever—no aerosol generating procedure		Urgent		
	Direct admit/same day post op admit—asymptomatic	Stat			
	Hospital to hospital transfer—surgical	Stat			
	Hospital to hospital transfer—medicine		Urgent		
	Asymptomatic now requiring aerosol generating procedure		Urgent		
	Psych Hospital (Vista and Unit 52)		Urgent		
	L&D patients		Urgent		
	Transfer to subacute care—symptomatic		Urgent		
	Urgent input procedure (within 24 h)—asymptomatic	Stat			
	Procedure anticipated greater than 24 h—asymptomatic		Urgent		
	Transplant donors and/or recipients	Stat			
Outpatient	Hospital Outpatient Depts (L&D clinic, burn clinic, BMT clinic, rad onc, etc.)		Urgent		
	UFP clinics—surgery tomorrow			Stat	
	Outpatient; high risk >60, Hex of respiratory disease, fever, CVD, immunosuppression, DM, HTN			Stat	
	Outpatient; Hex of respiratory illness/fever			Stat	
	Procedure anticipated greater than 24 h—asymptomatic		Urgent		
	HealthCare Worker Exposure				Routine[c]
	Florida Recovery Center				Routine

[a]Stat: ~2 h turn around time.
[b]Urgent: ~7 h turn around time.
[c]Routine: ~24–36 h turn around time.

listed in Table 1) based on the responses to the questions in the order form (Figure 3). We also configured our Epic system to interface with external commercial laboratories.

INFORMATICS SUPPORT FOR ON-SITE COVID-19 TESTING

At UF Health, clinical laboratory testing instruments are typically interfaced with Epic Beaker through the Data Innovations (DI) instrument manager (Data Innovations, South Burlington, VT). The DI instrument manager is connected to the NextGen Connect Integration Engine (Formerly MirthConnect), which pushes the results into Beaker. Unfortunately, not all instruments have DI compatible software drivers. In these cases, a laboratory technologist is required to enter results manually into Beaker LIS. One such instrument without native DI connectivity support is QuantStudio 12 Flex instrument (Thermo Fisher) that we used for implementing a CDC-based RT-PCR Panel for detection of the SARS-CoV-2. Without a feature for auto interfacing results, manual entry of results is a labor-intensive process and a workflow bottleneck.[7] More importantly, this process is prone to manual entry errors.[7] We developed a custom middleware solution for automatically interfacing the results from the QuantStudio into Epic Beaker. Our overall approach is shown in Figure 4, and the middleware solution is in Figure 4, Step B.

As shown in Figure 4, Step A, as soon as SARS-CoV-2 testing is ordered and a specimen is collected, it appears on the pathology lab worklist in Epic Beaker LIS. We configured our electronic interface software Epic Bridges and NextGen Connect for simultaneously sending an order HL7 message to a network folder. Once the specimen has been analyzed for SARS-CoV-2 on the testing platform, the result is stored in an excel sheet on the instrument. The RT-qPCR assay for a SARS-CoV-2 positive sample generates positive results for two conserved targeted regions of the SARS-CoV-2 genome (N1, N2—see Figure 4, Step B).[8] All samples are also tested for human RNAse P (RNP) genes as amplification control to assess specimen quality (RP column in Figure 4, Step B). Our middleware solution automatically matches the output files to the HL7 incoming order messages and generates an outgoing HL7 result message (Figure 4, Step C). The middleware functions in two steps. First, it translates target regions and RP values for each specimen into a result value (ie Detected, Not Detected, Indeterminate, and Invalid). Second, for each specimen, it detects the correct incoming HL7 order message file based on the specimen ID, and inserts a result value into the HL7 message generating outgoing HL7 message. This outgoing HL7 message is placed on the network drive and automatically picked up by NextGen Connect and pushed into Beaker.

TEST REPORTING AND MONITORING

Monitoring and reporting every SARS-CoV-2 test and its result is crucial for clinical management of the disease and for taking necessary precautionary steps towards minimizing community transmission of the disease. The UF Health command center and leadership team required real-time updates on SARS-CoV-2 testing. Such updates inform policy decisions, clinical care, isolation precautions, personal protective equipment use, and future projections of testing needs and

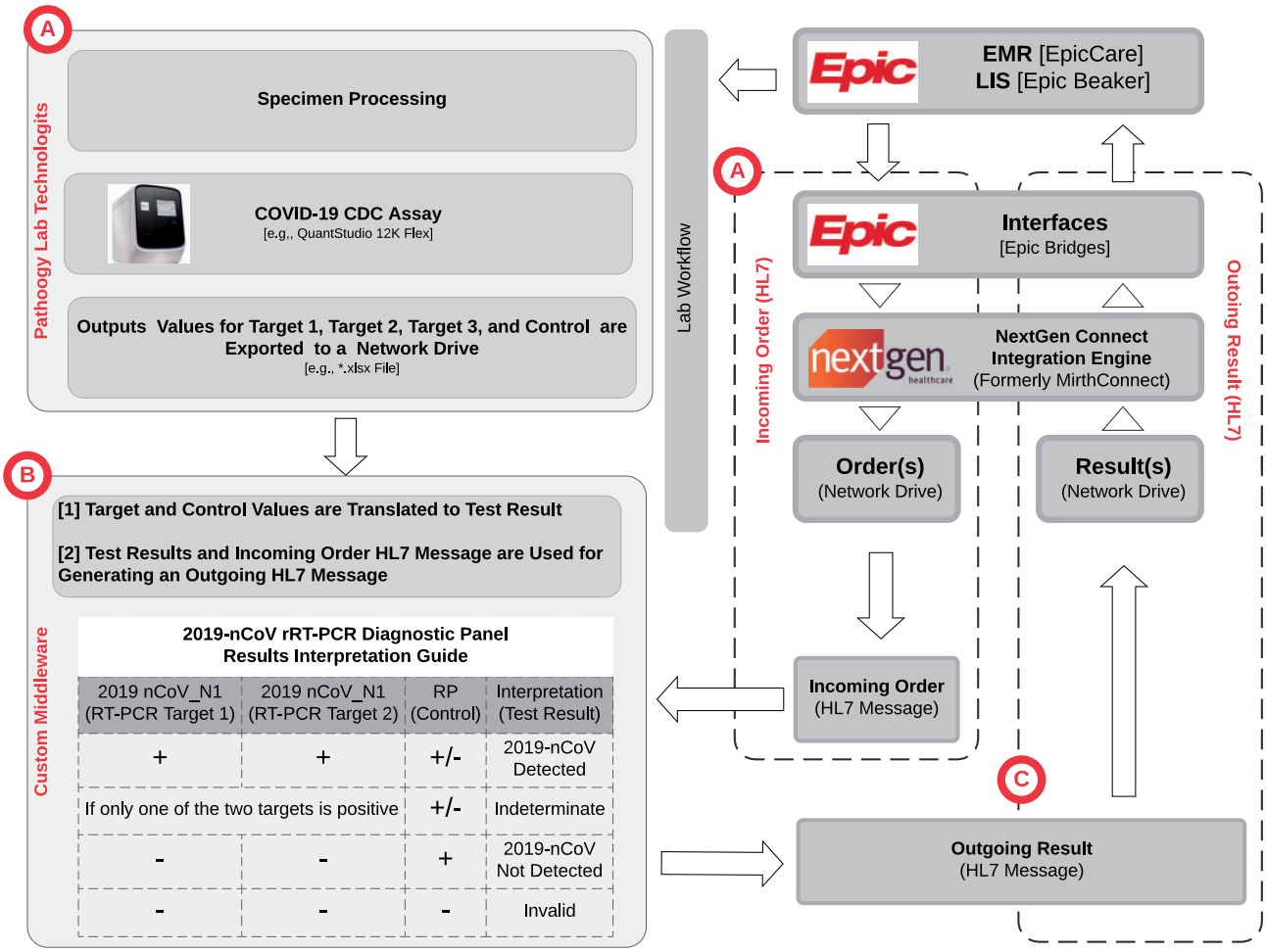

Figure 4. SARS-CoV-2 test custom middleware work flow for testing platforms that are not automatically interfaced with LIS/EHR.

patient care requirements. Our UF Health enterprise reporting team built a dashboard which automatically displays these real-time data (Figure 2, Step D). Specifically, the dashboard reports on the number of tests performed daily, the number of positive SARS-CoV-2 tests, the number of negative tests, and the number of indeterminate tests.

Pathology laboratory operations have additional data monitoring needs (Figure 2, Step D). A separate pathology dashboard was created specifically to meet pathology laboratory needs. These dashboards report on the volume of tests by hour/day/overall, health care facilities locations, and types (inpatient/outpatient/community screening) across different laboratories and testing platforms in the UF Health system. The dashboards are primarily used for allocating resources and scheduling batch testing in an optimal fashion.

Test orders with direct results interface with the UF Health system. The test results directly go to the patient chart. In contrast, results for test orders from external/nonintegrated healthcare submitters are emailed as pdf reports via NetDelivery (https://interbitdata.com/) (Figure 2, Step D). Additionally, positive test results are communicated by phone.

Timely reporting of test results to public health information systems is crucial for effectively managing pandemic outbreaks.[9] We submitted extrapolated data from the laboratory report electronically in compliance with required reporting to the DOH.[10] All test results including positive and negative tests were submitted. The reporting was accomplished with an existing Electronic Laboratory Reporting feed from UF Health to Florida DOH (Figure 2, Step D). The following data are reported: Resulting Lab, Result Time, Procedure Code, Procedure Name, Test, LOINC, Patient Name, MRN, Status, Accession #, Ordering Date.

CONCLUSION

In this article, we reported the development of informatics workflows at UF to assess the extent to which CDC guidelines for hospital assessment and decision making are being implemented before ordering tests. We demonstrated how we streamlined sample triage, testing, and distribution in the event that maximum testing capacity and efficiency is reached or exceeded. Our informatics instruments minimize errors in data collection, reporting to the clinician on call, analysis, and reporting these findings to patients for clinical management. We hope that our approach proves useful to other healthcare entities seeking to optimally respond to the enormous volumes of COVID-19 patients anticipated in the near future.

AUTHORS' CONTRIBUTIONS

All authors participated in the conceptualization and design of the COVID-19 testing protocol and workflows described in this manuscript. S.C., S.M., K.N., and M.D. lead the informatics implementation efforts. S.C., S.F., and T.L. took the lead in writing the

manuscript with all authors input. All authors provided critical feedback and approved the final version.

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CONFLICT OF INTEREST STATEMENT

None declared.

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