424. Sensitivity Results for the Abbott m2000 PCR Assay of SARS-CoV-2 at a Denver, Colorado Medical Center

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Background: The Abbott RealTime SARS-CoV-2 assay (Abbott Laboratories, Chicago, Illinois) is an RT-PCR test for qualitative detection of SARS-CoV-2 nucleic acid in NP and OP specimens performed on the Abbott m2000 System. Currently, no published data exists on the performance characteristics of the assay.

Methods: Denver Health Medical Center (DHMC) is a 550-bed hospital that is Denver County's safety net institution. The Department of Pathology and Laboratory Services at DHMC provides testing for both inpatient and outpatient populations. In March 2020, we validated the Abbott RealTime SARS-CoV-2 assay. Beginning March 19, inpatients and outpatients with SARS-CoV-2 symptoms were tested. On April 22, universal testing began on admitted patients, regardless of symptoms, and on May 2, testing began on asymptomatic outpatients prior to time-sensitive procedures. We evaluated the sensitivity and negative predictive value (NPV) for tests done March 19 through June 16 using a surrogate method. False negative (FN) results: patients with an initial negative test then a positive test within 7 or 14 days. True negative (TN) results: patients with two initial consecutive negative tests within 7 or 14 days. True positive (TP) results: patients with an initial positive test.

Results: There were 16,152 tests done for 13,673 patients. Test results are shown in Table 1. Sensitivity for 7 and 14 days was 99.1% and 97.6%, respectively. The NPV for 7 and 14 days was 94.7% and 91.4%, respectively.

Table 1

Test Result	7-Day Timeframe	14-Day Timeframe
	n	n
False negative	19	53
True negative	342	563
True positive	2196	2196

Conclusion: There are limitations to our analysis. First, our assumption of no false positives may be incorrect. Although PCR assays are known to have a low false positive rate, the rate likely is not zero, but in the absence of a true gold standard comparator, we could not calculate test specificity. Second, testing asymptomatic patients may artificially inflate the TN results and the NPV. Third, results depend on the quality of specimen collection, preservation, transport, and handling. We believe accounting for repeat testing in a short timeframe lends credibility to the sensitivity and NPV results. Without published gold standard data on SARS-CoV-2 testing, infection can be reliably ruled both in and out using this assay. Providers can confidently use the results to make clinical and infection prevention management decisions.

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425. The Utility of Paired Upper and Lower COVID-19 Sampling in Patients with Artificial Airways

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Session: P-13. COVID-19 Diagnostics

Background: The Centers for Disease Control and Prevention (CDC) recommends upper respiratory tract (URT) polymerase chain reaction (PCR) testing as the initial diagnostic test for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Lower respiratory tract (LRT) testing for patients requiring mechanical ventilation is also recommended. The goal of this study was to evaluate concordance between paired URT and LRT specimens in children undergoing pre-admission/procedure screening or diagnostic testing. We hypothesized that < 10% of paired tests would have discordant results.

Methods: Single center cross-sectional study including children with artificial airways who had paired URT and LRT SARS-CoV-2 PCR testing between 4/1/2020 and 6/8/2020. URT specimens included nasopharyngeal (NP) swabs and aspirates. LRT specimens included tracheal aspirates and bronchoalveolar lavages. URT and LRT specimens were classified as paired if the two specimens were collected within 24 hours. Artificial airways included tracheostomies and endotracheal tubes. Tests were classified as diagnostic versus screening based on the indication selected in the order.

Results: 102 paired specimens were obtained during the study period. Fifty-nine were performed for screening and 43 were performed for diagnosis of suspected SARS-CoV-2. Overall, 94 specimens (92%) were concordant, including 89 negative from both sources and 5 positive from both sources. Eight specimens (8%) were discordant, all of which were positive from the URT and negative from the LRT (Figure 1). Among patients undergoing screening, 3 of 4 positive tests were discordant and among symptomatic patients, 5 of 9 positive tests were discordant. There were no instances of a positive LRT specimen with a negative URT specimen.

Figure 1. Performance of upper and lower respiratory tract SARS-CoV-2 PCR testing in children with artificial airways

A. All paired URT and LRT samples (total N = 102 pairs)

Lower Respiratory Tract		Upper Respiratory Tract: Positive	Upper Respiratory Tract: Negative
	Positive	5	0
	Negative	8	89

B. Paired URT and LRT samples obtained pre-procedure/admission (screening) (N= 59 pairs)

Lower Respiratory Tract		Upper Respiratory Tract: Positive	Upper Respiratory Tract: Negative
	Positive	1	0
	Negative	3	55

C. Paired URT and LRT samples obtained for suspected SARS-CoV-2 (diagnostic) (N = 43 pairs)

Lower Respiratory Tract		Upper Respiratory Tract: Positive	Upper Respiratory Tract: Negative
	Positive	4	0
	Negative	5	34

Conclusion: Overall, most paired samples from the URT and LRT yielded concordant results with no pairs positive from the LRT and negative from the URT. These data support the CDC recommendation that URT specimens are the preferred initial SARS-CoV-2 test, while LRT specimens should be collected only from mechanically ventilated with suspected SARS-CoV-2.

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426. Use of Real Time IP-10 Measurements to Identify and Monitor the Dysregulated Immune Response in COVID-19 Patients

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Session: P-13. COVID-19 Diagnostics

Background: It is estimated that up to 10% of SARS-CoV-2 patients progress from early and pulmonary stages to the most severe stage of illness, which manifests as an extra-pulmonary systemic hyperinflammatory syndrome. Interferon gamma-induced protein 10 (IP-10) is an inflammatory marker that plays a role in the dysregulated host response of COVID-19 infected patients. Clinical monitoring of IP-10 has been restricted in the absence of a rapid diagnostic test. MeMed Key™ is a novel platform recently cleared to provide IP-10 measurements in 15 minutes. We hypothesized that providing physicians with real time IP-10 measurements would support detection and continuous monitoring of patients with a dysregulated immune response and potentially allow personalized immunomodulation to improve patient outcome.

IP-10 levels reflect corticosteroid treatment

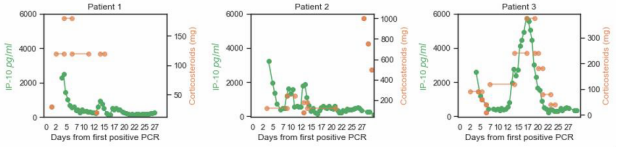

Figure 1 legend: These 3 patients had IP-10 >1000 *pg/ml* at the start of the study. Right Y axis shows the normalized levels of Corticosteroids administered (Solumedrol and Hydrocortisone). Left Y axis shows the levels of IP-10 measured by MeMed Key™. X axis shows days from first positive SARS-CoV-2 PCR. Patient 1 survived, Patients 2 and 3 died.

Methods: From 7th April 2020 to 10th May 2020 blood was routinely collected serially from 52 SARS-CoV-2 positive patients hospitalized at a COVID-19 dedicated medical center. A clinical decision support protocol was in place focused on managing viral response, oxygenation and inflammatory state (NCT04389645).

Results: The median age of the 52 patients was 69, 69% were male, 21% were ventilated, 4 died, 2 due to non-COVID-19 related complications. The most common comorbidities were Diabetes 40% and Hypertension 46%. IP-10 >1000 *pg/ml* correlated with ICU admission ($p < 0.05$) and increased COVID-19 severity score ($p < 0.01$). 19 of the 52 patients had IP-10 >1000 *pg/ml*, of these 12 were treated with corticosteroids.

Monitoring IP-10 within the clinical decision support protocol assisted with personalized corticosteroid regimens with the aim of reducing IP-10 < 1000 *pg/ml*. The 10 patients that survived exhibited IP-10 levels >1000 *pg/ml* for 2.6 days on average. In contrast, the 2 patients that died of COVID-19 related complications displayed an average of 7.5 days with IP-10 >1000 *pg/ml* (p< 0.05).

Conclusion: Providing physicians with real time measurements of IP-10 in COVID-19 patients proved a useful tool as part of the clinical decision support protocol. Timely identification, monitoring and personalized treatment of COVID-19 patients exhibiting a dysregulated immune response may aid in improving patient outcome. Further studies are warranted.

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427. Variation in SARS-CoV-2 molecular diagnostic test performance in symptomatic versus asymptomatic populations

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Session: P-13. COVID-19 Diagnostics

Background: Growing recognition of the importance of asymptomatic and pre-symptomatic transmission for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has led to a substantial expansion of testing from symptomatic to asymptomatic patients, and particularly those with risk factors for infection. Viral burden in asymptomatic individuals can differ from symptomatic patients, which can impact test performance. We therefore evaluated the impact of expanded testing indications upon the sensitivity and specificity of molecular diagnostic assays for SARS-CoV-2.

Methods: We performed a retrospective review of laboratory results from 5,122 emergency room patients and inpatients tested for SARS-CoV-2 between 05/03/2020 and 06/13/2020 using the Hologic Panther Fusion and the Cepheid Xpert assays at the Brigham & Women's Hospital in Boston, MA. Descriptive analyses were performed for trends in testing volume, rates of positivity and cycle thresholds (Cts) over time based on symptom status. We calculated the proportion of new diagnoses made on a patient's first test as an indirect measure of sensitivity. We calculated the proportion of first tests that are positive with a Ct value < 35 as an indirect measure of specificity.

Results: The overall rate of positivity over the study period was 8.7% (599/7,510 tests; 440/4,795 people) and declined by 1.8% (95% CI -2.2% - -1.4%, P< 0.0001) each week. Relative to tests in symptomatic people, the asymptomatic population had a higher mean Ct value (35.1 vs 32.3; P < 0.0001). Ct values increased by 0.7 (95% CI -0.1 - +1.4, P=0.07) and 0.8 (95% CI +0.3 - +1.4; p=0.01), sensitivity declined by 4% (95% CI -9% - +1%, P=0.08) and 12% (95% CI -20% - -5%, P-0.01) and specificity declined by 8% (95% CI -3% to 20%; P=0.13) and 9% (95% CI 7% - 11%; P=0.0002), over the time period of the study for asymptomatic and symptomatic patients, respectively.

Figure 1: Trends in Ct values by symptoms

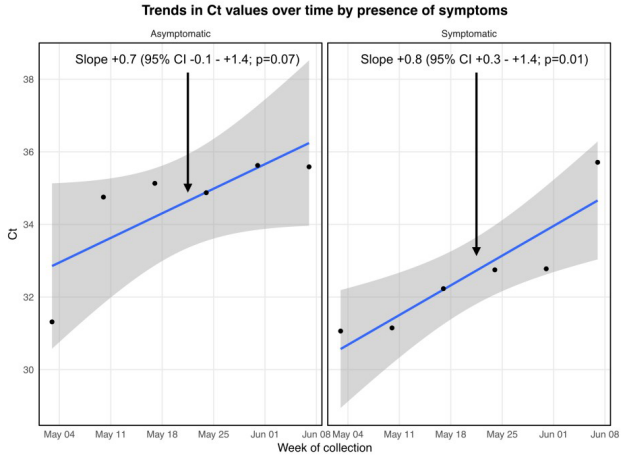


Figure 2: Trends in diagnosis by first versus second test by symptoms

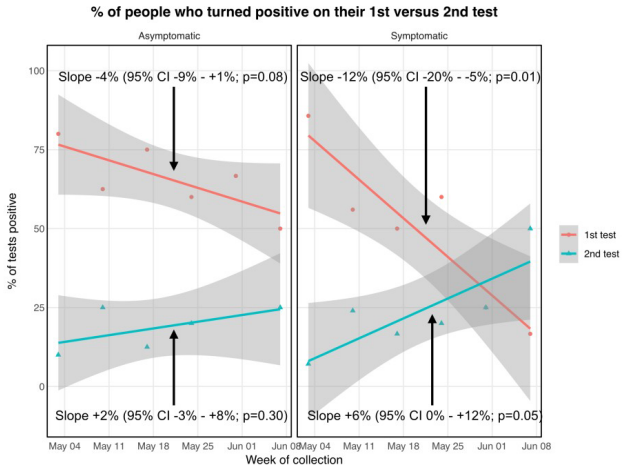
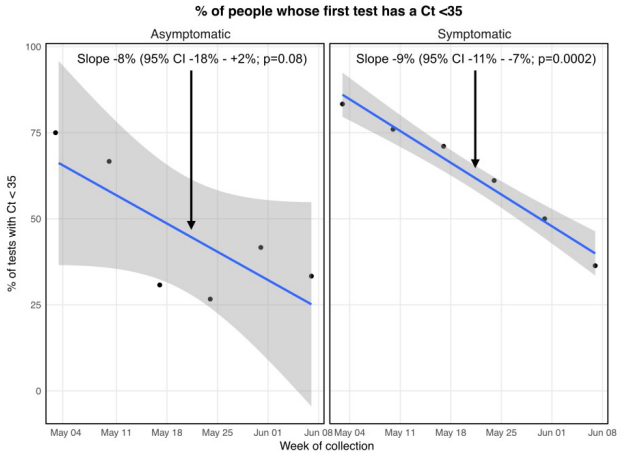


Figure 3: Trends in proportion of people with their first test having Ct < 35 by symptoms



Conclusion: We show that the proportion of patients with low SARS-CoV-2 viral loads has increased as testing has expanded to the asymptomatic population and as transmission wanes in the community. This negatively impacts the performance of molecular assays by increasing the risk of false negatives and the detection of non-viable virus. Decision algorithms based on molecular assay results may need re-evaluation in light of these dynamics.

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428. Very High Clinical Likelihood (VHCL) Of COVID-19 Infection: Peering Beyond A Negative Nasopharyngeal Swab

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Session: P-13. COVID-19 Diagnostics

Background: Diagnosis of COVID-19 relies upon RT-PCR assays for SARS-CoV-2 from a nasopharyngeal swab (NPS). However, results depend upon duration of illness at the time of testing and operator performance. False negatives occur 10–30% of the time. In our center we formulated & applied a clinical prediction tool for diagnosis of COVID-19 infection. Patients who satisfied criteria were designated as having COVID-19 regardless of NPS results. Herein, we describe the set of patients who fulfilled full and strict clinical criteria (VHCL) **(Table 1)** and had at least 2 negative NPSs on hospital admission.