Conclusion.  Of the markers studied, both d-dimer and CRP were considered useful by most respondents. LDH and ferritin were used less frequently and were not considered as useful in guiding medical decision making. Discontinuation of standing daily LDH and ferritin orders is believed to have potential to result in cost savings to the health care system with no adverse patient outcomes.

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366. Abbott BinaxNOW Rapid Antigen Test Performance in Detecting SARS-CoV-2 Infections in a COVID-19 Outbreak Among Horse Racer Track Workers
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Session: P-15. COVID-19 Diagnostics

Background. Rapid antigen tests (e.g., Abbott’s BinaxNOW) are cheaper and faster than nucleic acid amplification tests (e.g., real-time reverse transcription polymerase chain reaction [RT-PCR]) for SARS-CoV-2 infection, with variable reported sensitivity. A horse race track in California experienced a COVID-19 outbreak among staff in April 2021, so BinaxNOW was used to supplement RT-PCR. Utility of BinaxNOW in detecting SARS-CoV-2 infection in the workplace outbreak was assessed.

Methods. Between November 25–December 22, 2020, anterior nasal swabs were collected from race track staff for six rounds of paired BinaxNOW and RT-PCR tests. BinaxNOW tests were interpreted according to manufacturer instructions. RT-PCR was performed at the state public health lab using the Thermofisher TaqPath COVID-19 Combo Kit. Staff with positive results on either test were isolated and removed from subsequent testing. Viral cultures were attempted on specimens with cycle threshold (Ct) < 30.

Results. Overall, 769 paired results from 342 staff were analyzed. Most were of Hispanic ethnicity (62.0%) and ages ranged from 18 to 92 years (median 52). BinaxNOW performance compared to RT-PCR was 95% CI as follows: positive percent agreement (PPA) 43.3% (34.6–52.4%); negative percent agreement (NPA) 100% (99.4–100%); positive predictive value (PPV) 100% (93.5–100%); negative predictive value 89.9% (87.5–92.0%). Among 127 RT-PCR-positive specimens, those with paired BinaxNOW-positive results (n = 55) had a lower mean Ct value than those with paired BinaxNOW-negative results (n = 72) (17.8 vs. 28.5) (p < 0.001). In dual positive pairs, median time from specimen collected to RT-PCR result reported was 4 days (range 1-6), compared to the 15-minute BinaxNOW reporting time. Of 100 Cts < 30 specimens, 51 resulted in positive virus isolation, 45 (88.2%) of which were BinaxNOW-positive.

Conclusion. High PPA and PPV support immediate isolation of BinaxNOW-positive individuals, while low PPA supports confirmatory testing following BinaxNOW-negative results. BinaxNOW performed better in paired specimens with lower Ct, value and positive viral cultures, which could suggest that among RT-PCR-positive staff, those that are BinaxNOW-negative may be less likely to contain infectious virus than those that are BinaxNOW-positive.

Disclosures. David Seftel, M.D., M.D., M.B.A.; Enable Biosciences, Inc (Board Member, Employee, Scientific Research Study Investigator, Shareholder)

367. Role of Conventional Biomarker for Prediction of Chest CT-confirmed COVID-19 Pneumonia
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Session: P-15. COVID-19 Diagnostics

Background. The coronavirus disease 2019 (COVID-19) has a wide range of severity. Chest computed tomography (CT) had high sensitivity and specificity to identify COVID-19 pneumonia. However, chest CT was not available in almost all hospitals in pandemic settings, including developed countries. This study is to evaluate the potential role of conventional inflammatory biomarkers to predict COVID-19 pneumonia.

Methods. All 155 RT-PCR-confirmed COVID-19 patients were evaluated for pneumonia by chest CT from April 10, 2021 to May 3, 2021 in the outpatient unit, a hybrid capture probe to have a similar effect on coverage. We observed that mutations and compared the performance of these assays using clinical samples. Further, the miniaturized hybrid capture workflow was optimized and evaluated to support high-throughput (384-plex). The sequencing data was processed by COVID-DX software.

Results. We detected 101,432 viruses (27%) with > = 1 mismatch in the last 6 base pairs of the 3’ end of ARTIC primers; of these, 413 had > = 2 mismatches in one primer. In contrast, only 38 viruses (0.01%) had enough mutations ( > = 10) in a hybrid capture probe to have a similar effect on coverage. We observed that mutations in ARTIC primers led to complete dropout of the amplicon for 4/11 isolates and diminished coverage in additional 4. Twist probes showed uniform coverage throughout with little to no dropouts. Both assays detected a wide range of variants (~99.9% coverage at 5X depth) in clinical samples (CT value < 30) collected in NY (Spring 2020-Spring 2021). The distribution of the number of reads and on target rates were more uniform among specimens within amplicon-based sequencing. However, uneven genome coverage and primer dropouts, some in the spike protein, were observed on VOC/VOI and other isolates highlighting limitations of an amplicon-based approach.

Table 1. Demonstrated sensitivity, specificity, LR+, and LR- for each specific cut-off value of hsCRP

| Cut-off for hsCRP (mg/L) | Sensitivity (%) | Specificity (%) | LR+ | LR- |
|-------------------------|-----------------|-----------------|-----|-----|
| 1.90                    | 81.9            | 64.9            | 2.33| 0.28|
| 1.95                    | 81.9            | 67.6            | 2.53| 0.27|
| 2.00*                   | 81.9            | 70.3            | 2.75| 0.26|
| 2.05                    | 80.2            | 70.3            | 2.70| 0.29|
| 2.10                    | 80.2            | 70.3            | 2.70| 0.28|

*Indicated optimal cut-off value for hsCRP to predict chest CT-confirmed pneumonia.

This figure shows ROC curve for hsCRP to diagnose of COVID-19 pneumonia. The area under the ROC curve is 0.82. The optimal cut-off value for hsCRP is 2.00 given sensitivity of 81.9% and specificity of 70.3%.

Conclusion. The hsCRP was the conventional biomarker that had an excellent performance in predicting COVID-19 pneumonia lead to early anti-SARS-CoV-2 treatment. This study demonstrated the potential role of hsCRP combined with clinical assessment in negative chest X-rays to replace chest CT in a high burden COVID-19 country during pandemic situations.

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368. Performance Characteristics of Sequencing Assays for Identification of the SARS-CoV-2 Viral Genome
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Session: P-15. COVID-19 Diagnostics

Background. As the SARS-CoV-2 (SCV-2) virus evolves, diagnostics and vaccines against novel strains rely on viral genome sequencing. Researchers have gravitated towards the cost-effective and highly sensitive amplicon-based (e.g. ARTIC) and hybrid capture sequencing (e.g. SARS-CoV-2 NGS Assay) to selectively target the SCV-2 genome. We provide an in silico model to compare these 2 technologies and present data on the high scalability of the Research Use Only (RDUO) workflow of the SARS-CoV-2 NGS Assay.

Methods. In silico work included alignments of 383,656 high-quality genome sequences belonging to variant of concern (VOC) or variant of interest (VOI) isolates (GISAID). We profiled mismatches and sequencing dropouts using the ARTIC V3 primers, SARS-CoV-2 NGS Assay probes (Twist Bioscience) and 11 synthesized viral sequences containing mutations and compared the performance of these assays using clinical samples. Further, the miniaturized hybrid capture workflow was optimized and evaluated to support high-throughput (384-plex). The sequencing data was processed by COVID-DX software.

Results. We detected 101,432 viruses (27%) with > = 1 mismatch in the last 6 base pairs of the 3’ end of ARTIC primers; of these, 413 had > = 2 mismatches in one primer. In contrast, only 38 viruses (0.01%) had enough mutations ( > = 10) in a hybrid capture probe to have a similar effect on coverage. We observed that mutations in ARTIC primers led to complete dropout of the amplicon for 4/11 isolates and diminished coverage in additional 4. Twist probes showed uniform coverage throughout with little to no dropouts. Both assays detected a wide range of variants (~99.9% coverage at 5X depth) in clinical samples (CT value < 30) collected in NY (Spring 2020-Spring 2021). The distribution of the number of reads and on target rates were more uniform among specimens within amplicon-based sequencing. However, uneven genome coverage and primer dropouts, some in the spike protein, were observed on VOC/VOI and other isolates highlighting limitations of an amplicon-based approach.
369. Alternative Workflow for SARS-CoV-2 Testing Using a Heat Lysis Protocol for Respiratory Specimens

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Session: P-15. COVID-19 Diagnostics

Background. The SARS-CoV-2 pandemic has demonstrated the need for streamlined workflows in high-throughput testing. In extraction-based testing, limited extraction reagents and required proprietary instrumentation may pose a bottleneck for labs. As a solution, ChromaCode developed a Direct Extraction protocol for the HDP® SARS-CoV-2 Assay, distributed in accordance with the guidance on Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency, Section IV.C., which allows for the processing of specimens without an extraction system. In lieu of an extraction system, the Direct Extraction protocol uses a thermal cycler to lyse and inactivate specimens which are directly added to the Polymerase Chain Reaction (PCR).

Methods. The Limit of Detection (LoD), Clinical Performance, and effect of Interfering Substances was determined for the Direct Extraction Protocol. The LoD was established on 6 PCR platforms with dilutions of inactivated SARS-CoV-2 virus spiked into residual, negative nasopharyngeal swab (NPS) matrix. Clinical performance was assessed with 48 positive and 50 negative frozen retrospective samples using the Direct Extraction protocol compared to an external Emergency Use Authorized (EUA) comparator assays (cobas® LiaT SARS-CoV-2 & Influenza A/B assay and the Hologic Panther Fusion® SARS-CoV-2 Assay respectively) on three PCR platforms. The Direct Extraction protocol was evaluated for performance in the presence of 13 potentially interfering substances that can be present in a respiratory specimen.

Results. The LoD of the Direct Extraction protocol ranges from 1000 – 3000 genomic equivalents (GE)/mL. The clinical performance of the assay was 95.8% positive agreement (95% CI of 84.6% - 99.3%) and 100% negative agreement (95% CI of 90.9% - 100% or 91.1% – 100%) across all three PCR platforms tested. The viral target was detected at 3X LoD for all interferents tested.

Conclusion. The Direct Extraction protocol of ChromaCode’s SARS-CoV-2 assay is a sensitive test that eliminates the need for sample extraction and performs very well against traditional extraction-based workflows. The inclusion of this protocol can reduce costs, reliance on extraction systems, and time associated with extraction-based protocols.

Disclosures. Meghna Yadav, Ph.D. Molecular Biology; ChromaCode Inc. (Employee, Shareholder) Tiffany Martinez, n/a; ChromaCode (Employee, Shareholder) Isabel Regoli, MS, Bioinformatics; ChromaCode (Employee, Shareholder) Osvaldo Hernandez, B.S., Molecular Biology; ChromaCode (Employee, Shareholder) Phuong Le, B.S., Biochemistry; ChromaCode (Employee, Shareholder) Heather Carolan, Masters, Computational Molecular Biology; ChromaCode Inc (Employee, Shareholder) Brad Brown, B.S, Ph.D Biomedical Sciences; ChromaCode (Employee, Shareholder) Karen Menge, Ph.D. Biochemistry; ChromaCode (Employee, Shareholder) ChromaCode (Employee, Shareholder)

370. Examining the Relationship Between SARS-CoV-2 PCR Cycle Threshold, Disease Severity and Epidemiologic Trends

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Session: P-16. COVID-19 Epidemiology and Screening

Background. Real-time reverse transcriptase PCR (rRT-PCR) has become the primary method for detection of SARS-CoV-2. Specific measurements of cycle threshold (Ct) values can give an estimate of viral load. Previous studies have shown temporal trends in Ct values, which could be used to predict the phase of the pandemic. This study’s goal was to examine the relationship between Ct and disease severity, as well as Ct trends.

Methods. Testing was performed using the Abbott M2000 SARS-CoV-2 assay. Data was collected for 262 SARS-CoV-2 positive patients from March-May 2020.

Results. The majority of the patients had mild to moderate disease. Average time since symptom onset was 5.9 days, and 92% were symptomatic. Figure 2 demonstrates the distribution of Ct by disease severity at time of testing. There was no significant difference in cycle threshold by sex, age, race or ethnicity. Figure 2 shows weekly mean cycle threshold by total new cases in Massachusetts to reflect temporal trend of Ct and cases. In the multivariable linear regression model, Ct increased with days since symptom onset (P< 0.001). Cycle threshold was inversely associated with disease severity in multivariable logistic regression though (OR 1.06, 95%CI 1.01-1.11, p<0.03), even when controlling for time since symptom onset.

Figure 1. Distribution of Ct by disease severity at time of SARS-CoV-2 testing.

Boxplot showing distribution of Ct by disease severity at time of testing. There was no significant difference between groups.

Figure 2. Weekly Mean Cycle Threshold by Total New MA Cases.

Line represents mean Ct over time period included in this study overlaid on total new cases in Massachusetts. Lower Ct were seen in the course as cases were increasing which peaked as cases stabilized.

371. Estimating SARS-CoV-2 Seroprevalence from Spent Blood Samples, January–March 2021

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Session: P-16. COVID-19 Epidemiology and Screening

Background. Measuring SARS-CoV-2 antibody prevalence in spent samples at serial time points can determine seropositivity in a diverse pool of individuals to inform understanding of trends as vaccinations are implemented.

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