COVID-19 Evidence Accelerator Collaborative

Thursday, *June 4, 2020, 12:00-1:00 pm ET*

2nd Diagnostic Accelerator Call Summary

Evidence Accelerator

The goal of the Evidence Accelerator is to provide a learning and collaborative community of health technology, data and other partners to come together and be a part of the real-world data community with a set of common tools. The tools that are available are the research questions, common data elements, translation tables, parallel analysis of common research questions, meetings and forums for feedback and learning, and individual accelerator communities to focus on specific topics.

There are different workstreams that are available for participants such as the Therapeutic Evidence Accelerator that focuses on drugs and biologicals and the Diagnostic Evidence Accelerator which focuses on the diagnostic aspects of COVID-19. In the future, there may be a Vaccine Evidence Accelerator that will focus on the vaccine development. Each workstream has a lab meeting where study results are discussed and lessons learned are shared; and a parallel analysis meeting where shared workplans are developed, aligned upon and executed. Questions raised by this community are encouraged and go through a process to triage those that will be taken off-line, with the Accelerator as a potential matchmaker, and those that will be run through parallel analysis.

You are Here: Diagnostics Accelerator

There were 5 presentations given at the 2nd Diagnostic Accelerator meeting. Those presentations are as followed:

1. Assessment of the prevalence of Asymptomatic and Pre-Symptomatic SARS-CoV-2 Infections: The ACORN Study (Brad Woodward, Lilly)
2. Real- Time RWE COVID Insights and Evidence by Health Verity (Andrew Kress)
3. Case Finding via Lab Testing (Dan O'Connor, Ciox Real World Data)
4. University of California Health Systems COVID-19 Data (Atul Butte)
5. Feedback on Research Questions (Carla Rodriguez-Watson, Jeff Allen, and Sean Tunis)

Assessment of the prevalence of Asymptomatic and Pre-Symptomatic SARS-CoV-2 Infections (Brad Woodward, Lilly/ACORN Study)

The ACORN study is a cross sectional community based observational study with an enrollment of 3000 people that looks at the correlation between the test results and clinical symptoms in asymptomatic patients. The CDC reported that 18-50% of infections are asymptomatic. The population characteristics include adults 18 years of age or older with no prior positive tests and no COVID like illness in the last 7 days (e.g. fever, new or worsening cough or shortness of breath, and headache). The primary objective of the study is to determine the point prevalence of SARS-CoV-2 through nasopharyngeal swab collection and RT-PCR testing. The secondary objectives are to determine the prevalence by subgroup, symptom status over time and the RT-PCR status over time. The baseline characteristics of the sample size of 2953 consisted of a mean age of 49.6 with a standard deviation of 15.5, the age range was 18-88, 58.9% were females, and majority of the populations race was White. The cumulative weekly point prevalence 3.1% (95% CI 2.5-3.7). Investigators observed a low prevalence considering the high risk of transmission from asymptomatic group. This finding is supported by a study conducted by the State of Indiana and Indiana University, which found a stable prevalence across the base line characteristics.

A 14-day symptom follow up for the patients initially positive was conducted. From the 81 patients that were initially positive, 58 or 72% of patients remained asymptomatic at day 14. Also, a 14-day RT-PCR retest was conducted for the initially positive group. From the 65 patients retested, 16 or 25% of patients remained positive and 13 or 81% of the 16 patients that tested positive were asymptotic during the 14 day follow up between initial and repeat test. 33 or 67% of the 49 patient that retested negative were asymptomatic during the 14 day follow up between initial and repeat test. 16.7% of patients that were enrolled in the study were not eligible but enrolled in the study with nonspecific symptoms. 14.3% of the 91 participants with SARS-CoV-2 described other baseline symptoms with headache being the most common complaint. Exposure risk was also looked at as a risk factor. Patients that were exposed to COVID-19 has an increasing positive rate. Infection risk increased for people when they came into contact with 1 or more exposure risk factor, contact with a confirmed case, or traveled outside of the state.

Limitation of the study include non-random sampling, uncertainty if RT-PCR positive translates to infectiousness, self-reported nature of entry criteria and symptoms, and the generalizability of the population.

Real- Time RWE COVID Insights and Evidence by Health Verity (Andrew Kress)

Health Verity is assembling large-scale real-world data to power diagnostic studies and natural history studies related to COVID-19. The data is aggregated from different health providers data such as pharmacy, medical claims, lab results, hospital charge master data, and EMR data. The inclusion criteria for the cohort is the positive diagnosis or relevant treatment for COVID-19. Health Verity links lab data and hospital data to look at the broader impact of the data. Their sample size is 16 million patients and increasing. Patient data is loaded into their platform which allows for the automation of the study work. There have been 3.1 million RT-PCR tests conducted with a 17.4% positivity rate for COVID-19. Also, there have been 960,000 serology

tests conducted with a 14.1% positivity rate for COVID-19. There is a decline in the positivity rate with 5.0% reported on May 30, 2020 and a decline in the testing volume. Through this collection, data on age, gender, specimen data, diagnostic code, ordering site, ordering providers, results, and result date can also be collected. One limitation they faced was that they did not have data on the test manufacturer which can impact test sensitivity and specificity.

Case Finding via Lab Testing (Dan O'Connor, Ciox Real World Data)

Ciox is an IT company that serves as the medical record department for many of the nation's hospital and clinics. The problem that they are trying to solve is taking the friction out of aggregating the medical record data for various stakeholders. The medical record data is used for continuity of care, clinical research, and risk adjustment. Ciox partnered with LabCorp to develop a program to create a deep clinical and structured database for COVID 19 patients. They have developed a 5-part system to using medical records: beaconing analytics, digital and analog grid, machine and human curation, COVID-19 observation database, and evidence generation to answer COVID-19 related questions. Ciox's data model includes 20 plus clinical categories with approximately 280 data elements. They are literature and real-world data driven. The data model is able to look at the longitudinal and comprehensive patient clinical history. Their data model is able to look at patient demographics, social determinants, comorbidities, smoking, COVID 19 severity, and treatment levels. Their case study is in the pilot phase. They have data from 31 states and 60, 000 patient searches which will yield 180,000 medical records. They will use this data to answer COVID-19 related questions.

University of California Health Systems COVID-19 Data (Atul Butte)

The University of California Health System tests approximately 2500 of its patients every day and has the capacity to run approximately 10,000 tests per day for other hospital systems and community efforts. Within the health system across 12 hospitals and hundreds of care delivery sites, they have 32 different ways of ordering the test, which are all harmonized. At the time of the presentation, they had provided 79,560 patients with results and 2,136 patients have tested positive and 525 patients have a pending result. Their current challenge with the increasing number of positives is for people that live close to the US and Mexico border. Their results for the positivity between age and genders coincide with other studies that have been conducted. They may be just coming off a second peak in the number of hospital admissions, which was on June 1, 2020. At the time of the presentation, the University of California Health System has 54 patients in the ICU, 50 on ventilators, and 5 patients on ECMO. The number of ECMO patients may increase as they are getting more patients on ECMO. They have sent 405 patients home and 71 patients have passed away. The University of California Health System has seen that patients older than 25 are admitted to the ICU or passing away, with the likelihood of ICU or death much higher over age 50. Some in the oldest aged population is passing away but do not have an ICU admission and might be due to established advanced directive. They gathered race and ethnicity data and update it weekly to ensure that they do not see anything out of the ordinary. A case study was shown how one inpatient can be positive, then test negative and then back to being test positive for COVID-19. In collaboration

with the FDA, they have looked at the different medications to treat COVID-19. In their health system they saw an increase in the use of Heparin. They also looked at serology testing, with over 10,000 ordered serology tests and more than 4000 patients with both RT-PCR test and serology test. All University of California health research faculty, staff, and students are able to access this HIPAA Limited Data Set which will not require further additional IRB submissions. They still have additional questions that they want to look into. The questions are how we define COVID admission, what if the admission started a week before the test was run, what happens if the admission is not respiratory related and due to other admitting factors, and how do we define a resolved infection.

Feedback on Research Questions (Carla Rodriguez-Watson, Jeff Allen, and Sean Tunis)

There was a discussion of the research questions that were sent out during the 1st diagnostic meeting to scope out the data elements and variables that will be necessary to provide answers to COVID-19. They questions are divided into 3 parts: test, patient, and population. In order understand the importance of each question, organizations evaluated each questions, priority, timeframe, and feasibility. A summary of the question ranking was briefly discussed. This will be used to identify organizations who are able to answer specific questions. 15 organizations responded to the excel sheet discussed during the 1st meeting. Respondents included device manufacturers, clinical research organizations (CROs), health systems, clinical research networks, claims systems (payers), device manufacturers, data aggregators, and pharmaceuticals. Manufacturer felts that information about test devices is the key to answer questions of accuracy. Many respondents expressed concern about the ability to answer questions about test accuracy because of the lack of clinical or laboratory gold standard. The summary of the comments of Test question was shared. The common element between all the comments was that there is a need to define a reference standard for testing, which is complicated by incomplete testing of symptomatic patients, questionable accuracy of tests, and still limited understanding of "classic" COVID symptoms.

Next Steps

- Conduct a group by group analysis to match groups potentially interested in participating in analysis for the first couple of questions.
- Those groups will be able to run their own analysis of the key questions and variable and enable observations among a larger population more quickly using similar approaches
- Create an evolving framework as learning continues and testing increases
- Provide comments to MDIC for their Real-World Evidence Generation: Advancing Regulatory Science and Patient Access for IVDs. Participants can download framework and provide comment on www.mdic.org/ivdRWE2020 by June 15, 2020.