



COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #17

Thursday, *October 29, 2020, 12:00-1:00PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting 17

This week's Diagnostics Evidence Accelerator meeting consisted of 4 presentations.

1. Project One Feasibility Assessment (Carla Rodriguez-Watson, Foundation)
2. Presentation of Aim 1 Characterization from Analytic Partners

Project One Feasibility Assessment (Carla Rodriguez-Watson, Foundation)

The goal of the Feasibility Assessment was to inform inclusion criteria for study design. Also, we assessed within each partner if we can analyze the following questions: (1) can we identify where test characteristics (manufacturer) resides within the data ecosystem: EHR, LIS, Instrument; (2) can we access manufacturer/device ID? Without a UID, what data are available to distinguish unique products from the same manufacturer; and (3) are there sufficient pairs of +RNA plus serological test (positive & negative) to power a comparison of sensitivity across serological test types or manufacturers.

The important dates to identify are the exposure and symptom onset date. However, we saw that we were not able to obtain the exposure date, therefore, we used test date. We have 5 of 6 sites that are reporting with a cohort size of RNA+ range from 9,000-339,000, however, there is a drop off when RNA+ to serology test is looked at. Clinical history from visit (office, telephone) in ICD10 coding is available. Manufacturer test name is available for some sites. Cycle-threshold values are not available and IgM testing is very low, therefore, it will be excluded from the analysis.

We analyzed the number of people with a +RNA and at least one serology test and we found that there are many people who are receiving a serology test the same day as the RNA test. An interesting find that was seen was that there were 10-17% of people that had a +RNA and a positive serology test within 14 days of the +RNA test. Based on findings from the feasibility assessment, the following determinations were made:

1. Since specimen collection was not consistently available, test date will be defined hierarchically as follows: specimen collection, specimen receive date, test date, and result date.
2. Since symptom onset date is not available, we used RNA sample date as an index date from which to identify appropriate serological tests for comparison. We will attempt to evaluate the time from symptom onset to RNA sample date in partners who have access to such data.

3. Since some sites include data from laboratories (and not the associated clinical visit) for a portion of their data, we will require that all persons included have a visit date within +/- 14 days from the sample collection date. This will enable the collection of presenting symptoms (or lack thereof).
4. IgM tests will be excluded from analysis.
5. The high density of serology testing on the same day, or within 2 weeks of the RNA test raised much discussion and interest in exploring testing patterns and what it may reveal about clinician trust of test results. Furthermore, clinicians tend to re-test if the clinical picture of the patient does not match the results of the test; or because it is more efficient to test patients on the same day.

Aim 1 test characterization is as followed:

1. Describe RNA tested by demographic, behavioral and environmental characteristics, baseline clinical presentation, key comorbidities (e.g. diabetes and cardiovascular disease), and bacterial/viral co-infections (e.g. influenza)
2. Describe serological testing by demographic, behavioral and environmental characteristics, baseline clinical presentation, key comorbidities (e.g. diabetes and cardiovascular disease), and bacterial/viral co-infections (e.g. influenza)
3. Characterize the timing of serology testing relative to symptom onset or NAAT date by demographic, behavioral and environmental characteristics, baseline clinical presentation, key comorbidities (e.g. diabetes and cardiovascular disease), bacterial/viral co-infections (e.g. influenza), and test characteristics (e.g. manufacturer)
4. Describe demographic, behavioral and environmental characteristics, baseline clinical presentation, key comorbidities (e.g. diabetes and cardiovascular disease), bacterial/viral co-infections (e.g. influenza), and test characteristics (e.g. manufacturer) associated with positive serology (+Ab) vs. negative serology (-AB)

The study design inclusion criteria included the following: +RNA, serology test \geq 14 days after +RNA specimen collection date, and visit date within +/- 14 days of RNA test.

Presentation of Aim 1 Characterization from Analytic Partners

Below are the summary results for Aim 1 test Characterization from the analytic partners.

University of California Health System (Rohit Vashisht)

- 13,495 patients with a positive serology test which are tested at UCLA and UCI. They are using 3 manufacturers in their health system.
- Majority of individuals had serology tests on the day of a +RNA test while the median time to serological test is 33 days from a +RNA test.
- Serological tests are higher among individuals that are 18-44 years, males, and White.
- The tests are highest among patients with a preexisting condition related to cardiovascular disease.
- The tests are highest among individuals with presenting symptoms related to cardiovascular disease, shortness of breath, and pneumonia.
- Majority of serological tests are conducting using DZ-Lite SARS-CoV-2 IgG CLIA Kit Diazyme after May 2020 mostly among inpatient.
- Individuals that are 4-17 are tested early for antibodies with a median time of 1-13 days.
- Time to serological test does not appear to vary with respect to preexisting conditions of individuals.

- Serological test using DZ-Lite SARS-CoV-2IgG CLIA Kit are conducted soon after +RNA (median=3 days) compared to test from other manufacturer.

UnitedHealth Group (Natalie Sheils)

- The eligibility window for cohort entry is from January 2020 through October 2020. UHG is able to look at claims data going back 1 year. When the exclusion criteria is added, N is equal to 9,618 people with a +RNA and +serology test, however, all N listed are distinct people since many people have multiple tests.
- The timeline for those with multiple +RNA has shown strange patterns. In their cohort, they found that there are people that have a +RNA test, then a +serology test, and then another RNA test. They have also seen that patients are getting both tests the same day and patients that are having a weekly test. They have a database that shows hospitalization of patients.
- Serological tests are higher among individuals that are 18-44 years of age. There is a balance of distribution among male and female. Within their dataset, race is largely not known, however, White's do have a higher proportion of serological testing.
- The tests are highest among patients with a preexisting condition related to cardiovascular disease. However, their data does not add up to one since many patients have more than 1 condition.
- The follow up serology tests are highest among patients with cough and fever as a presenting symptoms.
- Patient geography is widely spread with more patients in the Mid-Atlantic and South-Atlantic having a greater access to serology testing.
- The 2 manufacturers that make up their data is Abbot IgG and Vitros IgG. However, a large amount of manufacturer data is missing from their data set.
- The median days to serology test by region was influenced by how the disease hit the specific region and the time that serology test was on the market.
- The median days to serology test by race and age is influenced by the small sample size.

Health Catalyst (Elizabeth Eldridge)

- Their COVID-10 National Registry shows summary metrics. Also, it shows the geographic regions, common COVID-19 medications, and the distribution for age, race, ethnicity and gender.
- When the exclusion criteria are added there are 3,523. They are seeing a lot of patients that had multiple tests on the same day, therefore they limited a subsequent serology test date of more than 0 days.
- Serological tests are higher among individuals that are 55-64 years of age and 12-17 years of age. There are more female with a positive serology test. There are more Whites that have a serological test compared to other races/ethnicity.
- The tests are highest among patients with a preexisting condition related to cardiovascular disease, diabetes, and hypertension.
- Geography is defined based on service location. The largest representation is from the Mountain area.
- Presenting symptoms is based on structured data and ICD 10 codes. There are more patients that have cardiovascular conditions, acute respiratory infection, acute bronchitis, and pneumonia.

Mayo Clinic (Ben Pollock)

- In the Mayo locations, there are a combined 2,100,000 molecular tests and more than 235,000 serology tests. There are 25,067 patients with +RNA test. 50.4% of patients are from Minnesota, 9.1% are from Arizona, 10.4% are from Florida, 1.7% are from Iowa, 25.9% are from Wisconsin, and the remainder are from other service locations.
- Mayo Clinics has a Unified Data Platform that has raw data in the bottom level which converts into integrated data and then into standardized data. However, the SCC Soft Laboratory system which is connected to EPIC is not in the Unified Data Platform.
- Out of the proportion of patients with +RNA, there are 88.6% of outpatient, 9.0% Emergency Department, and 2.4% inpatient.
- Serological tests are higher among individuals that are 18-44 years of age. There are more female with a positive serology test. There are more Whites that have a serological test compared to other races/ethnicity.
- There are patients that have multiple serology follow up. The median is 25 days.
- Mayo Clinic is in the process of linking their lab data to EHR data, so they will be able to better link manufacturer data. The molecular tests that they are using are Abbott Platform Roche cobas (high-throughput) Platform, Roche Liat, Cepheid Platform, Luminex Platform, ThermoFischer, Perkin Elmer, Hologic APTIMA, and Virology Lab LDT. The Serologic Assays that they are using are Euroimmun IgG ELISA on Dynex Agility platform (S1 based), Epitope Diagnostics IgG ELISA on Dynex Agility platform (NC based), Ortho-Clinical Diagnostics IgG CIA on VITROS3600 platform (S1 based), and Roche Diagnostics Total Antibody Elecsys on e800 platform (NC based).
- They do not have a precise way to measure symptom, but they are part of a cohort Entry C where they are using natural language processing to capture symptoms.

Action (Anthony Louder)

- The study period from March 1, 2020- July 31,2020, but the data extends back into March 2019.
- The master dataset is constructed from linking claims, CDM, and lab data in the HealthVerity Marketplace. The data is a random sample.
- There were more females compared to male who had a serology test. The rate of test was similar between the genders.
- There were more 45-64 years of age groups. The time to testing is 32-35 days between the first diagnostic test and the first serology test.
- There were more representation from the Mid-Atlantic region. The Mid-Atlantic region had a greater time of serology testing.
- By calendar time, there were more people that had serology test before May 1, 2020. After May 1st, 2020, there is a shorter time between the first +RNA test and the first serology test.
- Prevalence rates of most preexisting conditions is similar between groups, however, dementia is notably higher in the no serology test group.
- Testing and time to first serology test within most of the preexisting conditions exhibit fair amount of consistency. Kidney disease and dementia had lower rates of testing.
- Manufacturers that are used for RNA test are Roche PCR, Hologic Panther TMA, and LDT. Manufacturers that were primarily used for serological testing Abbott and Ortho.

From the Chat Box

- Negative RNA and Serology is also worth knowing, since it may contribute to a better understanding of serologic specificity, which is needed for epidemiologic purposes.
- An accelerator asked if the patients who are Ab positive only subsequently NAAT tested to see if Ab response is for current or prior infection?
- Another accelerator asked if all of this was clinical testing. Meaning not community surveillance or return to work/school, etc.
 - The presenter answered that the data is from clinical testing.
- When saying "is highest" does this mean: the highest users (group with highest rate of use) or does this mean that group that is the largest proportion of the sample?
- An accelerator was wondering if perhaps people are doing PCR and serology on the same day in patients who are presenting within a couple of weeks of possible covid-19 symptoms
- An accelerators states that their conversation with doctors a while ago was dual NAAT/Ab testing reflects uncertainty as to patient status - e.g., patient had some symptoms a few weeks earlier, a week ago, and now. So dual testing provides better sense of patient status.
- An accelerator stated that they see the same strange patterns in another commercial claims with linked labs data source. So, you are not alone.
- A participant was curious to see if the often mentioned association with dementia reflects bias towards long term care facility residents being tested with pre-existing dementia versus COVID-19 induced dementia.
- A participant states that the early surge in NY/NJ/New England often limited to NAAT only whereas subsequent time period has far more dual testing.

Next Steps

- Continue making data connections through the Evidence Accelerator.

Next Meeting: Thursday, November 5th, 2020 12-1 pm ET