COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #30

Thursday*, May 20, 2021, 12:00-1:00PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting 30

This week's Diagnostics Evidence Accelerator meeting consisted of 3 presentations:

- Diagnostics Parallel Analysis Project One Readout (Dr. Carla Rodriguez-Watson, Reagan-Udall Foundation for the FDA)
- COVID Testing Priorities (Dr. Thomas Inglesby, HHS/ASPR)
- CDC-NIH At-Home Testing Initiative (Dr. Elizabeth Di Nenno, CDC and Dr. Rachael Fleurence, NIH)

As always, thank you to all of the analytic partners, strategic advisors, and scientific advisors that are participating in this project.

Diagnostics Parallel Analysis (DxPA) Project One Readout (Dr. Carla Rodriguez-Watson, Reagan-Udall Foundation of FDA)

The objective of Aim 1 for DxPA Project One is to describe real-world serology testing patterns by instrument, clinical, and demographic factors. The cohort consists of approximately 931,000 patients across the six partners (2 claims and 4 EHR) participating in Project One. The study period for Project One was from March 1, 2019 to December 31, 2020. The follow-up serology sample period was 0-90 after the first positive RNA test. The inclusion criteria included persons with a positive RNA result from March 1, 2020 to September 30, 2020. Additionally, people with clinical encounter (from any care setting where COVID-19 symptoms, or lack thereof, would be reported) within +/- 14 days of RNA sample collection date, specimen receipt date, test date or result date were included in the cohort. The exclusion criteria included antigen test, IgM or IgA tests, and persons without evidence of at least six months of enrollment in the 365 days prior to index, exclusive of the index date (i.e. -365 to -1) for claims datasets.

The key findings from Aim 1 included:

- 15% of serology tests were conducted within 14 days of molecular test. This was driven by the surveillance for nosocomial infection.
- Additionally, the data showed that same-day molecular/serology testing is prevalent.
- COVID-19 has shown that there are racial disparities in exposure, infection rates and death. This was evident in the data collected for Aim 1. Four of 6 sites had adequate capture of race data, however, there was race/ethnicity data missing or unknown for some of the data partners.

- Distribution of Black population is lower among the serotested as compared to untested, suggesting lower serotesting in the Black population
- A shorter time to serotesting among Black patients who are tested may point to associations between race, pre-existing conditions, and/or more severe clinical presentation.

Aim 2 of Project One characterizes the positive percent agreement (PPA) between serology and positive molecular test. The objective was to describe real-world performance of serology (compared to positive molecular test) by instrument, clinical, and demographic factors. The study period is from March 1, 2019 through December 31, 2020. The inclusion criteria included persons with a positive RNA result from March 1, 2020 through Sept 30, 2020; a clinical encounter (from any care setting where COVID-19 symptoms, or lack thereof, would be reported) within +/- 14 days of RNA sample collection date, specimen receipt date, test date or result date; and at least one (1) serology test occurring 14-90 days after CED. The exclusion criteria included antigen test, IgM or IgA tests, persons without evidence of at least six months of enrollment in the 365 days prior to index, exclusive of the index date (i.e. -365 to -1) for claims datasets, and serological test occurring <14 days after CED.

The key finding from Aim 2 included:

- The total study numbers ranged from 977 to 6848 people with SARS-CoV-2 infection. We observed variability in the PPA. Although different, the range of PPA was quite tight across data types. In claims, the range was 90-92%; in EHRs 84-88%. These ranges are very different from the near 100% sensitivity on which EUAs were considered.
- The data partners looked at the PPA for test manufacturer and the Abbot Architect (IgG) was predominately used in the claims-based systems and has a PPA of 89% - 92%. Ortho Vitros IgG test was used broadly in the data partners that have provided data. The PPA was similar in both the claims and EHR datasets.
- For the Abbot Architect, the performance captured by the data partners is 10% lower than the performance captured by the Abbott Architect EUA study. However, in the EUA study, the sample size was 88 patients, whereas, the sample size captured by the data partners ranged from 891 - 1388.
- Stratification by race did not show much variability. The PPA in white patients tended to be lower than in Black patients. Though, sample sizes for whites tended to be much higher. Smaller sample sizes for the Asian, Pacific Islander and Native Hawaiian were very small and contributed unstable results; as suggested by wide confidence intervals.
- In the Hispanic Ethnicity stratification, there were differences in the PPA for the individuals that identified as Hispanic and the individuals that did not identify as Hispanic. However, the sample size was smaller for the individuals that identified as Hispanic.
- In the calendar time stratification, the data partners stratified by calendar time before and on/after June 15, 2020 by since it marks the start of the Summer surge in COVID-19 cases. There was no difference in the PPA within partners, but there was a difference across partners. Also, in one partner there was a significant drop in the sample size after June 15, 2020.

<u>Questions and Answers:</u>

- Are there ways to better capture these data?
    - This is something that we will have to answer ourselves.
- Any speculation on the source of the data gaps? At the clinical reference lab? At the insurer? At the EHR? During the data interchange between lab and EHR?

    - No, however, from our discussion from the partners, the gaps could occur anywhere. This could be a workflow issue or it is something that is not asked or answered. This is something that we need to look into.
- What are the trends in testing over time (months), both in total and disaggregated by race/ethnicity? Are we moving in the right direction?
- If one is biracial or multiracial, how are they categorized in the datasets?
    - The DX Ev Accel followed OMB directives on this issue. OMB discusses the options around multiracial respondents. The OMB directive applies to federal entities and federally funded entities but does not apply to private entities. The directive can be found here.
- Have you studied the data by locality or zip code as surrogate of economic status?
    - The data partners did look by locality and captured area percent poverty and percent COVID-19. However, only 1 partner was able capture those data. There are some issues regarding business agreements that prevent the partners from sharing geographic data needed to map those data. Nevertheless, we are working with the partner who captured the data to look at the effect of place on individual probability of seropositivity.

COVID Testing Priorities (Dr. Thomas Inglesby, HHS ASPR)

The current administration focus is on COVID-19 testing as a measure to diagnosing COVID-19 among people with symptoms and those with potential exposures to the virus; Identifying outbreaks early to prevent or respond to hotspots and conduct genomic sequencing to track variants; and Finding asymptomatic disease to stop outbreaks, especially in priority settings and high-risk populations like schools and congregate facilities such as long-term care. Due to this, the Administration secured $47.8B in American Rescue Plan funding for testing and mitigation, signed an Executive Order on Testing; established a National Pandemic Testing Board that brings together program leaders from across the federal government; and is ensuring that there is White House Coordinator on Testing.

The specific priorities and examples of the implementation of those priorities are as followed:

- Provide free COVID-19 testing that is widely available and accessible to all
    - The current administration issued new guidance to remove barriers to testing, including testing for asymptomatic people. The guidance makes it clear that neither private health plans or the United States Government (USG) would cost-share, require prior authorization or use screening criteria to deny coverage of COVID test.
    - Additionally, by making substantial new funding available to cover all uninsured costs associated with testing improves testing for the uninsured and community-based testing. Additionally, the administration is expanding testing at community testing sites and pharmacies, particularly communities with high Social Vulnerability Index (SVI) areas.
    - Also, the CDC released $2.25 billion in funding to address COVID health disparities, advanced health equity in high risk and underserved populations, including racial and ethnic minority communities and rural areas. This is intended to improve testing, contact tracing, mitigation and improve data collection.
    - HRSA is providing nearly $860 million to rural clinics and hospitals for COVID testing and mitigation measures.
    - The administration is expanding screening test development to find asymptomatic disease early. The FDA announced streamlined pathway for test developers to receive emergency use authorization for screening tests, including over-the-counter tests. Additionally, the new

FDA fact sheet to assist schools, workplaces, communities, and others in deciding which test to use when establishing testing programs to screen asymptomatic individuals.
    - The administration created innovative community health initiatives to support at-home testing. CDC and NIH launched "Say Yes! COVID Test," described more fully in the next presentation.
- Provide COVID-19 testing supply, materials and manufacturing capacity match testing needs
    - The administration is providing funding for investment in domestic production of tests and supplies.
    - The administration has procured tests to support COVID screening in long-term care facilities. HHS and DOD awarded $255 million for the production and delivery of 50 million Abbott BinaxNOW rapid point-of-care antigen tests for COVID-19 to support continued screening testing in long-term care facilities
    - Finally, the administration is making strategic use of Defense Production Act (DPA) authorities to provided large diagnostics company with a DPA priority rating to secure resin in order to ensure its continued production of 3.5 million tests a month.
- Testing to help protect those who live and work in vulnerable settings and who are in higher risk populations
    - CDC released an Operational Strategy for K-12 Schools through Phased Prevention which is a roadmap for schools to safely reopen for in-person instruction through consistent use of prevention strategies.
    - Additionally, the Administration invested $10 Billion in American Rescue Plan Funding to Support Testing to Help Schools Safely Reopen.
    - Finally, the CDC released testing guidance outlining how to use screening testing to identify, track, and mitigate asymptomatic transmission of COVID-19, including specific recommendations for workplaces, correctional facilities, shelters and higher education settings.
- Genomic sequencing is scaled up to identify more rapidly SARS-CoV-2 variants and inform public health action
    - The Administration invested in rapidly increasing virus genome sequencing.
    - The administration launched New Innovative Centers of Excellence in Genomic Epidemiology to focus on developing new genomic surveillance tools to better track pathogens.
    - Finally, the administration is building a National Bioinformatics Infrastructure which will provide substantial investment in bioinformatics in the U.S. public health system to create a unified system for sharing and analyzing sequence data. Additionally, this will support training to increase sequencing in clinical settings and expand CDC's Bioinformatics Fellowship program.
- Finally, the administration is sustaining the testing capacity and infrastructure to respond to COVID-19 surges and future infectious pathogen outbreaks.

Questions and Answers:

- Is the government also thinking about expanding surveillance from just testing? I know there's been some work on using wastewater. What about other sources or an upgrade to the ILINet that marries many sources of data flow (e.g. wastewater, OTC medication usage, testing results, etc.).
    - There is a possibility that there will be a wastewater surveillance. The administration will release information on this later.

- We need the manufacturer information to leak out of the instrument into the LIS and into the EHR so that the real-world performance of the test can be assessed--and the USG can know, beyond EUA, the highest value tests.
- Have you developed a centrally managed format to deliver the results in an interoperable way? We need to avoid any post-hoc manual mapping processing that will preclude a timely assessment of the data facts.

"Say Yes! COVID Test" CDC-NIH At-Home Testing Initiative (Dr. Rachael Fleurence, NIH and Dr. Elizabeth Di Nenno, CDC)

The CDC and NIH are collaborating to implement and quickly measure the effectiveness of rapid at home testing 2-3 times a week in reducing community transmission of SARS-CoV-2 in two large communities over a 4-week period. The test that is used in the study is Quidel's QuickVue at-home COVID-19 test and the communities that are part of this are Hamilton County (Tennessee) and Pitt County (North Carolina). They launched a public health campaign to notify residents of the availability of free tests by allowing for online fulfilment in partnership with Amazon, community center pick up, at local centers, churches, schools and other sites, and additional efforts to reach and engage with underserved communities.

NIH funded a team at University of North Carolina/Duke University to conduct an ecological study to identify signals in community transmission and matched controls. The outcome measures for the study are positive tests for SARS CoV-2, measures of SARS-CoV-2, including variants, in wastewater, mobility outcomes, hospitalizations attributable to SARS-CoV-2, and SARS-CoV-2 ICU admissions. The matching controls Pitt County, NC: Charlotte, NC, Cabarrus County, NC , Wake County, NC and Chattanooga, TN: Memphis, TN. There was an optional research study that participants can take part in. This study will evaluate feasibility of frequent testing and its associations with socio-behavioral mechanisms of community transmission, including social interactions, health behaviors, healthcare utilization, knowledge, and disease burden.

As modeled in Clinical and Economic Effects of Widespread Rapid Testing to Decrease SARS-CoV-2 Transmission, at-home testing is predicted to decrease community transmission. In the counties participating in this study, there was an overall decrease in community transmission. In Pitt County, NC, the intervention was from April 4 through May 19, 2021. There is a market research survey that is underway to understand local uptake. In Hamilton County, TN, the intervention began on May 4, 2021 and will end on June 4, 2021. The market research survey is planned to take place within the next few weeks. NIH is exploring a third location in Washtenaw County, Michigan due to large spring surge, high demand for testing, different demographic make-up and geographic setting from which to learn.

The takeaways from the research evaluation are that the signals may be impacted by uptake level, vaccination rate and existing local prevalence trends. The interim results are expected in July/August 2021. The takeaways for distribution of tests are that there are differences between NC and TN responses such as community size, urban/rural mix, lead time for public health campaign, level of awareness of test availability, opening to second kit orders in TN, relation with attitude towards vaccination. The takeaways for use are that there is a need for more data on the use of the test. the takeaway for access is that there was a higher rate of success when they collaborated with local leaders. Finally, the takeaway for the cost is to mitigate the potential barriers for a widespread adoption in household.

Questions and Answers:

- Did the users report the test results through the internet?
    - There was no requirement for the users to report test results. The pipes are built to report the results; however, no one has reported the results.

Next Steps

- Continue making data connections through the Evidence Accelerator and through www.EvidenceAccelerator.org.

Next Meeting: Thursday, June 3, 2021 12-1 pm ET