COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #13

Thursday*, September 3, 2020, 12:00-1:00PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting 13

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

1. Why Are We Here? "Heidi's Journey" (Gina Valo, FDA/OC)
2. Building THE Ideal Data Set (Martha Davis, Danaher Diagnostics, LLC)
3. COVID-19 antibody testing: performance variation across subgroups (Natalie E. Sheils, UnitedHealth Group)
4. Addressing Potential Bias in RWE (Tom Trikalinos, Brown University)

Why Are We Here? "Heidi's Journey" (Gina Valo, FDA/OC)

A review of last week's visual presentation of a patient that was tested multiple times for COVID-19 was shown. As we move from the instrument to the EHR, the fidelity of the data is lost. In order to solve this problem, the research community needs to look at one data element at a time. The goal is to keep the integrity of the data element through the system and be able to aggregate the data at the patient level.

Since developing COVID-19 tests, our next step is to understand test performance to improve public health and safety, understand the difference and variables in test performance as they relate to research and the development of therapeutics and vaccines, and identify viable paths to reopening the economy. The work that the research community is conducting is a bridge to go beyond the scope of COVID-19. We need to use RWD to generate RWE for use in regulatory science, generate RWE to inform clinical and medical policy decisions, and enable systems of learning, feedback, and iterative improvement.

Project One is a retrospective study that answers a single COVID-19 question. It is a manual clean up of unstructured data with few stakeholders (health systems and aggregators). Our goal is to use the lessons learned to go beyond COVID-19. This project is called "Project Mars". This project is designed to answer multiple questions for multiple conditions with structured, clean, and ready to use data. Also, it is designed to include many stakeholders. The pathway to Project Mars is through the Parallel Analysis Work Group which is looking at the manufacturer data elements.

Building THE Ideal Data Set (Martha Davis, Danaher Diagnostics, LLC)

This presentation consisted of a discussion on what an ideal data set will look like for Project "Mars". A data set that incorporated point in time analysis and longitudinal patient data is important. Point in time analysis can be used for population health and predicting and monitoring diseases distribution. Point in time analysis can be sliced based on location and patient demographics. Longitudinal patient data can be used to look at disease progression, characterization of alternate care pathways, and determining accuracy and effectiveness of tests, vaccines, and treatment. The challenge that both have is that it cannot connect multiple visits from the same patient making it difficult to sequence the visits.

The data does not completely flow to the aggregator from the instruments. That data that researchers are currently analyzing is point in time data, which is disconnected from the rest of the data that are available for a patient. The goal is to connect all of the data points to see a complete picture on a patient. There are different kinds of interactions that take place to generate data and all of these data elements are required to display a full story. We should be able to answer enough questions, so that we can understand where and why there are gaps in the data. Also, we should be able to see device data if a patient is tested across different devices.

One data element that is difficult to connect to data sets is date and time of reported diagnosis. The only way to connect is through the EHR. There are also elements that exist outside of an institution such as point of care device data. However, we should be mindful of laws surround PHI and HIPAA when trying to collect data because it can hinder the ability for researchers to gather the necessary data needed to advance our goals. Therefore, researchers should plan for information needed to troubleshoot inconsistent answers. Point of Care and at home testing data may not flow into an EHR system, therefore we have to find a solution to collect those data points. Answering questions such as how standards are being applied at a manufacturing level, how is data being collected, and how patient identifiers are being defined is crucial.

Depending on the system, not all recommendations for implementing health data standards may be followed and standards are open to interpretation by the manufacturer. There are health data standards that may include future data needs which can be implemented. In order to have an ideal data set, we will need to align the minimum interoperability standards across instrumentation and EMR systems. There needs to be new regulations and enforcing requirement standards for devices and data system interoperability with manufacturers. We need to be able to include standards for POC and emerging devices. There needs to be clarifications on the usage beyond infectious diseases. Therefore, enabling data content will support better medicine.

COVID-19 antibody testing: performance variation across subgroups (Natalie E. Sheils, UnitedHealth Group)

UnitedHealth Group and Harvard Medical School is publishing an article called "Variation Across Population Subgroups of COVID-19 Antibody Testing Performance" which discusses the results from their study. They evaluated 11,809 individuals who had a positive PCR test followed by an antibody test. They found that the serology test appeared to have a higher recall than popular media has reported. The recalls vary significantly across subpopulations and according to timing of the tests.

Their data set includes 2,445,907 tests that were collected between March 2, 2020 to August 1, 2020. In their data set, 66.8% of total tests are PCR test and 33.2% of total tests are antibody tests. They separated their data by LOINC codes and found that 98.21% of the PCR tests share a LOINC code, therefore, 65.54% of all their tests share a LOINC code. 83.01% of antibody tests share a LOINC code,

therefore, 27.57% of all tests share the same LOINC code. 10% to 15% of antibody tests were taken the same day as a PCR test. They have a 14 day restriction after a positive PCR test to do a recall test. IgG test outperformed the IgM and IgA tests with positive of 91.9%. The pathway that they took to evaluate their data was first to get individuals with test results. Next, they filter out individuals that had a positive PCR test, and then filter individuals based on when the second test was done (before 14 day, after 14 days, and an AB test). They then filter the data based on the IgG antibody test and other antibody test. Finally, filter patients based on a positive or negative result. For antibody tests, the test recall changes over time. They do not have test results for POC and at home testing.

They analyzed recalls by age and gender. The recall increases for patients 45 and older and for males compared to females. Also, they analyzed their data based on race and income. The recall test performs better in non-white populations. They found no statistical significance in income on test performance. They found that recall varies by manufacturer. They do have manufacturer data for 2,359 patients which includes Abbot and Vitros IgG tests. The Vitros test has a higher recall at 93.1%. There may be manufacturer data available for other tests that they will be including to connect the all data pipes.

Addressing Potential Bias in RWE (Tom Trikalinos, Brown University)

The objective of the project is to assess the risk of bias of RWD analytics to estimate the sensitivity of antibody testing. We have to distinguish between whether someone has received the test, been selected to receive the test, if someone has received a positive test result, and if someone has the disease. The sensitivity of the test includes the patients that have the disease. The answer for project one is about the individuals that were selected to get the PCR test and then, get a positive PCR test. We cannot deduce the sensitivity of antibody testing using the information that we have due to the non-identifiability or partial identifiability. To answer Project One, the approach needed requires first identifying the data elements that can be captured by typical RWD and what extra information is needed. The next step is to refine relevant quantities. Then, one must obtain information needed for identification from design studies and combine evidence from RWD and design studies. A proposed formula that consists of elements identifiable from study data and parameters from controlled studies was presented. An example of designed study (or controlled study) includes a cohort of patients with known time of infection who will receive antibody testing at regular predefined intervals. Such evidence from controlled studies can be combined with data from real-world studies to perform the analyses.

Discussion

- There are no systems that collects the interaction between the patient and the healthcare provider. The provider is the one that has to add that information into the EMR.
- In order to create a master database that can be used for regulatory and public health purposes, we need to improve the standards to protect patient privacy.

From the Chat Box

- If participants want to follow Heidi's Story, the story can be found on www.evidenceaccelerator.org.
- MDIC released its IVD RWE Framework and can be downloaded at the framework here
- A participant stated that there are fundamental problems that we need to address. Those problems are that we do not have automated data verification processes that can confirm that the data are generated and transmitted undamaged to the correct patient records and end users. We cannot track each person that has visited a doctor or other health provider with a unique identifier. LabCorp has 140,000 interfaces to and from their clients, and Epic and Cerner

has many changing interfaces. This leads to a lot of missing data, and patient data partitioned across multiple health systems. This complicates performing analysis.

- A participant stated that data linkage for observational research is hard. As we often write the only risk to the subject is loss of confidentiality, however linkage requires exchange of identifiers or individual level tokens. An overview of this linkage process is discussed further in an article called "Linking electronic health data in pharmacoepidemiology: Appropriateness and feasibility".
- A caller said patient ID linking between lab orders is sent from EMRs to reference labs and lab results sent from reference labs to EMRs is accomplished via MRN, name, and DOB. Errors in the data stream can pose significant patient safety risks, therefore, reference labs & EMRs have consistently tested the veracity of accurate patient ID linking, as far back as HL7 v2.x LIS interfaces.
- A participant suggest scrubbing to remove sensitive information using NLP is a promising approach.
- A caller suggested that developing Learning Health Systems would be a good framework for bringing stakeholders together as a collective enterprise to identify how interoperability would create value to each stakeholder.
- A caller shared a website discussing SARS-CoV-2 Diagnostics, if callers are interested.

Next Steps

- Continue making the data connection and learn about test performance for the next meeting.

Next Meeting: Thursday September 17, 2020 12-1 pm ET