COVID-19 Evidence Accelerator Collaborative

Diagnostics Evidence Accelerator #29

Thursday, *May 6, 2021, 12:00-1:00PM ET*

Call Summary

Introduction to Diagnostics Evidence Accelerator Meeting 29

This week's Diagnostics Evidence Accelerator meeting consisted of 2 presentations:

1. How Integrated Data and HIE Can Support COVID-19 Response (Dr. Shaun Grannis, Regenstrief Institute)
2. Assessing Vaccine Effectiveness: Israel's Case Study (Dr. Ran Balicer, Clalit Health Services, Israel)

As always, thank you to all of the analytic partners, strategic advisors, and scientific advisors that are participating in this project. As of the week of May 3, 2021, in our Diagnostics Parallel Analysis project, we are on step 6 where accelerators are revising Aim 1 manuscript on testing characterization and on step 9 where accelerators are running their Aim 2 analysis.

How Integrated Data and HIE Can Support COVID-19 Response (Dr. Shaun Grannis, Regenstrief Institute)

The basis of the work that Regenstrief Institute comes from The Indiana Network for Patient Care (INPC). This electronic health record (EHR) system collects data from a variety of sources such as hospitals, labs, pharmacy, payors, public health, physician offices, and ambulatory care. Additionally, in 2001, Regenstrief developed a syndromic surveillance system connecting hundreds of hospitals in Indiana to monitor critical public health end points such as carbon monoxide outbreaks and COVID-19 symptoms.

The Notifiable Condition Detectors (NCD) within the Regenstrief's system is an automated system that examines EHR system interactions to determine whether that specific interaction needs to go to the Public Health Department. NCD captured over 6000 notifiable symptoms, whereas, labs and providers capture very little amount of those conditions. Therefore, electronic capture of conditions is essential in supporting public health and population health. When COVID-19 became a pandemic, Regenstrief developed and maintained the laboratory LOINC codes for coronavirus through their NCD to identify COVID-19 cases. The NCD formulates 24-hour reports that captures anyone that is diagnosed with COVID-19 and any new conditions. Regenstrief implemented this as soon as their Governor declared a State of Emergency in the State of Indiana.

Regenstrief is able to capture the complete clinical journey of a patient allowing them to capture critical statistics such as demographics, comorbidity, recovery time, hospitalizations, and emergency

department statistics in real time. Additionally, the NCD system allows the research team to analyze where the COVID-19 cases are originating from such analyzing the current cases emerging from Michigan and their recent surge in cases. This system allows the capture of surges in cases, which allows the Public Health Department mitigate supplies to that specific area.

The Indiana State immunization registry, CHIRP, is connected to the health information exchange (HIE). The HIE captures all of the immunizations administered in the state including COVID-19 vaccines at the different vaccination sites. Since the data is captured in the HIE, they are able to integrate clinical and outcomes data. CDC asked couple states to develop a program, VISION, to evaluate COVID-19 vaccine effectiveness. There are 10 sites from around the country and the project period is from January 1, 2021 to August 30, 2022. Data are provided to CDC on a weekly basis on key outcomes, e.g., breakthrough positivity, emergency department (ED) visits, hospitalizations and death. The data is captured from COVID-19 Vaccine registry, INPC ED visits and inpatient hospitalizations for COVID like illness, and COVID-19 test data.

For the methods of this project, CDC has preferred to take a test negative approach to analyze these data. Regenstrief is using propensity score matching by matching vaccinated individuals who have encountered the health system with COVID-like illness with not-vaccinated individuals who have encountered the health system with COVID-like illness. This is defined by ICD-10 codes and chief complaints. Through this they are able to understand the key outcomes of interest. The preliminary results from this show that the rates of coronavirus infection after vaccination are rare. There is a manuscript in development that will discuss the results further.

Questions and Answers:

- How complete and timely are the mortality data that you can access and incorporate?
    - In real time, Regenstrief receives death data from various sources. The data will be noisy; however, it will be timely. The cause of death data is free text; therefore, they conduct NLP to identify the COVID-19 cases.
- What if people get care out of state? I should have added mortality data occurring outside hospitalization.
    - The data that they capture is primarily from Indiana.
- In support of the FDA BEST surveillance work: what percent of vaccination is not captured by administrative claims (NDC/CPT billing)? Do you have bidirectional data connectivity to report IIS data to the payers in support of FDA active medical product safety surveillance activities?
    - When a vaccine is administered, the information is entered into the software and is tightly controlled, therefore it is not claims data. At this point, they are not sure about the comparison about the data between claims and EHR.
    - Regenstrief does have the ability to conduct bidirectional data connectivity. These reports are called Clinical Value Reports. Vaccine status is under consideration to be added to those reports. In addition, when a clinician logs in to the HIE, they are able to see if their patient has been vaccinated.
- Data for breakthrough infection broken out by time since vaccination?
    - Yes! They are looking at partial and full vaccine efficacy in the patient population.
- Are there any limitations on use of the vaccine registry data? Under what authority can those data be used by CDC? Could the data be used by others (e.g., manufacturers) for research with proper agreements? State policies commonly limit use of immunization data, interested in how those barriers were handled.

- The data is placed in the HIE for patient care purposes. Regenstrief is the broker in dealing with the data sets. The datasets will be de-identified and limited data research.
- Can you link the vaccination data to the clinical data of each individual? Can you link the clinical data to viral variants?
  - Yes, this is person-level matching.
- Are you examining differences between the different vaccines?
  - Yes, Regenstrief is able to identify which manufacturer is administered.
- How does INPC differentiate between IIS data sharing/usage policy for public health vs. research use cases? How does tokenization and de-identification fit into that picture? What is your impression of how that varies with other states?
  - There are not many states that have a statewide HIE and an institute to conduct analysis with. Therefore, how it varies within the state is unknown.
- Can you connect V-Safe or VAERS cases in Indiana to get a denominator for AE reports?
  - It is feasible as long as there is enough information to connect. They will work with the state department to address this.

Assessing Vaccine Effectiveness: Israel's Case Study (Dr. Ran Balicer, Clalit Health Services, Israel)

Since Israel is using a digitized system, researchers are able to use integrated data to answer a wide array of public health questions such as vaccine effectiveness. There were three waves of COVID-19 in Israel. 90% of the infections during the third wave consisted of the B117 (UK Strain) virus. This changed their pubic health response since the standard public health response implemented during the first and second wave did not respond to lowering the rate of COVID-19. Their vaccination campaign began December 20, 2020 where they were vaccinating 2.5% of their population per day. They have vaccinated 40% of the population thus far allowing for the researchers to analyze vaccine effectiveness. With the vaccines being administered, the number of COVID-19 cases have declined significantly even with the B117 variant cases increasing.

With the Polack, et al. randomized control trail showing that the Pfizer/BioNTech vaccine has an efficacy of 95%, the researchers knew that in the real world, the efficacy of the vaccine will be lower. However, they also knew that the vaccine effectiveness may be more important than analyzing the efficacy of the vaccine. Therefore, they emulated a target trial where they did everything to make their retrospective analysis mimic a randomized control trial. In this methodology, researchers need to account for biases and confounding variables that may be in effect in the data otherwise the conclusions made will be misleading. During the target trial, they noticed baseline difference, vaccinated characteristics changed over time, infection rate changed over time, informative censoring, and indirect effects.

In their published real-world study, they had 600,000 vaccinated individuals matched perfectly with 600,000 unvaccinated individuals. They conducted rolling follow up. In the first round of data, they saw 94% reduction in the symptomatic infections and 92% reduction in illness. They distinguished this between the different number of doses of the vaccine. In the second round of the publication and data collection, they saw a 96% reduction in symptomatic infection and 95% reduction in severe illness. Additionally, from their data they saw that the effectiveness between the different age groups, the effectiveness was equal. However, under different comorbidities, there were a significant reduction in symptomatic infection (80% reduction in symptomatic infections among CHD/CKD patients).

Due to these data, they have updated their public health guidelines. To go into restaurant, people have to have a Green Pass vaccination certificate app which indicates either that the person is vaccinated,

had a past infection, or had a negative test result. Their infection rate as dropped to 50 cases per day, approximately 5 severe cases, and mortality rate is 0-1 per day. Through their breakthrough variant study, they saw a high proportion of the South African variant (B1351). This shows that the vaccine effectiveness might be lower.

Questions and Answers:

- In the early cohort, were the reductions observed comparing fully vaccinated (2 doses) and no vaccination; or was it at least 1 dose?
    - It was a rolling cohort follow up. Everyone from the first dose was followed up. The Kaplan-Meier curves are from the first dose. However, it does include individuals, after first and second dose also.
- Which is the penetration of the new Indian variant in Israel?
    - There have been several dozen cases. The researchers are keeping a close watch however, it is difficult to monitor cases that have a low incidence rate.
- With the completeness and granularity of your data, have you noticed any effects of long-COVID emerging?
    - This is something the researchers are working on.

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

Next Meeting: Thursday, May 20, 2021 12-1 pm ET