

COVID-19 Evidence Accelerator Collaborative

Lab Meeting #5

Thursday, May 14, 2020, 3:00-4:00 pm ET

Call Summary

Introduction to Lab Meeting 5

The theme for this week's lab meeting was "hard things are hard, but they are worth doing." Thoughtful approaches to the collection of data, design of studies, and interpretation of results garnered using real-world data is always important. This is particularly vital right now since there is currently no standard operating procedure for how to optimally operationalize the use RWD for COVID-19. Two presentations given at the lab meeting demonstrate how to thoughtfully design studies while moving rapidly to answer critical questions:

1. Presentation on COVID-19 Updates from the FDA Sentinel Initiative
 - a. Assessing Natural History, Drug Use and Treatment Impact for COVID-19 in the Sentinel System (Robert Ball, FDA)
 - b. TriNetX and COVID-19: Coding, Data, and Outcomes (Jennifer Stacey, TriNetX)
 - c. Translating Early Observations to Scalable RWD/RWE (Jeff Brown, Harvard Medical School and Harvard Pilgrim Health Care Institute)
2. Presentation on COVID-19 in the Cancer Population from the Syapse Learning Health Network (Jon Hirsch & Thomas Brown, Syapse)

The Accelerator hopes to draw learnings from and build off these approaches in its parallel analysis workstream.

Lab Meeting Presentations

Presentation on COVID-19 Updates from the FDA Sentinel Initiative

Assessing Natural History, Drug Use and Treatment Impact for COVID-19 in the Sentinel System

- The Sentinel System was launched in 2008 in response to the FDA Amendments Act of 2007 and is the FDA's premier real-world data system which historically has been used to monitor drug safety. This system can also be used to observe changes in how drugs are being used and to predict drug shortages.
- During the COVID-19 pandemic, the FDA is utilizing the Sentinel system to:
 - Monitor for shortages of drugs used for treatment of COVID-19 and its complications in hospitalized patients. The goal of this project is to set up sequential drug monitoring capability with an emphasis on in-hospital (especially critical care) drugs in up to 20 data partners for drug use data for 60 priority drugs by state and week.
 - Construct COVID-19 natural history cohorts which will be used to improve understanding of the characteristics and outcomes of COVID-19 patients.

- To aid interpretation of, or as an external control for, single-arm trials
 - To serve as a basis for creating cohorts for studies of impact of drug use on COVID-19 outcomes
- Cohorts currently of interest include:
 - Cohort of hospitalized patients to study drug treatment impact (e.g. hydroxychloroquine)
 - Cohort of hospitalized patients using certain drugs chronically to evaluate whether use of these drugs predict COVID-19 outcomes (e.g. ACE inhibitors)
 - Subcohorts with unique characteristics (e.g. cancer patients)

TriNetX and COVID-19: Coding, Data, and Outcomes

- TriNetX is a company known for fresh electronic medical record (EMR) data on global status that was originally established for clinical trial optimization but has shifted to include real-world studies. TriNetX has partnered with the FDA Sentinel Initiative for the construct of a natural history cohort whose data can be queried interactively in real-time to investigate COVID-19 treatment, natural history, medical care use, and outcomes.
- TriNetX data most often comes from a health care organization's data warehouse, but additional data is also garnered from third party sources. This data is mapped to a common data model.
- TriNetX began with initial query logic based off of diagnostic codes for the identification of patients 12-years or older with COVID-19 receiving inpatient care and produced a cohort of 580 patients. From this cohort, TriNetX ran analyses to see what percentage of patients were receiving mechanical ventilation, supplemental oxygen, and dialysis care.
- At first, it was observed that only ~ 3% of patients were identified as having received supplemental oxygen and ~ 15% were on mechanical ventilation. Upon further investigation, it was concluded that supplemental oxygen may not be coded in a patient's EMR accurately and/or in a structured manner:
 - Initial query did not include non-invasive ventilation codes (e.g. CPAP) for supplemental O₂ as they don't specify if an oxygen condenser was used or not, but making the assumption along with additional codes increased patients on O₂ from ~3% to ~5% of cohort
 - Adding hypoxia is another consideration. While not specifically stating O₂ was administered, when added to the query it indicated that 25% of patients in the cohort were in need of supplemental O₂.
- **Reality of RWD may be that oxygen supplementation may be noted in the patient's chart instead of being coded, especially if it's not a long-term supplement—RWD is not perfect and requires thoughtful consideration.**

Key Points Raised in WebEx Chat

- The timing heuristics of ventilation, supplemental oxygen, and confirmed COVID-19 diagnosis are unusual. Inpatient admission status could be used as the index event to measure an outcome such as supplemental oxygen or ventilation instead of the COVID-19 diagnosis.
- Initial pre-paralytic oxygen is likely not captured.

Translating Early Observations to Scalable RWD/RWE

- As demonstrated by looking across studies, factors such as stratifying by different covariates or adjusting the time frame used will alter the results we observe.
- COVID-19 creates a perfect storm for the promise and perils of real-world data.
- Rapid and real-time information versus definitive studies.
- Inpatient EMRs were the initial focus but registries and ambulatory EMRs are now contributing information.
- The utilization of real-world data sources for answering COVID-19 questions is akin to piecing together a puzzle:
 - At first, it is hard to see all the puzzle pieces or to know what is missing
 - Gathering data quickly is akin to organizing the pieces
 - Current information helps us to ask better questions
 - Flexibility and transparency are critical for understanding what was done
- **Analysis with RWD occurs in phases. The focus now is on rapid, iterative analysis with fresh data to organize the pieces. The focus now is on transparency, without which we are blind-sided. The next phase will be to refine data quality, methods and questions.**
- **Formal analyses should focus on matching the right data to the right methods to the intended use**

Presentation on COVID-19 in the Cancer Population from the Syapse Learning Health Network

- Syapse leveraged its Learning Health Network to gain a better understanding of how the COVID-19 pandemic is impacting cancer patients. Work from this partnership is considered a preliminary analysis and ongoing work is needed.
- Several objectives for this work were outlined:
 - Characterize the population via description of select clinical and demographic characteristics
 - Describe outcomes of interest including hospitalizations, ventilation support, and mortality
 - Explore potential risk determinants for COVID-19 severity including tumor site, comorbidities, etc.
- Several initial observations came out of this work:
 - Cancer patients (overall and with COVID-19) were skewed toward females in this population
 - Overrepresentation of Black or African American individuals in COVID-19 cohort relative to population representation in the Detroit metropolitan area
 - Overrepresentation of low-income individuals in COVID-19 impacted population relative to overall cancer cohort.
 - Younger patients had a higher rate of hospitalization than prior reported studies.
 - A majority of patients were admitted to the hospital within each solid tumor group.
 - Patients with active cancer were more likely to receive mechanical ventilation support.
 - Rate of mechanical ventilation flat across age groups.
 - A significant portion of patients received HCQ after COVID-19 diagnosis.

Key Points Raised in WebEx Chat

- A conceptual framework could be useful for determining a priori whether certain research questions are more or less likely to be answered using RWD.
- The level of tolerance for a “trial and error” approach for this determination may differ given the different consequences for different questions and contexts.