COVID-19 Evidence Accelerator Collaborative

Lab Meeting 54

Thursday, July 22nd, 2022, 3 - 4:00 pm ET

Call Summary

Overview of Lab Meeting 54

Lab Meeting 54 consisted of three presentations. First, Dr. Alecia Clary, consultant to the Reagan-Udall Foundation for the FDA, announced new data partners and their research questions. Next, the joint ISPE-FDA Foundation Editorial Committee provided an overview of the COVID-19 Real-World Evidence (RWE) Primer which is a new resource with guidance on using and designing RWD studies. Finally, Dr. Emily O'Brien of the Duke Clinical Research Institute discussed objectives and findings from the National Patient-Centered Clinical Research Network's (PCORnet) HERO Study.

Therapeutics & Vaccines Research Questions

Dr. Alecia Clary, consultant to the Reagan-Udall Foundation for the FDA

Grantee Announcement Research & Research Questions

- Komodo Health will examine the utilization of monoclonal antibodies as an outpatient treatment for individuals with COVID-19
- TriNetX will examine 1) the incidence of breakthrough infections in patients who have been vaccinated and treated on an outpatient basis and 2) characteristics of patients hospitalized with COVID-19 post-vaccination

COVID-19 Real-World Evidence (RWE) Primer: Campside Chat with the Authors

Joint ISPE-FDA Foundation Editorial Committee

The global response to the COVID-19 pandemic required the conduct of rigorous studies on the safety and effectiveness of diagnostics, drug repurposing, and novel therapies and vaccines in near real time. Given this need for rapid evidence generation using existing data sources, there was an emphasis on the importance of careful design and methodological approaches to support causal inferences in real-world data (RWD) studies to guide clinical and regulatory decision making. The editorial committee and chapter authors collaborated to create the COVID-19 RWE Primer to learn from evolving lessons of addressing the COVID-19 pandemic and bolster the future use of RWE.

The COVID-19 RWE Primer will be available to read and download for free on the Evidence Accelerator website early in the fall.

Chapter 1: Overview of RWE

- Key definitions and types of RWD
- Overview of key questions, common terms, key considerations (data linkages, data governance, etc.) for using RWD

- Unique considerations for using administrative data/electronic health record data to answer questions related to COVID

Chapter 2: Overview of Methods in RWE Generation – Study Design

- RCTs are not always feasible/ethical/timely for answering safety/effectiveness questions
- Chapter focuses on observational studies using best pharmacoepidemiologic practices to answer these questions
    - Target trial paradigm, between-person designs, within-person design, descriptive design
    - How each is used and what questions can be answered using each

Chapter 3: Methods in RWE Generation – Sources of Error

- Confounding, selection bias, immortal time bias, misclassification, missing data
- What each looks like in practice, why each is a problem, and how to handle them

Chapter 4: Examples of COVID-19 RWE Studies

- Target trial emulation, cohort studies, case-control studies, self-controlled case series studies, drug utilization studies, diagnostic test utilization studies
- Takes these examples and types of data and provides examples that are directly applicable to public health

Chapter 5: Major Multi-Stakeholder Initiatives – Defining the Future of COVID-19 Observational Research

- Overview of partnerships that provided data and helped answer questions using RWE throughout the pandemic
- Discusses the ways in which this global public health emergency altered the way we approach RWD and how it is used to generate RWE

Chapter 6: The COVID-19 Evidence Accelerator

- Overview of the COVID-19 Evidence Accelerator, analyses, workstreams, etc.

Chapter 7: Communicating about RWE

- Where to publish findings
- Tips for developing a communication plan and how to message findings from RWD studies – particularly amid a lot of misinformation

<u>The HERO Platform as a Living Registry and Vaccine Safety Surveillance System</u>

Dr. Emily O'Brien, Duke Clinical Research Institute

The National Patient-Centered Clinical Research Network (PCORnet)

- When COVID began in March 2020, PCORnet was research ready thanks to prior investments
- The Patient-Centered Outcomes Research Institute (PCORI) funded the Healthcare Worker Exposure Response & Outcomes (HERO) program to help address unanswered questions related to COVID & its impact on individuals working in, and affiliated with, healthcare

The HERO Program

- User-friendly online platform for healthcare workers (HCWs), their families & communities.
- Opportunities to contribute to research by answering short surveys, signing up to participate in future clinical trials, and share problems to address/questions to answer through research.

- **HERO Registry** – 55k+ members sharing their experiences through surveys on PPE, childcare, burnout, moral injury, vaccine hesitancy, and PASC
- **HERO HCQ** – 1.3k+ HERO members randomized to hydroxychloroquine (HCQ) or placebo to determine protective benefit against COVID-19 infection
- **HERO Together** – 20k+ HERO members who received a COVID-19 vaccination and report on safety for two years following, provided FDA with the earliest safety reports

HERO Registry

- **Objectives**
  - Create a virtual community of diverse adult HCWs
  - Establish research-ready community interested in engaging in upcoming research studies
  - Create a dataset of health-related measurements, risk factors, & outcomes
  - Share information about the HCW experience during COVID-19
- **Members**
  - 68% HCWs (mostly nurses, administrative/research staff, and physicians), 11% members of a healthcare worker's household
  - 21% community members of healthcare workers
- **Engagement**
  - Conducted "hot topic" surveys to capture participant perspectives of pressing issues
  - Example: "Intent to Leave Healthcare" Hot Topic Survey
    - Conducted in May 2021 and December 2021
    - % considering/planning to leave healthcare increased by 12% during this time
    - In December, more than 66% of nurses and 50% of physicians were considering/planning to leave or had already left
    - Major drivers behind leaving were burnout (74%), lack of appreciation from employer (50%) and lack of mental/emotional support from employer (36%)
  - Share results from research/surveys with members and with the broader public

Site-less Vaccine Safety Surveillance (HERO Together)

- **Primary objective:** estimate the real-world incidence of safety events of interest and other clinically significant events among vaccinated individuals.
- **Secondary objective:** Evaluate whether the vaccine recipients experience increased risk of events. Estimate rates of events among sub cohorts (e.g., pregnant women, immunocompromised, and stratified by age).
- **Community Pharmacy Campaign Effect in Reaching Broader Population:** Partnerships resulted in meaningful improvements in representation of Black and Latinx populations in PCORnet
- **Primary Safety Analysis Population (n=9513):** 36.6 median years old, 68.7% female, 65.9% white, 74.9% non-Hispanic or Latinx, median 3 days since first vaccine dose at enrollment
- Participants self-reported events which were reviewed and included if they met an event definition
- Top 4 Adjudicated Event Rates (per 1000 person-years)
  - All-Cause Hospitalization = 14.65
  - Any Adverse Event of Special Interest = 11.51
  - Arthritis/arthralgia = 5.02

- Non-anaphylactic allergic reaction = 2.09

Key Takeaways

- The HERO Registry offers a mechanism to understand the impact of the pandemic on a large number of HCWs and their families/communities over time
- Hot Topic polls offer flexibility in addressing emerging topics of interest
- Multimodal communication enhances engagement
- Post-vaccination AE rates have been low – the most common events included non-hospitalized arthritis/arthralgia and non-anaphylactic allergic reaction