



COVID-19 Evidence Accelerator Collaborative

Lab Meeting #18

Thursday, September 3, 2020, 3:00-4:00 pm ET

Call Summary

Introduction to Lab Meeting 18

The theme of this week's lab meeting was "Real World Data – What is it good for?" Presentations and discussion focused on uses of Real World Data and Evidence (RWD/E) in the context of COVID-19. Following discussion led by Peter Pitts (Center for Medicine in Public Interest) on More Comprehensive Use of Validated, Structured and Meaningful Data from Different Sources, two capabilities presentations were given on the following topics:

1. Smart Pharmacovigilance Tools – Brian Overstreet (Advera Health Analytics)
2. Open Access Data Resources for COVID-19 Research -- Niall Brennan (HCCI) and Jason LaBonte (Datavant)

RWD/E Presentation & Panel Discussion

Introduction to Topic: What does "Real World Victory" Look Like?

- **Real World Data** – Broadly defined as information collected that goes beyond data normally obtained through Phase 3 clinical trials.
- **Real World Evidence** – Evidence derived from analysis & synthesis of RWD.
 - Data are simple raw materials that alone are non-informative, whereas evidence is shaped and connotes the organization of the information to instruct a conclusion or a judgment.
- Real World Data and Evidence can be used *in addition* to data obtained through phase 3 clinical trial programs.
 - Accepting RWD/E does not mean discarding the gold standard (randomized clinical trials), but rather, it means augmenting it.
- These data are valuable because they investigate clinical, economic, *and* patient-reported outcomes.
- There is hesitation to use RWE/D because it challenges the status quo, and regulatory science for these data is still new.

- We tend to only think of using RWD for effectiveness studies. We risk debasing RWD/E because we tend to highlight “how it can’t be used,” rather than acting on “how it can be used” and the opportunities those represent.
- **Four Real World Musts:**
 1. Must reframe the need for data to answer questions as a critical task.
 2. Must broaden the types of questions being addressed.
 3. Must internalize it is not about RWE or clinical trials – it is about the *totality of evidence*.
 4. Must remember that evidence = answers not research design.

Panel Discussion

- It is important to recognize both randomized clinical trials (RCT) and RWD collection have strengths and limitations:
 - RCTs are slow and expensive.
 - RWD/E is new, there are quality issues, and it cannot alone predict safety and efficacy.
- Using the two together (RCTs and RWD), especially in times of crisis, would improve totality of evidence and help answer questions rapidly to inform action at speed.
 - Example: Using RWD to track distribution of EUA ventilators and their performance.
- RCT data collection methodology can incorporate RWD.
- RWD may be useful for looking at the long-term implications of COVID-19. Starting to collect data now on the following may help inform later action:
 - Cardiac effects
 - Cost and spending
- Our ability to understand this disease is limited which may affect our ability to evaluate therapies. Current interventions are designed for speed rather than efficacy/safety, RWD may be helpful for profiling the natural progression of the disease, how people respond to it, and what patient outcomes are.

Conclusion:

- To answer questions about COVID, we need a lot of data which can be gathered from RW and RCT/Clinical settings.
- Rather than either/or perspective of RCTs and RWD, we should shift the conversation to how can we use these data and information together to answer all the questions we have about COVID-19.

Capabilities Presentations

Pharmacovigilance Data Case Study: Emerging Even Signals with Covid-19 Therapies Smart Pharmacovigilance Tools – Advera Health Analytics

- **Pharmacovigilance** - science of detecting, assessing, and preventing adverse drug effects.
 - Limitations/Challenges of modern pharmacovigilance data:

- **Quality** – No reporting requirements, lack of data input control, potential for reporting bias
 - **Causality** -- Reporting of an AE does not prove causality. Requires access and review of case narrative which is not publicly available
 - **Incidence** -- Incidence is not calculable because not all AEs are reported.
 - Solutions:
 - **Quality** – Curating/cleaning data as much as possible.
 - **Causality** – Volume of data and validating across datasets.
 - **Incidence** – Disproportionality calculations and other statistical measures as alternative.
- **Pharmacovigilance for COVID Safety Review**
 - Using pharmacovigilance signal management systems to detect safety signals in drugs treating COVID-19.
 - Given lack of efficacy data for emerging COVID therapies, understanding the safety data becomes even more critical. All potential safety signals were listed on product labels except for 2 (embolic events for 2 potential COVID therapies)
 - Analyzed potential causality by looking at challenge and rechallenge stats as well as looking at comorbidities.
 - Reporting odds ratio (ROR), way of reporting disproportionate incidences
 - **Result (preliminary):** Remdesivir has Acute Renal Failure safety signal
 - Kidney issues associated with use of Remdesivir
 - Liver enzyme tests were off
 - All labeled issues for Remdesivir
- Although much of the attention on RWD is efficacy focused so-far, it can provide important safety data.
- Curated data and advanced analytics can accelerate the early detection of safety signals
- Pharmacovigilance data should be part of overall RWE generation

Open Access Data Resources for COVID-19 Research – Healthcare Cost Institute (HCCI) & Datavant

- Working collaboratively across industries to create an aggregated data source open to any researcher
- The group is composed of institutions donating technology services, healthcare expertise, and de-identified data
- This information can be used to help inform and combat the COVID-19 pandemic.
- Privacy principles are in place to protect the data—Access is limited to non-commercial public health and research purposes, and no data leaves the environment
- Current COVID-19 research database activity includes around 1600 registered researchers, over 130 submitted study proposals, 100 research groups conducting studies, and over 350 organization represented, include Harvard Medical school, the Yale School of Public Health, and Stanford School of Medicine
- Several studies have reported out results:

- Daily deaths during coronavirus pandemic by State
- Socioeconomic network heterogeneity and pandemic policy response
- Effects of State COVID-19 closure policy on non-COVID-19 healthcare utilization
- Many additional studies submitted by researchers are currently underway