



COVID-19 Evidence Accelerator Collaborative

Lab Meeting # 30

Thursday, April 1st, 2021 3 - 4:00 pm ET

Call Summary

Overview of Lab Meeting 30

During this week's lab meeting we heard three presentations on ongoing research in the COVID-19 space. First, Dr. Joshua Vogelstein of Johns Hopkins University provided an update on his research evaluating Alpha-1 blockers in COVID-19 patients. Next, Dr. Claire Cravero of Datavant presented on the COVID-19 Research Database which brings together data from various sources for researchers to access free of cost. Then, Jessica Federer and Dr. Mert Aral of Huma presented key learnings from their work using remote patient monitoring of COVID-19 patients in Europe and how smartphone-based apps can enable data collection. Finally, we shared the data visualization of the week which highlights the gap in the rate of vaccinations among Hispanic/Latino populations in the United States.

Alpha-1 adrenergic receptor antagonists (alpha-1 blockers) to prevent hospitalization and death from COVID-19

Dr. Joshua T. Vogelstein, Department of Biomedical Engineering, Johns Hopkins University

Disruption of self-amplifying catecholamine loop reduces cytokine release syndrome

- December 2018 study showed when mice were injected with catecholamine (key in cytokine storms) about 80% of them died.
- When mice were given an alpha-1 blocker and injected with [Lipopolysaccharide \(LPS\)](#), which promotes secretion of cytokines and about 90% of the mice survived.
- Provided information that led researchers to study alpha-1 blockers' ability to prevent cytokine storm syndrome in COVID-19 patients.

Preventing cytokine storm syndrome in COVID-19 using alpha-1 adrenergic receptor antagonists

- Alpha-1 adrenergic receptor antagonists are inexpensive, widely used among men with benign prostatic hyperplasia, generic drugs with a strong safety profile.

Alpha-1 adrenergic receptor antagonist to prevent hyperinflammation and death from lower respiratory tract infection

- Retrospective study of patients with acute respiratory distress (n=18,547) or pneumonia (n=338,674) taking any alpha-1 adrenergic receptor antagonist, Tamsulosin, or Doxazosin.
- 40-42% reduced risk for death/hyperinflammation among patients with acute respiratory distress who were taking Tamsulosin.
- 10-20% reduced risk for death/hyperinflammation among patients with pneumonia taking Doxazosin.

The Association Between A-1 Adrenergic Receptor Antagonists and In-Hospital Mortality From COVID-19

- Collaborated with the VA for data on patients.
- 80,000 male VA patients with COVID between 45-85 years old
- Collected comorbidity data including past year of medications with particular attention to alpha-1 blockers (Tamsulosin, Terazosin, Prazosin, Doxazosin, Alfuzosin, Silodosin) and mortality data
- 54-74% reduced relative risk for death among patients with COVID-19 taking Doxazosin.
- Limited because this was not a clinical trial and these people were taking a small dose of this medication. Could potentially have a greater effect when taken at higher doses.

Next Steps

- Compelling and robust results → important to do controlled trials
- New trial funding committed earlier this week

COVID-19 Research Database: Update & Common Data Schema Release

Dr. Claire Cravero, Datavant

COVID-19 Research Database

- **Goal:** Increase access to Real-World Data (RWD) to help inform response to COVID.
- **Need for an open platform for research with:**
 - Core real-world datasets (both smaller datasets with rapid data and more robust datasets from clinical trials that are slower) that can be joined in a privacy preserving manner.
 - Open, scalable technology to host data and link with additional datasets.
 - Robust governance structure to control access to datasets.

Solution: The Open Research Database Stack

- The COVID-19 Database brings together a group of companies/collaborators to provide technical assistance, manage data governance, data refreshes and loads, certify individual and linked datasets as de-identified, etc.
- Together they help ensure data is used and managed appropriately and is accessible for researchers.

Data Governance

- Robust process for governance of the database ensures all data are being used appropriately and in a privacy preserving manner.

- Researchers submit their study plan for review and it goes through a series of reviews (triage, assignment for review, scientific review) before being approved for using the database.
 - Triage – proposal is reviewed for compliance with DUAs and any conflicts to be resolved are identified.
 - Assignment for review – the Chair of the Scientific Review Committee assigns the proposal to be reviewed by a member with relevant experience and availability.
 - Scientific review – The reviewer completes a scorecard for the proposal which assesses the proposal for suitability of the data, approach and methodological rigor.
- If a proposal is not accepted, it may be resubmitted for consideration after changes have been made.

Database Statistics

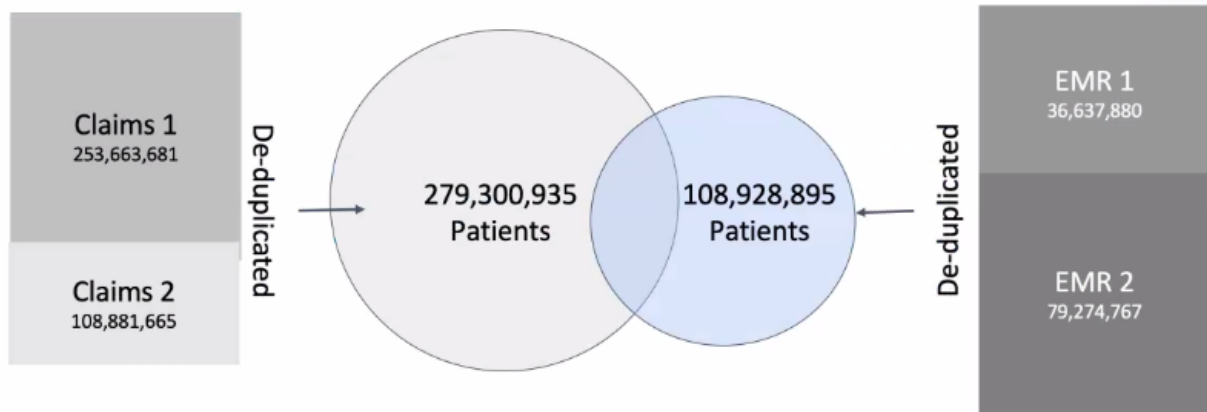
- Last time there was 5 databases and research projects.
- Now there are:
 - >2200 registrations at the website
 - >200 proposals for review
 - >150 projects ongoing
 - >400 researchers provisioned data
 - 55 public data sources (ICU capacity by state, forecasts by IHME, etc.)
 - 13 major private data sources (claims, EHR, COVID-19 metadata, health-related propensity data, disease specific datasets, life-insurance claims/mortality data, etc.)
 - \$0 cost to researchers (committed through 2021)

Outputs of the Database

- Opioids & COVID publication: Assessment of Filled Buprenorphine Prescriptions for Opioid Use Disorder During COVID-19
- Publication on the Impact of COVID on the Massachusetts Healthcare System and Considerations for Massachusetts Healthcare Policy – telehealth, pediatric behavioral health, etc.
- The Effects of School Re-openings on COVID-19 hospitalizations publication – found opening schools does not increase COVID infections that lead to hospitalization
- The Economist’s visualization/report on the risk of hospitalization and risk of death following positive COVID test in the US
- Others: COVID’s effect on healthcare utilization and mortality, effect of health insurance status on COVID mortality, surgery during the pandemic, the prevalence of hypercoagulopathy in COVID

Common Data Schema Release

- Research databased covers 316,087,395 individuals with claims or EHR data in the United States.
- Over 72 million linked patients (both claims and EHR data)
 - 790k vaccine doses recorded in linked data
 - 3.7 million COVID patients in the linked data
 - 146k COVID patients linked to mortality data (no cause of death, but have linked those that received a diagnosis for COVID to mortality data)



Next Steps

- Retrospectives: participation in landscape report, methods paper and conference abstracts to shared lessons learned.
- Researcher funding launch
- Expanding patient registries available and linked in the database
- Increase impact through research technical support and RWD education
 - Webinars
 - Documentation
 - Transparent timelines
 - Researcher technical support role

Key Learnings from Huma: International COVID-19 Deployments

Jessica Federer & Dr. Mert Aral, Huma

About Huma

- Technology company in healthcare and research
- Multiple national deployments (i.e., Germany, UK) and partnerships with other organizations.

Key Learnings

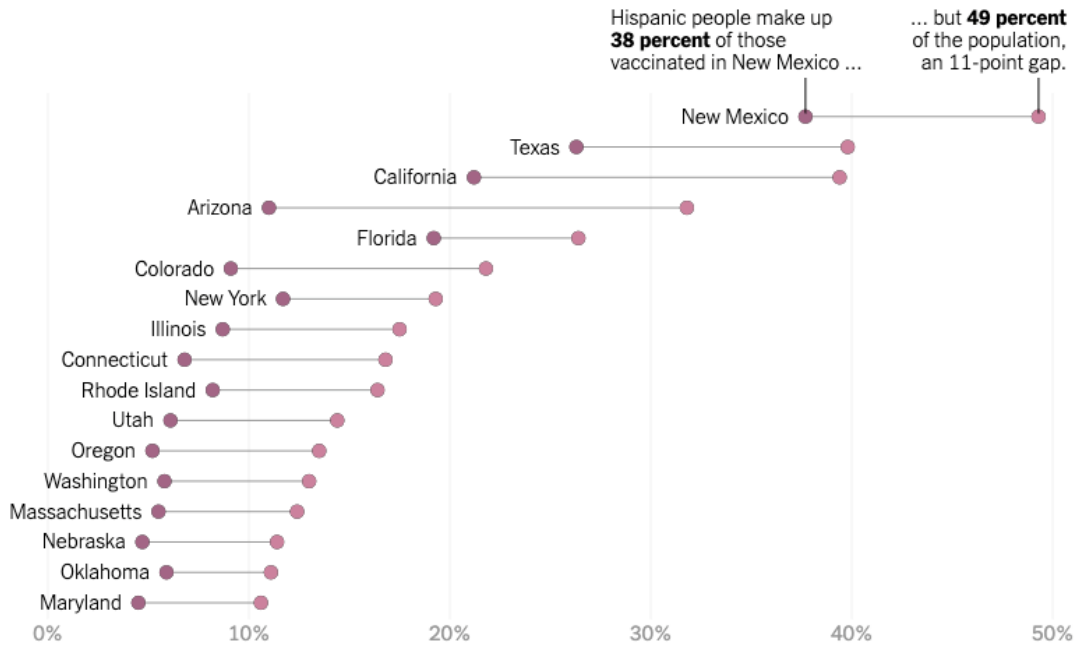
- **Learning 1: Remote patient monitoring (RPM) in a home setting can be successfully used during a pandemic**
 - Allowed hospitals to double patient capacity by monitoring patients through “virtual wards”
 - Zero mortalities reported across all monitored patients
 - Reduced hospital readmission rates (36% less likely to be readmitted when monitored by Huma)
 - Early detection and efficient reporting of adverse events
 - 90% adherence across patients 18+
- **Learning 2: Hospital at home can be rapidly & broadly scaled, but requires commitment & collaboration from all parties**
 - Currently the Live COVID-19 RPM is being deployed in Germany, UK, and UAE

- Can be deployed very quickly – 100 clinics in 1 day, deployed across countries in 3 to 4 weeks
- Technology is compatible, scalable, and requires minimal bandwidth to run the application
- **Learning 3: Phone-based apps can be utilized to optimize care of patients undergoing elective surgeries and to manage waiting lists**
 - Currently, significant backlog for patients waiting for elective surgeries in the UK. The number of patients waiting >52 weeks for elective procedures increased by over 138000% since February 2020.
 - Various phone-based apps for showing patient timelines, collecting patient reported information, tracking biometric/activity data, enabling telehealth visits, and logging symptoms can be used to address some issues related to this backlog.
 - Improved pre-operative and post-operative care
- **Learning 4: Sub-studies can be embedded into longitudinal studies in a pandemic to enable the collection of novel insights**
 - The Fenland Study
 - To investigate the interaction between environmental and genetic factors in determining type 2 diabetes, CVS, and other metabolic disorders.
 - >12500 patients participated over 15 years (2005-2020), all have thorough phenotype data on genetics collected over time
 - Combined existing data from the Fenland Study with prospectively collected digital data (through Huma) alongside bi-monthly COVID-19 testing
 - Data helping understand the natural history of COVID from pre-symptomatic to symptomatic stages, develop a pre-symptomatic model for early detection, evaluate the impact of social distances on health-related behaviors
- **Learning 5: Severity risk scores can be developed rapidly with potential to be implemented at scale digitally**
 - Developed a machine learning model using data from the collaboration with the Fenland Study
 - Results undergoing peer review for publishing in Nature Scientific Reports
 - Helped identify new risk factors for COVID
- **Learning 6: Existing mobile technology can enable site-less, investigator-less, EDC-less studies at scale**
 - Patients can complete study consent and verification, onboarding questionnaires, treatment information questionnaires, AE reporting, etc.
 - Mobile technology can also provide care plans/timelines and learning content on symptoms for patients.

Data Visualization of the Week

- In various US states, Hispanic individuals represent a lower proportion of the vaccinated population compared to the proportion of the general population they represent.
- This gap is related to the number of structural barriers Hispanic populations face when accessing healthcare and health information. (i.e. trust in providers, language barriers, technology/internet accessibility).

Known Hispanic share of the vaccinated population and of the general population



Note: The states that were included had Hispanic populations of 10 percent or more. Nevada and New Jersey were excluded because they do not report the race and ethnicity of vaccinated people, but rather of all doses given. States define race and ethnicity differently and with varying levels of completeness — in some states as much as a third of vaccinations are missing race and ethnicity data. Comparisons between states should be made with caution.