COVID-19 Evidence Accelerator Collaborative

Lab Meeting #8

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

Call Summary

Introduction to Lab Meeting 8

The theme of this week's lab meeting was "what is it like to have mild/moderate COVID-19? Describing the outpatient experience." Three presentations were given:

1. Presentation on the Behavior, Environment, And Treatments for COVID-19 (BEAT19) Preliminary Analysis: Patient-Powered Registry of People Before, During, and After COVID-19 (Mark Shapiro, xCures)
2. Presentation on Self-Reported and Passive Sensor Data to Understand Everyday Symptoms in Individuals with COVID-19 (Luca Foschini, Evidation)
3. Presentation on a Dynamic Near Real-Time Community Reporting System for COVID-19 (Nancy Dreyer, IQVIA)

The lab meeting began with a brief review of the COVID-19 Evidence Accelerator Collaborative, the workstreams the Accelerator has launched, and the Accelerator's role in the larger Real-World Data (RWD) Community. Notably, the Accelerator brings together a diverse group of health data and technology partners to advance RWD to urgently address questions about COVID-19, which is intended to overlap with those approaches being developed and utilized by stakeholders at the FDA and other government organizations.

The Accelerator does so by using a series of tools to make analyses more efficient and interpretable:

- Prioritized research questions
- Common data elements and translation tables between common data models
- Common protocol for repeated analysis of priority research questions across multiple data partners (the "parallel analysis")
- Meetings and forum for rapid cycle feedback and learning
- Individual Accelerator communities focused on specific topics (e.g., therapeutics, diagnostics)

Lab Meeting Presentations

Behavior, Environment, And Treatments for COVID-19 (BEAT19) Preliminary Analysis: Patient-Powered Registry of People Before, During, and After COVID-19

- XCures is a precision oncology company with a focus on collecting data from patients using patient-reported outcomes (PROs) to provide important insights into COVID-19.
- XCures views PROs as remote telemetry which can help augment other sources of real-world data that is typically collected from the patients care team.

- The Behavior, Environment, and Treatments for Novel Coronavirus Infection COVID-19 (BEAT19) study is a patient-powered longitudinal, observational registry enrolling anyone at risk for or with known or suspected SARS-CoVo2 infection.
- The scientific rationale for the BEAT19 study is to develop a longitudinal, observational dataset of patient-reported symptoms before, during, and after infection with COVID-19 in the community setting.
- The BEAT19 study has gone from concept to action in a rapid time period and as of June 3, all 50 states and DC are represented by 3,044 participants and 42,321 surveys.
    - Anonymized data from this study is available at: https://github.com/beat19-org/beat19-public-data
    - "Less anonymized" data is available to researchers under a MOU
- The BEAT19 patient-reported symptom domains use a standard 5-point Likert-style rating scale and include text drawn from CTCAE-PRO and DSS scales.
    - The questions were selected quickly based on validated items from scales available without a fee/license.
- The goals of the BEAT19 study are:
    - To develop a time series model for various symptoms from onset to resolution
        - To distinguish between symptoms associated with early and late onsets
    - To measure the relative symptom burden (severity and duration) across symptoms
        - Symptom persistence
        - Symptom frequency and latent class model
    - To identify contrasting symptoms between COVID-19 positive cases and COVID-19 negative cases
- It is challenging to develop a time series model for COVID-19 because, unlike with other diseases, it is often less clear when a patient got sick. Because of the broad range of symptoms and symptom severity with COVID-19, it is clear when a patient seeks care or is tested, but not when their illness begins.
    - To adjust for this, the BEAT19 includes a time lag in its model.
- Preliminary findings from the BEAT19 study's time-averaged symptom severity model include:
    - Fatigue was cited as the most prominent symptom on the time-averaged symptom severity model of confirmed & suspected COVID-19 cases.
    - Fatigue was also the most prominent symptom on the time-averaged symptom severity model when only looking at confirmed COVID-19 cases. There was little difference between the suspected and confirmed cases.
- The BEAT19 has constructed a preliminary COVID-19 symptom severity and trajectory model using Bayesian multilevel ordered logistic regression and adjusting for symptom-level time lag and participant-level time lag.
- Preliminary findings from the BEAT19 symptom severity and trajectory model include:
    - Higher severity symptoms include fatigue, coughing, and aches
    - Lower severity symptoms include temperature, nausea, and loss-of-smell
- Future directions for BEAT19 symptom modeling:
    - Incorporate mixture model with symptom trajectories including a mixture of positive/suspected/negative cases
    - Continue examination of latent class model and trajectories

    - Examine participant-level predictors including demographic and treatment covariates to predict time-lag to care seeking and participant level effects on symptom severity/duration
- Future goals of BEAT19:
    - To provide data and model to clinical researchers looking for PRO measures/questions that capture the COVID-19 patient experience

Self-Reported and Passive Sensor Data to Understand Everyday Symptoms in Individuals with COVID-19

- Evidation measures health in everyday life and enables anyone to participate in research and health programs.
- Evidation works with biopharmaceutical companies to integrate individually-permissioned patient generated health data (PGHD), defined as wellness and/or health-related data created, recorded, or gathered by individuals for themselves (or by family members or others who care for an individual) into RWE and clinical trials.
- Evidation generates RWE through:
    - Direct-to-participant research studies
    - The use of novel data (e.g., PGHD)
    - Having established a trusted relationship with approximately 4 million individuals through a platform called Achievement. Built upon a foundation of user privacy and control over permissioned health data, this platform can be accessed by everyone and allows members to be rewarded for health activities and to participate in research studies.
- The goal of Evidation's COVID-19 work is to understand the utility of PGHD for early detection, monitoring, and management of COVID-19 in everyday life. This goal includes:
    - The quantification of the prevalence and progression of COVID-19 symptoms both inside and outside the clinic, and contextualized with those from influenza or influenza-like illnesses (ILIs)
    - An understanding of behavioral and physiological parameters measured from wearable sensors
- The study utilized data from a participatory surveillance program run on Achievement, initially including 86k participants filling out 194k surveys, and performed analyses on three cohorts:
    - COVID-19: self-reported being diagnosed with COVID-19 (N=230)
    - Pre-COVID-19 flu: self-reported being diagnosed with flu prior to SARS-Cov-2 pandemic (N=6,270)
    - Non-COVID-19 flu: self-reported being diagnosed with flu during SARS-Cov-2 pandemic (N=426)
- This study includes two kinds of PGHD:
    - Surveys about SARS-Cov-2 & influenza tests, symptoms, risk factors, in addition to , comorbidities, symptom experienced during ILI episode
    - Data passively and continuously collected from commercial wearable sensors (e.g., Fitbit, Apple Watches, Garmin, ...): total sleep time, resting heart rate, total step count

- There is a lot of work which must go into making PGHD (survey and sensor data) fit-for-use. This work includes filtering for reported information which is implausible ("impossible to happen") and filtering for a higher level of coverage and quality. See here: for a white paper on the topic: https://healthpolicy.duke.edu/publications/determining-real-world-data%E2%80%99s-fitness-use-and-role-reliability
- Preliminary results from this study demonstrate:
    - Self-reported symptoms of COVID-19 present differently from the flu
    - COVID-19 cases tended to last longer and peak later than flu and are characterized by chest pain/pressure, shortness of breath, and anosmia.
    - The fraction of elevated resting heart rate measurement collected daily from wearable devices rose significantly in the two days surrounding the onset of COVID-19 symptoms compared to a baseline period.
    - Steps lost due to COVID-19 persisted longer than flu.
    - Compared to Non-COVID-19 flu and pre-COVID-19 flu patients,
        - COVID-19 patients were more likely to seek care in an emergency room.
        - COVID-19 patients were more likely to seek care via telehealth services.
    - COVID-19 patients were more likely to be hospitalized.
- Biases and limitations of this study include:
    - This study uses a convenience sample and is not representative of the US population. Only comparisons across cohorts are immediately meaningful, anything else needs reweighting.
    - Self-reported diagnosis may be affected by lack of understanding of testing results.
    - Patients that receive tests are not representative of all COVID-19 patients, since test administration is based on symptoms.
    - Symptom reporting and wearable sensor wearing may decrease as symptom severity increases.
- The Evidence Accelerator could use findings from this work to:
    - Complement the understanding of natural history of COVID-19 prior to hospitalization
    - Explore the feasibility of integrating PGHD into RWD common data models
    - Inform the design of future COVID-19 studies (observational and interventional)
    - Follow up/re-contacting/continuous evidence generation
- Next steps for the Evidation COVID-19 work:
    - Additional data is still coming into this study (which ends in August 2020) and will be shared as a part of a consortium of biometric data for COVID-19 on Sage Bionetwork Synapse
    - Further analyses on the current data are being done, including focusing on wearables other than Fitbit and looking at more items on the survey such as risk factors.
- This study can be found at: https://www.medrxiv.org/content/10.1101/2020.05.28.20115964v1

Dynamic Near Real-Time Community Reporting System for COVID-19

- IQVIA was formed in 2016 by merger of quintiles and IMS health and includes a tremendous number of data feeds which generate a lot of information.
- The IQVIA COVID-19 Active Research Experience (CARE) Project is designed to study factors that affect symptom severity and progression. Factors of interest include:

    - Non-prescription and prescription medicines
    - Vitamins, minerals, and herbals
    - Underlying health conditions
    - Occupational and community exposure, including and COVID-19 test results
- The CARE Project studies symptom severity and progression over three month periods and is able to push out special questions for supplementary data collection.
- At the beginning of the study, participants fill out a baseline survey with no identifying information. At the end of this questionnaire, they are asked if they would like to participate in follow-up and if so, they provide contact information.
- Patients participating in follow up are surveyed two times/week for the first month and 2 times/month for months 2 and 3 to avoid burnout.

- Unique features of the CARE Project include:
    - Consented study participants provide baseline information and
        - Agree to be re-contacted for follow-up, including supplementary information, and to receive alerts for research opportunities.
        - Are asked to provide alternate contacts to facilitate follow-up, including hospitalization or mortality.
    - Using a vetted process, IQVIA generates unique encrypted tokens that support linkage of de-identified participant data with de-identified IQVIA data assets, as feasible. This serves as an opportunity to validate and extend the PGHD.
    - The agile data hub technology supports linkage with external data too, including clinical details, genomic information, wearable data, and other connected devices.
- The CARE Project is able to link to several IQVIA RWD sources, which can help provide longitudinal patient level data.
    - Within medical claims data, there are 382,000 patients with confirmed diagnosis; However, the overlap with CARE data has not yet been determined.
- CARE Project Dashboard
    - Summary of patient characteristics (n=18,717 U.S. participants)
        - Median age is 38 years (range 18 - >90 years old)
        - 67% female
        - Ethnicity: 64% white; 11% black; 5% Asian; 7% American Indian; 11% multiracial
        - 7% hospitalized at baseline survey
    - Inquiring about specific supplement:
        - ~15% report using zinc
        - ~38% report using Vitamin D
    - Major signs and symptoms reported (from highest reported to lowest reported):
        - Fever, cough, aches & pains, decreased sense of taste, fatigue, shortness of breath, sore throat
- Additional information about the CARE Project can be found at www.helpstopCOVID19.com

Discussion

- The Oncology Center of Excellence (OCE) is interested in understanding the natural history of patients who have “recovered” from COVID-19. Because many cancer therapeutics cause symptoms like fatigue, and wearables and PROs are increasingly a part of the discussion in oncology trials, an understanding of baseline symptoms in trial participants based on prior history of COVID-19 would be immensely helpful.
- It will be important for the community to continue thinking about how best the “denominators” of this population can be determined. Patterns we are seeing now may reflect testing patterns, care seeking patterns, etc., but a true understanding of the denominator would contribute greatly to our understanding of COVID-19.