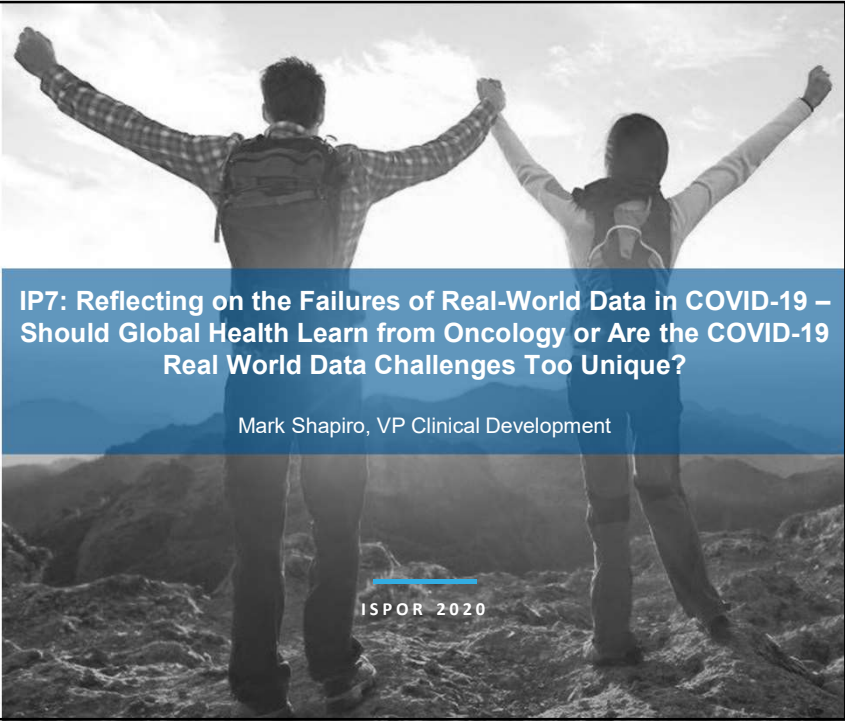




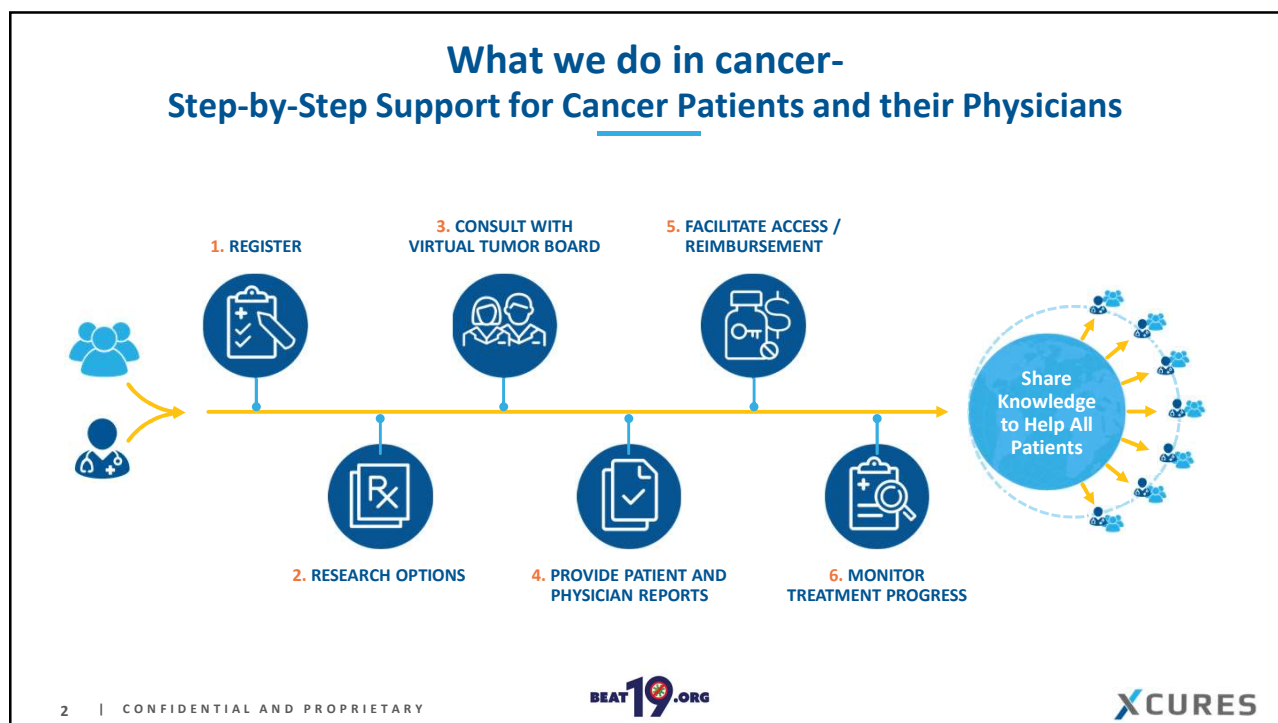



IP7: Reflecting on the Failures of Real-World Data in COVID-19 – Should Global Health Learn from Oncology or Are the COVID-19 Real World Data Challenges Too Unique?

Mark Shapiro, VP Clinical Development

ISPOR 2020

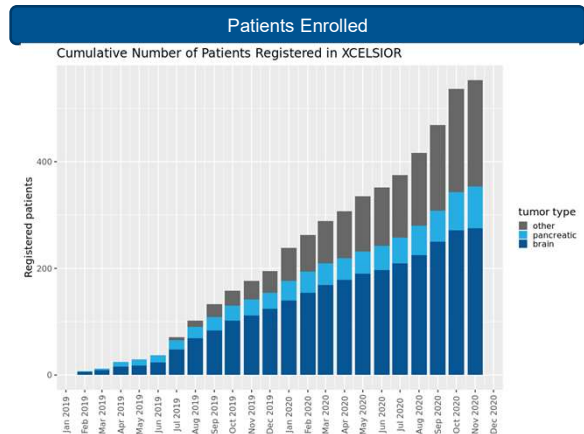
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2

XCELSIOR- A People-Powered Outcomes Registry in Cancer

- A patient-centric outcomes registry
- Data abstraction and ongoing tracking of more than 550 patients
- Complete medical records plus ePRO
- Tens of thousands of pages of medical records data collected, processed, and abstracted
- Document Classification
- Named-entity recognition
- Mapping to eCRF
- Data quality and QC



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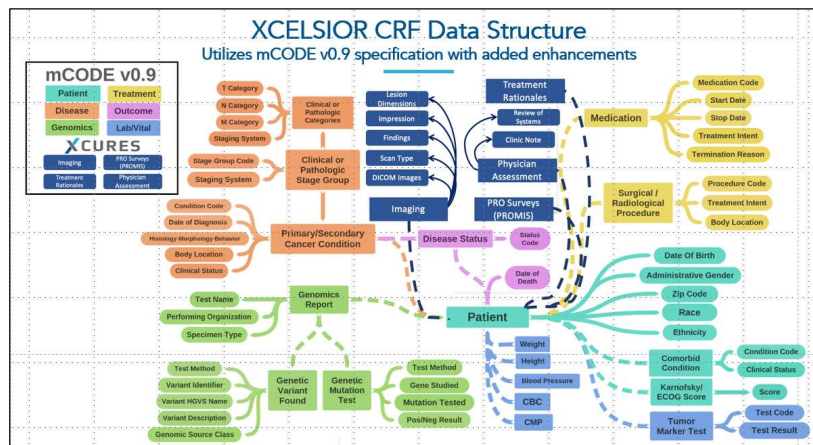
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Data Standards- Flexible, Bridging RWD (mCODE) and Clinical Trial Standards (CDISC)

- Ongoing collection of full medical records data
- Record abstraction into 21 CFR 11 compliant database
- Combines flexibility of RWD with clinical trial specific structure modeled on clinical trial standards
- Flexible eCRF with tumor-specific form variants
- Code and map to several ontologies
 - LOINC, SnOMED, NCIT, etc.



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Challenge- Design a Scientific Protocol During a Fast-moving Pandemic

- Study Design: A people-powered longitudinal, observational registry enrolling anyone at risk for or with known or suspected SARS-CoV-2 infection
- Scientific Rationale: To develop a longitudinal, observational dataset of patient-reported symptoms before, during, and after infection with COVID-19 in the community setting
 - Seemed like all focus was on hospitalized patients, but beds were filling up and we felt many people would be stuck home alone
- Study Timeline:
 - Initial Concept: March 19
 - IRB approval: March 21
 - NCT04321811: March 25
 - Website live: March 27
 - First participants enrolled: March 28
 - Current Protocol v3.1: April 20
 - EC approval in Brazil on May 26
- All 50 US states and DC represented with >5,000 participants, 108,000 surveys
- Anonymized data on GitHub: <https://github.com/beat19-org/beat19-public-data>
- **Manuscript in preparation**

5

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5

Challenge- Symptoms Assessment without Validated Scale

HEENT Symptoms

- Headache
- Loss of taste or smell
- Sore throat
- Runny nose
- Stuffy nose
- Itchy or gritty eyes
- Watery eyes
- Dizziness or vertigo

Respiratory Symptoms

- Wheezing
- Sneezing
- Cough
 - severity
 - Wet or dry cough
 - Bloody or red phlegm
- Shortness of breath

GI symptoms

- Nausea
 - Frequency
 - severity
- Vomiting
 - Frequency
 - severity
- Diarrhea

General Symptoms

- Fever
- Chills,
 - frequency
 - severity
- Body Aches/Muscle Aches
- Fatigue, Tiredness, or Lack of Energy
- Problems Sleeping

Standard 5-point Likert-style rating scales:

- Severity: none, mild, moderate, severe, very severe
- Frequency: None/never, rarely, occasionally, frequently, almost constantly

Text drawn from CTCAE-PRO and DSS scales

- Questions selected quickly based on validated items from scales available without fee/license
- **No validated scale specific for COVID-19, reported symptoms constantly changing early in pandemic**

6

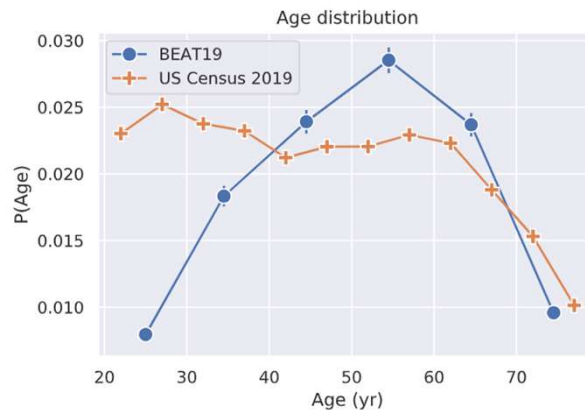
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6

Challenge- Controlling for Representativeness of Data

- Participants recruited via Social Media
- Zip code location data on participants
- Information about Zip codes
 - SES
 - Population Density
 - Prior voting behavior
- Numerous time-varying covariates examined
 - SIP orders
 - Self-reported mask-wearing
 - Cell-phone based location and proximity



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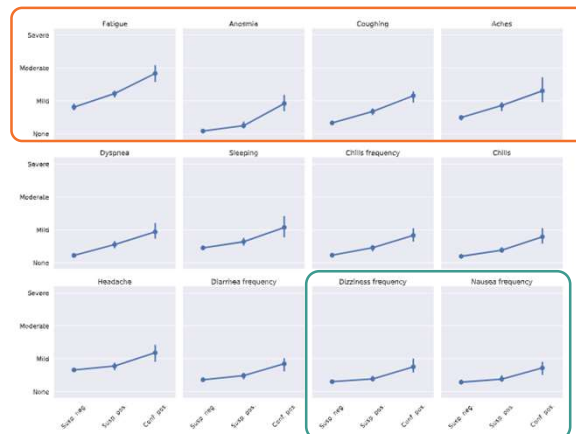
Challenge- Cohort Definitions and Causal Relationships

Need to define cohorts

- Few true negatives, many suspected negatives
- Strong testing biases early on
- Issues with test accuracy

Three cohorts defined

- Suspected Negative
- Suspected Positive
- Confirmed Positive



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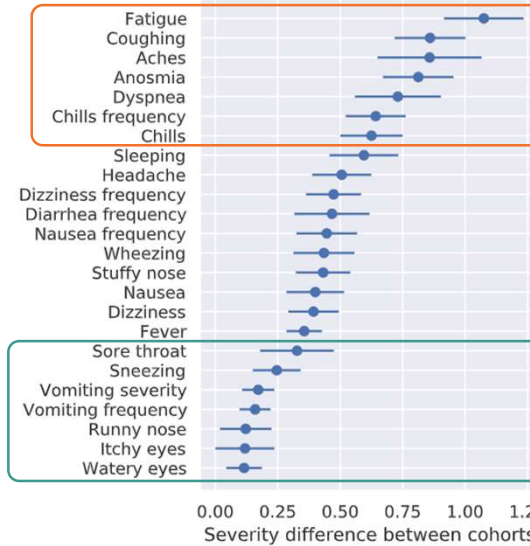
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Challenge- Causal Relationship versus Association

Clearly associated symptoms

Three cohorts defined

- Suspected Negative
- Suspected Positive
- Confirmed Positive



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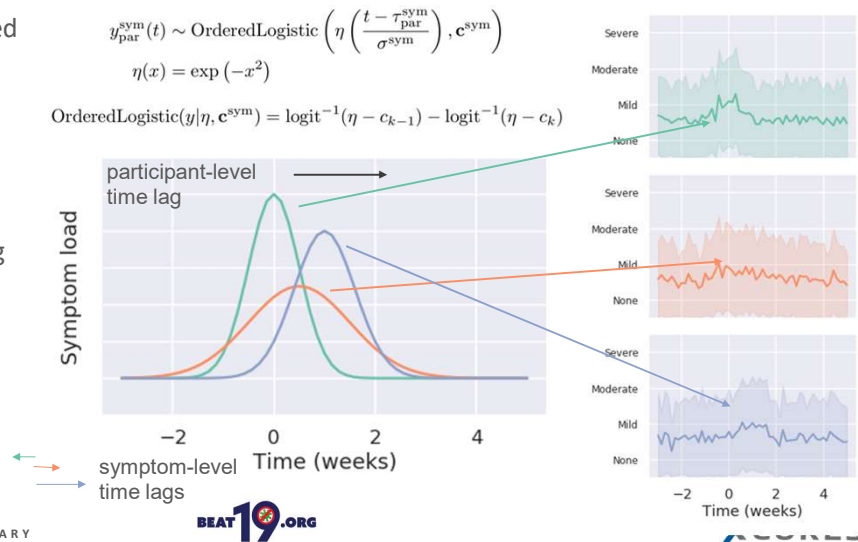
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Challenge- Time Series without Defined Start (When did someone get COVID-19?)

Lots of left- and right- censored data

Bayesian multilevel ordered logistic regression

- Symptom-level time lag
- Participant-level time lag

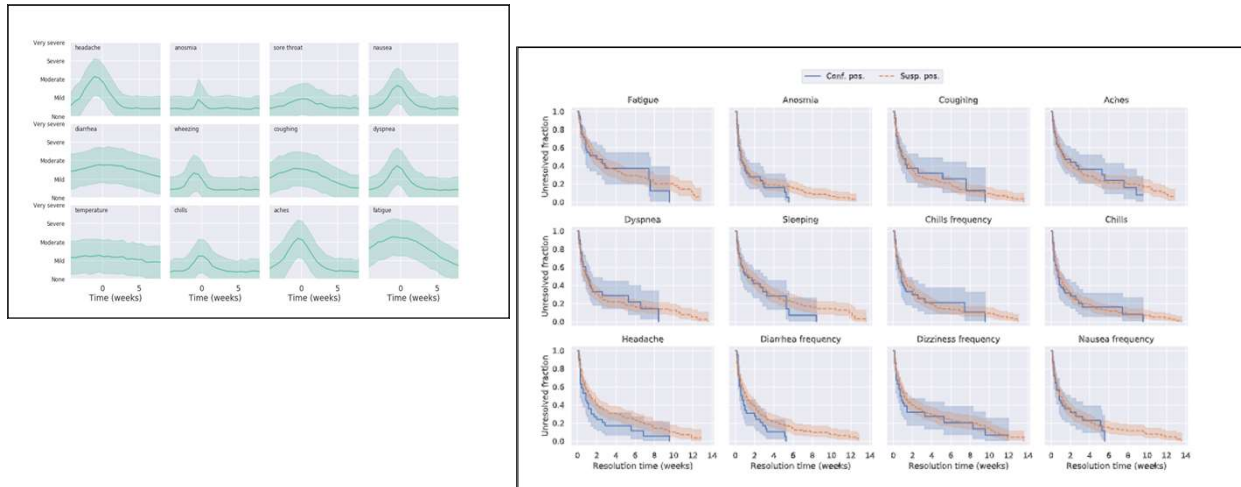


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10

Challenge- Within patient versus between group controls

Posterior predictive symptom trajectories:



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Parting thoughts

- Clinical research is typically slow, COVID-19 was FAST
 - Emergency research exceptions should be modified for pandemic response
 - More prospective RWD could help fill the gap
- Development of specialized rating scales takes time.
 - There is a need for:
 - Flexible and adaptable PROs in public domain
 - Standardized definitions of real-world endpoints
- Engage people, patients, and partners to collaborate

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