

## Randomized, Embedded, Multifactorial Adaptive Platform Trial Case Example: Evaluating Treatment Options for Community-Acquired Pneumonia

Embedding trials into health care delivery is possible. CTTI spoke with individuals from five different trials in which certain elements of the trial were embedded into clinical practice. We provide an example of one trial, [REMAP-CAP](#), below.

### TRIAL OVERVIEW

- ▶ Adaptive, randomized, open-label trial
- ▶ Number of sites (as of April 2022): ~359 (hospitals and community-based sites worldwide)
- ▶ Number of patients enrolled (as of April 2022): 11,131
- ▶ Ages eligible for study: Adult, Older Adult
- ▶ Interventions: Repurposed drugs (primarily), investigational drugs, and a biologic (convalescent plasma) for community-acquired pneumonia and in the event of a respiratory pandemic such as COVID-19
- ▶ Key outcomes/endpoints:
  - Primary: Days alive and not receiving organ support in ICU [ Time Frame: Day 21 ]
    - Primary end-point for patients with suspected or proven COVID-19 infection
  - Secondary: All-cause mortality [ Time Frame: Day 90 ]

### EMBEDDED TRIAL ELEMENTS

- ▶ Federated adaptive platform that runs on the back of an incentivized network for community participation and research (independent of an individual trial)<sup>1</sup>
- ▶ *Patient Identification & Eligibility*: Identify, enroll, and follow patients using the electronic health record (EHR)
- ▶ *Data Acquisition*: Aligned research outcomes and endpoints to data captured within routine care (appreciating the level of structured data existing and needed)

- ▶ *Evidence Integration*: Results of a diverse (representative) population are made available in close to real time and rapidly translated into clinical practice

## WORDS OF WISDOM

- ▶ Create a shared passion around the fact that knowledge generation is an arc across multiple study questions
- ▶ Ask questions that clinicians care about and allow them to feel like they are engaged in the process
- ▶ Executives at hospitals should foster a culture of research. We need to create a robust learning model that generates causal inference that we can believe in and that is actually embedded in clinical practice.
- ▶ Leverage a federated view of platform learning engines and allow for variation
- ▶ Consider clinical workflow and design the trial so that operations are integrated
- ▶ Create a robust learning model that is transparent
- ▶ Learn from models outside of research to develop the right infrastructure
  - Think modularly about an internal design that can have different protocols installed (similar to the way hardware and software are interchangeable with common protocols)
  - Commit to “product-ization” and standardization
- ▶ Develop better cooperative agreements
- ▶ Provide funding incentives
  - Tie reimbursement to clinical trial participation (as is seen in the U.K.’s National Health Service and the U.S. Veteran’s Affairs system)
  - Local funding agencies can take a position on international trials (e.g. NIH could bring a U.S. consortium into international learning networks or local funding agencies could fund a piece of an international trial)

CHALLENGES		SOLUTIONS
<b>Data</b>	Electronic health record (EHR) data elements in the U.S. are patchy and unstructured	Assessed what data elements were needed and what was present with adequate veracity in the data source (EHR)  “Spiked” the clinical care process with a collaboratively agreed upon structured intake form that aligns with clinical care and research needs
<b>Culture</b>	Current regulations (including for funding and responsibility) artificially segment studies nationally –but this is at odds with the nature of the problem and the fact that evidence is used internationally	Leverages a federated platform supported by governing bodies with an incentivized network for community participation and research  Operationalizes the trial in each place in a way that's consistent with local guidelines
<b>Process</b>	Training and certifying thousands of physicians to provide consent is difficult to scale in the U.S.	Clearly identifies research procedures and trains staff (coordinated by a central research center) to do those procedures  Provides flexibility in consenting approaches (i.e. via phone, video, etc.)

## REFERENCES:

1. Angus, D., Gordan, A., Bauchner, H. Emerging Lessons From COVID-19 for the US Clinical Research Enterprise. *JAMA*. 2021; 325(12):1159-1161.  
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