

Advancing Clinical Trials at the Point-of-Care: Integrating Research and Care Delivery to Close Critical Evidence Gaps

The Need and Opportunity for the Coalition for Advancing Clinical Trials at the Point-of-Care

Progress in addressing unmet medical needs and improving patient outcomes depends on our ability to generate robust evidence on the safety and efficacy of medical products through randomized controlled trials (RCTs). But the vast majority of patients and their providers don't participate in clinical trials. A principal reason is that it isn't easy: the conduct of clinical trials in the US has grown increasingly complex, and many trials are underpowered and not well designed to answer key questions. The result is high costs and delays in addressing key research questions, with many left unanswered or understudied.

Many of these unanswered questions involve drugs and other medical products with well understood mechanisms of action, and well-known safety profiles, which in principle should make it easier to conduct straightforward trials in frontline settings of care. For example, how effective is a drug in particular subgroups of patients? Is a drug effective in additional "off-label" indications? How does the effectiveness of alternative drugs or dosing schedules compare?

The consequences of inefficiencies and the limited value of much clinical research have been apparent in the COVID-19 pandemic. An analysis found that, of the 2610 trials of existing COVID-19 therapeutics registered on clinicaltrials.gov by December 1, 2020, only 5% had sufficient enrollment and/or other key design features that would enable the generation of definitive results about treatment efficacy.¹

Consequently, few of the studies actually conducted are likely to yield actionable evidence that could change the standard of care to combat COVID-19.² Further, only a tiny fraction of Americans diagnosed with COVID-19 have participated in clinical trials that led to actionable results.

The nation's COVID-19 response has highlighted the need for more simple, distributed trial capabilities to generate much needed evidence on the effectiveness of approved drugs for acute COVID-19 and for its long-term sequelae. Further, challenges similar to those experienced in COVID-19 trials have limited the development of key evidence for many other conditions in which there is unmet medical need. In particular, evidence generation is obstructed by a fragmented clinical trial enterprise that leaves out most health care providers and patients.

To address these challenges, we are forming the Coalition for Advancing Clinical Trials at the Point of Care. The ACT@POC coalition will drive the implementation of large-scale clinical trials to address

¹Bugin K, Woodcock J. Trends in COVID-19 therapeutic clinical trials. *Nature Reviews Drug Discovery*. 2021;20(4):254-255. doi:[10.1038/d41573-021-00037-3](https://doi.org/10.1038/d41573-021-00037-3)

² Exceptions include the US vaccine trials, which used straightforward methods of patient enrollment and follow-up, enabling large-scale participation by practicing clinicians in diverse communities across the country.

priority evidence questions in the frontline clinical settings that provide care to the vast majority of the US population. This enhanced clinical trial capacity would provide a much-needed complement to current trial networks that may be better suited for extensive research data collection on earlier-stage products, but that are often less well suited for addressing timely “real-world” research questions in diverse populations and health care settings.

The coalition will support the development of tools and resources aimed at integrating clinical research and clinical care. In particular, we expect that trial enrollment, randomization, and data collection would be streamlined relative to the requirements for participation in current trials designed for specialized settings to study products with limited evidence on safety. Building on these steps, the ACT@POC coalition will seek to enhance and boost participation in existing trial networks that support our principles, enabling a critical mass of participation by clinicians who are understandably focused on practical treatment issues and data collection that is relevant to improving patient care. The ACT@POC coalition will also help identify and enhance incipient networks in areas where current trials are inadequate and too small to answer priority researchable questions. The resulting networks may be better suited initially to assessing approved treatments where there is already a good understanding of mechanisms of action and safety profiles, or to complement academic sites that implement more complex study requirements and data collection. Over time, as the digital and other support tools improve and with more experience, we expect the range of studies involving frontline clinicians to expand.

Coalition Structure and Organizing Principles

The Coalition for Advancing Clinical Trials at the Point of Care will include health systems, community-based care organizations, health research organizations, and other collaborators to drive much more widely available and representative clinical trial participation to support rapid evidence development. The coalition will seek out the inclusion of patient groups, community hospitals and health centers, medical practices, research organizations, and biotechnology companies to identify a practical agenda and action steps to substantially augment the evidence generation capacity of the current clinical trial enterprise.

Organizing Principles

The coalition is built around the following organizing principles—

- I. Engagement of practicing clinicians in a broader range of care settings, to obtain much greater clinical trial participation so research will reflect large and diverse patient populations who are not typically able to participate in clinical research
- II. Development and adoption of tools that enable straightforward data collection from electronic data systems used to support and improve routine clinical care, to limit the burdens and maximize the benefits for frontline healthcare workers, who must carve out time during the provision of care to collect data
- III. Collaboration with clinical trial design leaders, regulators, funders, sponsors, and other stakeholders to assure that clinical trial design features are fit-for-purpose – with relatively simpler design and data collection requirements for products where mechanisms and safety issues are better understood
- IV. Enrollment of diverse trial participants through broader participation in effective frontline trials. The lack of representation in clinical trials continues to magnify health disparities. Without

sufficient representation, optimal prevention, diagnosis, and treatment decisions cannot be made.

- V. Reaching a critical mass of participation in existing and emerging platform trials in areas of unmet need (i.e. registry-based trials that assess multiple therapeutics simultaneously) to enable meaningful, large-scale trials that maximize learning from patient participation and minimize burden on participating hospitals, clinicians, and patients while collecting adequately reliable data
- VI. Expectation to improve technology supports and capabilities to conduct frontline studies over time, enabling increasingly streamlined trial participation and supporting care improvement

Coalition Actions and Deliverables

Actions

- 1. Develop tools and supports to enhance participation of practicing health care providers and community health systems in clinical trials**
 - a. Develop and implement digital tools to enable more automated and straightforward data collection, consent, and enrollment, including an adaptable common data model that can collect data from widely used electronic medical record platforms and other data sources. MITRE is strongly committed to building on their work in cancer, COVID-19, and other areas to assist the ACT@POC coalition with applying such electronic tools to simplify participation
 - b. Partner with precompetitive collaborations such as the FDA-NCATS/NIH-C-Path CURE Drug Repurposing Collaboratory (CDRC) to identify and improve trial site resources that support trial execution
 - c. Develop site readiness assessment resources to make it easier for health care providers to assess what's needed to participate in key trials (e.g., EHR interoperability, staffing, training, and pharmacy capacity as well as legal and financial review capacity)
 - d. Identify partner organizations to expedite trial-site contracting and participation

- 2. Identify, partner, and enhance promising clinical trial networks for practical trials in key clinical areas**
 - a. Engage leading potential clinical trial and platform partners to determine feasibility and funding for the coalition's initial trial activities, focusing on opportunities for greatest impact through study designs that can be implemented widely. These partners could include: **i)** Future pandemic preparedness networks (including an inpatient or outpatient practical respiratory trial network, or the network envisioned in the Federal government's future preparedness planning); **ii)** CDRC's (FDA-NCATS/NIH-C-Path CURE Drug Repurposing Collaboratory) COVID-19 network and potentially other infectious and chronic disease studies; **iii)** PCORNet's practical platform for cardiovascular studies and simple chronic drug trials (e.g., the PREVENTABLE study of the impact of lipids on certain cardiovascular outcomes and dementia onset); **iv)** anticipated practical platforms for postmarket randomized studies of treatments to delay progression of Alzheimer's disease; or other networks that could be expanded.
 - b. Partner with the most promising existing and emerging research networks identified in this trial network assessment

- c. Support the development and implementation of consistent platform trial features that can be used for multiple priority diseases

3. Improve coordination across existing trials and networks in the priority areas, limiting the need for new networks

- a. Partner with regulatory stakeholders as well as public and industry sponsors of research to assess priority research questions and data needs; match these needs with existing network availability and capacity
- b. Promote efficient regulatory oversight of trials, by engaging with regulators, funders, and other stakeholders including public-private partnerships to identify opportunities to reduce participation burdens resulting from regulatory compliance requirements while maintaining trial integrity and appropriate research protections
- c. Support the development of common trial design and data collection features that enable co-enrollment across multi-arm platform trials assessing multiple therapeutics

4. Implement culture change in partner health systems to increase network participation

- a. Partner with community based health care providers to understand clinician and patient motivation and needs for trial participation
- b. Partner with payers to refine incentives and supports for participation in meaningful trials (e.g. building on bonus payment for COVID-19 trial participation and other improvement incentives)
- c. Partner with payers and health system CEOs to develop plan for incentivizing adoption of electronic tools that can simplify trial participation and improve data collection quality
- d. Encourage industry participation in trial networks

Deliverables

1. Tools and resources to reduce burden of participation (e.g., automated data collection tools, site readiness and onboarding toolkit, best practice models, policies, and guidelines)
2. Recommendations and proposals for achieving broad participation by frontline providers in clinical trial networks and/or platforms to develop practical evidence that addresses key priority areas of unmet medical need (e.g., COVID-19/public health emergencies and high-burden chronic diseases)
3. A specific goal for increased health system participation in one or more clinical trial networks or platforms, alongside a parallel goal for increased participation of smaller and more diverse community health care providers

