Optimizing Clinical Trial Networks & Infrastructure

IDSA and HIVMA have developed recommendations to optimize clinical trial design for testing and therapeutics for COVID-19 as well as other existing and future infectious threats. These are intended to better balance the need for the rapid development and deployment of new therapeutics, while ensuring sufficient clinical trial data to support safe and optimal use.

Outpatient clinical trials for therapeutics can be challenging because they require large numbers of participants and a complex infrastructure to ensure participant follow-up and safety monitoring. Similar to the issues regarding safety considerations for vaccines, the risk-benefit calculus is more complicated in treatments for individuals with mild-to-moderate disease, who generally recover without intervention, as compared with therapies for patients hospitalized with severe COVID-19. Treatment for outpatients with mild disease must demonstrate meaningful clinical improvements and must be safe with few adverse effects, easy to store and administer, and scalable to both provide equitable access and demonstrate a population-level benefit for preventing disease progression. The current infrastructure of clinical trials limits the speed of innovation and makes the study of experimental treatments extremely difficult even in tertiary care academic medical centers. Safety precautions for staff add expense and complexity. In particular, therapies such as blood products that may not have much profit potential rely on federal or other non-commercial funders for development and study.

Historically, enrollment of communities of color and other underserved populations has been low in clinical trials due to multiple factors including, access limitations, concentration of studies in tertiary care academic centers, medical mistrust, racism and other forms of discrimination, and stigma. These are the populations most heavily impacted by COVID-19 and other infectious diseases epidemics and therefore must be prioritized for promising investigational therapeutics. Successful efforts should build on the progress of programs like the NIH Community Engagement Alliance (CEAL) Against COVID-19 Disparities, which expands existing community outreach by NIH-funded COVID-19 clinical trial networks, and the Rapid Acceleration of Diagnostics-Underserved Populations (RADx-UP) initiative, which focuses on hard-hit populations and aims to understand and alleviate barriers to access.

We recommend:

- Increase federal investment in research to study and develop COVID-19 outpatient treatment options, to address barriers to timely identification of infected patients for trials

and to support clinical trial engagement and outreach to those most vulnerable to COVID-19.

- Provide federal funding to maintain COVID-19 clinical trial infrastructure, including platform trials and networks such as NIAID's COVID-19 Prevention Trials Network, to streamline and incentivize research in areas of high unmet need. Provide additional funding to study COVID-19 seamless trial designs and master protocols to identify elements for future adoption. Facilitate the connection of clinical infrastructure with basic and translational researchers for the development of "personalized" markers of responses to vaccine and therapeutics.
- Increase federal investment in pragmatic trials networks, platform technologies, and research infrastructure to rapidly generate real world data and inform the development of therapies and diagnostics.
- Develop collaborations between the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Agency for Healthcare Research and Quality's (AHRQ), and the clinical research community to strengthen and improve the clinical trial infrastructure, expand funding mechanisms, and develop better analytical and predictive tools. Federally supported infrastructure should provide an integrated framework to link individuals diagnosed with COVID-19 to appropriate trials and encourage large-scale collaboration across many different types of facilities. Such an approach will increase the reach of trials of promising therapeutics to populations that are typically omitted from studies. This goal is best accomplished by performing studies on larger, more diverse populations, including in settings outside the traditional urban tertiary care academic centers, thereby increasing access to treatments for patients and the ability to gather data across a broader range of participants more rapidly.
- Support and expand the NIH Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public private partnership. NIH has committed to maintain ACTIV's inventory of clinical trial capacity within the National Center for Advancing Translational Sciences (NCATS) for future research efforts.
- Support the expansion of pragmatic trials networks (e.g., FDA Reagan Udall COVID-19 Diagnostics Evidence Accelerator, Sentinel, PCORnet, NIH Collaboratory), including networks that enroll children, to rapidly generate real world data and inform the development of therapies and diagnostics. Develop a more pragmatic trial network to reach more participants through community-based settings and run larger, simpler trials.

Outstanding Questions

- One challenge NIH faced in terms of launching research during the COVID pandemic was that seemingly high priority studies ended up competing with studies at different sites thereby limiting the ability of the US to perform studies comparable to the UK RECOVERY trial. How can IDSA work with NIAID to improve community-based research infrastructure moving forward? How can coordination with clinical ID practitioners advance these objectives and create opportunities for additional research?
- The 2020 National Action Plan for Combating Antibiotic-Resistant Bacteria calls for the creation of a network of clinical trial sites to reduce barriers to research and to establish a

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comprehensive understanding of the safety and effectiveness of new antibiotic agents in challenging clinical settings and indications. What is needed to advance this objective?

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