ACT@POC

Committed to Better Evidence and Better Care

Enhancing Integration of Clinical Research with Clinical Care: Empowering Health Systems to Lead on Evidence Generation

America is experiencing a life-threatening, backward slide in health. Overall life expectancy in the United States declined by 2.7 years from 2019 to 2021, the largest two-year drop in almost a century. Addressing this sharp decline will require health systems to lead the next wave of clinical evidence generation for improving disease outcomes.

Gaps in the US clinical research evidence generation system leave the nation vulnerable to health emergencies while also impeding its ability to efficiently produce practical, relevant evidence. Advancing point-of-care trials enables randomized trials in the real world to answer priority research questions while affording patients and providers an experience aligned with normal clinical care.

While the U.S. Food and Drug Administration (FDA) leadership has recognized challenges in the current evidence generation system, overcoming many of the hurdles to widespread use of point-of-care trials—especially for regulatory decision-making—means addressing both real and perceived policy barriers.

In November 2021, leaders of health care organizations launched the Coalition for Advancing Clinical Trials at the Point-of-Care (ACT@POC) in response to the continuing large and avoidable gaps in timely evidence to inform patient care. Today, the work of this coalition continues. In an open letter, ACT@POC's members describe our mission to support larger-scale, more efficient clinical trials. We outline ACT@POC's principles for its operational priorities, including engaging practicing clinicians in a broader range of settings for clinical research, supporting the development of digital tools, and assuring that clinical trial designs are fit for purpose to surface real-time, real-world information about the effectiveness of available therapies.

ACT@POC's recent actions to support its mission include:

- Providing technical assistance and recommendations to the Office of Science and Technology Policy, Advanced Research Projects Agency for Health, FDA and other policy leaders to advance point-of-care trial approach networks in important areas of evidence gaps
- Convening a major public workshop with health system leaders, Federal government stakeholders, frontline clinicians, and other organizations instrumental in achieving broader participation in clinical trials

- Launching Coalition working groups focused on addressing key challenges, such as regulatory barriers and data interoperability, to advance these issues and support dialogue with senior leaders throughout the health ecosystem
- Highlighting the Coalition's work in white papers and a *Health Affairs Forefront* blog

Through our work, **we have identified recommended actions for health systems to enact a culture that encourages and supports integrated clinical research at the point-of-care**. Our coalition/ACT@POC will work to advance these recommendations, develop supporting resources for other clinical research stakeholders, and launch and leverage pilot point-of-care trials to improve evidence generation systems for patients, providers, health systems, and all stakeholders.

ACT@POC Recommendations

- **Work with community leaders on research priorities** and engage with patients to foster patient trust in clinical research. Patients may be reluctant to enroll and trust the results of trials that are disconnected from the health needs of the community.[1]
- **Permit direct contact with potential research participants** to broaden awareness of and interest in clinical trial participation and enhance recruitment.[2] Health system patients already have a relationship with our providers, and patient recruitment policies can be designed to both protect privacy and expand access to trials.
- **Provide capacity and seek opportunities for external funding (e.g. from sponsors or payers) to support dedicated research time for providers** to participate in clinically relevant research, along with opportunities to investigate research questions of mutual interest.[3] Frontline providers often lack time to collect additional patient information and needed trial data as well as complete trial oversight and compliance activities. Dedicated research time should be paired with steps to simplify participation in research and streamline the ability to collect usable structured data at the point-of-care.
- **Work with legal teams to adopt a risk-proportionality framework** for indemnity agreements and Institutional Review Board (IRB) review based on considerations including the known safety data for the investigational therapeutic, the phase of the clinical trial, the unmet patient need, and the desired trial enrollment. Organizational risk management processes for research (e.g., IRB oversight, liability insurance) should be better aligned, simplified, and modularized with the risk proportional to the trial type and therapy in question.
- **Support clinical research infrastructure and digital technologies** that reduce burden on providers and create processes for generating evidence from data collected in point-of-care trials.[4] Coordination between private and public stakeholders can provide sustainable funding for real-world evidence generation.
- **Improve the interface between local and central/single IRBs** through a timely and effective process to address potential concerns while improving efficiency. Multi-site

trials that use a central or single IRB may face uncertainties around mutual decision-making between local health system IRBs and the central/single IRB.[5,6]

- **Work with trial sponsors and supporting organizations to help define staff responsibilities** and roles for engaging in research.[7] Staff providing routine care should be able to support point-of-care trials without being classified as research personnel and having the added burdens that result. Recent FDA draft guidance on decentralized trials distinguishes local health care providers from study investigators. However, additional considerations may still be needed to minimize staff and site burden. Health systems have a critical perspective to shape those considerations.
- **Establish policies that address ethical challenges** for staff supporting point-of-care research. Combining clinical research and care poses new challenges that require a rethinking of traditional research ethics. Patients and providers need clear expectations surrounding trial participation activities, including during informed consent.[8] Clear guidelines for the ethical conduct of point-of-care research can maintain and build patient trust.[1] Such ethical conduct guidelines could build off existing conflict of interest policies for providers and should not add additional burdens for them.

As health care leaders, our patient care mission demands better evidence. We are committed to this mission. Creating a culture of participation is only a first step in facilitating a necessary transformation to better integrate clinical care and clinical research, but it is a critical foundation for further progress. Better coordination and integration between care and research has the potential to close evidence gaps for patients with chronic and rare diseases as well as address key questions related to value in the provision of health care. It can also help achieve much needed increased representative enrollment in clinical trials and increased patient trust in clinical research through better engagement of their primary providers. Our goal is the formation of a learning health system that provides better care for all patients by generating practical evidence on how to improve disease outcomes that matter to patients and help reverse the downward trends in U.S. life expectancy.

Signed,

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References

1. Morain S, Kraft stephanie, Wilford B, et al. Toward Meeting the Obligation of Respect for Persons in Pragmatic Clinical Trials. *Hastings Cent Rep*. 2022;52(3):9-17.

2. McHugh KR, Swamy GK, Hernandez AF. Engaging patients throughout the health system: A landscape analysis of cold-call policies and recommendations for future policy change. *J Clin Transl Sci*. 2019;2(6):384-392. doi:10.1017/cts.2019.1

3. Tambor E, Moloney R, Greene SM. One size does not fit all: Insights for engaging FRONT-LINE clinicians in pragmatic clinical trials. *Learn Health Syst*. 2021;5(4). doi:10.1002/lrh2.10248

4. Fiore LD, Brophy M, Ferguson RE, et al. A point-of-care clinical trial comparing insulin administered using a sliding scale versus a weight-based regimen. *Clin Trials Lond Engl*. 2011;8(2):183-195. doi:10.1177/1740774511398368

5. Goldstein CE, Weijer C, Brehaut JC, et al. Ethical issues in pragmatic randomized controlled trials: a review of the recent literature identifies gaps in ethical argumentation. *BMC Med Ethics*. 2018;19(1):14. doi:10.1186/s12910-018-0253-x

6. Sugarman J, Califf RM. Ethics and Regulatory Complexities for Pragmatic Clinical Trials. *JAMA*. 2014;311(23):2381-2382. doi:10.1001/jama.2014.4164

7. *CTTI Recommendations: Embedding Clinical Trial Elements into Clinical Practice*. Clinical Trials Transformation Initiative; 2022:1-16. https://ctti-clinicaltrials.org/wp-content/uploads/2022/12/CTTI_Recommendations_Embedding_Trials_in_Clinical_Practice_December_2022.pdf

8. Fiore LD, Lavori PW. Integrating Randomized Comparative Effectiveness Research with Patient Care. *N Engl J Med*. 2016;374(22):2152-2158. doi:10.1056/NEJMra1510057