NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®

Getting the *Right* Evidence to Decision-Makers *Faster:* Insights From the NIH Pragmatic Trials Collaboratory

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This two-day workshop will explore the critical cycle of evidence generation to decision by health system leaders to implement the findings of pragmatic clinical trials (PCTs) conducted within health care systems. Pragmatic trials differ from traditional more explanatory clinical trials, as they test interventions or practices delivered in real-world settings. The NIH Pragmatic Trials Collaboratory has launched 23 PCTs that are conducted within a variety of US health care systems at over 1,000 clinical sites. One might expect that leadership in the health care systems would interpret and implement the evidence of statistical significance from these trials as anticipated during NIH's competitive review and approval process. But the reality is far more complex. Some interventions are implemented despite failure to achieve pre-specified primary outcomes, and some are not implemented despite a positive result.

Day 1 of the workshop will focus on the evidence that decision-makers use, with the critical question being: *How do we get the right information to decision-makers*? Panel 1 will highlight experience from Collaboratory studies to anchor a discussion about how health systems leaders make decisions based on evidence collected in PCTs. Panel 2 will discuss what outcomes and information are important for decision-makers. This discussion will involve how to convey this information to health care leaders, including qualitative and quantitative data (i.e., cost, burden, and systems data), data from secondary outcomes, and information about implementation and effectiveness in subsets of a clinical population. The Panel 2 discussion will also address the ability of embedded pragmatic trials to provide evidence about effectiveness in subsets of a clinical population, including underserved populations.

This issue of timeliness brings us to the topic of Day 2: *How do we develop the desired evidence as quickly as possible?* The Collaboratory currently focuses on identifying during the first year of funding whether the intervention is feasible and ethical, and to a lesser extent on whether it is possible to implement the intervention as anticipated. During the conduct of the trial, few of the PCTs have performed interim analyses of key outcomes to determine the likelihood that a trial will either achieve the desired outcome or will not do so. It is also uncommon for trials to routinely evaluate whether interventions are being delivered and uptake is sufficient to allow for testing of the hypotheses. Any of these determinations could constitute grounds for early modification of the protocol, implementation of strategies to enhance intervention fidelity, substitution of an alternative intervention, or early termination of the trial. Among the topics for discussion will be the criteria that should be considered and employed to end a study before its anticipated full term. The panel will consider whether these criteria should reflect the perspectives of a funder whose goal is to maximize the learning from a collection of trials, in addition to the perspectives of individual investigators, health care systems, payers, and delivery systems who focus on individual trials.

These considerations lead us to Panel 4: Potential structures and incentives for supporting early decisions to modify or end a particular pragmatic trial (failing fast or learning quickly and moving on). In this panel we will explore potential mechanisms that align incentives to maintain focus on accelerating the development of actionable evidence to support decision-makers. The panel will provide examples of trial designs (platform trials or factorial or adaptive design), infrastructure such as clinical trial networks, and funding mechanisms such as phased awards that require pilot implementation or vanguard site trial startup.