Endpoint Strategy in Pragmatic Trials: From Big Questions to Meaningful Outcomes
Sponsored by the National Institutes of Health
Virtual, September 8-9, 2026

This 2-day workshop will share knowledge from the NIH Pragmatic Trials Collaboratory and explore emerging issues to help advance pragmatic research that benefits providers and recipients of healthcare. The workshop will explore the factors involved in selecting endpoints and interpreting treatment effects in embedded pragmatic clinical trials (ePCTs) to best inform decision-making. A series of engaging panels will address considerations for selecting endpoints that reliably measure concepts of interest in ePCTs; influential factors in the analysis and interpretation of treatment effects; applications of multicomponent and hierarchical endpoints; and real-world examples of various endpoint strategies in ePCTs.

In 2012, the NIH Pragmatic Trials Collaboratory was developed to address issues of major public health importance by generating evidence during the delivery of routine care. To date, the NIH Collaboratory has launched 37 pragmatic trials that are conducted within healthcare systems at more than 1,400 clinical sites. Over the course of these trials, we have learned much about generating evidence capable of driving change in complex and evolving healthcare systems, including the many unique challenges and opportunities of pragmatic research.

Day 1 of the workshop will focus on selecting the endpoint strategy. An opening presentation will introduce the foundational connections between endpoints and meaningfulness, outline key concepts for endpoint selection, examine endpoint complexities encountered in the design and analysis of ePCTs, and describe differences for effectiveness and implementation trials. Panel 1 will explore considerations for choosing more distal outcomes versus more proximate outcomes. The discussion will include examples and lessons learned from endpoint selection in the NIH Pragmatic Trials. Panel 2 will define the estimand framework and its importance for pragmatic trials, address the populations of interest in ePCTs, and discuss strategies for handling intercurrent events, sharing examples of the estimand framework in the NIH Collaboratory Trials. Panel 3 will examine options for multicomponent endpoints and motivations for their use, discuss strategies for handling multiple endpoints in pain trials, and review hierarchical composite endpoints and considerations for using them.

Day 2 will focus on the meaningfulness of treatment effects. The opening presentation will outline key concepts in interpreting treatment effects and introduce statistical analysis considerations for handling complex endpoint scenarios in ePCTs. Panel 4 will explore considerations for determining when a treatment effect is large enough to be meaningful, discuss how precision and uncertainty are involved in these decisions, and assess how these decisions might differ for interpreting treatment effects for individuals versus populations. Panel 5 will identify best practices for specifying effect sizes for sample size estimation, review lessons from the NIH Collaboratory Trials in various settings, describe analysis pitfalls that can lead to misinterpretation of treatment effects, and discuss the potential for a more holistic interpretation across multiple endpoints.