NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®

Going From Zero to 100: Generating Evidence Through Pragmatic Research to Address Pressing Healthcare Issues

WORKSHOP SUMMARY

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Prepared by: NIH Pragmatic Trials Collaboratory Coordinating Center
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Executive Summary

The NIH Pragmatic Trials Collaboratory held a 2-day workshop, "Going From Zero to 100: Generating Evidence Through Pragmatic Research to Address Pressing Healthcare Issues," focusing on the preparatory actions researchers can undertake in the planning and application phase (Phase Zero) to ensure embedded pragmatic clinical trials (ePCTs) yield actionable evidence for a variety of settings. This report summarizes discussions from each workshop session.

Access the complete workshop materials and videocast recordings.

Panel 1: Phase Zero: Getting the Research Question Right

The NIH Pragmatic Trials Collaboratory has supported over 30 ePCTs conducted within healthcare systems. Over the course of these trials, it became evident that work begins well before submitting a grant application (Phase Zero). Critically, Phase Zero includes understanding how to align a research question with patient, funder, and healthcare system priorities. Panelists described the process for developing their trials and gave suggestions for research funding announcement (RFA) developers.

Panel 2: Engagement as the Cornerstone in Pragmatic Research

Panelists explored engagement with partners, including how and when researchers identify and approach front-line clinicians, patients, funders, and community partners. Methods of engagement included advisory boards, focus groups, interviews, meetings, and surveys. Panelists described challenges with engagement, including lack of funding; burden for those who participate, especially patients; and the potential for conflicting input.

Panel 3: How to Use Data From Disparate Data Systems

Panelists discussed challenges related to collecting data from disparate data systems, including the electronic health record (EHR), patient-reported outcomes, and devices. Mapping of data posed challenges, and took time and effort. Panelists noted that when collecting patient-reported outcomes, care must be taken to ensure all patients have internet connectivity.

Panel 4: Retrofitting, Reimagining, and Redesigning Healthcare Systems to Reach Populations Most Affected by Health Inequities

This session examined how researchers can help redesign health systems to make them more equitable. Panelists outlined levers for change employed in their NIH Collaboratory Trials, such as improving broadband, changing the clinical environment, and passing new legislation.

Panel 5: Overcoming Administrative Burden in Pragmatic Research

Overcoming administrative burden is a multipronged effort that involves multiple teams and work activities. One panelist shared a tool that enables all partners to quickly visualize where they are in the process as a way to detect delays and overcome them. Other helpful strategies described included repeatable processes for IRBs and data use agreements.

Introduction

The NIH Pragmatic Trials Collaboratory held a virtual workshop July 15-16, 2024, to examine the actions that researchers can take during the planning and application phase (Phase Zero) to ensure ePCTs generate evidence to drive change across diverse settings. The workshop also explored ways to overcome challenges associated with launching a trial in disparate environments, including making sense of data systems, diversifying sites, and overcoming administrative burden.

Pragmatic trials differ from traditional more explanatory clinical trials, as they test interventions or practices in real-world settings. NIH Collaboratory Trials have been conducted within a variety of US health systems and included over 1,400 clinical sites. From these trials, the program has learned about generating evidence in the context of complex and evolving healthcare systems, including the critical preparatory work that starts well before applying for research funding.

Panelists included ePCT investigators, research administrators, and leaders from the NIH Collaboratory. Access the complete workshop materials, including slides and videocast recordings.

Keynote: Connecting Lab, Clinic and Community: Communities Advancing Research Equity (CARE) for Health™

Speaker: Monica M. Bertagnolli, MD, director of the National Institutes of Health (NIH)

> "Our work at NIH is not finished when we deliver scientific discoveries, but only finished when all people are living long and healthy lives."

The new Care for Health program is designed to address the serious health problems of the nation. We still do not have the best evidence we need to make decisions with patients every day (only 7% of cancer care guidelines are from randomized controlled trials), the lifespan is declining across the nation, and the health equity gap continues to grow. One way to get more evidence is from the clinical care environment, and pragmatic trials can contribute to this effort. Primary care communities are on the frontlines of healthcare. Through the Care for Health program, NIH will connect research to primary care with a focus on practical and feasible research that can be executed in a primary care environment. The goal is to make sure that everything learned from research is rapidly and equitably adopted into clinical care.

Care for Health will create a clinical trials network that is also a learning network. As part of the network, primary care practices will be invited to participate in a long list of research protocols and can choose the studies that will have the greatest impact on the communities they serve. Importantly, the program will be sustainable, achieve longitudinal collection of data, help address health disparities, and focus on health across the entire lifespan.

Phase Zero: Getting the Research Question Right

Panelists: Kevin McLaughlin, Kushang Patel, Andrea Cheville, Gregory Simon; Moderator: Kevin Weinfurt

Panelists described how they carefully pieced together each element of their ePCT research question: population, intervention, control, outcomes, and time (PICOT). Both clinical need and feasibility were key considerations for each aspect. Researchers used existing empirical data and preliminary data from care delivery to inform their questions, and they worked in areas where they had clinical expertise and existing research partners. They had to navigate constraints such as available technology and affordability. One panelist described how they knew from experience that population-based care improvement programs were often not implemented because they were considered too expensive, so that influenced their research design.

The process starts with being excited about an idea, but it has to be translated into a hypothesis that is feasible to test. Guiding questions research teams used during the development process included:

- Where does a clinical need or challenge exist?
- What populations stand to benefit?
- What populations do we have access to?
- What can we measure?
- In what areas does our expertise and experience allow us to contribute?

Panelists emphasized the importance of crafting research questions that help decision-makers. In the case of SPOT, an alliance involving insurers, funders, researchers, and health systems was supporting the goal of addressing suicide risk, and health systems had started to focus on it in their quality and safety priorities. This created an environment ripe for ePCTs.

> "Sometimes after you think the research question is finalized and it's even been funded, it's not finalized, and you've got to go back and pull in more input."

Engaging with health systems was critical to the process for aligning research questions with healthcare system priorities and gaining access to patients, though researchers acknowledged that aligning research questions with healthcare system priorities can present both opportunities and challenges. Depending on the context of the clinical setting, an ePCT could be perceived as a threat to ongoing research.

It can also be challenging to match a research idea with available funding opportunities. On one hand, researchers want to get funded, but on the other, they have an idea about the best research question and approach. Recognizing their intervention was a big leap, one panelist made sure to apply for a funding opportunity that was asking for bold, innovative approaches.

To move their research concept forward, NOHARM built a multidisciplinary team, matured their idea, developed an approach, checked in with partners across their institution to ensure appetite and support, recognized challenges, and pushed ahead.

Nonlinear Process

Overall, researchers described the process for developing their trials as uncomfortable and nonlinear, involving false starts and a bit of serendipity. A common theme was the value of pilot work for helping to refine the research question and PICOT. For example, in NOHARM, parts of intervention and delivery strategy changed as a result of the pilot.

Panelists recognized that ePCT development is a continuous learning process requiring flexibility. The world changes over time, which is important to remember for ePCTs because they often have usual care as the comparison group. Researchers had to consider ways to prevent contamination and maintain fidelity, and these elements are resource dependent. Usual care can also vary when working with multiple healthcare systems, so researchers may need to characterize it across systems.

> "In retrospect, it's easy to make a linear story, but it was not. Every decision had ramifications for prior decisions. There was a lot of iterative and cyclical refinement of the idea."

Suggestions for RFA Developers

Panelists were asked to share thoughts on the type and format of RFAs for ePCTs. They offered the following suggestions:

- In a research portfolio, aim for a balance of some small steps (working with what is available right now) and some big steps (developing tools for the future).
- Ambiguous language can be discouraging to applicants, whereas specific language gives researchers more confidence to apply. Specific criteria and examples are especially helpful.
- When appropriate, use language about being creative, pushing the envelope, and how disruption is desired.
- Describe the type of innovation desired (eg, methods, setting, population). Everyone has their own definition of innovative.
- Indicate what level of prior evidence is required in terms of feasibility and the causal chain.
- Remind reviewers of the parameters.
- Put out multiple different types of RFAs. Have some that are very focused and others that are more open to investigator ideas.

Engagement as the Cornerstone in Pragmatic Research

Panelists: Natalia Morone, Julie Fritz, Anna Krupp, Sebastian Tong; Moderator: Gregory Simon

Several NIH Collaboratory Trials shared their experiences engaging with partners from various groups, including healthcare administrators, patients, advocates, clinicians and staff, and community members. The examples illustrated how partners can serve multiple roles and bring unique perspectives and expertise to an ePCT. Overall, panelists recognized partner contributions as critical to moving the research forward. They stressed the need for strong, trusting, longitudinal relationships, which take time to develop before a trial.

> "What's core to our engagement is longitudinal relationships—going to sites and communities and fully engaging—being open and receptive to a bidirectional way of doing research."

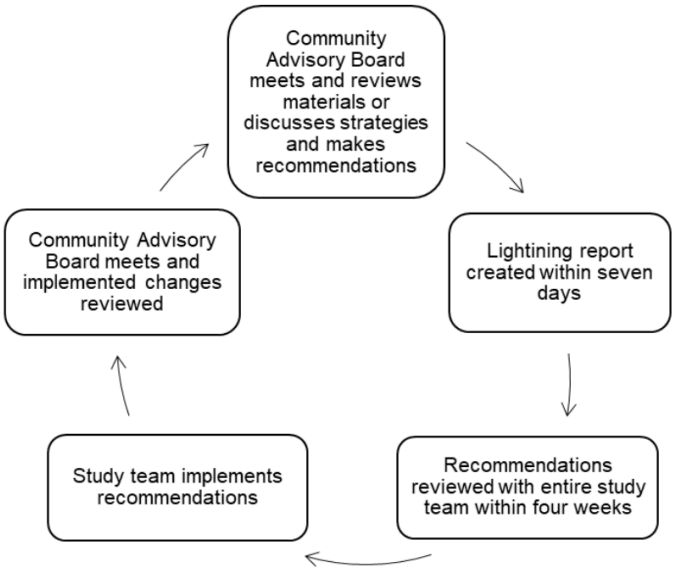
Methods of Engagement

Panelists described an array of methods for engaging research partners, including:

Advisory Boards

OPTIMUM had a community advisory board that met monthly and addressed different topics as the trial progressed. They provided feedback on patient needs, advised on the best way to engage providers and integrate the trial into the healthcare system, helped tailor recruitment methods, and played an important role in planning for dissemination and implementation after trial completion. At the outset, board members received a 2-hour training to ensure they had a clear understanding of their role. OPTIMUM used a rapid work cycle to collect and implement feedback, then follow up with the community advisory board to share the actions taken (Figure 1).

Figure 1. Community Advisory Board Rapid Work Cycle



Another panelist shared that advisory committees not specific to a single trial but instead participating across several trials could help make sure an institution or health system is not overburdening clinics or participants with research activities. The researchers discussed that while it can be beneficial to have longstanding advisory groups because of the education and familiarity needed to participate fully, it is also helpful to have some

turnover so you get new voices and perspectives. Hearing new perspectives could also be accomplished through other methods like individual interviews.

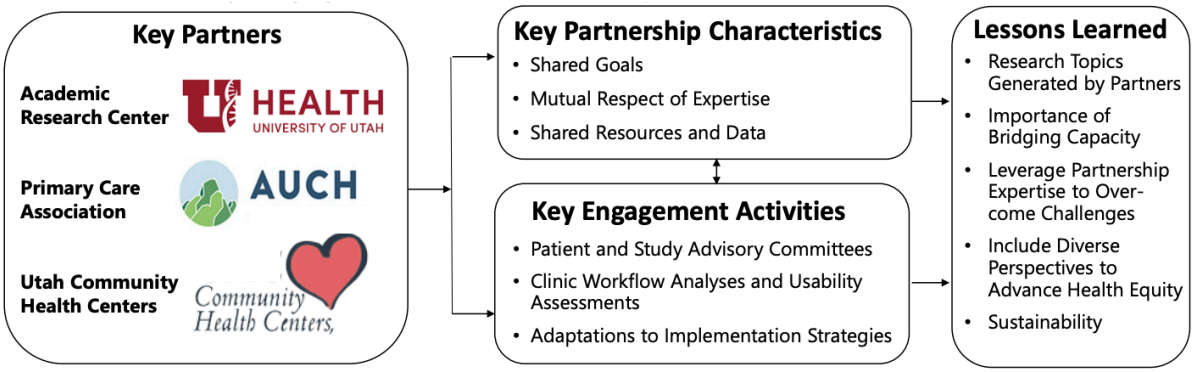
Focus Groups and Interviews

During their pilot phase, the OPTIMUM team conducted focus groups at each site to tailor the trial's implementation strategies. In addition, they conducted one-time interviews to understand barriers to integrating their intervention into primary care. They employed qualitative ethnographic interview guides to interview medical directors, advocacy group leaders, and family physicians.

Existing Partnerships

Several panelists described the ability to bring their research idea into an existing partnership model as invaluable. The BeatPain Utah team has found that engaging lower-resource, rural communities requires a consistent partnership model (Figure 2). They started by recognizing that any research topic has to reflect the priorities of the community health centers. Working together on an ongoing basis helps to build a mutual respect, and an existing relationship with a primary care association greatly benefited the trial. In their case, well-established primary care practice-based research networks do ongoing research at a number of primary care practices.

Figure 2. BeatPain Utah Partnership Model

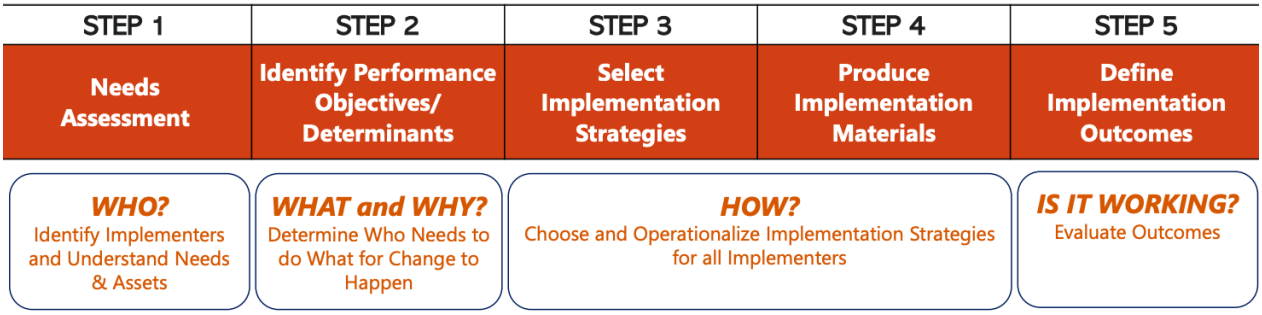


From: Schlechter et al. 2021.

Implementation Mapping

In successful ePCTs, researchers are aware of clinic workflows and aim to be minimally disruptive. The BeatPain Utah team found implementation mapping helpful to understand differences in clinic structure, learn about the nature of patient populations, and adapt implementation strategies accordingly (Figure 3). Implementation mapping is a systematic process for developing strategies to improve the implementation of evidence-based interventions in real-world settings. The BeatPain Utah team took time to understand how the research would fit into the workday of individual staff members, and this exercise revealed things that helped them modify trial processes.

Figure 3. Implementation Mapping



From: Walker et al. 2022.

Meetings

BEST-ICU found it helpful to have regular meetings between the research team and the health system to maintain buy-in at all levels, from executive leadership to unit leaders, nurse managers, and medical directors. Another suggestion was to attend sites' existing clinic meetings so researchers can hear what bothers the staff and challenges they may be facing, even when not speaking directly about the trial.

The AIM-CP trial is part of a research network that has a Steering Committee with regular meetings to guide research priorities and provide feedback on trials. The Steering Committee includes providers, pharmacists, primary care clinicians, and health system leadership. The network also hosts an annual meeting that brings together anyone representing a practice who is interested in research. Site champions can showcase quality improvement in their practices via posters. There are also collaborative small group discussions where clinicians can give feedback to investigators preparing a grant application about their study design, topic, and what aspects of the proposed trial are actually pragmatic.

Surveys

Through its research network, AIM-CP had access to a group of clinicians that have agreed to receive up to 5 surveys or qualitative interviews per year designed to help investigators get perspectives to refine or adapt their trials to primary care.

Engagement Challenges

Panelists described barriers and challenges encountered when conducting engagement for ePCTs:

Funding

While all acknowledged that engagement should begin before a trial even starts, there is often no funding mechanism for this. These activities require investigators and staff who are familiar with engagement to carry them out, along with time to build relationships—especially when engaging clinics and providers without a lot of experience in research. Yet, engagement often has to happen without any funding.

One panelist was able to fund engagement work through ongoing CTSA support at their institution. Another described a mechanism where the research network asks all funded studies that work through the network to provide a small amount of money that supports network infrastructure, including ongoing engagement.

In terms of ways NIH can better support engagement, panelists suggested:

- Providing funding for infrastructure building
- Allowing researchers adequate time to build partnerships
- Looking for community feedback being incorporated as a desired component of the grant application
- Having study review sections that include community members or other voices outside academic researchers (though there may be limitations based on regulations)

Burden

Panelists agreed on the importance of valuing partners' time by compensating them. One method is to provide compensation for each engagement activity (eg, meeting, survey). Such costs may be included with the ePCT grant, or a researcher may have access to ongoing infrastructure or support.

In addition, they cautioned that researchers need to be cognizant of the burden of various engagement activities: more isn't always better. Be efficient and attentive to the asks of the partners to avoid overburdening them. Carefully consider meeting frequency to strike a balance between keeping clinics engaged without asking for too much of their time.

Conflicting or Limited Input

Researchers sometimes receive inconsistent feedback from partner engagement, which can pose challenges. One panelist described that it helped to identify the core evidence-based components of their intervention. This allowed the research team to adapt some aspects at different sites but still have the intervention be comparable across the trial.

Panelists also discussed how to engage people who are disengaged or actively opposed to the research. Strategies suggested included conducting one-off interviews with these individuals instead of asking them to be involved in an ongoing way, asking partners who do volunteer what they hear from their colleagues, and having an intermediary or liaison so people can feel comfortable giving honest or critical feedback through a third party.

Researchers may encounter that partners or potential partners have opinions that are not evidence based and may conflict with the trial. A panelist described that, while this situation is challenging, researchers need to know all the different views because those are the people who will need to trust the trial's results for change to happen. The goal of engagement is not to settle differences of opinion but to broaden the researcher's understanding of the real-world context for the trial.

How to Use Data From Disparate Data Systems

Panelists: Elizabeth Wick, Chandra Almond, Leslie Crofford; Moderator: Keith Marsolo

The session highlighted 3 NIH Collaboratory Trials, covering the challenges of creating a single comprehensive dataset for analysis (Table). The ePCTs described relied on the EHR to varying degrees.

EHR Data

Table. EHR Challenges and Solutions in NIH Pragmatic Trials Collaboratory Trials

Trial	EHR type	Data challenge	Solution
IMPACt-LBP	EPIC and PCORnet claims data	2 of 3 sites provided EHR data in PCORnet format, with 1 site providing raw EHR data	Identified external group to map raw data to PCORnet framework, which necessitated additional data checking, increasing timelines and budget
FM-TIPS	5 different physical therapy–specific systems	Participating clinics did not have data or IT specialists, so front desk staff uploaded data	Time and effort was needed to map the data, which was delivered in many different formats
I CAN DO Surgical ACP	EPIC	Different workflows across 3 disparate healthcare systems, and risk of excessive representation from high-volume clinics	Due to the automation in the EHR, a dedicated team was needed for extracting information and close monitoring required to ensure the trial unfolded as planned

A common challenge described across trials was the impact of EHR updates, which can occur multiple times during a trial. Upgrading EHR systems during the trial can affect the operational build, requiring careful checks and change control to maintain consistency.

In some cases, data systems can influence trial design. Researchers noted that having more research data outside the EHR increased the potential for issues and meant sites needed to be more research savvy. Furthermore, choices such as linking survey data with the EHR can have implications for HIPAA and consent, which can affect recruitment. One study found one third less recruitment when there was a HIPAA authorization required with a survey.

> "We have received everything from an Excel file to a .jpg image screenshot."

In FM-TIPS, data uploads received from participating clinics were problematic. Clinics did not want to ask vendors to run reports because there is a cost. If a clinic failed to flag a research participant in the EHR, the research team had to look by hand for the record. Episodes of care were not necessarily matched. FM-TIPS advised that there is a limit to what you can do with sites who do not have professional data managers, so think about whether the data you will acquire will be worth it. In addition, it takes a long

time to build relationships with sites and maintain enthusiasm when you do something that interferes with their productivity workflow.

Patient-Reported Outcome Data

Multiple trials collected patient-reported outcomes via online surveys and described some difficulty and disparities with patient access. Some patients had to drive to the clinic or go to their local library to complete the surveys. Another trial also used a separate electronic data capture system (Redcap) in addition to the EHR.

> "Trying to find the negative of the things that did not happen is complicated."

One solution was to test trial surveys on a phone and make that an option because that is how many patients without internet access will complete them.

Data From Devices

The FM-TIPS trial included data from wearable devices, which posed its own set of challenges. The devices had to remain connected to the app and internet or data could be lost, and if patients did not follow the instructions for account setup, then it caused problems with data uploads. FM-TIPS found it vital to work with a vendor who collects data from wearables.

In summary, because each healthcare system is different, validating queries to identify the trial population and outcomes accurately is crucial. Data managers need to be integrated during all phases of an ePCT to understand the data coming from different sources and how it will be collected, extracted, and integrated into a dataset for the trial.

Retrofitting, Reimagining, and Redesigning Healthcare Systems to Reach Populations Most Affected by Health Inequities

Panelists: Diana Burgess, Eduard Vasilevskis, Gloria Coronado; Moderator: Rosa Gonzalez-Guarda

Panelists discussed how to best engage populations most affected by health inequities using examples from 3 NIH Collaboratory Trials. As the trials gained experience integrating health equity into their research, one thing that became clear is the design of healthcare systems systematically benefits certain populations. Therefore, panelists described a need to think more broadly about how to retrofit, reimagine, and redesign healthcare systems to make them more equitable.

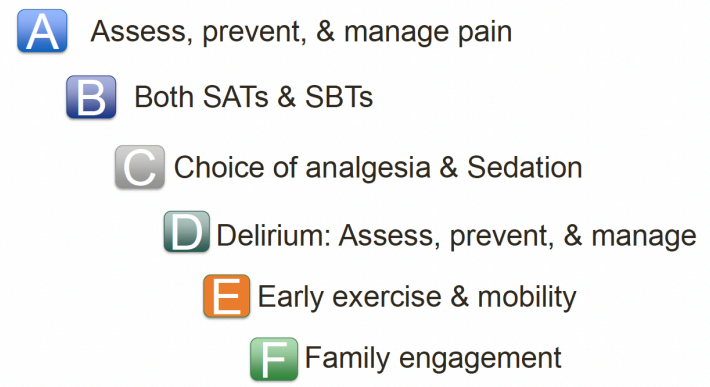
The RAMP trial is testing a scalable and integrated telehealth intervention delivered by whole health coaches to address the needs of patients and overcome existing barriers to pain care. The study includes rural-dwelling individuals within the Veterans Health Administration (VA). The team developed a Community Engagement Panel (CAP) of Veteran-Serving Organizations, with help from RAMP Veteran and patient expert consultants and referrals from participating organizations.

The investigators also formed a Veteran engagement panel consisting of 50% women and 50% from minoritized racial and ethnic groups, a range of ages (36-74), and a range of geographic locations. Veterans are considered a vulnerable population with greater physical and mental health burden than the overall population. Rural-dwelling Americans and Veterans are disproportionally affected by the dual crisis of chronic pain and opioids. While telehealth has helped increase access to services, there are problems with reliable broadband in many of these rural communities.

One way to **retrofit** the system is to build telehealth with clear processes for using resources to implement VA-approved interventions. More broadly, another way is to increase access to telehealth through subsidized broadband and equipment. To **reimagine** the problem, panelists suggested shifting the national consciousness about chronic pain prevention and treatment. To accomplish this, researchers could partner with other federal agencies to launch a national public education campaign on chronic pain and its treatment as part of a comprehensive approach that includes provider-level, payer-level, and policy-level initiatives. The **levers for change** that could help make this happen include the Broadband Equity, Access and Deployment (BEAD) program, which includes $42.45 billion in state block grant to build broadband infrastructure in unserved and underserved areas. The development of partnerships outside the VA system can also drive change.

The BEST-ICU trial aims to increase use of the ABCDEF bundle (Figure 4) in intensive care units. Each element requires coordination of care with providers and a lot of attention and effort, and thus the trial is testing real-time audit and feedback along with the use of a nurse facilitator.

Figure 4. ABCDEF Bundle

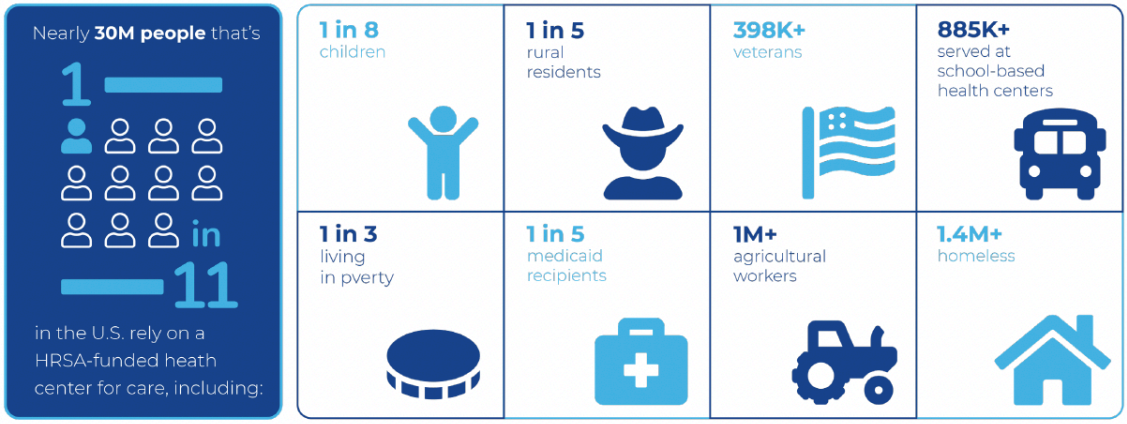


SAT, spontaneous awakening trial; SBT, spontaneous breathing trial.

BEST-ICU includes 3 geographically different safety net hospitals from different organizations that serve rural-dwelling patients. To **retrofit** the hospitals, the investigators' goal is to make the dashboard of the real-time audit visible to caregivers, which could encourage them to ask questions. Often, the ICU is not conducive for family members, so to **redesign**, hospitals can start by expanding the hours that family can visit, making comfortable spaces for family, and including family in information sharing, enabling them to be a better part of the care team for the patient.

STOP CRC was a cluster-randomized trial of 26 federally qualified health center (FQHC; Figure 5) clinics in Oregon and California to improve colorectal cancer screening. The study involved a partnership between the FQHCs, Kaiser Permanente Center for Health Research, and OCHIN, and the intervention was a mailed fecal test kit.

Figure 5. Characteristics of FQHCs



The biggest challenge the team faced was that some medical directors did not want to promote stool-based testing because patients would face out-of-pocket costs for a follow-up colonoscopy. A screening colonoscopy had no out-of-pocket costs (as part of the ACA Preventive Health Mandate). To **redesign**, the team went to their advisory board, and with the help of an Oregon State Representative, sponsored a bill that required insurance companies to cover out-of-pocket costs for follow-up colonoscopies. The bill passed into national law. To **reimagine**, they also helped make colorectal cancer screening an incentivized metric, so Medicaid health plans began to produce monthly reports on it.

In summary, the 3 trials used different levers of change to retrofit, redesign, and reimagine healthcare systems as part of their research. The levers included improving access to broadband, changing the clinical environment, and passing new legislation. There are many thoughtful ways to conduct research and reach those who experience health inequities.

Overcoming Administrative Burden in Pragmatic Research

Panelists: Karen Hartman, Geeta Swamy, Pearl O'Rourke, Keith Marsolo, Michael Kurilla, Michael Ho, Miguel Vazquez; Moderator: Adrian Hernandez

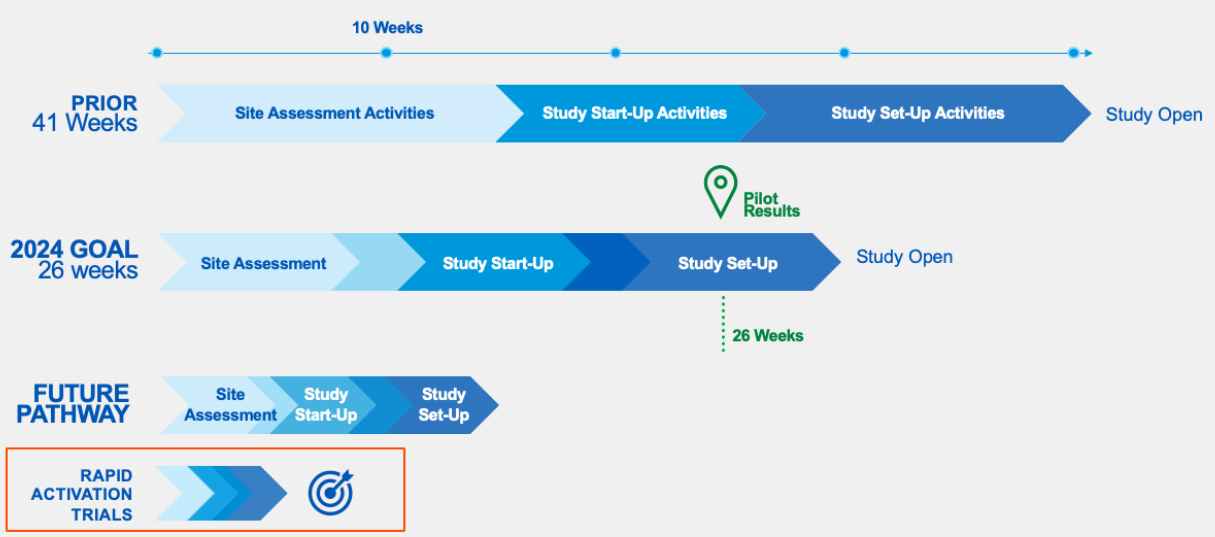
Panelists experienced with ePCTs offered ways to overcome administrative burden and shorten trial timelines. They included investigators, administrators, and people responsible for oversight of research who had developed streamlined and reuseable processes.

Administrative Startup

Trial activation is a complex process that involves workflows in and across many departments, including finance, contracts, operations, and regulatory departments. At Mayo Clinic, clinical trial activation used to take 41 weeks. The institution lacked high-level processes and standard, repeatable operating procedures.

To streamline trial startup, a team worked across all Mayo departments to identify pain points and develop a structure that would increase collaboration. Leaders and business units now meet weekly to discuss activities across the organization and identify opportunities for synergy and efficiency. This effort shortened the time for trial activation to 26 weeks (Figure 6). For high-priority areas, the group also developed "rapid activation trials," which shorten the timeline even more.

Figure 6. Accelerating the Trial Activation Process



The institutional approval process at Duke also involves numerous offices, overlapping workflows, and multiple systems. A Trial Innovation Unit was tasked with providing transparency into the process and reducing the timelines of 3 areas of trial startup:

- IRB approval
- Contract execution
- Billing

The Trial Innovation Unit partnered with process owners, investigators, research teams, and IT developers through a series of focus groups and working sessions during discovery and development. They developed a project tracking system with 2 main components:

- A metrics dashboard primarily for use by research administrators with retrospective view of data across units
- A status tracker primarily for use by study teams with status information for a trial awaiting approval

Both tools use the same defined milestones, mapped application variables, and combined data sources. Study teams and research administrators can access both tools, and the trackers show where the delays are so that teams can strategically respond.

Single IRBs

While they offer some benefits, single IRBs are not an administrative panacea. In the case of external IRB review, a formal institutional agreement is required *and is specific to reliance on the external IRB review.* All of the other organizational and institutional review processes are still required, including grants, contracts, policies, ancillary, and legal review.

Even when a single IRB is used (through a reliance agreement), the protocol must still be submitted to the local IRB office for tracking and communication purposes. While the initial review for a trial employing a single IRB may still be clunky, reliance agreements have been streamlined with SMART IRB. It enables approval of the protocol across all sites, handling of adverse events and unanticipated problems, and continuing review. Future work will include standardization and harmonization of forms and processes between institutions and better coordination between relying and reviewing institutions.

Data Use Agreements (DUAs)

Several NIH Collaboratory Trials have reported delays longer than 6 months because of DUA issues. Therefore, study teams are encouraged to start working on DUAs as soon as possible—potentially even before the protocol is finalized. Obtaining an example or template DUA can also be beneficial. Most institutions will have generic templates within their offices of research or contracts, but these may need to be modified to fit the specifics of an ePCT, which often use data collected in the EHR and through insurance claims. Institutions participating in the NIH Collaboratory have shared agreements for a specific trial when asked, but raised concerns about broad distribution.

Specific challenges that the trials have encountered include:

- Trials can enroll from private clinics, which may be part of a larger corporate chain that must sign the DUA.
- Relevant data may also be "owned" by the EHR/technology vendor, requiring a separate agreement.
- If linking trial data to external sources, each data holder may also have a separate DUA.
- Each data holder may have restrictions on how their data can be shared or further disseminated.

Collaboration with the healthcare system is key because enthusiasm of the data holder to participate in the project can also influence the time it takes to negotiate a DUA. The level of consent needed for the data requested may also affect the time it takes to get a finalized DUA. If personal health information (PHI) is involved, expect greater restrictions and scrutiny, particularly out of concern for data breaches. However, many trials that are using EHR data may be able to use a Limited Data Set, which results in fewer hurdles than with data that include PHI. Even if de-identified data are requested, institutions may have concerns if the size of the cohort is over a certain threshold (eg, 100K patients), which can have ramifications for studies of more common conditions or studies with a "usual care" observational control cohort.

If certain elements of the protocol are unworkable from the perspective of the data holder, the researcher may need to revise the trial design. It is best to have initial conversations to ensure issues are identified sooner rather than later.

Administrative Document Sharing

The IRB Reliance Exchange is a free web portal for review documentation and coordination. Over 500 institutions and 700 studies are using the portal, which streamlines the process so that "nobody has to reinvent the wheel" with administrative tasks. The Trial Innovation Network has created contract templates and research agreements that have significantly shortened timelines. Developments in electronic consent (eConsent) and are also streamlining the process. The network is in the process of developing the capability for better integration compliance with FDA requirements for data submission.

> "The Trial Innovation Network has focused on contract templates and agreements for accelerated research, which has been highly successful: times have been reduced from 55 days to 22."

Investigator Perspectives

An investigator described administrative experiences from their first NIH Collaboratory Trial (Nudge) to their second (Chat 4 Heart Health), which studied a similar intervention. They found that IRB familiarity with the first study and stability in the research team across both studies (including the NIH Project Officer) were helpful because all parties understood the logistics of the work.

They also noted that the skills required for initiating contracts for multi–health center studies are complex, and in the planning phase, it is often unclear if the trial will be funded for implementation. Thus, the health system could spend a lot of effort creating contracts for a trial that would not be implemented.

In summary, having a systematic administrative process that enables team members to quickly understand the status and causes for delays can help speed clinical trial startup. Programs that streamline IRB reliance, such as SMART IRB, can also create efficiencies, along with greater experience in ePCTs.

The complete workshop materials, including slides and videocast recordings, are available on the Living Textbook.