

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

WORKSHOP SUMMARY

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Executive Summary

The NIH Pragmatic Trials Collaboratory held a 2-day “Getting the *Right* Evidence to Decision-Makers *Faster*,” which explored the critical cycle of evidence generation by researchers to decision-making by healthcare system leaders to implement the findings of pragmatic clinical trials conducted within healthcare systems.

[Access the complete workshop materials and videocast recordings.](#)

Discussions from each workshop session are summarized below.

Panel 1: How Have Health Systems Made Decisions Based on Evidence Collected in PCTs?

In pragmatic clinical trials, the study interventions are designed to align with healthcare system priorities, infrastructure, and operations, with the goal of easing implementation during the trial and increasing the likelihood that effective interventions will be translated into practice. Yet, in the NIH Collaboratory’s experience, effective interventions are not always adopted into routine practice, and interventions that did not achieve their intended effects sometimes are. Using examples from NIH Collaboratory Demonstration Projects, panelists discussed reasons why healthcare system leaders might decide to adopt ineffective interventions, such as benefits for subgroups, improvements in secondary trial outcomes, and benefits for staff. Panelists also discussed reasons why healthcare system leaders might not elect to adopt or sustain interventions that were effective, including cost, feasibility, and alignment with policy incentives and other requirements or priorities.

Panelists: Devon Check, Vincent Mor, Lynn DeBar, Kathryn Glassberg, Douglas Zatzick, Eileen Bulger, Susan Huang, Kenneth Sands, Edward Septimus; Moderator: Gregory Simon

Panel 2: How Do We Generate the Right Evidence to Support Decision-Makers?

Researchers and healthcare system leaders who have worked on NIH Collaboratory pragmatic trials emphasized the importance of researchers being well connected to their healthcare delivery systems. Another major theme was the need to communicate usable results to healthcare system leaders, which may not always be reflected in the primary outcomes of traditional clinical trials. Panelists discussed considering composite and secondary outcomes as options during study design while still maintaining scientific rigor.

Panelists: Kenneth Sands, Eileen Bulger, Edward Septimus, Amy Kilbourne, Rosa Gonzalez-Guarda, Patrick Heagerty; Moderator: Hayden Bosworth

Panel 3: Learning Faster

A pragmatic clinical trial can provide generalizable effectiveness data about an intervention that is tested in the real-world settings where patients receive usual clinical care. These trials are at

higher risk for failure when the goals of the research and healthcare system operations are not aligned. Panelists discussed implications for data monitoring and the different expectations for fidelity and adherence that may require careful consideration of the rules for modifying or stopping the trial. Careful attention to ethical and regulatory considerations is also important, especially given the dynamic and real-world contexts of pragmatic trials.

Panelists: Gloria Coronado, Natalia Morone, Corita Grudzen, Kevin Chan, Pearl O'Rourke, Cheryl Boyce, Andrea Cook; Moderator: Kevin Weinfurt

Panel 4: Potential Structures and Incentives for Faster Learning

The NIH Collaboratory has facilitated better, faster learning by helping individual pragmatic trials be successful. The Coordinating Center infrastructure helps build relationships and bring peers together to reflect on challenges. It is these types of partnerships that are a critical element of being able to problem solve in a pragmatic trial. Researchers shared that while principal investigators may be hesitant to speak with their trial's NIH project officer, these conversations can be very productive in finding a way forward when roadblocks occur. Despite incredible efforts by investigators, studies often do not go according to plan. Rather than embracing failing faster, panelists advocated for a philosophy of learning sooner. In some cases, this may mean examining whether continuing a trial represents a good use of funding.

Panelists: David Chambers, Wynne Norton, Tisha Wiley, Kenneth Sands, Edward Septimus, Gloria Coronado, Natalia Morone, Corita Grudzen; Moderator: Richard Platt

Access the [complete workshop materials](#), including slides and videocast recordings, as well as the keynote presentation by Andrew Bindman, executive vice president and chief medical officer for Kaiser Permanente.

Introduction

The NIH Pragmatic Trials Collaboratory held a [virtual](#) workshop June 20-21, 2023, to explore the critical cycle of evidence generation to decision by health system leaders to implement the findings of pragmatic clinical trials (PCTs). 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 27 PCTs that are conducted within a variety of US health systems at over 1,000 clinical sites. One might expect that leadership in the health 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.

The workshop explored two critical questions:

- How do we get the right information to decision-makers?
- How do we develop the desired evidence as quickly as possible?

Panelists included experienced PCT investigators and leaders from the NIH Collaboratory, along with decision-makers from some of their partnering health systems. Access the [complete workshop materials](#), including slides and videocast recordings.

Keynote: Learning Health Systems—Reflections From the C-Suite

Dr. Andrew B. Bindman shared his experience as Executive Vice President and Chief Medical Officer of Kaiser Permanente. Dr. Bindman served on advisory and leadership roles for the US Health Energy and Commerce Committee, the US Department of Health and Human Services, the Agency for Healthcare Research and Quality, the California Medicaid Research Institute, and the Healthy California for all commission among many other agencies, and spent more than 30 years at the University of California San Francisco, where he practiced and taught clinical medicine while conducting research in health access and outcomes. Despite the promise of learning health systems to develop evidence, implementation of practice changes based on PCT findings remains challenging.

The barriers to implementing evidence-based care improvements include:

- Sifting through the deluge of articles and information to determine actionable steps to improving the health system is challenging, leading to a great reliance on systematic reviews or other ways of curating data externally so that it becomes manageable.

- Internally generated data are expected to be treated with the same rigor as externally generated data, creating the possibility of perceived reputational risk if the data are out of alignment with standards of care.
- Despite whether data are internally or externally generated, incorporating new activities into clinical workflows of the organization as a whole is difficult, especially when one considers the many competing demands for the time of clinicians.
- Many interventions require IT support automation and must therefore align with the priorities of the health system.

Partnerships of researchers and clinicians in real-world environments have increased the acceptance of research findings as relevant, particularly when the research is conducted locally. Additionally, meaningful advances have been made with regard to the nature of the clinical questions that are being asked from these robust partnerships. However reaching, the nonclinical audience—healthcare system leaders— is critical for addressing broader questions of how to make care more efficient, affordable, patient-centered, safe, and equitable.

Barriers to health system leadership support for practice changes include:

- Findings from studies are presented very late in the process, and the health system leaders are typically not informed about the incoming evidence and how they can incorporate it into their decision-making.
- Extramural funding provides researchers autonomy and prestige, yet confers a more distant relationship to the healthcare system than when getting internal funds.

To truly create a learning health system, researchers may require stronger incentives to commit to working in partnership with health systems. Consequently, if health system leaders are to provide these incentives, they need to better understand how the availability of evidence will improve their decision-making. However, as yet, health system leaders do not have enough working examples of how research findings have helped in their role as decision-makers. Therefore, leaders have not yet moved to provide incentives for a learning health system.

How Have Health Systems Made Decisions Based on Evidence Collected in PCTs?

Panelists: Devon Check, Vincent Mor, Lynn DeBar, Kathryn Glassberg, Douglas Zatzick, Eileen Bulger, Susan Huang, Kenneth Sands, Edward Septimus; Moderator: Gregory Simon

In PCTs, study interventions are designed to align with healthcare system priorities, infrastructure, and operations, with the goal of easing implementation during the trial and increasing the likelihood that effective interventions will be translated into practice. Yet, in

the NIH Collaboratory's experience, effective interventions are not always adopted into routine practice (Table 1), and interventions that did not achieve their intended effects sometimes are (Table 2). Using examples from NIH Collaboratory Demonstration Projects, panelists discussed reasons why healthcare system leaders might decide to adopt ineffective interventions, such as benefits for subgroups, improvements in secondary outcomes, and benefits for staff. Panelists also discussed reasons why healthcare system leaders might elect to not adopt or sustain interventions that were effective, including cost, feasibility, and alignment with policy incentives and other requirements or priorities.

Table 1. Intervention *Not Sustained* When Intervention *Did* Improve Primary Outcome

Primary Endpoint	Post Hoc/Secondary Findings	Implementation
PPACT		
<u>Significant</u> : Reduction in pain	<u>Significant</u> : Reduction in pain-related disability and benzodiazepine use	<u>Not sustained</u> : None of the participating health systems fully sustained the intervention, largely due to upfront staffing costs and feasibility considerations
TSOS		
<u>Significant</u> : Reductions in PTSD symptoms at 6 months (but not at 12 months)	<u>Significant</u> : Secondary stratified analyses showed significant 3, 6 and 12-month PTSD intervention treatment effects at sites with good/excellent implementation, but no significant intervention treatment effects at sites with fair/poor implementation.	Trauma centers must have protocols to identify and refer patients at high risk for psychological sequelae; no trauma center-based intervention required.

Table 2. Intervention *Sustained* When Intervention *Did Not* Improve Primary Outcome

Primary Endpoint	Post Hoc/Secondary Findings	Implementation
ABATE		
<u>Null</u> : No significant reduction in infections in the non-critical care population	In patients with medical devices, intervention was associated with reductions in all-cause bloodstream infections and multi-drug resistant organism cultures	<u>Sustained</u> : Health system sustained the intervention for patients with a medical device in participating hospitals that were in the intervention arm <u>Expanded</u> : Adopted intervention for patients with a medical device in all other health system hospitals
LIRE		
<u>Null</u> : No decrease in spine-related healthcare utilization after imaging	Slightly reduced subsequent opioid prescriptions	<u>Sustained (partially)</u> : Half of participating systems sustained the intervention based on its potential to reduce opioid use; no additional resources were required to

sustain the intervention, and there was a perception that it might help communication

PROVEN

Null: No significant reduction in hospital transfers

Significant reduction in hospital transfers among people who died

Sustained (partially): One-third of participating facilities chose to keep the intervention in place because staff liked it and found it rewarding to participate in; the intervention was low cost to keep in place

Based on the NIH Collaboratory's experience, factors in addition to a trial's primary result seem to drive subsequent adoption or non-adoption of an intervention tested in a PCT. The next session discussed what factors influence decision-makers' adoption choices beyond evidence of clinical benefit.

How Do We Generate the Right Evidence to Support Decision-Makers?

Panelists: Kenneth Sands, Eileen Bulger, Edward Septimus, Amy Kilbourne, Rosa Gonzalez-Guarda, Patrick Heagerty; Moderator: Hayden Bosworth

Researchers and healthcare system leaders who have worked on NIH Collaboratory PCTs emphasized the importance of researchers being well connected to their healthcare delivery systems. Another major theme was the need to communicate usable results to healthcare system leaders, which may not always be reflected in the primary outcomes of traditional clinical trials. Panelists discussed considering composite and secondary outcomes as options during study design while maintaining scientific rigor.

Key Drivers of Decision-Making

According to the panelists, the typical research paradigm where researchers identify a primary endpoint and measure it to a statistical significance of $P < 0.05$ is not really measuring what is needed to drive implementation decisions. Instead, key drivers of decision-making included perception of the intervention and buy-in from partners, local context, the importance of the research question, and subgroup and post hoc analyses.

Perception of the Intervention and Buy-in From Partners

The experience of healthcare systems, from the leadership level down to the frontline clinicians who are doing the intervention, can influence whether or not an intervention is sustained. Considerations included whether the staff liked the intervention, if it made them

feel better about their jobs, and whether it was consistent with the organization's mission. Alternatively, lack of complaints can also drive sustainability.

The PROVEN trial cited staff satisfaction as a motivator for health systems that adopted its intervention. At some facilities, staff found the trial's advance care planning videos to be extremely useful and wanted to keep using them. Furthermore, some facilities had major efforts focused on palliative care and moving patients into hospice, so they were very intrigued about seeing a reduction in hospital transfers among people who died. Finally, there were no complaints amongst the staff or administrators of PROVEN sites regarding the intervention.

For the TSOS trial, the success of the program hinged on the researchers' upfront engagement with the American College of Surgeons—getting buy-in for the study before it started. The College wants to follow the evidence, and also not create an unfunded mandate that does not fit the evidence. It is a thoughtful process.

Local Context

When trials are conducted in local hospitals, there is a perception that the results are more relevant and powerful.

For example, in the ABATE trial, the health system showed its own hospitals' data to its clinicians as part of the discussion about whether to sustain the intervention. They also had in-house thought leaders already engaged in the issue and personally invested in what had been happening with the trial. These close connections made the transition to long-term implementation smoother. The health system had also created an environment that embraced the philosophy of a learning health system, so its internal stakeholders were familiar with the process of conducting studies, and then moving from the study environment into implementation. This familiarity lowered the threshold for moving forward after the study.

When trials are conducted in local hospitals, there is a perception that the results are more relevant and powerful.

Importance of the Research Question

Whether or not a research question addresses a problem of strategic priority for the health system can drive implementation and sustainability. The leader of ABATE's partner health system described that when they had meaningful clinical questions, the research and clinician partnership was synergistic.

Relevant Secondary and Post Hoc Analyses

Implementation decisions are based on many considerations, not just statistical significance of a PCT's primary outcome. Subgroup and secondary analyses also provide useful information for decision-makers. An investigator from the PROVEN trial explained

that researchers are not speaking the same language as decision-makers when researchers are constrained by their particular standard of evidence ($P < 0.05$). People who are making real healthcare system decisions have a different standard of evidence.

A health system leader emphasized that there are plenty of decisions that get made every day in the absence of a strong randomized trial level of evidence. It is a luxury to have quality evidence, and any evidence is better than the *status quo* where decisions are driven by intuition and personal expertise and experience. The secondary analysis from the ABATE study—which was not pre-specified—provided ample evidence to drive change, especially because findings of the ABATE study had face validity. The findings were consistent with practice in the health system’s ICUs, consistent with the findings of a previous trial, and made sense to clinicians that the greatest benefit would be for patients with devices due to their high risk of bloodstream infection.

Investigators discussed that when planning PCTs, they pre-specify the subgroup and post hoc analyses as much possible. In these trials, it is not uncommon for the primary endpoint to be null and to have a subgroup that benefits. By pre-specifying these analyses, any benefits found gain broader acceptance, and even when the analyses are not pre-specified, as with the ABATE example above, the evidence may still be enough to drive change.

By pre-specifying subgroups and secondary analyses, the benefits found gain broader acceptance.

Getting Robust Evidence Is a Lengthy Process

Healthcare systems leaders emphasized the need to get actionable answers quickly. When healthcare systems, clinicians, patients, and payers really care about an issue, it creates a great opportunity for researchers. However, research typically takes 5 or 6 years to get a good answer. The time from developing the protocol, trying to obtain funding, executing the trial, cleaning the data, analyzing the data, and getting the results published can be a long cycle with large randomized controlled trials. When a problem is critical, healthcare system leaders want an answer quickly and may try a lot of strategies that might work, whether or not the testing is scientifically rigorous.

We need strategies that get answers quickly, not strategies that get the highest quality evidence in 5 or 6 years.

This issue of timeliness was explored further in the remaining workshop sessions.

Learning Faster

Panelists: Gloria Coronado, Natalia Morone, Corita Grudzen, Kevin Chan, Pearl O'Rourke, Cheryl Boyce, Andrea Cook; Moderator: Kevin Weinfurt

During the first year of a trial's funding, the NIH Collaboratory focuses on identifying 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 program's PCTs have performed interim analyses of key outcomes to determine the likelihood that the trial will achieve the desired outcome. It is also uncommon for the trials to routinely evaluate whether the intervention is being delivered and uptake is sufficient to allow for testing of the hypothesis. 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 discussed were the criteria that should be considered and employed to end a study before its anticipated full term. The panel considered 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 investigators, healthcare systems, payers, and delivery systems who focus on individual trials.

The panelists explored two critical questions:

- What are the opportunities and challenges for monitoring signals in real time about the intervention and the implementation of the intervention so an investigator might know as quickly as possible if a trial is unlikely to succeed?
- What are the considerations for deciding when and how to act on these signals?

Monitoring Signals in Real Time

Panelists discussed different methods for detecting early signals (Table 3). Qualitative interviews planned for the end of a trial are not actionable, so finding ways to learn earlier can be helpful to successful implementation of a trial.

Table 3. Methods for Detecting Early Signals

Method	Finding	Example
<u>STOP CRC</u>		
Plan-Do-Study-Act Cycles to support program implementation	The team found many implementation barriers that they would not have known about otherwise	Completed tests were being thrown out because they did not have a collection date, so materials were changed to bring attention to the collection date
<u>OPTIMUM</u>		
Pilot study with interviews and community advisory boards	Involvement from participants in the pilot improved understanding of how they were using technology	The team needed to invest a significant amount of time teaching participants how to use technology
<u>PRIM-ER</u>		
The intervention was complex and deployed in heterogeneous systems	While it is important to describe the intervention as precisely as possible so it can be replicated in other centers, the intervention itself can be delivered in different formats	Intervention could be delivered as an interruptive alert or a banner

Panelists suggested that complex interventions that are less amenable to adaptations in different settings might not work in other places.. Detecting early signals that the intervention is not working might be challenging, especially if part of the intervention is to adapt to different contexts. At a certain point, you cannot iterate further to make local adaptations because it changes the intervention too much. Then it is time to stop adapting the intervention and just stop the trial.

Because of the need to adapt and potentially pivot, all the panelists suggested that a 1 year planning phase was a bit too short, especially when working with safety net organizations and other federally qualified health systems.

Opportunities for detecting an early signal that adaptations are needed include:

- Piloting the trial at the most diverse site
- Conducting small pilots at each site
- Engaging with a multi-stakeholder panel to help determine what needs be learned and appropriate reactions

Considerations for Deciding When and How to Act on Signals

There are different situations with where it might be appropriate to modify or end a study:

- Early stopping because of inability to implement the intervention or lack of effectiveness

- Early stopping because the intervention has achieved its primary endpoint

Early stopping because of inability to implement the intervention or lack of effectiveness

In traditional explanatory trials, a Data and Safety Monitoring Board (DSMB) might advise stopping a trial because of overwhelming evidence of benefit or futility, but different issues may arise in PCTs. For example, adherence to the intervention is less tightly controlled by the research team in a PCT, and lack of fidelity can lead to inadequate separation between the study arms and, consequently, an inability to statistically detect a difference in outcomes. Data quality issues can also create challenges, as data from the electronic health record can be inconsistently or inaccurately captured across sites. Therefore, outcome or safety endpoints may not be uniformly ascertained across sites. Depending on the data source, there may also be lengthy delays in obtaining data, which can make detecting an early signal about a potential issue challenging.

Perspective From Scientific Officers at the NIH

Instead of trying to “hit the home run,” the NIH wants to reduce the risk of not obtaining sensible, useable information from a trial. Uncovering early and unanticipated signals that suggest there's a problem in how the trial is going can enable changes that ensure a trial can be completed. The process of engaging stakeholders is iterative: teams re-evaluate, change, and re-engineer because of unanticipated implementation barriers, especially given the complexity and heterogeneity of sites in PCTs.

We need to ask the question, is it okay to fail?

How project-officers make go-no go decisions on trials

Decisions are based on the totality of data, not one signal.

Program officers ask:

- Is the data quality from the electronic health record good enough to detect a treatment effect?
- Is the trial sufficiently powered for adequate separation and the ICC?
- Is there non-random bias?
- Are there patient safety concerns?

Panelists indicated a desire to help investigators overcome challenges. After a trial is started, project officers can help by engaging stakeholders in an iterative process to re-engineer the trial because of unanticipated problems. For example, if something is not going right with the first 10% to 20% of patients who are enrolled, there is an opportunity

to stop and change the course of the trial. Having robust, objective, and pervasive data is important to support this decision to pivot or pause. We need to ask the question, is it okay to fail?

Pragmatic tips for pausing or stopping a trial

- Have robust and persuasive data to support the decision
- Base the decision on the totality of the data, not individual metrics
- Ensure the evidence is clear and convincing (highly and substantively likely to be true)
- Prepare investigators, the DSMB, and sponsors of impending futility. Ideally, ending a trial should not be a surprise decision.
- A bioethicist can help frame key issues from a moral perspective to patients (i.e., it is unethical to continue a trial that is unlikely to provide an answer they were told it would provide).
- Finally, ending a trial is not personal, but it can feel that way to investigators, so ongoing communication is key.

A Community-Based Perspective

Patients, practitioners, teams, health systems, and communities are all a part of PCTs and the decisions involved. The impact of a PCT stopping early can be quite profound, and without involving patients and communities throughout the process, we are lacking an important perspective that could provide an opportunity to strengthen how we design, adapt, and change a PCT. A community-based review process can help make determinations about PCTs and advance science for society.

Ethical and Regulatory Perspectives

There are ethical and regulatory reasons for pivoting. Ultimately, there are 3 questions we must ask:

- Is the study worth doing?
- Does it matter?
- Will it really be implemented?

Patients give their time, healthcare providers give time and resources, and investigators need to be able to say that we can ethically and realistically answer the research question given early signals. Ethical review continues through the entire trial and is not limited to the initial IRB approval. If

interim results suggest that an answer to a research question has been found or is unlikely to be found, then there is an ethical imperative to pivot, and IRBs can help determine if there is justification for this. Panelists shared advice for investigators: If implementation is



If implementation is not working, change it. If you have the answer, stop the trial. Involve your team, your statisticians, and the IRB.

not working, change it. If you have the answer, stop the trial. Involve your team, your statisticians, and the IRB.

Many ePCTs are conducted with a waiver of individual consent, meaning consent is not required. However, changes may alter the risk-benefit analysis; if the changes increase the risk to such a degree that consent is required, new challenges will arise because participants may not be aware that a study is ongoing.. It may not always be reasonable to tell people there was an interim analysis, and that there is a possibility of change, early termination, or a new requirement for consent. Panelists reinforced the need to maximize benefit and decrease risk while being as transparent as possible.

Early stopping because the intervention has achieved its primary endpoint

Panelists discussed whether it could be acceptable to aim for less stringent "proof" as a tradeoff for timeliness. As stated in an earlier panel, p-values do not drive decisions, and Bayesian approaches, changing the allocation ratio in response to evolving results, or other approaches might be better suited to creating evidence faster.

In PCTs there are typically no formal stopping rules for effectiveness. It is not common to see planned interim analyses or planned assessments and thresholds around uptake or intervention fidelity (which DSMBs should probably consider interim analysis). There have been several trials get to the analysis stage before investigators realized there was a signal earlier in the process that could have initiated a discussion about stopping or pivoting. Because much of the data comes from the electronic health record, it is possible to monitor recruitment, fidelity, uptake of the intervention, and the intraclass correlation coefficient, all of which can impact the ability to discern a result. PCT interventions are complex and subject to change over time. However, stopping early might impact subgroup analyses or the evaluation of long-term outcomes. Most importantly, panelists recommended selecting a study design that permits monitoring and responding to signals. A stepped-wedge design makes responding to signals especially challenging.

For PCTs, it may help for DSMB members to have a formal process for monitoring and for the biostatisticians to update the sample size and intraclass correlation coefficient calculations over time. If there is a need to fully pivot to a new study design, investigators should work with the funder, DSMB, IRB, and biostatisticians to make sure the pivot has a reasonable chance of succeeding.

Select a study design that permits monitoring and responding to signals. A stepped-wedge design makes responding to signals especially challenging.

Potential Structures and Incentives for Faster Learning

Panelists: David Chambers, Wynne Norton, Tisha Wiley, Kenneth Sands, Edward Septimus, Gloria Coronado, Natalia Morone, Corita Grudzen; Moderator: Richard Platt

The NIH Collaboratory has facilitated better, faster learning by helping individual PCTs be successful by helping build relationships with program officers, health system leaders, and researchers and bringing peers together to reflect on challenges. These types of partnerships are a critical element of being able to problem solve in a PCT. Researchers shared that while principal investigators may be hesitant to speak with their trial's NIH project officer, these conversations can be very productive in finding a way forward when roadblocks occur. Despite incredible efforts by investigators, studies often do not go according to plan. Rather than embracing failing faster, panelists advocated for a philosophy of learning sooner. In some cases, this may mean examining whether continuing a trial represents a good use of funding.

It is not “failing faster,” it is learning sooner.

With PCTs, one often needs to adapt the intervention, but the distinction between adapting and changing the intervention falls on a spectrum. There are questions about how much change is acceptable in the context of the approved protocol.

Implementation Science Context

Communication between researchers, healthcare system leaders, and front-line staff can help anticipate challenges and develop strategies to address and learn from those challenges. Researchers described that no matter how much planning, the unknown is always lurking.

As much as we plan, the unknown is always lurking.

Ensuring that the research questions and milestones for PCTs are meaningful to partners at multiple levels of the organization or community settings can help make trials resilient to some unanticipated changes. Capturing contextual data as part of the trial can help investigators tease apart the impact of context on trial implementation and effectiveness of the intervention. Clinical and investigator partnerships enable joint planning for mitigation strategies. Ahead of the trial, investigators and their partners can conduct a “pre-mortem” by planning for what is going to go wrong. Ideally, the group involves investigators, clinicians, health system leaders, and community members to brainstorm the ways a trial is not going to work out and anticipate those challenges in a flexible design or with alternate strategies for continuing the trial.

It is important to engage with NIH program staff throughout the trial, especially in case of unexpected events. The more engagement and awareness of problems as they occur, the easier it is to try and mitigate the unexpected changes. Capturing contextual data can help to understand the impact of unexpected challenges and prepare for future trials.

Key Considerations

Panelists offered several tips to support implementation and plan for potential challenges:

- Have the right stakeholders around the table, including data scientists, community partners, and clinicians who will be implementing the intervention on the front lines.
- Ensure the outcomes are meaningful to multiple partners.
- Most trials have challenges with recruitment, so determine reasonable recruitment goals by working with your statistician.
- Develop strategies to improve recruitment, such as expanding eligibility criteria. Also consider how much effort is worth putting into increasing recruitment. If you are unable to recruit, what does that say about the research question?

Insights From NIH Program Officials

When things are going wrong, panelists stressed the need to interact with NIH program staff. Most program staff want to be a good steward of taxpayer dollars and make sure that investments in research advance public health. When an unexpected challenge arises, program officials ask these key questions:

- What is good science and where is the bigger scientific question going?
- How do we maximize the value of the investment that we've already made?
- What were the original goals of the study and what did we hope to learn?
- Does continued investment in the infrastructure that's been developed by this study represent a good stewardship of taxpayer dollars?

Are we moving the scientific needle? Are we improving the delivery of services that work for populations who need them?

There is almost always something that can be salvaged or thought about in a different way and still bring scientific value from the study. Even underpowered research can provide provocative data points that spur additional research. Pre-mortem approaches include structuring a study so that even if things do not go as planned, others can still learn from it. For example, if leadership will not adopt an implementation plan that was developed by a local change team, this information is of interest for future studies. When a study does not go as planned, the challenges should be published in the literature because people can learn from the experience. For example, in a study about getting referrals for treatment—including medications—for opioid use disorder: an important outcome was that while the rate of referrals increased, uptake of medications did not. Program officials are actively

seeking trials with scalability, sustainability, stakeholder engagement, and that connect practice with equity. Funders do not have resources to test every intervention in every possible setting. The question is, are we moving the scientific needle? Are we improving the delivery of services that work for populations who need them?

Infrastructure for Faster Learning

Panelists discussed that to conduct trials faster, a re-useable infrastructure would be helpful, where partners have worked together successfully before. An example is the ABATE trial, which had worked with its health system partner on a previous study, REDUCE MRSA. PCORI is a great example of a re-usable network that can be used to answer important questions.

Some questions a re-usable infrastructure could help with include:

- What's the highest priority question for right now?
- Is this the right question?
- Is the question being framed in the right way?
- Is this the right setting to answer the question?
- Are the right people being included?
- Are the sites qualified?
- Is this the best solution to test based on what we know right now?
- What is the backup plan? If this doesn't work, is there something else that we might test?

A re-usable infrastructure also allows for pivoting quickly. However, a different mechanism for grants is needed to allow for this type of pivot. Currently, the cost of the pivot is frequently beyond the scope of the award.

A theme of workshop discussion was that there is no substitute for planning for contingencies. Even the known unknowns are worth trying to articulate. Dealing with the unknown unknowns is tougher. In contingency planning, researchers describe as many of the possible situations that might arise as clearly as possible, as well as how one might deal with the different challenges. Monitoring for fidelity of the intervention is a step in the right direction, but a contingency plan is needed to solve problems that arise.

One strategy—particularly for interventions that have multiple components—is to specify what could change in terms of the form it might take versus the function of the intervention. In these situations, it is prudent to ask, *What is the minimum viable intervention that will produce our outcome?* Tracking adaptations is also important because there is a continuum between adapting an intervention and actually developing an entirely new intervention.

2023 NIH Workshop Summary

Bringing together a community with a shared commitment to transparency and mutual learning has been beneficial for the NIH Collaboratory trials. When thinking about trying to learn faster, there are lessons to be gleaned from the culture created and maintained in a network like the NIH Collaboratory. These lessons are illustrated throughout the shareable resources compiled in the program's [Living Textbook](#).

The [complete workshop materials](#), including slides and videocast recordings, are available on the [Living Textbook](#).