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Journal
Healthcare, 4(3)

ISSN
2213-0764

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Publication Date
2016-09-01

DOI
10.1016/j.hjdsi.2015.07.005

Perspectives

Trials without tribulations: Minimizing the burden of pragmatic research on health care systems

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ABSTRACT

Pragmatic clinicaltrialsareincreasinglycommonbecausetheyhavethepotentialtoyield findings that are directlytranslatabletoreal-worldhealthcaresettings.Pragmaticclinicaltrialsneedtointegratere- search into clinical workflow without placing an undue burden on the delivery system. This requires a research partnership between investigators and health care system representatives. This paper, organized as a series of case studies drawn from our experience in the NIH Health Care Systems Research Collaboratory, presents guidance from informational interviews of physician–scientists, health services researchers, and delivery system leaders who recently launched pragmatic clinical trials.

1. Introduction

Pragmatic clinical trials integrate healthcare research into everyday practice to address issues relevant to patients, clinicians, and delivery system leaders.[1–3] The results of pragmatic trials therefore reflect the effectiveness of interventions in diverse, real- world patient populations, as well as the ability of delivery systems to implement the interventions. These features of pragmatic clinical trials increase the generalizability of their findings. Funding is growing for pragmatic trials because of their potential to implement and sustain positive results.[4, 5]

Pragmatic clinical trials involve collaborations with diverse stakeholders including researchers, clinicians, and delivery system leaders and staff, from executives to information technology (IT) to frontline providers.[6] Increasingly, patient advisors are part of the research team.[3] Each of these stakeholders has different priorities, work cultures, and expectations. To guide multidisciplinary groups in establishing pragmatic clinical trial partnerships, we present case studies drawn from our experience in the National Institutes of Health (NIH) Health Care Systems Research Collaboratory, supported by the NIH Common Fund. We generated the case studies by interviewing researchers, physicians, and delivery sys- tem leaders of six pragmatic trials funded by the Collaboratory. Each case has a primary practical observation and several secondary insights. The findings address establishing a pragmatic trial partnership; identifying a research question of interest to all stakeholders; and designing and integrating a study into clinical practice in a way that minimizes the burden of research participation on the delivery system.

Case 1: Establish a partnership from the get-go

In the Collaborative Care for Chronic Pain in Primary Care study, clinical staff are testing a team-based program to help patients manage chronic pain. Principal investigator Dr. Lynn DeBar, Kaiser Permanente Center for Health Research, is collaborating with Kaiser Permanente regional health systems, including in Hawaii, where her collaborator Dr. Stacey Honda is the Associate Medical Director for Ancillary Specialties for the Hawaii Permanente Medical Group.

Dr. DeBar advises establishing a partnership from the beginning of a pragmatic clinical trial, starting with identifying the research question. “The idea for our study came directly from frontline clinical staff,” said Dr. DeBar. People with chronic pain are high users of healthcare and long-term opioid use is a strong concern of the delivery system partners. Making care for patients with chronic pain more effective could save time for the delivery system's primary care providers.

Even with a research topic that is a high priority for clinicians, Dr. DeBar said that researchers must respect the providers who interact with patients, for example by not scheduling study-related patient visits during the busiest clinical times. “Space is tight in primary care,” she said, “so we’ve been creative, like holding patient group sessions in lobbies.” Dr. DeBar also noted that the study's use of clinic space for meetings during slow times was a benefit to clinics, which are expected to run at full capacity all the time.

The delivery system must also make adjustments, said Dr. Honda. “It’s a two-way street,” she said. “We fit the project into our normal processes and the researchers incorporate the clinical processes and languages into their intervention to get the staff to buy into it. It feels a little foreign from both sides but in the long run it will pay off.”

Case 2: Do a pilot project

Even when researchers and healthcare system leaders are enthusiastic about a pragmatic clinical trial, Dr. Gloria Coronado, Kaiser Permanente Center for Health Research, advises starting small, with a pilot project. Dr. Coronado leads the pragmatic trial Strategies and Opportunities to STOP Colon Cancer in Priority Populations (STOP CRC) with Dr. Beverly Green, Group Health Research Institute. One of their collaborators is Dr. Christine Nelson from OCHIN, a national health information network.

STOP CRC is evaluating an evidence-based, culturally tailored approach to increasing colorectal cancer screening in underserved populations. Although the community clinics recruited for the study were committed to the research, Drs. Coronado and Nelson said that doing a small pilot project was essential for discovering unanticipated hitches, checking cost estimates, and optimizing study efficiency by adjusting the study protocol. “As a result of the pilot,” said Dr. Coronado, “we eliminated a study arm that turned out not to be feasible and refined our electronic medical record tools to automatically generate lists of patients eligible for each step in our step-wise intervention. Moreover, the early success of our pilot made it easier to recruit additional clinics into the trial.” “At each step,” adds Dr. Coronado, “we asked the clinic staff, ‘What would you normally do in this situation?’ and as much as possible, we designed our program to match their activities—that is, we incorporated our program into their standard workflows.” For the community clinics, said

Dr. Nelson, the pilot phase high- lighted the benefits of study participation. “Community clinics can be especially receptive to collaborative studies,” said Dr. Nelson, because the studies bring resources that they otherwise wouldn’t have, such as data analysts and biostatisticians and research expertise.”

Case 3: Take advantage of existing hospital and health system infrastructure

The Active Bathing to Eliminate Infection (ABATE Infection) pragmatic clinical trial also began with an established partnership and a pilot project. The ABATE team has now randomized about 50 hospitals to test interventions to reduce drug-resistant bacteria and healthcare-associated infections. The ABATE principal investigator is Dr. Susan Huang, University of California Irvine. The hospitals are part of Hospital Corporation of America (HCA), where Dr. Edward Septimus is the lead HCA investigator and medical director of infection prevention and epidemiology.

“Rule one,” said Dr. Septimus, “is listen to your frontline healthcare workers. They understand the workflow issues.” To add the study protocol to the clinical workflow as seamlessly as possible, the researchers took advantage of existing infrastructure. For example, nurses already answer a set of computerized questions about patients at each shift, so a single study question was added to that list. The healthcare system already has staffing resources and infrastructure for quality improvement campaigns that are led by local leaders such as infection preventionists, unit directors and managers. The study is using those existing resources and processes. “We’re implementing our intervention using usual hospital procedures,” said Dr. Huang. “The clinical staff will conduct this quality improvement campaign in the way their unit always has, and this gives them ownership.”

To further ease the burden of study participation, the hospitals do only the intervention—data collection is through a centralized data warehouse. Dr. Huang also said that getting Institutional Re- view Board (IRB) approval through a single trusted entity (Harvard Pilgrim Health Care) was crucial for moving the study forward, since it relieved individual hospitals from going through the complete IRB process.

Having local leadership involved and accountable, and making in-person visits to recognize local efforts is highly effective in maintaining compliance and enthusiasm, said Dr. Septimus. He said to ensure a successful research project, “make pride in participating in research a part of the culture.”

Case 4: Minimize the impact on clinical workflow

Even with healthcare system leaders and staff involved in streamlining study design and implementation, a pragmatic trial will often affect clinic workflow. Dr. Laura Dember, University of Pennsylvania, has suggestions for minimizing this impact from her collaboration with dialysis provider organizations Fresenius Medical Care North America and DaVita. Dr. Dember leads the TiME study, (Time to Reduce Mortality in End-Stage Renal Disease), which is evaluating how a facility-level approach to dialysis session length affects survival, hospitalization, and quality of life for patients with kidney failure.

By definition, the intervention will have an effect on the dialysis facilities, since some patients will have a longer treatment time, explained Dr. Dember. She said, “We recognize

the impact we're having on the clinical staff and tried to minimize it as much as possible. For example, we developed the eligibility criteria to enroll only patients new to dialysis. This was a compromise since now we're studying a subgroup instead of all patients, but it limits the number of patients with longer treatments that need to be accommodated by the facilities."

In addition, Dr. Dember and her collaborators are easing the burden of study participation on the clinical staff by collecting only the data that are necessary for answering the research questions. "We spent a lot of time deciding on the data elements for the trial —working closely with the provider organizations from the beginning," said Dr. Dember. "We limited the data elements to those that will be available through routine clinical care." The method of collecting data also considers the clinical staff, said Dr. Dember. Rather than implementing new electronic data capture systems just for the trial, the study is using systems already in place at the facilities to collect clinical information.

Case 5: Be as automated as possible

Automated interventions, when feasible, can make study participation easier for delivery systems, physicians and clinical staff. In the pragmatic trial Lumbar Image Reporting with Epidemiology (LIRE), Principal Investigator Dr. Jeffrey Jarvik is collaborating with five healthcare systems across the country on an intervention to improve interpretation of diagnostic tests for lower back pain. In an earlier version of the intervention, radiologists had to add in- formation about the prevalence of certain findings in patients without back pain to each lumbar spine imaging report, explained Dr. Jarvik. For the refined version used in LIRE, this information is included automatically, by default. "Providers don't need to do anything actively," he said.

Since LIRE was built on a previous collaboration, Dr. Jarvik and colleagues also had a way to ease the burden of the study on the delivery system's IT staff. "We already had code to get the variables of interest from the electronic health record," said Dr. Jarvik, "so we're using that—we're leveraging work we've already done." Another essential component of working smoothly with health- care systems, said Dr. Jarvik, is identifying co-investigators or primary contacts at each intervention site who are knowledgeable about the study and their own system and are respected by people within their system. For the LIRE study, this is a radiologist or general internist at some sites and a researcher at others. "We rely on our co-investigators at the sites to provide us with local solutions to problems," said Dr. Jarvik. "So we give them a fair amount of latitude."

Case 6: Researchers are the tail, not the dog

As a concluding observation, Dr. Gregory Simon, Group Health Research Institute, had a message specifically for researchers working with healthcare systems in pragmatic clinical trials. Dr. Simon leads a pragmatic trial comparing the effectiveness of two population-based programs to prevent suicide attempt. Identifying people at risk for suicide and measuring the effects of practical, scalable risk-reduction methods requires data on hundreds of thousands of people, so the study is possible only through co- operation with large health delivery systems. The delivery systems in this partnership have already prioritized reducing suicide at- tempts in their community, so they readily agreed to participate when they were approached. In arranging the details, however, Dr. Simon said that he and his research team needed to keep a simple rule in mind.

"Remember," he said, "the purpose of the healthcare system is not to do research, but to provide good healthcare. Researchers often have a tail-wagging-the-dog problem. We assume if we think something is a good idea, the healthcare system will too. We need to remember that the mission is to improve peoples' healthcare. We need to remember that we're the tail and the healthcare system is the dog."

An application of this philosophy, said Dr. Simon, is under- standing that even though

healthcare system leaders consider the study a high priority, they must consider other priorities both within mental health departments and broader health systems. Investigators should identify partners or champions in delivery system leadership but understand those partners will have competing priorities.

2. Conclusion

The interviews for these case studies were conducted as part of planning and cross-project learning during a pilot phase. In 2014, all studies described here transitioned from the pilot phase to a full pragmatic trial to run through 2017. Based in part on the success of the initial trials, the NIH Health Care Systems Research Collaboratory funded additional pilot pragmatic trials. Key observations from leaders of the first round of pragmatic studies were: 1) Establish a solid partnership between researchers and delivery system partners from the beginning, building on previous collaborations if possible; 2) Do a pilot phase to test the partner- ship and identify issues to correct before a larger trial; 3) Take advantage of existing delivery system resources and infrastructure, for example templates for quality improvement programs; 4) Consider ways to reduce the impact on the clinical staff wherever possible, for example in the patient recruitment and data collection steps; 5) Reduce data burden at the local level by automating interventions as much as possible without overwhelming delivery system IT staff; and finally, 6) Always keep in mind the main goal for all stakeholders: improving healthcare.

A cross-cutting theme from the case studies is the need to be flexible throughout and be prepared to adjust the study design as needed. Since each delivery system has a unique culture and workflow, to be feasible, pragmatic trial study procedures need to be tailored according to these features. Research teams operating in a pragmatic setting should “expect the unexpected,” because inevitable but unpredictable changes will occur in how services are delivered and in the staff and leadership responsible for their delivery. Thus, there will always be uncertainty as pragmatic trials move forward. That said, the type of setting does provide guidance about how to approach study design, which will vary depending on the type of care provided (ambulatory, hospital); ownership model (federally qualified health center, private); and payment mechanism. For example, some of the studies such as cases 1 and 2 are occurring in a capitated environment and would require adaptions for a fee-for-service setting. Some studies such as cases 3 and 5 are in systems with established quality improvement approaches and electronic health records. Studies in settings without these assets need a different approach, for example, to compile participant data and monitor the study. Case 2, in federally qualified health centers that are known for responding to client input, and Case 4, in a specialty setting, illustrate how study feasibility is ensured by tailoring approaches for a particular de- livery model. Finally, case 6 is a reminder to maintain focus on the common goal of improving patient care. The cases are from U.S. healthcare systems but since the contexts are diverse, the findings are relevant for designing studies in other countries.

The key observations and cross-cutting themes illustrate how pragmatic trial researchers can design study procedures that minimize clinical burden. All interviewees endorsed developing a keen understanding of the clinical setting, starting with a pilot so that procedures can be refined before scale up, and maintaining close coordination with stakeholders throughout the study.

Acknowledgments

This work is supported by the National Institutes of Health (NIH) Common Fund, through cooperative agreement U54 AT007748 from the Office of Strategic Coordination within the Office of the NIH Director, as well as NIH Awards 5UH3DK102384- 03, 5UH3CA188640-03, 5UH3NS088731-03, 5UH3AR066795-03,
4UH3MH007755-02 and 5UH3AI113337-03. The views presented here are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health. The sponsor did not have a role in designing, researching and writing this paper or deciding to submit it for publication.

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Conflict of interest disclosure statement

This statement accompanies the article Trials without tribulations: Minimizing the burden of pragmatic research on healthcare systems, authored by Karin E. Johnson and co-authored by Eric B. Larson, Chris Tachibana, Ella Thompson, Gloria D. Coronado, Lynn DeBar, Laura M. Dember, Stacey Honda, Susan S. Huang, Jeffrey G. Jarvik, Christine Nelson, Edward Septimus, Greg Simon and sub- mitted to *Healthcare* as an Original Article. Below all authors have disclosed relevant commercial associations that might pose a conflict of interest:

Consultant arrangements: None. Stock/other equity ownership: None. Patent licensing arrangements: None. Grants/research support: None.
Employment: None. Speakers' bureau: None. Expert witness: None.