NIH Funds Six Large Simple Trials to Rapidly Advance Answers

NIH Cites CTTI's Large Simple Trials Project in Funding Announcement

SUMMARY

Inspired by CTTI's Large Simple Trials work, the National Institutes of Health (NIH) funded six low-cost, pragmatic, patient-centered, randomized controlled intervention trials.

GOAL(S)

Like other sponsors, NIH trials have become increasingly expensive and complex. With strict budgets to adhere to, it is more challenging than ever to conduct trials, even as the clinical community suffers from unanswered questions. The NIH wanted to address these challenges by stimulating the conduct of large simple trials (LST), or randomized trials designed to only answer one or two questions in a broad patient population, making them more efficient and less expensive than traditional randomized trials.

CHALLENGES

Randomized controlled trials as the "gold standard" for research is well embedded in the clinical research community, and there was doubt across the research enterprise about the acceptability of LSTs. Specifically, trialists had: 1) concerns that regulators will require more granular data, 2) operational concerns, and 3) lack of incentives and interest.

SOLUTION(S)

In 2013, CTTI published a manuscript in *JAMA Viewpoint* addressing these concerns and making the case for LSTs as a viable pathway to side-step these challenges and advance human health. Novel uses of existing data collection platforms like administrative claims and electronic health record data, CTTI said, present opportunities to speed enrollment and minimize activities like data collection and onsite monitoring for certain research aims. NIH agreed and set forth to bring more LSTs to life.

TAKING ACTION

CTTI's work stimulated and informed NIH's release of a request for applications (RFA) that aimed to fund pragmatic, patient-centered randomized controlled intervention trials that leverage existing resources to answer important questions in a cost-effective manner. In addition, the RFA called for trials that would have high impact from a patient perspective and be rigorously conducted via randomization. The potential topics of the proposed interventions were broad within these requirements. NIH received a robust response and selected six applications to fund. They were diverse in terms of patient populations, conditions, interventions, and design. For example, one trial implemented an evidence-based program for insomnia among cardiovascular patients. The intervention was cognitive behavioral therapy for insomnia (CBT-I), which was made pragmatic by delivering therapy through electronic means rather than face-to-face with a clinician. Awards to these studies were phased, so teams achieved specific and pre-determined milestones to move forward. A key part of NIH's program was regular collaboration among funded project teams to assess progress and pragmatism. Investigators rated their own trials and those of their colleagues on various domains of pragmatism, which was an insightful process that helped keep teams aligned with the original goal. For example, there was a tendency as time progressed to add measures to get more insight. The collaborative meetings helped maintain the original designs by discussing and illustrating how it would detract from the pragmatic nature the Institutes sought in funding these projects.

IMPACT

Five of the six funded trials advanced to completion, and all have published results. NIH considers the program a significant success.

ADVICE

NIH was aware that LSTs had merit and potential to speed uptake of results in the clinical care setting. The additional information from this program was illustration of the benefit of regular investigator meetings to overcome challenges and consider pragmatic approaches that have been seldom explored. Study teams looked to CTTI's recommendations to orient their thought processes toward a streamlined, patient-focused way of thinking about how they might proceed. NIH cites its investment in a coordinating center for these studies as key to keeping the teams engaged with one another and ultimately successful. "You can do a lot with resources already available," said one NIH leader. "Not everything can be done pragmatically, but for clinical questions appropriate for this methodology, LSTs are a valuable framework to deploy." To those who challenge LSTs with the argument that the data routinely collected in electronic health records are inferior in detail and quality, NIH cites Eastman Kodak's first digital camera images. Because they were substantially inferior to film images, Kodak found it easy to dismiss the importance of digital camera technology. Missing that market was a massive contributor to Kodak's bankruptcy filing in 2012, and by the time Kodak launched the Instamatic, the market had passed it by. It is common, NIH said, for large organizations to have difficulty dealing with innovative technologies because they are successful with their current business model, the new technology is usually initially inferior, and their established customers are not asking for it. If you have the inclination to dismiss the LST model at its current stage of development, take a moment to consider if you are too beholden to the status quo. Don't be the Kodak Instamatic.

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ORGANIZATION

National Institutes of Health

CONTACT

ORGANIZATION TYPE

Government

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TOPIC

Large Simple Trials

RELATED CTTI PROJECT

Large Simple Trials

CTTI RESOURCES

The imperative of overcoming barriers to the conduct of large, simple trials