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New Clinical Trial Approach Reduces Time and Costs of Many Studies

Doctors at the Veterans Affairs Boston Healthcare System are testing a new kind of clinical trial that's not only less costly but guides doctors to switch to the best treatment even before the trial is completed. The new approach -- called a point-of-care clinical trial -- was developed by Stanford University biostatistician Philip Lavori, PhD, and a Boston-based team as an alternative to expensive, lengthy, double-blind, placebo-controlled clinical trials to compare drugs and procedures that are already in regular use.

"The goal of point-of-care clinical trials is to deliver the best care to patients while learning from each experience and redefining that care," said Lavori, a professor of health research and policy at Stanford's School of Medicine and the senior author of an article on the method to be published online April 4 in Clinical Trials. "This 'learning and improving' loop will enable health-care institutions to more rapidly fold improvements into their medical practices," he said.

The article's lead author is Louis Fiore, MD, director of the Department of Veterans Affairs Cooperative Studies Program Coordinating Center in Boston and associate professor of medicine at Boston University's schools of Medicine and of Public Health.

The high cost of medical care has spurred interest in weeding out costly, ineffective medical care, and in 2009, the economic stimulus package included $1.1 billion for studies, known as comparative-effectiveness research, that pit one treatment against another. Point-of-care clinical trials offer researchers a new tool for this research, combining the statistical validity of a traditional clinical trial, in which researchers take time-consuming and costly steps to randomize patient selection to minimize bias, and the real-world applicability of an observational study, in which researchers can more efficiently draw on data from medical records and databases but do not eliminate the potential bias of why certain patients got certain treatments.

The article provides a roadmap for carrying out a point-of-care clinical trial comparing two standard methods of treating hospitalized patients for diabetes: sliding-scale insulin and the weight-based regimen. In the sliding-scale regimen, short-acting insulin is given three to four times a day as directed by an algorithm that factors in blood sugar levels, planned activities and sugar consumption. In the weight-based protocol, patients receive longer-acting insulin throughout the day in doses based on their weight.

The roadmap is designed for the Boston VA, which began enrolling patients in the study in October 2010. One key element of the point-of-care approach is a flexible electronic medical record system that can be programmed to randomize patients and search for patterns within the clinical information. Before the trial, doctors at the Boston VA Medical Center could prescribe either protocol, using their personal preference to determine which.

"The idea of embedding research into clinical care has been around for quite awhile but to my knowledge this is the first time that a randomized trial has been fully integrated into a hospital's informatics system," said Fiore. "It demonstrates an effective way to use electronic medical records to improve health care at a local level."

"The pilot study has been successful so far, and we plan on rolling it out to other VA hospitals nationwide over the coming months," he said. "We have tested all the links in the clinical informatics chain, and know that we are not interfering with clinical practice; we have demonstrated good acceptance from patients; we have learned how to inform doctors about the study; and we have dealt with all the human subjects issues that arise from trying to do something new."

To launch the study, informatics specialists programmed the EMR system to incorporate recruitment and data collection as part of everyday caregiving. So now that the trial has

begun, when a doctor punches in an order for insulin, the electronic medical record system offers not only the two usual protocols but also a third -- labeled "no preference." If no preference is the choice, a nurse explains the trial to the patient. If the patient agrees to participate, the EMR software randomly assigns one of the two protocols and care continues as usual with the doctors entering the patient's clinical details into the system.

Meanwhile, the EMR software is tracking which of the two approaches is associated with the best outcome -- in this case, "best" means getting out of the hospital quicker. As the study progresses and new batches of patients enter the trial, the software will preferentially direct more patients to the treatment that's most successful at that time. The process continues with new batches until the estimated probability that one treatment is better than the other exceeds 99 percent.

An important advantage of a point-of-care clinical trial is that it allows researchers to quickly compare treatments on a local patient population, then immediately implement the best alternative into the physician ordering system of a clinic. That means no delays for peer-review or physician adoption. In addition, resulting decisions are tailored to specific populations, which can vary widely in their genetic, geographical and socioeconomic compositions.

The new approach seeks to strike the ideal balance between the two other predominant methods of conducting comparative-effectiveness research.

In an observational study, a comparison of these two diabetes treatments could likely be completed even more quickly and at less cost, but its results are not as reliable. In these studies, researchers evaluate treatments by analyzing patient medical records or disease databases, without actively enrolling study participants. The pitfall is the lack of control over patient selection. Results can be distorted if one of the treatments is more often given to patients with worse expected outcomes.

Traditional randomized clinical trials -- considered the "gold standard" for the regulatory approval of drugs, devices and surgical interventions, as well as comparisons of approved treatments -- remove this potential bias by randomly assigning treatments to patients. While this method produces highly reliable evidence, a large trial can cost many millions of dollars and can take a decade or more to complete.

A point-of-care trial -- once integrated into a clinic's informatics system -- can be conducted relatively quickly, for very little incremental cost. Such trials won't work for studies that need a control group or involve a new drug yet to be approved by the FDA, because neither is part of regular care. Still, point-of-care trials are useful for comparing efficacy of commonly used drugs, devices, treatments and interventions in which peer-reviewed evidence is lacking or inconclusive.

For example, a point-of-care trial could be used to determine which FDA-approved stent produced fewer adverse effects. Or to assess the value of providing cognitive processing therapy to sufferers of post-traumatic stress syndrome. Or to quantify whether a new emergency room checklist for suspected stroke patients improves outcomes. A point-of-care trial could also be used for personalized medicine, to look for correlations between genetic biomarkers and efficacy of drugs.

The ultimate goal is to cut through the barriers to medical care based on evidence from clinical trials. "Using evidence to decide what treatments to use seems like a good idea -- but as soon as it involves questions of coverage it becomes highly political," said Lavori, co-director of Spectrum, which administers Stanford's NIH Clinical and Translational Science Award program. "Our idea is that if systems of care like the VA can integrate implementation of research results directly into care, we will keep the decision-making where it belongs. It brings medical decision-making back down to expert physicians and their patients, and out of the political realm."

Fiore's and Lavori's co-authors are researchers at the VA Boston Healthcare System's Massachusetts Epidemiology Research and Information Center. Funding for the study came from the Department of Veterans Affairs Cooperative Studies Program and the National Institutes of Health.

Journal Reference: 1. R. A. Rosenheck, J. H. Krystal, R. Lew, P. G. Barnett, S. S. Thwin, L. Fiore, D. Valley, G. D. Huang, C. Neal, J. E. Vertrees, M. H. Liang. Challenges in the design and conduct of controlled clinical effectiveness trials in schizophrenia. Clinical Trials, 2011; DOI: 10.1177/1740774510392931