Clinical trials can be improved by managing the learning curve

EurekAlert

DURHAM, N.C. Practitioners of clinical medicine are familiar with learning curves, and strategies like simulation are increasingly used to minimize learning-curve effects on clinical care. Because similar learning curves have been hinted at in some clinical trials, researchers at Duke University Medical Center studied the phenomenon in the data record of a large, multi-site clinical trial. Their findings point to ways to improve the quality of future trials through better training and simulation exercises.

The team found that research conducted by investigators in the large VALsartan In Acute myocardial iNfarcTion (VALIANT) trial progressed in a way consistent with a learning curve. This trial compared long-term treatment of 12,367 patients at 931 sites with the drugs valsartan, captopril or both in high-risk patients after a heart attack (myocardial infarction).

Duke researchers found that departures from the trial protocol were more common for earlier-enrolled patients at the study sites. Departures were defined both as violations, or failure to comply with the final study protocol, and as deviations, instances of non-compliance resulting from unforeseen circumstances.

Queries questions about data generated in the study were also significantly more common for patients enrolled earlier in the trial.

Protocol departures were more common at sites with less frequent enrollment for example, two or fewer enrollees per month compared to six or more subjects per month.

"We embarked on this evaluation to begin to unravel how to further improve clinical trials," said Jeffrey Taekman, M.D., co-lead author and assistant professor in the Department of Anesthesiology at Duke, and director of the Duke University Human Simulation and Patient Safety Center. "We will take these findings and incorporate them into simulation programs for study sponsors. Through a careful 'walk-through' of a study protocol we can catch and address issues prior to first subject enrollment in a trial. With the use of simulation, just like sports team members, each of the research team members will be able to practice the protocol without involving subjects. Ultimately, we hope to further improve trials through the data obtained in our research studies. "

The study was published in the *Quality and Safety in Health Care* journal online on July 30.

Co-lead author Mark Stafford-Smith, M.D., a Duke professor of anesthesiology, said

that clinical trials that adhere to effective protocols from the very start are beneficial. "In a previous study of critically ill patients, researchers made observations suggesting a benefit for a drug, but the study didn't yield a positive finding, possibly because a learning curve affected early trial data," Stafford-Smith said.

Taekman described the two basic categories of problems with clinical trial protocols problems in educating or training people to run the trial effectively and human-factor problems.

Stafford-Smith said that in one instance a company that was having challenges investigating a new agent came to the Duke Human Simulation and Patient Safety Center to learn how to better conduct a clinical trial. "There was a sense that the drug wasn't working because it was tricky to learn how to use," Stafford-Smith said. A pilot simulation demonstrated potential value as a method for learning how to perform more efficiently during a clinical trial. The company was so impressed that it promptly invested in such training for further investigations of its drug, he said.

"While preparing simulations for the agent, we also uncovered human-factor concerns in the protocols -- issues that made the trial more difficult to conduct," Stafford-Smith said. "The protocols were elegant on paper but flawed in practice that is the human- factor error in a trial." Examples of human-factor problems in trials might be blood tests on patients that are poorly timed to show drug effectiveness, or instructions that are worded ambiguously, making the protocols hard to follow.

The team is now developing metrics to compare the effectiveness of different interventions to improve trial conduct. "Ultimately, we are interested in how our human factor and immersive education methods can impact the quality of a clinical trial," Taekman said. "Future studies may involve evaluating the best ways for trial coordinators and staff to learn, including the use of virtual environments."

SOURCE [1]

Links:
[1] http://www.eurekalert.org/pub_releases/2010-07/dumc-ctc072910.php