New statistical tool could mean clinical trials yield better information with fewer patients

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University of Alberta researchers have developed a new statistical tool to evaluate the results of clinical trials, with the aim of allowing smaller trials to ask more complex research questions and get effective treatments to patients more quickly.

In a paper published in the journal *BioMedInformatics*, the team reports on their new "Chauhan Weighted Trajectory Analysis," which they developed to improve on the Kaplan-Meier estimator, the standard tool since 1959.

The Kaplan-Meier test limits researchers because it can only assess binary questions, such as whether patients survived or died on a treatment, and it can't include other factors such as adverse drug reactions or quality-of-life measures such as being able to walk or care for yourself.

The new tool allows simultaneous evaluation and visualization of multiple outcomes in one graph.

"In general, diseases aren't binary," explains first author Karsh Chauhan, a fourth-year MD student at the U of A. "Now we can capture the severity of diseases—whether they make patients sick, whether they put them in hospital, whether they lead to death—and we can capture both the rise and the fall of how patients do on different treatments."

"This allows us to do a smaller, less expensive, quicker trial with fewer patients, and get the overall benefit of a new treatment more rapidly out there in the world," says John Mackey, a breast cancer medical oncologist and professor emeritus of oncology.

The two began working on the statistical tool three years ago when they were designing a clinical trial for a new device to prevent bedsores, which affect many patients with long-term illness. They wanted to look at how the severity of illness changed during treatment, but the Kaplan-Meier test wasn't going to help.

"Pressure ulcers range from just a red rash to wounds that can go down to the bone," Chauhan says. "What we wanted to be able to see was, can this device change the number of people who get a rash, but does it also change the number of people who get severe disease and may eventually need surgery?"

"Dr. Mackey said to me, 'If the tool doesn't exist, then why don't you build it yourself?' That was very exciting," says Chauhan, who also has a BSc in engineering physics, which he calls a degree in "problem-solving."

Chauhan wrote the software and then worked on the mathematical proof with postdoctoral fellow Kaiqiong Zhao, now an assistant professor of mathematics and statistics at York University. The team had initially been told by statisticians that their problem could not be solved, so they are now pleased to have the paper published in a peer-reviewed statistics journal.

The tool was tested for reliability on both simulated and real-world data, with help from John Walker, associate professor of oncology and head of medical oncology for northern Alberta at the Cross Cancer Institute.

Chauhan and Mackey will present their tool at a conference of cancer researchers in Vancouver next month, but they say it can be used for a wide range of medical trials, and for testing innovations in non-medical fields such as engineering or finance. They have created a website where researchers can run secondary analyses on previous trial results to gain

new insights. They also hope to begin work soon to design new trials and analyze those results.

"We're looking to collaborate with and promote the tool to clinical trial investigators," says Chauhan, who hopes to begin his medicine residency next year. "We have the ability to design entirely new clinical trials with much smaller sample size requirements. That's possible because the tool captures more nuance, so we can gather more information from a smaller number of people."

More information: Utkarsh Chauhan et al, Weighted Trajectory Analysis and Application to Clinical Outcome Assessment, *BioMedInformatics* (2023). DOI: 10.3390/biomedinformatics3040052

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