Taking the 'random' out: New approach to medical studies could boost participation

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Rather than the 50/50 odds from a coin toss, the odds that a patient will get the more effective treatment in a clinical trial increase over time in studies that use the Response-Adaptive Randomization approach. Credit: University of Michigan

It's a classic Catch-22: Medical researchers need to figure out if a promising new treatment is truly better than a current one, by randomly assigning half of a group of patients to get each treatment.

But when they approach patients about taking part in the study, those 50-50 random odds don't sound good enough – and the study struggles to get enough volunteers. That slows down the effort to improve treatment for that condition.

Now, new research shows the promise of an approach that takes some of the "random" out of the process, while preserving the ability to compare treatments.

Instead of every patient getting a randomly chosen treatment, the approach adjusts the odds as the study goes along. So if early results show that one of the two treatments appears to work better, each new patient's odds of getting that treatment increase. It's called response-adaptive randomization, or RAR.

In a new brief report in the journal *Stroke*, University of Michigan Medical School researchers report the results of how 418 emergency department patients responded to the two approaches to medical studies.

The researchers asked the patients to imagine they had just suffered a stroke, showed them a video describing a study that needed stroke patients, and asked them whether they would volunteer for that study if they had really just had a stroke.

What the patients didn't know is that half of them had randomly been shown a video that described a classic randomized study, and half had seen the same video but with an added section explaining that if one treatment appeared to be working better in earlier patients, their odds of getting it would improve.

Only 54 percent of the people shown the first video said they would volunteer for the study. But 67 percent of those shown the RAR video said they'd enroll.

If the results play out in real emergency stroke studies, this 13-point difference could make a big difference in the pace of medical research, says William Meurer, M.D., M.S., the U-M emergency physician who led the study.

"Although this is a hypothetical scenario, it shows we might increase recruitment for acute stroke studies using a response-adaptive randomization design," he says. "This could be especially important in emergency situations, when patients or their loved ones have just minutes to consider options."

The new study has already led to further research that will look at patients' comprehension of the explanation of their odds of getting one treatment versus another.

At the same time, a U-M-based clinical trial network for brain emergencies has already begun to use the RAR approach in some studies. The network, called NETT for Neurological Emergencies Treatment Trials, is a laboratory for adaptive designs (many using RAR) through a project called Adaptive Designs Accelerating Promising Trials Into Treatments (ADAPT-IT).

The main challenge in doing RAR studies comes in making sure that the researchers gather enough data about each treatment to make their findings statistically sound – that is, to be able to tell for sure that the differences between treatments are real and not due to chance.

Meurer notes that an RAR approach in a study comparing two treatments can benefit patients the most, but poses a greater challenge

for researchers. Using an RAR approach in a study comparing three (or more) options, so that the least effective of the three gets used less as the study goes on, presents an opportunity to improve the outcomes of the patients in the trial and learn more efficiently.

Other adaptive approaches to randomization, such as a breast cancer study where patients are randomized differently based on specific characteristics of their cancer, are also starting to be used.

Meurer and U-M emergency physician and NETT chair William Barsan, M.D., have helped colleagues at U-M design clinical studies where randomization adapts based on different criteria, including severity of a patient's disease. They're also surveying clinical trial researchers about what they think of the RAR approach.

Barsan says, "We think that using the RAR approach is very appealing in our network, where we are treating patients with life-threatening neurologic emergencies such as stroke and head trauma. Knowing that more patients will receive the more effective therapy just seems like the right thing to do."

Performing an RAR study does require more infrastructure and preparation for researchers, Meurer says – for example, instead of just making up equal numbers of treatment packs when the study begins, the research team must prepare increasing numbers of packs containing the option that's working better.

It's also important to keep the treating physician "blinded" to which option they're giving each patient, so they don't bias the study.

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