What Is an Example of How to Choose a Study Design?

Liz Turner:

The first Collaboratory ePCT I'd like to talk about is the SPOT trial, so the Suicide Prevention Outreach Trial. This is a large trial with approximately 16,000 patients across four clinical sites. It's a three arm MRCT evaluating two individual level interventions versus usual care. Those interventions are a skills training program, a care management program.

Now for both of these, the intervention contact is mostly through the EHR, so the Electronic Health Record. In this case, there's very low risk of contamination, and in this case, the unit of randomization is the patient. STOP CRC, so Strategies and Opportunities to Stop Colorectal Cancer in Priority Populations. Even more patients are involved across more sites, 26 clinical sites. It's a two arm design. The intervention is a health system based program to improve colorectal cancer screening rates. Now, being a health system based program, it's applied in this case to a clinical site. It's very natural to randomize the clinical sites, so as to perform cluster randomization. That is the unit of randomization is the clinical sites.

The LIRE trial, so this is the Lumbar Imaging with Reporting of Epidemiology trial with the goal to reduce unnecessary spine interventions. This is to be achieved by providing information on prevalence of normal findings. In this case it's large. There are all eligible patients of 1,700 primary care providers across a hundred clinics. The intervention is clinic levels. It's very natural to use cluster randomization, that is the unit of randomization is the clinic.

Now this is a pragmatic trial in a context where all clinics were going to eventually receive the intervention that was planned from the beginning.

OPTIMUM is optimizing pain treatment in medical settings using group-based mindfulness. The plan is to have about 450 patients across three clinical sites. It's going to be a two arm RCT, so randomized control trial to intervention versus usual care. The unit of randomization is the individual, but very importantly, the intervention is group based by design.

The first question would be is there a strong rationale for randomizing groups of individuals, so clusters of individuals? I'm using that term interchangeably, groups and clusters. Is there a strong rationale to randomize clusters rather than individuals to study conditions? Let's say the case is yes, let's see an example.

The STOP CRC colorectal cancer screening trial. The intervention was at the clinic level. It's really natural, in fact necessary to randomize the clinics. Likewise in the LIRE lumbar imaging trial, in that stepped wedge trial. But how to distinguish between a parallel arm and stepped wedge design or to choose? The question is there a strong rationale for rolling out the intervention to all clusters before the end of the trial? In the case of the STOP CRC colorectal cancer trial, the investigators determined that no, that was not the case, and could go with a regular parallel arm design, cluster randomized trial design.

Remember, collectively as the biostats working group of the NIH Collaboratory, we would recommend going with the parallel arm design as far as you possibly can.

In the case of the lumbar imaging trial, well, there was a strong rationale to roll out the intervention to all clusters before the end of the trial, so this naturally led to a stepped wedge cluster randomized trial design.

Now, suppose now just shifting away from the cluster randomized trial design. Let's say now there is not a strong rationale for randomizing these groups or these clusters and there is actually a rationale. It's very natural to randomize individuals.

Some examples, the SPOT, so the suicide prevention randomized control trial. They were two individual level interventions that were going to be evaluated. It was a three arm trial, so they were being evaluated in comparison to usual care. In this case, it's very natural to use individual level randomization, and additionally, we did not have concerns of contamination in the suicide prevention trial.

The next question, let's see how it links to these two trials. Do participants receive their treatment in a group format or from a shared interventionist?

You can probably imagine the response here is no in the case of the suicide prevention RCT. The intervention is totally targeted at the individual. It's predominantly delivered through the EHR, the Electronic Health Record. There is no shared interventionist, no group format.

In the case where there is a group format to the treatment or individuals are receiving the treatment from a shared interventionist, say it's from the same therapist. Yes. In this case, you can respond yes to this question and then you'll be in the class of what's called an individually randomized group treatment trial.

This is a design that is probably the least well-known, I would say, between the classes of designs we're talking about here, this example, the OPTIMUM trial.

That's given you a flavor and a bit of a framework to think about making some of these decisions. We recognize there are a whole host of many, many other decisions. It's never as simple as what's presented in this figure, but we hope that some of these questions could at least spur you and your team, your collaborators, to have good conversations around how to make these decisions.