PROJECT INFORMATION

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Improving Trial Design and Analysis for Treatments for Rare Diseases

Principal investigator

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Organization

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What was the project about?

A rare disease is one that affects fewer than 200,000 people in the United States. Because few people have these diseases, clinical studies on treatments can be hard to conduct. One way to study rare disease treatments is with an snSMART study.

snSMART studies have two stages. In the first stage, researchers assign patients to a treatment by chance. In the second stage, patients may stay with the same treatment or switch treatments. Patients stay on the same treatment if it's working well. If the treatment isn't working, researchers assign patients by chance to a new treatment.

snSMARTs can help researchers learn more from a smaller number of patients than a standard clinical study. But most current methods for analyzing snSMARTs use data only from the first stage, which can lead to inefficient results.

In this project, the research team developed and tested new methods that use data from both stages to analyze snSMARTs. The team compared results from the new methods to actual treatment effectiveness to see

- Bias, or whether results are too high or too low
- Efficiency, or how big the difference is between the results and actual treatment effectiveness

What did the research team do?

The research team created two Bayesian and two frequentist methods. Bayesian methods use findings

from previous studies in the analysis, but frequentist methods don't.

Using a computer program, the research team created test data sets with 45–300 patients that looked like data from an snSMART study. Using the test data, the team compared the new and current methods to see which worked better to find the best

- First stage treatment
- Sequence of treatments

Clinicians that treat rare diseases, a patient with a rare disease, and a family member gave input on the study.

What were the results?

All methods worked well enough to see which first stage treatment or sequence of treatments worked best. To find the best first stage treatment, the Bayesian methods using data from both stages worked better than methods using only first stage data and the frequentist methods. To find the best treatment sequence, the Bayesian method was the most efficient but could result in biased estimates.

The research team also created an online sample size calculator that figures out how many patients should be in an snSMART study.

What were the limits of the project?

The research team compared the methods using test data. Bayesian methods may not get accurate results if assumptions about data aren't met. The new methods don't apply to designs using a placebo, or a pill that

doesn't contain medicine. Also, the snSMART design is most appropriate to study diseases with symptoms that are stable over time and don't change.

Future studies could test the methods when data are missing. Researchers could also develop methods to analyze data from an snSMART with a placebo.

How can people use the results?

Researchers can consider using the new methods and the online calculator when designing and analyzing snSMART studies.

To learn more about this project, visit www.pcori.org/Kidwell341.