◆ What to Look for in a Randomized Controlled Trial

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Sylvan B Green, professor of epidemiology and biostatistics at Case Western Reserve University School of Medicine, addressed the comparative advantages of randomized controlled trials and observational studies. According to Green, observational studies often provide useful information about care patterns, patient preferences, and costs, and they can generate hypotheses for future trials. However, observational studies generally should not be used for comparing alternative treatments because patient selection might have been biased. In addition, observational studies might be comparing groups of patients who differ with regard to unmeasured or unknown prognostic factors or who have inherently different prognoses because of time trends in disease characteristics, diagnostic methods, or supportive care. For those reasons, observational studies could lead to erroneous conclusions about the comparative benefits of different interventions.

In contrast, the randomized controlled trial provides an unbiased, balanced, and reliable method for determining whether drugs or devices are effective. Randomized controlled trials are superior for comparing interventions for the following reasons:

- Bias, whether conscious or unconscious, is avoided.
- Predictive factors, both known and unknown, tend to be balanced between intervention and comparison groups.
- Using a concurrent comparison group controls for trends in time.
- Randomization provides a valid means for evaluating the probability that two groups of patients receiving equivalent drugs or treatments will have different outcomes because of chance alone.
- Results from well-designed clinical trials are more likely to be convincing.

When reviewing a published article that reports the results of a randomized controlled trial, Green advised, readers should look for the following elements of a well-designed trial:

- A proper randomization procedure for allocating patients to treatment groups in an unbiased manner.
- A sample size that is large enough to provide adequate statistical power and to allow for a meaningful comparison.
- A simple design that yields conclusions about specific end points.
- An intention-to-treat analysis that includes all individuals randomized to treatment who were counted in the group to which they were randomly allocated, regardless of whether each individual completed the treatment.
- Statistical results that present a specific *P* value and a confidence interval that quantifies uncertainty and indicates a range of values in which the true treatment effect is thought to lie.

In addition, data from well-designed controlled trials can be combined for meta-analyses that compare data across trials to produce a more precise estimate of the effects of a treatment. Because randomized controlled clinical trials permit unbiased treatment comparisons, they present the best choice to patients who need state-of-the-art treatment alternatives, and they benefit science.

To gain more information about randomized controlled trials, consult the Web site of the Society for Clinical Trials, *www.sctweb.org*.