into two groups based on the order of treatments. In the first time period of the clinical trial, patients are randomly provided either the candidate compound or the standard of care. After a set time interval, the treatment groups are reversed, and the study is continued to its conclusion. As the trial proceeds, the patients are monitored to determine the impact of the therapeutic regimens. In this instance, since all of the patients receive both the new treatment and the standard of care, they are their own control group. As a result, fewer subjects are required for crossover trials. This trial design is an effective means of determining the utility of potential new therapies for chronic conditions in which symptomatic relief is the desired outcome (e.g., chronic pain, allergy suppression, etc.). Crossover trials are also useful in demonstrating that two therapeutic agents are bioequivalent.

There are some important limitations that should be considered before embarking on a crossover trial. First, the change of therapy should take place with minimal carryover effect of the first treatment regimen. Significant residual effects that carry over into the second phase of a crossover trial can make the results difficult to interpret. The amount of time required for the treatment regimens to "wash out" depends on the pharmacokinetic properties of the candidate compound and should be considered when determining the time lag between regimens at the crossover time point. It is also important to understand whether or not the disease or condition reverts back to its baseline level during the washout period, and to determine whether or not the treatment order has an impact on the results of the clinical trial. (Is patient improvement significantly different when treatment A is followed by treatment B versus when treatment B is followed by treatment A?) If these items are not easily addressed and accounted for, a standard, parallel trial may provide more meaningful results.

One of the fundamental drivers in the value and cost of a phase III clinical trial is the number of patients in each arm of the trial. In order for a phase III clinical trial to be supportive of a licensing effort for a candidate compound, the number of participants must be large enough to provide a statistically significant result. This is typically set at 5%. In other words, the chance of identifying an effect when one is not actually present is 5%. Viewed in a more positive light, there is a 95% chance that results observed in the course of the trial are real and not a result of random chance. The trial must also include enough patients such that its statistical power is high enough. Typically, the number of patients needs to be high enough that there is an 80–90% likelihood of detecting a difference between treatment groups if such a difference exists. The number of patients required to meet these criteria also depends on the size of the expected effect. As one would expect, larger effects are more easily detected and generally require smaller patient populations. None of these calculations are easily accomplished, as they require complex statistical