

Phase III clinical trials can be divided into some general categories based on their overall goal relative to the current standard of care. The goal of a superiority trial is, as the name implies, to demonstrate that the candidate compound is more effective in dealing with the targeted disease or condition. In this case, a competitor treatment may be run in parallel to the candidate compound so that a direct comparison may be made. Historical data may be available, but it is rarely suitable for inclusion in a licensure request (NDA). If there is no current treatment, a placebo control is used as a comparator group. In theory, a placebo control group could be used even when a treatment is available, but the ethics of not using at least the standard of care in the control group is questionable.

In some cases, phase III clinical trials are designed to demonstrate that a candidate compound is similar in efficacy to the current standard of care (an equivalency trial) or that it is not less effective than the current standard of care (a non-inferiority trial; the candidate compound could also be better). In these instances, a placebo control is generally not sufficient as a direct comparison with the standard of care is the desired end result. These types of studies are most often employed when the candidate compound's advantages over the standard of care are tied to something other than overall efficacy. A candidate compound that is expected to be safer, more convenient for the patient (e.g., once a week dosing versus daily dosing), or more cost-effective could be studied in an equivalency or non-inferiority trial.

The choice of outcome measures in a phase III clinical trial is a critical aspect of the trial design. They must be chosen very carefully and be well defined so that it is clear whether or not the trial has met its objective. In addition, the results must be capable of convincing regulatory officials and health professionals that a change in the standard of care is warranted and that the candidate compound is suitable for market approval. Although the primary endpoints will vary based on the targeted condition or disease, they must be clinically relevant to both the researcher and the patient. Examples of primary endpoints include increased survival (e.g., cancer survival), shortened duration of an event (e.g., shorter recovery time from an infection), or changes in patient habits (e.g., smoking cessation). In some cases, it may be necessary to track more than one endpoint in order to demonstrate utility of a candidate compound, which necessitates a composite endpoint. Consider, for example, a trial designed to evaluate a potential new treatment for cardiovascular disease. In this case, there are multiple, relevant clinical events (e.g., myocardial infarction, stroke, acute coronary syndrome) that could be positively impacted by the new treatment. Individually, positive changes in a single outcome measure might not be statistically significant, but collectively they could demonstrate a benefit to patients. Importantly, only the first clinically relevant event is included in the results of a clinical trial, as treatment or disease management will generally shift to more adequately support the patient post-event. It would be difficult to distinguish between shifts in patient outcome that are based on the changes in patient management versus the candidate compound.