



*Accelerating research towards a
cure for multiple sclerosis*

Clinical Research – A Deeper Look

Clinical research is the study of health and illness in people. It is the way we learn to prevent, diagnose and treat illness. Clinical research helps translate basic research (done in labs) into new treatments and information that will benefit patients. A clinical trial is one type of clinical research study. Clinical trials are done to determine whether new drugs or treatments are safe and effective. Clinical trials can also look at other aspects of care, such as improving the quality of life for people with chronic illnesses. Clinical trials can vary in size and cost, they can be done on an inpatient or outpatient basis, and they can involve a single site or multiple sites. Some clinical trials involve healthy subjects, and others pertain to patients with specific health conditions who are willing to try an experimental treatment.



The testing of medical treatments in clinical trials has two main goals. The first is to determine the treatment's "efficacy" or "effectiveness" (whether the treatment works well enough for its intended purpose). The second goal is to determine the treatment's "safety" (whether the treatment is safe enough). Neither efficacy nor safety is an absolute criterion. Both are evaluated relative to the treatment's intended use, what other treatments are available, and the severity of the disease or condition. In all cases, the benefits of the treatment must outweigh the risks.

The person that leads a clinical study is called a principal investigator (PI). People often confuse clinical research or clinical trials with medical care, especially when an individual's doctor is also the PI of their clinical trial. When a patient receives medical care, it is according to a doctor's plan of care developed specifically for each patient. If a patient participates in a clinical research study, the PI and the patient must follow a set plan called the "study protocol", which is designed by the study sponsor. The sponsor is the person or company that is responsible for the initiation, management and financing of the clinical study. The protocol ensures that all researchers perform the trial in the same way on similar subjects and that the collected data is comparable across all subjects. Protocols cannot be adjusted for individual patients, however protocols do include steps to follow if patients aren't doing well. It's important to understand that a clinical trial is an experiment, which means that the answer to the research question is unknown. Patients may or may not benefit directly by participating in a clinical trial, which is why whether or not to participate in one is an important topic to discuss with your doctor.

If a clinical trial is "open label", subjects and researchers are aware of the drug being given. In some clinical studies, participants may be assigned to receive a placebo (an inactive product that resembles the treatment being studied). Comparing a new treatment with a placebo can be the fastest and most reliable way to demonstrate the new treatment's therapeutic effectiveness. Placebos are not used if a patient would be put at risk by not having effective therapy. Potential study participants are told if placebos will be used in the clinical trial before they enroll. A "randomized study" is one in which subjects are randomly assigned to separate groups to receive different treatments (neither the researchers or subjects can choose which group). At the time of the clinical trial it is not known which treatment is best. In some randomized studies subjects receive either the study treatment or a placebo. A "blinded study" is one in which the participants do not know which study treatment they receive. If the clinical trial is "double-blind", the researchers also do not know which treatment participants receive. The double blind study method helps minimize the effects of any bias on the part of participants or researchers. If participants do not know which group they are in, their beliefs about the treatment are less likely to influence the outcome. If researchers do not know which group subjects are in, their feelings or biases will not influence how subjects may respond or how data is collected.



One way of classifying clinical trials is by the researcher's role in the study. In an "observational study", the investigators observe subjects and measure their outcomes. The participants in such trials do not receive any treatment but may be asked to provide information or blood samples. The ACP Repository and iConquerMS™ are examples of observational studies. In an "interventional study" (or clinical trial), the investigators give participants a particular medicine or other therapy to compare the treated subjects with those receiving no treatment, or the standard treatment. The researchers then measure how the participants' health changes.



The U.S. Food and Drug Administration (FDA) and the National Institutes of Health (NIH) classify clinical trials according to their purpose. "Prevention trials" look for better ways to prevent disease. These trials may include medicines, vitamins, vaccines, or lifestyle changes. "Diagnostic trials" are conducted to evaluate the presence or absence of disease as a basis for treatment decisions in symptomatic individuals. "Screening trials" look for the best way to detect early disease or risk factors for disease in large numbers of apparently healthy individuals. "Treatment trials" test new treatments, or medical devices. "Quality of life trials" explore ways to improve the comfort and quality of life for individuals with chronic illness. "Epidemiological studies" look to identify the patterns and causes of diseases in groups of people. Finally, "genetic studies" aim to better understand how a person's genes and illnesses may be related. For example, genetic research may explore ways in which a person's DNA makes him or her more or less likely to develop a disease. This may lead to development of tailor-made treatments based on a person's genome.

A third classification of clinical trials is whether the trial design allows changes based on data collected during the trial. "Adaptive trials" allow modifications to the trial and/or the statistical procedures of the trial, and then use interim results to modify the trial as it proceeds. In this way, drugs that have a therapeutic effect and patient populations for whom the drug is appropriate can be more quickly identified. "Fixed trials" are not modified once initiated and results are not assessed until study completion.

Clinical trials can also be classified according to whether or not they are considered beneficial. A "therapeutic trial" is one in which the treatment being studied is likely to benefit participants in some way (for example, a clinical trial for a new MS drug). A "non-therapeutic trial", on the other hand, is one that is unlikely to produce any direct benefit to

the participants involved (for example, tracking the long term health effects of chemotherapy). Non-therapeutic studies often lead to therapeutic ones.

Therapeutic clinical trials are classified by phase. Each phase relates to how close the drug is to being both approved for use by regulatory authorities, and proven clinically safe and effective for its stated purpose. Each phase has a different purpose and helps researchers answer a different question. Phase 1 trials are often the first trials for the treatment under study done in humans (with prior testing being done in lab animals). Testing in phase 1 trials is done in a small group of people (20 to 80) to determine safe dose ranges, and begin to identify side effects. Phase 2 trials involve a larger group of participants (100 to 300) to determine the treatment's effectiveness and to further evaluate its safety. Phase 3 trials test with large groups of people (1,000 to 3,000) to confirm the treatment's effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the treatment to be used safely. Phase 4 trials are post-marketing studies that identify more information about the long-term effects of new drugs and treatments. Phase 4 studies involve patients that have been taking the new drug for a considerable period of time and can continue throughout a drug's lifetime of active medical use.

People participate in clinical trials for a variety of reasons. Many, with and without disease, participate to help others and to contribute to moving science forward. Individuals with an illness may also participate to receive the newest treatment. Clinical trial participants often see clinical trial staff more frequently for study visits than they would normally see their physician for standard care. Some see this additional care and attention as a benefit. Participation in clinical trials is key as they offer hope for many people and an opportunity to help researchers find better treatments in the future.