

Understanding Clinical Trials basic level

Overview

When researchers discover a new drug or treatment, they first conduct extensive laboratory and animal studies called preclinical trials. When these laboratory studies show benefits, researchers develop a clinical trial protocol (plan) for testing in people.

What are clinical trials?

The Food and Drug Administration (FDA) is a government agency that regulates the use and testing of drugs and medical treatments. The FDA requires that all new drugs and treatments pass the clinical trial process before being approved for use by the public. During clinical trials, researchers evaluate the safety and efficacy of these new drugs and treatments.

Types of clinical trials

There are several types of clinical trials described below.

- **Treatment trials** study the following: drugs (e.g., pain medicines, anticonvulsants); treatments (e.g., steroid injections, radiation treatments); new approaches to surgery (e.g., spinal instrumentation, dural sealants); and novel methods (e.g., gene therapy, deep-brain stimulation).
- **Prevention trials** study medicines, vitamins, minerals, or exercises that may lower risks of developing certain diseases.
- **Screening trials** test the best way to find a disease or condition through methods such as magnetic resonance imaging (MRI), mammography, or blood tests.
- **Quality of life trials** study the benefits of treatments (e.g., side-effect reducing drugs) or lifestyle changes (e.g., support groups, dietary changes) that may improve quality of life.

Phases of clinical trials

The four phases include the following.

- **Phase I** determines the safety of a treatment that showed positive results in laboratory and animal studies. Phase I trials are neither designed to be therapeutic nor guarantee therapeutic benefits because little is known about the

treatment's effectiveness in people. Drug metabolism and safety are tested in a small group (20-80) of patients or healthy volunteers.

- **Phase II** tests the effectiveness (efficacy) of a drug or procedure on a disease or condition in a larger group of 100-300 patients. Particularly, the treatment is evaluated to identify its benefits and side effects. When the benefits of treatment outweigh side effects and/or risks, the next phase of testing can begin.
- **Phase III** tests a drug or procedure among 1,000-3,000 participants. Its risks and benefits are evaluated and compared with standard, proven treatments.
- **Phase IV** tests a newly FDA-approved drug or procedure for optimal use or efficacy in the treatment of another disease or condition. For example, aspirin, which was initially approved as a pain reliever, was later found to be useful as a blood thinner. This phase is not required.

Role of the Institutional Review Board

An institutional review board (IRB) approves the protocol (trial plan) and monitors all clinical trials. The board is an independent committee of doctors, administrators, consumers, and ethicists from the institution where the trial will occur. The IRB ensures that a trial does not pose unreasonable risks to participants. It scrutinizes recruitment, advertising, and treatment side effects.

Participating in a clinical trial

Participation in a clinical trial is voluntary. Some patients opt to be part of a trial for access to medical treatment (e.g., cancer drug) not yet on the market. During clinical trials, the treatment is still experimental. Thus, although treatment will not benefit all patients, doctors learn more about specific conditions. Participants are part of a larger effort that, in the future, may help others with the same disease.

If you are interested in finding out more about participating in a clinical trial, discuss this with your doctor to learn more about a specific protocol.

Potential benefits

Participants in a clinical trial may:

- Have access to new treatments and drugs before they become available to the public.
- Be carefully monitored to assess the effects of treatment, including any side effects, by doctors and health care staff.
- May benefit early if treatment is effective.
- Contribute to research that will help patients in the future with the same condition.

Potential risks

Participants also must consider some of the following potential risks.

- The new drug or treatment may have side effects or risks that doctors do not yet know about.
- The new drug or treatment may not be better than the standard care.
- In a randomized study, participants may not choose which treatment they will receive.
- Health insurance may not cover all the costs for some test drugs or treatments.
- Participation in a clinical trial may require more visits to the doctor than normal.
- Although a new treatment has benefits, not everyone will benefit.

Who sponsors clinical trials?

A clinical trial may be sponsored by a pharmaceutical company, national organization (e.g., National Cancer Institute), government (National Institute of Health), or academic hospital.

How is a trial conducted?

A clinical trial requires a well-designed protocol, collaboration among various medical specialties, and effective reporting of the findings. It is conducted under the direction of the principle investigator (PI).

Protocol

Clinical trials follow a strict *protocol*—a scientific plan of action. The PI and/or co-investigators may design or assist in its design. The protocol explains who and how many patients will participate, what tests will be performed, how results will be measured, and why the trial may be discontinued. Every doctor (co-investigator) and research facility involved in a trial must follow the protocol designed for that new drug or treatment.

Location

Clinical trials are conducted in different settings (e.g., community hospitals, academic hospitals, specialty treatment centers) and locations. Trials initiated by the PI may be single or multi-center. Single-center trials are available only at the PI's academic hospital.

Multi-center trials are conducted at various locations and offer some advantages versus single center trials.

- Patient enrollment may be quicker because more institutions are involved from different geographic regions.
- Participants will better represent the general population.
- When conducted in various centers around the country, multi-center trials make participation more convenient and cut travel for some patients.

Although investigators at various locations follow the same protocol, some variability in results may occur at different centers.

During a clinical trial, cooperative groups, that is, networks of organizations and researchers at academic hospitals and community practices, may collaborate to conduct research in their medical specialty. For example, oncologists and pediatricians may join a pediatric cancer cooperative group; neurologists and other brain specialists may join a brain tumor cooperative group.

Inclusion/exclusion criteria

All clinical trials have guidelines with criteria about who can participate or not, called inclusion/exclusion criteria. Inclusion criteria list the conditions for eligibility (e.g., disease type, patient age and sex, previous treatment). Exclusion criteria list all conditions that prohibit enrollment.

Randomization

Clinical trial participants may be randomly divided into two or more groups; this is called randomization. For two groups, there is a 50% chance of assignment into either group; a computer program makes the assignment. One group receives the experimental treatment (test group), and the second group (control group) receives either standard or placebo treatment. If one group shows better results, researchers can say with confidence that one treatment is better than the other.

Randomized trials may be “blind”, meaning that participants do not know which treatment (i.e., control, test) they will receive. “Double-blind” trials mean that neither participants nor researchers know to which group participants are assigned. Randomization is part of the scientific method to minimize bias and maximize objectivity in the results. Participants should understand that they may or may not receive the new treatment.

Results

After a clinical trial is completed, researchers analyze and report their findings to the FDA and medical community. Sometimes these findings are published in a medical journal. If the results are good, the study moves onto the next clinical trial phase until the drug or product is found to be safe and effective. The FDA will then approve the drug

for specific use in people, listing all side effects and recommended dosages.

Confidentiality

In reporting the results of a clinical trial, every effort is made to maintain the confidentiality of patients' study records. Patients are informed about who will inspect their medical and study records. Patients are not referred to by name and, unless required by law, patient identity is kept confidential.

Enrolling in a clinical trial

Informed consent *

*Adapted from OHRP "Tips on Informed Consent"

When all inclusion and exclusion criteria are met, an informed consent form is given to the patient. Informed consent is a written and signed agreement required for participation in a clinical trial. It provides the participant with key facts about a clinical trial, including the purpose and length of the study, required procedures, contacts, as well as possible risks and benefits.

Doctors and nurses involved in the study will discuss this information in a simple, concise language. They will:

- Describe why a patient is being asked to participate and what the overall experience might be.
- State the purpose of the study and identify the researcher and/or study sponsor.
- Describe possible benefits expected (this may be nothing more than a sense of helping the public) and risks/discomfort.
- Identify standard treatment options versus experimental treatment.
- Inform participants about the extent that personal private information will be kept confidential.
- Explain if compensation and treatment are available if more than a minimal risk of research-related injury exists.
- List contacts if any questions arise.
- Participants can withdraw from the study at any time without penalty.

If you are interested in participating in a clinical trial, talk with your doctor and those close to you about your options. Before making an informed consent, make sure that you understand the protocol and ask questions if you need more information.

Participants will receive and should keep a copy of the signed consent form. It contains important information that may be referred to during the trial.

Cost

Health insurance coverage varies and may not include partial or complete costs associated with a clinical trial. This occurs because some health plans define clinical trials as "experimental" or "investigational" procedures.

The informed consent form outlines costs for care associated with participation in the clinical trial that will be billed to the patient or insurance company. The FDA does not prohibit charges to patients for treatment or services in a trial. Routine care costs are usually billed to the patient or insurance company. Routine care costs include the medical care needed (whether or not you were in a trial), such as diagnostic tests, hospital care for an emergency injury, or check-up visits to monitor the injury or disease. Participants should be sure to get an estimate of out-of-pocket expenses for which they will pay.

In most clinical trials, the treatment, tests, and doctor's visits are free. Some clinical trials may pay participants for their time and travel.

Questions to ask your doctor

1. What kinds of therapies, procedures or tests will I have during the trial? Will they hurt, and if so, for how long?
2. How do the tests in the study compare with those outside of the trial?
3. Can I take my regular medications while in the clinical trial?
4. Where will I have treatment and who will be in charge of my care?
5. How could being in this study affect my daily life?
6. What are my responsibilities if I participate?
7. Will my health insurance cover the costs of the trial?
8. What charges and how much will I have to pay during the trial, for example, for tests or study drugs?
9. How long will the trial last?
10. What are the potential short- and long- term benefits and risks?

For more information

If you have more questions, please contact the Mayfield Clinic, Department of Clinical Trials (associated with the University of Cincinnati Department of Neurosurgery) at 513-558-3590 or 800-325-7787.

Links

For a current listing of clinical trials that Mayfield physicians are conducting see,
www.mayfieldclinic.com/ClinicalTrials.htm

For current listings of national clinical trials,

www.centerwatch.com
www.clinicaltrials.gov
www.cancer.gov
www.mycure.com
www.virtualtrials.com

Glossary

bias: a point of view preventing impartial judgment on issues. In clinical studies, blinding and randomization minimize bias.

blind: a randomized clinical trial is "blind" when the participants do not know to which group (experimental or control) they are assigned.

control group: the group that receives standard treatment.

cooperative groups: networks of organizations and researchers at academic hospitals and community practices that collaborate to conduct research in their medical specialty.

double-blinded study: a clinical trial in which neither medical staff nor participants know which therapy the participant will receive.

efficacy: the maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. Phase II clinical trials gauge efficacy, and Phase III trials confirm it.

Institutional Review Board (IRB): a committee of scientists, doctors, and consumers at each health care facility where a clinical trial takes place. IRBs review and must approve protocols for all clinical trials. They check to see that the study is well designed, does not involve undue risks, and includes safeguards for patients.

multi-center clinical trials: trials that are conducted at many treatment centers at the same time.

placebo: an inactive pill, liquid, or powder that has no treatment value.

randomization: a method used to prevent bias in research. People are assigned by chance to either the treatment or control group, like the flip of a coin.

single-center clinical trials: trials initiated by one researcher that are only available at one center.

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