NIH Clinical Research Trials and You

http://nih.gov/health/clinicaltrials/basics.htm

What are clinical trials and why do people participate?

Clinical trials are part of clinical research and at the heart of all medical advances. Clinical trials look at new ways to prevent, detect, or treat disease. Treatments might be new drugs or new combinations of drugs, new surgical procedures or devices, or new ways to use existing treatments. The goal of clinical trials is to determine if a new test or treatment works and is safe. Clinical trials can also look at other aspects of care, such as improving the quality of life for people with chronic illnesses.

People participate in clinical trials for a variety of reasons. Healthy volunteers say they participate to help others and to contribute to moving science forward. Participants with an illness or disease also participate to help others, but also to possibly receive the newest treatment and to have the additional care and attention from the clinical trial staff. Clinical trials offer hope for many people and an opportunity to help researchers find better treatments for others in the future.

What is clinical research?

Clinical research is medical research that involves people like you. People volunteer to participate in carefully conducted investigations that ultimately uncover better ways to treat, prevent, diagnose, and understand human disease. Clinical research includes trials that test new treatments and therapies as well as long–term natural history studies, which provide valuable information about how disease and health progress.

The idea

The idea for a clinical research study—also known as a clinical trial—often originates in the laboratory. After researchers test new therapies or procedures in the laboratory and in animal studies, the most promising experimental treatments are moved into clinical trials, which are conducted in phases. During a trial, more information is gained about an experimental treatment, its risks, and its effectiveness.

The protocol

Clinical research is conducted according to a plan known as a protocol. The protocol is carefully designed to safeguard the participants' health and answer specific research questions. A protocol describes the following:

- Who is eligible to participate in the trial
- Details about tests, procedures, medications, and dosages
- The length of the study and what information will be gathered

A clinical study is led by a principal investigator (PI), who is often a doctor. Members of the research team regularly monitor the participants' health to determine the study's safety and effectiveness.

Protocol review

Each clinical trial in the United States must be approved and monitored by an Institutional Review Board (IRB) to ensure that the risks are minimal and are worth any potential benefits. An IRB is an independent committee that consists of physicians, statisticians, and members of the community who ensure that clinical trials are ethical and that the rights of participants are protected. Federal regulation requires all institutions in the United States that

conduct or support biomedical research involving people to have an IRB initially approve and periodically review the research.

Sponsors

Clinical trials are sponsored or funded by various organizations or individuals, including physicians, foundations, medical institutions, voluntary groups, and pharmaceutical companies, as well as federal agencies such as the National Institutes of Health and the Department of Veterans Affairs.

Informed consent

Informed consent is the process of providing potential participants with the key facts about a clinical trial before they decide whether to participate. The process of informed consent (providing additional information) continues throughout the study. To help someone decide whether or not to participate, members of the research team explain the details of the study. Translation or interpretive assistance can be provided for participants with limited English proficiency. The research team provides an informed consent document that includes details about the study, such as its purpose, duration, required procedures, and who to contact for further information. The informed consent document also explains risks and potential benefits. The participant then decides whether to sign the document. Informed consent is not a contract. Volunteers are free to withdraw from the study completely or to refuse particular treatments or tests at any time. Sometimes, however, this will make them ineligible to continue the study.

Types of clinical trials

There are different types of clinical trials.

- **Natural history studies** provide valuable information about how disease and health progress.
- **Prevention trials** look for better ways to prevent a disease in people who have never had the disease or to prevent the disease from returning. Better approaches may include medicines, vaccines, or lifestyle changes, among other things.
- **Screening trials** test the best way to detect certain diseases or health conditions.
- **Diagnostic trials** determine better tests or procedures for diagnosing a particular disease or condition.
- **Treatment trials** test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.
- **Quality of life trials** (or supportive care trials) explore and measure ways to improve the comfort and quality of life of people with a chronic illness.

Phases of clinical trials

Clinical trials are conducted in "phases." Each phase has a different purpose and helps researchers answer different questions.

- **Phase I trials**: Researchers test an experimental drug or treatment in a small group of people (20–80) for the first time. The purpose is to evaluate its safety and identify side effects.
- **Phase II trials**: The experimental drug or treatment is administered to a larger group of people (100–300) to determine its effectiveness and to further evaluate its safety.
- **Phase III trials**: The experimental drug or treatment is administered to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it with standard or equivalent treatments, and collect information that will allow the experimental drug or treatment to be used safely.
- **Phase IV trials**: After a drug is approved by the FDA and made available to the public, researchers track its safety, seeking more information about a drug or treatment's risks, benefits, and optimal use.

Some concepts to understand

Typically, clinical trials compare a new product or therapy with another that already exists to determine if the new one is as successful as, or better than, the existing one. In some studies, participants may **b**e assigned to receive a **placebo** (an inactive product that resembles the test product, but without its treatment value). Comparing a new product with a placebo can be the fastest and most reliable way to demonstrate the new product's therapeutic effectiveness. However, placebos are not used if a patient would be put at risk—particularly in the study of treatments for serious illnesses—by not having effective therapy. Most of these studies compare new products with an approved therapy. Potential participants are told if placebos will be used in the study before they enter a trial.

Randomization is the process by which two or more alternative treatments are assigned to volunteers by chance rather than by choice. This is done to avoid any bias with investigators assigning volunteers to one group or another. The results of each treatment are compared at specific points during a trial, which may last for years. When one treatment is found superior, the trial is stopped so that the fewest volunteers receive the less beneficial treatment.

In ***single-*** or ***double-blind studies*****,** also called single- or double-masked studies, the participants do not know which medicine is being used, so they can describe what happens without bias. "Blind" (or "masked") studies are designed to prevent members of the research team or study participants from influencing the results. This allows scientifically accurate conclusions. In single-blind ("single-masked") studies, only the patient is not told what is being administered. In a double-blind study, only the pharmacist knows; members of the research team are not told which patients are getting which medication, so that their observations will not be biased. If medically necessary, however, it is always possible to find out what the patient is taking.

Who participates in clinical trials?

Many different types of people participate in clinical trials. Some are healthy, while others may have illnesses. A **healthy volunteer** is a person with no known significant health problems who participates in clinical research to test a new drug, device, or intervention. Research procedures with healthy volunteers are designed to develop new knowledge, not to provide direct benefit to study participants. Healthy volunteers have always played an important role in research.

Healthy volunteers are needed for several reasons. When developing a new technique, such as a blood test or imaging device, healthy volunteers (formerly called "normal volunteers") help define the limits of "normal." These volunteers serve as controls for patient groups and are often matched to patients on characteristics such as age, gender, or family relationship. They receive the same test, procedure, or drug the patient group receives. Investigators learn about the disease process by comparing the patient group to the healthy volunteers.

Factors like how much of your time is needed, discomfort you may feel, or risk involved depends on the trial. While some require minimal amounts of time and effort, other studies may require a major commitment in time and effort on behalf of the volunteer, and may involve some discomfort. The research procedure may also carry some risk. The consent process for healthy volunteers includes a detailed discussion of the study's procedures and tests.

A **patient volunteer** has a known health problem and participates in research to better understand, diagnose, treat, or cure that disease or condition. Research procedures with a patient volunteer help develop new knowledge. These procedures may or may not benefit the study participants.

Patient volunteers may be involved in studies similar to those in which healthy volunteers participate. These studies involve drugs, devices, or interventions designed to prevent, treat, or cure disease. Although these studies may provide direct benefit to patient volunteers, the main aim is to prove, by scientific means, the effects and limitations of the experimental treatment. Consequently, some patients serve as controls by not taking the test drug, or by receiving test doses of the drug large enough only to show that it is present, but not at a level that can treat the condition. A study's benefits may be indirect for the volunteers but may help others.

All clinical trials have guidelines about who can participate, called **Inclusion/Exclusion Criteria**. Factors that allow someone to participate in a clinical trial are "inclusion criteria." Those that exclude or not allow participation are "exclusion criteria." These criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Before joining a clinical trial, a participant must qualify for the study. Some research studies seek participants with illnesses or conditions to be studied in the clinical trial, while others need healthy volunteers.

Some studies need both types. Inclusion and exclusion criteria are not used to reject people personally; rather, the criteria are used to identify appropriate participants and keep them safe, and to help ensure that researchers can find new information they need.

How Am I Protected?

Ethical guidelines

The goal of clinical research is to develop knowledge that improves human health or increases understanding of human biology. People who participate in clinical research make it possible for this to occur. The path to finding out if a new drug is safe or effective is to test it on patient volunteers. By placing some people at risk of harm for the good of others, clinical research has the potential to exploit patient volunteers. The purpose of ethical guidelines is both to protect patient volunteers and to preserve the integrity of the science. Ethical guidelines in place today were primarily a response to past research abuses.

Informed consent

Informed consent is the process of learning the key facts about a clinical trial before deciding whether to participate. The process of providing information to participants continues throughout the study. To help someone decide whether to participate, members of the research team explain details of the study. The research team provides an informed consent document, which includes such details about the study as its purpose, duration, required procedures, and who to contact for various purposes. The informed consent document also explains risks and potential benefits.

IRB review

Each clinical trial in the United States must be approved and monitored by an Institutional Review Board (IRB) to ensure that the risks are minimal and are worth any potential benefits. An IRB is an independent committee that consists of physicians, statisticians, and members of the community who ensure that clinical trials are ethical and that the rights of participants are protected. Federal regulation requires all institutions in the United States that conduct or support biomedical research involving people to have an IRB initially approve and periodically review the research.