Clinical Trials and CAM

Introduction

Clinical trials are an important part of medical research. They help scientists find better ways to prevent, detect, and treat diseases and medical conditions. This fact sheet provides an introduction to clinical trials in general and also to trials involving complementary and alternative medicine (CAM).

Key Points

- Clinical trials are research studies in which the safety and efficacy of treatments and therapies are tested in people. Clinical trials are essential for determining which treatments work, which do not, and why.
- There are clinical trials for healthy people (for example, to prevent disease) and trials for many different types and stages of diseases and conditions.
- Participating in a clinical trial can have benefits and risks; the Federal Government requires that participants in federally funded clinical trials are protected and closely monitored. All known risks must be disclosed to participants before they enter a study.
- If you are interested in taking part in a clinical trial, talk with your health care provider. Also, be sure that you understand the information contained in the consent form, have had all of your questions answered, and have discussed the decision with family, friends, or other people you trust.

About CAM and NCCAM

CAM is a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. Complementary medicine is **used together with** conventional medicine, and alternative medicine is used **in place of** conventional medicine.

The National Center for Complementary and Alternative Medicine (NCCAM) is the Federal Government's lead agency for scientific research on CAM. NCCAM's mission is to explore CAM practices using rigorous scientific methods and build an evidence base for the safety and effectiveness of these practices.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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National Center for Complementary and Alternative Medicine

Overview of Clinical Trials

A clinical trial is a research study in which a treatment or therapy is tested in people to see whether it is safe and effective. Clinical trials also help researchers learn which treatments are more effective than others. The information gained from clinical trials helps to improve medical care and contributes to the understanding of diseases and conditions (for example, how a disease progresses or how it affects different systems in the body).

Clinical trials are also called medical research, research studies, or clinical studies. Each trial follows a protocol, which is a written, detailed plan that explains why the study is needed, what it is intended to do, and how it will be conducted. The protocol is written by the trial's principal investigator (the person in charge of the trial).

Types of Clinical Trials

Clinical trials are used to study many aspects of health care:

- **Treatment trials** test treatments for a specific disease or condition.
- **Prevention trials** study ways to reduce the chance that people who are healthy, but possibly at risk for a disease, will develop the disease.
- **Early detection or screening trials** study new ways of finding diseases or conditions before they produce signs or symptoms.
- **Diagnostic trials** test new ways to identify, more accurately and earlier, whether people have diseases and conditions.
- Supportive care trials, also called **quality-of-life trials**, study ways of making patients more comfortable and giving them a better quality of life.

There is a common misunderstanding that clinical trials are a last resort for those who have a disease and have tried all other treatment options. However, there are trials for healthy people (for example, to study disease prevention) and for all different types and stages of diseases.

Clinical Trial Phases

Because a clinical trial tests treatments in people, there needs to be some evidence before the clinical trial starts that the therapy is likely to work. This evidence can come either from previous laboratory research studies or from reports on the therapy's use by people.

Clinical trials take place in phases. In **Phase I** trials, researchers test the treatment in a small group of people, focusing on safety, adverse effects, and sometimes dosage and schedule of administration. In **Phase II** trials, the treatment is given to a larger number of people to determine potential usefulness and to further evaluate its safety and adverse effects. This phase can last several years. In **Phase III** trials, the treatment is usually given to several hundred or more people to confirm its efficacy and more fully define any adverse effects. Phase III trials often compare the treatment under study with standard treatments.

In each phase, different research questions are answered:

- **Phase I:** What is the safe dose? How does the treatment affect the human body? How should the treatment be given?

- **Phase II:** Does the therapy cause any adverse effects? Are the adverse effects tolerable? Is there evidence that the therapy is useful in treating the disease or condition?
- **Phase III:** Is the treatment better than, the same as, or worse than placebo or a standard (and widely accepted) treatment or approach? (See the explanation of placebos below.)

Common Elements of Clinical Trials

Trials can be randomized. In a randomized trial, each participant is assigned by chance—through a computer or a table of random numbers—to either an investigational group or a control group. Randomization is used in all Phase III studies and in some Phase II studies. It helps ensure that the study results are attributable to the treatment and not to unrelated factors that might bias the outcome or the interpretation of the results.

Each participant has an equal chance of being assigned to any group. Some complex trials include several groups.

Trials are often double blind. This means that neither the researchers nor the participants know who has been assigned to which group. Blinding is another way to help minimize the chance of bias influencing the trial results. The information is kept on file at a central office so the research team can find out who was assigned the active treatment if they need to know.

Researchers design clinical trials to have one or more endpoints. An endpoint is a measure that determines whether the treatment under study has an important effect. An example of an endpoint is whether a person's pain improves following acupuncture treatment.

About Placebos

A placebo is an inactive treatment designed to resemble the treatment being studied. An example of a placebo is a pill containing sugar instead of the drug being studied. By giving one group of participants a placebo and the other group the active treatment, the researchers can compare how the two groups respond. This gives the researchers a truer picture of the active treatment's effects.

Another type of placebo, called a "sham," is used when the treatment under study is a procedure (e.g., acupuncture), not a drug or other substance. A sham procedure is designed to simulate the active treatment but does not have any active treatment qualities. For example, in a clinical trial of acupuncture, the sham procedure might consist of placing acupuncture needles in areas of the body that are not expected to have any therapeutic response.

Placebos are necessary because many factors other than the treatment being studied can influence either the course of an illness or the response of a patient to treatment. For example, many illnesses or symptoms resolve on their own, and interactions with the provider or a patient's expectations about the treatment may influence the patient's response. These and other factors are part of what is known as the "placebo effect," which researchers try to separate from the effects of the treatment they are studying.

About Participants

Each clinical trial is unique in its eligibility criteria—i.e., rules for who can participate. The purpose of the criteria is to identify appropriate participants, based on what is being studied and the questions the researchers hope to answer. Examples of criteria include type or severity of disease, presence of other illnesses, and history of prior treatment.

As much as possible, clinical trials include people of various ages and ethnic groups and both genders so the results can apply to the general population. Sometimes, because of what is being studied, it makes sense for a trial to be limited to a particular group, such as women or older people.

Eligibility criteria are also intended to make the trial as safe as possible for participants. For example, it might not be safe for someone with a serious illness to participate if they would have to stop taking their regular medicine to do so. The criteria are never used to exclude someone for reasons not related to the study itself.

Protections for Participants

The Federal Government requires many protections for people who participate in federally funded clinical trials. Before a clinical trial can start, the written protocol must be approved and monitored by an institutional review board (IRB)—an independent group of health care providers, other experts, and people from the community who make sure that the study is set up and run safely and fairly. IRBs also review and approve the consent documents that people must sign in order to participate in a clinical trial. An IRB can stop a clinical trial if the researcher is not following the protocol or if the trial appears to be causing unexpected harm to the participants. An IRB can also stop a clinical trial if the evidence is clear that the new intervention is effective so that it can be made widely available as soon as possible.

At NIH, clinical trials also require additional data and safety monitoring. Some clinical trials—especially Phase III clinical trials, which often involve many institutions—use a Data Safety Monitoring Board (DSMB). A DSMB is an

NIH Protections for Study Participants: Historical Context

The National Institutes of Health (NIH) has established policies and procedures to protect people involved in research studies. The foundation of the NIH protections is *The Belmont Report—Ethical Principles and Guidelines for the Protection of Human Subjects*. Published in 1979, the *Belmont Report* provides the philosophical basis for current Federal laws governing research that involves people. It established three fundamental ethical principles for such research: respect for persons, beneficence (maximizing benefits and minimizing harms), and justice (treating subjects fairly).

Another document in the history of protections for research participants is *The Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects*, issued in 1964 by the World Medical Association. *The Declaration of Helsinki* broadened concepts initially set forth after World War II in *The Nuremberg Code*, which named 10 conditions that must be met to justify research involving people. The two most important conditions were the need for voluntary informed consent of participants and a scientifically valid research design that could produce fruitful results for the good of society.

For more information about regulations and ethical guidelines, see the NIH Office of Human Subject Research Web site: http://ohsr.od.nih.gov/guidelines/index.html.

independent committee made up of statisticians, physicians, and patient advocates (a majority of whom are not connected with the clinical trial) who regularly monitor data from the trial to ensure that the risks of participation are as small as possible. Their priority is patient safety—they can stop a trial if safety concerns arise or if the trial's objectives have been met.

Participants are also protected by a process called informed consent. People who are considering taking part in a clinical trial meet with a member of the research team, who provides key facts about the study, such as:

- Who is sponsoring and conducting the research
- Who has reviewed and approved the study
- What the researchers want to learn
- How the research team will monitor participants' health and safety
- What participants will be required to do during the trial, and for how long
- Possible benefits and risks of participating
- Other treatments that are available for the disease or condition
- How the privacy of participants' medical records will be protected.

Informed Consent Process

When you talk to a member of the research team during the informed consent process, you have a right to have all of your questions answered. If you do not understand an answer you receive, ask again. It can be helpful to make a list of questions and concerns before you talk to the study team.

The staff will also give you a consent form, which explains the study and should be written in straightforward language. Consent forms can be long, and they contain a lot of information that you need to consider carefully. It is a good idea to take the consent form home, so you can think about it and review it with family members or friends. If you are interested in joining a study, it is also very helpful to discuss it with your primary health care provider. By signing the form, you are providing your consent to participate in the trial. However, participating in a clinical trial is completely voluntary. You can leave the trial at any time—and for any reason—even after you have signed the consent form.

What Happens During the Trial

What happens depends on the type of trial and the study protocol. However, some activities are similar for all clinical trials:

- The research team will check the participants' health at the beginning of the trial, give specific instructions for participating, and monitor their health carefully during the trial.
- Participants may be required to perform some tasks between appointments, such as taking medication according to a schedule, completing logs, or answering questionnaires.

Clinical trials take place in a variety of settings depending on the type of trial and what is being studied. For example, participants in a trial of an herb might follow the protocol at home, while a trial that involves specialized equipment (such as acupuncture) might be carried

out in a clinic or other health care setting. Other trials may require participants to be in a hospital, clinic, or research center while the therapy is given.

What Happens After the Clinical Trial

The researchers carefully analyze the data from the trial and then consider what their findings mean. If the trial has been completed and the results have medical importance, the researchers share their findings with the medical community and the public. The results are usually reported in a peer-reviewed medical journal ("peer-reviewed" means that the report is reviewed before publication by a group of experts in the same field) and/or discussed at scientific meetings. The media may also cover the results of the study. The research team also will inform the participants about the study results soon after the study is completed and all its data are analyzed. Participants should ask the study team when they expect to know the results.

A treatment that has been found to be safe and effective in a carefully conducted clinical trial may become a new standard practice.

CAM Clinical Trials

Although many CAM treatments have been in use for a long time (sometimes for centuries), there may be less scientific knowledge available about them than for conventional medical approaches. Without scientific evidence, people already using CAM treatments may be at risk—for example, for serious effects from taking the wrong dose, using the treatment in the wrong way, or using it with other medications that may cause a dangerous interaction. Or, the treatment may be ineffective.

Researchers, including many supported by NCCAM, are studying CAM treatments in clinical trials to find answers to questions such as:

- Does it work?
- If so, how does it work?
- For which diseases and conditions does it work?
- What dose is safe?
- What dose is effective for a specific disease or condition?
- What are the adverse effects?
- How should it be given?
- Are there situations in which it might be harmful?
- Can it be used safely with other forms of treatment?
- Is it better than, or a useful option compared with, other treatments that are available?

NCCAM funds studies on a variety of CAM treatments. A few examples include acupuncture; natural products, such as herbs and other dietary supplements; massage; meditation; and chiropractic or osteopathic manipulation. Examples of diseases and conditions for which CAM therapies are studied include cancer, cardiovascular disease, neurological disorders, and osteoarthritis. Some of these studies involve partnerships with other components of NIH. Institutions outside the Federal Government are conducting studies as well.

If You Are Thinking About Participating in a Clinical Trial: Possible Benefits and Risks

Benefits

- You may have the chance to receive expert medical care and have your health closely watched throughout the study.
- Clinical trials can offer an opportunity for excellent treatment or prevention of a disease or condition.
- In some types of trials, you may be among the first to benefit from a new treatment or new knowledge about a current treatment.
- You will help others by helping to advance medical and scientific knowledge.

Risks

- The treatment under study does not always turn out to be better than, or even as good as, standard treatment. The researchers hope that it is, but they need to do the study to find out for certain.
- The treatment may have adverse effects that are unknown to the researchers or different from what they expect.
- If you are in a randomized trial, you may be assigned to a treatment other than the one you hope to receive. You usually will not know what group you are in.
- The treatment under study may not work for everyone.
- Participation may require more tests and more visits or treatments than regular care.
- There may be costs to participate, and these costs may not all be covered by health insurance plans. Be sure to talk with the research team about any costs involved.

Finding CAM Clinical Trials

The NCCAM Web site contains a listing of NCCAM-funded clinical trials. ClinicalTrials.gov is a database of thousands of clinical studies being sponsored by NIH, other Federal agencies, and the pharmaceutical industry. You can also find out more by contacting the NCCAM Clearinghouse. See “For More Information” below for these and other resources.

For More Information

NCCAM Clearinghouse

The NCCAM Clearinghouse provides information on CAM and NCCAM, including publications and searches of Federal databases of scientific and medical literature. The Clearinghouse does not provide medical advice, treatment recommendations, or referrals to practitioners.

Toll-free in the U.S.: 1-888-644-6226
TTY (for deaf and hard-of-hearing callers): 1-866-464-3615
Web site: nccam.nih.gov
E-mail: info@nccam.nih.gov

National Institutes of Health (NIH)

NIH—the Nation's medical research agency—includes 27 institutes and centers and is a component of the U.S. Department of Health and Human Services. It is the primary Federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases.

Web site: www.nih.gov
E-mail: nihinfo@od.nih.gov

ClinicalTrials.gov

ClinicalTrials.gov is a database of information on federally and privately supported clinical trials (research studies in people) for a wide range of diseases and conditions. It is sponsored by NIH and the U.S. Food and Drug Administration.

Web site: www.clinicaltrials.gov

PubMed®

A service of the National Library of Medicine (NLM), PubMed® contains publication information and (in most cases) brief summaries of articles from scientific and medical journals. CAM on PubMed®, developed jointly by NCCAM and NLM, is a subset of the PubMed system and focuses on the topic of CAM.

Web site: www.ncbi.nlm.nih.gov/sites/entrez
CAM on PubMed®: nccam.nih.gov/research/camonpubmed/

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