NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE
National Institutes of Health

About Clinical Trials and Complementary and Alternative Medicine

Clinical trials are an important part of the medical research process. Through clinical trials, scientific discoveries can lead to better ways to prevent, detect, and treat diseases and medical conditions. This fact sheet will provide you with an introduction to clinical trials and to trials of complementary and alternative medicine (CAM).

Key Facts

- 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 are a key part of the process in finding out which treatments work, which do not, and why. Clinical trial results also contribute new knowledge about diseases and medical conditions.
- There are clinical trials for healthy people (for example, to prevent disease) and trials for many different types and stages of diseases and conditions. Some people think that clinical trials are only a last resort for those who have a disease and have tried all other treatment options, but this is not true.
- There are clinical trials being conducted on CAM throughout the United States and the world.
- Participating in a clinical trial can have benefits and risks.
- Participants in clinical trials are protected and closely monitored.
- If you are interested in taking part in a clinical trial, talk to your health care practitioner. Also be sure that you understand the consent form, have had all your questions answered, and have discussed the decision with people you trust.

What is CAM?

Complementary and alternative medicine, as defined by the National Center for Complementary and Alternative Medicine (NCCAM), is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.[*]

[*]Conventional medicine is medicine as practiced by holders of M.D. (medical doctor) or D.O. (doctor of osteopathy) degrees and by their allied health professionals, such as physical therapists, psychologists, and registered nurses. Other terms for conventional medicine include allopathy; Western, mainstream, orthodox, and regular medicine; and biomedicine. Other terms for CAM include unconventional, non-conventional, unproven, and irregular medicine or health care. Some conventional medical practitioners are also practitioners of CAM.

The list of practices that are considered CAM changes continually, as those therapies that are proven to be safe and effective become adopted into conventional health care and as new approaches to health care emerge.

What is NCCAM's role in the field of CAM?

NCCAM, which is part of the National Institutes of Health (NIH), is the Federal Government's center for scientific research on CAM. As part of its mission, NCCAM explores complementary and alternative healing practices through rigorous science. This effort includes supporting carefully selected, designed, and conducted clinical trials of CAM therapies.

What is a clinical trial?

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. The information learned from clinical trials helps to improve health care and to keep people healthier. Researchers also conduct clinical trials to find out which treatments are more effective than others. The results from trials can also contribute to our 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—a written, detailed plan that explains why there is a need for the study, what it is intended to do, and how it will be conducted. The protocol is written by the trial's principal investigator (the person who is in charge of the trial).

What are the major types of clinical trials?

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

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

Clinical trials have sometimes been thought of as a last resort, for those who have a disease and have tried all other treatment options. This is not true. There are trials for healthy people (for example, to study disease prevention) and trials for all different types and stages of diseases.

What are the different phases of a clinical trial?

Because the therapy will be tested in people, before a clinical trial can start, there needs to be some evidence that it is likely to work. This evidence can come either from previous research studies in animals or from reported information on its use by people.

Clinical trials take place in phases. In each phase**,** different research questions are answered. The following are types of questions that each phase helps to answer:

- **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 treatment treat the disease or cure the condition?
- **Phase III**: Is the treatment better than, the same as, or worse than the standard (or most widely accepted) treatment? If there is no standard treatment available, is it better than, the same as, or worse than a placebo? (Placebos are explained below.)

What are some common elements of clinical trials?

Researchers might include randomization in the trial design. Randomization is used in all phase III studies and in some phase II studies. It gives the best chance of knowing that the study results are caused by the treatment and not some other factor, such as people's choices or beliefs.

Each participant in a randomized trial is assigned by chance (through a computer or a table of random numbers) to one of two groups:

- The investigational group, made up of people who will receive the therapy, also called the active treatment; or
- The control group**,** made up of people who will receive either the standard treatment (if there is one) for their disease or condition, or a placebo.

Each participant has an equal chance of being assigned to either group. In some complex trials, there are more than two groups.

Trials can be 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 if there is an urgent need for the research team to find out who was assigned the active treatment, they can.

Researchers design clinical trials to have one or more endpoints. An endpoint is a measure that determines whether the treatment under study has an effect. An example of an endpoint is whether a person's tumor shrinks after receiving chemotherapy.

What is a placebo?

A placebo is designed to resemble as much as possible the treatment being studied in a clinical trial, except that the placebo is inactive. 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 and get a truer picture of the active treatment's effects.

Another type of placebo is called a "sham" procedure. When the treatment under study is a procedure (not a drug or other substance), a sham procedure may be designed that resembles 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 (from previous knowledge) to have any therapeutic response.

In recent years, the definition of placebo has been expanded to include other things that could have an effect on the results of health care. Examples include how a patient and a health care provider interact, how a patient feels about receiving the care, and what he or she expects to happen from the care. Therefore, when a treatment is compared to a placebo in clinical trials, the patients should differ only in whether they receive treatment, and not in other aspects.

Not all clinical trials compare an active treatment to a placebo. No patient is denied treatment in a clinical trial if there is a standard therapy available that could improve the comfort and survival of the patient.

Who can participate in a clinical trial?

Clinical trials include people of various ages, ethnic groups, and both genders as much as possible, so that the results can apply to the general population. Each clinical trial, however, is unique in its eligibility criteria (rules for who can and cannot participate). Examples of criteria include sex, age, type of disease, severity of disease, and history of prior treatment. If a disease is being studied in a trial, participants must have a similar degree of illness, so that there is a good chance they will respond in similar ways to the treatment being studied.

Are there protections for people who participate in clinical trials?

Yes, 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 IRB is an independent group of health care providers, other experts, and lay people from the community who make sure that the study is set up and run safely and fairly. IRBs review protocols and the consent documents that people must sign in order to participate in a clinical trial.

Participants are also protected by a process called informed consent. If you are considering taking part in a clinical trial, during this process you will meet with a member of the research team. He or she will provide you with 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 your 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 your disease or condition.
- How the privacy of your medical records will be protected.

You have a right to have all 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, an agreement that you will sign if you decide to join the trial. Consent forms can be long, and they contain a lot of information. It is a good idea to take the consent form home, so that you can think about it and review it with family members or friends. If you have an interest in joining a study, it is also very helpful to discuss it with your health care practitioner and others whose advice you trust.

Participating in a clinical trial is completely voluntary. You can leave the trial at any time, for any reason—even after you have signed the consent form.

What happens once a clinical trial starts?

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 do some things between appointments, such as take medication according to a schedule or make a phone call to report their experiences.

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. Still other trials may require participants to be in a hospital, clinic, or research center while the therapy is given.

What happens after a clinical trial ends?

The researchers carefully analyze the data from the trial. Then they consider what their findings mean and whether there should be further testing. If a trial has been completed and the results have medical importance, they usually report the results first in a peer-reviewed medical journal ("peer reviewed" means that each report is reviewed before publication by a group of experts in the same field). A new treatment that has been found to be safe and effective in a carefully conducted clinical trial may become the new standard practice.

If you are a trial participant, the research team will inform you about the study results soon after the study is completed and all its data are analyzed. Ask the study team when they expect to be able to let you know the results.

What are the possible benefits of being in a clinical trial?

- You will receive expert medical care.
- Your health will be closely watched throughout the study.
- Clinical trials can be one treatment or prevention option for 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.

What are the possible risks to being in a clinical trial?

There are possible risks to being a clinical trial, as there are with any form of treatment and with illness itself. In a clinical trial:

- 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 sure.
- The treatment may have side 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 the control group, where you will not receive the treatment under study.
- Like standard treatments, 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 and your situation.

Are clinical trials being done of CAM?

Yes, clinical trials of CAM are taking place throughout the United States and the world.

While many CAM treatments have already been in use for a long time (sometimes for centuries), there is not the kind of scientific knowledge available about them that has been gained from studies of conventional medicine. Many people are already using CAM, and without this scientific knowledge, they 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 another treatment with which it interacts.

Researchers, including many supported by NCCAM, are studying CAM treatments in well-designed clinical trials to find answers to such questions 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 side 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 an adequate alternative to, other treatments that are available?

NCCAM is funding studies on a variety of CAM treatments. A few examples include acupuncture; herbs such as *Ginkgo biloba*; dietary supplements such as glucosamine, chondroitin, saw palmetto, and soy; and massage. Examples of diseases and conditions for which these CAM therapies are being studied include arthritis, neurological disorders, cardiovascular disease, and cancer. Some of these studies involve partnerships with other institutes at NIH. Institutions outside the Federal Government are conducting studies as well.

How do I find out more about 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 the National Institutes of Health, 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

Toll-free: 1–888–644–6226
International: 301–519–3153
TTY (for deaf and hard-of-hearing callers): 1–866–464–3615

E-mail: info@nccam.nih.gov
NCCAM Web site: nccam.nih.gov
Address: NCCAM Clearinghouse, P.O. Box 7923, Gaithersburg, MD 20898-7923

Fax: 1–866–464–3616
Fax on Demand Service: 1–888–644–6226

The NCCAM Clearinghouse provides information about CAM, including clinical trials, and about NCCAM.

National Institutes of Health (NIH)
1 Center Drive
Bethesda, Maryland 20892
Web site: www.nih.gov

NIH's mission is to uncover new knowledge that will lead to better health for everyone. Comprised of 27 separate components, mainly Institutes and Centers, NIH works toward that mission by conducting and supporting research, training researchers, and fostering communication of medical information. Descriptions of each of the Institutes and Centers, along with their research priorities and links to their Web sites, can be accessed from the main NIH Web site at: www.nih.gov.

ClinicalTrials.gov
Web site: clinicaltrials.gov

ClinicalTrials.gov provides patients, family members, health care professionals, and members of the public easy access to information on clinical trials for a wide range of diseases and conditions. NIH, through its National Library of Medicine (NLM), has developed this site in collaboration with all NIH Institutes and the Food and Drug Administration (FDA). The site currently contains approximately 6,200 clinical studies sponsored by NIH, other Federal agencies, and the pharmaceutical industry in over 69,000 locations worldwide.

CAM on PubMed
Web site: www.nlm.nih.gov/nccam/camonpubmed.html

CAM on PubMed, a database accessible via the Internet, was developed jointly by NCCAM and the National Library of Medicine (NLM). It contains bibliographic citations (1966 to the present) to articles on research findings that have been published in scientifically based, peer-reviewed journals on CAM. These citations are a subset of the NLM's PubMed system that contains over 11 million journal citations from the MEDLINE database and additional life science journals important to health researchers, practitioners, and consumers. CAM on PubMed also displays links to publisher Web sites, some of which offer the full text of articles.

Computer Retrieval of Information on Scientific Projects (CRISP)
Web site: www-commons.cit.nih.gov/crisp

CRISP is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other research institutions. The database, maintained by the Office of Extramural Research at NIH, includes projects funded by NIH and other health-related Federal agencies.