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For patients

Clinical Trials and Screening: What You Need to Know

What is a Clinical Trial?

At A Glance

- A clinical trial is a research study that tests how well new medical techniques work in people.
- The different types of trials include observational and randomized controlled trials (RCT). A RCT is considered to be the most reliable way to learn whether a certain test or treatment works.
- Screening trials evaluate new tests for detecting cancer and other health conditions in people before symptoms are present. The goal is to determine whether the screening test saves lives and at what cost.
- Patients should consult their own physicians for assistance in interpreting what clinical trial research results may mean for them.

A clinical trial is a type of research study that tests how well new medical techniques work in people. Individual research trials are designed to answer scientific questions and to find better ways to prevent, screen for, diagnose or treat a disease. Clinical trials vary greatly in size: from a single researcher in one hospital or clinic to an international multicenter study with several hundred participating researchers on several continents.

Every clinical trial has an action plan, or protocol, for conducting the trial. The plan describes how the study will be conducted. Each study has rules about who can and cannot participate. These rules are called "eligibility" criteria and they describe characteristics that must be shared by all participants.

In the United States, an independent committee of physicians, statisticians and members of the community called an Institutional Review Board (IRB) must approve and monitor the action plan to ensure that any risks to participants are minimized and are worth the potential benefits.

Different Types of Research Studies

Observational Studies

There is a distinct difference between **observational studies** and **randomized, controlled trials**. In **observational studies**, researchers monitor a group of people for a period of time without trying to change their lives or provide special treatment and then draw conclusions about the frequency or course of disease in the group. However, only further research can prove the findings of observational studies.

Randomized, Controlled Trials and Blind Studies

A **randomized, controlled trial** (RCT) provides the most compelling medical evidence and is considered to be the most reliable way to learn whether a certain test or treatment works. Randomized means each study subject is randomly assigned to receive either the new treatment being studied or a **placebo**, which is either a fake treatment or the available standard of care to which the new treatment is being compared. Patients who receive the placebo treatment serve as the control group, which allows researchers to isolate and study the effect of the treatment received by the other group.

A **blind study** means the subjects involved in the study do not know which they receive—the study treatment or placebo. If the study is double-blind, the researchers also do not know which treatment is being given to any given subject. This "blinding" is to

prevent researchers' biases from affecting the results.

Types of Clinical Trials

Different types of clinical trials have specific goals. For example:

- treatment trials to test the effectiveness of a new drug or procedure and
- screening trials to test new ways of detecting cancer or other health conditions in people before they have any symptoms.

Treatment Trials

Current Trials Online

The National Institutes of Health (NIH) maintains a current list of clinical trials being conducted throughout the United States and in 203 other countries online at www.clinicaltrials.gov (https://www.clinicaltrials.gov) . Nearly 266,043 trials sponsored by NIH, other federal agencies and private industry are listed in the database. The National Cancer Institute lists cancer-related trials (https://www.cancer.gov/clinicaltrials) at Cancer.gov.

Randomized, controlled clinical trials are separated into different phases based, in part, on the number of participants, and the interim goals for each phase.

- Phase I trials are the first step in testing a new approach in people. In these studies, researchers enroll a small number of patients (fewer than 100) at a few centers and evaluate safety issues, watching closely for any harmful side effects.
- Phase II trials usually include 100-300 patients. The study drug or treatment is given to this larger group of people to see if it is effective and to further evaluate its safety.
- Phase III trials are randomized, controlled multicenter trials involving large groups of 300-3,000 patients. The study drug or treatment is given to this larger group to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely.
- Phase IV trials are conducted to further evaluate the long-term safety and effectiveness of a treatment. They usually take place after the treatment has been approved for standard use and involve up to several thousand people.

From Trial Results to Clinical Practice

After a clinical trial is completed, researchers analyze the data before making decisions about the meaning of the findings and further testing. They will determine whether to move on to the next phase or, especially after a Phase III trial, whether the results have medical importance.

Results are often published in scientific journals that are reviewed by experts to ensure the analysis and conclusions are solid. The results may be featured by the media and discussed by patient advocacy groups before they are published.

Once clinical trials indicate that a new approach is safe and effective, it may become a standard practice—widely accepted and used by medical practitioners and part of guidelines offered by health organizations.

Screening Trials

Screening trials evaluate new tests for detecting cancer and other health conditions in people before symptoms are present. The goal is to determine whether or not the screening test saves lives and at what cost.

The methods of detecting disease, often called **screening tests**, can include:

- **imaging tests** that produce pictures of areas inside the body.

- **laboratory tests** that check blood, urine, and other body fluids and tissues.
- **genetic tests** that look for inherited genetic markers linked to disease. A genetic marker is a specific gene or other identifiable portion of DNA that can be used to identify an individual disease or trait.

Reducing Mortality: The Ultimate Screening Goal

Before a screening program is widely accepted and recommended by medical practitioners, it must do more than detect disease at an early stage. The accepted measure of screening effectiveness is a reduction in the number of deaths from the given disease.

Successful screening programs must produce greater benefit than harm and do so at a cost that society can afford. Following the early detection of disease through screening, diagnostic and treatment services are available that may result in better outcomes for those patients.

Screening trials are instrumental in determining to what extent screening methods actually reduce mortality (death rate)—and at what cost. Examples of screening tests that have become standard medical practice, based on research findings that demonstrated reduced death rates, are Pap tests for cervical cancer and mammography for breast cancer.

Imaging Tests in Screening

Imaging Screening Trials

American College of Radiology Imaging Network (ACRIN) provides information on clinical trials using imaging (for screening as well as diagnosis and treatment) at the Patients section (http://www.acrin.org/PATIENTS/INTRODUCTION.aspx) of ACRIN.org.

A great deal of attention is focused on using imaging tests to screen for the presence of disease. Medical technologies such as computed tomography (CT), magnetic resonance imaging (MRI) and molecular imaging are increasingly capable of detecting disease and other abnormalities at their earliest stages.

Although these highly sensitive imaging tests can detect some diseases, such as cancer, at the most curable stage, they can also produce a high rate of false positives (test results that indicate disease is present when it is not). Imaging screening tests may also detect small tumors that might never become life threatening. This phenomenon, called "over-diagnosis," can put individuals at risk for unnecessary biopsies, surgeries and other treatments. (Over-diagnosis is also an issue with other types of screening tests, not just imaging.)

The life-saving potential of imaging tests to detect cancer must be weighed against the health and socioeconomic costs incurred by using the technologies—both by society and individual patients. Medical providers and healthcare organizations carefully and regularly review the results of screening trials and all other available medical evidence in order to help guide patients and healthcare consumers.

Screening for Lung Cancer

The Impact of Lung Cancer

Lung cancer is the leading cause of cancer deaths in both the United States and throughout the world. It is estimated that more than 94 million current and former smokers in the U.S. are at high risk of developing the disease.

This process is reflected in the **National Lung Screening Trial** (NLST), a large-scale, randomized and controlled clinical trial that compared the effects of two ways of detecting lung cancer—low-dose helical CT (LDCT) and standard chest x-ray—on deaths from the disease.

Researchers have long looked for a way to diagnose lung cancer at an earlier, more treatable stage. Like many cancers, lung

cancer that is detected early—before spreading to other areas of the body—is easier to treat. Unfortunately, when lung cancer is typically diagnosed today, the disease has already spread outside the lung in 15 to 30 percent of all cases.

Both chest x-rays and CT scans have been used to find lung cancer early; however, researchers have been uncertain as to whether the screening techniques reduced the number of deaths from the disease. Although chest CT is capable of detecting small abnormalities that cannot be seen on x-rays, many of those abnormalities turn out not to be cancer, resulting in additional testing and anxiety for patients.

Recent Developments

The U.S. Preventive Services Task Force (USPSTF) has issued a recommendation in favor of annual screening for lung cancer with low-dose computed tomography (LDCT) in persons at high risk for lung cancer based on age and smoking history. For more information, please visit task force website (https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening) . Be sure to check back at *RadiologyInfo.org* for updates.

The NLST was launched to determine whether screening CT or x-ray could reduce mortality rates from lung cancer among those at high risk for the disease. The trial involved more than 53,000 men and women who were current or former heavy smokers between the ages of 55 and 74 enrolled at 33 sites across the country. Each participant was randomly assigned to receive three annual screenings with either CT or standard chest x-ray.

The results of the trial revealed that there were 20 percent fewer lung cancer deaths among the trial participants screened with CT. From a statistical viewpoint, this finding was highly significant—in other words, the mortality reduction was not due to chance but to screening with CT.

"This is the first time that we have seen clear evidence of a significant reduction in lung cancer mortality with a screening test in a randomized controlled trial," said NLST project officer Christine Berg, M.D., when announcing the results.

Harold Varmus, M.D., director of the National Cancer Institute, added, "Lung cancer is the leading cause of cancer mortality in the United States and throughout the world, so a validated approach that can reduce lung cancer mortality by even 20 percent has the potential to spare very significant numbers of people from the ravages of this disease."

If you have questions about lung cancer screening, it may be helpful to discuss with your physician and refer to the National Comprehensive Cancer Network (NCCN) guidelines for lung cancer screening (https://www.nccn.org/patients/guidelines/lung_screening/) .

In the meantime, NLST trial investigators emphasize that the single best way to prevent deaths from lung cancer is to never start smoking, or if already smoking, to quit permanently.

A Final Word on Interpreting Clinical Trial Results

Results of medical research—such as the findings of the NLST trial—are big news. Knowing the basics of clinical research and where to turn for additional guidance can help when it comes to evaluating the results of new medical studies.

A resource designed to help consumers understand scientific studies and research results is an article titled *Understanding Risk: What Do Those Headlines Really Mean (https://permanent.access.gpo.gov/lps53495/risk.asp.htm)* published by the National Institute of Health's National Institute on Aging (NIA).

When evaluating a new medical finding, the NIA encourages consumers to ask a series of questions, including:

- Was the study conducted in the laboratory, in animals or in people? The results of research in people are more likely to be meaningful.
- Does the study include people like you? Check to see if the people in the study are of the same age, sex, education level,

income group, ethnic background and with the same health concerns.

- Was the study a randomized, controlled clinical trial involving thousands of people? Such studies are the most expensive and time consuming but, provided that the technology used in the trial is up to date, they give scientists the most reliable results.
- The bottom line: talk to your doctor or healthcare provider for help on understanding research results and what they can mean for your health.

The primary goal of any well-structured research project is to protect the safety of the clinical trial participants…you! First, your participation is voluntary and never required. Many protective steps must follow when conducting clinical trials to ensure your safety and privacy.

Protocol and Informed Consent

Every clinical trial has a protocol. This is a plan for the trial, and includes background and reasoning for the trial, study objectives, trial design, methods and statistical considerations. The protocol describes who may participate in the trial. It also provides the schedule of tests, procedures, medications and dosages. The protocol justifies the research, ensures it is safe for participants, and is designed to answer the researcher's question.

An important part of the protocol is informed consent. Informed consent is an FDA requirement for your safety. It ensures you are given complete information about a clinical trial prior to your participation. You must read and sign an informed consent before any treatment or testing related to the trial is provided. Read this carefully and discuss with your family and doctors.

The FDA required informed consent includes:

- Trial approach (what will be done)
- Nature of the trial (that the trial involves use of an unproven test)
- Purpose
- Procedures involved and expected length of the trial
- What happens during the trial and which parts of the trial are experimental
- Possible benefits and risks
- Other treatments that might be considered
- Guarantee that identity will remain confidential
- Guarantee that participants have the right to leave the trial at any time
- Contact information in case the participants have questions about the trial or experience side effects or problems during the trial

You have a right to ask questions about any aspect of the clinical trial

Institutional Review Boards and Data Safety Monitoring Boards

An Institutional Review Board (IRB) is an independent committee made up of scientists, doctors, advocates and community members. The committee meets to review and monitor a hospital or research institution's clinical trials. These committees ensure that trial participants are exposed to the minimum possible risks and that the risks associated with the trial are reasonable in relation to the expected benefits. Any institution that conducts clinical trials is required to have the trials reviewed and approved by its IRB before participants can enroll.

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