Chapter 30

Finding Clinical Trials

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Introduction

The rapid advances in the causes and management of telomere biology disorders (TBDs) provide increasing opportunities for individuals with TBDs to participate in clinical trials aimed at improving the lives of those affected by these complex disorders.

Please note: Information about clinical trials should always be used along with the advice of your health care team.

What is a Clinical Trial?

A clinical trial is a research study performed in people to evaluate a medical, surgical, or behavioral intervention.

There are two main study types:

- **Clinical Trials:** Participants receive specific interventions according to the research protocol. Interventions include medical products (such as drugs, devices, procedures, changes to participants' behavior [such as diet]). Clinical trials may compare a new medical approach to a standard one that is already available, to a placebo that contains no active ingredients, or to no intervention.
- **Observational Studies:** Investigators assess health outcomes in groups of participants according to a research plan or protocol. Participants may receive interventions (which can include medical products such as drugs or devices) or procedures as part of their routine medical care, but participants are not assigned to specific interventions by the investigator (as in a clinical trial).

Where Do I Look for Trials?

ClinicalTrials.gov contains a database of federally and privately supported clinical trials being conducted around the world. This searchable registry can be used to locate information regarding a trial's purpose, inclusion/exclusion criteria, study locations, study coordinator's contact information, etc.

How Do I Find Appropriate Trials?

Search Fields

- The **Condition or disease** field tells the database to find all the studies with the disease that was entered. (For example, "Dyskeratosis Congenita" or "Telomere Biology Disorder.")
- The **Other terms** field can be used for additional terms you would like to search, such as a specific National Clinical Trial (NCT) number (unique study identifier in the format "NCTXXXXXXXX"), drug name, an investigator's name, etc.

- The **Country** field can be used to limit one's search to a specific country. If the United States is selected, search fields for State, City, and Distance will appear.

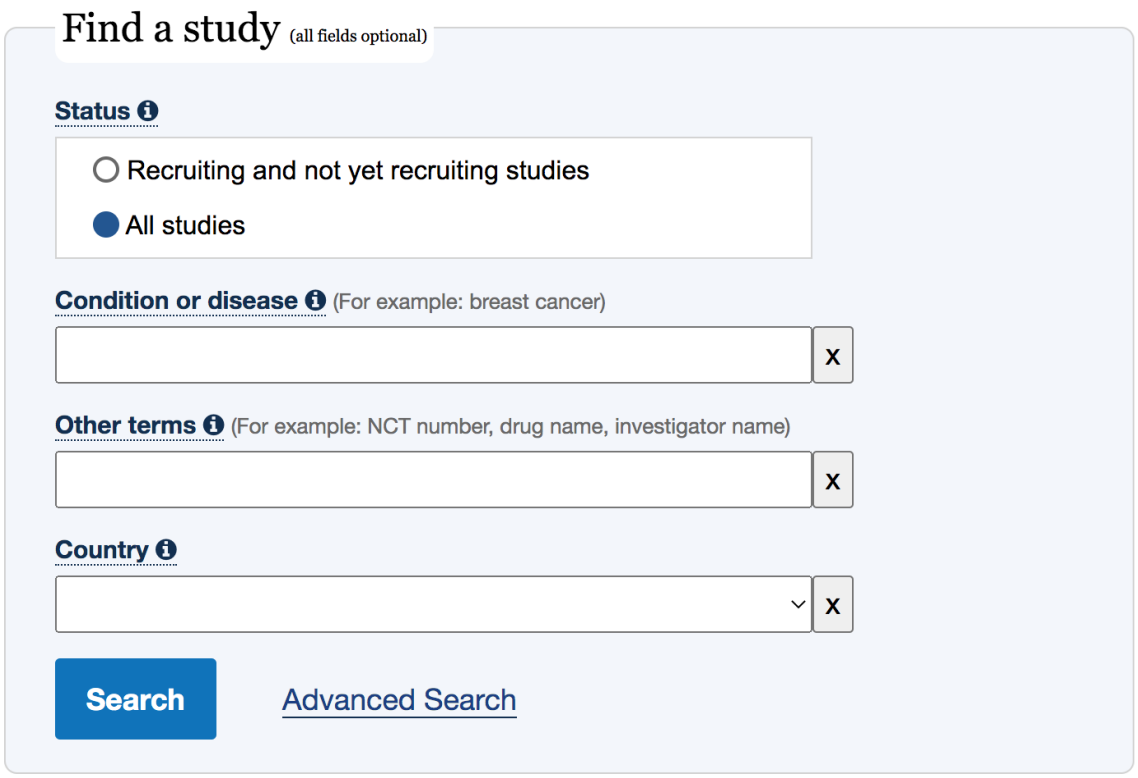

Figure 1. Searching for a clinical trial at ClinicalTrials.gov.

Searches Using Operators: OR, NOT, and AND

Words such as OR, NOT, and AND (in uppercase), are known as search operators. These words can be used in the search function to broaden or narrow a search. For example:

- Use OR to find studies that contain any of the words connected by OR.

  Example: Dyskeratosis Congenita OR Telomere Biology Disorder

  This search finds study records containing either the words "Dyskeratosis Congenita" or "Telomere Biology Disorder." Using OR broadens your search.

- Use NOT to find study records that do not contain the word following NOT.

Example: inherited NOT acquired

This search finds study records containing the word "inherited" but excludes records containing the word "acquired" from the search results. Using NOT narrows your search.

- AND is not necessary because the search function will automatically find study records that contain all the words specified in the search. However, AND can separate distinct concepts.

Additional Filters

Using the left sidebar, one can use the **Status**, **Eligibility Criteria**, **Study Type**, **Study Results**, **Study Phase**, **Funder Type**, and **Study Documents** filters.

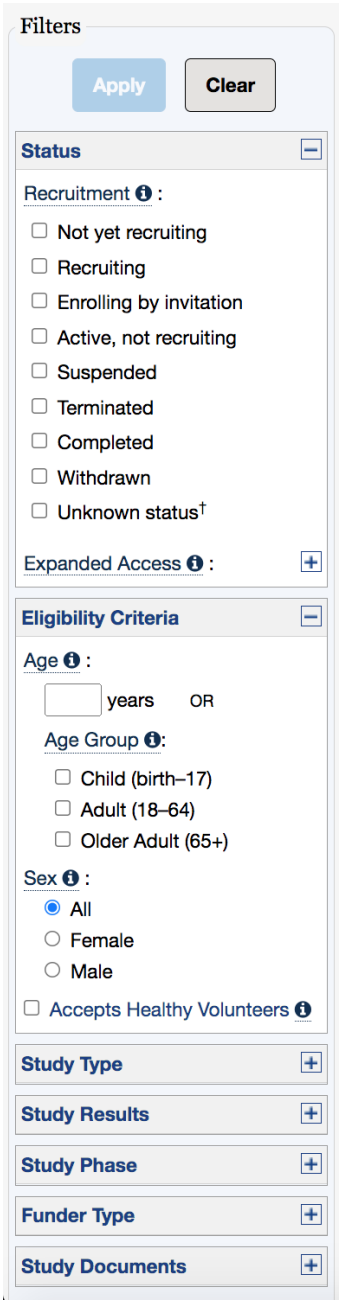

Figure 2. Additional search filters at ClinicalTrials.gov.

Recruitment Status

- **Not yet recruiting:** The study has not started recruiting participants.
- **Recruiting:** The study is currently recruiting participants.
- **Enrolling by invitation:** The study is selecting its participants from a population, or group of people, decided on by the researchers in advance. These studies are not open to everyone who meets the eligibility criteria - only people in that population, who are specifically invited to participate.
- **Active, not recruiting:** The study is ongoing, and participants are receiving an intervention or being examined, but potential participants are not currently being recruited or enrolled.
- **Suspended:** The study has stopped early but may start again.
- **Terminated:** The study has stopped early and will not start again. Participants are no longer being examined or treated.
- **Completed:** The study has ended normally, and participants are no longer being examined or treated.
- **Withdrawn:** The study stopped before enrolling its first participant.
- **Unknown:** A study's status was recruiting; not yet recruiting; or active, not recruiting but has passed its completion date. The status has not been verified within the past 2 years.

Eligibility Criteria

Eligibility criteria is the key requirements that people who want to participate in a clinical study must meet. Eligibility criteria consist of inclusion criteria (which are required for a person to participate in the study) and exclusion criteria (which prevent a person from participating).

Eligibility criteria can include whether a study accepts healthy volunteers, has age requirements, or is limited by biological sex. Additional information regarding eligibility criteria is often found under the details of a study.

Clinical Trial Phases

Clinical trials used in drug development are sometimes described by phase. These phases are defined by the Food and Drug Administration (FDA).

- **Preclinical:** Preclinical studies are sometimes called laboratory studies and can include studies on cell lines and animals. While pre-clinical studies give a lot of useful information, humans may differ in the way that the drug or treatment is absorbed, processed, and excreted. After the pre-clinical studies are completed and if the treatment still seems promising, the Food and Drug Administration (FDA) must give permission before the treatment can be tested in humans.
- **Phase I:** Describe clinical trials that focus on the safety of a drug. The goal is to determine the drug's most frequent and serious adverse events and how the drug is broken down and excreted by the body. These trials usually involve a small number of participants and healthy volunteers.
- **Phase II:** Gather preliminary data on whether a drug works in people who have a certain condition/disease. The drug may be compared to similar participants receiving a placebo (inactive substance) or a different drug. Safety continues to be evaluated; short-term adverse events and effectiveness are studied.
- **Phase III:** Gather more information about a drug's safety and effectiveness by studying different populations and dosages. The drug may be used in combination with other drugs. These studies typically involve more participants.
- **Phase IV:** Occurs after the FDA has approved a drug for marketing. These trials gather additional information about a drug's safety, efficacy, or optimal use.

In certain circumstances, phases may necessitate combining (e.g. Phase I/II), such as when trial on healthy participants is not possible.

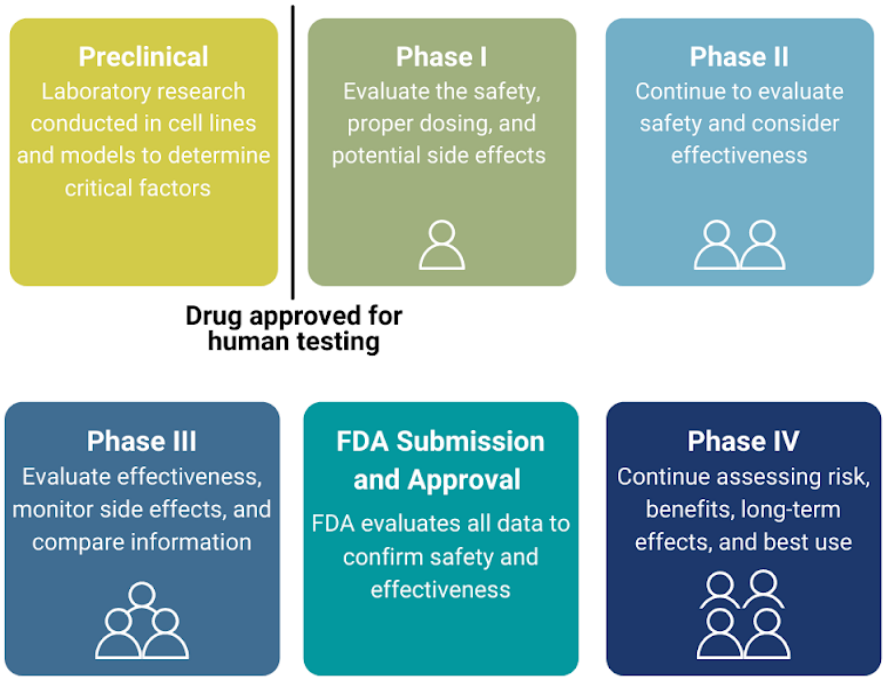

Figure 3. Clinical trial phases infographic. (Figure adapted from hepb.org.)

How are Study Participants Protected?

Informed Consent

Informed consent is a process used by researchers to provide potential and enrolled participants with information about a clinical study. This information helps people decide whether they want to enroll or continue to participate in the study. The informed consent process is intended to protect participants and should provide enough information for a person to understand the risks, potential benefits, and alternatives to the study. In general, a person must sign an informed consent document before joining a study to show that he or she was given information on the risks, potential benefits, and alternatives and that he or she understands it. Signing the document and providing consent is not a contract. Participants may withdraw from a study at any time - even if the study is not over.

Institutional Review Boards (IRB)

Every study must be reviewed, approved, and monitored by an institutional review board (IRB). An IRB is made up of doctors, researchers, and members of the community. Its role is to make sure that the study is ethical and that the rights of participants are protected. This includes making sure that research risks are minimized and are reasonable in relation to any potential benefits (among other responsibilities).

Future Implications

By participating in a clinical study, one contributes to medical knowledge. Much of what is known today about TBDs has been derived from clinical trials. The results of studies can make a difference in the care of future individuals with TBDs by providing information about the benefits and risks of diagnostic, preventative, therapeutic products, or interventions.

Questions to Consider Before Participating in a Trial

- What exactly is being studied?
- Why do researchers believe the intervention being tested might be effective? Why might it not be effective?
- Has it been tested before? What were the results from those tests?
- What are the possible interventions that I might receive during the trial?
- How will it be determined which intervention(s) I receive (for example, by chance)?
- Who will know which intervention I receive during the trial? Will I know? Will members of the research team know?
- How do the possible risks, side effects, and benefits of this trial compare with those of my current treatment?
- What will I have to do?

- What tests and procedures are involved?
- How often will I have to visit the hospital or clinic?
- Will hospitalization be required?
- How long will the study last?
- Who will pay for my participation?
- Will I be reimbursed for other expenses?
- What type of long-term follow-up care is part of this trial?
- If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?
- Will the results of the study be provided to me?
- Who will oversee my medical care while I am participating in the trial?
- What are my options if I am injured during the study?

Additional Resources

Additional clinical trials and information may be present under Team Telomere's Resources tab: https://teamtelomere.org/resources.

For information on the National Institutes of Health Inherited Bone Marrow Failures Syndromes study, please go to http://marrowfailure.cancer.gov/index.html.

References

1. Ferris, Robert L. "Why Are Clinical Trials Important?" *Oley.org*, Mar. 2017, oley.org/page/clinical_trials.
2. National Institutes of Health. "Finding a Clinical Trial." *National Institutes of Health (NIH)*, 6 Nov. 2018, www.nih.gov/health-information/nih-clinical-research-trials-you/finding-clinical-trial.
3. NIH National Library of Medicine. "About Clinical Studies." *ClinicalTrials.gov*, Dec. 2015, clinicaltrials.gov/ct2/about-studies/.