CLINICAL TRIALS AND ME

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Clinical Trial Terminology

Considering to participate in a clinical trial can raise a lot of questions for potential participants. You may be searching for answers to your questions on the internet, by asking your doctor, or through information obtained from clinical trial personnel. A lot of information is available through a variety of channels and choosing to be a part of a clinical trial should be an educational process.

One key part of this process is learning to speak the "clinical trial language." This means becoming familiar with clinical trial terms that you may hear certain personnel use and understanding clinical trial methods that you may be a part of.

Before we get to the in-depth terminology used to describe the details of clinical trials, let's clearly define what clinical trials are and get a clearer understanding of their value.

Clinical Trials Explained: The Value of Research

The life expectancy of humans has been rapidly increasing throughout history. Pharmaceuticals are partly responsible.[1]

For instance, before the early 20th century and the discovery of antibiotics, human life expectancy was about 30 years less than it was in 2016 (78.8 years).[2] With the discovery of antibiotics, the major contributors to non-age-related death changed from infectious and communicable diseases to diseases such as cardiovascular disease, cancer, and stroke.[2]

Despite the incredible power of pharmaceuticals and their historic role in changing our health and our lifespan, there are still many human ailments for which no known treatments exist. Many scientists and doctors are focused on fixing this issue, driving medicine forward, and discovering treatments that will further increase life expectancy and improve human quality of life.

Running a clinical trial is one critical step in solving this problem and identifying drugs that can help achieve this goal.

A Clinical Trial Definition

A clinical trial is a research study involving human subjects that test new treatment methods, new drugs, and methods for measuring the effectiveness of a test treatment on a disease or medical condition. Often, human volunteers are given one or more investigational therapies to test the effects on their health of behavior.[3] In other words, clinical trials allow researchers to test whether or not an exploratory medication or medical method is safe for a certain disease or condition.

Clinical trials allow scientists and doctors to answer questions like: "Does drug A work better than drug B?" or "Do participants recover faster if they get this study drug before or after cardiac surgery?" Scientists can accurately evaluate medications by studying their effects

on healthy people and on those with the condition the drug is designed to target.

As a potential clinical trial participant, you may be interested in understanding the various types of clinical trials, their different methodologies, and in what instance each one is used. Below, we go beyond a clinical trial definition and delve further into clinical trial terms, with more in-depth descriptions of the methods used—*placebo-controlled, randomized* or *blinded*—and the clear distinctions between them.

For more information on what a clinical trial is, see "What is a Clinical Trial?"

Understanding Clinical Trial Terms

To conduct a clinical trial, scientists and doctors use intricate clinical trial methods designed to maintain the accuracy or integrity of the data collected during a clinical trial. These methods may appear overly complicated to you as a participant, however; in addition to maintaining data integrity, these methods are meant to keep you as safe as possible.

The discovery of an effective treatment for a disease requires that several types of clinical trials be conducted before the investigational treatment can be approved by a regulatory agency, such as the U.S. Food and Drug Administration (FDA). The type of trial will determine how many participants are involved, the trial design, and many other factors.

To help decode some of the jargon that you may hear from researchers or personnel while you are engaged in your clinical trial, let's clearly define some of the more common clinical trials names, acronyms, and terminology.

The following clinical trial terms have been organized into specific categories:

Terms Related to the Risks and Benefits of a Clinical Trial

- **Adverse Event:** an unfavorable change in the health of a participant, including abnormal laboratory findings, that happens during a clinical study or within a certain amount of time after the study has ended.[4]
- **Contraindication:** a situation in which a specific treatment should not be used because it may be harmful.[5]
- **Efficacy and Effectiveness:** efficacy is the performance of an intervention under ideal and controlled circumstances, as in a clinical trial. Effectiveness is the performance under "real-world" conditions.[6]
- **Informed Consent:** a process used by researchers to communicate the risks and potential benefits of participating in a clinical study to potential and enrolled participants.[4]

Terms Related to the Types of Clinical Trials and Methods Used

- **Biologic:** a class of drugs isolated from a variety of natural sources (human, animal, or microorganism), may be produced by biotechnology methods, and are composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues.[7]
- **Blinding:** a method used in certain types of clinical trials that keeps study participants from knowing what study treatment they are receiving. This is called single-blinding.[8]
- **Diagnostic Trials:** a research study that evaluates methods of detecting disease.[9]
- **Dose-Ranging Study:** a type of clinical trial where different doses of a drug are tested to determine which is the safest and most effective.[10]

- **Double-Blind Study:** when both study participants and clinical trial personnel are blinded from knowing what study treatment the individual participants are receiving.[8]
- **Pre-Clinical Research:** small studies designed to provide detailed information on dosing and toxicity levels. These studies occur before clinical trials in humans and can be in vitro, meaning in a test tube, and/or in vivo, meaning in animals.[11]
- **Phase 1 Research:** a phase of research that describes clinical trials that focus on the safety of a drug. They are usually conducted with healthy volunteers, and 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.[4]
- **Phase 2 Research:** a phase of research that describes clinical trials that gather preliminary data on whether a drug works (that is, the drug's effectiveness) in people who have a certain condition or disease. Safety is evaluated, and short-term adverse events are studied.[4]
- **Phase 3 Research:** a phase of research that describes clinical trials that gather more information about a drug's safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. These trials typically involve larger numbers of participants than phase 1 and phase 2 trials.[4]
- **Phase 4 Research:** a phase of research that describes clinical trials that occur after the FDA has approved a drug for marketing. They include so-called postmarket requirement and commitment studies that are required of or agreed to by the study sponsor. These trials gather additional information about a drug's safety, efficacy, or optimal use.[4]
- **Open-Label Trial:** a type of study in which both the health providers and the participants are aware of the drug or study treatment being given to an individual participant.[12]
- **Pilot Study:** a small-scale test of the methods and procedures to be used on a larger scale for the purpose of examining the feasibility of an approach.[13]
- **Placebo and Placebo-Controlled:** an inactive substance or other intervention, called a placebo, that looks the same as, and is given the same way as, an active drug or treatment being tested. The effects of the active drug or other intervention are compared to the effects of the placebo. This is called a *placebo-controlled* study.[14]
- **Principal Investigator (PI):** the person who is responsible for the scientific and technical direction of the entire clinical study.[4]
- **Protocol:** the written description of a clinical study. It includes the study's objectives, design, and methods. It may also include relevant scientific background and statistical information.[4]
- **Randomization:** random, meaning by chance, assignment of clinical trial participants to the study treatments being tested in a clinical trial.[4]
- **Screening Trials:** trials that test the best way to detect certain diseases or health conditions.[3]
- **Sponsor:** the organization or person who initiates the study and has authority and control over the study.[4]
- **Study Coordinator:** The study coordinator, also called a clinical research coordinator (CRC), is responsible for carrying out many key operational procedures in the management of clinical trials, including administrative, feasibility analysis, regulatory compliance, recruiting, patient care, and evaluation of study data.[15]
- **Study Nurse:** The Study Nurse, or Clinical Trial Nurse, interacts with patients participating in clinical trials by ensuring the patient understands benefits and risks, informed consent, and other decisions pertaining to

the pending trial, and once enrolled, can administer medications or perform other critical procedures.[16]

- **Sub-Investigator (Sub-I):** The Sub-investigator is a research fellow, resident investigator, or other member of the team who assists the investigator in the conduct of the clinical investigation. They may or may not perform any significant clinical investigation-related duties at the discretion of the Primary Investigator.[17]
- **Toxicology:** The study of poisons, including the source, effect, and treatment of poisoning. It is a branch of pharmacology (the study of drugs).[18]
- **Treatment Regimen:** a structured treatment plan designed to improve or maintain health.[19]
- **Pharmacokinetics:** the activity of drugs in the body over a period of time, including the processes by which drugs are absorbed, distributed in the body, localized in the tissues, and excreted.[20]

Terms Related to Recruiting Participants to Clinical Trials

- **Clinical Trial Registry:** a collection of information about individuals with a specific diagnosis or condition that may be used to seek out people who are good candidates to participate in clinical trials.[21]
- **Inclusion/Exclusion Criteria:** the specific characteristics that determine whether a person is allowed or not allowed to participate in a clinical trial. Together, these make up the eligibility criteria.[4]
- **Healthy Volunteer:** a person with no known significant health problems who participates in clinical research to test a new drug, device, or intervention.[3]
- **Patient Volunteer:** a person who has a known health problem and participates in research to better understand, diagnose, treat, or cure that disease or condition.[3]

Terms Related to Analyzing Clinical Trial Data

- **Intent-To-Treat (ITT):** a population of clinical trial participants that includes all randomized participants in the groups to which they were randomly assigned, regardless of their adherence with the entry criteria, regardless of the study treatment they actually received, and regardless of subsequent withdrawal from study treatment or deviation from the protocol.[22]
- **Modified Intent-To-Treat (mITT):** a subset of the Intent-to-Treat population that excludes randomized subjects in a justified way, such as participants who were deemed ineligible after randomization or certain participants who never started study treatment.[22]
- **Per-Protocol Analysis:** interpretation of randomized clinical trial results that removes data from participants who didn't comply with a clinical trial protocol.[23]
- **Statistical Significance:** describes a mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone.[24]
- **Study Endpoint:** in clinical trials, an event or outcome that can be measured objectively to determine whether the intervention being studied is beneficial.[25]

Terms Related to Regulatory Review and Approval

- **Good Clinical Practice (GCP):** a set of principles that helps ensure the safety, integrity, and quality of clinical trials by addressing elements related to the design, conduct, and reporting of clinical trials.[26]
- **New Drug Application (NDA):** an application by which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the United States.[27]
- **Off-label Use:** use of an FDA-approved drug as treatment for an unapproved condition.[28]

- **On-label Use:** use of an FDA-approved drug as treatment for an approved condition.[28]
- **Peer Review:** a quality control measure in research, where professionals review each other's work to make sure it is accurate, relevant, and significant.[29]
- **PICO Framework:** a framework for building and answering a clinical or health care related question. PICO is an acronym for:[30]
  - **Patient population or problem:** *how would you describe a group of patients in the study?*
  - **Intervention (i.e., a cause, prognostic factor, treatment, etc.):** *which main intervention is of interest in the study?*
  - **Comparison intervention (if necessary):** *is the study including placebo or standard to compare to the exploratory intervention?*
  - **Outcomes:** *what is the hope for the intervention and what will it accomplish?*

References:

1. Life Expectancy. Our World in Data website: https://ourworldindata.org/life-expectancy. Accessed April 26, 2018.
2. Adedeji WA. The treasure called antibiotics. Ann Ib Postgrad Med. 2016;14(2):56-57.
3. NIH Clinical Research Trials and You. NIH website: https://www.nih.gov/health-information/nih-clinical-research-trials-you/glossary-common-terms. Published February 2016. Accessed April 26, 2018.
4. Glossary of Common Site Terms. ClinicalTrials.gov website: https://clinicaltrials.gov/ct2/about-studies/glossary. Published April 2018. Accessed April 26, 2018.
5. Contraindication. MedlinePlus website: https://medlineplus.gov/ency/article/002314.htm. Published April 2018. Accessed April 26, 2018.
6. Singal AG, Higgins PDR, Waljee AK. A Primer on Effectiveness and Efficacy Trials. Clin Transl Gastroenterol. 2014;5(1):e45.
7. What Are "Biologics" Questions and Answers. U.S. Food & Drug Administration website: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm. Published February 2018. Accessed April 26, 2018.
8. Day SJ, Altman DG. Blinding in clinical trials and other studies. BMJ. 2000; 321:504.
9. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/diagnostic-trial. Accessed April 26, 2018.
10. Dose-Ranging Trial. AIDSinfo website: https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/1560/dose-ranging-trial. Published April 2018. Accessed April 26, 2018.
11. Step 2: Preclinical Research. U.S. Food & Drug Administration website: https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405658.htm. Published January 2018. Accessed April 30, 2018.
12. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/open-label-study. Accessed April 30, 2018.
13. Leon AC, Davis LL, Kraemer HC. The Role and Interpretation of Pilot Studies in Clinical Research. J Psychiatr Res. 2011;45(5):626-629.
14. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/search?contains=false&q=placebo. Accessed April 30, 2018.
15. The Anatomy of a Great Clinical Research Coordinator. Association of Clinical Research Professionals (ACRP) Website: https://acrpnet.org/2018/08/14/the-anatomy-of-a-great-clinical-research-coordinator/ Published August 14, 2018. Accessed March 4, 2019.
16. What is a research nurse and what do they do? Clinfield Limited website: https://clinfield.com/what-is-a-research-nurse-and-what-do-they-do/ Published February 11, 2013. Accessed March 5, 2019.
17. Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs. U.S. Food & Drug Administration website: https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf Published May 2010. Accessed March 4, 2019.
18. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/toxicology. Accessed April 30, 2018.
19. HIV/AIDS Glossary. AIDSinfo website: https://aidsinfo.nih.gov/understanding-hiv-aids/glossary/1641/treatment-regimen. Accessed April 30, 2018.
20. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/pharmacokinetics. Accessed April 30, 2018.
21. List of Registries. NIH website: https://www.nih.gov/health-information/nih-clinical-research-trials-you/list-registries. Published March 2018. Accessed April 26, 2018.
22. Gupta SK. Intention-to-treat concept: A review. Perspect Clin Res. 2011;2(3):109-112.
23. Ranganathan P, Pramesh CS, Aggarwal R. Common pitfalls in statistical analysis: Intention-to-treat versus per-protocol analysis. Perspect Clin Res. 2016;7(3):144-146.
24. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/statistically-significant. Accessed April 30, 2018.
25. NCI Dictionary of Cancer Terms. NCI website: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/endpoint. Accessed April 30, 2018.
26. Good Clinical Practice Training. NIH website: https://grants.nih.gov/policy/clinical-trials/good-clinical-training.htm. Published December 2017. Accessed April 26, 2018.
27. New Drug Application (NDA). U.S. Food & Drug Administration website: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm. Published March 2016. Accessed April 30, 2018.
28. Understanding Unapproved Use of Approved Drugs "Off Label." U.S. Food & Drug Administration website: https://www.fda.gov/ForPatients/Other/OffLabel/ucm20041767.htm. Published February 2018. Accessed April 30, 2018.
29. Peer review: what is it and why do we do it? MedicalNewsToday website: https://www.medicalnewstoday.com/articles/281528.php. Published August 2017. Accessed April 30, 2018.
30. PICO Framework. PubMed Health website: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0029906/. Accessed April 30, 2018.