Conducting and Managing Cancer Clinical Trials
A Library of Resources

VIII. Clinical Trial Design and Methodology

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This library of resources was compiled to centralize resources related to conducting and managing clinical trials. The resources are particularly helpful for physician investigators and research staff. A Task Force of the Research Community Forum, representing a range of community research stakeholder groups with a wealth of experience, compiled this list to help make it easier for research sites to find needed resources. Decisions to include resources were solely based on the Task Force’s own go-to resources, consultation with colleagues, and an environmental scan of available resources on these topics. Resources from commercial, for-profit entities are generally excluded from the library. The items listed are not necessarily endorsed by ASCO; they are listed based on the discretion and expertise of the Task Force.

This list is not exhaustive and will be updated periodically. Your feedback is welcomed! If you have ideas for content to add or edit, please email your suggestions to the ASCO Research Community Forum.

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VIII. Clinical Trial Design and Methodology

These resources describe key terms in precision medicine and clinical trial types and designs. Definitions are provided below.

This section includes the following topics:

A. Precision Medicine Trials and Important Definitions
B. Other Types of Trials and Important Definitions
C. Statistical Considerations for Trial Designs and Methodologies
D. Clinical Trial Terms — Resources

A. Precision Medicine Trials and Important Definitions

Precision medicine is an approach for disease treatment and prevention that considers individual variability in genes, environment, and lifestyle for each person. It allows doctors and researchers to more accurately predict treatment and prevention strategies for a particular disease that will work best in specific groups of people. This approach is in contrast to traditional disease treatment and prevention strategies that are developed for the average person, with less consideration for individual differences. (National Institutes of Health Genetics Home Reference)

- **Basket Trial**: Basket trials test the effect of one drug on a single mutation in a variety of tumor types, at the same time. These studies also have the potential to greatly increase the number of patients who are eligible to receive certain drugs relative to other trials designs. (National Cancer Institute [NCI] Dictionary of Terms)

- **Umbrella Trial**: Umbrella trials have many different treatment arms within one trial. People are assigned to a particular treatment arm of the trial based on their type of cancer and the specific molecular makeup of their cancer. (National Cancer Institute [NCI] Dictionary of Terms)

- **Targeted Therapy**: Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific types of cancer cells and limiting harm to normal cells. Some targeted therapies block the action of certain enzymes, proteins, or other molecules involved in the growth and spread of cancer cells. Other types of targeted therapies help the immune system kill cancer cells or deliver toxic substances directly to cancer cells to kill them. This type of therapy may have fewer side effects than other types of cancer treatment. (National Cancer Institute [NCI] Dictionary of Terms)

- **Molecular Profiling**: Molecular profiling is a method of testing genetic characteristics as well as any unique biomarkers of a cancerous tumor. The results are used to identify and create targeted therapies, which are designed to work most effectively for specific cancer tumor profiles. (Leukemia and Lymphoma Society Cancer Molecular Profiling)

- **Genomic Profiling**: Genomic profiling is laboratory method use to learn more about the genetic makeup of a person or cell type and the way those genes interact with each other and the environment. This method may inform why some people get certain diseases while others do not, or why people react in different ways to the same drug. It may also be used to help develop new ways to diagnose, treat, and prevent diseases, such as cancer. (National Cancer Institute [NCI] Dictionary of Terms)
• **Precision Medicine Initiative:** The PMI is a $215 million proposed investment in President Obama’s 2016 Budget to accelerate biomedical research and provide clinicians with new tools to select the therapies that will work best in individual patients. The PMI’s near-term emphasis is on cancer, and other disease areas will be included over the longer term. ([National Cancer Institute [NCI] and the Precision Medicine Initiative](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))

B. Other Types of Trials and Important Definitions

• **Cancer Care Delivery Research:** Cancer Care Delivery Research (CCDR) examines how social factors, financing systems, organizational structures and processes, health technologies, and healthcare provider and individual behaviors affect cancer outcomes, access to and quality of care, cancer care costs, and the health and well-being of cancer patients and survivors. Ultimately, it aims to reduce the incidence, associated symptoms, and morbidities of cancer and its treatment, and enhance the quality of life of those affected by cancer. ([National Cancer Institute Community Oncology Research Program [NCORP] Research Areas](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))

• **Treatment Trials:** Treatment trials are designed to test new ways to treat cancer. For a treatment to become standard, it must usually go through 3 or 4 clinical trial phases. The early phases make sure the treatment is safe. Later phases show if it works better than the standard treatment. ([National Cancer Institute Types of Clinical Trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))
  
  o **Phases of Clinical Trials:** For a treatment to become standard, it must first go through 3 or 4 clinical trial phases. The early phases make sure the treatment is safe. Later phases show if it works better than the standard treatment. Each phase of a clinical trial is designed to provide different information about the new treatment, such as the dose, safety, and efficacy (how well it works). The phases are described as I, II, and III. ([National Cancer Institute Phases of Clinical Trials; Cancer.net Phases of Clinical Trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))
  
  o **Phase I Clinical Trial:** An experimental drug or treatment, which has proven to be safe for use in animals, is tested in a small group of people (15-30) for the first time. Data are collected on the dose, timing, and safety of the treatment. The purpose is to evaluate its safety and identify side effects. ([National Cancer Institute Phases of Clinical Trials; Cancer.net Phases of Clinical Trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))
  
  o **Phase II Clinical Trial:** An experimental drug or treatment is tested in a larger group (100 or less) to provide more detailed information about the safety of the treatment, in addition to evaluating how well it works for a broader range of people. Phase II trials usually take about two years to complete. ([National Cancer Institute Phases of Clinical Trials; Cancer.net Phases of Clinical Trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))
  
  o **Phase III Clinical Trial:** Before an experimental drug or treatment is approved by the FDA and made available to the public, Phase III trials are conducted on a large group of people (from 100 to several thousand). At least two (and often more than two treatment options, including standard of care) are compared to find out whether the new treatment is better, and possibly has fewer side effects, than the current standard treatment. Phase III clinical trials are usually randomized, meaning that patients receive either the investigational drug or treatment or another drug or treatment in a non-ordered way. ([National Cancer Institute Phases of Clinical Trials; Cancer.net Phases of Clinical Trials](https://www.cancer.gov/about-cancer/treatment/clinical-trials/types/))
Phase IV Clinical Trial: After a drug is approved by the FDA and made available to the public, researchers track its safety, seeking more information about a drug or treatment’s risks, benefits, and optimal use. Several hundred to several thousand people participate in Phase IV trials. (Cancer.net Phases of Clinical Trials)

- **Health Services Research**: Multidisciplinary research that examines how social factors, financing systems, organizational structures and processes, health technologies, and personal behaviors affect access to health care, the quality and cost of health care, and ultimately our health and well-being. Its research domains are individuals, families, organizations, institutions, communities, and populations. (Agency for Healthcare Research and Quality An Organizational Guide to Building Health Services Research Capacity)

- **Cancer Prevention Studies**: A cancer prevention trial is a study of a large group of people. A prevention trial tries to find better ways to prevent people from getting cancer or lower the chances that people will get it. (U.S. Department of Health and Human Services [HHS] If You Want to Find Ways to Prevent Cancer... Learn About Prevention Clinical Trials)

- **Prognostic Studies**: Studies that aim to understand the course, determinants, or probability of a given outcome in cohort (Cochrane Methods Prognosis About Us)

- **Experimental Studies**: As part of an experimental study, researchers provide an intervention (such as a treatment) to a group of individuals and compare their results to those of another group that does not receive the intervention (known as the control group). The researchers decide who receives the intervention and who does not either randomly (for reasons explained below) or through intentional selection. Experimental studies can investigate treatments, correlative science (testing whether specific genes or proteins affect the development or spread of cancer), new imaging techniques, and quality of life issues. (Cancer.net Understanding Cancer Research Study Design and How to Evaluate Results)

- **Observational Studies**: During an observational study, the researchers observe groups in which the intervention that each person receives is not controlled by the researchers. Observational studies tend to be epidemiologic (relating to how various risk factors cause or affect the development of a disease in a population). (Cancer.net Understanding Cancer Research Study Design and How to Evaluate Results)

- **Comparative Effectiveness Research**: Comparative effectiveness research is the conduct and synthesis of systematic research comparing different interventions and strategies to prevent, diagnose, treat and monitor health conditions. The purpose of this research is to inform patients, providers, and decision-makers about which interventions are most effective for which patients under specific circumstances. (National Library of Medicine Resources for Informing Comparative Effectiveness Research)

C. Statistical Considerations for Trial Designs and Methodologies

- **Statistical Considerations in Oncology Trials** | ASCO eLearning Fundamentals of Clinical Trials
- Clinical Trial Eligibility Criteria. This asco.org web page provides an overview of ASCO’s initiative on broadening eligibility criteria.
D. Clinical Trial Terms — Resources

- Genetics Home Reference. This website from the U.S. National Library of Medicine provides consumer-friendly information about human genetics, including the effects of genetic variation on human health.
- NIH Clinical Research Trials and You.
- ASCO Cancer.Net Information for Patients
- National Cancer Institute Dictionary of Genetics Terms. This resource provides technical definitions for many terms related to genetics.
- National Cancer Institute Dictionary of Cancer Terms. This resource provides definitions for many terms related to cancer and medicine.
- ASCO eLearning Fundamentals of Clinical Trials