Module II: Basic Concepts In Clinical Research

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Clinical Research Concepts

• Human Subjects Research
  • Ethical Considerations
Human Subjects Ethics 101

1947- **Nuremberg Code** - a set of research ethical principles (10) for human experimentation set as a result of the Nuremberg Trials at the end of the WWII as a result of the atrocities that were committed by the Nazis.

Includes such principles as **voluntary consent and absence of coercion**; properly formulated scientific experimentation; and **avoiding physical and mental suffering**.

1964- **Declaration of Helsinki** incorporated the 10 ethical principles of the Nuremberg Code. In 1975, it introduced the concept of oversight by an 'independent committee' which became a system of Institutional Review Boards (IRBs).
Tuskegee Syphilis Study - conducted from 1932 to 1972 in rural Tuskegee, Alabama, 600 poor and mostly illiterate African-American men, 400 of whom were infected with syphilis, were monitored for 40 years.

- Free medical exams were given, however the men were never told about their diagnosis.
- In the 1950’s, when penicillin became available, the men were denied proper treatment or given fake treatments instead.
- Most of the “participants” died slow and painful deaths of syphilis during the study.
- The study continued until 1973 when the US Dept. of Health, Education and Welfare stopped the trial after it was publicized.
- Congressional intervention eventually led to the publication of the Belmont Report in 1979- the cornerstone of ethic principles in Human Subjects Research.
The Belmont Report (1979)  
Ethical Principles and Guidelines for the Protection of Human Subjects of Research

<table>
<thead>
<tr>
<th>Ethical Principals for Research</th>
<th>Applications of Ethical Principles for Research</th>
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<tbody>
<tr>
<td><strong>Respect for Persons</strong></td>
<td><strong>Informed Consent</strong></td>
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<tr>
<td>• Individuals should be treated as autonomous agents</td>
<td>• Volunteer research participants, to the degree that they are capable, must be given the opportunity to choose what shall or shall not happen to them</td>
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<td>• Persons with diminished autonomy are entitled to protection</td>
<td>• The consent process must include three elements:</td>
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<td>o Information,</td>
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<td></td>
<td>o Comprehension,</td>
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<td></td>
<td>o Voluntary participation</td>
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<td><strong>Beneficence</strong></td>
<td><strong>Assessment of risks and benefits</strong></td>
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<td>• Human participants should not be harmed</td>
<td>• The nature and scope of risks and benefits must be assessed in a systematic way</td>
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<tr>
<td>• Research should maximize possible benefits and minimize possible risks</td>
<td>Subjects must be told of all possible risks and benefits of the treatment/intervention</td>
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<td><strong>Justice</strong></td>
<td><strong>Selection of participants</strong></td>
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<tr>
<td>• The benefits and risks of research must be distributed fairly</td>
<td>• There must be fair procedures and outcomes in the selection of research participants</td>
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Why do Institutional Review Boards (IRBs) exist?

• The primary function of the IRB is to protect the rights and welfare of human subjects- remember, not formalized until 1974!

• IRBs help reduce the potential for researchers to lose sight of individual rights and welfare because of a focus on advancing science/knowledge
What does IRB review concentrate on?

- Ensuring it is as safe as possible for people to take part in a study

- If there are serious risks, ensuring they are as low as possible and the right kind of monitoring is in place to prevent adverse effects or identify adverse outcomes as soon as possible

- Ensuring the subject population is the appropriate population to answer the study question

- Ensuring the study design is acceptable so that
  - the question posed can be answered by the research
  - the right number of people will be enrolled (not too many or too few) so that as few people are exposed to risk as possible

- Ensuring the information given to potential research participants is sufficient to allow them to make an informed choice about whether they want to take part in the research study
Clinical Research Concepts

• Human Subjects Research
• Ethical considerations
• Federal Regulations/ ICH GCP
Overview of Clinical Research Regulations

• Depending on the type of research study and funding agency/sponsor, there may be multiple levels of regulatory and compliance oversight, including federal regulations, state laws, institutional policies and guidelines, and funding agency/sponsor policies and guidelines.

• Understanding the levels of oversight for your study will ensure that you have the appropriate procedures in place.

• Most clinical research studies that take place at an Academic Health Center (AHC) are regulated by one or more US Department of Health and Human Services agencies.

• Most commonly studies are regulated by the Office for Human Research Protection (OHRP) and/or Food and Drug Administration (FDA). These agencies function under different sets of regulations (i.e. DHHS vs FDA)
Governmental Organizational Chart: Human Subjects Research oversight

US Department of Health and Human Services (DHHS)

- National Institutes of Health (NIH)
  - National Cancer Institute (NCI)
- Food and Drug Administration (FDA)
- Office of the Assistant Secretary for Health (ASH)
  - Office for Human Subject Protection (OHRP)

- The **Common Rule** (US Department of Health and Human Services Title 45 CFR 46) is a rule of ethics regarding biomedical and behavioral research involving human subjects in the US
  - It is the *baseline standard of ethics* by which any government-funded research in the US is held
  - Most academic institutions hold their researchers to these statements of rights regardless of funding

• The FDA is the regulatory body responsible for the regulation and oversight of human subjects research studies that involve investigational products (e.g. drugs, biologics and devices)

• Studies subject to FDA regulations are those conducted in the United States under an IND or IDE and must adhere to the Code of Federal Regulations (CFR) Title 21:
  - 45 CFR 56: Institutional Review Boards (IRBs)
  - **21 CFR 50: Protection of Human Subjects**
  - 21 CFR 312: Investigational New Drug Application
  - 21 CFR 54: Financial Disclosure
  - 21 CFR 11: Electronic Records
  - **45 CFR 46: Common Rule (DHHS)**
**IND: Investigational New Drug**

- Prior to using the drug on humans, the sponsor must submit to and receive approval from FDA for an investigational new drug application (IND). This is an FDA application process developed to standardize the process of testing a new medication, or the new use of an FDA approved medication with human subjects.

- The FDA has two primary objectives in reviewing an IND: (1) to assure the safety and rights of subjects in all phases of an investigation and (2) to help assure that the quality of the scientific evaluation of the drug is adequate to permit an evaluation of the drug’s effectiveness and safety (21 CFR 312.2).

- An Investigational Drug is still in the developmental stage, and is the object of a clinical investigation(s) to determine the safety and effectiveness of the drug, and is not available for commercial sale or distribution.

- When all phases of clinical studies (described in more detail below) are successfully completed, the sponsor may then submit a **New Drug Application (NDA)**.
IDE: Investigational Device Exemption

• An IDE is an FDA submission that permits clinical investigation of devices. This investigation is exempt, and doesn’t meet the PreMarket Approval (PMA) regulatory requirements.

• The term “IDE” stems from this description in 21 Code of Federal Regulations (CFR) 812.1: “An approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose”.

• An Investigational Device is still in the developmental stage, and is the object of clinical investigation(s) to determine the safety and effectiveness of the device, and is not available for commercial sale or distribution.

• PreMarket approval (PMA) is the FDA process of reviewing scientific and regulatory data to evaluate the safety and effectiveness of Class III medical devices prior to approval of the device for commercial sales and distribution.
Basic Concepts in Clinical Research:
ICH Guidelines - E6: GCP

• ICH- International Committee for Harmonization
  • Developed with consideration of the GCP of the EU, Japan and the US, as well as Canada, Australia, the Nordic Countries and the World Health Organization (WHO)

• ICH Good Clinical Practice (GCP)
  • A standard for designing, conducting, performing, monitoring, auditing, recording, analyzing, and reporting clinical trials that provides assurance that the data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial subjects are protected (ICH E6 GCP 1.21)
Basic Concepts in Clinical Research: Federal Regulations vs. ICH GCPs

• ICH GCP is published as a GUIDELINE

• Federal regulations are LAW

*FDA recognizes the ICH GCP as strongly suggested guidelines*

• UWCCC upholds to the higher standard of ICH GCP
Clinical Research Concepts

• Human Subjects
  • Ethical considerations
  • Federal Regulations/ ICH GCP

• Sponsor Types
Sponsor Types

Sponsor (definition): An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial (ICH GCP E6 1.53)

• Types of study sponsors:
  • Industry
  • Sponsor-Investigator
  • Federal
Sponsor Types: Industry Sponsored

- Pharmaceutical companies develop protocols and approach a site or a PI to participate in a study
- UWCCC typically participates as one of a number of sites
- A Clinical Research Organization (CRO) is most often utilized to manage the conduct of the trial
Sponsor Types: Sponsor-Investigator

- Study conceptualized, designed and authored or co-authored by a UWCCC investigator, often referred to **Investigator Initiated Trials (IIT)**

- An investigator may seek funding for such studies from industry, non-profit organizations and foundations, private funding, departmental/institution funding or federal agencies

- However, even if the study is funded by an industry sponsor, the PI is still a Sponsor-Investigator with additional responsibilities
Sponsor Types: Federally Funded

• A Federally Funded clinical research study is a peer-reviewed protocol sponsored under a broad charter by a Government agency (or agencies) for the purpose of performing, analyzing, integrating, supporting, and/or managing basic or applied research and/or development

• NCI-sponsored trials

• Cooperative Group trials (i.e. ECOG, Alliance, NRG)
Clinical Research Concepts

• Human Subjects
  • Ethical considerations
  • Federal Regulations/ ICH GCP
• Sponsor Types
• Protocol Types
Basic Concepts in Clinical Research:
Protocol Types

Protocol Types identify the type of protocol based on the study outcomes and methodology used (intervention, surveys, specimen analysis, etc.) The following classifications are based on the NCI 05/13 P30 CCSG Data Guide:

- Treatment
- Supportive Care
- Prevention
- Screening
- Diagnostic
- Health Services Research
- Basic Science
- Extension (Rollover)
- Compassionate Use
- Registry/Database
- Biospecimen Repository
- Other
Basic Concepts in Clinical Research: Protocol Types

**Treatment:**
- Protocol designed to evaluate one or more interventions for treating a disease, syndrome, or condition using interventional methods:
  - Drug, Device, Biologic, Gene Therapy, Radiation Therapy, Stem Cell Therapy, Nutrition, Behavioral, Psychosocial
- Intended to treat the cancer

Protocol Examples:
- *A Phase 2 Randomized Multicenter Study of PEGPH20 (PEGylated Recombinant Human Hyaluronidase) Combined with nab-Paclitaxel and Gemcitabine Compared to nab-Paclitaxel and Gemcitabine alone in Subjects with Stage IV Previously Untreated Pancreatic Cancer*
  - Objective: To estimate the progression-free survival (PFS) duration of PEGPH20 combined with nab-paclitaxel (NAB) plus gemcitabine (GEM) (PAG treatment)
Basic Concepts in Clinical Research: Protocol Types

**Supportive Care:**

- Protocol designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects, or mitigate against a decline in the participant’s health or function.
- In general, supportive care interventions are not intended to cure a disease.
- Types of Supportive Care:
  - Drugs, Nutrition/Dietary, Behavioral/Other
- Protocol Example:
  - *Impacts of Exercise on Prognostic Biomarkers in Lung Cancer Patients*
    - Objective: To determine the effect of an eight-week exercise intervention on biomarkers of inflammation, oxidative stress, exercise capacity, and quality of life in lung cancer patients.
  - *Reducing work disability in breast cancer survivors (WISE symptom driven intervention)*
    - Objective: To determine the feasibility and usability of the WISE and empirically evaluate its effect on short-term work ability among BCS
Prevention:

- Protocol designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition.

- Prevention intervention and Chemoprevention are not synonymous.
  - Prevention can have many different interventions
  - Chemoprevention uses agents/drugs only

- Nutritional/Dietary – addition of soy, green tea (Chemoprevention)
- Behavioral/Other – smoking cessation, exercise (Prevention)
  - A Phase IIA Exploratory, Randomized, Placebo controlled Trial of Pomegranate Fruit Extract/Pom-X in Subjects with Clinically Localized Prostate Cancer Undergoing Active Surveillance
  - Objective: To determine the effect of Pomegranate Fruit Extract (PFE) 1000mg, taken daily for 1 year, on the plasma levels of Insulin-like Growth Factor (IGF-1) from baseline to end of study (52 weeks) in participants undergoing Active Surveillance (AS) for early stage prostate cancer.
Basic Concepts in Clinical Research: Protocol Types

**Screening:**

- Protocol designed to assess or examine methods of identifying a condition (or risk factor for a condition) in people who are not yet known to have the condition (or risk factor).

- Protocol example:
  - **Cytologic Analysis of Distention Media as a Screening Test for Endometrial Cancer**
    - Objective: Perform cytologic analysis of sonohysterographic distention media in patients with known endometrial carcinoma in order to predict sensitivity of using such fluid for cancer screening
  - **Free Oral, Head and Neck Cancer Screening at UWHC**
    - **Objective:** What are the participant characteristics of people who attend a free public screening for oral, head and neck cancer? How many people who attend the screening will receive an abnormal screening that prompts recommendation for further follow up and/or leads to a head and neck cancer diagnosis?
Basic Concepts in Clinical Research: Protocol Types

**Health Services Research:**

- Protocol designed to evaluate the delivery, processes, management, organization, or financing of health care.

- Methods: Risk assessments, Surveys, Outcomes, Environmental and/or Behavioral assessments
  
  - Protocol example:
    
    - *Primary Care Provider Barriers to Colon Cancer Screening*
    - Objective: To assess the barriers to Colorectal Cancer screening in our community as perceived by primary care providers.

    - *Oncologists’ Perspectives on the Goals and Perceived Responsibilities for Breast Cancer Follow-up*
    
      Objective: To examine how the goals and perceived responsibilities for breast cancer follow-up differs amongst different types (medical, radiation, surgical) of oncologists
Basic Concepts in Clinical Research: Protocol Types

**Basic Science:** (includes what we used to refer to as “Correlative”)

- Protocols designed to examine the basic mechanisms of action of an intervention (e.g., physiology, biomechanics, radiologic).

- Protocol Example:
  - *Collection Protocol of Bone Marrow Tumor Cells and Stromal Cells from MM Patients*
    - Objective: To obtain and separate sufficient viable tumor cells and non-malignant cells in patients with MM undergoing routine BM aspiration;

- These studies are separate from other studies – for studies linked to another study see “Ancillary/Companion”
Chart Review:

- Studies that use subject medical records to answer a clinical research question

- Retrospective in nature

Protocol Examples:

- *Adjuvant Radiation for Stage II Endometrial Cancer: An Update of the University of Wisconsin Experience*
  - Objective: describe treatment techniques, dose and fractionation, and specified tissue tolerances of previous studies

- *Retrospective Observational Study of Subjects with Cytokine-Refractory Metastatic Renal Cancer Treated with Axitinib (AG-013736) to Estimate 5-Year Survival*
  - Objective: to retrospectively collect current survival data for the patients originally included in A4061012 study to estimate the 5-year survival rate in subjects with cytokine-refractory mRCC treated with axitinib.
Basic Concepts in Clinical Research: Protocol Types

**Extension (Rollover):**

- Experimental therapeutic studies that are extended under a new protocol (that is exactly the same as the initial protocol) to provide treatment to patients that are benefiting from the treatment on the initial protocol.
- One or more existing subjects (no new subjects) from the previous trial are allowed on a rollover study.
- No new subjects are allowed to enroll
- **Protocol Example:**
  - *A Rollover Protocol for Patients Who Received CP-675,206 (Tremelimumab) in Other Protocols*
    - Objective: To allow access to tremelimumab (CP-675,206) for patients who received it in other trials
Basic Concepts in Clinical Research: Protocol Types

Compassionate Use:

• Provide experimental therapeutics prior to final FDA approval for very sick individuals who have no other treatment options. The study is open to one or more new subjects (not continuing from other treatment options)

• Also referred to as ‘Expanded Access’ studies

Protocol Examples:

• Multi-Patient Expanded Access of Prochymal® (Ex-vivo Cultured Adult Human Mesenchymal Stem Cells) Infusion for the Treatment of Pediatric Patients Who Have Failed to Respond to Steroid Treatment for Acute GVHD
  • Objective: To allow pediatric patients who have failed to respond to steroid treatment for acute GVHD expanded access to Prochymal

• Compassionate Use Protocol for the Use of AMD3100 to Mobilize Peripheral Blood Stem Cells for Collection and Transplantation
Basic Concepts in Clinical Research: Protocol Types

Registry/Database:

- Individual databases that collect data on subjects that meet a pre-determined set of criteria

- Protocol Example:
  • *Head and Neck Database*
    • Objective: Improve understanding of cancer survival and quality of life in patients with head and neck cancer, and to further study the effects of new treatments on outcome for these patients
  • *Benchmarking UW Health Breast Imaging and the National Mammography Database for Improved Clinical Outcomes*
    • Objective: The goal is to evaluate the internal performance on which to assess strengths and weaknesses of the Breast Imaging services as compared to the NMD
Basic Concepts in Clinical Research:
Protocol Types

**Biospecimen Repository:**

- Studies that involve the collection of biospecimens from cancer patients or healthy volunteers for use in ongoing lab studies or for preservation in a repository for future studies.

- Protocol Examples:
  - *North American Mantle Cell Lymphoma Project*
    - Objective: To analyze clinical features and biomarker expression utilizing tissue microarrays for prognostication of disease outcome and response to therapy.
  - *Protocol for a Research Sample Repository for Allogeneic Hematopoietic Stem Cell Transplantation*
    - Objective: To make blood samples available for research studies related to histocompatibility and HSC transplantation.
Basic Concepts in Clinical Research: Protocol Types

Other:

- Studies involving healthy populations and/or cancer patients that do not involve intervention/alteration in the status of participants
- Includes some Epi/Ob studies, Survey studies, Quality of Life studies
- Protocol Examples:
  - A Multicenter Study of Hematopoietic Stem Cell Donor Safety and Quality of Life
    - Objective: to compare the incidence of serious and severe adverse events in related hematopoietic stem cell (HSC) donors in Age Group 1 (ages 18-40) and Age Group 2 (ages 41-60) versus a comparative cohort of unrelated HSC donors within the same respective age groups; and 2) to describe the incidence of serious and severe adverse events in related HSC donors ages <18 and >60.
Basic Concepts in Clinical Research:

Clinical Research Categories (Data Table 4 Report Type)

- Interventional
- Observational
- Ancillary or Correlative
**Interventional:**

- A clinical research category in which individuals are assigned by an investigator based on a protocol to receive specific intervention.
- The participants may receive diagnostic, therapeutic, behavioral or other types of intervention.
- The assignment of the intervention may or may not be random.
- The participants are followed and biomedical and/or health outcomes are assessed.
Observational:

• A clinical research category in which the studies focus on cancer patients and healthy populations that involve no intervention or alteration in the status of the participants.

• Biomedical and/or health outcome(s) are assessed in pre-defined groups of participants.

• The participants in the study may receive diagnostic, therapeutic, or other interventions but the investigator of the observational study is not responsible for assigning specific interventions to the participants of the study.
Ancillary or Correlative:

- Ancillary studies are stimulated by, but are not a required part of, a main clinical trial/study, and that utilize patient or other resources of the main trial/study to generate information relevant to it.
- Ancillary studies must be linked to an active clinical research study and should include only patients accrued to that clinical research study.
- Correlative studies are laboratory based studies (including radiology) using specimens to assess cancer risk, clinical outcomes, response to therapies, etc.
Clinical Research Concepts

- Human Subjects
  - Ethical considerations
  - Federal Regulations/ ICH GCP
- Sponsor Types
- Protocol Types
- Phases of Clinical Research Studies
Basic Concepts in Clinical Research: Phases of Clinical Studies

• **Phase I**
  • Looks at safety parameters
  • The first step in testing a new treatment in humans after animal research. These studies test the best way to give a new treatment and the best dose. The dose is typically increased a little at a time in order to find the highest dose that does not cause harmful side effects

  Dose escalation          Maximum Tolerated Dose (MTD)

Because little is known about the possible risks and benefits of the treatments being tested, in oncology, phase I trials usually include only a small number of patients who have not been helped by other treatments

• Characteristics:
  • Short duration
  • Typically involves:
    • **Pharmacokineti**c**s (PK)**- study the absorption and safety of an agent over a period of time
    • **Pharmacodynamics (PD)**- study of the physiological effects (e.g. blood pressure, heart rate, ECG) of an agent
Basic Concepts in Clinical Research: Phases of Clinical Trials

• Phase II

• Designed to evaluate the safety and **effectiveness** of a new drug using the dosing determined to be safe in Phase I studies

• These trials typically focus on interventions (biomedical or behavioral) for specific types of cancer or related cancers

• Characteristics:
  • Enrollment of less than 100 subjects
  • Patients may or may not have already been treated with standard of care therapy for their cancer type
  • Assesses safety and efficacy
Basic Concepts in Clinical Research: Phases of Clinical Studies

• **Phase III**
  • A study to compare an experimental/treatment intervention (or new use for treatment) with a standard or controlled intervention or comparing two or more existing treatments
  • In most cases, studies move into Phase III only after a treatment appears to be safe and effective in Phases I and II
  • Characteristics:
    • May include hundreds or thousands of study subjects
    • Usually randomized and consists of 2-3 treatment groups
    • Broader eligibility criteria than Phase II studies
    • Typically involves:
      • Efficacy and safety evaluations in population subgroups
      • Dosing intervals
Basic Concepts in Clinical Research:
Phases of Clinical Studies

• **Phase IV**

  • Conducted after a treatment has been approved and is being marketed. Evaluates side effects that were not apparent in the Phase III trial
  
  • Characteristics:
    • Hundreds to thousands of study subjects
    • Monitors long-term safety
  
  • Phase IV studies are not conducted until after the regulatory authority has approved an investigational agent
Clinical Research Concepts

• Human Subjects
  • Ethical considerations
  • Federal Regulations

• Research Protocol
  • Study Types
  • Phases of Clinical Research Studies
  • Study Design Concepts
Basic Concepts in Clinical Research: Clinical Study Design Concepts

• **Randomization**: Method used to prevent bias in research

  • A computer or table of random numbers generates treatment assignments and participants have an equal chance to be assigned to one of two or more groups (e.g. the control group or the investigational agent)
Basic Concepts in Clinical Research: Clinical Study Design Concepts

• **Stratification** - Categorizes subjects into subgroups by specific characteristics
  - Enables researchers to look into separate subgroups to see whether differences exist (e.g. Individuals are divided up into two groups, smokers and non-smokers, and then randomized into either the control group or investigational group)
Basic Concepts in Clinical Research: Clinical Study Design Concepts

**Blinding**

- **Purpose:** To distinguish the effects of investigational agents from influences of biased observation, course of disease, or placebo effect
- **Types:**
  - **Open Label (unblinded)** - Subject, investigator, and evaluator know the treatment
  - **Single-blind** - Subject does not know if they are in experimental or control group
  - **Double-blind** - Neither the subject nor the researcher knows which subjects are in which group
  - **Double-dummy** - Used to blind 2 treatments dissimilar in appearance - subjects take both dosage forms (e.g. oral and intramuscular) but one is active and one is placebo
Basic Concepts in Clinical Research: Clinical Study Design Concepts

Controls:

- **Uncontrolled** - Contains no control group. Everyone receives the same treatment/intervention.

- **Placebo** - compares one or more active treatments to a dosage form that does not contain the active treatment.

- **Active** - Compares two or more treatments, each with different active ingredients. Common in studies intended to demonstrate differences in treatment outcomes or when the use of a placebo is unethical.
Adjuvant therapy is additional treatment that is given after primary treatment for apparently localized cancer.

The idea is to prevent recurrence by wiping out any metastases which are presently too small to detect.

They are designed to prevent the recurrence of cancer in people who no longer show clinical evidence of disease.

The primary treatment is usually surgery and the adjuvant therapy is usually drug therapy or radiation therapy.

- For example, radiotherapy or systemic therapy is commonly given as adjuvant treatment after surgery for breast cancer.
Neoadjuvant Treatment Studies:

- Neoadjuvant trials are additional therapy before standard treatment or intervention (i.e. surgery).

- Neoadjuvant therapy aims to reduce the size or extent of the cancer before using radical treatment intervention, thus making procedures easier and more likely to succeed, and reducing the consequences of a more extensive treatment technique that would be required if the tumor wasn't reduced in size or extent.
  - i.e. neoadjuvant hormone therapy prior to radical radiotherapy for adenocarcinoma of the prostate.
Basic Concepts in Clinical Research: Prospective vs Retrospective

- **Prospective studies** look at information starting at a baseline and continue to follow into the future.
  - i.e. Identify smokers and non-smokers at baseline and compare their risk of developing specific diseases.

- **Retrospective studies** (‘historic’) look at information that has already occurred, post-hoc.
Clinical Research Concepts

• Human Subjects
  • Ethical considerations
  • Federal Regulations
• Sponsor Types
• Study Types
• Phases of Clinical Research Studies
• Study Design Concepts
• The order of things
Basic Concepts in Clinical Research: The order of things

Before a protocol can be conducted:

- It must be approved by a scientific review committee and an IRB
Basic Concepts in Clinical Research: The order of things

Before a subject can participate in the protocol:

• Informed Consent must be obtained

Informed Consent Form (ICF)
A document that describes the rights of participants in a clinical trial and includes details about the study, including its purpose, duration, required tests and procedures, potential risks and benefits, costs, and subject rights

Informed Consent Process (ICP)
An ongoing process for which the goal is to provide sufficient information to the potential subject regarding the study so that he/she can make an informed decision as to whether or not to participate in the research
Basic Concepts in Clinical Research: The order of things

Before the consented subject can be accrued to the study:

• Eligibility must be determined by systematically going through all of the protocol’s eligibility criteria to ensure they are eligible to be in the study
  • Inclusion Criteria
  • Exclusion Criteria
Once an eligible subject is registered to the study...

- The treatment of that subject must follow the strict guidelines set out in the protocol
The logical next step is learning...

Module 3: What is a Protocol?