Al-Mustaqbal University

Pharmacy Ethics 3rd stage
Ethical Issues In Clinical Research
Part I

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Clinical (research)Trial: An experiment to compare the effects of two or more healthcare interventions.

Population: The group of people being studied
e.g. geography, age group, certain diseases.

Types of studies

- Observational study
  - A study in which the investigators do not seek to intervene, and simply observe.
- Experimental study
  - A study in which the investigators actively intervene to test a hypothesis.
- Retrospective study
  - A study in which the **outcomes** have occurred to the **participants** before the study.
- Prospective study
  - Evaluations of the effects of healthcare interventions,

Types of Study Designs

1. Observational Designs
2. Experimental Designs – interventional studies

• Types of Observational Studies

I- Cohort Studies

- A group of subjects followed over time(selected period)
- Purpose: defining the incidence and investigating potential causes of a condition (incidence)
- Can be prospective – investigator chooses a sample group and measures characteristics in each subject over a period of time that might predict outcomes
- Can be retrospective – same as prospective, except all data collection and follow-up has happened in the past; only possible if adequate data is available

Types of Observational Studies

II- Cross-Sectional Studies

- Similar to cohort studies except all the measurements are made at one time point with no follow-up
- Purpose: describing variables and their distribution patterns (prevalence)
- Strength – fast and inexpensive since there is no follow-up or waiting time for outcome

Types of Observational Studies

III- Case-Control Studies

- Two groups of people examined for the same outcome
  - Group 1 – “cases” or a population of people with a certain disease
  - Group 2 – “controls” or a population of people without that same disease

- Purpose: compare prevalence of risk factor(s) in subjects with the disease (cases) versus subjects without the disease (controls

IV- Experimental Studies

- These studies evaluate the effects of an intervention
  - Types of interventions:
    - Behavior modification (eg. a walking program to improve weight loss)
    - Drug (eg. a new investigational drug or studying a drug for off-label use – subject to FDA regulations)
    - Device (eg. a new investigational stent – subject to FDA regulations)
- Strength: Can demonstrate causality

- Randomized controlled trial

intervention is assigned to each individual randomly.

- Blinding

The process of preventing those involved in a trial from knowing to which comparison group a particular participant belongs.

- Single blind (patient does not know)
- Double blind (patient and investigator)
- Triple blind (No one know)

Clinically significant

that is large enough to be of practical importance to patients and healthcare providers

- Statistically significant
  - $p < 0.1, 0.05, 0.01$ or 0.001.

    Where p is probability of being mistaken

- Review
- A review article in the medical literature which summarizes a number of different studies.

Pre-clinical studies

Animal populations.

preliminary efficacy and pharmacokinetic

Clinical Trials Phases

Clinical trials are conducted in phases. The trials at each phase have a different purpose and help scientists answer different questions.

Clinical Trials Phases

- Phase 0
- Subtherapeutic doses
- (10 to 15) Human subjects.
- Pharmacokinetics and Pharmacodynamics

- PHASE I
- Safe dosage range and identify side effects.
- Healthy and/or patients.
- Small group of people (20-80).

PHASE I Cont.

- SAD (Single Ascending Dose)
  - This is continued until pre-calculated pharmacokinetic safety levels are reached, or intolerable side effects start showing up
- MAD (Multiple Ascending Dose)
  - Understand the pharmacokinetics & pharmacodynamics

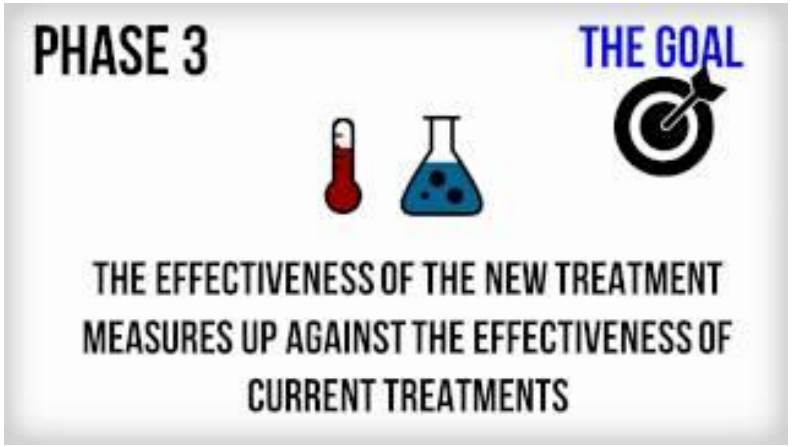
- Food effect
  - a short trial designed to investigate any differences in absorption of the drug by the body, caused by eating before or after the drug is given.

- PHASE II:
- Controlled clinical studies
- the effectiveness.
- short-term side effects and risks.
- larger group of people (100-300).
- further evaluate its safety.

- Phase IIA
  - is specifically designed to assess dosing requirements.
- Phase IIB
  - is specifically designed to study efficacy.
- New drug failure usually in this phase

PHASE III:

- Expanded controlled and uncontrolled trials.
- Additional information to evaluate the overall benefit-risk.
- 1,000-3,000 Human subjects
  - disease/medical condition.
- Effectiveness, side effects, compare it to commonly used treatments.



PHASE III: Cont.

- The most expensive, time-consuming and difficult trials to design and run.
- At least two successful Phase III trials, demonstrating a drug's safety and efficacy to be accepted by organizations like FDA (USA), TGA (Australia), EMEA (European Union), etc..
- Most drugs undergoing Phase III clinical trials can be marketed under FDA standards.

PHASE IV:

- Post-marketing studies to describe additional information including the drug's risks, benefits, and optimal use.
- Harmful effects discovered by Phase IV
- e.g. Cisapride (It was recently **withdrawn** in number of countries due to the increased risk of arrhythmias).
- Also Cerivastatin (brand names Baycol and Lipobay), Troglitazone (Rezulin) and Rofecoxib (Vioxx).

References:

-Robert J. Pharmaceutical Care Practice: The Clinician's Guide, 2nd Edition.

- Internet search.