

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

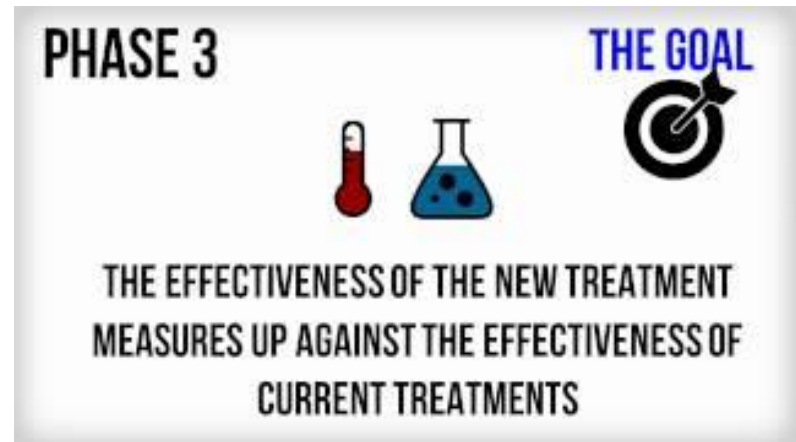
- is specifically designed to assess dosing requirements.

- 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.

