

# Research on Humans

# Functional Classification of Medicine

Medicine and medical intervention can take any of five forms:

- (1) **Therapeutic** (curative): seeks to cure a disease or ailment.
- (2) **Palliative**: seeks to lessen the symptoms of a disease/ailment.
- (3) **Preventive**: seeks to prevent the onset of a disease.
- (4) **Diagnostic**: seeks to arrive at an understanding of a disease (typically with the hope of curing it).
- (5) **Experimental**: seeks knowledge (like diagnostic), but not regarding any particular patient.

## Therapeutic vs Experimental

The **only goal** of the **medical therapist** is the **well-being of the patient**.

The **primary goal** of the **medical researcher** is the **acquisition of knowledge** (patient well-being is secondary).

# Testing New Drugs

Before being allowed by the Food and Drug Administration (FDA) to market a drug in the United States, pharmaceutical companies need to subject the drug to a three-stage review:

- (1) **Investigational New Drug** (IND) application,
- (2) **Clinical Trials**, and
- (3) **New Drug Application** (NDA).

About **20%** of the investigational new drugs (IND) filed with the FDA clear all three stages.

The **clinical trials** occur in four phases...

# Clinical Trials

**Phase 1:** focus on **safety**, uses healthy volunteers (N=20-80).

**Phase 2:** focus on **efficacy**, uses volunteers from the target pool of end-users. (N>100)

**Phase 3:** continued study of safety and efficacy in different populations, dosages, and drug combinations. (N>1000)

**Phase 4:** after the drug is approved. Studies long-term effects over large populations.

# Clinical Trials

Populations are **randomized** and placed into groups: one with the new drug (etc.), the other with a **placebo**; some involve healthy populations, while others involve subjects who might benefit from the drug.

The first modern clinical trial was published in 1948. Sponsored by the British Medical Research Council, the trial compared streptomycin, a new antibiotic, with bed rest alone in patients with tuberculosis.

# Professional Codes and Laws

## Hippocratic Oath

(implied)

The physician is a therapist; research on human subjects is not allowed. The physician *qua* physician may not perform research.

“I will use those dietary regimens which will benefit my patients according to my greatest ability and judgement, and I will do no harm or injustice to them.”

“Into whatever homes I go, I will enter them for the benefit of the sick...”

# Professional Codes and Laws

## Nuremberg Code (1949)

Human experimentation is permitted on condition of:

§1: **informed consent**,

§2: a **worthwhile goal** unattainable in any other way,

§3: preceded by **animal studies**,

§4: structured to **avoid all unnecessary harm** and suffering,

§5: where there is no *a priori* reason to believe **that death or disabling injury** could happen,

§6: the **degree of risk** never exceeds the humanitarian importance

§7: and with **precautions** against these risks,

§8: research is conducted by **qualified personnel**,

§9: the **subject can quit** the study at any time,

§10: and the study **must be terminated** if the scientist believes that continuation will lead to death or disability.



# Nuremberg Doctor Trials (1946)



Dr. Klaus Karl Schilling, convicted of using 1200 concentration camp prisoners for malaria experimentation, beginning in 1942. Thirty of these died directly from the infections. Hanged on May 28, 1946 (Landsberg, Germany).

# Informed Consent

The principle of informed consent derives from the principle of autonomy. A patient's consent must meet the following criteria:

**Disclosure of Information:** the patient is told the risks, harms/benefits, and alternatives to the course of action — in short, whatever information that a patient might reasonably need in deciding on one course of action over the alternatives.

**Understanding:** the information is given in a way understandable by the relevant parties.

**Mental Competence:** the patient must be mentally competent.

**Voluntary Consent:** the consent is granted without coercion or fraud. (A person might also be coerced by a lack of practical choice, e.g., someone in desperate financial straits might agree to serve in a risky study because of the compensation.)

# Professional Codes and Laws

## Helsinki Declaration (1964, etc.)

A set of guidelines for experimenting on human subjects, developed in 1964 by the World Medical Association at its General Assembly in Helsinki (thus the name). This declaration was intended to replace and expand upon the Nuremberg Code.

- Human experimentation is now permitted on **incompetents**, with informed consent made by a legitimate proxy.

# Professional Codes and Laws

## National Research Act (1974)

Mandated the approval of an institutional review board (IRB) for all federally funded research with human subjects.

## Belmont Report (1979)

Written by a U.S. government committee to regulate government funded research involving human subjects.

The report focuses on **autonomy** and **beneficence**, and adds to the previous codes the requirement of **justice**: both **in selecting subjects** and in **designing the research**, the most vulnerable populations must be given extra protections (from coercion and abuse).

# Human Experimentation, badly done

## Tuskegee (syphilis)

(1932-1972) 400 black men with syphilis were matched against 200 uninfected controls to chart the natural progress of the disease. They were given standard heavy metal therapy, but denied penicillin when it was found (in the 1940s) to be effective against syphilis. No informed consent. [Led to the National Research Act of 1974 (use of IRBs)]

## Willowbrook (hepatitis)

(1956-1970) Mentally retarded children at the Willowbrook State School were intentionally infected with hepatitis, both to test a vaccine and to trace the illness's progress. No consent by proxy.