Volgograd State Medical University
Department of Philosophy, Bioethics and Law

Lectures on Bioethics

Lecture 5.

# Clinical Research Ethics

# What is Clinical Research?

- Human subjects research is research which involves humans, as opposed to animals, atoms, or asteroids, as the subjects of study.
- Clinical research refers to the subset of human subjects research which focuses on improving human health and well-being.
- The social value of clinical research lies in its ability to collect information that might be useful to identifying improved methods to treat diseases.

- The process of testing potential new treatments can take 10-15 years, and is standardly divided into phases.
- Phase 1 studies are the earliest tests of a new intervention and are conducted in small numbers of individuals. Phase 1 studies are designed to evaluate how the drug influences the human body and how the human body influences the drug.

- If phase 1 testing is successful potential new treatments go on to larger phase 2 studies which are designed to further assess risks and also to evaluate whether there is any evidence that the treatment might be beneficial.

- Successful phase 2 studies are followed by phase 3 studies which involve hundreds, sometimes thousands of patients. Phase 3 studies are designed to provide a rigorous test of the efficacy of a treatment and frequently involve randomization of subjects to the new treatment or a control, which might be standard existing treatment or a placebo.
- Finally, post-marketing or phase 4 studies evaluate the use of interventions in clinical practice.

# History

- Modern clinical research may have begun on the 20th of May, 1747. James Lind, the ship's surgeon, was concerned with the costs scurvy was exacting on British sailors. He chose 12 sailors who were suffering from scurvy, and divided them into six groups of 2 sailors each. Lind assigned a different intervention to each of the groups, including two sailors turned research subjects who received 2 oranges and 1 lemon each day. Within a week these two were nearly healthy; the others were sicker, and several were dying.

- The ethics of clinical research begins by asking how we should think about the fate of these latter sailors. Do they have a moral claim against Lind? Did Lind treat them appropriately?
- To put the fundamental concern raised by clinical research in its simplest form: did Lind sacrifice sailors, patients under his care, for the benefit of future patients?

- The ethical guidelines in various parts of the world were formulated only after discovery of inhumane behaviour with participants during research experiments. World War II led the states to take more interest in science and research resulting in initiation of larger, systematic clinical investigations to gain knowledge for better treatment of patients, specially the soldiers. Most of the studies were carried out through defence efforts and used mainly the prisoners without concern of their consent and well being.

- The experiments by the Nazi doctors in their concentration camps were the cruellest of all of them. Death was the end point in most of the experiments . The discovery of these experiments stunned the whole world which led to formulation of Nuremberg code.
- The Nuremberg Code (1947) is often regarded as the first set of formal guidelines for clinical research.
- The first and longest principle in the Nuremberg Code states that informed consent is “essential” to ethical clinical research.

- Representatives of the World Medical Association began meeting in the early 1960s to develop guidelines, which would become known as the Declaration of Helsinki, to address the perceived shortcomings of the Nuremberg Code. They recognized that insisting on informed consent as a necessary condition for clinical research would preclude a good deal of research designed to find better ways to treat dementia and conditions affecting children, as well as research in emergency situations..

- Regarding consent as necessary precludes such research even when it poses only minimal risks or offers subjects a compensating potential for important clinical benefit. The challenge, still facing us today, is to identify protections for research subjects which are sufficient to protect them without being so strict as to preclude appropriate research designed to benefit the groups to which they belong.

# Subject selection

- Who does the study need to include, to answer the question it is asking? The primary basis for recruiting and enrolling groups and individuals should be the scientific goals of the study - not vulnerability, privilege, or other factors unrelated to the purposes of the study. Consistent with the scientific purpose, people should be chosen in a way that minimizes risks and enhances benefits to individuals and society.

- Groups and individuals who accept the risks and burdens of research should be in a position to enjoy its benefits, and those who may benefit should share some of the risks and burdens. Specific groups or individuals (for example, women or children) should not be excluded from the opportunity to participate in research without a good scientific reason or a particular susceptibility to risk.

# Informed consent

- For research to be ethical, most agree that individuals should make their own decision about whether they want to participate or continue participating in research. This is done through a process of informed consent in which individuals (1) are accurately informed of the purpose, methods, risks, benefits, and alternatives to the research, (2) understand this information and how it relates to their own clinical situation or interests, and (3) make a voluntary decision about whether to participate.

- There are exceptions to the need for informed consent from the individual — for example, in the case of a child, of an adult with severe Alzheimer's, of an adult unconscious by head trauma, or of someone with limited mental capacity.

# Ethics committee

- The first appearance of need of ethics committee (EC) was made in Declaration of Helsinki in 1964.
- The establishment of EC requires 5-15 members with at least one basic medical scientist (preferably one pharmacologist), one clinician, a legal expert, a social scientist / philosopher or theologian and a lay person from the community.
- Every institute, where research is going on should have its own EC with its head preferably from outside the institute.

- The ECs should have independence from political, institutional, professional, and market influences, in their composition, procedures, and decision-making.
- ECs are responsible for carrying out the review of proposed research before the commencement of the research. The basic responsibility of EC is to ensure an independent, competent and timely review of all ethical aspects of the project proposals received in order to safeguard the dignity, rights, safety and well-being of all actual or potential research participants.