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Ethics in Clinical Research: A Review

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Abstract **Review Article**

Clinical trials involve human beings so ethics become very important because everyone in the medical profession has forgotten the ethics for making more profits in terms of finance. In the world every country has their own rules and regulations and they work accordingly and follow their own behavior towards humans in clinical trials. For the humanity ground it is necessary for all countries to follow the same and ethical rules that are universal and worldwide acceptable. Several documents refer to codes of ethics that are *Belmont Report, Declaration of Helsinki, Nuremberg Code, U.S. Common Rule* etc. The core principles are designed on the basis of above reports. In this we discussed various biases in clinical trials with possible solutions.

Keywords: Ethics in clinical trials, Codes of ethics, Core principles, bias in trials and solutions.

INTRODUCTION

Clinical Research

The National Institutes of Health (NIH) includes all research involving human participants. It does not include secondary studies using existing biological specimens or data collected without identifiers or data that are publicly available [1].

Clinical Trials

Clinical Trials are clinical research studies involving human participants assigned to an intervention in which the study is designed to evaluate the effect(s) of the intervention on the participant and the effect being evaluated is a health-related biomedical or behavioral outcome [1].

Goals of Clinical Research

The ultimate goal of clinical research is to increase medical knowledge and improve patient care. For the conclusions resulting from clinical research to be valid and applicable, the research must be conducted deliberately via systematic investigation and data collection [2].

Types of Clinical Research: As per USFDA [3]

- Treatment research typically studies new medicines, psychotherapy approaches, medical devices, surgical and therapeutic techniques, and other intervention innovations.
- Prevention research focuses on ways to stop the development or return of diseases via medicine, vitamins, vaccines and lifestyle changes.
- Diagnostic research looks for effective techniques to identify disorders and provide doctors and clinicians with prediction rules for spotting the diseases in patients.
- Genetic studies examine the link between genes and disease with the goal of improving disease prediction and estimating the chances of an individual contracting a specific disease.
- Epidemiological studies are intended to spot patterns, causes and ways to control diseases in certain populations by identifying risk factors and protective factors for those diseases.
- Clinical studies are also referred to as observational studies, as the NIH's National Institute on Aging explains. Clinical studies observe people in normal settings to group volunteers by characteristic and note changes over time. The results of these studies often lead to potential new clinical trials.

Codes of Ethics

Several formal documents and ethical frameworks provide moral guidance for clinical researchers. A few of the most prominent examples include the following:

1. The Belmont Report codifies basic ethical principles that underscore biomedical research. This document was created by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research [4].

It involves three basic principles:

a) Respect of Persons

Respect for persons incorporates at least two ethical convictions: first, that individual should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

b) Beneficence

Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

c) Justice

Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

It provide base for clinical research like a) collection of informed consent form b) Assessment of risks and benefits and c) selection criteria of subjects for the clinical research.

2. The Declaration of Helsinki is an international agreement put forward by the World Medical Association and amended many times over the years to address new ethical concerns [5].

The declaration of Helsinki was formed under the organization world Medical Association. As rules and principles of clinical research varies country to country and they follow the rules according to their need. The world medical Association decided to bind all the countries in single rules and principles involve clinical trials in any field. In 18th WMA General Assembly, Helsinki, Finland, June 1964 the ‘The Declaration of Helsinki’ was developed. It has total 35 points including introduction, principle for all medical research and additional principle for medical research combined with medical care.

3. The Nuremberg Code was ratified following World War II, in response to the abusive and exploitative clinical trials undertaken by Nazi scientists. It provides an international standard for clinical research ethics [6].

It has total 10 basic principles for the clinical research that give clear guidance to the all research organizations that hoe they can conduct the clinical research in ethical manner.

4. The U.S. Common Rule: ratifies key protections for the patients who participate in clinical trials [7].

It is a complete guideline to from documentary evidence with respect to human welfare and their rights and possible risks and benefits.

Core Principles: [8]

In addition to these ethical codes, some core principles guide the work of clinical researchers. Noteworthy examples include the following:

- Ensuring that testing is scrupulous and fully compliant with stated clinical protocols.
- Verifying the scientific validity of the results.
- Choosing clinical trial participants in a way that is fair and free of prejudice.
- Fully informing all volunteers about what the trial involves and potential risks before they offer their consent.

NIH Clinical Center researchers published seven main principles to guide the conduct of ethical research:

a. **Social and Clinical Value:** Every research study is designed to answer a specific question. The answer should be important enough to justify asking people to accept some risk or inconvenience for others. In other words, answers to the research question should contribute to scientific understanding of health or improve our ways of preventing, treating, or caring for people with a given disease to justify exposing participants to the risk and burden of research.

b. **Scientific Validity:** A study should be designed in a way that will get an understandable answer to the important research question. This includes considering whether the question asked is answerable, whether the research methods are valid and feasible, and whether the study is designed with accepted principles, clear methods, and reliable practices. Invalid research is unethical because it is a waste of resources and exposes people to risk for no purpose

c. **Fair Subject Selection:** The primary basis for recruiting participants should be the scientific goals of the study — not vulnerability, privilege, or other unrelated factors. Participants who accept the risks of research should be in a position to enjoy its benefits. Specific groups of participants (for example, women or children) should not be excluded from the research opportunities without a good scientific reason or a particular susceptibility to risk.

d. **Favorable Risk-Benefit Ratio:** Uncertainty about the degree of risks and benefits associated with a clinical research study is inherent. Research risks may be trivial or serious, transient or long-term. Risks can be physical, psychological, economic, or social. Everything should be done to minimize the risks and inconvenience to research participants to maximize the potential benefits, and to determine that the potential benefits are proportionate to, or outweigh, the risks.

e. Independent Review: To minimize potential conflicts of interest and make sure a study is ethically acceptable before it starts, an independent review panel should review the proposal and ask important questions, including: Are those conducting the trial sufficiently free of bias? Is the study doing all it can to protect research participants? Has the trial been ethically designed and is the risk–benefit ratio favorable? The panel also monitors a study while it is ongoing.

f. **Informed Consent:** Potential participants 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.

Bias in Clinical Trials [9]

a) Selection Bias: Assigning patients with better oral hygiene to the treatment group favored by the investigator.
Solution: Appropriate randomization.

b) Study Management or Performance Bias: Following more closely the patients in the treatment group favored by the investigator.
Solution: Standardization of procedures Personnel training Blinding, when feasible.

c) Detection Bias: Recording outcomes in a way that proves the investigator's or the participant's beliefs.
Solution: Blinding, when feasible.

d) Attrition or Post Randomization Bias: Participant loss related to the outcome (eg, severe side effects).
Solution: Intention to treat analysis.

e) Publication or Reporting Bias: Selective reporting of only statistically significant results.
Solution: Trial registration, prepublication of trial protocol, reporting not only interesting or positive results, but also negative results.

CONCLUSION

Nowadays, a number of pharmaceutical companies and medical research institutes conduct a large number of clinical trials to beat the market in a competitive way. They try to produce solutions to every medical situation in society before other companies. In this competitive environment they sometimes forget the basic ethics because of poor knowledge, influence company managers and for capturing the market. In the current review we tried to summarise all the basic ethical

principles in one place so everyone can follow it in their daily life and various research activities.

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