

The Belmont Report: An Ethical Framework for Protecting Research Subjects

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INTRODUCTION

In 1979, a select group of 11 American men and women were in the midst of a congressional assignment. The assignment was to “identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles.”¹ In 1979, these principles were published in what is commonly known as The Belmont Report. While never formally adopted, The Belmont Report has become the primary ethical framework for protecting human research subjects in the United States.



Most of us have some knowledge of the U.S. Food and Drug Administration (FDA) statutes, which are published in Title 21 of the Code of Federal Regulations (CFR), or those of U.S. Public Health Service (PHS) which are published in Title 45 CFR. However, we may be less familiar with non-regulatory guidelines, such as *The Belmont Report*, that have importance in research involving human subjects. Our goal is to briefly explain some of the historical events that led to *The Belmont Report* and to provide an overview of the Belmont principles and the underlying message of the report.

BACKGROUND

At its basic level, the U.S. Congress is an agent of change, enacting laws as a response to events or problems requiring national uniformity. On July 12, 1974, Congress passed the National Research Act, primarily in response to the USPHS-sponsored syphilis studies that were conducted on indigent African-American males in Tuskegee, Alabama from 1932 to 1972. When the story broke, the tragic events of these studies were widely reported in the press. In fact, the syphilis studies are still newsworthy as exemplified by the made-for-television movie, *Miss Evers' Boys*, broadcast on HBO earlier this year.

It is interesting to note that during the 40 years of the syphilis studies,

two international codes were adopted for physicians and scientists conducting research with human subjects. They were *The Nuremberg Code* in 1947 and the *Declaration of Helsinki* in 1964, which has since been revised and updated. At the time, each of these international standards delineated ethical principles for informed consent and medical care of research subjects, both of which were disregarded in the syphilis studies. For whatever reasons, the United States government continued to sponsor research in humans that should have been guided by the Nuremberg and Helsinki principles. While the United

States was the primary sponsor of *The Nuremberg Code*, the United States was not a signatory to the *Declaration of Helsinki*.

However, codes and principles are not regulations, and therefore are not enforceable by law. With the 1974 National Research Act, Congress mandated the establishment of institutional review boards (IRBs) to review all federally funded human research. Until this time, hospital or institutional review of research activities for purposes of protecting human subjects was voluntary, informal, and without established criteria.

The National Research Act also created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The 11 members of the Commission, who represented science, law, ethics, and society, published several statements or reports on various aspects of research with human subjects. These reports outlined recommendations to the Secretary of the Department of Health, Education, and Welfare (DHEW), now known as the Department of Health and Human Services (DHHS).

One of the Commission's statements was *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* commonly referred to as *The Belmont Report*. The Commission recommended to the DHEW Secretary that *The Belmont Report* be adopted in its entirety, representing DHEW policy. While *The Belmont Report* was never officially endorsed, many of the Commission's recommendations in this statement

became the basis for future DHHS laws. In 1981, Congress enacted three DHHS statutes that demonstrated a remarkable collaborative effort within DHHS. They are FDA regulation 21 CFR Part 50 and PHS regulation 45 CFR Part 46, both titled Protection of Human Subjects. The third 1981 statute is FDA regulation 21 CFR Part 56, titled Institutional Review Boards.

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Since neither Congress or DHEW (now DHHS) moved to formally adopt *The Belmont Report* in its entirety, arguably, the United States does not have a national policy for protecting research subjects. Yes, there are the aforementioned DHHS statutes, but these are mandates too restrictive and inflexible to be used as a dynamic foundation for evolving biomedical ethics.

Despite the lack of endorsement by either DHEW or Congress, *The Belmont Report* is indeed alive. It is recognized by many, albeit quietly, as the United States' contribution to the short list of international guidelines for protecting human subjects involved in research.

THE BELMONT REPORT

The objective of *The Belmont Report* “is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.”² The framework of *The Belmont Report* is presented in three discussion topics: boundaries between practice and research, basic ethical principles, and applications.

1. Boundaries Between Practice and Research

Practice refers to interventions that are intended to solely improve the well being of the patient. They are accepted standards that have a reasonable expectation of success. The goal of practice is to provide a diagnosis, preventive treatment, or therapy that will enhance the patient's wellness. In most cases, practice standards are supported by research findings.

Research refers to activities that are designed to develop or contribute to the general body of knowledge. General knowledge includes theories, principles, and relationships. Research activities test a hypothesis, are validated by statistical measures, and allow conclusions to be drawn.

Research is written in a formal protocol that can be reviewed and replicated by others. In research, benefits are not always known nor are they assured. Because harm may result during research, the protection of subjects is paramount.

It is not uncommon to have practice and research occur simultaneously in clinical trials, particularly if the safety and efficacy of the investigational treatment are being evaluated. During the informed consent process,

subjects must clearly know which study activities are standard practice and which are research.

2. Basic Ethical Principles

The Belmont Report identifies three fundamental principles that underlie all research involving human subjects: respect for persons, beneficence, and justice.

a. Respect for Persons

Respect for persons includes two ethical presumptions. The first is that persons should be treated as autonomous individuals, capable of making their own decisions. Autonomous individuals possess the capacity for self-determination. We demonstrate our respect for persons when we encourage and accept an individual's opinions and choices. We show a lack of respect for persons when we withhold information and deny individuals the freedom to make an informed decision.

The second presumption is that not every person is capable of self-determination. The capacity for self-determination develops during a person's life. Therefore, the very young have diminished autonomy. Additionally, some individuals may lose the capacity for self-determination because of physical illness, mental disabilities, or situations that restrict personal freedom, such as prisons and the military. Respect for persons who are immature, incapacitated, or restricted requires that we provide them protection as human subjects.

b. Beneficence

The second basic ethical principle is beneficence. Beneficence is the practice of doing good, making all

efforts to improve an individual's well being. The principle of beneficence is firmly embedded in the ethical tradition of medicine as defined by Hippocrates: "As to diseases, make a habit of two things — to help, or at least to do no harm." However, in order to help and avoid harm, we must first learn what is harmful.

For research that will benefit society, subjects may be exposed to a risk of harm with no personal benefit. In research, an ethical dilemma occurs in deciding when it is proper to pursue certain benefits despite the risks involved, and when the benefits should be foregone because of known or potential risks to the subject.

c. Justice

Justice is the third basic principle identified in *The Belmont Report*. Justice requires that each person is treated fairly, equitably, and given what he or she is due. There is an equal distribution of benefits as well as burdens. An injustice occurs when a benefit to which a person is entitled is denied without good reason or when an excessive burden is imposed.

In clinical research, we should always be mindful that certain classes of persons, e.g., the indigent, ethnic groups, or the institutionalized may be selected because of their availability, dependence, or because they are easy to manipulate rather than for reasons related to the problem being studied. These classes are frequently referred to as "vulnerable populations" and require protection as human subjects.

3. Applications

We can gain an understanding of the Belmont principles by applying them to some of the steps in the clinical research process. *The Belmont Report* singles out the following

activities: informed consent, assessment of risks and benefits, and selection of research subjects.

a. Informed Consent

The first Belmont principle, respect for persons, requires that research subjects be given the opportunity to decide what will or will not happen to them. This opportunity occurs during the informed consent process, which contains three components: information, comprehension, and voluntariness.

Information. When presenting information, it is essential for subjects to understand the research is neither necessary for their well being nor are the effects of the research fully known or understood. Understanding this, subjects can decide if they wish to participate in the research for the purpose of contributing to general knowledge. If a direct benefit to subjects is expected, they should clearly understand the range of risks.

The minimum information required to be provided to subjects is found in 21 CFR 50.25 for FDA reviewed research and 45 CFR 46.116 for all federally funded research. These sections contain the 14 elements of informed consent. While these regulations pertain to DHHS activities, they have become a framework for preparing and reviewing informed consents in all types of research involving human subjects.

Comprehension. Another component of informed consent is comprehension. Comprehension is the capacity to understand. The information provided to a subject must be in a language and at a level that he or she can comprehend. Informed consent is invalid if the consentor does not

understand the information upon which the consent was based. Investigators are responsible for determining that a subject has comprehension of the information.

Voluntariness. Voluntariness is the third component of informed consent. The informed consent process must be free of coercion, undue influence, and unjustifiable pressures. Coercion is the threat or intention of harm by one person to another in order to gain compliance. For example, the subject may be denied medical care unless the subject enrolls in the study.

Undue influence is an offer of an excessive or unwarranted reward in order to gain compliance. An example of this might be the amount of money offered to healthy subjects who participate in Phase 1 trials, or making compensation contingent upon the subject completing the study.

Unjustifiable pressure occurs when a person in a position of authority urges a course of action for the subject. This may occur with the investigator as well as with any member of the investigator's team, when presenting the informed consent to the subject. The dilemma is to recognize when objective discussion of the research study becomes unjustifiable pressure to participate.

b. Assessment of Risks and Benefits

The second Belmont principle,

beneficence, is applied in the assessment of risks and benefits. Risk refers to the possibility that harm may occur. Benefit refers to something of positive value related to well being. Assessment of risks and benefits deals with the probabilities and magnitudes of possible harms and anticipated benefits. In general, risks to the subject should be outweighed by the sum of anticipated benefits to the subject and to society in the form of new knowledge. It is commonly stated that risks and benefits should be "balanced." Unfortunately, there are few quantitative measures available to provide this kind of objective assessment for investigators or IRBs.

c. Selection of Subjects

The third Belmont principle is justice and this is applied during the selection of subjects. Justice in the selection of subjects occurs at two levels: individual justice and social justice. Individual justice requires the investigator to consistently demonstrate fair procedures in selecting subjects. For example, investigators should not offer potentially beneficial research to their favored patients while offering riskier studies to less favored patients.

Societal justice is based on a fair and equitable selection of subjects across economic, ethnic, and gender classes. No class of subjects should bear the burdens of research particularly if disabilities, restrictions, or a hostile social environment already burdens them.

SUMMARY

The Belmont Report, which was published in 1979, was a direct response to the notorious syphilis studies that were conducted by the USPHS from 1932-1972. While it was

never officially adopted or endorsed, *The Belmont Report* has served as an ethical framework for protecting research subjects in the United States for nearly 20 years. Many of its recommendations have been incorporated into Title 21 CFR Parts 50 and 56, and Title 45 CFR Part 46.

To gain a full appreciation of *The Belmont Report*, readers are encouraged to obtain a copy of the statement and to review it in its entirety. *The Belmont Report* and the *Declaration of Helsinki* can be found in the March 1996 edition of the FDA's *Information Sheets for Institutional Review Boards and Clinical Investigators*. The *Declaration of Helsinki* may also be found in 21 CFR 312.120(c)(4); Foreign clinical studies not conducted under an IND.

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References

- ¹ The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research: *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. DHEW Publication No. (OS) 78-0012, Washington, 1978, p. 2.
- ² *Ibid.* p. 3.

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