

Ethical and moral aspects of human based research

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The term “research” refers to a class of activity designed to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference. In the present context “research” includes both medical and behavioural studies pertaining to human health. Usually “research” is modified by the adjective “biomedical” to indicate its relation to health.

Progress in medical care and disease prevention depends upon an understanding of physiological and pathological processes or epidemiological findings, and requires at some time, research involving human subjects. The collection, analysis and interpretation of information obtained from research involving human beings contribute significantly to the improvement of human health.

All research involving human subjects should be conducted in accordance with the first article from the Universal Declaration of Human Rights: “All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood” (1).

The first international instrument on the ethics of medical research, the Nuremberg Code, was promulgated in 1947 as a consequence of the trial of physicians (the Doctors’ Trial) who had conducted atrocious experiments on unconsenting prisoners and detainees during the Second World War. The Code, designed to protect the integrity of the research subject, set out conditions for the ethical conduct of research involving human subjects, emphasizing their voluntary consent to research (2).

The Declaration of Helsinki, issued by the World Medical Association (WMA) in 1964, is the fundamental document in the field of ethics in biomedical research and has influenced the formulation of international, regional and national legislation and codes of conduct. The Declaration, amended several times, most recently in October 2008, is a comprehensive international statement of the ethics of research involving human subjects (3). It sets out ethical guidelines for physicians engaged in both clinical and nonclinical biomedical research. It is the duty of the physician to promote and safeguard the health of patients, including those who are involved in medical research. The physician’s knowledge and conscience are dedicated to the fulfilment of this duty. The Declaration of Geneva of the WMA binds the physician with the words, “The health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that: “A physician shall act in the patient’s best interest when providing medical care”. In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.

Some articles of the Declaration are mentioned below. The design and performance of each research study involving human subjects must be clearly described in a research protocol. The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits (3).

The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration (3). The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee.

For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There might be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research may be done only after consideration and approval of a research ethics committee. When seeking informed consent for participation in a research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such

situations the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.

Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have the duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication (3). Reports of research which are not in accordance with the principles of this Declaration should not be accepted for publication.

Other important publications in the field of medical research regulation are those of the Council for International Organizations of Medical Sciences (CIOMS). Since the first publication in 1982 of the Guidelines (4), several international organizations have issued ethical guidance on clinical trials.

At the Council of Europe's level, the Convention on Human Rights and Biomedicine signed in Oviedo in 1997, in its Article 18, establishes that it is up to each country to decide whether to authorize or not embryo research (5). Each country is only obliged to respect two conditions: "to ensure adequate protection of the embryo", that is to say to adopt a legislation fixing the conditions and limits of such research and to prohibit "the creation of human embryos for research purposes". The Directive 98/79/EC on in vitro diagnostic medical devices (including the use of human tissues) provides that "the removal, collection and use of tissues, cells and substances of human origin shall be governed, in relation to ethics, by the principles laid down in the Convention of the Council of Europe for the protection of human rights and dignity of the human being with regard to the application of biology and medicine and by any Member States regulations on this matter". At this same level, the Charter on Fundamental rights of the European Union approved by the European Council in Biarritz (France) on October 14, 2000 prohibits different kinds of practices possibly related to embryo research, namely "eugenic practices, in particular those aiming at the selection of persons" and "the reproductive cloning of human beings" (5).

Research involving human subjects includes:

studies of a physiological, biochemical or pathological process, or of the response to a specific intervention – whether physical, chemical or psychological – in healthy subjects or patients;

controlled trials of diagnosis, preventive or therapeutic measures in larger groups of persons, designed to demonstrate a specific generalized response to these measures against a background of individual biological variation;

studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures;

studies concerning human health-related behaviour in a variety of circumstances and environments.

Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice (4).

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

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. 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: do not harm and maximize possible benefits and minimize possible harms.

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.

3. 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. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are: to each person an equal share; to each person according to individual need; to each person according to individual effort; to each person according to societal contribution, and to each person according to merit.

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent – Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, may adversely affect a subject's ability to make an informed choice. Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance.

2. Assessment of Risks and Benefits. -- The assessment of risks and benefits requires a careful array of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether to participate or not.

The Nature and Scope of Risks and Benefits. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favourable ratio." This ideal requires making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically.

3. Selection of Subjects – Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects. One special instance of injustice results from the involvement of vulnerable subjects.

In conclusion is underlined that in our era of brilliant medical scientific achievements it is of exceptional importance to set up rules, regulations and protocols, that will allow maximum benefit nations wide and that will block the mistakes which may cost our identity as human beings.

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