

## RESEARCH INVOLVING HUMAN SUBJECTS- ETHICAL PERSPECTIVE

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**ABSTRACT:** Research involving human subjects are important to develop new therapeutics for the betterment of the human race. To take part in such research as volunteers is moral duty of any human. But such experiments should be justifiable and minimal risky for the participants. History of unethical research involving humans led to the development of many guidelines to make such research ethical as well as to gain maximum possible output. Several guidelines have been formulated to ensure research with human participants ethical. All the guidelines emphasize on one thing in particular- informed consent of the human subjects. Other considerations include rational benefit-harm ration, beneficence, justice, adequate research design and approval from proper authorities. All these guidelines aim to prevent any unethical research involving humans against their will.

**Key words:** Research, Human, Ethics, Consent

**INTRODUCTION:** Research refers to a class of scientific activities designed to develop or contribute to generalizable knowledge. The term “human research”, then, refers to research that involves human subjects. Research is a public trust that must be ethically conducted, trustworthy, and socially responsible if the results are to be valuable<sup>1</sup>. All parts of a research project – from the project design to submission of the results for peer review – have to be upstanding in order to be considered ethical<sup>2</sup>. When even one part of a research project is questionable or conducted unethically, the integrity of the entire project is called into question<sup>3</sup>.

**TYPES OF RESEARCH INVOLVING HUMAN:** Two subtypes of human research can be identified. (1) Therapeutic research is closely akin to therapy. Therapeutic research has dual purpose: it is performed primarily for the benefit of the patient subjects; at the same time, the treatments are administered in a systematic and controlled way, so that treatment results can be applied to other contexts or to future subjects and patients. An example of therapeutic research is a study that compares the relative effectiveness of two similarly promising anti-cancer drugs administered to cancer patients. (2) Nontherapeutic research, on the other hand is performed primarily for the purpose of gaining new knowledge, not for the benefit of the subjects involved in the study. For example, healthy human

volunteers who need no drugs for therapeutic purposes frequently participate in the early phases of drug testing, when the safety of new drugs for human use is being evaluated<sup>4</sup>.

**THE MORAL JUSTIFICATION OF RESEARCH INVOLVING HUMAN SUBJECTS:** The primary argument in favor of human research appeals to the principle of beneficence. It asserts that the social benefits to be gained from such research are substantial and that the harms resulting from the cessation of such investigations would be exceedingly grave<sup>3</sup>.

A second approach to the justification of human research is based on a joint appeal to the principles of beneficence and justice. According to this view, beneficence requires that each of us make at least a modest positive contribution to the good of our fellow-citizen or the society as a whole. If our participation in research promises significant benefit for others, at little or no risk to ourselves, then such participation may become a duty of beneficence. In addition, if we fail to fulfill this modest duty, while most of our contemporaries perform it, we may be acting unjustly, since we are not performing our fair share of a communal task<sup>5</sup>.

Every person currently alive is the beneficiary of earlier subjects' involvement in research. To be specific, the willingness of past human volunteers to take part in studies of antibiotics (like penicillin) and vaccines (like the polio vaccine) contributes to the health of us all. Accordingly, it seems unfair for us to reap the benefits of already-performed research without making a reciprocal contribution to the alleviation of disability and disease<sup>4</sup>.

Investigators should be free to decide what kinds of research they will perform and how they wish to conduct that research. According to this view, the freedom of scientific inquiry should be protected from outside interference, unless there are strong reasons for overriding the presumption of freedom. Thus, if an investigator can find human subjects who are willing to take part in some proposed research, he or she should generally be allowed to proceed with the research<sup>6</sup>.

**RESEARCH DESIGN AND BENEFIT- HARM RATIO:** The requirement of adequate research design is end-oriented or utilitarian in character. The central aim of this requirement is to ensure that human research will be conducted efficiently- that is, in a way that maximizes the amount of information gained from exposing human subjects to the minimum amount of risk. The codes of research ethics add a second stipulation, that research involving humans should be based upon prior laboratory and animal studies<sup>7</sup>. A third stipulation is that all studies involving human subjects should be carefully controlled, so that the biases of the investigator do not invalidate research results. Fourthly, careful methods of statistical analysis should be employed in interpreting the data derived from human research, so that the greatest possible informational benefit is derived from each study<sup>8</sup>.

Even if the optimal research is selected for a particular study, questions about the probability and magnitude of anticipated harms and benefits resulting from the study may remain. A maximum level of anticipated harm is suggested in the Nuremberg Code: "No experiment should be conducted where there is a priori reason to believe that death or disabling injury will occur"<sup>9</sup>.

**INFORMED CONSENT:** Since the Nuremberg trials, no aspect of human research has received greater attention than the issue of consent. In parallel fashion, several codifications of research ethics, including the Helsinki Declaration, have gradually developed the concept of informed consent in the context of research<sup>10</sup>.

Informed consent is designed to protect individuals participating in clinical research trials. An individual interested in participating in a medical research trial will receive a document that contains information about the benefits and risk of the trial, the research procedures and the reasons for the research. The participant should be able to review the document with doctors and ask questions about things they do not understand. Official consent to participate in the trial is given when this document is signed, with the researcher and the participant retaining a copy. The researchers are obligated to keep the participant updated and answer any questions the participant has. Informed consent does not obligate the participant to finish the trial. A participant has the right to leave the trial at any time during the study<sup>11</sup>.

The principle of informed consent is the cardinal canon of loyalty joining men together in medical practice and investigation. The law of battery protects patients and subjects against unauthorized interventions while the law of negligence holds investigations liable for falling short of the customary standard in informing patients or subjects about the potential risks of a particular intervention. It is the duty of the investigators to provide full information to subjects concerning both the fact of randomization and the progress of the trial<sup>12</sup>.

The requirement of adequate research design, favorable benefit-harm ratio and reasonably free and sufficiently informed consent are generally regarded as necessary conditions of ethically acceptable human research. Some also add that all subjects who accept the risks of research for the sake of the society should also receive equitable compensation for injuries sustained in the course of their participation in that research<sup>13</sup>.

**PRIVACY AND CONFIDENTIALITY:** Privacy and confidentiality are very important components for research involving human subjects. People have a right to protect themselves, and information gathered during research participation could harm a person by violating their right to keep information about themselves private. The information gathered from people in biomedical studies has a unique potential to be particularly embarrassing, harmful, or damaging<sup>14</sup>.

Recently, a number of research projects have focused on unlocking genetic information. Genetic information may violate a person's right to privacy if not adequately protected. The very fact that genetic information contains information about identity provides a unique challenge to researchers. Many genetic experiments may seem harmless, but during the process of collecting genetic information on, for example, breast cancer, a researcher will inevitably collect a wealth of other identifiable information that could potentially be linked to research participants as well<sup>15</sup>.

**BENEFICENCE:** Beneficence is a principle used frequently in research ethics. It means, "doing good."48 Biomedical research strives to do good by studying diseases and health data to uncover information that may be used to help others— through the discovery of therapies that improve the lives of people with

spinal cord injuries or new ways to prevent jaundice in infants. The crux of this issue lies in the fact that uncovering information that may one day help people must be gathered from people who are living and suffering today<sup>16</sup>. While research findings may one day help do good, they may also cause harm to today's research participants. For example, research participants in an AIDS study could be asked to take an experimental drug to see if it alleviates their symptoms. The participants with AIDS take on a risk (ingesting the experimental drug) in order to benefit others (information on how well the drug works) at some time in the future. Researchers must never subject research participants to more risk than necessary, be prepared to cease research if it is causing harm, and never put participants at a level of risk disproportionate to the anticipated benefits<sup>17</sup>.

**JUSTICE:** The principle of justice demands that individual research subjects be selected fairly and that appropriate populations are selected as research subjects. Because historical abuses of research subjects tended to occur among those who were in some way disadvantaged or vulnerable, justice in the selection of subject populations was typically considered as the need to protect such populations from inclusion in research<sup>18</sup>. However, justice has come to be understood in some situations as fairness in access to the benefits of participating in research, for individuals and for groups. AIDS and other disease-based activism in the 1980s offered powerful arguments for access to potentially life-saving but experimental drugs as well as an appreciation that a protective stance towards research participants could lead to serious inequities in the availability of medical treatments (e.g., if drugs are not tested with children, there may not be good drugs available for use with children). As a consequence, there are now multiple policies of government and professional groups requiring the inclusion of various population subgroups in research<sup>19</sup>.

The principle of justice means giving people what is due to them. This means that the risks and benefits of research should be shared in a fair way, between all parties involved, e.g. sponsors, trial participants and communities. So it is fair to:

- Invite people and communities to take part in the research because it helps researchers achieve their scientific goals. But they should not be invited for reasons that have nothing to do with the research, e.g., because it is convenient for the researchers to ask them. For example, in phase III HIV vaccine trials, people at high-risk of HIV infection will be recruited<sup>5</sup>.
- Select participants in a way that lowers the risks involved. For example, researchers should choose those who are less vulnerable. So, adults should be involved in HIV vaccine trials first, then older adolescents, then younger adolescents and so on<sup>20</sup>.
- Ask a person to take on the risks of research, as long as they or the population or community they represent, have a chance to benefit from it. Anyone who stands to benefit should also take on some of the risks. For example, it would not be fair to ask poor participants living in Africa to take on the risks of HIV vaccine research if only persons in the West will benefit. Similarly, if sponsors stand to benefit from a successful vaccine, they must take on some of the risks like the cost of making the vaccine<sup>21</sup>.

**RESEARCH INVOLVING CHILDREN:** Ethical guidelines for human research generally presuppose that the subjects who take part in research are adults who have normal mental capacities and who are not pregnant, seriously ill, institutionalized, or in desperate need of money. Special subjects groups who differ

in one or more respects from this model of the normal adult human subject include the mentally retarded, the dying, the comatose, fetuses and children<sup>6</sup>.

The general justification for including children in biomedical research is that physiologically children are not merely "little adults". For example, many drugs produce totally different effects in adults and children, or even in newborn infants and two-year-olds. Unless carefully controlled studies of pediatric reactions to such drugs are performed, children are likely to receive either ineffective or highly toxic doses of drugs<sup>22</sup>.

In general, parents are legally empowered to give permission-often termed proxy consent. No nontherapeutic research should be performed without the informed consent of the research subject. Young children are incapable of giving informed consent. Therefore, no nontherapeutic research involving young children should be performed. In some cases the risks of nontherapeutic pediatric research may be minimal, while the potential benefits of the research to children as a class may be substantial<sup>23</sup>.

All members of society are mutually interdependent and therefore owe to each other the performance of certain minimal moral duties. Among these duties is the obligation to take part in minimally risky nontherapeutic research that promises great promises to the society as a whole. Since, children, too, are members of the society; they stand under a similar obligation, although they may be too immature to recognize the fact. According to this argument, it is permissible for parents to provide proxy consent for their children's participation in minimally risky non-therapeutic research<sup>24</sup>.

**DOES INCENTIVES ETHICAL?** There is considerable confusion regarding the ethical appropriateness of using incentives in research with human subjects. Previous work on determining whether incentives are unethical considers them as a form of undue influence or coercive offer. Incentives become problematic when conjoined with the following factors, singly or in combination with one another: where the subject is in a dependency relationship with the researcher, where the risks are particularly high, where the research is degrading, where the participant will only consent if the incentive is relatively large because the participant's aversion to the study is strong<sup>25</sup>.

Incentives in medical research induce people to do something inherently good (assuming of course that the research is necessary, sound in design, and conducted with integrity), not to violate their duties. So they are not bribery. Neither is they blackmail, since incentives are offers and not threats; one can refuse them and remain no worse off than before. The problem centers around the claim that incentives, particularly relatively large incentives, are a form of undue influence or undue inducement<sup>26</sup>. An offer can be irresistibly attractive so that a destitute person may be induced to do something against his or her better judgment, and even almost against his or her will, by the offer of a large amount of money. Thus, the debate in this form is unresolvable because the positions arise out of irreconcilable paradigms. The argument that incentives maximize choice and therefore maximize freedom arises from the economic paradigm according to which an incentive is simply one form of trade. The alternative argument that incentives can constitute undue influence evaluates incentives as one form of power<sup>27</sup>.

Grant and Sugarman<sup>28</sup> suggested that the use of incentives in medical research will not pose ethical problems. According to them, most of the time for most research studies, the use of incentives to recruit

and retain research subjects is entirely innocuous. The ethical responsibility to improve medical care must be balanced against the ethical responsibility to treat research subjects as autonomous individuals deserving of respect. Incentives used in an ethically appropriate manner can play an important role in striking that balance.

**ETHICAL APPROVAL FOR RESEARCH INVOLVING HUMAN PARTICIPANTS:** In carrying out their work researchers inevitably face ethical dilemmas which arise out of competing obligations and conflicts of interest. All research proposals involving data collection involving human participants normally requires prior ethical approval to ensure the safety, rights, dignity and well-being of the participant and those of the researcher. Ethical approval should not be considered as a bureaucratic obstacle; it is a mechanism for ensuring and demonstrating that the design of your research respects the rights of those who are the participants of the research<sup>29</sup>.

**Ethical Guidelines:** Guidelines for the use of human subjects in research are relatively recent, with the first modern and formal efforts to protect human subjects coming after World War II. The birth of modern research ethics began with a desire to protect human subjects involved in research projects. The first ever ethical guideline was that of **Nuremberg Code** formulated in 1946 which was resulted due to abhorrent and torturous “experiments” with concentration camp inmates by the Nazi Doctors<sup>18</sup>. The Nuremberg Guidelines paved the way for the next major initiative designed to promote responsible research with human subjects, the **Helsinki Declaration**. The Helsinki Declaration was developed by the World Medical Association and has been revised and updated periodically since 1964<sup>30</sup>. Following the Helsinki Declaration, the next set of research ethics guidelines came out in the **Belmont Report** of 1979 from the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Council for international organization of Medical Science in collaboration with WHO developed international ethical guidelines for biomedical research in 1993 with special attention to developing country in response to common research as HIV/AIDS<sup>20</sup>.

Each set of regulations and internationally adopted principles concerning research with human subjects consider the following issues to be of tantamount concern:

- Human subjects must voluntarily consent to research and be allowed to discontinue participation at any time.
- Research involving human subjects must be valuable to society and provide a reasonably expected benefit proportionate to the burden requested of the research participant.
- Research participants must be protected and safe. No research is more valuable than human well being and human life.
- Researchers must avoid harm, injury, and death of research subjects and discontinue research that might cause harm, injury, or death.
- Research must be conducted by responsible and qualified researchers.
- No population of people can be excluded from research or unfairly burdened unless there is an overwhelming reason to do so.

**CONCLUSION:** Participation of human subjects is a must to make any clinical research successful while the guidelines direct the researchers to perform such project ethically. Under-developed and developing countries are more vulnerable in terms of unethical clinical research due to loose monitoring and under-implementation or lack of appropriate law. Scientists and regulatory authorities should be aware of the basic principles of bioethics regarding human participation in research. This article will provide readers basic understanding on ethical principles regarding inclusion of human participants in clinical research.

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