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Topic 2: Central ethical principles of clinical research involving human Subjects

In patient-care today, the idea of paternalism is not accepted today. The idea of the doctor deciding a course of treatment thereby eliminating the patient’s right to make a choice regarding their own treatment violates the key ethical principle of autonomy and is thus not acceptable today in medical practice. Clinicians and care staff are expected to promote patient autonomy and empower them to make autonomous decisions as much as reasonably possible (Rhodes and Schiano 508). However, such ethical clarity is not as probable when it comes to clinical research. Clinical research often involves testing new medical interventions within the laboratory to observe important findings and information, often by first subjecting animals to the same trials and eventually testing them in humans. The practice raises critical ethical and bioethical issues, and because many physicians are themselves involved in clinical research today, any misinterpretation when it comes to boundaries between care and research can have potentially serious consequences. It is therefore important to engage in an ethical analysis of clinical research to arrive at an answer. In the paper, I will be discussing various key ethical principles of clinical research that involves human subjects, highlighting important ethical and philosophical concerns raised by bioethicists and physicians associated with human recruitment in clinical research, and finally attempt to arrive at an appropriate ethical model for the protection of human subjects.

The goal of clinical research is to determine which medical intervention is most appropriate to a disease and whether one form of intervention is more adequate than the other while offering a greater clinical benefit than risk. Yet, the human subjects on which these medical interventions are tested are themselves prone to risks regardless of preceding animal trials. It is thus evident that subjecting the participants to risks in order to collect useful health and clinical data is to seek benefit for future patients. Nevertheless, the practice is still ethically problematic since it can potentially lead to an Individual being possibly harmed (Beauchamp 24). Many current regulations and guidelines attempt to address the issue by admonishing researchers to subject test participants to risks only when the value of the study can sufficiently justify it, yet, there are no easy answers. Several observers are of the view that the ethical principles of clinical care govern the ethics of clinical research, utilizing methods that are deemed acceptable within clinical care while exposing participants to only as much risk as is acceptable within a clinical setting.

These concerns by bioethicists and physicians regarding the ethics of clinical research are not without context. Clinical research history is rife with abuses which continues to influence how ethicists and policymakers perceive clinical research-related concerns. Numerous guidelines were developed to prevent the recurrence of horrific abuses, such as the hypothermia experiments conducted by Nazi scientists during the Second World War (Berger 1435). The Nuremberg Code was one such formal guideline developed in response, which was also later deemed inadequate to address the ethical issues related to clinical research (Buchanan and Miller 372). For instance, the requirement to have independent ethical approvals and reviews was not existent in the Nuremberg Code (The Nuremberg Code 1448). The guideline was then followed by the Declaration of Helsinki to address the former’s shortcomings. The presence of informed consent was emphasized as a mandatory condition for clinical research testing various conditions and emergency situations in patients, even if the research posits minimal harms or risks, or offers the human subject certain compensation (Declaration of Helsinki 1964 1449). The increased emphasis on informed consent was due to the fact that clinical research always relied on volunteer participation who would agree to assume certain risks to themselves. The informed consent process seeks to inform the test subjects of the benefits, risks, and their rights when they agree to participate in a clinical test (Buchanan and Miller 384).

 Following the Helsinki Declaration, The Belmont Report of 1979 provided clear guidance to behavioral and biomedical researchers by outlining some key ethical principles that had to be taken into consideration to ensure the protection of human subjects, namely justice, beneficence, and respect for individuals. It followed after the abuses committed in the Tuskegee syphilis study came to light four decades after the research was initiated. The infamous study involved testing and documenting the natural course of syphilis among 400 African American males in Tuskegee county (Rothman 5). Clinically proven treatments were withheld from the test subjects who were instead told that the processes involved were for therapeutic purposes. After the incident came to light, a U.S. National Commission was formed following public outcry, who were tasked to develop appropriate safeguards and re-evaluate ethical principles for clinical research (Brandt 27). The Commission’s findings and recommendations created a code of conduct for future regulations surrounding clinical research

Even as improved guidelines started to govern clinical research, the philosophical and bioethical debate among ethicists and physicians continues in light of emerging ideas. Any misinterpretation between the boundaries of clinical care and research can lead to serious consequences, for instance, it can lead test subjects to believe that the research studies will involve the physician prescribing the best therapy, while the intervention provided within the test is governed by research protocol. Such issues have prompted many observers to assume the position that the ethics of clinical care should also govern the ethics of clinical research. Such a view finds it ethically unacceptable for a physician to support a research unless it stands consistent with the medical interests of the patient since the contrary view would violate their duty as a clinician (SEP n.p). The view has been mostly applied to randomized controlled trials wherein the intervention received by a test subject is based on a random process instead of a proper clinical judgement deciding the most appropriate therapy (Levine 532). Another principle adopted by this camp is that the treatments selected for the trial must be the best currently available for that particular disease and that the test subject's interests must not be compromised when scientific information is collected. The position is based on the philosophical notion of virtue, which believes that clinical research must protect and reassure the test subjects as well as the public that they are protected, just as the norms of clinical medicine are. In turn, it is assured that any enhancements in clinical research and medicine are not achieved at the cost of exploiting Individuals.

However, the reality is that many procedures and studies which were crucial in developing or identifying enhanced methods for protecting health are not consistent with the medical interests of the test subjects. In this regard, classifying certain research as therapeutic or nontherapeutic is also problematic since nearly all clinical research involves some components that are nontherapeutic in nature (Levine 531). Similarly, an evaluation of the risk-benefit of many clinical studies would reveal that certain interventions and procedures are contrary to the norms of medical practice, for instance, studies that use healthy subjects to test a drug’s safe dosage level. Such a study clearly violates the position taken by ethicists who believe a trial should be consistent with the individual’s clinical interests. A prima facie view in this regard would be to view the physician’s responsibilities to exist only within the domain of clinical care for patients requiring treatment, which cannot apply to clinical research (Beauchamp 27). Moreover, most bioethicists have begun to recognize the former’s view’s limitation in ensuring that research subjects are not exposed to risks beyond that which falls within the risk threshold of clinical medicine, without obscuring the actual clinical research and its objectives.

One way to address the conflict between the two positions would be to find a reasonable justification for exposing the test subjects to overall net risks against the society’s benefit (Beauchamp 25). Moreover, it will also involve identifying certain protections for human subjects so that they can remain safe while not being as strict as to obstruct the necessary clinical research intended to bring benefit to a group or community. In such a case Rhodes and Alfandre (69) bring forth a set of principles that help decide which particular principle should have priority in a certain case, in a way that helps avoid the ethical dilemma. Such meditative methods have been applied by other researchers, for instance, in the case of defining the ethics of placebo-controlled trials. According to Emanuel and Miller (918), such trials are ethical only when they have compelling methodologic reasons, wherein a strict ethical assessment makes it clear that placebo-taking subjects will not be exposed to serious harm and at the same time, certain arrangements have been made to minimize any potential risks associated with receiving the placebo.

In order to arrive at an appropriate model for protecting the human subjects, the Belmont report (1979) is a useful guiding tool to understand the underlying principles which should govern the model. Among the principles, the first is that any study involving human test subjects should be necessary to improve the welfare and health of human beings. Secondly, a recognition that the ability to engage in research is not a right, but rather a privilege extended to the researchers by the subjects and the overall society itself. Thirdly, the costs and risks of the clinical research must not outweigh the potential benefits (Ryan, Brady and Cooke 4). Following these basic principles, some further governing principles to define a model includes ‘respect for persons’ which involves treating individuals as autonomous agents and entitling them to protection if their autonomy is diminished. The principle of beneficence and justice generally cover the aforementioned principles under the former’s doctrine of minimizing potential harms and maximizing possible benefit (Beauchamp 24). An injustice is said to have occurred if an individual is denied what is entitled to them as a result of some undue burden or without good reason (Beauchamp 26). The principle of justice also applies in the case of selecting research subjects who have to be examined whether they have been selected owing to their manipulability, belonging to a certain class, or a compromised position, instead of the selection being governed directly by the requirements of the clinical research.

The important doctrines governing ethical principles in research lead researchers Buchanan and Miller (372) to define what makes clinical research ethical. These requirements include: informed consent, presence of independent review, a favorable risk to benefit ratio, a known scientific or social value, fair selection of subjects, scientific validity, respect for participants, and community collaboration. Together these fair terms would allow human subjects to be used in clinical research while avoiding potential exploitation and ensuring particular safeguards for them (Buchanan and Miller 372). Additionally, there must be uncertainty within the clinical community regarding which intervention or treatment is better, and the outcome should be helpful in determining the preferred treatment. Furthermore, since the objective of clinical research is to obtain knowledge to enhance human health, the findings and investigations of the research must be placed in the public domain.

In addition, the model should also consider the incentives offered to human subjects for participating in the research. In order to avoid concerns of exploitation, bias, inducement, any monetary compensation must be dependent on the time needed to complete the research procedures and activities, as well as the nature of the research (Buchanan and Miller 382). Incentives should be offered that minimize any potential conflict of interest. At the same time, the presence of IRBs is also necessary to protect the safety, well-being, privacy and rights of the vulnerable subjects (Buchanan and Miller 373). Furthermore, no study or procedure should be performed if it is not a clear part of approved IRB protocols, and other requirements such as maintenance of records and documentation, reporting adverse events, and obtaining prior approval before changes are initiated must also be followed, while ensuring that all applicable regulations are complied with (Beauchamp 30).

Appreciating the engagement of the research subjects is also useful to build a level of trust between the subjects and investigators, while ensuring that the complete requirements of informed consent are fulfilled and it is evident that the human subjects used an autonomous and voluntary choice to participate. The informed consent procedure must involve a descriptive statement of discomforts and risks in the study, a disclosure of alternatives, benefits to the test subject, statement of compensation and confidentiality, the availability of treatment in case of an adverse event, a statement outlining the voluntary nature of the participation, and contacts in case the subject has questions related to the risks, benefits, or their rights (Buchanan and Miller 384). Additionally, any circumstances for exclusion, unforeseeable risks, potentially additional costs, information about other members of the study, and consequences to withdrawing during the research must also be outlined where appropriate.

To conclude, the adherence to guidelines are crucial for conducting ethical research to protect the vulnerable population while ensuring that all clinical research is conducted without undue influence, coercion, or through deceptive means. However, there is still a need to evaluate and examine other methods to further enhance the test subject's protection as well as retention, providing them with incentives that maximize positive outcomes and minimize conflict of interest. A careful assessment of risks, proper collection of informed consent and compliance with regulatory bodies is essential to minimize any potential harms to the vulnerable test subjects, who must be treated with concern, beneficence, justice and respect in accordance with the applicable codes of conduct.

# Works Cited

Beauchamp, Tom L. "Ethical Theory and Bioethics." *Contemporary Issues in Bioethics*. Ed. Beauchamp and Walters. 6th. New York, NY: Wadsworth, 2003. 2-34.

Berger, Robert L. "Nazi Science - The Dachau Hypothermia Experiments." *The New England Journal of Medicine* 222.20 (1990): 1435-1440.

Brandt, Allan M. "The Case of the Tuskegee Syphilis Study." *The Hastings Center Report* 8.6 (1978): 21-29.

Buchanan, David and Franklin G. Miller. "Justice in Research on Human Subjects." *The Blackwell Guide to Medical Ethics*. Ed. Rosamond Rhodes, Leslie P. Francis and Anita Silvers. Malden, MA: Blackwell Publishing, 2007. 373-393.

"Declaration of Helsinki 1964." *BMJ* 313 (1996): 1448-1449.

Emanuel, Ezekiel J. and Franklin G. Miller. "The Ethics Of Placebo-Controlled Trials — A Middle Ground." *The New England Journal of Medicine* 345.12 (2001): 915-919.

Levine, Robert J. "The Need to Revise The Declaration of Helsinki." *The New England Journal of Medicine* 341.7 (1999): 531-534.

Rhodes, Rosamond and David Alfandre. "A systematic approach to clinical moral reasoning." *Clinical Ethics* 2 (2007): 66-70.

Rhodes, Rosamond and Thomas D. Schiano. "Justice in Transplant Organ Allocation." *Medicine and Social Justice*. Ed. Rosamond Rhodes, M Pabst Battin and Anita Silvers. 2nd. New York, NY: Oxford University Press, 2012. 505-522.

Rothman, David J. "Were Tuskegee & Willowbrook 'Studies in Nature'." *The Hastings Center Report* 12.2 (1982): 5-7.

Ryan, Kenneth John, et al. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Commission Report. Bethesda, MD: National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979.

SEP. *The Ethics of Clinical Research*. 30 January 2009. 16 May 2019. <https://plato.stanford.edu/entries/clinical-research/>.

"The Nuremberg Code." *BMJ* 313 (1996): 1448-1449.