

Chapter 13

The Holocaust as an Inflection Point in the Development of Research Ethics



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Abstract Modern research ethics arose as a response to the scientific and medical communities' participation in the Holocaust. The Holocaust remains the only example of medically sanctioned genocide and thus can provide critical lessons regarding the importance of valuing basic ethical principles ahead of the potential for scientific progress in the contemporary context of research ethics. This chapter will explore the trajectory of research ethics using the Holocaust as an inflection point. It will briefly describe the difference between medical and research ethics before and after the Holocaust, and then show how the lessons of the Holocaust not only influenced the creation of the Nuremberg Code but also the subsequent development of the Declaration of Helsinki, the Belmont Report, the Federal Policy for the Protection of Human Subjects (The Common Rule) and the International Ethical Guidelines for Biomedical Research Involving Human Subjects.

13.1 Introduction

The Holocaust is a unique event, both in the history of genocide and in the history of professional ethics. As an incidence of mass murder, the Holocaust is the only instance of medically sanctioned genocide, where mass murder was framed as an issue of public health and implementation of the state's ethnic cleansing was overseen by the medical community through systematic labeling, persecution, forced sterilization and eventual killing of those deemed "unfit" or racially inferior. In the history of professional ethics, the Holocaust serves as a unique inflection point, where ethical standards in medicine and research went from being a priority internal to the medical profession to one that became subject to the oversight of society at large. The worldwide shock of hearing about the abrogation of ethics on the part of the

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229

medical and scientific communities during the Doctors' Trial at Nuremberg became the impetus for the Nuremberg Code, which is widely accepted as the "constitution" of bioethics and research ethics (Caplan 2010). Exploring the genesis of the Nuremberg Code and its impact on subsequent codes of ethics is essential to understanding the development of modern research ethics.

Bioethics consists both of medical ethics and research ethics, which are distinct fields with their own practical applications. The former consists of regulating the ethical relationship between patients and physicians, while the latter regulates the relationship between subject and researcher. These two relationships are not exactly the same, since the goals of medicine and the goals of research differ. However both subfields of bioethics are each founded on the same moral principles: i.e. respect for autonomy, nonmaleficence, beneficence, and justice (Beauchamp and Childress 1979). While entire books have been written offering definitions for these terms, for the purpose of this chapter they will be defined as follows: Respect for autonomy is the principle that recognizes the right of individuals to make informed decisions and the need for health care professionals to respect those decisions. Nonmaleficence and beneficence are complementary ethical principles; the former refers to the duty of researchers and medical providers to avoid harming patients and minimize potential risk to them, and the latter refers to the duty of maximizing benefit either to the subject/patient and/or the larger community. Justice takes two forms, procedural justice is the principle which implies the duty to treat "like cases alike," in other words, to provide fair and equal treatment of humans; substantive justice demands an equal distribution of the benefits and burdens of research so that the burden of research does not fall on any individual or particular population (Beauchamp and Childress 1979). These principles existed as part of the ethics of medicine and research dating back to the beginning of the nineteenth century even before the Nuremberg Trial; however, these principles were only formally incorporated as the foundation of bioethics and research ethics in the 1970s. Only after the Holocaust were these principles given priority. Moreover, only after the Holocaust did society at large take an active role in attempting to emphasize and hold physicians and researchers accountable for them, especially the principle of respect for autonomy, even if each of these four principles is a fundamental element of current research ethics.

When physicians who took an oath to heal were put on trial at Nuremberg for unspeakable crimes against humanity including torturous experiments performed on prisoners of war who did not—and could not—consent, both the prosecution and the defense were immediately tasked with seeking out historical examples of research ethics to bolster their arguments. A review of the history of international research ethics and those specific to Germany were necessary.

This chapter will provide a brief history of research ethics, noting the change in priority after the verdict and the publication of the Nuremberg Code. The influence of the Nuremberg Code on the development of subsequent codes of ethics, including the Declaration of Helsinki, the Belmont Report, the Federal Policy for the Protection of Human Subjects, and the International Ethical Guidelines for Biomedical Research Involving Human Subjects will be examined. The latter portion of the chapter will shift focus to address significant issues that have arisen from the

codification of research ethics, such as the necessity of informed consent and the practical difficulties caused by a lack of adequate definitions for key terms within the codes. The current debate regarding what constitutes a vulnerable population and what types of special protection should be offered to these groups of people will be considered. The rapid pace at which medical science continues to advance necessitates a thorough reevaluation of the current state of research ethics in order to ensure the protection of human dignity regardless of the possibility of scientific or societal advancement. Finally, the chapter will end with the suggestion of a paradigm shift away from the rigid protectionism that has resulted from the codification of ethics towards a moral professionalism that uses the Holocaust as the historical framework for developing a personal and professional code of ethics that guides future generations of researchers. While the Holocaust served as an important inflection point in research ethics, since it was the impetus for developing formalized regulations that were created and enforced by entities external to the medical profession, a consequence of this has been a reduction in the internal moral motivations of professionals to demand ethical integrity of the profession, as was found in pre-Holocaust medical ethics. Finding a balance between internal and external ethical requires synthesizing the ideological goals of traditional medical ethics with the practical needs of modern research ethics in order to encompass the benefits of both.

13.2 History of Research Ethics Pre-World War II

While the explicit purpose of the Doctors' Trial at Nuremberg was not to explore the concept of research ethics, the nature and magnitude of the trial led to the recognition of the need for a universal set of standards established by a governing body to ensure ethical human subject experimentation rather than continued reliance on ethical compliance that was internally motivated (Grodin 1992). This recognition stemmed from the strategies of both the prosecution and the defense in the trial, which utilized the (brief) history of research ethics as part of their legal strategies to show how research ethics should be understood as an affair internal to the medical profession. The prosecution based their historical arguments on the work of Hippocrates, Thomas Percival, William Beaumont, and Claude Bernard, while the defense argued that in order to appropriately contextualize the behavior of German physicians operating under National Socialist rule, German codes of ethics must be used as the benchmark.

The Hippocratic Oath is perhaps the most well-known and influential example of an explicit ethical standard to which physicians committed themselves. It was written between 470 and 360 B.C.E. and unequivocally states that the physician's foremost responsibility is to act in the best interest of the patient: "I will follow that system of regimes which, according to my ability and judgement, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous" (Grodin 1992, p. 123). While the Hippocratic Oath was written well before the introduction of the four principles upon which modern bioethics and research ethics are founded,

Hippocrates' writings emphasize the necessity of beneficence and nonmaleficence in the care of the patient, despite never specifically referencing any type of human experimentation.

In 1803, an English physician named Thomas Percival wrote what is believed to be one of the earliest codes of medical ethics, where he mentioned research ethics explicitly. Although Percival's code focused mostly on clinical practice, he included a section expressly dealing with human experimentation:

Whenever cases occur, attended with circumstances not heretofore observed, or in which the ordinary modes of practice have been attempted without success, it is for the public good, and in especial degree advantageous to the poor (who, being the most numerous class of this society, are the greatest beneficiaries of the healing art) that new remedies *and new methods of surgical treatment* should be devised but, in the accomplishment of the salutary purpose, the gentlemen of the faculty should be *scrupulously and conscientiously governed by sound reason, just analogy, or well-authenticated facts*. And no such trials should be instituted without a previous consultation of the physicians or surgeons according to the nature of the case (Grodin 1992, p. 124).

William Beaumont's 1833 code of ethics expanded upon Percival's work and included a directive regarding the absolute necessity of voluntary consent. Beaumont wrote, "The voluntary consent of the subject is necessary...The experiment is to be discontinued when it causes distress to the subject" (Grodin 1992, p. 125). Beaumont's work is significant in that it is the first documented code that includes the concept of informed consent, or what Beauchamp and Childress would later refer to as respect for persons/autonomy. Informed consent became the cornerstone upon which the Nuremberg Code was founded and, to this day, continues to be a source of great debate within the field.

In 1865, French physiologist Claude Bernard published his seminal work, *An Introduction to the Study of Experimental Medicine*, in which he proposed his own principles of ethical human experimentation:

It is our duty and our right to perform an experiment on man whenever it can save his life, cure him or gain him some personal *benefit*. The principle of medical and surgical morality, therefore, consists in never performing on man an experiment which might be harmful to him in any extent, even though the result might be highly advantageous to science, i.e., to the health of others...Christian moral ethics forbid only one thing, doing ill to one's neighbor. So, among the experiments that might be tried on man, those that can only *harm* are forbidden. Those that are innocent are permissible, and those that may do good are obligatory (Grodin 1992, pp. 125–126).

While Bernard's code does not deal with informed consent, it does reference beneficence and nonmaleficence. It also touches upon the concept of justice by explicitly prohibiting human experimentation solely for utilitarian purposes.

The prosecution used each of these codes to argue that the history of research ethics mandates that the physician act in the best interest of the patient. The experimentation that had taken place during World War II were clearly not examples of physicians acting in the best interests of their patients. However, the defense argued that the experiments performed by National Socialist physicians under the Third Reich could only be understood in context of German standards. Thus, they aimed to provide a brief history of German medical ethics pre-World War II.

13.2.1 German Research Ethics

Much like German medicine and science, German research ethics at the beginning of the twentieth century was much more advanced than the rest of the world. On December 29, 1900, the Prussian Minister of Religious, Educational and Medical Affairs published a statement regarding human experimentation (Grodin 1992). It is important to note that this document was issued by an official government organization, as opposed to the academic codes of ethics written by Hippocrates, Percival, Beaumont, and Bernard. This document is also unique in that it specifically references both the needs of vulnerable populations and the necessity of informed consent. Not only does this document set forth theoretical principles, it also enumerates the exact methodology for conducting ethical experimentation with human subjects (Grodin 1992). On February 28, 1931, the German Ministry of the Interior published a Reich circular entitled, “Regulations on New Therapy and Human Experimentation,” which included the majority of the tenets later cited in the Nuremberg Code (Grodin 1992). Again, it is crucial to understand that these regulations did not arise from within the medical community, but rather from the government (Bruns and Chelouche 2017). This document, published not long before the Third Reich formally rose to power, was considered to be far superior to any guidelines that had come before it and, ironically, even to many that came afterwards, specifically the Nuremberg Code and the Declaration of Helsinki (Grodin 1992). However, these documents did not invest authority to international or other regulating bodies to hold researchers accountable for unethical conduct, leading medical researchers to justify their actions as ethical when they complied with the politics of the Third Reich.

As World War II was officially beginning, Germany was advancing medical ethics for physicians, yet in truth was politicizing medicine and medical research. The Nazis created an entirely new field within medical education called Medical Law and Professional Studies. The goal of this field was to merge medicine and politics by inculcating a new generation of doctors with the ideological goals of the Nazi party, including “the unequal worth of human beings, the moral imperative of preserving a pure Aryan people, the authoritarian role of the physician, the individual’s obligation to stay healthy, and the priority of public health over individual-patient care” (Bruns and Chelouche 2017, p. 591). The paradigm shift that took place between the ethical codes issued by the government in 1900 and even in 1931 and the new curriculum that took hold in 1939 is significant. The new code of ethics under the Nazis abandoned the traditional ideals of respecting the person and acting in the patient’s best interest in favor of an ethos that valued the health of society and viewed the patient as a utilitarian means to an end who was useful only so far as he or she could benefit the greater good. It was this *transformation* of ethics, rather than what has traditionally been seen as a lack of ethics, that the defendants used to argue their case at the Doctors’ Trial.

13.3 Doctors' Trial and the Publication of the Nuremberg Code

On December 9, 1946, Chief Prosecutor Telford Taylor argued in his opening statement, “[T]he defendants in this case are charged with murders, tortures, and other atrocities committed in the name of medical science” (1992, p. 67). He continued:

Whatever book or treatise on medical ethics we may examine, and whatever expert on forensic medicine we may question, will say that it is a fundamental and inescapable obligation of every physician under any known system of law not to perform a dangerous experiment without the subject's consent. In the tyranny that was Nazi Germany, no one could give such consent to the medical agents of the States; everyone lived in fear and acted under duress” (1992, p. 89).

His opening statement included descriptions and accusations of the horrific acts of the physicians, however it also served as a call to action regarding the broader topic of appropriate guidelines for human experimentation. As a result, while the main focus of the tribunal was on the behavior of the physicians on trial, questions about the lack of guidelines regulating human experimentation persisted throughout the tribunal.

The conclusion of the trial followed the same pattern. On August 20, 1947, 16 of the 23 physicians were convicted of war crimes and crimes against humanity and 7 were sentenced to death (Judgment and Aftermath 1992). However, just as Telford Taylor advocated for a larger ethical accounting to the medical profession writ large than simply charging the defendants with murder and torture, the judgment at Nuremberg likewise did not stop with giving its verdict on the individuals on trial. Fully cognizant of the significance of the testimony and documentation before them, the court established universal guiding principles to govern human subject experimentation. The Nuremberg Code set forth ten principles for the ethical conduct of human experimentation, beginning with “The voluntary consent of the human subject is absolutely essential” (Nuremberg Military Tribunal 1947). The purpose of the code was to:

set the general agenda for all future ethical and legal questions pertaining to the conduct of human experimentation. What are the individual and societal values that justify science and technology? What are the source and the imperative of the quest for knowledge? Who decides on the limits of scientific endeavors? Who determines the benefits and who sets the research agenda? ... How willing are we to risk human life to serve individual or societal ends? ...” (Annas and Grodin 1992a, b, p. 6).

The publication of the Nuremberg Code was a pivotal moment within the history of research ethics. The creation of a universal standard for the ethical approach to human subject experimentation was revolutionary: however, the difficulty in translating the ideological goals of the Nuremberg Code into practical application soon became apparent.

13.4 Codification of Ethics Post Nuremberg

The Nuremberg Code was created in response to unspeakable abuses of human dignity and ethical misconduct within the medical profession. While the creation of the Nuremberg Code was a necessary step in the codification of research ethics and the development of accountability within the field, its unwavering focus on informed consent ultimately proved to be problematic for those attempting to conduct research with populations incapable of meeting the very strict requirements for informed consent laid out by the Nuremberg Code. Over the next few decades, several other codes of ethics were created in response to similar scandals. Each code attempted to fix perceived inadequacies found in earlier codes and respond to the violations of ethics brought to light by the most recent scandal.

13.4.1 Declaration of Helsinki

The Nuremberg Code was published in 1947 and mandated the absolute necessity of obtaining voluntary informed consent. Coming at the end of a trial in which the lack of voluntary informed consent became a focal point of the prosecution's argument, informed consent seemed to be a necessary prerequisite for any meaningful code of ethics. The closing arguments for the United States at the Doctors' Trial included a statement by James McHaney, the Chief Prosecutor for the Medical Case, in which he maintained:

There are, indeed, other prerequisites to a permissible medical experiment on human beings...*important as these other considerations are, it is the most fundamental tenet of medical ethics and human decency that the subjects volunteer for the experiment after being informed of its nature and hazards. This is the clear dividing line between the criminal and what may be noncriminal. If the experimental subjects cannot be said to have volunteered, then the inquiry need proceed no further. Such is the simplicity of this case* (Grodin 1992, p. 137).

However, as research ethics developed as a field, the idea of voluntary informed consent began to come into question. From a theoretical perspective, it made sense that a researcher would always attempt to secure informed consent from a subject. However, this requirement precluded the possibility of engaging in potentially valuable research involving children or the mentally ill, who cannot give voluntary informed consent. This perceived obstacle established by the Nuremberg Code to protect vulnerable populations seemed to be preventing them from receiving possible advantages that could be gained through productive medical research.

In response to this challenge, *The Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects* was published by the World Medical Association in 1964. Providing a mechanism for allowing research on populations who could not provide voluntary informed consent that conformed to the strict guidelines laid out in the Nuremberg Code appeared to be a primary factor in the decision

to draft this document (Emanuel 2003a, b). The Declaration of Helsinki offered provisions for the consent of a legal guardian when the voluntary informed consent of the subject could not be obtained, thus meeting the practical challenges associated with conducting clinical research in the 1960s.

13.4.2 Belmont Report

When the Nuremberg Code was first published, medical researchers in the United States did not immediately see the relevance between what took place in Nazi Germany and research that was being done stateside. Dr. William Silverman described the experience of American physicians as part of the Advisory Committee on Human Radiation Experiments' Ethics Oral History Project as follows: "There was a disconnect... The interpretation of these Codes was that they were necessary for barbarians but [not for] fine upstanding people" (Faden et al. 2003, p. 8). However, after Beecher's (1966) article in the *New England Journal of Medicine* exposed 22 research violations conducted by leaders in the field at major research institutions throughout the country, the ethics of human experimentation began to receive more attention. Only after the details of the Tuskegee Syphilis Study were made public was the National Research Act passed into law in 1974 and the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was created (Emanuel 2003a, b).

One of the most important tasks of the National Commission was to produce a statement of ethical principles that would govern research with human subjects and prevent ethical transgressions like Tuskegee from recurring. On April 18, 1979, the *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was published (Emanuel 2003a, b). This document was founded on three principles that were "generally accepted in our cultural tradition: "respect for persons, beneficence and justice" (Emanuel 2003a, b, p. 26). The Belmont Report also attempted to delineate boundaries between practice and research and provide clear definitions for terms so as to avoid issues in a practical setting.

13.4.3 Federal Policy for the Protection of Human Subjects

Despite the previous international and national codes, the United States recognized the need for administrative law that could implement practical guidelines for ethical research and delineate particular norms that could be followed in practice. The US Department of Health and Human Services, National Institutes of Health, and Office for Human Research Protections published the Federal Policy for the Protection of Human Subjects, also referred to as The Common Rule, in 1991. The Common

Rule was heavily influenced by both the Declaration of Helsinki and the Belmont Report, however it differs in certain significant ways. First, the Common Rule established guidelines that were mandatory for institutions receiving financial support from the federal government. It also created a method for overseeing these experiments in the form of Institutional Review Boards, or committees that review research methodology to ensure the ethical nature of the experiment at various points within the process. The Common Rule also extends special protections to experiments pertaining to vulnerable populations: pregnant women, human fetuses, neonates, prisoners, and children. Within the United States government, there are currently 20 agencies that have signed on to follow the revised version of the Common Rule that went into effect in July 2018 (<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html>). The fact that these regulations are compulsory for institutions receiving federal support and that the document established a means by which to enforce these guidelines makes the Common Rule unique among ethical codes.

13.4.4 International Ethical Guidelines for Biomedical Research Involving Human Subjects

In 1982 the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) established a set of International Ethical Guidelines for Biomedical Research Involving Human Subjects. A major impetus for the development of this document was the rapid growth of international human subject research, particularly between developed and developing nations looking for a solution to the HIV/AIDS crisis (Emanuel et al. 2000). The need to balance research and protect human subjects is reflected in the opening of the CIOMS guidelines:

The ethical justification of biomedical research involving human subjects is the prospect of discovering new ways of benefiting people's health. Such research can be ethically justifiable only if it is carried out in ways that respect and protect, and are fair to, the subjects of that research and are morally acceptable within the communities in which the research is carried out (CIOMS 2002).

The CIOMS guidelines incorporate the principle of justice and aim to ensure that those who are exposed to the risks of research also benefit from potential rewards, which had been a concern raised by the advent of clinical trials for HIV/AIDS drugs conducted by pharmaceutical companies in developing countries.

13.5 Key Issues

13.5.1 *Informed Consent*

The goal of the Nuremberg Code was to create a set of moral principles that would guide international research involving human subjects in the wake of the ultimate example of what can happen without any type of ethical regulations. However, due to the unique circumstances in which the code was developed, special emphasis was placed on the need for voluntary informed consent. The prosecution at the Doctors' Trial "did not rest their case on the distastefulness of the purposes of the researchers or on the epistemological style or value of the research design or even on the pain and suffering experienced by the human subjects" (Feldman 2014, p. 303). Rather, the prosecution chose to focus their argument specifically "on the failure of the researchers to treat those they experimented with as autonomous individuals capable of giving or declining consent to participate" (Feldman 2014, p. 303). Seen from this perspective, the emphasis on informed consent aligns with the bioethical principle of respecting the person and treating him or her as an autonomous agent. The lack of respect for the individual's ability to make autonomous decisions is a key component of the dehumanization that was so crucial to the systematic mass murder of millions of people deemed "unfit" or "racially inferior."

Feldman argues:

the point of making autonomy central to human subjects research regulation is to ensure that potential subjects understand such risks, and then choose for themselves whether to participate in research. The significance of autonomy does not vary according to the type of possible injury, although risks of different kinds of injury may require different techniques for ensuring autonomous participating in human subjects research (Feldman 2014, p. 310).

Those who take this view contend that autonomy is the key component not only to the Nuremberg Code, but to any meaningful code of ethics. It is the autonomy of the individual that is paramount, not the level of risk or the methodology by which one obtains consent.

Autonomy and respect for persons has always been a central tenet in bioethics and research ethics, however its practical application and regulatory oversight has proven to be problematic in many cases. This was the primary motivating factor behind the development of the Declaration of Helsinki and subsequent legislation. Removing the strict requirements for voluntary informed consent was seen as a way to make it easier to include a broader audience of research participants, thus fulfilling other bioethical principles such as justice due to fair subject selection, and later laws like the Common Rule made sure that researchers would comply with these rules in order to secure their funding.

The argument against the standards of informed consent set forth in the Nuremberg Code is that not all human subject experimentation poses the same amount of risks, therefore not all experiments should be subjected to the same strict regulations. Rhodes argues that:

the Nuremberg Code, the original 1964 version of the Declaration of Helsinki, and the Common Rule all explicitly endorse a view that research risks should be balanced against societal benefits that the project promises. Nevertheless, implementation of the current rules often seems to ignore the importance of adopting a balanced approach (2014, pp. 37–38).

Seen from this perspective, mandating voluntary informed consent negates potential societal benefits that could be gained from experiments that pose extremely minimal risks to the subject. Rhodes contends that the strict regulations make it impossible to conduct what she terms “*de minimis* risk” experiments, i.e.: those “involving only negligible physical, social, or psychological risk where nothing inherently dangerous, such as using identifiable leftover blood sample, is done to the body” (2014, p. 37). She states that there should be no requirement to obtain informed consent for studies that pose *de minimis* risk, and that attempts to protect individuals from any and all potential risks are hindering scientific advancement. “Policies that consider only the risk, and deliberately ignore the possible social benefits that research could provide,” Rhodes asserts, “express a distorted view of what ethics entails and therefore produce regulations that are ethically flawed” (2014, p. 38). The concept of informed consent that was at core of the Doctors’ Trial at Nuremberg remains the focus of much debate within modern research ethics.

13.5.2 *Lack of Adequate Definitions*

In addition to the problems surrounding the term “informed consent,” the lack of adequate definitions for key terms within subsequent documents have continued to cause ambiguity and controversy for the field. Designating where research ends and therapeutic treatment begins, in particular, has generated much contention. The American Medical Association was concerned that the Belmont Report would intrude upon the “ordinary practice of medicine,” and thus ensured that the final document would contain a section delineating the “boundaries between biomedical or behavioral research involving human subjects and the accepted and routine practice of medicine.” (Schrug 2014, pp. 288–289). Ultimately, after confusion about phrases such as “social research” and “generalizable knowledge,” the Belmont Report defined practice as referring to “interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventative treatment, or therapy to particular individuals” (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979). Research is defined as “an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements or relationship). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective” (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979).

While the National Commission and the American Medical Association worked in tandem to create definitions that would be mutually beneficial to professional organizations and associations working in both the fields of medicine and research, scholars have noted that in practice, it is extremely difficult to differentiate between clinical research and medical practice, when patients are recruited for clinical trials. Chalmers stated, “Because episodes of illness and individual people are so variable, every physician is carrying out a small research project when he diagnoses and treats a patient” (Levine 2003, p. 103). Annas and Grodin assert, “It is probably fair to say that modern physicians believe that *anything* they do to one of their patients is, by definition, treatment. This, of course, is consistent with the Hippocratic ethic of acting only for the benefit of one’s patient” (1992, p. 308).

Even in instances that are purely research-based, the history of the doctor-patient relationship can unwittingly cause issues. While their intentions may be good, researchers who stand in front of their subjects wearing a white coat may automatically bring about images of the doctor-patient relationship which can complicate the researcher-subject relationship. Experiments that take place in hospitals can further confuse subjects who are conditioned to thinking of hospitals as a place to go for treatment (Katz 2003). In order to effectively distinguish research from the practice of medicine, bioethicist Edmund Pellegrino argues that definitions alone are not enough. The process of informed consent must include a conversation in which the separation between physician-scientist and physician-healer is made abundantly clear. He states that “[t]he physician can easily obtain consent to an experimental protocol simply by emphasizing the hope of cure and downplaying the risk and the experimental nature of the treatment” (Katz 2003, p. 211). Conflating the relationship between clinical research and medical practice clearly poses potential risks to patient-subjects.

13.6 Current Debate

13.6.1 *What Makes Human Subject Research Ethical?*

It has been over 70 years since the publication of the Nuremberg Code, yet society continues to struggle with the same question: “what makes human subject research ethical?” The codification of ethics rests on the four basic principles of bioethics: autonomy, beneficence, non-maleficence, and justice. Yet despite the theoretical similarities within the codes, each of these principles is reflected differently in various documents and their practical applications remain problematic.

Different codes of ethics were created in response to different scandals within different countries within different historical eras. As a result, the codes lack a universal applicability making them difficult to employ in a real-world setting. Without any type of unifying, cohesive ethical framework, everyone involved in

the process is left without an answer to what most would argue is the single most important question in the field, “what makes human subject research ethical?”

Emanuel, Wendler, and Grady attempted to answer that question by outlining seven requirements for ethical research involving human subjects. They devised these guidelines after analyzing key research and literature in the field, including the Nuremberg Code, the Declaration of Helsinki, the Belmont Report, and the CIOMS guidelines. First, they addressed the goals, definitions, and theoretical foundations of these requirements by stating:

The overarching objective of clinical research is to develop generalizable knowledge to improve health and/of increase understanding of human biology; subjects who participate are the means to securing such knowledge. By placing some people at risk of harm for the good of others, clinical research has the potential for exploitation of human subjects. Ethical requirements for clinical research aim to maximize the possibility of exploitation by ensuring that research subjects are not merely used but are treated with respect while they contribute to the social good (Emanuel et al. 2000, p. 2701).

The article then contends that while there are no guidelines currently in existence that include all seven requirements, each condition was chosen because it represents a “fundamental protection” that exists at the foundation of every document that was synthesized as part of the creation of these guidelines. In addition, these requirements were created to be universally applicable, although their specific use may entail adapting the document to the needs of a particular culture. The seven requirements proposed by Emanuel and his colleagues include: social or scientific value, scientific validity, fair subject selection, favorable risk–benefit ratio, independent review, informed consent, and respect for potential and enrolled subjects (Emanuel et al. 2000).

Judging the seven requirements against the four moral principles on which modern bioethics and research ethics were founded, it is obvious that there is much overlap. Emanuel and his colleagues began with the foundation of research ethics, reviewed and synthesized various codes of ethics, and then essentially developed an updated list of principles that are easier to utilize in practical settings and more relevant to a global audience. In the seemingly unending quest to answer the question, “What makes human subject research ethical?” these seven requirements are a seemingly logical next step in the trajectory of research ethics.

13.6.2 Reevaluation of Research Ethics: How Can Codes of Ethics Be Standardized and Enforced?

Ethical guidelines for human subject research continue to be reevaluated in order to better protect the dignity of the individual while still allowing for the advancement of medical science. The history of the codification of research ethics has proven that despite the theoretical and foundational similarities, there is a lack of standardization and cohesiveness among ethical guidelines. Differing opinions regarding the definitions of key terms and an absence of a centralized governing body to enforce these

guidelines further complicate their use. These issues were clear to the judges during the Doctors' Trial at Nuremberg and have been cited as one of the reasons behind the including the Nuremberg Code as part of the legal judgment that was delivered at the tribunal. Their strategy was to incorporate the Nuremberg Code into international criminal law, thereby ensuring that its repercussions would be felt throughout the world for generations to come. In addition, the judges recognized that while the legal validity of ethical codes was uncertain, violating international law would have definitive harsh penalties (Grodin 1992). However, because the judges did not offer a concrete method for enforcing the Nuremberg Code it was impossible to practically implement (Emanuel 2003a, b). The history of research ethics has proven that "although a code is necessary, it is insufficient to safeguard human rights in human experimentation...The courts of individual countries, including the United States, have consistently proven incapable of either punishing those engaged in unlawful and unethical experimentation or compensating the victims of such experimentation" (Annas and Grodin 1992a, b, p. 309).

As each new code of ethics was introduced in response to a major scandal within the field of research ethics, it became even more apparent that these codes were not preventing legal or ethical abuses within human subject research. Since the publication of the Nuremberg Code, examples of unethical instances of human subject research abound: the Willowbrook Study, the Brooklyn Jewish Chronic Disease Hospital, the Tuskegee Syphilis Study, drug trials in developing countries are just a few of the instances that triggered revisions in pre-existing codes of ethics. As medical technology has continued to advance, criticism about the usefulness of ethical regulations within the current research environment are growing. There are increasing concerns regarding "new medical devices, genomics, the Internet, mobile technologies, and stem cell research—all of which have revolutionized how and by whom research is conducted" (Davis and Hurley 2014, p. 12). The rapid pace of medical and scientific advancement is going to create new challenges for the development of ethical guidelines for human subject research.

In his groundbreaking work, *The Structure of Scientific Revolutions*, Thomas Kuhn presented a theory explaining the cycle of progress within scientific fields. Very simply put, Kuhn asserted that change does not result from the accumulation of an abundance of new knowledge. Rather, scientific knowledge advances when the old way of thinking about a topic no longer works and a new model must arise to take its place. In this situation, a paradigm shift occurs. The old model is no longer able to sufficiently serve as a reliable guide for solving problems, and a new model emerges that is better equipped to handle the challenges of the field (Kuhn 1962). While this model crisis first occurred after the Nuremberg Trial, it is occurring again today. Rather than continuously revising codes of ethics, it is necessary to reevaluate the entire approach to research ethics and create a paradigm shift. This does not mean abandoning the values that became dominant as a result of the Nuremberg Trial; rather, it means that new regulations and ethics codes must incorporate those values in a way that allows them to remain consistently prioritized in our changing world of medical research.

13.7 From Codification to Moral Professionalism: Teaching Bioethics and the Holocaust

The Nuremberg Code was written in response to the medical community's blatant and egregious disregard for the dignity of human beings that took place during the Holocaust. This unique example of medically sanctioned genocide led to a codification of ethics that has become increasingly incompatible with the current research environment. Cohen and Lynch argue:

[T]he fundamental issues at stake are the same as they have always been—balancing protectiveness against autonomy, risks against benefits, efficiency against deontological concerns. But several decades after the current human subjects regulatory framework was first adopted...it is not well suited for the reality of much of the research that will emerge in the twenty-first century and the institutions that will be conducting it (2014, p. 6).

Modern research ethics must redefine itself in a way that will both protect the rights and dignity of individuals while also meeting the demands of an ever-changing scientific world whose goal is to improve the welfare of society.

The system in use is failing both researchers, subjects and society. Instead of constantly attempting to revise ethical guidelines, as has been the case since the inception of the Nuremberg Code over 70 years ago, a new paradigm must be established that emphasizes the responsibility of the researcher to prioritize the well-being of the subject first and foremost. Even before Beecher's landmark 1966 article exposing research violations in major US institutions, he had already expressed doubts about the efficacy of using guidelines to regulate ethical human subject research in his response to the publication of the Nuremberg Code: "It is not my view that many rules can be laid down to govern experimentation in man. In most cases, these are more likely to do harm than good. Rules are not going to curb the unscrupulous. Such abuses as have occurred are usually due to ignorance and inexperience" (Advisory Committee on Human Radiation Experiments 1996, p. 90). Instilling a moral ethos within the profession will ensure that researchers are treating individuals with dignity and respect not because a code of ethics tells them to, but because it is the right thing to do. This is a synthesis between the priority of maintaining an internal morality of the profession that existed before the Holocaust and the priority of external oversight and regulation that existed after the Holocaust and continues today.

It is a fallacy to believe that Nazi doctors acted without any type of moral motivation. The history of medical ethics in Germany up to and including World War II has proven that there was, in fact, a very advanced formalized system of ethics being taught and instilled into physicians. Rather, their ethics were corrupted by a National Socialist political ideal that stressed the worth of certain individuals over others based on their value to the nation (Proctor 1992). Thus, it is important to understand that medical and research ethics do not exist independent of society, yet physicians and researchers must also have the ability and integrity to go against society's mores when they become corrupted. As Bruns and Chelouche have argued, "[t]he prevailing medical ethos can be strongly determined by politics and the zeitgeist and therefore

has to be repeatedly negotiated” (2017, p. 591). We have seen that ethical guidelines are often created in response to events within a culture or within a historical time period. As a result, these guidelines are equally likely to be influenced by the prevailing cultural or political zeitgeist. This is why they have been—and continue to be—repeatedly negotiated.

Recognizing that the Holocaust served as a historical inflection point in the history of developing medical and research ethics can allow us, as a society and a community of bioethicists, to develop a personal and professional ethos that values the dignity of the individual in a new paradigm, one that also emphasizes moral professionalism. While regulatory systems like peer review and informed consent can certainly help prevent ethical abuses from occurring, ultimately moral professionalism argues that a person’s moral compass will always be a better guide than an ever-changing series of documents. Teaching about the ways in which the moral compass of the Nazi doctors was corrupted by forces from outside the medical profession is important. Understanding how these physicians abandoned their Hippocratic Oath and transformed from healers to killers demonstrates the “ease with which a contemporary ideology—one that promises a better future for our country—can undermine ordinary, “good” doctors’ core ethical obligations to the primacy of patients’ interest” (Cohen 2010, p. 205). External codes of ethics have proven time and again to be a double-edged sword, regulating professionals while also being subject to the pitfalls of politicization. Shifting away from the failing paradigm of codification towards one that also consists of moral professionalism will allow future generations of researchers to develop an internal motivation to act ethically that will guide them to do the right thing, not because they are required to do so, but because they truly believe it is the ethically sound decision.

References

- Advisory Committee on Human Radiation Experiments. (1996). *The human radiation experiments: Final report of the President's Advisory Committee*. New York: Oxford University Press.
- Annas, G.J., and M.A. Grodin. 1992a. Introduction. In *The Nazi doctors and the Nuremberg Code: Human rights in human experimentation*, ed. G.J. Annas and M.A. Grodin, 3–11. New York: Oxford University Press.
- Annas, G.J., and M.A. Grodin. 1992b. Where do we go from here? In *The Nazi doctors and the Nuremberg Code: Human rights in human experimentation*, ed. G.J. Annas and M.A. Grodin, 307–314. New York: Oxford University Press.
- Beauchamp, T.L., and J.F. Childress. 1979. *Principles of biomedical ethics*. New York: Oxford University Press.
- Beecher, H.K. 1966. Ethics and clinical research. *New England Journal of Medicine* 274 (24): 1354–1360.
- Bruns, F., and T. Chelouche. 2017. Lectures on inhumanity: Teaching medical ethics in German medical schools under Nazism. *Annals of Internal Medicine* 166 (8): 591–595.
- Caplan, A.L. 2010. The stain of silence: Nazi ethics and bioethics. In *Medicine after the Holocaust: From the master race to the human genome and beyond*, ed. S. Rubinfeld, 83–92. New York: Palgrave Macmillan.

- Cohen, I.G., and H.F. Lynch. 2014. Introduction. In *Human subjects research regulation: Perspectives on the future*, ed. I.G. Cohen and H.F. Lynch, 1–8. Cambridge, MA: The MIT Press.
- Cohen, J.J. 2010. Medical professionalism: Lessons from the Holocaust. In *Medicine after the Holocaust: From the master race to the human genome and beyond*, ed. S. Rubinfeld, 201–208. New York: Palgrave Macmillan.
- Davis, A.L., and E.A. Hurley. 2014. Setting the stage: The past and present of human subjects research regulations. In *Human subjects research regulation: Perspectives on the future*, ed. I.G. Cohen and H.F. Lynch, 9–24. Cambridge, MA: The MIT Press.
- Department of Health and Human Services. (1991). *Federal policy for the protection of human subjects*. Washington, D.C.
- Emanuel, E.J. 2003a. Scandals and tragedies of research with human participants: Nuremberg, the Jewish Chronic Disease Hospital, Beecher, and Tuskegee. In *Ethical and regulatory aspects of clinical research: Readings and commentary*, ed. E.J. Emanuel, R.A. Crouch, J.S. Arras, et al., 1–5. Baltimore, MD: The Johns Hopkins University Press.
- Emanuel, E.J. 2003b. Ethical and regulatory guidance for research with humans. In *Ethical and regulatory aspects of clinical research: Readings and commentary*, ed. E.J. Emanuel, R.A. Crouch, J.S. Arras, et al., 25–28. Baltimore, MD: The Johns Hopkins University Press.
- Emanuel, E.J., D. Wendler, and C. Grady. 2000. What makes clinical research ethical? 2000. *JAMA* 283 (20): 2701–2711.
- Faden, R.R., S.E. Lederer, and J.D. Moreno. 2003. U.S. medical researchers, the Nuremberg Doctors Trial, and the Nuremberg Code: A review of the findings of the Advisory Committee on Human Radiation Experiments. In *Ethical and regulatory aspects of clinical research: Readings and commentary*, ed. E.J. Emanuel, R.A. Crouch, J.D. Arras, et al., 7–11. MD: The Johns Hopkins University Press, Baltimore.
- Feldman, H.L. 2014. What's Right about the "medical model" in human subjects research regulation. In *Human subjects research regulation: Perspectives on the future*, ed. I.G. Cohen and H.F. Lynch, 299–311. Cambridge, MA: The MIT Press.
- Grodin, M.A. 1992. Historical origins of the Nuremberg Code. In *The Nazi doctors and the Nuremberg Code: Human rights in human experimentation*, ed. G.J. Annas and M.A. Grodin, 121–144. New York: Oxford University Press.
- Judgment and Aftermath. (1992). In: Annas GJ., Grodin MA (eds) *The Nazi doctors and the Nuremberg Code: human rights in human experimentation*. New York: Oxford University Press, pp 94–104.
- Katz, J. 2003. Human experimentation and human rights. In *Ethical and regulatory aspects of clinical research: Readings and commentary*, ed. E.J. Emanuel, R.A. Crouch, J.D. Arras, et al., 210–213. Baltimore, MD: The Johns Hopkins University Press.
- Kuhn, T.S. 1962. *The structure of scientific revolutions*. Chicago, IL: University of Chicago Press.
- Levine, R.J. 2003. Research and practice. In *Ethical and regulatory aspects of clinical research: Readings and commentary*, ed. E.J. Emanuel, R.A. Crouch, J.D. Arras, et al., 103–107. Baltimore, MD: The Johns Hopkins University Press.
- Nuremberg Military Tribunal, from *U.S. v. Karl Brandt, et al.* 1947. *The Nuremberg Code*.
- Proctor, R.N. 1992. Nazi doctors, racial medicine, and human experimentation. In *The Nazi doctors and the Nuremberg Code: Human rights in human experimentation*, ed. G.J. Annas and M.A. Grodin, 17–31. New York: Oxford University Press.
- Rhodes, R. 2014. *De minimis* risk: A suggestion for a new category of research risk. In *Human subjects research regulation: Perspectives on the future*, ed. I.G. Cohen and H.F. Lynch, 31–44. Cambridge, MA: The MIT Press.
- Schrag, Z.M. 2014. What is this thing called research? In *Human subjects research regulation: Perspectives on the future*, ed. I.G. Cohen and H.F. Lynch, 285–298. Cambridge, MA: The MIT Press.

Taylor T (1992) Opening statement of the Prosecution, December 9, 1946. In *The Nazi doctors and the Nuremberg Code: Human rights in human experimentation*, ed. G.J. Annas and M.A. Grodin, 67–93. New York: Oxford University Press.

The Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization. (2002). *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, Geneva.

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979). *The Belmont Report: ethical principles and guidelines for the protection of human subjects of research*. Washington, D.C.: Department of Health, Education, and Welfare.

United States Department of Health and Human Services. (2018). Office for human research protections. <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html>. Accessed 20 Aug 2018

World Medical Association. (1964). *Declaration of Helsinki: ethical principles for medical research involving human subjects*. Finland.

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