

Coercion in Research: Are Prisoners the Only Vulnerable Population?

Barbara E. McDermott, PhD

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Research plays an essential role in advancing medical and behavioral sciences and in improving our ability to understand and treat illness. However, unlike clinical care, which is intended for the sole benefit of the patient, research has the broader goal of advancing knowledge and does not necessarily provide the subject with an ensured clinical benefit, raising obvious ethics-related concerns and making voluntary consent to participate essential. For certain participant populations, consent may be problematic. Such individuals include those who may be unable to make informed, voluntary decisions about participation in research, either because of impairments in cognition or reasoning or because they live in an environment that is potentially coercive.

History of Research on Prisoners

Prisoners are considered a group of individuals for whom coercion is a major concern, primarily because of the supposition that prisons are inherently coercive institutions. Previous research conducted on prisoners makes the rationale for this evident. Historically, prisoners have been considered an ideal population on which to conduct research because they are readily accessible and in a controlled environment. As an example, in the early 1900s, pellagra had reached epidemic levels in the rural southern United States. The U.S. Public Health Service

(USPHS) commissioned Dr. Joseph Goldberger to study the problem in an effort to find a cure.¹ The widely held belief at the time was that pellagra was caused by some type of micro-organism. Dr. Goldberger began observational studies and formulated the hypothesis that diet was primarily responsible for the disease. To test this theory, he recruited 11 prisoners from Rankin State Prison in Mississippi to undergo dietary modifications in an effort to induce pellagra in these otherwise healthy volunteers. In exchange for their participation, the prisoners were promised a full pardon. After five months, during which time several prisoners began to develop symptoms of the disease, the study concluded, with 6 of the 11 evidencing symptoms of pellagra. During those months, inmates who developed the disease suffered so greatly that some were willing to forgo the pardon to discontinue the study.

A much more extreme example highlighting the subtlety of the coercive process was the malaria study at Stateville Penitentiary in Illinois.² The prison was built as a panopticon, meaning that the housing units were arranged in a circle surrounding a central tower. A guard was placed in the tower but was not visible to the inmates. Thus, the guard could be watching the inmates at any time without their knowledge, imposing a subtle form of authority. During World War II, malaria was devastating U.S. soldiers fighting in the Pacific Ocean theatre. At that time, quinine was the only effective treatment, although supplies were limited. Between 1942 and 1945, the United States reportedly lost eight million man-days to the disease. In 1944, the malaria studies began at Stateville Penitentiary. Although inmates were not promised early

Dr. McDermott is Professor of Clinical Psychiatry, Division of Psychiatry and the Law, Department of Psychiatry, UC Davis School of Medicine, Sacramento, CA. Address correspondence to: Barbara E. McDermott, PhD, UC Davis School of Medicine, Department of Psychiatry, Division of Psychiatry and the Law, 2230 Stockton Boulevard, Sacramento, CA 95817. E-mail: bmcdermott@ucdavis.edu.

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release initially, the governor of Illinois eventually guaranteed that all inmate participants would have their parole decisions reviewed at the end of their sentences. It ultimately was determined that inmates participating in the malaria studies were released an average of two years earlier than were nonparticipants. At the initial announcement of the effort, 200 volunteers were solicited; 487 men offered their services. Although the prisoners signed consents for these studies, no risks were mentioned in the consent forms. According to reports from the infamous inmate Nathan Leopold,³ each volunteer was fully apprised verbally of the risks; one risk was death. Yet, inmates volunteered in increasing numbers. As a result of these studies, brought to light during the Nuremberg trials as evidence that the United States had also performed atrocious medical studies on prisoners, the Governor of Illinois (Dwight Herbert Green) convened a committee (dubbed the Green Committee) to determine the conditions under which prisoners could serve as subjects in medical experiments and whether a reduction in sentence could be offered as a reward for such service.⁴ Published, in part, in the *Journal of the American Medical Association* in 1948⁵ were three rules that the committee proposed for conducting medical research on prisoners: consent must be obtained in the absence of coercion and with knowledge of the potential risks; the studies must be based on the results of animal experimentation and on knowledge of the natural history of the disease, and must be expected to yield results not obtainable in any other fashion; and the study must be conducted by scientifically qualified personnel and avoid unnecessary physical or emotional suffering, and there should be no reason to believe that death or a disabling injury would occur. The ultimate conclusion of the committee was that medical research could be conducted ethically with prisoners if those criteria were met and, to avoid undue influence or coercion, the reduction of sentence was not excessive.

With the endorsement of the American Medical Association, medical research on prisoners flourished. In the last year of World War II, the National Institutes of Health received approximately \$700,000 in federal funding; by 1955, this amount increased to \$36 million and reached \$1.5 billion by 1970.⁶ Much of this funding was allocated to medical research that was conducted on prisoners. Noteworthy examples include Dr. Albert Sabin, who

tested a polio vaccine on prisoners at the Federal Reformatory in Ohio because he believed that the vaccine was not yet ready for the general public; Dr. Jonas Salk's use of Michigan inmates in his work with the influenza vaccine; and Sloane-Kettering's collaboration with Ohio State University and the use of prisoners in Ohio for cancer research that involved injecting live cancer cells into supposed volunteers. Although the Green Committee encouraged the disclosure of risks to each prisoner, there were no procedures in place to ensure that such a disclosure occurred. Researchers were left with the responsibility of assuring that participants knew the risks associated with the studies and were presumed to police themselves in this regard.

In 1962, the thalidomide scandal changed Food and Drug Administration (FDA) regulations regarding drug testing. Thalidomide was routinely administered to pregnant women in Europe for the control of nausea. Although the FDA withheld approval of thalidomide for use in the United States, thousands of U.S. women, many of child-bearing age (including some who were pregnant), participated in studies conducted by pharmaceutical companies on its safety and efficacy. When the link between thalidomide and birth defects became clear, the FDA modified its procedures for drug testing and ultimately required that such studies be conducted in three phases. Phase 1 studies required the use of healthy subjects to evaluate the safety of experimental medication (Phases 2 and 3 were for establishing efficacy). Prisoners were ideal subjects for Phase 1 studies. They were willing to accept more risk for less money and, according to the assistant medical director of one pharmaceutical company, were guaranteed to show up. Medical research in prisons continued to grow. One particularly egregious example was a study by Dr. Austin Stough, an Oklahoma physician who used prisoners in Oklahoma, Arkansas, and Alabama for drug and blood plasma studies in mostly unregulated conditions. One report indicated that in a prison in Alabama, 28 percent of the prisoners participating in Dr. Stough's studies developed viral hepatitis compared with 1 percent of the prisoners who did not participate. One inmate was quoted as saying, "They're dropping like flies out here."⁷ The studies conducted in Holmesburg Prison in Pennsylvania further illustrated the abuse of prisoners for medical research. Prisoners were routinely used for testing of cosmetics, details of which were documented by

Allen Hornblum in his book, *Acres of Skin: Human Experiments at Holmesburg Prison*.⁸ The title was derived from a comment by Dr. Albert Kligman, a professor of dermatology at the University of Pennsylvania Medical School. When he first entered the prison, he reportedly recalled in a newspaper interview: “All I saw before me were acres of skin. It was like a farmer seeing a fertile field for the first time” (Ref. 8, p 37).

Although not conducted on prisoners, the Tuskegee syphilis study set in motion a chain of events that effectively halted medical research in correctional institutions.⁹ In the early 1900s, syphilis was seen as a major health problem, with as many as 35 percent of people in their reproductive years exhibiting symptoms of the disease. The Tuskegee study, initiated by the USPHS in 1932, was designed to provide evidence of the significant effects of untreated syphilis, presumably in an effort to encourage the development of new treatments for the disease. The study involved 600 African-American sharecroppers from Alabama, 399 infected with syphilis before the study began and 201 noninfected. Participants in the study were provided medical care, meals, and burial insurance; all participants were led to believe that they were receiving treatment; and none provided informed consent. In 1947, penicillin was established as an effective treatment for syphilis, but rather than close the study and treat all the subjects, investigators withheld penicillin from study participants. The participants were never told that they had syphilis, they were told that they had bad blood, and the researchers prevented the men from accessing the rapid-treatment centers established by the USPHS for those infected with syphilis. The study ended in 1972 when it was made public in an article appearing in *The New York Times*. By the time the study ended, 128 men had died, 40 wives had been infected, and 19 children had been born with congenital syphilis. A class-action lawsuit resulted in a \$10 million settlement by the U.S. Government and sweeping changes in the conduct of research. On May 16, 1997, President Bill Clinton issued a public apology to all participants in the Tuskegee study as well as to their wives and children.

As a result of the Tuskegee study, in 1974 Congress passed the National Research Act, which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was charged with devel-

oping guidelines for the ethical conduct of research; the Belmont Report,¹⁰ named for the conference center in which it was penned, was drafted in response to this charge. The report described three basic principles of ethical research: respect for persons: persons should be treated as autonomous, and if autonomy is diminished, additional protections should be in place; beneficence: human subjects should not be harmed and the research should maximize benefits and minimize risk; and justice: benefits and risks of research should be distributed fairly. Many of the recommendations of the Belmont Report were incorporated into the Department of Health and Human Services (DHHS) Title 45 Code of Federal Regulations (CFR) Part 46, known as the Common Rule.¹⁰ One major aspect of the Common Rule was the requirement that research be reviewed by a committee on ethics: an institutional review board (IRB). These bodies were intended to provide oversight of research (researchers?) to ensure that the three basic principles of the Belmont Report are not violated.

In 1976, the Commission effectively banned medical research in prisoners. Two concerns were deemed most relevant for prisoners: whether prisoners bore the fair share of burdens and benefits (justice) and whether they could truly give voluntary consent (respect for persons). The Commission commented:

... [T]he strong evidence of poor conditions generally prevailing in prisons and the paucity of evidence of any necessity to conduct research in prisons have been significant considerations of the Commission. An equally important consideration has been the closed nature of prisons, with the resultant potential for abuse of authority [Ref. 12, p 12].

They issued multiple recommendations, many of which were adopted in the Common Rule. However, the Commission went beyond the recommendations to propose a requisite standard of living for inmates in prisons conducting research, making research out of the question for most, if not all, prisons. Such standards included limiting prison populations, providing single-occupancy cells, segregation of offenders by age and offense as well as potential for violence, and “effective procedures assuring that parole boards cannot take into account prisoners’ participation in research and that prisoners are clearly informed that there is absolutely no relationship between research participation and determinations by their parole boards” (Ref. 12, p 19).

Modern-Day Research on Prisoners

The Common Rule identifies certain “vulnerable” populations, including pregnant women, human fetuses and neonates, prisoners, and children. The definition of prisoner includes not just individuals incarcerated in prisons, but any individual committed to a facility in lieu of incarceration as well as individuals detained in jails awaiting arraignment, trial, or sentencing. Only minimal-risk research is allowed; for prisoners, minimal risk is defined as “the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.” Further, only four types of research are permissible: studies of the causes, effects, and processes of incarceration or criminal behavior; studies of prisons as institutions or prisoners as incarcerated persons; research on conditions particularly affecting prisoners as a class; and research on practices that have the intent and probability of improving the health or well-being of the subject. Both Types 3 and 4 require approval by the Secretary of Health and Human Services, a task so onerous that most federally approved research is limited to Types 1 and 2. However, only federally funded research and certain other federal agencies are required to comply with these regulations; biomedical research can continue in prisons if it is not federally funded (e.g. funded by pharmaceutical companies), and state laws allow such conduct.¹³

Because the Common Rule imposes severe restrictions on federally funded research but allows other biomedical research to continue unregulated in prisons, the DHHS requested that the Institute of Medicine (IOM) form a committee to re-evaluate the guidelines contained in Subpart C of the Common Rule, which were codified in 1981 and revised in 1991, to determine if revisions were necessary. The committee, in a 265-page document published in 2007,¹⁴ presented their recommendations, which in essence consisted of five changes: expand the definition of prisoner to include individuals whose liberty is restricted by the criminal justice system (e.g., individuals on probation or in diversion programs); widen the scope of the regulations to include all research conducted on prisoners regardless of the funding source; eliminate the category-based approach to allowable research and shift to a risk-benefit approach, allowing research on prisoners

only when the benefits outweigh the risks; require that all research be conducted with collaboration from key stakeholders (prisoners and prison staff) and enhance oversight of research involving prisoners.

Because these recommendations were so controversial, with some factions expressing concern that the IOM was imposing even further restrictions on research¹⁵ and others believing that the revisions would open the door to further unethical research,^{16,17} the recommendations have not yet been adopted and incorporated into the Common Rule.

Has the Pendulum Swung Too Far? The Question of Voluntary Consent

As the arguably unethical research of the past has exemplified, the Green Committee’s expectations that researchers police themselves regarding obtaining voluntary, informed consent fell short. The Tuskegee Study was a particularly egregious example. Participants not only did not provide consent, they were unaware that they were being enrolled in a research study. The biomedical and psychological studies conducted on prisoners, too numerous to document in this article, made it clear that voluntary consent was particularly problematic in this population. The primary impediment to voluntary consent in prisoners is coercion: the forces that exist inside prison walls that may subtly or not so subtly encourage participation in research, so that participation is not technically voluntary. In 1948 the Green Committee proposed that granting a pardon to an inmate serving a life sentence in exchange for research participation was excessive and clearly coercive. In the case of the Stateville Penitentiary, where correctional officers were ever-present and could be watching at any time, the exercising of authority and potential encouragement for research participation was more subtle. The IOM has suggested that protections afforded prisoners should extend to parolees and probationers. These individuals are under the jurisdiction of the criminal justice system, with clear consequences (including incarceration) for failure to cooperate with the terms and conditions of probation or parole. However, they are not residing in a controlled environment, locked behind closed doors and high walls, which is in part what led to the abuses in the past. Are probationers and parolees less likely to be able to provide voluntary, informed consent because of their involvement in the criminal justice system? Are they as susceptible to coercion?

A recent study highlights the complicated questions regarding voluntary consent and vulnerability to coercion.¹⁸ A sample of IRB members was recruited and provided written vignettes documenting hypothetical research studies. Participants in the hypothetical studies were varied along illness type (psychiatric versus medical) and illness severity (low versus high). IRB members were asked to make judgments of decisional capacity, coercion, and risk. Their judgments of vulnerability to coercion varied, depending on illness severity and type. For low-severity illnesses, vulnerability to coercion was higher in psychiatric patients; for high-severity illnesses, there were no differences in IRB members' judgment of vulnerability to coercion: psychiatric patients and medically ill participants were viewed as equally vulnerable. These results suggest that vulnerability to coercion is not simply based on one's living environment and may be based, at least in part, on how high-stakes the research is.

Along these lines, how many research participants actually provide informed, voluntary consent? Consent forms for clinical trials often exceed 15 to 20 pages, as the researcher dutifully outlines all the procedures and the risks and benefits of participation, according to all established regulations. What level of understanding do these participants truly have? Many of them have life-threatening illnesses and may be desperate for a treatment that could effect a cure. One particularly poignant example was publicized in a local newspaper. Two surgeons were performing an experimental treatment on patients with a particularly aggressive type of cancer. The prognosis for individuals diagnosed with this disorder is poor; it is almost always fatal, with death occurring within months of diagnosis. The procedure was experimental and according to news reports (which included confidential letters from the university) had not been fully tested according to FDA guidelines. Three patients consented to the procedure and, according to public documents, two of the three actually requested the procedure. Given that these individuals had been in essence given a death sentence and were eager to undergo any type of experimental treatment to extend their lives, could any type of informed consent be truly voluntary? The results of the study of the IRB members suggested that such individuals (i.e., those with extremely high-severity illnesses) are clearly at risk of coercion and may be less able to provide voluntary, informed consent.

Conclusions

There are no simple solutions to these questions. Clearly, research conducted on prisoners in the past involved coercion, both from the authority imposed by prison officials and the fact that release decisions indeed were based on participation. The IOM attempted to resolve many of the problems associated with the conduct of research with prisoners in its recent review of Subpart C of the Common Rule. The committee met with stakeholders, including both prisoners and researchers, for a thorough review of the scope of the problem and to determine if revisions to the current standards were necessary. Prisoners are not the only research participants vulnerable to coercion, as the IOM acknowledged by including nonincarcerated individuals under control of the criminal justice system in its definition of prisoners. Yet, the recommendations stirred such controversy that five years later, none of them has been adopted.

The study by Luebbert and colleagues¹⁸ makes it clear that IRBs believe prisoners are not the only research participants vulnerable to coercion. When life is at stake, whether within the confines of prison walls or not, it appears that many research participants are willing to take excessive risks. Can a terminally ill individual intelligently weigh the risks associated with dangerous research when facing death? Is the answer to create more and more restrictions to protect classes of participants? Perhaps not. Perhaps the answer is to explore more systematically the questions associated with consenting to participate in research, both in prisoners and other vulnerable populations. While capacity to consent has been researched extensively, especially in individuals for whom capacity is suspected to be impaired, coercion in research has been substantially less extensively researched. Coercion was clearly a force in prisoners when freedom was granted in exchange for research participation. Under what specific circumstances and with what specific participants is coercion also a problem? Instead of expanding and changing definitions, it seems most appropriate to explore in a more systematic way the role that coercion plays in biomedical research in all participants, not simply those who reside in (presumably) coercive environments.

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