2007

Biomedical Research Involving Prisoners: Ethical Values and Legal Regulation

Lawrence O. Gostin
Georgetown University Law Center, gostin@law.georgetown.edu

297 JAMA 737-740 (2007)

Biomedical Research Involving Prisoners
Ethical Values and Legal Regulation

Lawrence O. Gostin, JD

Until the early 1970s, R. J. Reynolds, Dow Chemical, the US Army, major pharmaceutical companies, and other sponsors conducted a wide variety of research on prisoners—a captive, vulnerable, and easily accessible population.[1,2] During that time, approximately 90% of all pharmaceutical research was conducted on prisoners, who also were subjected to biochemical research ranging from testing diet drinks and simple detergents to studies involving dioxin and chemical warfare agents.[3] From 1962 to 1966, for example, 33 pharmaceutical companies tested 153 experimental drugs at Holmesburg Prison in Philadelphia, including a Retin-A (tretinoin) study in which researchers did not seek informed consent and prisoners were not adequately treated for pain.[4] By the mid-1970s, biomedical research in prisons sharply declined as knowledge of the exploitation of prisoners began to emerge and the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was formed.[5]

Federal regulations to protect human subjects of research were established in 1974 and modified and codified in 1981.[6] The regulations were revised in 1991 as the Federal Policy for the Protection of Human Subjects and became known as the Common Rule. The Common Rule applies to research funded by the Department of Health and Human Services (DHHS); to private institutions that undertake a Federal-Wide Assurance of Compliance; and, with broad exceptions, to 16 additional federal agencies.[6] The US Food and Drug Administration has similar regulations for research involving the products it regulates. The Common Rule contains requirements for institutional review board (IRB) review, informed consent, and risk/benefit analysis.

These regulations also provide extra protections for particularly vulnerable populations: pregnant women, fetuses, and neonates (subpart B); prisoners (subpart C); and children (subpart D). Subpart C, promulgated in 1978 in response to recommendations from the national commission,[7] strictly limits research involving prisoners. However, federal agencies (except for the DHHS, Central Intelligence Agency, and Social Security Administration) have not adopted subpart C, perhaps because it is so restrictive. In 1981, Food and Drug Administration regulations specifically applicable to prisoners were blocked by a lawsuit brought by prisoners wishing to participate in research.[8] In 1997, the Bureau of Prisons adopted its own additional regulations for research involving prisoners in federal custody.[9]

Under subpart C, research on prisoners must present no more than minimal risk, defined as the risk of harm normally encountered in their daily lives or in the routine medical, dental, or psychological examination of healthy persons. Subpart C identifies 4 categories of permitted research relating to (1) possible causes, effects, and processes of incarceration; (2) prisons as institutional structures or prisoners as incarcerated persons; (3) conditions particularly affecting prisoners as a class; and (4) practices that have the intent and reasonable probability of improving the health or well-being of research participants. Categories 3 and 4 may proceed only after the Secretary of Health and Human Services has consulted with experts and published a *Federal Register* notice of the intent to approve. A fifth category of research was permitted when subpart C was amended in 2003 to allow epidemiologic research on specified diseases in which prisoners are included in the population of interest but are not the sole study group. In such a case, the IRB must determine that the epidemiologic research involves minimal risk or no more than inconvenience to prisoner-subjects.[10]

The definition of minimal risks is so narrow and confusing (eg, are the risks to be measured in terms of threats encountered in life on the outside, or within prison?), and the secretarial review is so onerous (taking months or years to review), that research subject to subpart C is often avoided.[1] Because these regulations apply only to a few federal agencies and institutions that voluntarily comply with them through a Federal-Wide Assurance of Compliance, the majority of prison research is conducted outside the purview of subpart C. Federal oversight of research in prisons, therefore, is either too restrictive (effectively impeding responsible research) or inapplicable (opening the door to exploitation or abuse). It is in this context that the DHHS asked the Institute of Medicine (IOM) to consider the need for de-

Author Affiliations: O'Neill Institute for National and Global Health Law, Georgetown University Law Center, Washington, DC; and Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, Md.
Corresponding Author: Lawrence O. Gostin, JD, Georgetown University Law Center, 600 New Jersey Law Center NW, Washington, DC 20001 (gostin@law.georgetown.edu).

veloping a new ethical framework for prisoner research and to identify regulatory safeguards.[1]

The Correctional Environment and Prisoner Research

The US correctional system has undergone major changes since the adoption of federal regulations. The overall correctional population (including persons in prison or jail and on parole or probation) has increased 5-fold between 1978 and 2005, to nearly 7 million people.[11] The US currently has the world's largest incarcerated population and highest incarceration rate, accounting for one quarter of the world's prison population.[12] Correctional facilities are often overcrowded and many inmates have limited access to programs, services, and health care.[13] Despite prisoners' constitutional right to humane medical care, several large prison systems have been placed under judicial supervision due to inadequate treatment.[14] The percentage of disadvantaged individuals under correctional supervision is increasing, including racial minorities, women, and children. For example, in 2005, nearly 12% of US black males aged 25 to 29 years were incarcerated, and 60% of offenders in local jails were racial or ethnic minorities.[11] A high proportion of inmates have communicable (human immunodeficiency virus [HIV]/AIDS, hepatitis C, tuberculosis) or chronic (mental illness, diabetes) diseases, drug or alcohol dependency, and low literacy.[15]

Prisoners are vulnerable to exploitation not only because of their low socioeconomic status and poor health but also because of their restricted autonomy and liberty. Highly vulnerable, often poorly educated prisoners may not be able to give informed consent or have a reasonable expectation of privacy within closed prison settings. In this research environment, prisoners may not be able to meaningfully choose between research participation and nonparticipation.

Toward a System for Ethical Research Involving Prisoners

Finding a balance between encouraging beneficial research and safeguarding prisoners is challenging and politically controversial. The history of prisoner exploitation cautions against allowing research. However, modern science might be able to improve understanding of the intractable problems faced by prisoners, including the treatment of substance abuse and mental illness, and the effectiveness of programs designed to help prisoners make a successful transition to the community. Such research is important, not only to prisoners but also to the broader community, especially because approximately 95% of prisoners will eventually be released from prison.[11] However, a comprehensive and stringent continuum of safeguards is required to protect this vulnerable population against abuse. The following proposals would provide such a system of safeguards while allowing responsible research.

Expand the Definition of Prisoner. Subpart C currently defines a prisoner as any person who is "involuntarily confined or detained in a penal institution"; detained in a facility as an alternative to prosecution or incarceration; or detained pending arraignment, trial, or sentencing. The emphasis on custodial detention, however, is too narrow. With the advent of "alternatives" to incarceration (including house arrest, day reporting centers, and halfway houses), the existing definition extends the protections of subpart C to only 2.1 million of the nearly 7 million persons under adult correctional supervision.[1] This leaves nearly 5 million people who lack the protections of the regulations. To ensure protection for this vulnerable group, a new definition of the term "prisoner" should comprehensively cover all individuals whose autonomy and liberty are restricted by the justice system.

Ensure Universal, Consistent Ethical Protection. Prisoner research regulations offer a patchwork of protection, ranging from no safeguards at all (for research not funded by a Common Rule agency), to basic Common Rule oversight, to heightened, overlapping, or possibly inconsistent regulations. Instead, all research on prisoners should be regulated uniformly, irrespective of the source of funding, supporting agency, or type of correctional facility. There is no ethical justification for lower levels of protection for prisoners simply because the funder is not a Common Rule agency or is a private corporation.

Create a National Database of Prisoner Research. Because most prisoner research is currently unregulated, there is no reliable basis to know how many studies have been undertaken, what safeguards have been used, and what has been learned as a result of the research. Consequently, the DHHS or another appropriate agency should create a publicly accessible national prison research registry. The registry would permit greater accountability, provide a scientific method for assessing the success of research projects, and facilitate the implementation of beneficial research findings to prisoner populations. By creating a national registry and uniformly regulating all prisoner studies, there would also be greater transparency and public accountability.

Shift From a Category-Based to a Risk-Benefit Approach to Research Review. The categories of permissible research established under subpart C do not provide consistent, reliable, or sufficient protection for prisoner research. Investigators and IRBs have difficulty placing research protocols into particular categories, and the structure does not focus attention on the conditions of confinement or the precise risks and benefits of the particular research protocol, which are the key ethical factors. Instead, a risk-benefit approach that provides a continuum of protections depending on the stringency of the correctional setting (similar to subpart D for children) is a more practical approach to ensuring safe and ethical prisoner research. Under this framework, research with prisoners should be conducted only if it offers a distinctly favorable benefit-to-risk ratio,

not because prisoners are a convenient source of research participants or have no access to therapeutic treatment.

Update the Ethical Framework to Include Collaborative Responsibility. The National Commission viewed respect for persons and justice as the 2 principal values that should guide research. However, collaborative responsibility is also important, meaning that to the extent possible, stakeholders (eg, prisoners, correctional officers, medical staff) should participate in the design, planning, and implementation of research. Participation helps ensure that all relevant groups have a stake in ensuring responsible research. A collaborative, cooperative approach to human subjects research is also likely to clarify the study's methods and objectives, enhance the process of securing meaningful informed consent, and maximize the likelihood of usable scientific knowledge flowing from the research.

Enhance Systematic Oversight of Research. Current oversight of prisoner research, where it takes place at all, is effectively limited to IRB review, which has been criticized as highly variable.[16] Instead, safeguards should be strengthened, made consistent, and applied in relation to the levels of risk and restriction of liberty experienced by prisoner-subjects. A prison research participant advocate, who is familiar with the local correctional setting but not an employee of the facility, should monitor the ethical conduct of the study. This advocate would provide more systematic and ongoing safeguards for prisoners.

Should Research Be Permitted in Prisons?

The proposals in the IOM report on research involving prisoners were intensely controversial, with some prisoner advocates decrying what they saw as a relaxation of existing safeguards[17] and investigators complaining that the proposed new rules are overly restrictive.[18] Certainly, the prerequisites for ethical research—informed consent and privacy—are difficult to ensure in many correctional settings. The prison environment, moreover, is rarely conducive to ethical research: overcrowded, inherently coercive, secretive, and unaccountable. The poor quality of some prison health care systems is also a major concern because inmates may volunteer for research simply to gain access to basic medical care, and prisoners may not receive effective treatment for harms that occur during the research study. Consequently, critics assert that only research posing minimal risk should be permissible.[17]

Although these are valid concerns, human subject research not only imposes risks and burdens but can also confer benefits. Modern advocacy movements have called for greater, not less, access to clinical trials by women, persons living with HIV/AIDS, and patients with cancer.[19] Epidemiologic, sociological, psychological, and biomedical research might be able to improve the health of prisoners and their living conditions. The opening of otherwise closed institutions to outside health professionals also could increase transparency and public accountability. Research can help society better understand how to improve prisoners' chances to succeed. This is an especially worthy endeavor, with 600 000 prisoners reentering the community each year.[20]

Much of the controversy surrounding the IOM's proposals concerned biomedical research, which carries the greatest risks. The IOM recommended particularly strict safeguards for biomedical research.[1] Such research should be limited to phase 3 trials that offer potential benefits to the research participants and not simply to prisoners as a class or the public at large. Further, the ratio of prisoner to nonprisoner study participants should not exceed 50%, to ensure a fair distribution of research burdens. With a high proportion of nonprisoner participants, the potential for prisoner abuse will be substantially reduced. In addition, research should not take place in institutions that cannot ensure prompt access to adequate medical services. These additional safeguards could lead to beneficial research, helping to find answers to the most intractable problems in institutions, such as HIV/AIDS, hepatitis C, tuberculosis, mental illness, and substance abuse.

The IOM report[1] recounted the painful history of medical mistreatment in the Tuskegee syphilis trials and Holmesburg prison, as well as prisoner abuse at Guantánamo Bay and Abu Ghraib. It reawoke debates stemming from as far back as the Nuremberg Code, which requires that human subjects have "the capacity to give consent . . . [and] be able to exercise free power of choice, without . . . constraint or coercion."[21] The ethical issues are of great importance because, as Dostoyevsky observed, "The degree of civilization in a society can be judged by entering its prisons."[22] But near-absolute prohibitions on research based on the sordid history of exploitation would leave prisoners without the benefits of modern science that could improve the quality of their lives and conditions unique to prisons. With systematic oversight, human dignity and scientific progress need not be incompatible.

Financial Disclosures: None reported.

1. Gostin LO, Vanchieri C, Pope A, eds. *Ethical Considerations for Research Involving Prisoners.* Washington, DC: National Academy Press; 2006.
2. Hornblum AM. They were cheap and available: prisoners as research subjects in twentieth century America. *BMJ*. 1997;315:1437-1441.
3. Urbina I. Panel suggests using inmates in drug trials. *New York Times*. August 13, 2006.
4. Hornblum AM. *Acres of Skin: Human Experiments at Holmesburg Prison.* New York, NY: Routledge; 1998.
5. The Belmont Report. *Ethical Principles and Guidelines for the Protection of Human Subjects of Research.* Washington, DC: National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; 1979.
6. 45 CFR §46.101 (1991).
7. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (NCPHS). *Research Involving Prisoners.* Washington, DC: NCPHS; 1976.
8. *Henry Fante et al v Department of Health and Human Services et al*, Civil Action No. 80-72778 (US District Court, ED Mich, S Div, 1981).
9. 28 CFR §512 (1997).
10. 68 *Federal Register* 36929 (2003).
11. Harrison PM, Beck AJ. Prison and jail inmates at midyear 2005. Washington, DC: US Dept of Justice, Bureau of Justice Statistics; 2006. http://www.ojp.usdoj.gov/bjs/pub/pdf/pjim05.pdf. Accessed January 9, 2007.
12. Center on Juvenile and Criminal Justice. The punishing decade: prison and jail

estimates at the millennium. http://www.cjcj.org/pubs/punishing/punishing.html. Accessed January 9, 2007.
13. Murphy D. Health care in the Federal Bureau of Prisons: fact or fiction. *Cal J Health Promotion*. 2005;3:23-37.
14. Coleman CH, Menikoff JA, Goldner JA, Dubler NN. *The Ethics and Regulation of Research with Human Subjects.* Dayton, Ohio: Lexis/Nexis; 2005.
15. Raimer BG, Stobo JD. Health care delivery in the Texas prison system. *JAMA*. 2004;292:485-489.
16. National Bioethics Advisory Commission. Ethical and policy issues in research involving human participants. http://www.georgetown.edu/research/nrcbl/nbac/human/overvol1.pdf. Accessed January 9, 2007.
17. Hornblum AM. When prisoners are victims. *Chron High Educ*. October 6, 2006.
18. Test drugs on inmates? yes [editorial]. *USA Today*. August 21, 2006.
19. Mastroianni A, Kahn J. Swinging on the pendulum. *Hastings Cent Rep*. 2001; 31:21-28.
20. Hughes T, Wilson DJ. Reentry trends in the United States: inmates returning to the community after serving time in prison. Washington, DC: US Dept of Justice, Bureau of Justice Statistics; 2004. http://www.ojp.usdoj.gov/bjs/reentry/reentry.htm. Accessed January 9, 2007.
21. *Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law No. 10.* Washington, DC: US Government Printing Office; 1953.
22. Dostoevsky F. *The House of the Dead.* London, England: Penguin Books; 1985.

Pay-for-Performance
Will the Latest Payment Trend Improve Care?

Meredith B. Rosenthal, PhD
R. Adams Dudley, MD, MBA

PAY-FOR-PERFORMANCE PROGRAMS ARE NOW FIRMLY ENsconced in the payment systems of US public and private insurers across the spectrum. More than half of commercial health maintenance organizations are using pay-for-performance, and recent legislation requires Centers for Medicare & Medicaid Services (CMS) to adopt this approach for Medicare.[1] As commercial programs have evolved during the last 5 years, the categories of providers (clinicians, hospitals, and other health care facilities), numbers of measures, and dollar amounts at risk have increased. In addition, acceptance of performance measurement among physicians and organized medicine has broadened, with the American Medical Association committing to the US Congress in February 2006 that it would develop more than 100 performance measures by the end of 2006.[2]

To date, widespread experimentation has yielded important lessons and highlighted critical challenges to paying for performance. Several recently published evaluations have demonstrated both the potential of pay-for-performance and the need for careful design of programs to ensure their effectiveness.[3,4] Despite purchasers' enthusiasm for pay-for-performance, it has become clear that it should not be a foregone conclusion that these programs will benefit patients or even significantly assist providers who want to improve care.[4,5]

While recognizing the shortcomings of current pay-for-performance programs, it is critical to reaffirm what most physicians and health care purchasers alike believe: the current payment system thwarts high-quality care and needs to be reformed. Furthermore, the basic intent of pay-for-performance—to encourage and assist providers in offering the most clinically appropriate care—would be a positive step from the current payment system. Nonetheless, there are many details about how pay-for-performance would actually be implemented that could mitigate or even reverse some of its good intent.

Our objective is to review dimensions of pay-for-performance programs that economic theory or available data suggest would be important determinants of their influence. With CMS poised to enter the fray and many commercial payers evaluating, expanding, and updating their first-generation pay-for-performance programs, the time is right to examine critically the various approaches to pay-for-performance.

Five Key Design Elements of Pay-for-Performance

Purchasers must make many decisions when implementing pay-for-performance programs.[6] Based on our experience studying incentive programs,[4,5,7-9] 5 aspects of program design that are likely to be most consequential have been identified. These 5 dimensions govern the types of provider behavior being influenced and the degree to which incentives are felt by clinicians. The TABLE presents the options available for each of these dimensions and includes examples of empirical or theoretical literature addressing the rationale for and against each option, as well as what is known about currently operating pay-for-performance programs. In discussing targets of pay-for-performance, the term *provider* is used to refer collectively to physicians, hospitals, and any other clinician or clinical entity that can bill for services.

Pay-for-Performance as Individual vs Group Motivator. In markets in which there are larger medical groups, phy-

Author Affiliations: Department of Health Policy and Management, Harvard School of Public Health, Boston, Mass (Dr Rosenthal); and Department of Medicine and Institute for Health Policy Studies, University of California, San Francisco (Dr Dudley).
Corresponding Author: Meredith B. Rosenthal, PhD, Department of Health Policy and Management, Harvard School of Public Health, 677 Huntington Ave, Boston, MA 02115 (mrosenth@hsph.harvard.edu).