MODULE 2

The Legacy of the Tuskegee Syphilis Study

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Introduction

Any consideration of ethics in public health research and practice must acknowledge the legacy of what has come to be called the Tuskegee Syphilis Study. Indeed, all public health research is conducted in the shadow of the actual study and the cultural icon that it has become. In some contexts and communities, mere reference to "Tuskegee" conjures images and reflects ideas that public health workers need to confront, as a practical matter, in order to provide services and conduct research. This following issue essay discusses the history of the Tuskegee Study of Untreated Syphilis, its legacy, and the way in which it functions as both a cultural icon and a framework for consideration of ethical concerns in public health.

What does it mean to say that a public health study has become a "cultural icon," indeed a symbol of what it means to conduct unethical research on human beings? The charge that something is "just like Tuskegee" summons emotionally charged meanings for researchers, the American public in general, and African-Americans in particular. "Just like Tuskegee" has rhetorical force: it immediately suggests a set of ethical concerns that warrant attention. However, the rhetoric surrounding "Tuskegee" can cloud careful and accurate analysis of what is actually at stake. With respect to the three cases following the issue essay, readers are invited to consider the ways in which the cases really are, or are not, just like Tuskegee. Such an initial analysis provides a starting point for deeper consideration of the ethics of research that appears to involve issues of race and racism, vulnerability of particular communities or populations, power, deception, exploitation, and questions about consent, appropriate study design and research hypotheses, distinctions between research and treatment, and standard of care—all issues raised by the original Tuskegee Syphilis Study.

Two initial issues of ethical relevance must be raised before the essay can commence. These are issues of terminology that have more than typical semantic importance. First, what should the Study be called? The official title of the study was "The Tuskegee Study of Untreated Syphilis in the Negro Male," but those with various interests have argued that other appellations would actually be more historically accurate. One commentator suggests the "US Public Health Service Study of Untreated Syphilis in the Negro Male" (Brawley 1998), while a Public Health Service (PHS) spokesman termed it a cooperative project of the PHS, the Tuskegee Institute, the Tuskegee Medical Society, and the Macon County Health Department in Alabama (Jones 1993, p. 7). Some contend that referring to it as the *Tuskegee*

Syphilis Study unfairly marks the Tuskegee Institute and taints its good name (Brawley 1998), when it could be argued that the Institute was manipulated into its institutional participation almost to the same degree as the individual men who were convinced to participate in the study. Unfortunate as it may be that the Institute is probably most widely known for this study, and unfair as it may be to single out the Institute for its participation, nevertheless it is important to refer to the Study by its common—indeed almost iconographical—name, for it is not just the history of the Study, but its cultural legacy that concerns us. For this reason, we shall refer to it as the Tuskegee Study of Untreated Syphilis or the TSUS. In addition, some refer to the TSUS as "the Tuskegee Syphilis Experiment," presumably to emphasize that the men enrolled in the study were experimented upon, were treated as guinea pigs, and perhaps to emphasize that people have reason to be wary of such research.[1] On the other hand, the TSUS was not an experiment in the sense that an intervention was tested. Its initial methodology involved collecting data to trace the course of a disease in members of a population and the prevalence of the disease in that population; it resembles an epidemiological study. Since penicillin eventually became widely available but was not given to men enrolled in the TSUS, the TSUS might be viewed as an "experiment in withholding treatment," an experiment designed to discover what occurred under conditions of non-treatment. Nevertheless, we shall avoid 'experiment' as a less appropriate term.

The second question is what the men enrolled in the study should be called. Current parlance suggests that those enrolled in research be called 'participants'; however, this term suggests a far more collaborative interaction than the men enrolled in the TSUS actually experienced. At the same time, to refer to them as 'subjects' seems to perpetuate their status as people to whom things were done—subjects, subjugated and acted upon—rather than as agents in their own right. As the account below reflects, these images are perhaps the most accurate in describing how the men in the TSUS were treated. Nevertheless, to refer to them today as 'subjects', in light of both contemporary understanding of that term and historical understanding of the wrongs done to them may seem to perpetuate the lack of respect for their dignity and agency. Finally, although the men were certainly enrolled in the study, referring to them as 'enrollees' is misleading if it suggests the contemporary notion of individuals who enroll in research through a process of informed consent. Having raised these considerations, in the following discussion, we tend to refer to those enrolled in the TSUS as 'the men in the study' or as the study 'enrollees'.

Issue Essay

Questions for Consideration

In addition to its historical and cultural importance, one of the reasons for considering the Tuskegee Study of Untreated Syphilis (TSUS) is that it raises so many ethically rich questions. First, ethical concerns attach to the premise of the study, its research design, its use of deception and social pressures to enroll, and the lack of informed consent. Next, background questions can be raised about the appropriateness of conducting research with members of "vulnerable populations" (and how to define or identify such vulnerability), about research in the context of a lack of access to adequate health care, and about research conducted against the social backdrop of racism or other social injustice and prejudiced cultural attitudes. These background issues raise questions about the practical

[1] Research has shown that people have a more positive attitude toward a study that is described as being "research," and are more wary when it is termed "an experiment." 'Research' or a 'research study' seems to imply cutting edge and possibly beneficial interventions, while 'experimentation' suggests images of scientists using people as guinea pigs. See Sugarman *et al.* 1998.

possibility of ensuring the voluntariness of participation in research, *informed* consent, and public trust in the conduct of research and the use of research results. That the TSUS's inception predated, but its cessation postdated, the Nazi experiments and the Nuremberg Trials only intensifies questions about the adequacy of regulations to ensure ethical conduct of research. Finally, because the TSUS involved a traditionally exploited group—African-American men—who were also poor, rural, and uneducated, consideration of the TSUS raises a variety of questions for current and future research: How should the concept of 'race' be used in research? How will society respond to identification of disease risks (e.g., dietary customs or genetic factors) associated with racially or ethnically defined populations? How should research on such questions be designed? How may research results be used to avoid further disadvantaging racially or ethnically defined groups? Finally, given the past and current structure of American society, how can social and economic factors (e.g., educational and economic background, or rural/urban environment) be meaningfully distinguished from racial categories in both the conduct and the reporting of research? In fact, particular features of the TSUS raise questions about the conceptual foundation and practical implementation of what may be considered the tools for best practice in conducting research with vulnerable populations or in minority communities.

Brief History of Tuskegee Study

In the 1920s, the medical and public health communities hypothesized that blacks and whites differed in their response to disease (King 1998, pp. 92-7). In Macon County, Alabama, where 35-40% of those tested were positive for syphilis, the PHS felt that it had an ideal opportunity to study the course of syphilis in blacks and to compare the course of the disease against a study on syphilis in whites, done several years earlier in Oslo, Norway. The impetus for the Tuskegee Study of Untreated Syphilis was rooted in earlier work by the US Public Health Service (PHS) in the rural south. In 1928, the PHS completed a study in Mississippi in which 25% of the sample (all black) tested positive for syphilis. With financial backing from the Julius Rosenwald Fund, the PHS planned to continue studies of syphilis in rural blacks and to provide treatment, which at the time was comprised of doses of arsenic, mercury, and bismuth. However, the beginning of the Depression in 1929 wiped out the finances for the project, and the PHS scaled down its plans and tried to salvage a much smaller-scale study (Thomas and Quinn 1991).

Nurse Eunice Rivers, a black woman who graduated from the Tuskegee Institute in 1922 and then worked for the state of Alabama on various public health projects, was hired as coordinator of the TSUS. She set up transportation, organized clinics, and generally served as the primary contact for the men enrolled in the study. With her help, the PHS was able to efficiently reach the men of Macon County, holding clinics in schools and churches and enlisting the enthusiasm of both leaders in the black community and white plantation owners, who had an interest in the health of their employees. The cooperation of the Tuskegee Institute—whose earlier involvement in syphilis treatment programs gave the appearance to the public that these efforts were being renewed—helped to set blacks at ease with the government doctors (Thomas and Quinn 1991). The Institute was persuaded to participate by promises of training and employment for its doctors and nurses, as well as credit for aiding an important scientific study (Jones 1993, p.102).

The men in the study were told that they were being tested for "bad blood," a Southern catchphrase for a variety of illnesses. They were not informed that they had syphilis or given information about what syphilis was, how it was transmitted, or how it could be treated. Originally, the study was to last only 6-12 months, not enough time to deliver a full course of treatment, but at the insistence of the Alabama state health officer involved in the study, enrolled men who tested positive for syphilis received a

minimal course of treatment: eight doses of an arsenic compound and some mercury pills. This would not have been enough to cure the men, though it might have rendered them noninfectious (Jones 1993, p. 99). However, the study was soon extended in an attempt to examine the men periodically until their death, and then to perform an autopsy, to give the doctors a chance to track the complete course of syphilis left untreated (Jones 1993, p. 132). Nurse Rivers and area doctors encouraged dying men to enter the hospital, and after death Rivers would sit with the grieving families and eventually ask permission to perform an autopsy, carefully explaining that no one at the funeral would be able to tell that the body had been opened. After 1935, the Millbank Memorial Fund in New York provided $500 each year to be given out as $50 burial stipends to each family in exchange for permission to perform the autopsy (Jones 1993, pp.153-4).

It was not difficult to persuade enrollees to continue in the study past the original few months. The men were given iron and aspirin as placebo treatments, which did in fact improve the their general health and make them enthusiastic participants in the study (Jones 1993, pp.147-8). They were aware that they were receiving far more medical care than they could otherwise afford, just as today some uninsured Americans enroll in research studies to gain access to basic medical care. The illusion of treatment was carefully perpetuated by the researchers, who even advertised spinal taps—a painful and potentially debilitating procedure—as "special free treatment" in addition to the "great deal of treatment for bad blood" that the men had already received (Brandt 1978). The spinal taps had no therapeutic value whatsoever and were performed solely to gather information on the presence of neuro-syphilis.

Soon, with awareness of venereal diseases rising, it was deemed important by those running the study that it not be compromised by enrollees' receiving treatment. In the late 1930s and early 1940s, PHS clinics in the rural south were dispensing an accelerated, week-long course of an arsenic derivative and bismuth to those with syphilis. Nurse Rivers was assigned to coordinate with these clinics to ensure that the men in the study were not given treatment (Jones 1993, p. 162). In 1943, the PHS clinics began using penicillin to treat syphilis, and Alabama passed a law that all citizens between 14 and 50 be tested for venereal diseases and TB and that those testing positive be treated (Jones 1993, p. 178). TSUS enrollees were not tested or treated (Jones 1993, p. 178). During World War II, the PHS arranged with the draft board that draftees from the study population would not need to take the penicillin treatment given to all other drafted men diagnosed with syphilis (Thomas and Quinn 1991). The men, identified to local and state doctors on a list provided by the Tuskegee researchers, did not know enough about their condition to question being turned away. Accustomed to having no access to health care, with their enrollment in the study, the men believed that they were already receiving adequate medical care (Brandt 1978).

In 1951, penicillin became the standard treatment for syphilis, but despite a full-scale review of the study by the PHS, and despite the new attention that was being cast on the ethics of research after the Nazi experiments were revealed, the study continued (Jones 1993, p. 181). Throughout this time, occasional papers on the study were given at conferences and published in medical journals with no ethical objections being raised (White 2000). Continued conduct of the TSUS was clearly unethical according to the guidelines set forth in the Nuremberg Code in response to the Nazi war crimes trials, which emphasized informed consent and the researcher's duty to avoid causing harm to the subject. The Code was followed in 1964 by the World Health Organization's Declaration of Helsinki, which also set out guidelines on human experimentation and insisted on a stringent informed consent process. In the late 1960s and early 1970s, the PHS developed guidelines for clinical trials that it funded; these established the first structures for peer review at the investigators' institutions—the forerunners of today's

institutional review boards (IRBs)—and eventually required that community members and those without scientific backgrounds sit on these panels. However, these guidelines were not applied to the PHS' own studies like the TSUS (Jones 1993, p. 190).

In 1964, an article was published about the last thirty years of the study. In response, Irwin Schatz, a Michigan doctor, wrote to the authors raising questions about the ethics of denying effective therapy for a potentially fatal disease, but the study continued (White 2000). In the late 1960s, Peter Buxton, a physician who worked for the PHS in San Francisco, began scrutinizing the study and voicing his concerns. Because of this attention, the PHS convened a blue ribbon panel to decide whether the study should continue. The panel was comprised entirely of white physicians, of whom all but one had previous knowledge of the study. The sole previously uninvolved member, Gene Stollerman, was the only panelist in favor of examining the men and providing appropriate treatment. The others, who wanted to continue the study without change in its protocol or provisions, emphasized the risks of penicillin treatment: it could cause adverse and allergic reactions, such as fibrillations and anaphylaxis, and in addition there was some evidence that penicillin cured syphilitic lesions but sometimes failed to kill the spirochetes that were the source of the disease. One panelist made the groundless assertion that the men would not accept treatment even if it were offered (Jones 1993, pp. 193-6).

The panelists also determined that informed consent was impossible to obtain from men with so little education and social status, and decided to approach the Macon County Medical Society (MCMS) to ask for a sort of surrogate consent. The MCMS, which was mainly comprised of black doctors, agreed that the experiment could go forward and promised not to give anyone in the study antibiotics for syphilis or for other diseases. At this time, the PHS also increased its efforts to find men who had been lost to the study in the preceding years, going so far as to enlist the assistance of the assistant postmaster in Tuskegee and to hire a retail credit agency to locate the men (Jones 1993, p. 196-200).[2] Buxton finally told the story of the Tuskegee study to Associated Press reporter Jean Heller in 1972. Her article, entitled "Human guinea pigs: syphilis patients died untreated," appeared in the *Washington Star* and alerted the nation and the world to the existence and details of the TSUS. The article and the reaction to it finally forced the study to end, forty years after its inception and nearly 20 years after penicillin had become standard treatment for syphilis (White 2000).

The Legacy of the TSUS

There are, in fact, multiple legacies of "Tuskegee." Public and political attention focused on the TSUS led to regulatory changes regarding the conduct of research. African-Americans who became aware of the conduct of the TSUS were outraged, and the TSUS served to reinforce and magnify the mistrust many African-Americans feel toward the government, its services, and those in power in the "establishment," including the medical establishment. Researchers must now confront this widespread and magnified mistrust, as well as fulfill the regulatory requirements spawned by Tuskegee and other research scandals and outrages (e.g., Nazi experimentation, viral hepatitis research at Willowbrook State School, cancer research at the Jewish Hospital for Chronic Diseases). Enrollment of members of minority groups in research studies is more difficult because of prevalent mistrust and lack of

[2] Thus it is not only since the events of September 11, 2001, that US government officials have proposed the use of public and private employees to track citizens for the sake of some supposed public good. While in the TSUS such employees were asked to locate study enrollees, in the 21st century "war on terrorism," it was proposed that postal employees and meter readers be officially encouraged to report suspicious activities observed in their daily work.

community-researcher collaboration, and therefore, members of these groups may fail to benefit maximally from research advances (e.g., drugs and other interventions) as these are developed without participation of people relevantly "like them" (Merton 1996, King 1998). (Moreover, such mistrust affects minority members' seeking of health care services, especially preventive interventions, and their interactions with health care providers [e.g., Roberts 1996].)

The regulatory legacy. In 1973, the Department of Health, Education and Welfare completely revamped regulations on human subjects protection. A class action suit was filed by TSUS enrollees and was settled out-of-court the next year; all of the participants or their families were compensated (Thomas and Quinn 1991). The total settlement amount of $10 million was distributed in amounts ranging from $5,000 to $37,500, according to whether the participants were still alive and whether they had been part of the syphilitic or control group (Jones 1993, p. 217). A task force was created in 1975 to consider whether injured research subjects should be entitled to compensation. In its 1977 report, it argued that just as military personnel who incur risks on behalf of society are compensated for service-related injuries, research subjects should be compensated for research-related harms suffered. No action was taken on the task force's recommendation.

In 1974, federal legislation created a national commission to oversee human subjects in research, and the National Research Act mandated the establishment of IRBs to review all federally funded grants involving human subjects (Corbie-Smith 1999). In 1991, the US Department of Health and Human Services (HHS) issued revised regulations on human subjects research. They have been accepted by almost all federal departments that fund such research, and have therefore come to be referred to as the Common Rule (Title 45 Code of Federal Regulations Par. 46 [45 CFR 46]). Many institutions not legally obligated to abide by the Common Rule have nevertheless adopted it, and many states have similar regulations. According to the regulations, in order for persons (or their legally authorized representatives) to give "legally effective informed consent," the researchers seeking participation must disclose eight elements of information about the study:

1. a statement that the study involves research, and description of that research and its purposes;
2. a description of reasonably foreseeable risks;
3. a description of reasonably expected benefits;
4. a disclosure of appropriate alternatives;
5. a statement about maintenance of confidentiality;
6. an explanation of possible compensation in case of injury, if the study involves more than minimal risks;
7. information about how subjects can have questions answered;
8. and a statement that participation is voluntary.

In some cases, participants must also be told about unforeseeable risks, circumstances under which their participation will be terminated, additional costs they might incur, consequences of a decision to withdraw, dissemination of findings during the study related to their willingness to continue, and the approximate number of total subjects. Some studies which involve no more than minimal risk to participants are eligible for expedited review, and some studies (e.g., many surveys, observations, or studies of existing data) are exempt from these informed consent requirements; however, it is the IRB—not the research investigators—who must determine whether a project is exempt or eligible for expedited review.

Prospective review by an IRB offers several ethical advantages: IRB panelists examine the importance of the study question, the reasonableness of the risk-benefit ratio, and the provisions for informed consent. This process, in theory at least, prevents participants' rights from being violated and ensures that participants incur the risks of research only for the sake of producing meaningful research results. In contrast, outside of the research context, when informed consent to treatment is lacking, criticism only emerges after the intervention has taken place. More stringent requirements for informed consent are considered necessary in a research context, as opposed to a purely therapeutic context. In the therapeutic relationship, doctor and patient typically share the same goal of the patient's good health or personal benefit. In research, the researcher and subject have at least some divergent goals, and the risk is that the subject's interests could be sacrificed for what the scientist or society considers the greater good served by the experiment (Berg *et al.* 2001, pp. 279-84).

Despite its important advantages, there are several limitations to prospective IRB review. IRBs are often staffed by volunteers or appointees who are not compensated for their time, yet appropriate review of research protocols is time-consuming and demands substantial commitment and expertise or education on the part of IRB members. Moreover, after an IRB has deemed a study design to be ethically acceptable, moral complacency—on the part of researchers, or IRBs in their overseer capacities—can set in. Finally, IRB review is subject to factual and ethical error, and in practice often focuses more on the completeness of the consent form the researchers plan to use than on the overall design of the study (Berg *et al.* 2001, pp. 259-66).

Members of some communities or study populations—so-called special or vulnerable populations—have additional reasons to worry that compliance with research regulations and award of IRB approval are inadequate to ensure that their participation is non-exploitive and even advantageous. The notion of "vulnerability" in the context of research is employed to describe groups of potential research subjects who may be more than usually susceptible to exploitation in the process of research, either because they may be more likely to be pressured to participate, or may be more likely to fail to understand the full implications of participation and may therefore be misled into participation.

The regulations in the Common Rule identify the following as "vulnerable populations" in the context of human subjects research: children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons" (45 CFR 46 §III[b]). These regulations provide for IRBs to appoint consent auditors and provide special regulatory protections of fetuses and pregnant women, children, and prisoners (45 CFR 46, Subparts B, C, and D).

Of course, in reality, a variety of individuals may be rendered vulnerable in virtue of various situational or persistent social factors. People who are sick or in pain, frightened, or overwhelmed by information or "bad news" may be vulnerable in virtue of these situational factors. Those who lack the education, emotional maturity, or language and communication skills to understand and appreciate what is disclosed to them during an informed consent process may also be vulnerable to inappropriate pressure to participate (or, instead, to reject precipitously the option of research participation that might benefit them). Those who feel disempowered in virtue of the social roles they occupy, or who lack economic resources to investigate the proposed research or alternatives to it, may not feel free to refuse participation. With respect to research risks, protection of competent adults who are economically or educationally disadvantaged has proved complicated and highlights concerns about both respecting autonomy and achieving social justice (Berg, *et al.* 2001, pp. 271-2; Kahn, *et al.* 1998).

After the TSUS, heightened sensitivity to the use of vulnerable populations in research resulted in many studies completely excluding these populations. Minority members and women were simply not recruited for trials, which protected them from the research-associated risks, but also meant that they were less likely to share in any benefits, both during the study and later when results were generalized to populations in which the interventions had not been studied (Corbie-Smith 1999, DeBruin 1994, Dresser 1992, Merton 1996, Kass 1998, King 1998). In addition, conditions more prevalent among, or disproportionately affecting, minority group members or women simply went unstudied (e.g., Faden *et al.* 1996). Finally, in 1993, the National Institutes of Health Revitalization Act mandated proportional representation of minorities and women as subjects in all research projects, unless there was a compelling reason to exclude them (Corbie-Smith 1999), and researchers are recognizing advantages with respect to funding priorities of studying conditions affecting minority members and women.

The legacy of mistrust among minority community members. Despite strict regulations on research, requirements of informed consent, and requirements that they be adequately and appropriately represented in study populations, minority populations often distrust both the government and the medical community. This mistrust is largely due to past injustices, such as the TSUS, which still plays a great role in African-Americans' reluctance to participate in research (Richardson 1997, Freimuth *et al.* 2001, Thomas and Quinn 1991, Corbie-Smith *et al.* 1999, Corbie-Smith 1999, King 1998). This prevalent mistrust is particularly harmful in light of the AIDS crisis, which affects so many blacks and other marginalized populations, such as gay men and intravenous drug users (IDUs). A phone survey on medical research and the TSUS revealed that 9% of 500 black households believed that HIV and AIDS were part of a plot to kill blacks. Only 1% those in a survey of the general population responded similarly (Richardson 1997).[3]

The history of mistrust carries over to the very informed consent process designed to protect research participants, with a substantial number of African-Americans viewing informed consent as primarily a legal protection for physicians and researchers and considering their signing a consent form as a relinquishment of their rights (Corbie-Smith *et al.* 1999).[4] Increasing African-Americans' understanding

[3] Again terminology carries important ethical and social implications. To contrast African-Americans and "the general population" in reporting the survey results conveys the message that African-Americans are not part of the general population. To take a similar example, talking about different levels of risk of HIV among urban gay men and in "the general population," marks gay men as being outside the general population. The "us vs. them" message implicitly conveyed has been shown to undermine HIV risk reduction education efforts, for example, and perpetuates the disenfranchisement of already marginalized groups (Grover 1988, Treichler 1998). The term 'subpopulation', rather than conveying that, for example, African-Americans or gay men constitute a group *within* a larger group, is often considered to emphasize the "sub" or lower status of the included group and to reinforce its subjugation.

[4] In focus-group interviews with African-Americans, researchers have discovered many misconceptions about the informed consent process (Freimuth *et al.* 2001, Corbie-Smith *et al.* 1999). Many participants believed that signing a consent form meant that they were waiving their rights, including those to sue if something went wrong, and that the primary purpose of a consent form is to protect doctors and hospitals from legal liability. In addition, they stated that the forms were often incomprehensible to them, and it was therefore impossible to fully understand what they were agreeing to. The process of informed consent itself could be improved most radically by providing information, both written and spoken, in terms that can be understood by laypersons. This is particularly important for members of minority groups, who may be disadvantaged educationally (Freimuth *et al.* 2001, Corbie-Smith 1999). Those who sign consent documents should be given copies of those documents to keep (Corbie-Smith 1999). Focus group participants also stated that they wished to have time to make a decision about participation in research, so that they could consult family members and do some research on their own about what they were being asked to do. They suggested it was important to have information from several different points of view (Corbie-Smith 1999).

of and trust in the informed consent process will be necessary to encourage their increased participation in research. Yet investigators who have studied the reluctance of African-Americans to join studies identify reason for African-Americans to be wary of recent policies that permit a waiver of consent for some types of research (specifically, emergency research) (Corbie-Smith *et al.* 1999). They are also concerned that incentives to participate in research could be unintentionally coercive (Freimuth *et al.* 2001). Since community ties are often particularly strong in minority groups, some form of community consent—in addition to individual consent—has been advocated as an important and valuable addition to the consent process (Corbie-Smith *et al.* 1999; Freimuth *et al.* 2001). Studies have also revealed that many African-Americans—indeed many Americans—do not understand the process and purpose of human subjects research (Berg *et al.* 2001, pp. 288-95). Gaining greater understanding of the purpose and process of research could allay many fears about participation. Education, both in schools and in the wider community, should seek to define the vocabulary of research and to explain its procedures and purpose (Freimuth *et al.* 2001, Corbie-Smith 1999). It should also address head-on the realities of and the misconceptions and myths surrounding the TSUS and other research controversies (Freimuth *et al.* 2001).

Responding to this legacy: steps to restore trust. In 1997, President Clinton took a major, at least symbolic step, toward addressing the realities of the TSUS and enabling productive confrontation of its cultural legacy. President Clinton apologized for the government's involvement in the Tuskegee study and introduced several initiatives to make amends, including establishment of a memorial and scholarships for minority bioethics students (http://clinton4.nara.gov/textonly/New/Remarks/Fri/19970516-898.html).

It may seem unlikely, or trivializing of a serious wrong, to suggest that the offer of a formal apology for wrongs as great as those committed in "Tuskegee" could provide grounds for the restoration of trust. Apologies—even or perhaps especially formal official ones—may seem more a matter of manners than of substantive ethics. Nevertheless, showing courtesy—or in this case specifically, offering an apology—is a means of showing respect, of demonstrating directly that the person to whom the courtesy or apology is paid is a person *worthy of respect* (Buss 1999). Although in most instances *doing* the right thing is more important than, after the fact, saying the correct thing—"I/we am sorry; we apologize for having done wrong"—the apology most directly acknowledges that the wronged parties were worthy of better treatment, were worthy of having their rights and their dignity respected. Such direct acknowledgment, if followed by attempts at both restitution or atonement, and appropriate future action, may constitute an initial step toward restoration of the trust of those previously wronged. In contrast, apology coupled with uncorrected action in the future would seem hollow, false, disrespectful, and manipulative. An apology not coupled with "follow through," i.e., with appropriate future action and with attempts to restore those wronged in the past or to atone for past wrongs, would further erode conditions of trust.

The establishment of the memorial and scholarship fund, the payment of some monetary compensation to study enrollees or their descendents, as well as the implementation of research regulations to prevent future similar wrongs, suggest that the Presidential Apology is not mere rhetoric, but instead is a formal statement of assumption of responsibility, recognition of wrongdoing, and acknowledgment of the moral standing of those wronged. Coupled with action, the Apology may indeed help to rebuild trust between African-Americans and the government and researchers.

In recent years, the important role of trust in morality has gained the attention of a number of moral philosophers, especially Annette Baier (1986). They observe that whatever ethical system is adopted—e.g., a set of principles and rules, a social agreement or contract about how to live, or a system of duties—that system relies on trust. Trust grounds a person's reliance on another to fulfill his duty or to follow established rules or abide by terms of a social contract. Morality requires trust in order to thrive (Baier 1986, p. 232). Indeed, trust is a necessary condition for many important human activities; because we need the assistance of others to accomplish what we care about, we must trust others with what we value in ways that make us vulnerable. We assume some risks—for example, the baring of our bodies before our physicians and the sharing of intimate details about our lives with friends—in order to seek benefits we cannot achieve without incurring such vulnerability. "We must allow many other people to get into positions where they can, if they choose, injure what we care about [e.g., our bodies, reputations, or confidences], since those are the same positions that they must be in in order to help us take care of what we care about [e.g., by treating our symptoms or sharing our dreams]" (Baier 1986, p. 236).

Health, aspirations, friendship, education, promise-making, secret-sharing—all of these goods flourish within an environment of trust. Of course, much that is negative and immoral may flourish when trust is misplaced and betrayed, including ridicule, exploitation, and conspiracy. "Trust alters power positions, and both the position one is in without a given form of trust and the position one has within a relation of trust need to be considered before one can judge whether that form of trust is sensible and morally decent" (Baier 1986 p. 240). Thus Baier suggests that when the parties to a possible trust-relationship occupy very different positions of power (e.g., teacher-student, researcher-study participant, doctor-patient, employer-employee), the terms of an appropriate trust-relationship must be different than if the parties were in a position of relative equality (e.g., classmates, buddies). Of course, contextual and structural factors can render apparent equals vastly unequal in power. Pain of injury can make one team member quite dependent on her fellow athletes. Persistent sex inequalities can make one parent (Mom) a less powerful wage-earner than her co-parent (Dad). An appropriate trust-relationship must not rely on or exploit these underlying power differences.

What are conditions of appropriate, morally decent trust? Baier proposes an expressibility test to determine whether a situation is one of morally decent (non-exploitive) trust: a trust relationship is morally decent if the maintenance of trust need not rely "on successful threats held over the trusted, or on her successful cover-up of breaches of trust" (1986, p. 255). Trust is appropriate only if the reasons for each party's confident reliance on the other could in principle be expressed openly without deterioration of either party's reliance. "To the extent that mutual reliance can be accompanied by mutual knowledge of the conditions for that reliance, trust is above suspicion" (Baier 1986, p. 259).

Clearly, the men in the TSUS did not have appropriate trust in the PHS researchers and Nurse Rivers. Had they had known that they were not being treated for their "bad blood," if they had known what researchers meant by "bad blood," or if they had known that the researchers' actions were undertaken primarily for the benefit of others, they would probably not have entrusted their bodies for spinal taps and other examinations. The researchers relied on "successful cover-ups of breaches of trust" to maintain the trust of study enrollees. They were successful in their exploitation because of the lack of educational and economic power of the men they enrolled and because those factors and racism combined to render those men more complaint with authority figures than others were likely to be.

It remains to be seen whether the regulatory steps taken to prevent future successful cover-ups of trust, future exploitation, coupled with the government's admission of wrongdoing, its acts of compensation and atonement, and the formal seeking of forgiveness successfully restore public trust, particularly that of African-Americans and other vulnerable groups. Complicating both this restoration of trust and a sense that clear lessons from the TSUS have been learned is ongoing debate about the "facts" of the TSUS and about what ethical lessons should be learned from it.

Debate about TSUS itself. Several authors have sought to show that the study's original design was scientifically appropriate and ethical, and that even after penicillin became available, it was not wrong to deny it to TSUS enrollees. These arguments focus on the decision to examine *untreated* syphilis, and whether this study design can be justified. Benedeck and Erlen (1999) point out six potential justifications that were relevant at the study's inception in 1930.

First, syphilis was recognized as a major public health problem, worthy of study. Second, it was more prevalent in the black population, there was significant evidence that blacks and whites were affected by the condition differently, and because whites had already been studied in Oslo, it made sense to focus a study on a black population. Third, there was plenty of disagreement about how best to treat syphilis, with different doctors recommending different dosages and lengths of treatments with a variety of compounds, including mercury, bismuth, and arsenicals. No standard treatment had been established and proven. Fourth, all treatment courses were lengthy (months to years), painful (involving frequent injections), and potentially toxic. They were completed by a very low percentage of patients who began treatment. Fifth, a large proportion of those with syphilis never obtained treatment, or were treated but not sufficiently to cure the disease. Because of their race and socioeconomic class, the men in the Tuskegee study were not denied treatment that they would otherwise have had access to in the 1930s. And sixth, according to the Oslo study, a majority of syphilis cases were cured spontaneously, with no treatment, leading doctors to believe that denying treatment to the men in the study would not adversely affect most of them. Doctors hoped that the study would yield significant knowledge about syphilis: the effects of the heavy metals and arsenicals were so variable, as was the course of syphilis itself, that observation of a significant number of untreated patients would hopefully give a baseline against which to measure the efficacy of various treatments.

White adds that in 1935 it was standard medical practice not to treat latent syphilis in men over fifty (White 2000, p. 587). Thirty percent of the men in the TSUS fell into this category, and 52% had had syphilis for more than fifteen years, making them ineligible for treatment in almost any medical institution in the 1930s and 1940s (p. 594). There was a study of untreated syphilis conducted at Stanford University, as well, with white subjects who were affluent enough that without the study, they would almost certainly have received the treatment to which rural blacks never would have had access. No one, White asserts, complains about this study (p. 595).

Most of those who accept that the study was ethical at its inception view the introduction of penicillin and the study's continuation—including attempts to prevent participants from being treated with penicillin even for other conditions besides syphilis—as the point at which the TSUS went wrong. However, some still argue that the doctors had no ethical obligation to provide penicillin to the men in the study and that they were looking out for the participants' best interests when they decided not to offer penicillin. Though the "miracle drug" was first used to cure syphilis in 1943, penicillin was not without problems. As with the heavy metals and arsenicals before it, there was no set dosage, route of administration, or duration of treatment known to be effective, and administration varied widely. This

was partly because new preparations were continually being invented, so none was the focus of the intense investigation that would have been necessary to determine the optimal course of treatment. At the beginning, the strength of the drug also varied, until techniques for its manufacture were standardized. And as with previous treatments, some people reacted to the drug or to the resulting buildup of dead spirochetes. As late as 1958, scientists were questioning penicillin's efficacy and safety for those in the late stages of syphilis, the condition from which the men in the TSUS suffered (Benedek and Erlen 1999, p.18). Most doctors believed that a cure at such a late stage, after being infected for so many years, was highly unlikely (Benedek and Erlen 1999, p. 25).

Even if failing to offer penicillin to TSUS participants could be justified on grounds that the men would not likely benefit from it, there is no question that the men in the TSUS never gave informed consent. In 1972, the Tuskegee Syphilis Study Ad Hoc Advisory Panel was formed and charged with determining "whether the study was justified in 1932 and whether it should have continued when penicillin became generally available" (see King 1998). Focusing on the lack of informed consent, the panel concluded that "in retrospect" the study was unjustified in 1932. The panel failed to consider whether the study would have been justified had the enrollees consented, and many commentators suggest that the panel's focus on the absence of consent obscured underlying issues of the justice of conducting the study in the environment of racism and racial segregation, poverty, and lack of education that characterized the TSUS enrollees' situation (King 1998).

Benedek and Erlen admonish against succumbing to "presentism"; the concept of informed consent was not formulated until 1957, and the doctor-patient relationship before that time was extremely paternalistic and often secretive (p. 24). In response, however, it should be argued that the TSUS involved timeless putative ethical wrongs. Deception, telling less than the whole truth, causing pain to some for the benefit of others, taking advantage of other's trust, treating others as one would not want to be treated oneself—all of these actions have raised ethical suspicions for centuries. It is those who would seek to employ them with impunity in a particular context (e.g., research) who must provide a justification for doing so. That no specific regulation, or specific social practice like informed consent, prohibited what the TSUS researchers undertook in 1932 does not provide such justification.

The legacy of race as a variable in research. A final thread of the legacies of the TSUS deserves particular attention: race. Assumptions about race and racial difference provided the scientific justification (such as it was) for the TSUS. In two senses, the men enrolled in the TSUS were enrolled because they were black: first, because syphilis in blacks was the study question; second, because if they had been white, they probably could not have been enrolled and retained in the study. This second claim is contestable. One of the physician-researchers involved in the TSUS, in fact, responded in an interview that he believes non-blacks could have been convinced to enroll (ABC News 1992). He suggests, for example, that "hillbillies" could have been enrolled instead, if only they had possessed the medical and quasi-scientific features of interest to the scientists. The social features that he considered critical to enrollment in the study—relative isolation and lack of education and sophistication—were not race-dependent. However, such socially-disempowering features did attach almost uniformly to blacks in the 1930s in the rural south.

But what of "race" as a non-social, scientific concept? Whether 'race' is a meaningful concept in any scientific sense, with relevance for public health care and medical interventions, or whether it is merely a social construct (and an often pernicious one at that), is the topic of much current scholarship (Bradby 1996, Graves 2002, King 1998). We have made progress since the days when African slaves

were diagnosed with a peculiar disease that manifested itself in the symptom of their absconding from the service of their masters (i.e., *Drapetomania*; Cartwright in Caplan *et al.* 1981), yet experience with sickle cell screening programs and other interventions targeting African-Americans suggests the need to increase conceptual and scientific clarity and to employ these accurate understandings to combat persistent prejudice (Seton Hall Law Rev. 1997).

Yet controversy surrounds the use of racial categories for research, for offering appropriate health care, and for understanding and addressing health disparities across various populations (King 1998, Roberts 1996, Epstein and Ayanian 2002, Laveist 1993, Daniels *et al.* 1999). With growing attention to both social determinants of health and advances in understanding genetic components of disease, the relevance of 'race' as a variable in research will garner greater attention. As one of the lawyers for the men seeking compensation for the TSUS wrote: "the Human Genome Project will bring to the forefront of human consciousness awareness of the range of variability not only among individuals but among groups. To acknowledge those differences, while insisting on their irrelevance to respect for individual dignity and equality of right, is a challenge we shall have to face" (Edgar 1992, p. 25). In this essay, we can only identify, but not fully or resolve what may be called the "dilemma of difference": "If…racial difference is ignored and all groups or persons are treated similarly, unintended harm may result from the failure to recognize racially correlated factors. Conversely, if differences among groups or persons are recognized and attempts are made to respond to past injustices or special burdens, the effort is likely to reinforce existing negative stereotypes that contributed to the racial differences in the first place" (King 1992, p. 35). Awareness of these pitfalls and open discussion of steps to avoid them may help to avoid at least the most flagrant abuses of trust, greatest injustices, and serious harms.

Rhetorical Advantages and Analytical Disadvantages to Being "Just Like Tuskegee"

Since the details of the TSUS became public, several subsequent research studies have been accused of being "just like Tuskegee." (The TSUS legacy extends beyond the borders and context of the United States; one commentator on an ethically suspect oncology study in New Zealand entitled her paper "New Zealand's 'Tuskegee'? Some Comparisons between the Tuskegee Syphilis Study and a Study at National Women's Hospital" (Crosthwaite 1995).)

Assessing whether this claim is strictly accurate may be less important than, asking, initially, whether "Tuskegee" provides a useful framework for considering the ethical issues raised in a particular case, and then more importantly, carefully analyzing the present ethical concerns. The following three cases may be considered in light of the legacy of and considerations raised by Tuskegee. The cases involve study of a needle exchange program in Alaska, a study of different lead abatement efforts and their effects on blood lead levels in children, and various studies to prevent the transmission of HIV/AIDS. In each case somewhat inflammatory emotional rhetoric reflecting the legacy of Tuskegee directs public attention to the cases. The legacy of Tuskegee also, very directly and practically, creates (or perpetuates) some of the attitudes, social conditions, and problems of trust and communication that give rise to ethical concern.

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Additional Resources

Tuskegee Syphilis Study

The Least of My Brothers. a self-contained, Web-based module on the ethics of research with human subjects that uses a dramatization of the TSUS, http://poynter.indiana.edu/sas/lb/

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Fact Sheet: AIDS Clinical Trials in Developing Countries

- Approximately 1600 HIV-infected infants are born each day, or over one half million annually (Fowler 2000). In the US in the late 1990s, there were approximately 280-370 cases of maternal-fetal HIV transmission annually.

- AIDS Clinical Trial Group Study 076 interim results released in 1994 showed a 25.5% mother-to-child transmission rate in the placebo group and a 8.3% transmission rate in the group receiving zidovudine, which led a US PHS Task Force to recommend that zidovudine be offered to all HIV-infected pregnant women and their newborns (MMWR 1994). The original 076 protocol enrolled women with only early or mild HIV infection. It is not known whether administration of zidovudine during the later stages of pregnancy may reduce the drug's future effectiveness thus limiting the woman's treatment options when her own disease progresses.

- The incidence of HIV infection in babies born to HIV-infected women who *do not breastfeed* is approximately 25%, and the majority of infection seems to occur at the time of delivery not *in utero*. Cesarean delivery (under standard surgical conditions of developed nations) reduces the risk of transmission to approximately 10% *without* zidovudine treatment.

- Parents are generally allowed to refuse, on behalf of their already born children, a burdensome therapy with only a 10% chance of benefit.

- The long-term risks of using zidovudine in newborns is unknown.

- Zidovudine (ZDV) is also known as Azidovudine (AZT).

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Fact Sheet: Kennedy Krieger Institute Lead Abatement Study

Lead levels. Elevated blood lead levels are dangerous for adults, contributing to hypertension and cardiovascular disease, but are particularly harmful to children (Kitman 15). Children are 4-5 times more susceptible to lead than adults because their digestive systems absorb 40-50 percent of lead ingested as opposed to 10-15 percent for adults (Kitman 38). Young children in particular are often exposed to more lead than their elders because they frequently put in their mouths objects on which airborne lead has settled (Kitman 38). Even low exposures of lead can lead to reduced IQ, behavioral problems, reading and learning disabilities, and hyperactivity (Kitman 16, 38). Pregnant women are also very susceptible to miscarriages and their fetuses to poor development if there is excessive lead exposure (Kitman 16). These problems are due to the fact that lead both retards neuro-anatomical development and degrades neurotransmitters (Masters 15).

There is no "safe" level of lead in the blood, but levels of 10 or more mcg/dl (micrograms per deciliter) is generally considered the threshold for concern, since at this point intelligence, behavior, and development can be adversely affected (http://www.cdc.gov/nceh/lead/lead.htm). When a child's blood lead level is between 10 and 20 mcg/dl, parents and communities should begin making changes to reduce lead exposure, such as more careful housecleaning and handwashing, and better nutrition to support the body's recovery. When the blood lead level is 20 or more mcg/dl, oral medication—chelation therapy—is considered, particularly if the child is showing symptoms. These medications bind to lead so that it will be excreted in the urine. Such therapy is always instituted (as standard care) at levels above 45. A reading of 70 or more mcg/dl is deemed a life-threatening emergency (http://www.keepkidshealthy.com/welcome/lead/leadtreatment.html).

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Kitman JL. "The Secret History of Lead," The Nation pp 11-14, 16-22, 24-28, 30-40, 42-22 (March 20, 2000).

Masters RD, Hone BT and Doshi S. Environmental pollution, neurotoxicity and criminal violence. RJ Rose (ed) *Aspects of Environmental Toxicology*. London: Gordon and Breach, 1997, pp. 132-148.

Fact Sheet: Research with children, from the "Common Rule," 45 CFR.

§46.404 Research not involving greater than minimal risk [see below].
DHHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

§46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
DHHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

(a) the risk is justified by the anticipated benefit to the subjects;
(b) the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
(c) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §46.408.

§46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
DHHS [Department of Health and Human Services] will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

(a) the risk represents a minor increase over minimal risk;
(b) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
(c) the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
(d) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in ∋46.408.

§46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
DHHS will conduct or fund research that the IRB does not believe meets the requirements of §46.404, ∋46.405, or §46.406 only if:

(a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
(b) the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) finds

(I) that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406, as applicable, or

(2) the following:

(i) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(ii) the research will be conducted in accordance with sound ethical principles;

(iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in §46.408.

Fact Sheet: Anchorage Needle Exchange Program (and Kennedy Krieger Institute Study)

From the Common Rule, 45 CFR:

§46.102 Definitions.

(i) Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Case Study 1: AIDS Clinical Trials in Developing Countries

In 1994, AIDS Clinical Trial Group Study 076, conducted in the United States and France, showed that a regimen of zidovudine administered to pregnant mothers and newborns decreased the likelihood of HIV transmission from mother to child. At that point, the ACTG 076 regimen became the standard of care in the developed world for the treatment of HIV-positive pregnant women. However, the regimen is expensive and intensive, and as a consequence, is not generally available for use in the developing countries of Asia and Africa. Therefore, several trials in the mid-1990s sought to determine whether reduced regimens of drugs, or other methods of treatment, would decrease transmission. These trials were funded by the US and other governments, or by international AIDS organizations, since the developing countries where they were carried out did not have the financial resources or public health infrastructure to fund and conduct the studies themselves.

According to 1993 World Health Organization (WHO) guidelines on human-subjects research, "the ethical standards applied [to a study in a host country] should be no less exacting than they would be in the case of research carried out in [the sponsoring] country" (CIOMS 1993, see Brody 1998, pp. 36, App. 1.8). Earlier, the WHO, in its Declaration of Helsinki IV, had decreed that "in any medical study, every patient—including those of a control group, if any—should be assured of the best proven diagnostic and therapeutic method" (WHO 1989, see Brody 1998, App. 1.2). According to these guidelines, because of the efficacy of the ACTG 076 regimen and its demonstrated superiority to no care at all, the control group of any study within or funded by the United States would have to receive the 076 regimen rather than a placebo. However, 15 of the 16 trials in developing countries begun after the ACTG study was completed involved a control arm in which participants were not provided with any antiretroviral drugs (Lurie and Wolfe 1997).

Case Study 1: Discussion

Opponents of these trials—including Peter Lurie, MD, MPH, and Sidney Wolfe, MD, of the Public Citizen's Health Research Group, and Marcia Angell, MD, former editor of the *New England Journal of Medicine*—claim that equivalency studies (which compare investigative interventions to a proven treatment), rather than placebo-controlled trials, are the best and most ethical way to assess less expensive interventions. They argue that researchers should search for a regimen that equals the 076 regimen in efficacy, rather than trying to determine whether various treatments are better than nothing. In addition, these opponents respond to claims that no care is the standard of care in developing countries by insisting that "standard of care" is a medical term that indicates a scientifically-determined effective level of care, which is not dependent on social context. The lack of treatment to prevent maternal-fetal transmission of HIV in the developing world is due to economic and social constraints rather than scientific knowledge, and therefore cannot be termed a "standard of care" (Angell 1997, Lurie and Wolfe 1997). Furthermore, these critics of placebo-controlled trials point out that manufacturers make drugs available for free for use in clinical trials, so money, at least in the experimental stages, should not be a barrier to the use of zidovudine (Lurie and Wolfe 1997). In addition, the number of trial participants and length of time necessary to do an active-controlled trial rather than a placebo-controlled trial are not prohibitively larger (Lurie and Wolfe 1997).

Marcia Angell condemned placebo-controlled trials in Africa, pointing out that "only when there is no known effective treatment is it ethical to compare a potential new treatment with a placebo" (Angell 1997). She claims that justifications for the use of placebos with women in the third world are similar to those used to justify the Tuskegee study: the women, without the study, would not receive treatment anyway, and the placebo-controlled studies are the fastest way to get information that will be useful in developing countries. Lurie and Wolfe outlined these points of comparison:

> *We invoked the Tuskegee study analogy in the perinatal AZT trials because (i) both were prospective studies in which participants were denied known effective treatments; (ii) both were conducted or funded by the U.S. Public Health Service; (iii) both involved people of color; (iv) both included violations of informed consent; (v) both were justified by claiming that this was the only appropriate study design; (vi) both were defended by positing differences between previous and present study populations; (vii) both were justified by asserting that study participants would not have been treated anyway; and (viii) both were terminated only after exposure in the lay press. (Lurie and Wolfe 1999)*

Amy Fairchild, PhD, MPH, and Ronald Bayer, PhD, respond, "Of the eight criteria Lurie and Wolfe list, four might apply to any ethical, well-designed, publicly funded study involving people of color" (Fairchild and Bayer 1999a). The argue that "for Tuskegee to serve as a useful analogy for illuminating research abused, the challenged study must meet some reasonable, general criteria. It must involve deception regarding the nature and very existence of the research study, it must capitalize on social deprivation or vulnerability, and not only must it fail to provide the best available effective therapy but it must also contrive to keep individuals from receiving such therapy" (Fairchild and Bayer 1999b).

Harold Varmus, MD, and David Satcher, MD, PhD, of the National Institutes of Health (NIH) answered critics of placebo-controlled studies by attempting to explain the complexities of AIDS research in the

third world, where economic and social conditions make deviations from first-world standards necessary (Varmus and Satcher 1997). They also pointed out, against Angell's comparison to Tuskegee, that the Tuskegee study did not test *any* intervention, whereas the purpose of all of the NIH-sponsored studies was to find effective treatments for AIDS and to prevent HIV-transmission. The first point made by Varmus and Satcher was that the ACTG 076 regimen is not feasible in most places in Asia and sub-Saharan Africa, since it requires that women are tested and counseled early in pregnancy, take a long course of oral zidovudine, have the drug administered intravenously during labor, refrain from breast-feeding, and administer a six-week course of the drug to their newborns. Mother and infant also must be carefully monitored for side effects. In the third world, women do not usually have early prenatal care, if any, customarily do not deliver in the hospital, and rely on breastfeeding to nourish and protect their children.

The second point emphasized by Varmus and Satcher was that in the developing world, where delivering the 076 regimen is not feasible because of economic and social circumstances, comparing other, more accessible treatments with it may not result in useful information for patients in those areas. "If the affordable intervention is less effective than the 076 regimen—not an unlikely outcome—this information will be of little use in a country where the more effective regimen is unavailable. Equally important, it will still be unclear whether the affordable intervention is better than nothing and worth the investment of scarce health care dollars."

A final relevant point was raised by Edward Mbidde, chairman of the AIDS Research Committee of the Uganda Cancer Institute. He reminds critics that, although funding originated with the NIH, "it is not NIH conducting the studies in Uganda but Ugandans conducting their study on their people for the good of their people" (Varmus and Satcher 1997). All of the studies in question have been developed with the help and approval of doctors and organizations in the countries where they have been conducted.

The placebo-controlled design would be considered unethical in the United States, where it is economically possible to provide the best-known treatment both within and outside of the clinical trial environment. Insistence on using the standards of the funding country is a protection designed to prevent the governments and companies of first-world countries from exploiting the citizens of developing countries, by enrolling them in studies and providing no treatment because no treatment is the norm in the host country. However, the question of whether the study will be relevant and beneficial for the people enrolled is an equally important one: if it is true that a placebo-controlled study has been devised by African scientists as the most useful study for Africans, taking into account the circumstances in those nations, then placebo-controlled studies may be the most ethical way to proceed if the goal is to find workable solutions to the African AIDS epidemic. In the Tuskegee study, the intervention that was denied was a series of doses of penicillin over a fairly short period of time, which could have been easily transported to affected populations in the United States and efficiently administered using existing public health infrastructures. In contrast, to provide the best-known treatment to prevent the transmission of HIV in the trials in question would have involved an intense regimen of very expensive drugs over a long period of time, requiring resources and facilities not currently available in sub-Saharan Africa and requiring the introduction of an entire health care infrastructure. Perhaps developed nations are ethically obligated to assist developing countries in creating this infrastructure, but doing so is generally considered beyond the scope of the individual studies.

Unlike the Tuskegee Study, the protocols for the placebo-controlled HIV/AIDS trials were developed by members of the population targeted for study. However, despite their common racial and ethnic background, those who proposed the study were generally more economically and educationally advantaged than those who enrolled as subjects. Also unlike Tuskegee, deception was not an integral part of the participant recruitment plan, and the studies sought to test interventions rather than to observe the natural progression of disease. Complicating this positive picture of the HIV/AIDS trials, however, are questions about whether the participants and similarly situated residents of the host countries would benefit from the findings of the studies, or whether those societies would lack resources and political commitment to provide treatment following the end of the trials. Might the study results be used instead in developed countries to argue for providing a less expensive, and probably somewhat less effective course of treatment to poor residents in developed nations who could not themselves afford the more expensive standard of care? In addition, investigation of what participants—especially those in the placebo-control arms—actually understood about the HIV/AIDS trials suggested that the informed consent process had not been effective in enabling them to make an informed, voluntary decision about study participation, nor in some cases were social structures conducive to their participation in the very Western or Anglo-American practice of obtaining informed consent. Some participants lived in cultures where deference to authority figures or elders, or where non-individual decision making was the cultural norm.

Questions for Additional Discussion

- Is it always better to do something than nothing; in other words, is it better to conduct the trials described above with the intention of developing some at least partially effective, potentially affordable intervention now, rather than waiting for broad social changes that would enable delivery of what is standard of care in the developed world? On the other hand, does permitting such studies and the eventual implementation of inferior (but better than nothing) therapy in developing nations reduce pressure to do more, e.g., to develop the public health infrastructure and political will to provide care more closely approximating that of the developed world? Susan Wolf makes this argument about current efforts to address genetic discrimination in the US; she argues that an anti-discrimination approach in health insurance, for example, "blunts any challenge to the rating system itself by suggesting that the problem is adequately handled by prohibiting disadvantage based on … genetic information" (I95, p. 348). In what other areas of health policy and research do you recognize a similar concern that by doing something rather than nothing, people undertaking these "band-aid measures" relieve pressure to address the problem more fully?

- What role should individual researchers play in the development of another country's public health infrastructure? What are the elements of such an infrastructure? Are there communities in the US—geographically defined or defined in other terms—that could similarly benefit from researchers' efforts?

- If an investigator undertakes a "non-intervention" epidemiological study—for example, a study of the prevalence of disease *x*—in a developing country, what responsibilities might that investigator incur and toward whom? Can an argument be made that *all* studies, even observational studies or assessments of disease prevalence, are in some sense interventions in the community studied? Which responsibilities of researchers are connected to the researchers'

awareness of a problem and which are attached to the researchers' intervention to study the problem?

- Of the criteria offered by Lurie and Wolf, and by Fairchild and Bayer, for being relevantly "like Tuskegee," which do you think are the most salient criteria? Why does it matter whether the AIDS trials are "just like Tuskegee" or not?

Additional Resources

Ho, D. (1997, September 29). It's AIDS, Not Tuskegee. *Time*, http://www.time.com/time/magazine/1997/dom/970929/viewpoint.its_aids_not_.html

London, L. (2002). Ethical Oversight of Public Health Research: Can Rules and IRBs Make a Difference in Developing Countries? *American Journal of Public Health* 92 (7), 1079-1084.

Case Study 2: Kennedy Krieger Institute Lead Abatement Study

In 1993-1995, the Kennedy Krieger Institute (KKI), an affiliate of Johns Hopkins University (JHU), conducted the Lead Poisoning Prevention Study in Baltimore, Maryland, to determine the effectiveness of various levels of lead removal ("abatement") from housing. Identification of the minimal effective level of lead abatement was deemed a socially and scientifically valuable goal because of both the health risks of lead and the need to maintain the availability of low-rent housing in Baltimore.
There were five study arms, involving 108 houses and their residents. The first group of homes received about $1650 worth of repairs such as lead paint scraping, the second about $3500 worth, and the third about $6500 worth. Abatement became increasingly more extensive and more nearly complete with the additional increments of cost. Group four homes received the most extensive abatement possible, and finally group five consisted of houses built after 1978 that presumably were free of lead paint although located in neighborhoods known to have many houses with lead paint. All the houses in the study, even the ones repaired "minimally," were freer of lead than about 95% of housing stock in Baltimore, and the lowest level of repair reduced lead dust by 80%. The repairs were paid for through a loan program from the Maryland Department of Housing and Development, and probably would not have occurred without such a program, because of the high cost of lead abatement measures in relation to the value of the housing stock that needed it. The owners of the properties were given assistance in obtaining the loans by KKI. Landlords were also strongly encouraged to rent to tenants with small children; the study design called for enrolling families with young children in the study and testing the children's blood for lead levels.

All children enrolled in the study received blood lead testing four to five times per year during the two-year duration of the study, and the houses, soil, and drinking water of each property were tested immediately after abatement was completed and then 1, 3, 6, 12, 18, and 24 months later. Participants were paid $15 for completing a questionnaire "about other potential sources of lead exposure in your home and activities which relate to exposure" every six months, and were given free transportation to the KKI clinic for blood testing. The study's consent form promised that "we would provide you with specific blood lead results. We would contact you to discuss a summary of house test results and steps that you could take to reduce any risks of exposure" (Clinical Investigation Consent Form).

Two mothers residing in houses that received less than full abatement later sued KKI, alleging that they had not been informed in a timely manner that their children's lead levels were elevated, that they had not been adequately warned about the risks of lead exposure and risks of the study, and that the study design placed their children at unnecessary risk. (*Grimes v. Kennedy Krieger Institute* 2001; Mastroianni and Kahn 2002). Their suits received a great deal of media attention, perhaps in part because KKI's insurance lawyers initially responded by claiming that the Institute had "no legal duty" to report lead levels to families.

Case Study 2: Discussion

KKI's rather hard-hearted and legalistic response, coupled with reports that at least one plaintiff was a minority member on pubic assistance, fueled concerns that poor minority families may have been exploited or mistreated by the more powerful university-affiliated institute. After a Maryland trial court refused to hear the suits, Judge Dale Cathell of the Maryland Court of Appeals not only declared that the cases should go to trial, but severely condemned the study itself. He likened the lead study to Nazi experimentation and the Tuskegee Syphilis Study, and held that parents and guardians could not consent to nontherapeutic research in which there was *any* risk to the child, a far more stringent standard than the nationally accepted one of minimal risk in research involving children. His ruling, if it had stood, would have resulted in shutting down much research on childhood vaccines and diseases in Maryland, and may have set a crippling, albeit not legally binding precedent,[5] nationally for research involving not only children, but also mentally disabled or demented patients, who are subject to the same research protections as minors (AHRP 2001). Two months after offering its initial decision, the court clarified that it had not intended the "no risk" standard to apply to nontherapeutic pediatric research studies and that it endorsed the federal regulations in this regard (see Fact Sheet).

Several children in the study suffered effects of lead poisoning and had elevated blood lead levels. Three more families have since filed charges against KKI, but none of the cases have yet gone to trial. Because the legal cases are ongoing, it is likely that many relevant facts remain to be discovered. Readers are cautioned about engaging in ethical analysis on the basis of an incomplete set of facts. Nevertheless, ethical criticisms and comparisons to the Tuskegee Syphilis Study focused on several aspects of the design and execution of the study about which enough is known that some preliminary discussion may take place. First, the subjects were children, a vulnerable population due to their inability to understand and consent personally and their particular susceptibility to toxins in the environment. Second, it was alleged that the study encouraged families to live in dwellings where lead, a known toxin, was present. Third, the scientists may have downplayed or failed to mention all of the risks of participation in the study to the children's parents, and failed to disclose in a timely fashion elevated blood lead results that would have indicated that children were at risk of lead poisoning. Similarly, in Tuskegee, the poor, uneducated black enrollees were vulnerable to exploitation, and were not informed of their syphilis, of what could be done to prevent its transmission or to cure it, or of the risks of participating in the study, including undergoing such invasive procedures as spinal taps.

Although we cannot possibly reach any conclusions about the actual legal charges and arguments being made, for the purpose of discussion, we can identify two distinct sets of issues concerning the ethics of the KKI study: questions concerning the basic *design* of the study, and concerns about how the study was *conducted*. In the first category are questions such as, should children have been used for this study? Children are more susceptible to lead poisoning than adults, but that fact also makes it more important that ways are found to lessen their exposure (Kitman 2000). The researchers knew that some of the children in the study were being exposed to more lead than others, but every house in the study had far less lead than most dwellings available for similar rental costs in the city. This meant that that the children in the study were generally better off in terms of lead exposure through their living environment by participating in the study, although it is conceivable that a family could have moved

[5] Although individual state court decisions are not binding on citizens or courts of other states, in the relatively uncharted terrain of human subject protections, researchers and funding agencies could be justifiably reluctant to undertake practices deemed wrong in such strong terms at a state appellate level.

from a more highly abated house to one with more lead present. The only way to have determined whether individual families (children) were better or worse off in virtue of their study participation decision would have been to have traced every family and determine the relative levels of lead in their previous and study dwellings.

The second set of questions focuses on the conduct of the study, including the provisions for informed consent, which could have been inadequate even if the basic design of the study was appropriate. The design met the approval of the JHU IRB, but did the researchers fully explain the study and the risks to the parents? In the consent form, the purpose of the study was explained as follows:

> *As you may know, lead poisoning in children is a problem in Baltimore City and other communities across the country. Lead in paint, house dust and outside soil are major sources of lead exposure for children. Children can also be exposed to lead in drinking water and other sources. We understand that your house is going to have special repairs done in order to reduce exposure to lead in paint and dust. On a random basis, homes will receive one of two levels of repair. We are interested in finding out how well the two levels of repair work. The repairs are not intended, or expected, to completely remove exposure to lead.*
> *We are now doing a study to learn about how well different practices work for reducing exposure to lead in paint and dust….This study is intended to monitor the effects of the repairs and is not intended to replace the regular medical care your family obtains.*

The form then explains that the study will sample lead levels in and around the dwellings and in children's blood, only hinting at the fact that the children's blood lead levels were to be used as indicators of the efficacy of the lead abatement procedures. The form also fails to explain the symptoms or effects of lead poisoning (see accompanying Fact sheet). Further, the consent form refers to "two levels of repair work," when there were actually five different levels of lead abatement (or lead-freeness) involved in the study. Although a consent form should be used only to guide and to document the process of informed consent, it is troubling when the information contained in the form is confusing, inaccurate, or incomplete. In addition, it appears that researchers did not follow through on the benefits or protections promised in the consent form. In at least one of the cases now slated for trial, the results of dust collection in a home was not reported to the family for nine months, and then only after the child's blood showed elevated levels of lead (Mastroianni and Kahn 2002).

A further interesting topic for ethical discussion was raised by Judge Cathell's initial decision that children could not take part in any nontherapeutic research that posited *any* risk to the child, rather than the existing "minimal risk" standard (see Fact Sheet). Though this judicial opinion was later reinterpreted, it highlights the conflict between protecting vulnerable populations and undertaking research that could benefit people like them (although not the participants themselves). This echoes similar debates over the inclusion of other vulnerable populations in research. Indeed, after recounting research abuses including the TSUS, Nazi experiments in concentration camps, and Japanese military "disease bomb" experiments in World War II, Judge Cathell claimed that "in the present case, children, especially young children, living in lower economic circumstances, albeit not as vulnerable as the other examples, are nonetheless, vulnerable as well." (http://www.claimrep.com/laws/cases/Md/caseMDGrimes.htm)

Because few health care interventions have been tested for use with pediatric patients, it would seem critical to encourage such pediatric studies, particularly drug testing. However, if the individual child's best interest is to be the overriding standard as the initial decision in *Grimes* suggested, then parents and guardians cannot be expected (or allowed) to consent to the participation of their children in research that is not designed to afford their children direct therapeutic benefit. Most important for public health research, no currently healthy child could be placed at potential risk in a study of preventive interventions for the sake of other children. Similar arguments could be made for others who cannot consent for themselves, e.g., the mentally disabled or "never competent," senile demented elderly and other "previously competent" people.

Questions for Additional Discussion

- In what ways does this study resemble features of the TSUS, and in what ways is it dissimilar?

- Could this study have been done, as a practical matter, if the families enrolled in the study were more affluent, for example, affluent enough to live in lead-free homes or to hire private lead-testing of their properties?

- What is the relevance for the ethical assessment of this study of the "current reality" that landlords would simply abandon their properties if the highest, most effective, and most costly lead abatement measures were required in order for them to rent their properties? How can the reality of this assumed "current reality" be determined? Would it be relevant to the assessment of this study if it could be predicted that landlords would generally be willing to invest, for example, $1700 per property for lead abatement? How is the "current reality" of housing economics in Baltimore similar or dissimilar to the "current reality" of the lack of public health infrastructure and funding for HIV treatment in developing nations?

- Is it relevant to the ethical evaluation of this study that most, indeed almost all, of the participants probably benefited, i.e., most lived in houses more free from lead than they otherwise would have? Did the KKI researchers rely on the "background level" of risk of lead poisoning to justify offering less than maximally effective interventions in the course of the study? How, if at all, did this justification differ from that made by Tuskegee researchers?

- How, if at all, was the design of the study faulty? Would the study have been unethical even if the researchers had reported testing results to parents in a timely fashion? What other measures, if any, should the researchers be required to undertake to protect the enrolled children from dangerous lead levels? At what blood lead level should such measures be undertaken (refer to Fact Sheet)?

- The appeals court held that in nontherapeutic research studies in which subjects are compensated in any amount or form, a contract is created between the researcher and subject which creates legally binding obligations for the researchers, such as a duty to warn of impending harm (Glantz 2002). Should researchers be held to obligations other than those stated in the consent document and discussed in the informed consent process?

- Is the informed consent document revealing enough? What information should researchers be obligated to disclose in this study? Although regulations govern the elements of disclosure in

the research context is there other information that should be disclosed to prospective research participants? What would a "reasonable person," or a typical parent in this situation, want to know? How should researchers respond if a prospective participant expresses the desire for more information? In the therapeutic context this would be called a request for disclosure according to a subjective (or individualized) standard. Is this appropriate in research?

- Nontherapeutic research on children can be carried out if the risk presented is "no greater than minimal risk," where 'minimal risk' "means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" (45 CFR §46.102(i); see Glantz 2002). However, children living in different environments have very different daily exposures to risk. Should the acceptable risk be greater for inner-city Baltimore children than suburban New York children, and if not, which group's daily life should be chosen as the standard?

Additional Resources

Keiger, D. and De Pasquale, S. (2002). Trials and Tribulation. *Johns Hopkins Magazine* Feb 2002. Accessed at http://www.jhu.edu/~jhumag/0202web/trials.html on 13 March 2002.

Kopelman, L.M. (2002). Pediatric Research Regulations under Legal Scrutiny: *Grimes* Narrows their Interpretation. *Journal of Law, medicine & Ethics 30(1),* 38-49.

Putney, S.B. and Gruskin, S. (2002). Time, Place, and Consciousness: Three Dimensions of Meaning for US Institutional Review Boards. *American Journal of Public Health* 92 (7), 1067-1070.

Case Study 3: Anchorage Needle Exchange Program

An NIH sponsored study in Anchorage, Alaska was designed to determine whether over-the-counter sale of sterile drug injection equipment was more effective than needle exchange programs (NEPs). The study randomly assigned 600 intravenous drug users (IDUs) and 500 former IDUs to one of two arms: those in one arm were enrolled in a needle exchange program, and those in the other were given a map of pharmacies in Anchorage that sold syringes. Researchers also sought to determine which method of needle distribution was more effective in preventing infectious diseases such as hepatitis and HIV, which are transmitted by shared needles. To this end, subjects were tested for hepatitis and HIV before and after the study period, with the number of new cases of those diseases indicating which method was preferable. Researchers additionally wanted to determine whether the availability of clean needles would cause a relapse in recovered users. Hepatitis B vaccination vouchers were provided to all participants. The conclusion of the researchers was that NEPs do not increase IV drug use.

Case Study 3: Discussion

Many ethical objections to this study were raised. Sidney Wolfe, MD, director of Public Citizen's Health Research Group, opposed the study on the grounds that it was unnecessary since the study questions have already been answered by other experiments (Caplan and Annas 1999). Art Caplan, PhD, and George Annas, JD, MPH, add that the study would be unethical regardless of whether or not it was redundant: "the ethical argument invoked in defense of this morally repugnant design was that the knowledge to be gained could not be gained by any other methods and was of such value as to justify the design. This, of course, is precisely the justification some defenders of the Tuskegee trial argued at the time the study was being challenged as unethical" (Caplan and Annas 1999).

The most frequent objection centers on the fact that one group of study participants was deprived of the option of obtaining free needles and was thereby at increased risk of contracting hepatitis or HIV. Drug users assigned to the pharmacy arm might be prevented from buying needles due to poverty, lack of transportation, or denial by pharmacists (Recer 1996). "The clinical trial at issue was constructed so as to leave subjects open to preventable infection by a serious disease by limiting their knowledge and their options" (Caplan and Annas 1999). Further criticisms focused on the use of the incidence of hepatitis B and HIV as endpoints of the study. George Annas believes that the use of Hepatitis B (for which there is a vaccine) as an end point of the study is in violation of the 1947 Nuremberg Code, under which "no human experiment is to be conducted that could induce life-threatening—and preventable—harm" (in Benowitz 1997). However, the question of whether the experiment can be considered to "induce" hepatitis B is also a subject of debate. Nonetheless, in response to such claims, the NIH added the provision that participants be given vouchers for Hepatitis B vaccines. However, some critics argue that the vaccines themselves, and not just vouchers, should have been given (Recer 1996). Caplan and Annas argue that the study allowed researchers to "stand by and observe as their subjects develop devastating diseases that could be prevented." (1997). Others suggested that "treatment of the underlying medical condition and the social context were not addressed by the intervention, leaving the subjects persistently vulnerable to the possibility of disease. The disconnect between the researchers' agenda and the needs of the community under study parallels the Tuskegee study" (Corbie-Smith 1999b). Finally, the study was criticized for encouraging participants to break the law: "drug injectors in the study…are also instructed how to talk and dress in order to convince a pharmacist to sell them a syringe, a violation of local Anchorage law" (Lurie and Wolfe 1999).

Other commentators seek to justify the Anchorage study in its own terms and to distinguish it from the Tuskegee study. "Whereas in Tuskegee the PHS used the social circumstances of poor African-American men to manipulate them into a study that would deprive them of treatment, proposals to provide sterile injection equipment seek to address the vulnerable situation of those exposed to HIV by offering a potentially life-saving intervention….Only insofar as the original study failed to offer hepatitis B vaccination to participants did it arguably involve an ethical lapse—a lapse addressed by the NIH despite the recommendations of its ethical review panel" (Fairchild and Bayer 1999b). Needle exchange programs didn't exist in Anchorage before the study, so drug addicts were not deprived of a service that they had grown used to—their access either improved or stayed the same. Like the men in the Tuskegee Study, some of the participants in the Anchorage trial were actively denied one type of intervention: they were refused access to the NEP. In addition, none of the men were offered counseling or assistance in treating their addiction, just as the Tuskegee men were not told how to prevent the transmission of syphilis. However, the Anchorage participants were not prohibited from entering drug rehabilitation if

they so chose, while at least some TSUS enrollees were actively prevented from seeking treatment for syphilis. Entrance into the Anchorage study was voluntary, and none were deceived.

Questions for Additional Discussion

- What aspects of the Anchorage study, if any, make it unethical? Would it make a difference if the research question had already been answered satisfactorily elsewhere, or if a NEP had been operating in the area previously and had been open to all, or if the pharmacy arm participants hadn't been instructed in breaking the law? Does the inclusion of former IV drug users in the study, in a situation in which they might be tempted into a relapse by the easy availability of sterile needles, raise any ethical problems?

- As in the TSUS, the AIDS perinatal studies, and the KKI lead study, in the Anchorage study the development of disease was used as one of the study's endpoints. Under what conditions, is the transmission or development of disease an appropriate endpoint?

- What is the level of risk that participants in this study might justifiably be asked to incur? Why? Is the Common Rule's definition of 'minimal risk' relevant in this study (see Fact Sheet)? Does the actual level of risk faced in daily life by the current and former IDUs enrolled in this study differ?

- The Anchorage study was an NIH-sponsored study conducted by non-IDUs. To what extent is it ethically beneficial or ethically problematic that the study was conducted by "outsiders" to the community being studied (i.e., the drug-using community). Would it have been appropriate, for example, for former IDUs to have been recruited to work with researchers to recruit current IDUs as participants in the Anchorage study? In what ways would they have played a role like that of Nurse Rivers in the TSUS?

- Imagine yourself as a researcher hoping to enlist the support of African-American community leaders in a large urban setting for a pilot needle exchange project targeting African-American IDUs. First, who, or what sorts of leaders, would you approach? What would you anticipate their response would be to your proposed project? How would your plans differ if you were approaching another minority community in your area, and how might leaders of that community respond?

- How would you respond if African-American community leaders charged that you were pursuing a NEP as a cheap alternative to providing effective drug treatment and that such NEPs are in reality part of a genocidal conspiracy to eliminate poor African-Americans, just like the Tuskegee project was (see Fairchild and Bayer 1999b)?

Additional Resources

Fisher, D. (2000). Does Needle Exchange Cause an Increase in Drug Use? Presented at APHA meeting, abstract online at http://apha.confex.com/apha/128am/techprogram/paper_1914.htm.

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Tools for Best Practice

Community consultation has been proposed as a tool with multiple benefits for public health research and practice. It is suggested that if researchers and public health practitioners were encouraged, or even required, to consult with members of the communities in which they conduct research and offer interventions, their research questions and health services might better fit the actual needs of community members (Strauss *et al.* 2001, Green and Mercer 2001). Such consultation might help to restore trust and promote a collaborative relationship between researchers or service providers and members of the public. And, depending on the degree of influence that community members exerted (or were recognized to have), community consultation could reinforce the goals of the process of obtaining individual informed consent—namely, the protection of well-being and the promotion of self-determination. As module 4 discusses, some commentators suggest that communities have interests, just as individuals do, that these interests are distinct from those of individuals, and that community consultation (or even a process of obtaining community consent) is necessary to protect those community interests. This perspective is the subject of much debate (e.g., see Foster *et al.* 1998, Juengst 1998, Sharp and Foster 2000, Weijer and Emanuel 2000).

In relation to the Tuskegee Syphilis Study, however, one issue is interesting to consider. The PHS officials conducting the TSUS might be thought to have engaged in a form of community consultation at various stages of the study, and it may be argued such consultation did little to promote the enrollees' autonomy, protect their welfare, or protect the interests of the rural and African-American community which they formed. (Others might suggest that the TSUS did bring more health care to Macon County Alabama than it had ever experienced before, or otherwise would have, and therefore that the TSUS did serve some community interests.) Nurse Rivers was in some ways a member of the African-American community of Macon County, although she was more educated and more affluent than the men she enrolled in the study. Was she a representative of the research community (the PHS) or of the African-American men she enrolled and treated? Can one person be a representative of both "communities?"

The Macon County Medical Society (MCMS) was consulted to provide a form of surrogate consent, presumably because its members were geographically and racially of the same community as the study population, and the Tuskegee Institute itself was approached for its initial involvement in part because of its ties to the African-American public in the area. Were these consultations and collaborations duplicitous and co-opting of those consulted, or were they appropriate attempts to consult representatives of, or at least people more similar to, those being studied? One commentator notes that during the history of the study, fourteen articles about it were published in nine medical journals, and the peer-review process and readership failed to discern ethical problems with the methodology of the study; moreover, black physicians were an integral part of the study and never raised ethical concerns, even after the project's focus changed from its initial commitment to treatment into a strictly observational study (White 2000). Given the conditions of racism and segregation that constitute the context of the TSUS, perhaps no appropriate community consultation could have been conducted, or could have resulted in redesign of the TSUS as an ethical study.

What about today? Consult Module 4, "Community-Based Practice and Research: Collaboration and Sharing Power." In light of the methods it suggests and the potential ethical pitfalls discussed above,

design a process of community consultation to implement a (hypothetical) research study or community-based intervention. Here are some ideas that you might study or implement:

- A program to increase the activity level of low-income elderly
- A program to assess whether school lunch programs address nutritional needs
- A study to determine whether, in an effort to improve diet among African-American heads of household, group-based education or individual mentoring is more effective
- A study to assess the effectiveness of various media messages to encourage use of car seats
- A study to increase enrollment of minority group members in cancer screening programs, including prostate and breast cancer
- A study of a program to reduce the presence of firearms in various neighborhoods through a "buy back" system
- A study to compare the effectiveness of programs that "buy back" firearms for cash and those that trade firearms for gift vouchers at local stores
- How do you identify the relevant communities in which to conduct your work? Are these "vulnerable" communities, and if so, in what ways? Does their vulnerability relate to the *voluntariness* of the community members' participation, their ability to be adequately *informed* about participating in your study or program, or some other factors?
- Who are the community representatives or leaders? What do you anticipate their concerns will be? How will your approach them? How will you approach members of the community, beyond these leaders? What role will community input into your study or program have and at what stages (e.g., study design or data analysis)? What risks are there of community leaders being (or being perceived) as being co-opted by you? What is the likelihood that you would be co-opted by them to serve interests that are not really your own (i.e., the interests of promoting public health)?
- How does the process of community consultation that you design resemble what was done in the TSUS? How does it help to avoid some of the ethical problems raised about the TSUS?

If possible (and appropriate within the framework of your educational program), conduct your hypothetical community consultation (as an individual, small group, or class). You will need to be clear that your objective is to learn about the process of consulting members of the public who come from and perhaps represent different communities. You will need to express your appreciation to those who are willing to talk with you, and you should invite their critique of the process you propose and stress that your goal is to learn from them. At the same time, you should be prepared to discuss the process of conducting research and providing public health services, and you should be prepared to productively confront the multiple legacies of Tuskegee in your discussions of your education, future work, and current hypothetical project.