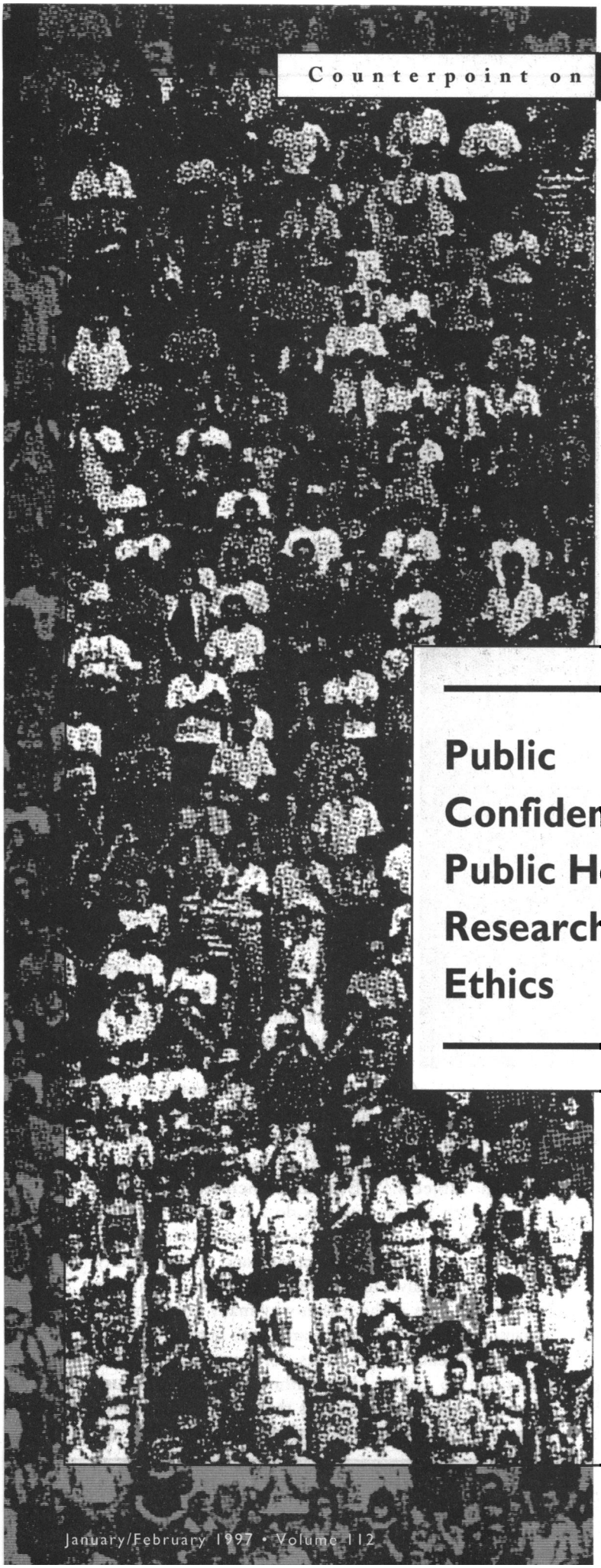

Public Confidence in Public Health Research Ethics

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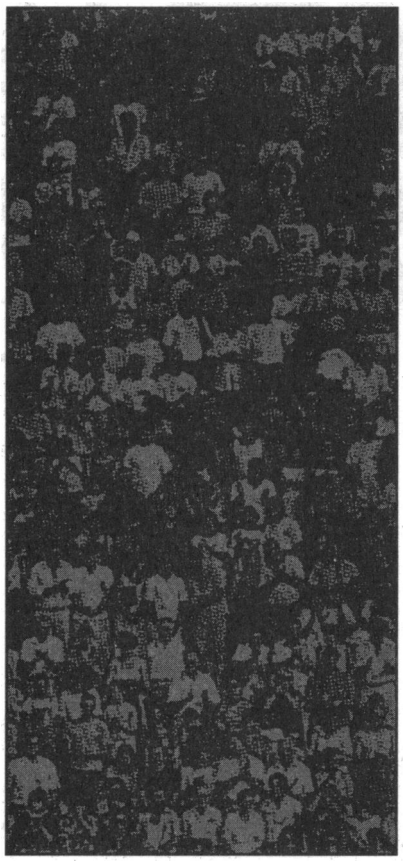
Beginning in December 1946, 23 Nazi physicians, scientists, and officers were prosecuted for war crimes and crimes against humanity in Nuremberg, Germany. The defendants, 16 of whom were convicted by an American military court, defended their acts of torture and murder by claiming that they were conducting medical research of importance to their country.[1] They were seduced by racial hygiene theories—supported by Nazi ideology—to consider Jews, Gypsies, people with physical and mental disabilities, and homosexuals as less than human and threats to the body politic, the Aryan *Volk*.[2,3]

On this 50th anniversary of the Nazi physicians trial, Annas and Grodin remind us that its greatest legacy was the Nuremberg Code.[4] The judges at the trial laid out the Code's 10 principles as part of the judgment.[1] The first is that "[t]he voluntary consent of the human subject is absolutely essential." The other nine require that the experiment avoid all unnecessary suffering, exclude foreseeable death or disabling injury, be conducted by qualified researchers who protect subjects against even remote possibilities of injury and who will terminate a study that is likely to result in death or injury, ensure that the subject can withdraw at any time, and be designed to yield fruitful results unprocurable by other methods.

Continuing Need for Ethical Principles

These principles form the foundation of research ethics around the world. Yet, researchers rarely refer to the Nuremberg Code today. This may be because they are not Nazis and rightly resent any association with Nazism. But it may also be because they find the Code too restrictive. The Code's first and primary principle—that human beings cannot be used as research subjects without their voluntary, informed, competent, and understanding consent—can be inconvenient. Not sur-

prisingly, in 1964, physicians developed their own statement of research ethics, the Declaration of Helsinki, which permits research without consent in some circumstances.[5] Physicians have also influenced other international guidelines that create exceptions to the requirement of voluntary, competent consent in order to permit the conduct of important scientific research.[6] These exceptions are also justified on the ground that researchers who are genuinely trying to find cures for human ills would not stoop to unethical conduct—at least not knowingly. Yet, research subjects who believe that researchers will do nothing to put them at risk can be inadvertently misled and sometimes physically harmed. We still need ethical principles even when research is good.



Good intentions can have bad consequences. One need only recall the Tuskegee experiment begun in the early 1930s to observe the natural course of syphilis in 399 black men in Alabama.[7] The men were not told that they were being used as research subjects and were not offered penicillin until the study became public in 1972. The U.S. Public Health Service initiated the Tuskegee project for a laudable purpose. Physicians wanted to provide additional health services to African Americans but were unable to obtain the necessary funding; the Tuskegee project was intended to demonstrate the need for additional services. The research ethos overtook the original impetus, however, and the researchers became more concerned with the scientific question than with the lives of their research subjects.

In this issue of *Public Health Reports*, Snider and Stroup appear to fall into this trap in their discussion of public health practice and research.[8] They argue that certain activities by public health professionals should not be considered research because "society has regarded the benefits as greatly outweighing the risks to individuals." However, the fact that the benefits of a project outweigh its risks is a *prerequisite* for ethical research with human subjects, not a reason to exclude it from the category of research.[9,10,11] Of course, public health practice activities are also predicated on the predominance of benefits over risks. Therefore, although this standard is a threshold for acceptable public health activities of all types, it cannot serve to differentiate research from practice.

Still, Snider and Stroup should be commended for drawing renewed attention to ethical principles for public health research and practice. After all, since Nuremberg, principles of research ethics have developed primarily with reference to medical and behavioral clinical research.[12] Their application to public health—although well understood by scholars of research ethics—are not often discussed in the literature. Snider and Stroup give us an opportunity to remind ourselves not only where ethical principles apply, but why.

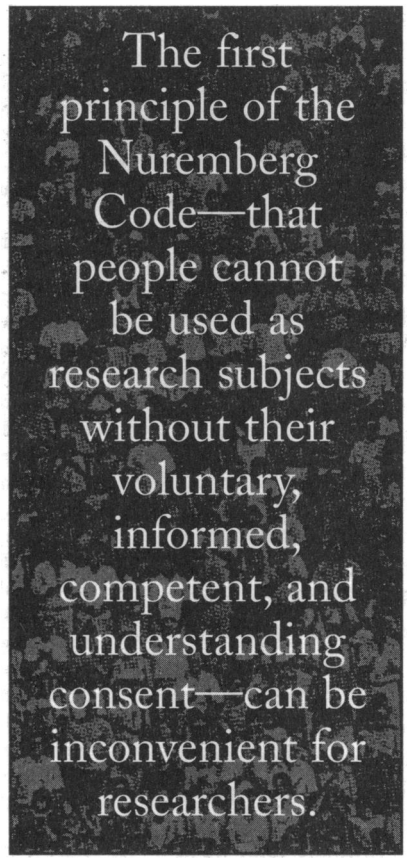
Distinguishing Research from Practice

Snider and Stroup appear to be concerned that Federal regulations governing research funded by the Federal government define the scope of research too broadly when applied to public health. They seek to remove certain public health activities from the category of research, apparently to avoid the burdens of Institutional Review Board (IRB) approval and subjects' consent. The "problem" of an overinclusive definition of research, however, is illusory. Much of the work that Snider and Stroup fear might be inappropriately considered as research is not research with human subjects at all or is exempt from IRB approval. The real problem may lie elsewhere—in failing to apply ethical principles to the conduct of public health practice as well as public health research.

The Nuremberg Code reminds us that principles of ethical research were adopted to protect human research subjects. Thus, they apply where human beings are used as subjects of research. In the United States, IRBs have been created to protect human research subjects.[10] Ethical principles governing research with human subjects do not restrict activities that do not use human beings as research subjects (other than to require honesty, objectivity, and confidentiality in collecting, analyzing, and reporting data, and similar basic rules). This is the reason why many public health activities do not qualify as research with human subjects. Disease surveillance programs, for example, are often structured to collect data without the need to use research subjects at all. Studies that collect data anonymously do not use research subjects because they do not

use individually identifiable information; they pose no threat to human beings and do not require individual consent. In order to avoid subjecting such programs to IRB approval, it is not necessary to claim, as Snider and Stroup do, that such programs are not research. One need only recognize that there are no human subjects to protect.

Another basis for distinguishing between research and practice lies in determining whether an activity is intended to produce generalizable knowledge (research) or to serve or benefit an identifiable individual (therapy). For example, contact tracing programs that seek to identify contacts of persons with a contagious disease are intended to prevent disease transmission or educate people at risk of disease and to reduce the incidence of disease in a population. They are not research studies. This does not mean, however, that people are obliged to participate. Contact tracing programs typically request the names of contacts from index cases, and the index case individuals can provide the information or not, as they wish. The fact that physicians and other professionals may have a legal obligation to report cases that they diagnose or identify is irrelevant to the status of the contact tracing program and to the right of individuals to consent to or refuse to provide information about their contacts.



Similarly, emergency responses to public health threats may not be research studies when they are intended to directly benefit individuals, not to develop generalizable knowledge. It is true that, in the literature, the concept of individual benefit has been discussed primarily in terms of medical care and that the terminology can appear awkward when applied to public health practice where there are lots of individuals to treat or serve and where the benefits are sometimes unevenly distributed among them. Nonetheless, the core idea remains that professionals are *serving* people for their own benefit rather than using human subjects as a source of data to answer a research question.

Snider and Stroup recommend that people who are contacted by emergency response personnel should give their consent to participate and that emergency response consent forms should be developed for that purpose. This recommendation appears to be based on the mistaken assumption that the only time individuals currently have the right to consent to or refuse to participate is when they are research subjects. The general rule of existing law is, of course, that no one is obliged to give information involuntarily, whether the request is made as part of a public health investigation, a criminal investigation, a consumer survey, or a research study. (Tax forms are an exception.) There is no reason to create an emergency response consent form; people can consent or refuse to give information without a form.

It is possible that, at a later date, public health professionals may wish to use information collected during non-research public health activities for the purpose of doing a research study. In that event, it *would* be necessary to obtain the informed consent of an individual for the use of information that would identify them individually. It is at that point that the person becomes a research subject. An individual's consent to be helped or to give information in an emergency does not mean that the person has agreed to the use of his or her information for research purposes. But, such later studies are typically conducted at a more leisurely pace and can properly be subjected to ethical review without jeopardizing a non-research emergency response to a threat to public health.

Program evaluation presents more complex questions because it encompasses activities ranging from research studies to routine forms of quality assurance monitoring. Current examples include studies of managed care enrollees to identify efficient treatment protocols; many such studies described as quality assurance may actually be research. Here again, the distinction depends on the purpose of the evaluation.[12] In addition, if identifiable information is being collected from human beings for the purpose of answering a research question, it is research with human subjects. If routine procedures are being studied to see whether they are consistent with established quality standards, it is not.

Conclusion

Snider and Stroup support the generally accepted principle that activities should be classified as research or practice by their intent. Procedures should be classi-

fied as research if they are intended to contribute to generalizable knowledge or use experimental or unproved interventions. This standard is already in effect and answers most of their concerns.

The problem with using intent as the touchstone of the definition of research is also well known: it does not address the difficulty many researchers have in being honest about their own intentions. There is ample evidence that medical researchers have often characterized experimental interventions performed for their own research purposes as therapeutic care for a patient.[13] Public health researchers may similarly attempt to disguise their own research agendas by claiming that they are just practicing public health. The converse may also occur when researchers unnecessarily compare known effective preventive measures with a placebo (or no prevention) in randomized trials, thereby converting standard practice into research. For example, the National Institutes of Health has recently been challenged for approving a study that would compare rates of hepatitis B in injection drug users who do and do not receive sterile syringes from needle exchange programs (Letter from Peter Lurie and Sidney M. Wolfe to Harold Varmus, Director, National Institutes of Health, dated October 17, 1996). Researchers who deny syringes to the control group could be violating ethical principles by withholding a potentially life-saving measure.

These dangers suggest that public health researchers should be held to at least as high an ethical standard as medical researchers. After all, by definition, public health activities affect large numbers of people, many more than will participate in clinical trials. The public's confidence in the public health community's ethical standards will often mean the difference between a program's success or failure. Moreover, because public health activities are so often conducted by government agencies as part of their official functions, they have a patina of coercion that is not present in privately conducted research. Public health practitioners who focus primarily on avoiding compliance with ethical research standards are likely to contribute to public suspicion of government efforts to improve everyone's health. Government programs to educate people about how to prevent HIV transmission, for example, have been resisted by those who fear another Tuskegee.[14]

Finally, the concern that too many public health activities might be mistakenly classified as research seems to turn the problem on its head. Where are the examples of public health programs that have been stopped by or even subjected to unnecessary ethical research review? On the contrary, there are too many examples of well-intentioned research projects that used human beings without their knowledge or consent.[15,16,17] The legacy of these undisclosed research studies has often been the public's loss of trust in the public health enterprise as a whole.

Rather than seek new ways to avoid adherence to ethical standards, the public health community would do well to voluntarily adopt higher ethical standards for all its activities.

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References

1. Annas GJ, Grodin MA, editors. The Nazi doctors and the Nuremberg code: human rights in human experimentation. New York: Oxford University Press, 1992.
2. Proctor R. Racial hygiene: medicine under the Nazis. Cambridge (MA): Harvard University Press, 1988.
3. Lifton RJ. The Nazi doctors: medical killing and the psychology of genocide. New York: Basic Books, 1986.
4. Annas GJ, Grodin MA. Legacies of Nuremberg: medical ethics and human rights. JAMA 1996; 276:1682–1683.
5. Declaration of Helsinki, as revised. In: Reich WT, editor. Encyclopedia of Bioethics. Vol. 5: appendix. New York: Simon & Schuster MacMillan, 1995:2765–2767.
6. Council for International Organizations of Medical Sciences and the World Health Organization. International ethical guidelines for biomedical research involving human subjects. Geneva, Switzerland: CIOMS, 1993.
7. Jones JH. Bad Blood: the Tuskegee syphilis experiment. New York: Free Press, 1981.
8. Snider DE Jr., Stroup DF. Defining research when it comes to public health. Public Health Rep 1997;112:29–32.
9. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: ethical principles and guidelines for the protection of human subjects of research. Washington DC: Government Printing Office, 1978.
10. Levine RJ. Ethics and regulation of clinical research. 2nd ed. Baltimore: Urban and Schwarzenberg, 1986.
11. Office for Protection from Research Risks, National Institutes of Health [US]. Protection of human subjects. CFR Title 45, Part 46. 1996.
12. Brett A, Grodin M. Ethical aspects of human experimentation in health services research. JAMA 1991;265:1854–1857.
13. Annas GJ. Judging medicine. Clifton (NJ): Humana Press, 1988:384–390.
14. Mariner WK. Distinguishing "exploitable" from "vulnerable" populations: when consent is not the issue. In: Bankowski Z, Levine RJ, editors. Ethics and research on human subjects: international guidelines. Geneva, Switzerland: CIOMS, 1993: 44–55.
15. Katz J. Experimentation with human beings. New York: Russell Sage Foundation, 1972.
16. Advisory Committee on Human Radiation Experiments. Final Report. 1995. New York: Oxford University Press, 1996.
17. Goldby S. Experiments at the Willowbrook State School. In: Katz J. Experimentation with human beings. New York: Russell Sage Foundation, 1972:1007–1010.