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Social Benefits of Human Subjects Research

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Introduction

The primary ethical justification for conducting research with human subjects is to benefit society.[1-5] This normative principle is stated explicitly or implied in many codes, guidelines and regulations pertaining to research with human subjects.[6-10] For example, according to the Nuremberg Code, an experiment with a human subject should "be such as to yield fruitful results for the good of society" and "[t]he degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment."[6] The CIOMS Guidelines put the matter this way: "The ethical justification of biomedical research involving human subjects is the prospect of discovering new ways of benefiting people's health."[8] According to U.S. federal research regulations, the risks of research must be reasonable in relation to the benefits to the subjects and the knowledge that may be gained, the latter of which is generally understood as a social benefit.[2,10] Federal regulations also require investigators to inform subjects about the benefits of the research to the subjects or others.[10]

Although there is a broad consensus that research with human subjects should benefit society, there has been relatively little discussion in the bioethics literature about specific social benefits.[11] Articles addressing social benefits tend to focus not on social benefits per se, but rather on topics related to social benefits, such as individual benefits, the ratio of risks to benefits, or the distribution of benefits.[12-16]

There is also very little discussion of social benefits in typical informed consent documents. In a random sample of 44 informed consent forms from U.S. oncology clinical trials, the average number of words describing social benefits was 19.7, as compared to 49.3 words describing individual benefits and 930 words describing risks. Five documents (11%) did not even mention how the research could benefit others. Many of the documents used only generic language to describe social benefits, such as "this research may benefit other patients in the future."[17]

What Are Social Benefits?

A "social benefit" of clinical research can be defined as a good outcome received by someone other than the research subject. A social benefit can be received by other patients with the subject's disease, various sectors of the population, or society as a whole. People can disagree about whether particular clinical research studies produce socially worthwhile results because they have different understandings of what is good for society. These different understandings often reflect disagreements about moral, political or religious values. For example, a pacifist might hold that research on vaccines to protect soldiers against biological weapons does not offer any net social benefits, because the research may lower barriers to starting wars.[11] Someone who opposes birth control would not consider research on new methods of contraception to be a social benefit, because it may increase the use of birth control. An atheist might have little interest in a study on the effects of prayer on recovery from heart surgery. A utilitarian, who believes that the good of society outweighs the good of the individual, may take a very different view of the importance of the social benefits of placebo controls in clinical trials than someone who emphasizes individual human rights and dignity.[5] As long as people disagree about fundamental moral,

political or religious values, they are likely to also disagree about the social benefits of research.

It is commonly assumed that clinical and other research that involves human beings is useful because it produces social benefits by generating knowledge with practical applications. Sometimes the road from research to practical application is clear, smooth and immediate. For example, a study on a method for reducing errors related to pharmacotherapy in hospitals could produce life-saving applications soon after it is completed. However, the road from human research to social benefits is often long, winding and uncertain.[18] For example, Phase I clinical trials on healthy subjects can be justified on the grounds that they are essential to developing new treatments that will help people who have the target diseases.[19] Yet most drugs that are tested in Phase I trials never make it to the marketplace due to lack of safety or efficacy.[20] Some studies that involve human subjects contribute to general knowledge about human biology or behavior but are not intended to yield practical results for quite some time, if ever. For example, the Human Genome Project (HGP), an effort to sequence and map the DNA in an entire human genome, was begun in 1990 and completed in 2002. Although the HGP has provided researchers with a wealth of information about human DNA, it may take several decades to translate this research into medical treatments and diagnostic tests.[21] Some of the practical applications of research with human subjects include:

- New drugs, biologics, surgical techniques, and other medical therapies
- Public health interventions, practices and policies
- Nutrition and exercise
- Psychological counseling and social work
- Social or economic policy
- Environmental or other regulations
- National security
- Law enforcement and criminal justice
- Public education
- Food, recreation and other consumer products
- Workplace safety and ergonomics
- Transportation and communication

Assessing Social Benefits

As mentioned earlier, the risks imposed on human research subjects must be justified by virtue of potential benefits for the subject or society. In other words, the risk/benefit ratio must be reasonable.[1,2,13,22] In the U.S., committees known as institutional review boards (IRBs) review and oversee research involving human subjects. Other countries have similar committees. To decide whether risks are reasonable in relation to benefits, IRBs must assess and compare risks and benefits. In the U.S., IRBs are not allowed to consider the long-term risks of research, such as possible social policy implications, but must focus on the risks and benefits to the subject and the benefits to society.[22] Because people disagree about how to compare risks and benefits, quantitative methods of comparing risks and benefits, such as cost-benefit analysis or expected utility theory, are seldom useful in making decisions about research on human subjects.[9,13] To compare risks and benefits, IRBs must therefore describe and evaluate them subjectively.

A great deal has been written about the assessment of risks to human subjects in research.[2,23] However, much less has been written about the assessment of benefits to human subjects, and even less about the assessment of social benefits. The process outlined below

can help IRBs and investigators assess social benefits systematically by answering the questions in Table 1.

Table 1: Assessing Social Benefits in Research: Key Questions

Benefits identification	What are the possible benefits to society?
Benefits estimation	What is the social significance of the benefits? How likely are the benefits to occur?
Benefits distribution	Who will receive the benefits?

Benefits Identification

The assessment of benefits has much in common with the assessment of risks. The first step of risk assessment in human subjects research is to identify the possible risks.[2,13] Likewise, the first step in benefits assessment is to identify the possible benefits. For example, will the research project help test a new medical therapy? Will it lead to a new public health intervention? Will it help to improve an educational program? Will it have important implications for social or economic policy? As we have already seen, there are many different types of benefits that a research project might produce for society.

Benefits Estimation

The next step is benefits estimation, which involves determining the social significance, if any, of the benefits and the probability that they will materialize. When estimating the social significance of a possible benefit, one may consider questions such as: Is the benefit important or trivial? Will it affect many people or only a few? Will it save human lives? Relieve suffering? Have economic impacts? Advance human knowledge? And so on. Benefits should be quantified when it is possible to do so. For example, one might estimate that a new oncology drug will extend the lives of 10,000 patients with advanced ovarian cancer by 2 years. However, it is not always possible to quantify benefits, due to insufficient knowledge or disagreements about benefits. As noted earlier, people often disagree about whether a research project has social benefits at all, or the degree of social benefits of the project.

People who agree about the social significance of possible benefits may still disagree about the probability that the benefits will materialize, due to the many factors that influence practical application. However, disagreements about probabilities need not prevent benefits assessment, since rough approximations will do in most cases. Although it would be unethical to use human subjects in research that cannot produce any benefits (individual or social), human subjects may be used when the benefits have a realistic (i.e., more than merely speculative) chance of occurring.[2] Investigators should help IRBs assess social benefits by including evidence concerning the significance and probability of social benefits in their research proposals.

Benefits Distribution

The next step in benefits assessment is to ascertain how benefits will be distributed. Questions about the distribution of the benefits of research are different from questions about the social significance of benefits because distribution questions address the fairness of the research project. In thinking about the distribution of benefits, one should ask: Who may benefit from the research? Will other patients benefit? Healthy people? School children? Soldiers? Private companies, universities, or other organizations? People in other countries? And so on. In many cases, disagreements about the social benefits of a research project center on questions about who will benefit from the project. For example, commentators and organizations have expressed the concern that many pharmaceutical clinical trials conducted in developing nations benefit people in developed nations more than they benefit

people in developing nations, because people in developing nations may not be able to afford the drugs being tested.[15,16] International codes of research ethics, such as the Helsinki Declaration and the CIOMS guidelines, have provisions that address distribution of the benefits of research. The CIOMS guidelines require research conducted in resource-poor countries to be "responsive to the health needs and the priorities of the population or community in which it is to be carried out; and any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community."[8]

Analysis of an Ongoing Controversy Concerning Social Benefits

Use of the above process can be illustrated by applying it to an ongoing controversy: testing pesticides on human subjects.[24,25]

Background

In the 1990s, several companies sponsored over a dozen experiments in the U.S. and the U.K., in which human subjects ingested small doses of pesticides. One of the purposes of the research was to generate data to convince the U.S. Environmental Protection Agency (EPA) to increase the amount of allowable levels of pesticide residues on foods, which had been reduced as the result of a law the U.S. Congress passed in 1996 requiring pesticide residue on foods to be decreased by a factor of ten, to provide extra protection for children. The companies subsequently submitted their data to the EPA, but the agency declined to accept the data until ethical and regulatory issues relating to the research were resolved. The EPA had been making its decisions concerning pesticides based on animal toxicology experiments, not on human experiments. The agency asked the National Research Council (NRC) to study the issues. In 2001, Croplife America, an agricultural industry trade association, sued the EPA for engaging in improper rule-making without public comment, and in 2003 a federal court sided with Croplife. The court ordered the EPA to issue new rules, following appropriate public comment. After the NRC completed its report, the EPA complied with the court's order and issued new rules for accepting data from human pesticide experiments sponsored by private companies in 2006.[25] The EPA's new human subjects rules have generated considerable controversy and are opposed by environmental groups.[26]

The Arguments

Environmental interest groups and other critics of the pesticide experiments argued that they were poorly designed, statistically underpowered, coercive (some experiments used company employees), dangerous to the subjects, and offered no useful social benefits.[24, 27,28,29] Other commentators, including the NRC, argued that while these particular experiments were flawed, pesticide testing on human subjects is not inherently unethical and could be carried out under stringent scientific and ethical standards.[25,28] Some of these proposed standards were that:

- Experiments should be well-designed.
- Experiments should be expected to provide information that contributes to our understanding of how pesticides affect human health and could be used by regulatory agencies to protect the public from the hazards of pesticide exposure.
- Experiments should not expose research subjects to a dose that would be expected to cause any permanent harm or damage.
- Subjects should give their fully informed consent.
- Subjects should not be members of a vulnerable group, such as children or pregnant women.

Although this dispute involved a number of different issues related to research with human subjects, much of the controversy centered on questions about the social benefits of pesticide experiments on human subjects, or lack thereof. Some opponents of the research claimed that pesticide experiments can never yield any morally worthwhile consequences for society.[27] Other opponents conceded that some experiments might produce valuable results, but that the results would not be important enough to justify intentionally exposing human subjects to pesticides.[24] Opponents were also concerned about the distribution of benefits. They argued that pesticide companies and other agribusiness interests would benefit more than consumers.[24,27,30]

Defenders of pesticide testing on human subjects argued that well-designed studies that expose people to low doses of pesticides under carefully controlled conditions could yield important knowledge about how the human body absorbs, distributes, metabolizes and eliminates pesticides, and that this knowledge could help to protect people from the harmful effects of pesticides.[25,28] The benefits of testing would outweigh the risks, provided that human subjects are not exposed a dose that would cause any permanent damage.[25]

Benefits Assessment

A systematic approach to assessing the social benefits of human pesticide testing could enhance our understanding of this controversy and point the way toward a resolution of some of the issues. By focusing on questions concerning the identification, estimation and distribution of benefits, it may be possible to pinpoint the disputants' sources of disagreement. The opposing parties may, in fact, agree on matters relating to research design, the minimization of risks, and informed consent, but may have major disagreements concerning whether the research could have social benefits and whom the research might benefit. Once questions about social benefits are separated from questions concerning other issues, opposing parties may be able to determine whether their differences of opinion can be resolved by obtaining additional information, or whether their differences stem from fundamental disagreements about moral values. Table 2 applies the benefits assessment framework described in this article to this particular dispute, in order to provide structure to the arguments above.

Table 2: Assessing Social Benefits in Pesticide Research

Benefits identification	Knowledge about how pesticides affect human beings Stricter (safer) food and pesticide regulations More cost-effective food and pesticide regulations, thereby increasing company profits and/or reducing consumer costs
Benefits estimation	Knowledge about how pesticides affect human beings has broad implications for society and public health However, this knowledge may not be very significant, since we already have safety data from animal studies that has been validated to some extent in "accidental experiments" Knowledge may (or may not) lead to safer and/or more cost-effective food and pesticide regulations would benefit many people
Benefits distribution	The general public may (or may not) benefit from stricter food and pesticide regulations Pesticide companies, farmers, farm workers, and food handlers may benefit Benefits will vary by country Organic food is unavailable to most people, especially poor and urban people

Conclusion

While few people dispute the idea that research with human subjects should produce socially worthwhile results, people often disagree about whether particular research projects actually will yield social benefits. Although considerable attention has been devoted to the assessment of subjects' risks in research, relatively little attention has been directed toward the assessment of social benefits. This article attempts to shed some light on social benefits in research. It proposes a method for examining social benefits systematically. Because so little has been written about the social benefits of research, the field should be fruitful for other investigators.

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