Community Involvement in the Ethical Review of Genetic Research: Lessons from American Indian and Alaska Native Populations

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The National Bioethics Advisory Commission has proposed that regulatory oversight for research with human subjects be extended beyond the protection of individual research participants to include the protection of social groups. To accomplish this, the commission recommends that investigators and ethics review boards *a*) work directly with community representatives to develop study methods that minimize potential group harms, *b*) discuss group implications as part of the informed consent process, and *c*) consider group harms in reporting research results. We examine the utility of these recommendations in the context of research with American Indian and Alaska Native communities. Because much attention has been given to the question of how best to consult with members of these communities in the design and conduct of research, we believe it behooves investigators to consider the lessons to be learned from research involving American Indians and Alaska Natives. After describing several difficulties surrounding the application of the commission's approach to these research contexts, we propose a research agenda to develop best practices for working with local communities in the ethical assessment of epidemiologic and environmental health research. *Key words*: ethics, indigenous populations, informed consent, participatory research, research oversight. *Environ Health Perspect* 110(suppl 2):145–148 (2002). *http://ehpnet1.niehs.nih.gov/docs/2002/suppl-2/145-148sharp/abstract.html*

Environmental health research can present challenges to institutional review boards (IRBs) and others charged with protecting the rights and welfare of research participants (*1*). Existing regulatory guidelines on research involving human subjects were developed primarily for clinical investigations, making their application to epidemiologic and community-based research problematic (*2*). Where epidemiologic studies present limited risks to participants, for example, clinical standards for informed consent may be inappropriate (*3*). Conversely, in community-based studies that present risks to all community members, existing regulatory standards focused on the protection of individual research subjects may be insufficient (*4*).

Concerns of this second sort—that is, concerns about research-related harm to identifiable communities—have been spurred on by advances in genetic technologies (*5*). Studies of human genetic variation can present risks to all members of a social group, not just those individuals who choose to participate in research (*6*). Findings that associate an ethnic group with a genetic predisposition to disease, for example, could lead to group discrimination or stigmatization (*7*). Such risks have been the subject of much discussion surrounding studies of the so-called breast cancer genes *BRCA1* and *BRCA2*, as some polymorphisms in these genes appear to be more common among persons of Jewish ancestry, specifically Ashkenazi Jews (*8*). This finding creates the possibility that all Ashkenazi Jews may be asked to pay higher insurance premiums or face other more subtle forms of discrimination on the basis of the apparent association between these genetic variants and increased risk of developing breast cancer (*9*). These collective risks are not unique to genetic research, however (*10*). Studies of population-specific characteristics, research on stigmatizing behaviors in a particular community, or the identification of local environmental contaminants can present risks to all members of a study population. Nonetheless, current federal regulations governing research with human subjects do not require researchers or ethics review boards to consider potential harm to nonparticipants (*11*).

In response to this apparent regulatory gap, the National Bioethics Advisory Commission (NBAC), a presidential commission on the protection of human subjects in research, has proposed that regulatory oversight be extended to include the protection of social groups (*12*). The NBAC recommendations, presented in the report, "Research Involving Human Biological Materials: Ethical Issues and Policy Guidance," maintain that in addition to considering potential risks to individual research volunteers, investigators and review boards should consider how to minimize group harms (Recommendation [Rec.] 17). When significant risk to an identifiable community can be identified before a study has begun, the commission suggests that researchers work directly with community representatives to develop study methods that minimize the potential for harm (Rec. 17) and discuss collective risks as part of the informed consent process (Rec. 18). The commission also recommends that in reporting research results, investigators and journal editors consider potential implications for social groups (Rec. 19).

The NBAC recommendations, if adopted by investigators and ethics review committees, would significantly extend regulatory perspectives beyond their present focus on risks to individual participants. Like other commentators on the protection of human subjects in research (*13–15*), we support this regulatory expansion. Developing additional oversight policies designed to protect identifiable groups is an important part of acknowledging the broader social implications of contemporary biomedical research and the need to think more expansively about the consequences of research practices. Nonetheless, we also recognize that soliciting community views regarding ethical conduct and responsible research practices can be difficult (*16,17*).

In this article we describe some of the benefits and challenges of directly involving communities in the ethical review of research. The analysis we propose focuses on genetic research with American Indian and Alaska Native communities, as several participatory models have been tried in these contexts (*18*). We believe these experiences with indigenous communities can illuminate broader ethical issues and practical challenges present in research studies involving other historically disadvantaged communities. Because there have been few successful examples of direct consultation with communities in the design of appropriate ethical

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protections, we also propose a research agenda to develop best practices for consulting local communities regarding the ethical conduct of epidemiologic and environmental health research.

Protecting Communities from Research-Related Harm

As noted above, existing regulatory policies and ethical guidelines concentrate on immediate risks to individual study participants and do not require researchers or ethics review boards to consider potential harms to nonparticipants (*11,19*). Thus, the recommendations proposed by the presidential commission represent a significant departure from current regulatory perspectives. Nonetheless, a compelling case can be made in support of the idea that when research studies place nonparticipating members of social groups at risk, these potential harms should be considered by persons conducting, reviewing, and participating in research (*4*). The potential benefits of addressing collective research-related harms include a more complete appreciation of the risks and benefits of research, increased public confidence in the research enterprise, and the promotion of increased diversity among research participants. Considering potential group harms also demonstrates respect for the diverse social and cultural traditions of many communities and acknowledges that research findings can disrupt social relationships within and between communities. These considerations suggest that protecting identifiable communities from research-related harm is a moral imperative in conducting and reviewing research (*20*).

Under current federal regulations, ethics review boards are required to include at least one community representative. There are times, however, when this is inadequate and the involvement of community representatives requires more elaborate consultation with members of the communities placed at risk, as often is the case in research with American Indian and Alaska Native communities and studies conducted outside the United States (*21,22*). In many cases, directly involving members of identifiable social groups, particularly members of historically underserved communities (e.g., communities of color, patient communities, or occupational communities), in the ethical review of research can help identify local risks that otherwise might go unnoticed.

A recent study of the effects of polychlorinated biphenyls on the health of American Indians living along the St. Lawrence River illustrates some of the potential benefits (and drawbacks) of soliciting community perspectives on the ethical conduct of environmental health research (*23*). The cooperative relationship between the Akwesasne people and scientists at State University of New York (SUNY; Albany, NY) was based on three principles: mutual respect, mutual equity, and mutual empowerment (*24*). These guiding principles were jointly agreed upon by community representatives and members of the research team from SUNY. Approval of the research was obtained from both the Akwesasne community and individual research participants. Project goals were determined jointly and designed to maximize data quality while simultaneously minimizing the disruption of community activities. Community members were involved in the project as research assistants, and after receiving proper training, these research assistants collected tissue samples and conducted interviews. The SUNY researchers believed the success of their research project was based largely upon the early stage at which the cooperative relationship with the Akwesasne developed, the formal approval of the study given by the Akwesasne, the participation of community members as field staff, the involvement of community partners in communicating research results, and shared authorship on the publication of research papers and reports (*25*).

The success of projects like this illustrates how the commission's proposals might be implemented and what benefits might be expected (*26*). Nonetheless, we should acknowledge the limitations of this approach. In the following sections we highlight two difficulties facing proposals to expand the scope of regulatory oversight to include the protection of social groups: how best to anticipate potential research-related harms to identifiable communities, and how best to manage the many practical challenges of expanding an already overburdened regulatory system. We again examine these two challenges in the context of research with American Indian and Alaska Native communities, as research with indigenous communities, particularly genetic research, has received considerable attention from commentators on ethical issues in research. Although it would be a mistake to naïvely generalize from these research settings to studies involving other identifiable communities where very different social relationships may characterize collective interests and concerns about biomedical and genetic research, we believe it behooves us to consider the lessons to be learned from past experience with American Indian and Alaska Native communities.

Anticipating and Assessing the Significance of Group Harms

No protectionist policies or regulatory structures can fully embody their guiding moral principles or anticipate all ethical issues that might emerge over the course of a research study (*27*). Nevertheless, the protection of nonparticipants and socially identifiable communities is particularly difficult to capture in regulatory language because of problems surrounding the definition of an affected community (*28–31*). Often, at the beginning of a study it is not clear which particular social groups will be affected by the research—much less how they might be affected. Similarly, there are numerous challenges surrounding how best to capture abstract notions such as "respect for communities" in formal research guidelines. As a result, investigators sincerely committed to conducting research in an ethical and respectful manner (and who are familiar with guidelines for ethical conduct in research) can nonetheless struggle with how to apply these guidelines and principles in the context of their studies. These and related problems are evident when one considers the commission's recommendations more carefully.

The commission's recommendations hinge on the ability of researchers or IRB members to anticipate collective research-related harms prospectively. Consider Rec. 17, the most detailed of the commission's proposals pertaining to group risks (*12*):

> Research using stored human biological materials, even when not potentially harmful to individuals from whom the samples are taken, may be potentially harmful to groups associated with the individual. *To the extent such potential harms can be anticipated* [emphasis added], investigators should to the extent possible plan their research so as to minimize such harm and should consult, when appropriate, representatives of the relevant groups regarding study design. In addition, when research on unlinked samples that poses a significant risk of group harm is otherwise eligible for exemption from IRB review, the exemption should not be granted if IRB review might help the investigator to design the study in such a way as to avoid those harms.

Although the type of community consultation proposed by the commission is useful in addressing collective risks that have been identified prior to the start of a study, this approach is limited by the fact that even experienced researchers and IRB members can fail to anticipate significant research-related risks before a study begins (*4*). For example, researchers and reviewers can find it especially difficult to identify risks involving the disruption of social relationships within communities of which they have little knowledge or familiarity. Similarly, risks that researchers or review boards view as minor may be viewed by study participants (or other members of the group placed at risk) as substantial.

These difficulties can be seen in two examples from research with American

Indian and Alaska Native communities (*32*). Studies of population histories and patterns of population migration can affect the legal standing of claims made by sovereign Native American tribes for the repatriation of human remains or the return of tribal artifacts held in federal museums (*33*). Researchers unfamiliar with these repatriation efforts are unlikely to anticipate such potential risks, although they may be quite salient to members of those communities. Similarly, studies involving genetic markers found more commonly in American Indian and Alaska Native populations can disrupt the social equilibrium that exists within a community by revealing that participants and their families are more "European" in ancestry than they themselves believe. Such findings have social consequences in many indigenous communities, as the ability to occupy a political office often is contingent upon establishing one's ancestry as sufficiently "Native" (*34*). Here too, it is unlikely that researchers who are not themselves members of these communities could anticipate such research-related risks or fully appreciate their significance for the community and its members.

The challenge of identifying potential group harms is especially difficult when researchers never have direct contact with members of the study population (*35,36*). Because many types of environmental health research can be done using information or biological samples that were collected for unrelated purposes (e.g., epidemiologic studies based on previous exposure assessments), researchers and the individuals from whom information or samples have been collected may never interact with each other. Additionally, as new risks may present themselves as the research progresses, it is important that consultation with members of study populations continue throughout the process of data collection, analysis, and reporting.

These difficulties highlight the importance of early and ongoing involvement of community representatives in the review of research proposals. To the extent that the commission's proposal depends upon the ability to anticipate group harms at the beginning of a research study, and many local or population-specific risks may still go unnoticed if there is significant sociocultural distance between members of the research team and study participants, the commission's recommendations are problematic. This is unfortunate, as it is precisely in those circumstances where collective risks are difficult to identify prospectively that the involvement of local study populations is most critical for minimizing potential harm.

Expanding the Scope of Regulatory Oversight: Future Research Needs

The expansion of regulatory oversight to include the protection of social groups would have significant consequences for a regulatory system that many believe is overburdened and undersupported (*17,37*). Thus, it is understandable why the commission attempted to limit community involvement in the ethical review of research to those studies in which significant group harms could be anticipated. Interestingly, applying this anticipatory principle would not only preclude the involvement of community representatives from some studies in which community consultation is critical for the identification of collective risks (as noted above) but would expand the scope of regulatory oversight to include many types of research currently viewed as exempt (e.g., research using anonymous samples from identifiable populations). This highlights a second challenge facing proposals to involve community members in the ethical review of research, namely, how to define the range of research studies where community consultation is needed.

One way to address this practical challenge is to concentrate on involving community representatives at the earliest possible stage in the research process. If this approach is used, attention should be given to the different methods through which community views might be solicited. Because presumably some studies require more involved community participation than others (because of the level of collective risk presented), the question becomes which features of the community and/or study can be used to determine the nature and extent of this involvement. For example, researchers might solicit input from participating communities through relatively informal mechanisms, through the identification of a subset of community members that are broadly representative of community interests, or by actively involving communities as research partners (*4*). In addition, as the balance of research benefit and harm can change over the course of an investigation, it is important to assess the effectiveness of various oversight mechanisms in protecting group interests throughout the entire duration of a research study. Examining the respective merits and problems with various approaches to community consultation and partnership and describing best practices with regard to each are essential to the continued development of policy in this area.

Of particular importance are empirical studies assessing how various social, religious, economic, cultural, and political communities view risks associated with research. Presently, little is known about how members of various underserved or marginalized communities weigh individual research risks against group risks, how salient collective risks are in relation to other risks encountered in daily life, or how individuals attempt to reconcile potential conflicts that may exist between personal interests in research participation and collective opposition to proposed research. Because not all collective harms carry the same weight—that is, some group harms are more significant than others—it is important to assess how members of historically underserved communities evaluate collective research-related harms. Moreover, without such information it will be difficult, if not impossible, to tailor oversight processes to specific communities.

There also is need for additional ethical and philosophical analysis of the goals of involving community representatives in the review of research. Whereas members of the presidential commission appear to view community involvement as a supplemental method of identifying risks, others have described the involvement of community representatives as something akin to seeking individual informed consent (*38*). Proponents of this second perspective maintain that there are reasons for involving community representatives in the review of research that are distinct from efforts to protect such groups. For example, seeking community advice can show respect for different cultural perspectives on how to balance individual and group interests in research. Further conceptual analysis is necessary to determine whether these are distinct value commitments and how the various goals of community consultation are served to greater or lesser degrees by different approaches to working with community representatives.

Another key area in which additional conceptual analysis is much needed concerns the notion of collective harm. Like individual harms, research-related harms to communities can be of two sorts—tangible and dignitary. Tangible collective harms include discrimination or stigmatization of community members, loss of social opportunities, and so forth. Dignitary harms to communities, by contrast, involve violations of collective rights or disrespectful treatment of the affected community. For example, using stored biological materials in a manner that the community would find morally objectionable can constitute a dignitary harm not only to the individuals who contributed those materials but to the community as a whole. How to assess the ethical salience of dignitary harms to communities and how to determine which of these harms are significant and which are not remains largely unexplored in the philosophical literature on community consultation in research.

In the final analysis, however, it is important to acknowledge in a very clear and candid way that expanding the scope of federal oversight to include the protection of identifiable communities will require a substantial investment of resources. Indeed, it may be the case that the additional costs (and practical difficulties) of developing these protections will result in fewer research studies being conducted, raising difficult issues regarding the proper balance between protectionist concerns and concerns for the advancement of knowledge. Although considerations of cost and practicability are inevitable features of biomedical research, we hope that these concerns are not allowed to trump discussions surrounding the development of new regulatory policies. Additional empirical data and conceptual analyses will be critical to resolving these questions about when some type of community consultation is needed and how it can be best carried out in the context of specific communities.

Conclusion

We have identified several challenges facing the expansion of regulatory oversight to include the protection of identifiable communities. Sociocultural distance between researchers and members of study populations can make it difficult to identify and fully appreciate the significance of collective research-related risks. This makes regulatory proposals based on the anticipation of collective risks problematic. Implementing new oversight requirements also would place significant strain on an already overburdened regulatory system. Thus, how to accomplish this regulatory expansion is complicated by the need to develop clear principles for determining when additional oversight mechanisms should apply.

These difficulties suggest that protecting social groups from research-related harm is far more nuanced than the analysis suggested by the commission. Nevertheless, the commission should be commended for its efforts. Their recommendations are the first substantive attempt by a national advisory group to advance regulatory protections beyond their current focus on individual risks and benefits. In proposing this regulatory expansion, the commission has raised a number of profound questions about how to balance individual and collective interests in research, as well as questions about what the goals of research guidelines should be with regard to meeting the needs of historically underserved communities. Thus, perhaps the most significant contribution of the NBAC report will be its promotion of continuing dialogue on the identification of risks to social groups, irrespective of whether investigators or regulatory agencies choose to adopt the commission's recommendations.

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