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360 Degrees of Human Subjects Protections in Community Engaged Research

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Abstract

With the introduction of the new National Institutes of Health Roadmap in 2003, there has been a growing emphasis on translational research. Translational research challenges current human subjects protections guidelines that were written in the 1970s and were focused on the protection of the individual participant in a clinical drug trial. Community engagement requires a critical examination of the range of risks that may arise when communities are both participants and partners in research in order to promote appropriate and effective protection of human subjects as individuals and members of communities. Given that the principal investigator has ultimate responsibility for ensuring the ethical integrity of the research, researchers should be aware of the human subjects protections delineated in the federal regulations that must be fulfilled and the other entities that can help ensure human subjects protections.

INTRODUCTION

In the wake of numerous abuses of human subjects in the United States including the United States Public Health Service Syphilis Study at Tuskegee (1) and the Willowbrook Hepatitis Studies (2). Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) in 1974. In its 1979 Belmont Report, the National Commission identified the underlying ethical principles that would be the foundation for human subjects protections (HSPs) in biomedical and behavioral research (3). The three principles—respect for persons, beneficence (that is, actions to advance wellbeing and minimize harms and risks, and justice—focused on protecting the rights of the individual subject. The Belmont Report and other reports by the National Commission were the basis for the Federal Regulations for the Protection of Human Subjects (Fed Regs) that were first written in the 1980s and with minimal modification, remain the basis for HSP in the United States today (4).

In the 30 years since the Belmont Report, the role of the community in research has evolved and translational research is now frequently performed with the active engagement of individuals and communities as research partners rather than merely upon them (5). The

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Witness for Wellness (W4W) project is a very successful case-study of this approach in which a community based agency called HAAF (Healthy African-American Families) helped foster a collaborative academic-community participatory partnership focused on reducing racial and ethnic disparities in mental health care (6). While the academic partners suggested the initial research topic, HAAF served as both community partner and project host by organizing a community-based depression conference that sought to examine “depression issues in racial and ethnic minority communities and to discover, refine, and promote the adoption of evidence-based interventions in these communities.”(6) The qualitative data gathered at the conference was then used by the academic-community partnership for collaborative agenda-setting and for defining and implementing next research steps (6).

Community engagement in research was spurred on both by the need to develop effective means to translate research discoveries that would be acceptable and adopted by individuals and communities and by individuals and communities that realized the value of the data, samples, and information that they provided at all stages of discovery and who therefore demanded to engage as both partners and participants (5). With the introduction of the National Institutes of Health (NIH) Roadmap in 2003 (7), the emphasis on translational research has gained more traction as funding from the NIH for academic medical centers evolved from supporting General Clinical Research Centers (GCRCs) to supporting Clinical and Translational Science Award (CTSA) programs with their greater community engagement (8).

Collaboration with communities in research occurs along a continuum, the whole of which is called Community-Engaged Research (CEnR). In 2008, the National Center for Research Resources of the NIH funded a supplement to the University of Chicago CTSA to develop a research ethics framework for HSP for CEnR. The final products were three manuscripts approved by the CTSA Consortium Publications Committee that were published in the *Journal of Empirical Research on Human Research Ethics* (9–11). The first manuscript describes a research ethics framework for CEnR. The other two manuscripts provide points to consider for HSP entities and for community-academic partnerships regarding the broader conception of risks that CEnR entails. Below are highlights from this project to provide an overview of HSP in CEnR for those involved in translational research and HSP oversight.

SEVEN ENTITIES THAT PROVIDE HSP

Although most academic researchers equate HSP with their institutional review board (IRB), as many as 7 distinct entities may be involved with the protection of human subjects: (i) the investigator, (ii) the IRB, (iii) the Data and Safety Monitoring Plan (DSMP), (iv) the Conflict of Interest (COI) Committee, (v) the Research Ethics Consultation (REC) program, (vi) the Research Subject Advocacy (RSA) program, and (vii) the Community Advisory Board (CAB) (11). The first three (the investigator, the IRB, and the DSMP) are enumerated in the Fed Regs.

First, the investigator has primary responsibility for the protection of human subjects enrolled in his or her research. Second, all research must have a DSMP, which should

outline how adverse events will be addressed, when review and possible modification of the methodology might be required, and when, if ever, interim data will be examined. The constitution of a Data Safety Monitoring Committee as part of the DSMP is usually reserved for clinical trials in which the endpoints are morbidity and mortality. A more informal monitoring plan is acceptable for CEnR that employs a broad range of low-risk interventions including social, behavioral, and environmental modifications with only a subset including any invasive biomedical interventions.

The structure, membership, and responsibilities of an IRB are delineated in the Federal Regulations. The Fed Regs also place constraints on the IRB, restricting the IRB to “consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research JS comment: WHY ADD THIS?)” (42). They also state that “The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility” (4). These statements are not meant to suggest that these concerns are not legitimate, only that they are not within the purview of the IRB and should be addressed by one of the other HSP entities.

One such entity that may consider these other risks is the Research Subject Advocate program, which was originally established for NIH-funded GCRCs (12). With the move from the GCRC to the CTSA, some institutions have maintained the RSA program solely within their clinical research centers, others have expanded the scope of the RSA to include outreach and monitoring in CEnR, and still others have dismantled their RSA program, incorporating the RSA functions into the responsibilities of other HSP entities.

REC is another entity that can provide HSP. REC entails a collaboration between investigators and research ethicists in the design and implementation of a research project that poses new or complex ethical issues in HSP. REC was first described in the literature in 1989 when a surgical team consulted with an ethics team to develop a protocol to remove part of a parent’s liver that would serve as a graft for a child with liver failure (13). Since the establishment of CTSAs, the number of REC programs has expanded, although they are not a mandatory component of CTSA programs and not all CTSA programs provide this service.

COI committees are another source of HSP. Although such a committee is not required by the Fed Regs, both the Association of American Universities and the Association of American Medical Colleges recommend that institutions have a written COI policy with a focus on disclosure and management, and in certain circumstances the prohibition of research at a particular institution or the performance of such research by a particular researcher (14, 15). For example, a COI committee at an institution may decide that it should not be a trial site for a phase 3 clinical trial for a drug developed by its own faculty member, particularly when the faculty member and the institution have a large financial interest in the drug’s success. (16) Rather, the COI committee may decide that there is a conflict or the appearance of a conflict in its participation and proscribe active participation in the trial.(17).

As more communities engage in research partnerships, some have considered what protection they should provide their members. Although the Fed Regs require community membership on an institution's IRB, current sources of HSP emanate mainly from the academic institutions. Communities may want to provide their own source of HSP, ranging from oversight by an established political body to the creation of a community IRB or, less formally, by the creation of a CAB. Whereas one form may fit in a specific community—e.g., the Indian Health Service has established its own IRB to ensure culturally-sensitive oversight of the ethical conduct of research on Native American communities—other communities may prefer the greater flexibility that a CAB provides.

THE NINE FUNCTIONS THAT SERVE AS THE BACKBONE OF AN HSP PROGRAM

The backbone of an HSP program is the fulfillment of nine functions that are delineated in the Fed Regs (4): (i) the risks of the research are minimized; (ii) the risks to subjects are reasonable in relation to anticipated benefits; (iii) the selection of subjects is fair; (iv) each participant gives a voluntary and informed consent; (v) when appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects; (vi) there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data; (vii) conflicts of interest are transparent and appropriately managed; (viii) consideration is given to what additional protections, if any, are needed for vulnerable populations; and (ix) proper training in human subjects protections is provided for research personnel.

The 9 functions have traditionally been interpreted solely with respect to individual participants, overlooking the risks (and benefits) that may occur to groups and communities. Research risks include both process risks (risks that occur as part of research participation) and outcome risks (risks that occur because the research occurred). For example, process risks to participants include the risk of bruising from a blood test or the side effects of a drug. Outcome risks to participants include the risk of learning one's carrier status for a late-onset genetic condition. There are also risks to the research participant's moral agency—that is, the authority of an individual to decide for him- or herself whether to participate in research. For example, if the researchers fail to respect the participant's wishes with respect to enrollment or withdrawal, they breach the participant's agency.

Both groups and communities may also be exposed to research risks in CEnR. To understand these risks, one must understand the difference between a group and a community (18). Although it is common to hear people talk about the "African American community" or the "HIV community," these entities are not established communities with internal structure, but groups of individuals with a shared characteristic (race/ethnicity or disease, respectively). Individuals may belong to many such groups, some of which they belong to voluntarily, and others involuntarily, some of which they embrace, and others which are imposed upon them. A community, by contrast, is a structured group—a group with its own social organization, often with identifiable leaders. Some communities have existed for centuries, others are newly formed, and others still are formed only for service delivery. Within a community, there is often a defined leadership with whom researchers

may seek collaboration. To collaborate with an unstructured group, the group (or at least a subset of the group) must be “structured.” The structure may come externally (e.g., by partnering with a community based organization) or internally (e.g., by empowering the group to organize and establish leadership). In CEnR, the term “community” refers both to pre-existing structured groups (established communities) as well as to unstructured groups that are structured for the purpose of the research either by external or internal sources. Individual members of long-established communities and members of groups structured for research participation can both be harmed by research participation, and both “communities” can be harmed by research findings, including for example, risks to group identity and social standing. However, it is only established communities that can experience the loss of sociopolitical authority and experience risks to well-established structure and function.

Table 1 delineates the 3 categories of risk in CEnR from the perspective of the individual participant (A-level risks) and from the perspective of the groups to which the individual belongs. When a community engages as a research partner, these risks apply to the community itself (C-level risks). For example, process risks include the risk of group dissension if some of the members support research participation and others do not. Outcome risks include the risk of social stigma if a certain trait is found to be more common in an ethnic or religious community. There are also risks to the moral agency of the community if the researchers fail to respect the community’s decision regarding participation, or if the researchers act so as to denigrate the community with respect to its peers.

B-level risks occur at the intersection between the individual and the groups in which he or she is a member. For example, imagine the case in which a group decides to participate in a research study but the individual does not want to do so. Although the individual has the right not to participate, he or she may experience some degree of peer pressure that poses threats to individual agency. And even if the individual does not participate, the findings may be ascribed to him or her as an individual by association. Thus, there are both process and outcome risks to the individual participants and to the group, and some of these outcome risks may implicate non-participants.

Using this expanded conception of research risks, the discussion of the nine key functions must be revised to account for the additional types of risks and harms that may arise from research partnerships, both to the individuals who participate and the groups in which they are members, as well as to non-participant community members.

CONCLUDING THOUGHTS

Risks to research participants occur at the level of the individual, the individual as a member of a group, or the group. These risks include process, outcome, and agency risks that may be dynamic over the course of a partnership. To ensure that the rights and safety of all subjects are promoted, and that the benefit: risk ratio is favorable, a variety of HSP mechanisms exist. Protection is best achieved if these mechanisms are coordinated to ensure that no gaps exist, to minimize unnecessary redundancy, and to provide checks and balances between the different entities of HSP and the nine functions that they must realize.

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Fig. 1.

Table 1

Risks to well-being and agency at the individual and group level.

	Process Risks to Well-Being	Outcome Risks to Well-Being	Risks to Agency
Individual (A-level)	Physical and psychosocial risks of the research interaction	Physical and psychosocial risks of research findings	Risk of undermining personal autonomy/authority
Individual by group association (B-level)	Physical and psychosocial identity risks of the research interaction	Physical and psychosocial identity risks of research findings	Risk of group decisions undermining personal autonomy/authority Risk of individual decisions undermining group autonomy/authority
Community (C-level)	Risks to group's structure and function because of engagement in research	Risks to group's structure and function because of research findings	Risk of undermining the group's moral and sociopolitical authority