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Back to the Rough Ground: Working in International HIV Prevention as Ethical Debates Continue

We are in a period of ethical uncertainty regarding the design and conduct of biomedical and public health research in developing countries.[1,2] While some of the assumptions and practices associated with this research warrant questioning, doing so has resulted in some conflicting guidance and opinion about when and how this research is appropriate. At the same time, the HIV/AIDS epidemic has surged, especially among populations in the developing world, making even more urgent the need for proven methods of prevention and treatment of the disease.[3]

The HIV Prevention Trials Network (HPTN) constitutes one of the major U.S.-based sponsors of HIV prevention research in both the U.S. and international settings (see www.hptn.org). To accomplish its mission, the HPTN must navigate a morally defensible path between ethical uncertainty about research and the public health imperative of halting a global epidemic. Tasked with addressing this need, the HPTN Ethics Working Group commissioned the authors to draft an ethics guidance document that would be responsive to the complexity of the network and the types of research it conducts. Here we describe the process we are using to perform this task.

The Rough Ground of HPTN Research

The first step in the process of drafting a practical guidance document entailed gaining an understanding of the structure and culture of the research network. The HPTN consists of six science working groups that have primary responsibility for establishing the network's research agenda and each taking unique approaches toward HIV prevention research. The Antiretroviral Therapy Working Group develops and examines strategies in which antiretroviral therapy can be used to reduce the sexual or parenteral transmission of HIV. The Microbicide Science Working Group focuses on testing topical microbicides, that is, antimicrobial agents formulated for application to the surface of the vagina or rectum to prevent HIV transmission during sexual intercourse. The Substance Use Science Working Group focuses on HIV prevention among drug-using populations. The Behavioral Science Working Group focuses on the role of sexual behavior and prevention. The Perinatal Science Working Group focuses on preventing HIV transmission from mothers to their children. The STD Control Science Working Group focuses on sexually transmitted diseases as important cofactors in acquisition and transmission of HIV. In addition to the science working groups, the HPTN includes a Community Working Group and regional subgroups to facilitate partnership among researchers and communities by advocating for community issues within the network, identifying priority community issues, strategically planning for community participation at all levels within the network, and documenting the participatory process.

The complexity of the HPTN structure and an already intricate review process place a premium on integrating specific actions needed to implement the ethics guidance with existing procedures wherever possible. Mechanisms for ethical review, oversight, and accountability exist at multiple levels, including HPTN-specific procedures, National Institutes of Health procedures, U.S. regulatory requirements for human subjects protections, and host country ethics committee reviews. The guidance document must support decisionmaking that will satisfy a broad range of requirements rather than impose a set of inflexible, prescriptive rules. In fact, the document should serve as a map for navigating existing, multiple requirements in a thoughtful, responsive,and consistent manner.

The guidance must also reflect the issues specific to prevention research and a public health mission, though

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the ethical implications of this research and public health practice are only now being explored in a systematic way. [4,5] Participants in prevention research are generally healthy, and the likelihood of direct personal benefit from trial participation is usually less than that found for research on therapies. However, the community-wide potential for benefit may be substantial. The extent to which individual risks can or should be balanced against community level benefits in public health research is an important concern in the design of much HPTN research.

Finally, the guidance must respect and be responsive to a wide divergence of local contexts and cultures. An absolutist approach risks generating harm through insensitivity to the needs of people in unique circumstances, while a relativistic stance runs the risk of fostering exploitation of repressive or discriminatory cultural norms and traditions in order to expedite the research agendas of outsiders. Thus the guidance needs to be culturally sensitive and responsive to local conditions, yet nonetheless grounded in fundamental ethical principles.

The Approach

To develop guidance equipped to face these challenges, we first reviewed the results of an email-based survey and ad hoc interviews of a subset of HPTN collaborators around the world asking them to identify the types of ethical issues that they encountered. This was supplemented by a review of HPTN protocols, both in development and in the field, and the procedures used for managing the network. We then reviewed international ethical guidance documents and the U.S. federal rules regarding the oversight of research. Ongoing conversations with members of the Ethics Working Group and science working groups and visits by one of the us (Kathleen MacQueen) to three HPTN sites in Africa provided further depth.

Based on the information and perspectives we obtained, we developed a set of obligations that focused on process and participation rather than prescription. Many of the obligations are procedural, in that they describe procedures to be used to ensure that research is designed and conducted in an ethically appropriate fashion and is aimed at promoting the welfare of HPTN research participants and communities. For example, the guidance for establishing standards for health care for research participants describe procedures for delineating care directly associated with research outcomes, for involving stakeholders in decisions regarding care to be provided solely as a research benefit, and for balancing factors related to levels of care in the control arm of a trial. Similarly, given the need for consensus regarding some of the ethical aspects of public health research, emphasis is placed on participatory approaches that bring stakeholders together in discussion leading to consensus.

We recognize that in some cases, the procedures to be followed may not guarantee that the ethically most desirable outcomes will be achieved. While this inability to guarantee desirable outcomes does not prevent the research from going forward, it is obviously morally preferable to make efforts toward their achievement. For example, researchers cannot be held accountable for the failure of host country governments to implement successful research results but they can build partnerships with Ministries of Health, international aid and development organizations, foundations, non-governmental organizations, pharmaceutical companies, and others who could facilitate the transfer of research benefits to host countries that enhance the potential translation of such results. In other cases, the actions aim toward enhancing conditions to promote the health of all, representing domains where creativity, partnership, and persistence are needed to more closely link HPTN research to HIV prevention practice specifically and public health practice more broadly. For example, there may be opportunities for researchers to contribute to the improvement of local conditions through advocacy for and fostering of relationships to bring in new resources for health care in the community. Discussion around such cases with HPTN collaborators revealed both a desire to strive for these desirable or supererogatory outcomes and a concern that publicly proclaiming such outcomes as goals and then failing to achieve them would result in a backlash of criticism that could undermine HPTN research and its primary aims as a whole. In this regard, we have found it important to stress that the document is not intended to carry the weight of regulatory authority. Rather, it emphasizes mutual accountability among peers and the thoughtful translation of ethical concept into action. The goal is to foster best efforts and best practices by raising awareness of ethical considerations, engaging collaborators at all levels in dialog about those considerations, and facilitating ethical decision-making at key points in the research process.

While we have taken the lead on the initial draft of the document, we have incorporated commentary and suggestions from the members of the HPTN Ethics

Working Group, and at the time of this writing are undertaking additional revisions based on internal reviews. Over the next year the document will continue to evolve in an iterative fashion as it is vetted both within and outside of the HPTN, and especially as it is applied to cases on the ground. We are now working with HPTN protocol teams to ensure that the guidance can be translated into practical, achievable guidelines for implementation. Ongoing critique and evaluation both within and outside the HPTN will be an essential component of the maturation and ultimate utility of this guidance.

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