Legal and Ethical Values in the Resolution of Research-Related Disputes: How Can IRBs Respond to Participant Complaints?
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Legal and Ethical Values in the Resolution of Research-Related Disputes: How Can IRBs Respond to Participant Complaints?

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ABSTRACT: **under US federal regulations,** participants providing informed consent must receive information regarding whom to contact in case of a research-related injury or complaint. Although informed consent processes routinely direct participants to contact institutional review boards (IRBs) with questions or concerns, there has been little empirical study of the ways in which IRBs act to resolve participants' research-related complaints. This article explores available literature on participant complaints, considers the responsibilities of IRBs in dispute resolution, and outlines a research agenda. As a case study, this review considers disputes arising from HIV/AIDS research, focusing on novel issues arising from biomedical HIV prevention trials.

KEY WORDS: dispute resolution, participant complaint, institutional review board, research-related injury.

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- "If you have any complaints about the study, you may contact the IRB."
- "If you would like to talk with someone other than the researchers to discuss problems or concerns … or to discuss your rights as a research participant, you may contact the IRB."
- "If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the IRB."

These statements, taken verbatim from informed consent forms at research institutions, are familiar language to anyone involved in human subjects research. Institutional review boards (IRBs), principal investigators (PIs), and study sponsors make every effort to ensure that research protocols are scientifically and ethically sound, and that any risks to participants are "reasonable in relation to anticipated benefits … and [in relation to] the importance of the knowledge that may reasonably expected to result" (45 C.F.R. § 46.111(a)(2), 2012). But despite these efforts, human subjects protocols may give rise to a variety of grievances brought against investigators or research institutions. Unlike prior research that has focused on researcher-IRB conflicts, this article is primarily concerned with research-related complaints made by participants, who may experience confusion, distress, and harm when the experience of research does not meet their expectations.

A case study from HIV prevention illuminates some of the difficulties in resolving research-related disputes:

> Approximately ten years ago, international protests contributed to the early closure of two of the first placebo-controlled trials of antiretroviral pre-exposure prophylaxis (PrEP)—oral pills for preventing HIV infection in uninfected people (Editorial, 2004; Global Campaign for Microbicides, 2009; Grant et al., 2005; Haire, 2011; McGrory, Irvin, & Heise, 2009; Mills et al., 2005; Singh & Mills, 2005). One of these trials took place in Cameroon; the design was to enroll healthy adult women with multiple sex partners, including female sex workers, and to randomize these women to receive either placebos or antiretroviral pills intended to reduce the risk of acquiring HIV. Endpoints included the incidence of HIV infection in each group. Before enrollment began, the trial came to the attention of the international HIV activist group Act-Up Paris, as well as the local Cameroonian activism group REDS. Advocates in both groups identified concerns about the protocol, including the lack of provision of female condoms and the lack of a formalized plan to provide antiretroviral treatment to participants who acquired HIV during the trial. The activists' attempts to resolve these issues through direct conversation with the study team were unsuccessful, leading them to engage international media and organize protests at the International AIDS Conference and the Cameroonian embassy in Paris. The ensuing media

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> attention was unwelcome for some trial participants; for example, one participant complained to the researchers that she had been contacted directly by a reporter. Intense scrutiny eventually prompted the Cameroon Ministry of Public Health to suspend the study midway through enrollment; investigators formally discontinued the protocol several months later (McGrory et al., 2009).

A detailed report of the Cameroon case study chronicles unsuccessful, ad hoc efforts to resolve the activists' complaints without a planned process for dispute resolution (McGrory et al., 2009). Subsequent interviews with stakeholders found that the activists perceived researchers to be unresponsive to their concerns, while the researchers believed that they had done everything within their control. As the report notes, "[The activists'] inability to get the study team to respond made them feel that they were not being taken seriously and was a key factor in their continuing efforts to interrupt the trial" (ibid., p. 33). The role of the IRB in resolving the dispute appears to have been minor; although the study was approved by the National Ethics Committee of Cameroon, the report mentioned only one discussion between the committee head and the activists.

Overall, this episode may represent a procedural failure that affected not only one trial, but the entire program of early PrEP research. Even if it was impossible for the study team to make the activists' recommended changes, the perceived absence of a dispute resolution *process* that allowed for voice, trust, respect, and a neutral decision (i.e., a lack of procedural justice—Hollander-Blumoff, 2010; Hollander-Blumoff & Tyler, 2011) may have been even more damaging. Although this case study is more focused on complaints made by third parties (activists) than by participants, it demonstrates the essential need for research institutions to plan for complaints and their resolution.

Background

A Role for IRBs in Dispute Resolution?

IRBs reviewing informed consent processes in the United States are subject to regulatory and ethical duties to ensure that participants have recourse in the event of a research-related complaint, particularly a complaint alleging injury. For example, the US Code of Federal Regulations requires IRBs to ensure that participants receive an "explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject" (45 C.F.R. § 46.116(a)(7), 2012). IRBs typically ensure that this requirement is fulfilled by directing complaints back to the IRB itself (Klitzman, 2011). The Office for Human Research Protections (OHRP, part of the US Department of Health & Human Services [DHHS]) also suggests that questions about the rights of research subjects be directed to "the IRB, an ombudsman, an ethics committee, or other informed administrative body" (Office for Human Research Protections, 1993a).

Informed consent templates from the World Health Organization and the US Agency for Healthcare Research and Quality assume that IRBs are available for complaints (Agency for Healthcare Research and Quality, 2009; World Health Organization, 2013). In recent years the Association for the Accreditation of Human Research Protection Programs (AAHRPP) has also listed written procedures for "handling complaints, non-compliance, and unanticipated problems involving risks to participants" as a requirement for institutional accreditation (Association for the Accreditation of Human Research Protection Programs Inc., 2013).

Despite the premise that responding to participant complaints is an essential IRB function (Stoddard, 2010) and the regularity with which informed consent forms make IRBs available to receive grievances, little is known about how IRBs manage these issues. IRBs' procedures for handling participants' research-related complaints may overlap with procedures for handling anticipated adverse events, unanticipated problems, and protocol noncompliance, but systematic study is lacking.

IRBs' processes for addressing participants' research-related complaints demand further study for both ethical and pragmatic reasons. Some complaints of research participants have culminated in litigation naming individual researchers, IRBs, IRB members, research institutions, and sponsors as defendants (Mello, Studdert, & Brennan, 2003). Research-related litigation has drawn attention in the United States, where the majority of research institutions do not provide an alternative system for compensating injured participants (Elliott, 2012; Pike, 2012). Litigation, however, may not be the most appropriate mode of dispute resolution for addressing research-related conflicts, which may involve disparities in knowledge, resources, sophistication, and access to the legal system. Alternatives to litigation may be less costly and more accessible, especially for grievances that may not be cognizable to the legal system, or for injuries that may fall outside the remit of insurance programs. But it is unclear what processes are feasible and effective for addressing participants' grievances.

This review aims to identify current literature on the resolution of research-related disputes involving human subjects. The following sections will first examine the type and frequency of participant complaints, followed by a

discussion of venues available to participants who believe they have experienced injury or mistreatment. The review will then discuss the roles and responsibilities of IRBs in addressing participant complaints, considering factors that may influence the effectiveness of IRB-led systems for resolving these disputes. A concluding section will consider the application of research-related dispute resolution processes to the emerging generation of biomedical HIV prevention research protocols. (Throughout, this article will use the term "IRB" to encompass equivalent institutions such as research ethics committees.)

Research-Related Disputes

Identifying Participant Complaints

When research protocols are subject to regulation by the DHHS or the FDA, the institution must have a procedure for promptly reporting unanticipated problems involving risks to others (Prentice et al., 2002). Unlike systems for unanticipated problems, however, there are no requirements or centralized systems for tracking other participant-initiated complaints submitted to IRBs. Available literature on the incidence, frequency, and categories of participant complaints is therefore scarce. Moreover, given the lack of investigation in this field, it is not known what subset of participant complaints is in fact reported to IRBs; many may be resolved by research teams without IRB involvement, and still more may go undetected and unresolved.

INCIDENCE AND FREQUENCY OF PARTICIPANT COMPLAINTS

Several studies have attempted to estimate the frequency of participant complaints. In 2011, AAHRPP collated data on complaints from 193 human research protection programs, including programs at hospitals and medical centers, universities, and Veterans Administration facilities (Association for the Accreditation of Human Research Protection Programs Inc., 2011). Analyses excluded independent IRBs overseeing multi-site studies. Findings indicated that, on average, each IRB had encountered 3.8 complaints during the past year, at an average of 7.9 complaints per 1000 protocols (ibid.). There appeared to be a small increase in the frequency of complaints from 2009–2011, but exact numbers were not reported. The study did not indicate the origin of complaints (e.g., participants, research staff, or others). An unrelated study examined 84 instances of participant questions and complaints submitted to an IRB in an HMO setting over a one-year period; 20% of participant contacts represented concerns and complaints, although the subject matter of these complaints was not specified (Ayala, Durazo, & Apel, 2006). Other commentators have differed in characterizing the frequency of participant-initiated complaints (Klitzman, 2011; Moss, 2007; Stoddard, 2010), but empirical data are largely unavailable.

A low frequency of complaint reporting does not mean that complaints are absent. Data suggest that research participants often do not understand the entirety of information disclosed during the informed consent process (Flory & Emanuel, 2004), and as a result, participants may find that the research experience does not align with their expectations. IRB personnel have also expressed concern that study participants are uncomfortable complaining to research institutions (Klitzman, 2011), causing complaints to go unreported.

CATEGORIES OF PARTICIPANT COMPLAINTS

Despite uncertainty regarding the incidence and frequency of participant complaints, scholars in the regulation and ethics of human subjects research have identified various categories of participant grievances. These complaints may be classified in several dimensions, including whether or not the complaint has resulted in litigation, the source of the perceived misconduct, whether the complaint alleges noncompliance with the protocol, and the type of harm alleged.

Many scholars have studied complaints that have led to research-related litigation, typically civil suits brought by individual participants or groups of participants against researchers, IRBs, and research institutions (DeVille, 2002; Mello et al., 2003; Morreim, 2003, 2004, 2005; Rose & Lodato, 2006). The central claim in this type of litigation is inadequate informed consent giving rise to physical injury, emotional distress, or dignitary harm (Mello et al., 2003; Morreim, 2003). Additional claims have included fraud and misrepresentation, battery, negligence, medical malpractice, products liability, breach of the right to privacy, breach of contract, wrongful death, breach of state law obligations, and conspiracy (DeVille, 2002; Gibbs, 2004; Jansson, 2003; Mello et al., 2003; Mishkin & Dolan, 2006; Morreim, 2004). Research-related litigation alleging misconduct by IRBs has commonly focused on improper use of expedited review, inadequate informed consent procedures, failure to report serious adverse events, protocol deviations, and neglect of preclinical studies (Mishkin & Dolan, 2006).

Another set of novel complaints in research-related litigation includes violations of the "right to be treated with dignity," premised on federal regulations, the US and state constitutions, and international and national ethics documents such as the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report (DeVille, 2002; Mishkin & Dolan, 2006; Morreim, 2003; Saver, 2006, 2009). To date, dignitary claims have included allegations of negligent

design or implementation of scientific protocols, failure to obtain informed consent, intentional infliction of emotional distress, unjust enrichment, fraud, breach of contract, and participant abandonment (Saver, 2006). Participant abandonment claims may encompass failure to provide posttrial access to the experimental treatment (Saver, 2009), failure to disclose individual research results (Gordon, 2009), premature study termination, denial of interventions, and failure to disseminate trial results (Saver, 2006). Such claims have generally been unsuccessful when tested in court (Morreim, 2003; Saver, 2006).

Outside the litigation context, little information is available about the types of complaints made by research participants. Robert Klitzman has noted that complaints may allege that research staff deviated from the protocol, or that the study did not meet participants' expectations (Klitzman, 2011). Jonathan Moss has described complaints regarding delayed participant payments, "unwanted intrusion" in the form of requests for study participation, and perceived violations of the Health Insurance Portability and Accountability Act (Moss, 2007; Stoddard, 2010, p. 803). One inquiry by the General Accounting Office found that "complaints about the lack of privacy and confidentiality were among the most common complaints made by research subjects" to IRBs, but specific data on complaint frequencies were not available (Kass et al., 2003; US General Accounting Office, 1999). Kathleen Motil and colleagues have described an IRB system responding to participant complaints, which suggested differences between complaints regarding "subject-related issues" (including noncompliance with the IRB-approved protocol or reporting requirements) and complaints regarding scientific misconduct (Motil, Allen, & Taylor, 2004, p. 10).

Venues for Resolving Research-Related Disputes

When a participant complains about an aspect of his or her research participation, including complaints that allege physical, emotional, or dignitary harm, several fora may be available for resolving the dispute. These may include a study-specific dispute resolution scheme, a dispute resolution process organized by the institution (often through the IRB), compensation through insurance for physical injury, or recourse to a third-party decision-maker through litigation or arbitration.

STUDY-SPECIFIC SYSTEMS

At least two research teams have published descriptions of grievance processes created for individual studies. Each of the two available articles has mentioned a grievance procedure specific to biomedical HIV research. For example, the Richmond AIDS Consortium instituted a three-step approach for resolving complaints brought by participants in clinical trials for AIDS treatment (Cox & Kerkering, 1993). This process was guided by the policy that the study participant "ha[d] the right to be treated with dignity as a human being at all times, regardless of [his or her] need for testing, treatment, or other services" (ibid., p. 20). The process first required participants to express their complaints verbally and in writing, followed by the option of speaking with a social worker who reported directly to the consortium panel. The panel issued written decisions about disputes within 10 days, and participants could then appeal to the full IRB for a final resolution. Data were not reported regarding the uptake or outcomes of the system, but the authors suggested that such a grievance procedure "may foster better patient-physician relationships," compared to conducting the trials without a formal process (ibid.).

A more recent series of trials sponsored by the International AIDS Vaccine Initiative evaluated the safety and efficacy of HIV prevention vaccines in India. Before the studies began, a local committee asked IAVI to create a study-specific "local arbitration board" composed of three experts on law, social science, and medicine. This board was retained during the trial to resolve any disputes and participant grievances that arose (Excler et al., 2008, p. 533), but further information about this board was unavailable.

Existing descriptions of study-specific complaint resolution procedures are rare and incomplete; research is needed to understand how procedures are designed, what values they serve, how effective they may be, and how they are experienced by IRB personnel, research teams, and participants.

INSTITUTION-SPECIFIC SYSTEMS

Institutions where multiple studies take place may provide their own processes for resolving research-related complaints. For instance, an institution may set up a single complaint resolution procedure that is available for all types of protocols, or it may set up study-specific complaint resolution procedures. Where a procedure exists, it may be supervised by the IRB, an ombudsman, or another institutional official. In a guidebook for IRBs, OHRP has pointed out that some IRBs maintain processes dedicated to resolving participant complaints (Office of Human Research Protections, 1993b), suggesting that it is optional but common for institutions to have these procedures. But such systems have received little attention; a recent systematic review of the empirical literature evaluating IRBs identified no study examining the strategies IRBs use to respond to participant grievances (Abbott & Grady, 2010).

Several case studies have described IRB-led complaint resolution processes, most notably an article by Motil and colleagues from the Baylor College of Medicine (Motil et al., 2004). These authors describe an iterative nine-step process supervised by the IRB chair and supported by indirect costs from grants (estimated costs were not reported). Basic steps include recording the complaint, notifying compliance administrators, auditing the research team, review by an IRB subcommittee, a formal hearing, deliberation by the full IRB, notifying the PI of a corrective action plan, permitting the PI to appeal the decision, and issuing a final notification. Further study is needed to understand how other institutions resolve complaints, especially when complaints do not allege protocol noncompliance.

Institutions may also rely on arrangements for dispute resolution that are separate from the IRB. Some institutions provide dedicated ethics consultation services to handle ethical concerns, including disputes that may arise from research. For example, the NIH Department of Bioethics has instituted a Bioethics Consultation Service available to researchers, staff, and participants involved in research at the NIH Clinical Center; the service provides either small consult teams or a full ethics committee to consider research-related issues (NIH Department of Bioethics, 2013). Research universities or hospitals may provide other resources for handling research-related disputes, including research subject advocates or ombudsmen separate from the IRB. Institutions that manage research enrolling culturally or geographically distant populations (e.g., participants in international settings) may also choose to establish partnerships with neutral local personnel to help manage disputes, such as a trusted community leader or advisory board. This may help to strengthen community-research connections, as well as making processes more accessible to participants with concerns.

INSURANCE

Where a participant complains of a physical injury arising from research, a minority of institutions provide insurance funds to compensate the participant for this harm. At present, regulations governing human subjects research do not require that research sponsors or institutions compensate participants for research-related injuries (Scott, 2003); informed consent processes need only disclose whether any medical care or compensation will be provided in the event of injury (45 C.F.R. § 46.116(a)(6), 2012). This distinguishes the United States from almost every other country with significant human subjects research programs, including 31 European countries, Australia, Brazil, China, India, Israel, Japan, South Africa, and Uganda (Pike, 2012).

Despite repeated recommendations by US national advisory committees to institute no-fault compensation for research participants (Ladimer, 1988), insurance programs are rarely available (Pike, 2012). As of 2005, 84% of US academic medical centers failed to provide free care or treatment for injured research participants, and none offered compensation for lost wages, pain, or suffering (Elliott, 2012; Pike, 2012; The Lewin Group, 2005). Participants in industry-supported research may have greater access to compensation for research-related injury. For example, one survey of research injury compensation policies in US medical schools found that 61% offered coverage for medical bills when the research was sponsored by industry, while 22% offered coverage when the research was not industry-supported (Paasch-Orlow & Brancati, 2005; Resnik, 2006). Outside the US, insurance coverage by US-sponsored trials varies. A recent study surveyed 12 principal investigators of NIH-sponsored HIV/AIDS clinical trials in Africa: 9 provided compensated treatment for injuries and 7 had insurance policies (Mamotte, Wassenaar, & Singh, 2013).

Although insurance is an important venue for resolving research-related grievances, even the most expansive research-related insurance systems do not extend to every type of participant complaint. These systems may neglect significant financial burdens in their failure to offer compensation for lost wages or pain and suffering (Pike, 2012). Insurance may also be unhelpful for remedying complaints that do not allege physical injury. For this reason, even institutions with effective insurance programs may need alternative processes for resolving the full range of complaints.

THIRD-PARTY LEGAL DECISION-MAKERS: LITIGATION AND ARBITRATION

When a participant has experienced a physical or intangible injury for which compensation is unavailable, he or she may seek to redress the injury through litigation in state or federal court. Litigation through the tort system is one means for aggrieved participants to obtain redress in the United States, and the previous section of this article described the types of legal claims that may be available. The tort system, however, has limitations that may hinder the resolution of research-related complaints. Pike (2012) has identified several barriers to litigation. First, the tort system is out of reach or undercompensatory for most injured participants, given the problems of demonstrating that researchers had a duty to participants, breached that duty, and thereby caused compensable injury (ibid.). When litigation does succeed it may tend to over-compensate the few participants whose cases are successful (ibid.). Third, research-related litigation is entirely unavailable to several classes of

research participants, including US-based participants in federally conducted research and international participants in federally or privately conducted research. In addition, courts are often inexperienced in adjudicating research-related disputes, and several of the legal theories described in the previous section have proven unsuccessful bases for researcher liability (Morreim, 2003). Litigation therefore entails significant uncertainty, and some of the harms perceived by research participants may find no remedy in court. Mello and colleagues (2003) have pointed out additional drawbacks of using litigation to resolve research-related disputes. The high costs of the legal process may increase the overall costs of research, particularly if juries award participants punitive damages. The fear of suit may also reduce individuals' willingness to serve on IRBs or encourage IRBs to make excessively conservative decisions (Mello et al., 2003).

In some settings where litigation is unavailable, such as research with international participants, arbitration may be the only dispute resolution mechanism capable of achieving a legally binding solution. In theory, participants and research institutions could contract before or after the study to submit research-related disputes to binding arbitration, in which a third-party arbitrator or group of arbitrators would render a legally enforceable decision. Some institutions, however, may find arbitration arrangements inappropriate for research-related disputes. Scholars have voiced concerns regarding the use of binding pre-dispute arbitration agreements to resolve medical malpractice disputes, finding that arbitration agreements may lead patients to unknowingly waive their rights to access the courts (DeVille, 2007), and analogous arguments may apply to the research context.

Resolving Research-Related Disputes

IRB Duties and Potentially Conflicting Roles

Before further examining IRB-led processes for the resolution of participant complaints, it is useful to consider the duties and potentially conflicting roles that the IRB may play when confronting a participant grievance. IRBs' responsibilities may stem from several sources, including federal regulation, AAHRPP accreditation, foundational ethical duties, and obligations to stakeholders.

FEDERAL REGULATION

IRBs for institutions in receipt of federal research funding are bound by the Code of Federal Regulations to ensure that participants are provided with contact information for "answers to pertinent questions about the research and research subjects' rights, and … in the event of a research-related injury to the subject" (45 C.F.R. § 46.116(a)(7), 2012). The FDA has imposed a parallel obligation for research intended to fulfill requirements for FDA approval (21 C.F.R. § 50.25(a)(7), 2012). Although these regulations do not bind the IRB to act on complaints, IRBs who provide their contact information to participants for this purpose imply that they will take an active role in resolving their concerns. OHRP does not formally require IRBs to maintain a complaint resolution procedure.

ACCREDITATION STATUS

AAHRPP standards for accrediting a human research protection program require that "Researchers and Research Staff have a process to address participants' concerns, complaints, or requests for information" (Association for the Accreditation of Human Research Protection Programs Inc., 2009, p. 8). AAHRPP also requires that the organization as a whole "respon[d] to the concerns of research participants"; specifically, the organization must "ha[ve] and follo[w] written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants … that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan" (ibid., p. 3). To date, no published study has identified how accredited human research protection programs have fulfilled these criteria.

ETHICAL PRINCIPLES AND IRB OBLIGATIONS

Beyond the regulatory obligations and accreditation standards for IRBs, the responsibility to address participants' complaints may also arise from IRBs' ethical obligations to protect the well-being of research subjects. Considering the Belmont Report as just one source of ethics guidance, each of the Belmont principles bolsters the need for IRBs to be involved in addressing participants' concerns (US Department of Health and Human Services, 1979). IRBs approving research studies may not perfectly anticipate the risks and benefits that participants will experience (Fisher, 1999, 2002, 2011), and they may similarly misgauge efforts to safeguard participants' autonomy. The opportunity for participants to lodge complaints provides an essential source of feedback for the IRB to update its assessment of study risks, benefits, and burdens.

RESPONSIBILITIES TO STAKEHOLDERS

Although the primary mandate of IRBs is to protect research participants, participants are not the only stakeholders in the resolution of research-related complaints. Moss has proposed four "necessary functions" of IRBs, of

which the first is "to ensure patient safety and equipoise" (Moss, 2007, p. 802). A second key IRB function is to protect investigators, and Moss notes explicitly that this protection is realized through IRBs' investigative and corrective responses to participant complaints. This function may be valuable to investigators because the legitimacy of complaints is not uniform (Klitzman, 2011). A third IRB function is safeguard the institution (Guillemin et al., 2012; Moss, 2007), which may also shape IRBs' responses to participant complaints. Participants' negative research experiences may culminate in litigation or affect the relationship between institutions and communities; given these possibilities, institutions may prioritize IRBs' capacity to respond effectively to participant complaints. Additional institutional stakeholders in the complaint process may also include study sponsors, drug and device manufacturers, partnering community-based or nongovernmental organizations, and organizations providing research oversight beyond the IRB. Moss's final IRB function is to preserve public trust in the scientific enterprise (Moss, 2007). An IRB contemplating its response to a participant's grievance may well consider implications for overall scientific legitimacy, including downstream effects such as community trust and willingness to participate in research.

The divided loyalties of IRBs may be a source of tension in their response to participant complaints, but the design and function of a complaint resolution process is intimately tied to participant well-being. Even if complaint resolution is handled by another body, it is advisable to involve IRBs in designing the process, monitoring accessibility, and acting on complaints that suggest ethical deficiencies in ongoing studies.

Resolving Research-Related Disputes in HIV Prevention Research

Research-related complaints may arise in every field, and the responsibilities of IRBs do not differ depending on the research area of the study protocol. But as this paper began with an HIV-related example, it is useful to consider the specific relevance of complaint resolution procedures for research on HIV/AIDS prevention and treatment. The unique context of HIV/AIDS research presents opportunities to engage participants in the development and implementation of dispute resolution processes, as well as challenges in working with disadvantaged populations and testing new prevention technologies.

OPPORTUNITIES FOR ENGAGING HIV/AIDS RESEARCH PARTICIPANTS IN DISPUTE RESOLUTION

HIV/AIDS research benefits from a history of community engagement. Community-led activism and advocacy in HIV/AIDS have set precedents for community consultation and research involvement at every stage (Harrington, 2009). Even some of the earliest clinical trials suggested that "AIDS clinical trial study participants prefer to be active participants rather than passive participants … [who] want to process their concerns and experiences about participating in clinical trials" (Cox & Kerkering, 1993, p. 20). Empirical research has since examined practices for engaging participant populations in community-based research (Harris, 2006; Logie et al., 2012; Rhodes, Malow, & Jolly, 2010; Ross et al., 2010), clinical trials (Essack et al., 2010; Newman et al., 2011; Sahay & Mehendale, 2011; Shagi et al., 2008; White et al., 2011), and outreach-based recruitment (Alvarez et al., 2006), to cite just a few papers. This article has previously discussed two study-specific grievance procedures: the Richmond AIDS Consortium process and the IAVI vaccine trial arbitration board. Research for this article did not identify any other research areas with study-specific grievance processes. This suggests that the resolution of research-related complaints may have particular salience in HIV-related research, and participants in these protocols may seek to take advantage of dispute resolution venues.

CHALLENGES FOR DISPUTE RESOLUTION IN HIV/AIDS RESEARCH

Although HIV/AIDS research often prioritizes community involvement, it often is also characterized by heightened participant vulnerability. The stigmas associated with HIV risk, HIV infection, and AIDS diagnosis persist (Earnshaw & Chaudoir, 2009), and the burden of infection is concentrated in communities with histories of disempowerment and socioeconomic marginalization (UNAIDS/WHO, 2012). Historical and contemporary incidents of exploitation have often led to a mistrust of medical research, including research on HIV (Corbie-Smith et al., 1999; Fisher et al., 2008; Fisher & Wallace, 2000; Oransky et al., 2009). Distrust of institutions that conduct HIV/AIDS research may also complicate this process, affecting not only participation (Dhalla & Poole, 2011), but also willingness to resolve subsequent research-related conflicts through a process organized by the research institution. A large proportion of HIV research takes place in international settings, where systems for remedying disputes or injuries may be unavailable (Mamotte et al., 2013; Pike, 2012). Furthermore, some behaviors associated with HIV carry criminal penalties, such as drug use (Wolfe & Cohen, 2010), same-sex sexual activity in some settings (Poteat et al., 2011), transactional sex (Rekart, 2006), and nondisclosure of HIV infection to sexual partners (Burris & Cameron, 2008). In this context, participants who

perceive an injury during their research experience may be less willing to seek resolution.

Little is known about participant grievances in HIV/AIDS research, but further research might focus especially on complaints that may arise from biomedical HIV prevention trials. In recent years, HIV prevention research has shifted from behavioral approaches toward biomedical prevention, as well as combination strategies integrating the two (Padian et al., 2008; Rotheram-Borus, Swendeman, & Chovnick, 2009). This shift has brought new challenges for researchers and IRBs, such as concerns about antiretroviral resistance and posttrial access (Chua et al., 2005; Jay & Gostin, 2012; Macklin, 2011, 2012; Millum, 2011; Weijer & LeBlanc, 2006). Trials have raised the possibility of posttrial access disputes even when the product is shown to be *ineffective*. For example, a South African trial of a vaginal microbicide found in 2000 that the product was ineffective in preventing HIV; one year after the trial ended, some participants expressed continuing disappointment and frustration about losing product access, even though they had been informed that product did not work (Mantell et al., 2006). These women commented in focus groups that losing access to the vaginal gel deprived them of protection against pain and discharge, and some rejected trial findings of ineffectiveness in preventing HIV. Further investigation is needed to understand participants' perceptions of harm and to identify effective procedures for hearing these concerns.

Conclusion

This literature review aimed to summarize existing knowledge on the incidence and typology of participant complaints, the availability of venues for resolving these complaints, the regulatory and ethical basis for IRBs' involvement in the complaint resolution process, features that may affect the design and effectiveness of IRBs' complaint resolution systems, and unique concerns that may influence the incidence and resolution of complaints arising from HIV/AIDS research. Although literature from other fields may assist in the theoretical development and advancement of this work, empirical data on research-related complaints are almost entirely absent. This review, therefore, serves best as a catalog of knowledge gaps and a call for a research agenda.

Best Practices

At present, the lack of knowledge about the resolution of research-related complaints makes it difficult to recommend best practices. Currently, limited venues are available for remedying participants' concerns. There is a deficit of insurance programs to compensate participants who sustain research-related injuries, and litigation is expensive and comparatively inaccessible. Neither insurance nor litigation may be an appropriate mechanism for redressing some categories of participant complaints, such as dignitary harms, or some categories of participants, such as those in international research. These deficiencies highlight the need for alternative processes for resolving complaints, and there are regulatory and ethical reasons to assert that IRBs should play a central role in, at minimum, overseeing the design and operation of such programs. Given the lack of attention to this topic in research ethics, IRBs developing dispute resolution systems may seek specific guidance from prior work in alternative dispute resolution (Smith & Martinez, 2009), social psychology concepts such as procedural justice (Hollander-Blumoff, 2010; Hollander-Blumoff & Tyler, 2011), medical malpractice dispute resolution (Szmania, Johnson, & Mulligan, 2008), and workplace grievance procedures (Walker & Hamilton, 2011).

Research Agenda

To date, research has insufficiently addressed participants', investigators', and IRBs' experiences with participants' research-related complaints. Although complaints may rarely be brought to the IRB, this does not mean that they are absent. Research in this area should proceed with both top-down and bottom-up approaches. From the top down, research is needed to understand the roles that IRBs currently play in the resolution of participant complaints; the structure, functioning, values, and outcomes of existing systems; and potential avenues for improving the accessibility and effectiveness of these processes. From the bottom up, it is important to investigate not only what happens to complaints once they are brought to the IRB, but also the factors that influence participants' expectations of fair treatment, perceptions of mistreatment or harm, and decisions to access an available complaint resolution process. Research is also needed to understand the expectations and experience of investigators and their staff when a complaint occurs.

Given recent changes in HIV prevention science, researchers in this field should investigate ways in which participant expectations and complaints are evolving. Scientific advances are paving the way for novel research-related complaints, and the field has already experimented with several types of study-specific dispute resolution processes. The dual experience of community advocacy

and participant vulnerability in the HIV/AIDS field also provides a unique dynamic for further study on participant complaints.

Educational Implications

The research agenda proposed here may be of most interest to IRB chairs and members, researchers in empirical research ethics or alternative dispute resolution, institutional risk management personnel, institutional ombudsmen and participant advocates, and potentially research oversight bodies such as OHRP and AAHRPP. Efforts to study this field may gain strength from institutional concerns about liability in research-related litigation, growing calls for the compensation of research-related injuries (Mamotte et al., 2013; Pike, 2012), and the expansion of empirical research evaluating IRBs (Abbott & Grady, 2010). IRBs, researchers, and participant communities have much to gain from opening this field to rigorous empirical inquiry, and improving the resolution of research-related disputes can benefit all stakeholders in the scientific enterprise.

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