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It Takes Two to Tango: Ethical Issues Raised by the Study of Topical Microbicides with Adolescent Dyads

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Auslander, Rosenthal and colleagues describe a difficult dialogue with their Institutional Review Board (IRB) [1]. Recruitment and data security restrictions imposed by the IRB hampered investigators' ability to recruit male partners in a topical microbicide study, or to link records of male and female participants, making the few male responses difficult to interpret. Their brief raises timely issues in the ethical review of research on adolescent sexual behavior.

Dual Role of IRBs

The "Common Rule" requires that IRBs conduct an ethical review of research, ascertaining that risks are minimized and reasonable in relationship to benefits, subject selection is equitable, informed consent is obtained, and investigators respect participant privacy and maintain data confidentiality [2]. Ethical functions derive from the Belmont Report and the principles of beneficence, justice, and respect for persons [3]. IRBs also have a regulatory role, assessing research in terms of national, state and institutional regulations, laws, and professional practice standards [2]. Regulatory functions have received increased attention due to high profile university sanctions related to federally-funded research [4]. While ethical and regulatory functions generally act synchronously and provide a consistent review, in some instances regulatory concerns produce a more restrictive perspective.

New Research Paradigms

As our understanding of relational and contextual influences on adolescent health deepens, investigators are recruiting dyads and social networks, and research is moving into community settings. This shift challenges the prevailing research paradigm which is based on recruiting individuals. Additionally, sexual behavior is a sensitive topic and adolescents are considered a vulnerable population. IRB regulatory guidance is not well-suited for behavioral research with adolescents. For example, regulations specify that "children" need special protections [5], but adolescents do not fit neatly into that category. Unfortunately, little data exist on ethical aspects of sexual behavior research with adolescents. Our understanding of how to assess social harm, or the extent to which research participation can cause psychological distress, is limited. The combination of newer methods and little empirical data presents challenges to IRBs.

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Respect for Persons, Beneficence and Justice: The Devil is in the Details

There is no disagreement about basic ethical principles. Who could find fault with respecting persons, balancing risks and benefits, and a fair participant selection such that some groups are not asked to shoulder more of the burden or have less access to benefits? However, there frequently are marked differences in how these principles are interpreted, ranked, or balanced [6]. These investigators and their IRB perceived a vastly different potential for social harm in the proposed recruitment method and for breaches of confidentiality in linking participants' records.

How could this happen? First, data on risks and benefits of behavioral research are scarce, but what data exist provide a crucial empiric perspective. For example, only 44% of IRB chairs categorized the risk of a confidential survey of sexual activity as minimal [7]. However, Halpern and Udry established that asking about sex on a survey does not lead to increased sexual behavior [8]. Empiric data can also substantiate a particular line of ethical reasoning. While bioethicists debate the appropriateness of pediatric research that does not offer direct benefit to individuals [9], empiric data support the acceptability of non-beneficial research among different populations of adolescents and parents [10–12]. In the absence of data, there can be marked variation in how IRBs quantify research risk [13,14], as well as systematic errors in this quantification [15].

Research risk can be difficult to specify. Federal regulations define research risks as “minimal” when risks are not greater “than those ordinarily encountered in daily life” or during “routine physical or psychological examinations” [2]. IRB members often make risk assessments based upon personal experience [16]. So whose daily life should be used as baseline? Investigators? IRB members? IRB member's adolescent children? Or adolescents from the community under study? Adolescent risk assessment is even more difficult because, developmentally, adolescents are moving targets. A 13 year old may perceive research as uncomfortable, whereas a 17 year old is perfectly comfortable. These investigators add another wrinkle, by recruiting through sexual partners. The additional uncertainty raised by innovative approaches in the absence of data may reinforce conservative (i.e., risk minimizing) IRB decision-making.

Legal issues present another challenge in adolescent sexual behavior research. IRBs and investigators must make sense of laws related to mandated reporting and statutory rape, and decide whether it is possible to put into place research procedures that would be in compliance with state law, but still prevent the harms to participants related to the mandated reporting of consensual sex. Because IRBs are responsible to universities to uphold regulations and safeguard research, IRBs default to conservative approaches. These investigators originally offered to educate participants about statutory rape laws prior to partner recruitment; Their IRB did not accept this. Other investigators have not asked the ages of male partners, instead screening for coercion (Fortenberry, personal communication).

One key aspect of justice, infrequently considered by IRBs, is whether it is unfair to limit access to potentially beneficial research. Excessive restrictions on adolescent research participation, ostensibly to protect a vulnerable population, can deprive adolescents, as a group, of the benefits of research. If investigators cannot study dyads and social networks, we are unlikely to see marked advances in the field of health behavior.

The Tango

Adolescent investigators have facilitated ethical review several different ways. First, the most effective way to argue benefits and harms is to generate data on adolescents' experiences of research participation. In the absence of data, consultation with community members can provide a valuable perspective on research risks and benefits. Many experienced investigators

get to know IRB staff and members, making themselves available for consultation during review. Some IRBs require investigators to attend meetings; others have no requirements, but often allow investigators to make a statement and answer questions. Finally, federal regulations require that IRBs contain at least one individual knowledgeable about and experienced in working with vulnerable populations [2]. Frequently, the “pediatric” representative is a bench scientist. Many adolescent research groups have a member serve on the IRB to educate and provide the relevant developmental, methodological, and theoretical expertise.

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