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Adolescent Self-Consent for Biomedical Human Immunodeficiency Virus Prevention Research

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A B S T R A C T

Purpose: The Adolescent Medicine Trials Network Protocol 113 (ATN113) is an open-label, multisite demonstration project and Phase II safety study of human immunodeficiency virus (HIV) preexposure prophylaxis with 15- to 17-year-old young men who have sex with men that requires adolescent consent for participation. The purpose of this study was to examine factors related to the process by which Institutional Review Boards (IRBs) and researchers made decisions regarding whether to approve and implement ATN113 so as to inform future biomedical HIV prevention research with high-risk adolescent populations.
Methods: Participants included 17 researchers at 13 sites in 12 states considering ATN113 implementation. Qualitative descriptive methods were used. Data sources included interviews and documents generated during the initiation process.
Results: A common process for initiating ATN113 emerged, and informants described how they identified and addressed practical, ethical, and legal challenges that arose. Informants described the process as responding to the protocol, preparing for IRB submission, abstaining from or proceeding with submission, responding to IRB concerns, and reacting to the outcomes. A complex array of factors impacting approval and implementation were identified, and ATN113 was ultimately implemented in seven of 13 sites. Informants also reflected on lessons learned that may help inform future biomedical HIV prevention research with high-risk adolescent populations.
Conclusions: The results illustrate factors for consideration in determining whether to implement such trials, demonstrate that such protocols have the potential to be approved, and highlight a need for clearer standards regarding biomedical HIV prevention research with high-risk adolescent populations.

IMPLICATIONS AND CONTRIBUTION

This study illustrates the complexity of practical, legal, and ethical factors that researchers and Institutional Review Board members must consider in determining whether to implement biomedical human immunodeficiency virus prevention trials with high-risk adolescent populations, demonstrates that such protocols have the potential to be approved, and highlights a need for clearer standards.

Disclaimer: The comments and views of the authors do not necessarily represent the views of the National Institute of Child Health and Human Development or those of the Department of Health and Human Services.

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An emerging approach to the prevention of human immunodeficiency virus (HIV) transmission is preexposure chemoprophylaxis (PrEP) using daily oral doses of the antiretroviral drug combination Emtricitabine/Tenofovir (FTC/TDF). FTC/TDF PrEP has been approved by the U.S. Food and Drug Administration (FDA) for high-risk adult populations [1,2]. Although young

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men who have sex with men (YMSM) are disproportionately affected by HIV [3,4], minor youth were excluded from clinical trials informing this FDA indication for use.

Minor adolescents are frequently excluded from biomedical HIV prevention research because of the legal and ethical complexity of including them. Researchers often have ethical concerns about adolescent vulnerability and capacity for research-related decision-making and legal concerns about navigating laws that may require parental consent [5–8]. Mandates for parental consent pose even greater barriers to recruitment in studies that address sensitive issues such as sexuality and sexual practices [7–9]. In the case of YMSM, for example, youth may be unwilling to participate in a study in which the informed consent process is likely to result in their sexual status and/or sexual activity being revealed to their family, potentially resulting in rejection or violence [10,11]. In certain circumstances such as these, ethical considerations supporting adolescent inclusion in research (e.g., the critical importance of clinical trials data on PrEP safety for YMSM or the high vulnerability of YMSM to HIV) may overshadow those requiring parental consent [5,8,12].

Federal regulations governing research conducted with FDA oversight stipulate parental consent for research with minors, and waiver of parental consent is therefore not permitted [13,14]. However, in limited circumstances where adolescents meet criteria for emancipation, are considered "mature minors," or are otherwise allowed to consent on their own behalf to the treatment or care being studied under state law, they may legally be permitted to consent to the research on their own behalf without parental consent [8,15]. Local Institutional Review Boards (IRBs) routinely determine whether the consent procedures proposed in a study are both ethically justified and compliant with state and federal law [16]. No biomedical HIV prevention trial has previously been conducted in the United States among adolescents aged 15–17 years without parental consent, and the process by which researchers and IRBs undertake the difficult task of reviewing and implementing such protocols with high-risk minor populations has never been examined.

Adolescent Medicine Trials Network for Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome Interventions Protocol 113

The Adolescent Medicine Trials Network for HIV/acquired immune deficiency syndrome (AIDS) Interventions (ATN), funded primarily by the National Institute of Child Health and Human Development, conducts HIV prevention and treatment research among youth aged 12–24 years in 14 clinical sites and surrounding communities. The challenge of balancing the legal and ethical justifications for and against minor self-consent was addressed by the ATN during a Phase II PrEP safety study (ATN Protocol 113, subsequently identified as ATN113) for 15- to 17-year-old YMSM. Motivated by the reality that FTC/TDF is likely to be used off-label for PrEP purposes among YMSM, the ATN sought to obtain safety data for this indication, including assessments of patterns of use, adherence, and changes in sexual risk and protective behaviors. The protocol also included an efficacious behavioral risk reduction intervention to address potential risk compensation associated with PrEP.

ATN113 was open to all sites, based on a common protocol that was approved by experts within the ATN and the National Institutes of Health. Additional opinions regarding adolescent self-consent were provided by the ATN Ethics Advisory Panel, the Office of Human Research Protection and the FDA. These bodies concluded that it was legally and ethically appropriate for minor adolescents to consent to ATN113 participation on their own behalf when permitted under state law as interpreted by their local IRB, and the protocol was written to require adolescent self-consent. As part of routine network protocol implementation procedures, an IRB submission packet was provided to all sites that included an IRB submission cover letter summarizing the protocol, an IRB submission template, and the ATN113 protocol itself. Materials specific to the external consultations described previously were also provided.

A summary of the ATN113 recruitment and consent process, as described in the protocol, follows. Recruitment is to be conducted using venue-based methods and/or online-based methods. For venue-based recruitment, potential participants are to be approached in coffee houses, gay youth centers, book clubs, House Ball community gatherings, parent groups, and clinics caring for the target population. ATN study sites have the option of also using social networking sites and geosocial networking mobile applications to approach potential participants. For venue-based recruitment, verbal consent is to be obtained before screening potential participants for preliminary eligibility using a handheld device, and for online-based recruitment, a Web-based screener is to be used. If a participant is deemed eligible based on preliminary criteria, he is to be offered an in-person screening appointment at the study site. On the day of the in-person screening, before determining final eligibility, the purpose, procedures, requirements, risks, and benefits of the study are to be thoroughly discussed with the potential participant and written consent obtained. Before screening for final eligibility, an "assessment of understanding" questionnaire must also to be administered to ensure understanding.

Study purpose and aims

The specific aims of the ATN113 substudy described in this article were to examine the following: (1) the initiation process by which ATN investigators and other study personnel, in collaboration with their local IRBs, evaluated the issue of adolescent self-consent and reached decisions regarding whether to approve and implement the ATN113 protocol and (2) reflections on valuable lessons learned. Understanding this initiation process is critically important as new biomedical HIV prevention technologies, including microbicides and vaccines, continue to emerge. Lessons learned during this process may help guide researchers, IRB members, and policy makers in the responsible conduct of future biomedical HIV prevention research with minor participants who are at substantial risk for HIV infection.

Methods

Qualitative descriptive methods, which provide an in-depth description of experiences shared by a group facing a common challenge [17], were used to meet the substudy's aims. The qualitative descriptive approach is particularly useful for generating straightforward summaries of information to guide future intervention. It relies on purposive sampling, moderately structured interviews with key informants, and low-inference content