Routledge
Taylor & Francis Group

Journal of Homosexuality

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/wjhm20

Challenges in Arranging to Waive Parental Consent in HIV Prevention Studies of Adolescent Men Who have Sex with Men: The Case of HPTN 078

Robert Klitzman, Robert H. Remien & Chris Beyrer

To cite this article: Robert Klitzman, Robert H. Remien & Chris Beyrer (2024) Challenges in Arranging to Waive Parental Consent in HIV Prevention Studies of Adolescent Men Who have Sex with Men: The Case of HPTN 078, Journal of Homosexuality, 71:6, 1584-1604, DOI: 10.1080/00918369.2023.2185093

To link to this article: https://doi.org/10.1080/00918369.2023.2185093

JOURNAL OF HOMOSEXUALITY
2024, VOL. 71, NO. 6, 1584–1604
https://doi.org/10.1080/00918369.2023.2185093

Routledge
Taylor & Francis Group

Challenges in Arranging to Waive Parental Consent in HIV Prevention Studies of Adolescent Men Who have Sex with Men: The Case of HPTN 078

Robert Klitzman, MD[a], Robert H. Remien, PhD[b], and Chris Beyrer, MD, MPH[c,d]

[a]Vagelos College of Physicians and Surgeons and the Joseph Mailman School of Public Health, Bioethics Program, Columbia University, New York, New York, USA; [b]HIV Center for Clinical and Behavioral Studies, Clinical Medical Psychology (In Psychiatry), Columbia University and in the NY State Psychiatric Institute, New York, New York, USA; [c]Public Health and Human Rights, Johns Hopkins University, Baltimore, Maryland, USA; [d]Epidemiology, International Health, Health Behavior and Society, Nursing, and Medicine, Johns Hopkins, the Bloomberg School of Public Health, Baltimore, Maeryland, USA

ABSTRACT

Including adolescent men who have sex with men (AMSM) in HIV prevention and treatment studies without parental permission is vital, but has often faced barriers. We examine the case of recent Institutional Review Boards (IRB) reviews of an HIV treatment and prevention study that requested waiving parental permission at four United States sites, but received different responses from each institution. IRBs varied in whether and how they weighed parental rights against AMSMs' rights and individual and social benefits, and potential harms (e.g., if a parent disapproves of the adolescents' sexual behavior). One IRB "tabled" the decision to receive advice from the university Office of General Counsel (OGC), despite state laws allowing minors to consent to HIV testing and treatment without parental permission. Another IRB consulted the university's Chief Compliance Officer (CCO), which thought the waiver was inconsistent with state law, which discusses "venereal disease," but not HIV. University attorneys may have competing priorities, however, and thus interpret relevant laws differently. This case raises critical concerns, highlighting needs for advocates for AMSM, researchers, IRBs and others at institutional, governmental, and community levels to educate policymakers, public health departments, IRB chairs, members, and staff, OGCs and CCOs about these issues.

KEYWORDS

Adolescent men who have sex with men (AMSM); homosexuality; adolescents; consent; HIV; IRBs; public health

Background

Inclusion of adolescent men who have sex with men (AMSM) in HIV epidemiologic, prevention, and other studies without obtaining their parent's permission is critically important, but has frequently faced barriers. AMSM are at high risk of HIV, and those living with HIV infection are at high risk for acquiring and having undiagnosed or untreated infection. According to the

CONTACT Robert Klitzman rlk2@cumc.columbia.edu Vagelos College of Physicians and Surgeons and the Joseph Mailman School of Public Health, Bioethics Program, Columbia University, 1051 Riverside Drive, Mail Unit #15, New York, New York 10032, USA.

Centers for Disease Control and Prevention (CDC), in the U.S., MSM constitute only about 2% of the population, but around 57% of those living with HIV and 67% of newly diagnosed HIV cases (Centers for Disease Control and Prevention [CDC], 2018). Among new HIV diagnoses in 2017, 70% were among adult and AMSM—especially those of certain ethnic and racial groups that have faced economic and health disparities. Specifically, among MSM newly diagnosed with HIV, 37% were African-American, 29% Latino, and 28% white. Moreover, one in six MSM with HIV are unaware of their infection (CDC, 2018). In a random sample of AMSM (ages 15–29) in six cities from 1994 to 2000, 77% (including, 91% of Blacks, 69% of Hispanic, and 60% of whites) were unaware of their infection, of whom 55% had not tested in the previous year, and 59% thought they were at low risk (MacKellar et al., 2005). Studies on how to prevent infection and optimize treatment are thus critically needed.

Many questions remain concerning whether and how to engage AMSM who are at risk, and/or living with the virus, in order for them to achieve and sustain viral suppression and avoid infecting others. The Society of Adolescent Medicine and the National Academy of Science have called for both more clinical and health research on adolescents, and for consideration of waivers of parental permission in certain situations (Santelli et al., 2003). The World Health Organization (WHO) similarly recognizes that obtaining permission from a parent or guardian for a child to participate in research is not always feasible—e.g., regarding sexual activities, substance abuse, street children, sexual abuse, physical abuse, or neglect. The WHO report, *Guidance on ethical considerations in planning and reviewing research studies on sexual and reproductive health in adolescents* (2018), and The Council for International Organizations of Medical Sciences (CIOMS) in collaboration with WHO (2016) have issued similar statements. The WHO states, for instance, that institutional review boards (IRBs) "should base its decision on whether waiver is in the best interest of the child" (World Health Organization [WHO], 2018), and that the research does not involve more than minimal risk.

HPTN's 2009 *Ethics guidance for research* (Rennie et al., 2009) likewise states, "The permission of parents or legal guardians is typically a prerequisite for the participation of children in research," but that:

> Orphans and street children who are exposed to HIV infection may have no legal guardians and might therefore be automatically excluded from HIV prevention research if the requirement for parental or guardian permission is applied strictly (Rennie et al., 2009).

In such cases,

> . . . investigators should seek protective ways of including these groups in close consultation with community representatives, regulatory authorities, ethics committees, and local or national organizations devoted to the rights and welfare of children (Rennie et al., 2009).

Yet while these guidelines suggest that waiver of parental consent may be permissible in certain situations (e.g., regarding orphans and street children), this document was written before the widening importance and use of Pre-exposure Prophylaxis (PrEP) (Centers for Disease Control and Prevention [CDC], 2021) among adolescents, and thus needs to study such use, making needs to include adolescents in research without parental permission even more pressing. Legal mechanisms permitting adolescents to consent without permission of parents or guardians are thus becoming increasingly critical.

In the U.S., the "Common Rule" (the Code of Federal Regulations [45-CFR -46] states that IRBs can waive parental consent in a study if such permission (Office for Human Research Protections [OHRP], 2004, 2019):

> is not a reasonable requirement to protect the subjects ... provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law (OHRP, 2019).

Additional federal guidance elaborates that IRBs may waive consent requirements if the research "is no more than minimal risk," the waiver "will not adversely affect the rights and welfare of the subjects," and the study "could not feasibly be carried out otherwise and whenever appropriate, subjects will be given additional pertinent information after they participate" (Office for Human Research Protections [OHRP], 1993).

Ethical considerations

Waivers of parental permission are, ethically, critical in HIV prevention treatment research with AMSMs for several reasons (Bauman et al., 2020). Proponents of requiring parental permission may argue that parents have rights to decide these adolescents' activities. But many such potential participants may not have disclosed their sexual orientation or HIV risk behaviors or status to their parents (or guardians), due to feelings of shame and fears of stigma or discrimination. Requiring such parental permission could thus lead to harms to these adolescents, including discrimination, stigma and/or physical or mental abuse, with some gay/bisexual adolescents being ousted from the home if a parent is unaware and/or disapproves of their sexual orientation. Moreover, adolescents have certain rights to autonomy, and laws exist that give "mature" and "emancipated" minors (e.g., 16- or 17-year-olds), who understand the associated risks and benefits, rights to initiate certain treatments without parental permission when such approval may be problematic (Klitzman et al., 2008; OHRP, 2004, 2019). An IRB's requirement of parental permission thus violates principles of non-maleficence and adolescents' autonomy, and can also reduce the potential subjects' willingness to participate, and hence the feasibility and potential scientific and social benefits of

a study. Adolescents who are already "out" to the parents, and thus potentially able to participate if parental permission is required, may not be at most risk. Hence, including only this group will significantly lower the generalizability and applicability of the eventual research findings to the populations who are most in need of HIV prevention and treatment.

Indeed, studies have shown that requiring parental permission in research on "at risk" adolescents can alter and impede research results (Mustanski, 2011). For instance, among 198 AMSM aged 14–17 in a study of oral vs. injectable PrEP, 62% would participate in general, but only 27.7% would participate in an HIV testing study if they had to obtain their parent's or guardian's permission (C. B. Fisher et al., 2018). Most (76.3%) disagreed that getting their parents' permission would be important "so that they can help me if the test showed I had HIV." Only 29.8% said that their parent or guardian knew that they were sexually active with male partners (C. B. Fisher et al., 2018). Similarly, among 74 sexual and gender minority adolescents in an online focus group, most would be unwilling to participate in an HIV study if parental permission were needed (Mustanski et al., 2017). Rural MSM may face even higher levels of closetedness and guardedness (C. M. Fisher et al., 2014; Lee & Quam, 2013). AMSM are also able to perceive benefits of such studies (Mustanski et al., 2017).

Among AMSM in a phase II study of PrEP, 100% reported feeling that they had received all the information they needed to decide to enroll in the study, and none felt that they had been talked into enrolling, or had enrolled even though they did not want to do so (Knopf et al., 2017).

Justice concerns arise as well since HIV disproportionately affects African-American and Latino AMSM, who may encounter higher levels of homophobia, and thus added difficulties coming out and potential harms (Brooks et al., 2005).

Yet IRBs have not always waived parental permission, despite calls to do so (Bauman et al., 2020). For example, for the Adolescent Medicine Trials Network Protocol 113 (ATN 113), an open-label Phase II safety study of PrEP among 15- to-17-year-old AMSMs, only seven of the 13 sites in 12 states that considered the protocol approved the waiver of permission that the researchers requested (Gilbert et al., 2015). IRBs in two states with similar laws arrived at opposite conclusions about waiving parental permission (Gilbert et al., 2015). Other researchers, in Chicago, saw their IRB's similar requirement of parental permission for an HIV prevention study among black AMSM as "paternalistic" (Miller et al., 2006).

Critical questions thus emerge regarding these tensions—how exactly IRBs respond to requests for waivers of parental permission in different contexts, why and how IRBs decide to accept or reject such requests, and how the ethical challenges involved might be addressed. While several broad ethical issues involved regarding this issue, in general, have been described at a relatively

theoretical level (OHRP, 1993), crucial questions remain concerning how these issues in fact arise and play out in various institutional contexts in the real world—how various IRBs and researchers approach these dilemmas and why.

In this paper, we present and analyze a case in point. HIV Prevention Trials Network (HPTN) 078, "Enhancing recruitment, linkage to care and treatment for HIV-infected MSM in the U.S.," an HIV prevention study, recently attempted to obtain approval for waivers of parental permission at four sites, but received different responses from the IRBs at each location. We present here our experiences and interactions since they raise crucial questions and concerns regarding current and future public health research in HIV and other areas, and suggest needs to improve future research ethics guidelines, practice, policy, education and scholarship.

The HPTN 078 experience

As described elsewhere (HIV Prevention Trials Network [HPTN], 2011), HPTN 078 investigated the effectiveness of a combined strategy to identify, recruit, and link MSM to HIV care, and an intervention to help HIV-infected MSM achieve and maintain HIV suppression. The study included MSM in Georgia, Maryland, Alabama, and Massachusetts. Given ongoing spread of HIV, new methods are essential to identify HIV-infected MSM who are not virally suppressed, and help them become virally suppressed. HPTN 078 therefore used deep-chain respondent-driven sampling (DC-RDS), a method to find marginalized populations, which identifies "seed" participants who then refer members of their social or sexual networks (HPTN, 2011). Seeds receive coupons for reimbursement to give to peers in their networks. Eligible peers then receive coupons to refer additional peers (Baral et al., 2015; Coombs et al., 2014; Volz & Heckathorn, 2008). We thus aimed to identify MSM who were living with HIV and were virally non-suppressed, whom we then invited to join the second phase of the study. After enrollment, we randomized them either to standard of care (SOC) to link to HIV care, initiate antiretroviral therapy and remain in HIV care, or to the study intervention, which consisted of working with a case manager (CM) to achieve these treatment goals. The study aimed to compare viral suppression over time.

We sought to include minors ages 16–17, in addition to adults aged 18 and over. We chose states in which the relevant state laws appeared to permit HIV testing without parental consent. The researchers asked IRBs for waiver of parental permission for screening, and in one case, enrollment. If a minor didn't want his parents involved, it would end that DC-RDS chain. Yet, as described below, at two of these sites, the IRB and their universities ultimately interpreted the relevant state laws otherwise, and did not permit HIV testing without parental consent as part of the protocol.

Table 1. Summary of IRB approval with regard to minors (16–17 years old) participating in HPTN.

Location	IRB Decision about Screening Minors		IRB Decision about Enrolling Minors (16–17)	
	Parental permission waived	Parental permission required	Parental permission waived	Parental permission required
Alabama	✓			✓
Massachusetts	✓		✓	
Maryland		✓		✓
Georgia		✓		✓

IRBs' response to HPTN 078

As seen on Table 1, the protocol received very different responses at each of the four sites. While the IRB at one site (Alabama) accepted the local site investigators' request to waive parental permission for screening, though not enrollment, the other sites deviated, as described below, raising critical questions as to why, and revealing needs to address obstacles to IRB approval of such parental waivers in research.

The case of a medical institution in Massachusetts

At the Massachusetts medical institution, which has considerable experience with the care and treatment of lesbian, gay, bisexual, transgender, and questioning or queer (LGBTQ) patients, the local site investigators requested waivers for both screening and enrollment, which the IRB immediately approved. Massachusetts explicitly allows minors over 14 years to receive HIV testing and treatment without parental permission (Guttmacher Institute, 2022). The institution's IRB also has experience with studies enrolling minors in studies of HIV-infected and at-risk adolescents.

The local site investigators' request to the IRB presented key ethical considerations, stating:

> HIV-related services offered at our site are confidential and do not require parental/legal guardian notification or permission to treat under state regulations. The vast majority of youth at our site do not visit the site with a parent, and it would be practically difficult for many eligible participants to obtain parental consent and may even pose a threat to their well-being. Contacting a parent/legal guardian could constitute a breach of confidentiality for these high-risk and potentially HIV-positive participants. It could also potentially put some HIV-positive youth at risk for abuse or ousting from their home if parents/guardians are not aware of their sexual orientation or HIV status and/or unaware of their seeking care at our site.
>
> It is expected that there will be participants who have not disclosed their HIV status or sexual orientation to parents/guardians. Nor will the parents/guardians be aware of the participant's risk behaviors. A requirement for parental permission in this type of study could not only affect a person's willingness to participate, but could also potentially impact the ability of researchers to engage in this type of HIV-related research with young people. . .Massachusetts State Law provides that there are certain circumstances under which a minor may consent to HIV testing and treatment without parental

> consent (Boston College Law School's Juvenile Rights Advocacy Project, 2006). These circumstances included reasonably believing one may have come into contact with a STD [sexually transmitted disease] (Guttmacher Institute, 2022).

The case of an institution in Alabama

In contrast, at the Alabama institution, the principal investigators (PIs) requested a waiver of parental permission for 16–17-year-olds for screening but not for enrollment (N. Stanfield to M. Mugarvero, personal communication, February 26, 2016), and explained to the IRB that:

> According to Alabama state laws, minors are allowed to consent for diagnosis and treatment of STDs. They are also allowed to consent for HIV/AIDS testing and treatment. Based on these laws, we request that 16-17-year-olds be allowed to provide consent for screening activities without requiring parental consent (N. Stanfield to M. Mugarvero, personal communication, February 26, 2016).

The researchers explained why the wavier was important to the research methods and thus the scientific and social benefit of the study.

> This waiver is being requested for screening activities only. In order for the DC-RDS methodology to work, participants must undergo screening activities and then serve as recruiters to being in new individuals for screening. If a minor needs parental consent to undergo the screening activities, and he doesn't want to involve his parents or his parents do not allow participation, the chain of recruitment will end, and interfere with the methodology's ability to find our target population (N. Stanfield to M. Mugarvero, personal communication, February 26, 2016).

The IRB decided that the risks were not greater than minimal and approved the protocol with limited modifications (to include in the consent form information about payment for participation).

The case of a medical institution in Maryland

In Maryland, the local site researchers requested permission to include 16–17 year-olds, and waive parental permission. Maryland laws allow minors to consent to HIV testing and treatment without parental permission (Maryland Department of Public Health, 1995; Maryland Department of Public Health, 2018a). Regarding "all patients . . . including minors" whose HIV test result is positive, "the healthcare provider shall ensure the patient is linked to an appropriate source of HIV medical care and support services" (Maryland Department of Public Health, 2018a). Providers "may, but need not, give a parent" or guardian "information about [the] treatment needed . . . except information about an abortion" (Maryland Department of Public Health, 1995).

Yet the IRB "tabled" the issue to receive advice from the university Office of General Counsel (OGC). The researchers were concerned about delaying the study (which could otherwise be approved for participants who were at least 18-years old), and thus withdrew their request.

The case of an institution in Georgia

In Georgia, too, the IRB was unsure about screening 16–17 year-olds for eligibility for the study, and referred the decision to their institutions' OGC, which then interpreted the relevant state laws very narrowly. These decision-making processes necessitated much back-and-forth communication with the researchers, the details of which highlight key issues and considerations involved.

The Georgia PI first asked the IRB how it might consider a request to waive parental permission for 16-year-olds for screening, since Georgia,

> allow[s] for STD testing of youth without parental consent, with the understanding that parental assent will be required for any eligible youth who want to enroll in this study and complete any further study procedures." (C. Root to R. Rousselle, personal communication, September 4, 2015).

The IRB responded, citing the relevant section of 45-CFR-46 that would need to be followed to waive parental permission.

The IRB added,

> There is also the fact that state law does, as you mention, allow minors to consent for themselves to STD testing. That could apply here, to allow them to also consent for this research screening, except that it sounds like there are other screening tools as well – questionnaires of some sort. If you have those available, [that] would be helpful (T. Gamble to K. West, personal communication, November 2, 2015).

The researchers sent the questionnaires to the IRB, but after two weeks, did not hear back and thus followed-up. The IRB then responded:

> . . . the way [the Georgia state law is] written is that minors can seek *treatment* (not testing) for STIs without parental consent, and the reference [included by the researchers] interprets the law to say that minors can seek HIV testing without parental consent (since the law is actually silent on HIV testing/treatment specifically (R. Rousselle to C. Root, personal communication, October 11, 2015).

The IRB asked as well whether the researchers,

> On the off-chance our IRB didn't go for parent-less screening, are there alternatives, or would we not be able to do the study? Would we (a) get parents to give permission for the screening, or (b) only enroll 18-up at our site? (R. Rousselle to C. Root, personal communication, October 11, 2015).

The IRB also asked whether the researchers,

> . . . had any concerns about parent reaction when they found out their child did participate in some of the study prior to the parent being informed: will the parents in fact be told that their child already was screened by the researchers? (R. Rousselle to C. Root, personal communication, October 11, 2015).

The IRB then asked the university's Chief Compliance Officer (CCO) to review the law and provide an opinion since the law "appears to allow minors

to seek treatment (but not testing) for STIs [sexually transmitted infections] without parental consent" (Georgia Code § 31–17-7, last modified, 2012). The law discusses "venereal disease," but not specifically HIV.

The researchers replied that they didn't think the DC-RDS component would work if parental permission were required, and that they would then enroll only adults. Concerning parental reactions if their child were screened without their permission, the researchers said the answer would depend on why the consent was waived. If the state allows HIV testing, in general, for minors, then the parents could be told that these offspring could seek this testing anywhere, that the questionnaires are minimal risk, and that IRBs can approve minimal risk research in adolescents without parental consent in certain circumstances.

The IRB replied that the CCO would like to talk to the researchers and that the CCO thought that the waiver "would not be consistent with state law," but that the CCO stated that it was "open to another interpretation." The researchers then spoke to the CCO. The IRB then wrote to the researchers that the CCO's,

> . . . reading of state law is that HIV testing is not included in the set [of] tests that can be done without parental notification. There are apparently sites in Georgia that do HIV testing without parental notification, thus who interpret the law differently. [The CCO] and our OGC agreed that they'd like a statement about it from the Georgia Department of Health [DOH], before we allow it (R. Rousselle to K. West, personal communication, November 2, 2015).

The CCO asked the researcher to contact the Georgia DOH to find out if the DOH providing HIV testing to adolescents without parental consent.

The DOH Assistant Manager of HIV Prevention eventually confirmed that the state DOH *did* provide HIV testing to anyone 13 years of age and older without parental consent, but that when a minor tests HIV-positive, the parents are notified and must provide permission for the minor to receive HIV care. The DOH representative said that he did not know of any cases where parents had gotten upset that their teenager had been tested for HIV at the Georgia DOH (T. Gamble to C. Root, personal communication, .

The DOH representative said that the DOH was providing such HIV testing to adolescents without parental consent under Georgia Code § 31–17-7, which states that a minor can "consent to *medical or surgical care*" if he/she "professes to be afflicted with a *venereal disease*, provided that any *such treatment* shall . . . [be] related to . . . the *venereal* disease . . . The consent of no other person or persons . . . shall be necessary" (Georgia Code § 31–17-7, last modified, 2012). The physician "may, but shall not be obligated to, inform the spouse, parent, custodian, or guardian of any such minor as to the treatment" (Georgia Code § 31–17-7, last modified, 2012). Such information may be given "even over the express refusal of the minor" (Georgia Code § 31–17-7, last modified, 2012).

The DOH representative also suggested that the IRB contact the DOH's OGC.

After a week, the researchers followed up with the IRB to see if the IRB had contacted the DOH's OGC. The IRB did not respond by e-mail, and it is not clear if the IRB contacted the DOH OGC. However, the researchers were concerned about delaying the study further and therefore decided to proceed with the study without including AMSM.

Discussion

This case raises several serious concerns and needs for mechanisms to ensure fuller consideration of the public health and ethical issues involved in studies of AMSM. Unfortunately, despite prior calls by scholars and professional associations for IRBs to waive parental permission for similar studies (Bauman et al., 2020; Gilbert et al., 2015; Mustanski, 2011), and institutional ethics guidance documents (Rennie et al., 2009; WHO, 2018) barriers clearly persist, given the realities of complex institutional and legal contexts that can exist. Specifically, Maryland's law appears to explicitly permit waivers of parental consent, but the IRB nonetheless sought the OGC's opinion and "tabled" the decision. Funded for only a limited period of time, the researchers felt that delaying the study would pose problems.

The Georgia IRB also did not approve the waiver because the law allowed waivers for "venereal disease," but not explicitly HIV, and because of the CGO's interpretation of the law, which allows waivers for treatment but not testing of minors who "profess" a venereal disease, but does not explicitly state that testing is permitted. Such laws may have been written when diagnoses of a venereal diseases were based solely on patients reporting symptoms (e.g., pus) rather than on objective diagnostic laboratory tests. Yet the CCO's interpretation of the law thus appears to be overly narrow, and to miss the spirit of the law or countervailing ethical arguments. The Georgia DOH, when asked, said that parental permission was required for treatment of offspring 13-years old and older, but did not specify whether the state considered emancipated or mature minors (e.g., 16–17-year olds) differently than other minors (e.g., 13-year olds). Yet states generally recognize mature or emancipated minors as able to make healthcare decisions on their own. Presumably, the state may well have considered these age groups differently, but the researchers, wanting to avoid delaying the study, did not pursue the matter further.

In the case of HPTN 078, in addition to the ethical considerations that support waiving of parental permission (respect for adolescents' autonomy, avoiding harm to participants, social and scientific benefits and social justice), the study also directly benefits individual participants' health, protecting them from HIV through PrEP. Although this medication may have potential side

effects, it is now part of standard of care, and these potential adverse events have been well-described, and shown to be relatively minor, and can thus be well presented in consent forms. Moreover, these adolescents are at high risk of acquiring HIV if not on PrEP. Critics argue that adolescents may not sufficiently comprehend the relevant risks and benefits, but studies suggest that AMSM can grasp the risks and benefits (Knopf et al., 2017; Mustanski et al., 2017), and researchers could address such a possible challenge—e.g., by carefully assessing each potential participant's comprehension.

Given that studies have found that around 75% of AMSM would not participate in HIV research if permission is required (C. B. Fisher et al., 2018), requiring such permission would also thus significantly bias the sample and reduce the generalizability and usefulness of the entire study and thus its scientific and social value.

An IRB's insistence on obtaining parental permission is of added concern since certain vulnerable groups, including AMSM, and especially African-American and Latino AMSM, are at increased risk of HIV. Hence, studies to assess these vulnerable, hard-to-reach populations are especially critical, and barriers to conducting such research can serve to perpetuate social injustices.

Robert Levine, who was involved in writing The Belmont Report (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979) thus called for reconsiderations of policies concerning the involvement of adolescents in research, seeing current regulations as overly protective (Levine, 1995). He pointed out that regulations have in fact strengthened protections for all research, and altered public perceptions of research. He suggested several recommendations—e.g., assessing whether the minor is already obtaining healthcare services independently, and possibly having adolescents identify an adult who comprehends their situation, is dedicated to their well-being, and can offer support. The Society for Adolescent Medicine has also argued that the regulations concerning adolescent health research should be reviewed and modified (Levine, 1995; The Society for Adolescent Medicine, 1999).

The HPTN 078 example highlights how difficulties can persist for investigators and IRBs, who may at times feel compelled to alter their recruitment or other aspects of their study design to avoid delaying the research, given that projects supported by the National Institutes of Health (NIH) and other funders are invariably time-limited. IRBs, policymakers, and others should thus take into account these costs and decrements in the potential quality and quantity and thus social benefits of the research.

IRBs have been criticized for tending to focus on procedural, regulatory and logistical issues, rather than underlying substantive ethical issues and considerations *per se* (Schrag, 2017). IRBs have also been found to vary, often for idiosyncratic reasons rather than because of differences in community values. For instance, 34% of IRB chairs would require parental consent for an

interview on support for abortion, and 69% said their IRB requires parental consent for all research on minors, with chairs who review fewer adolescent protocols more likely to say so (Mammel & Kaplan, 1995). Goldman and Katz (1982) reported inconsistencies among IRBs as well, but did not examine why. The HPTN experience reveals a key factor—differing perceptions and interpretations of a state's laws.

This case therefore reveals barriers to public health ethics that have received little, if any, attention in the prior literature, regarding not only *which* ethical considerations should affect decisions, but also *who* is ultimately making these decisions, and in *what* particular institutional and legal contexts—particularly, the critical roles of OGCs and CCOs, to whom IRBs may defer, and the fact that these offices have competing priorities, protecting the institution from possible legal risks and reputational damage that they perceive. OGCs and CCOs thus appeared to weigh protection of the institution over public health ethics. The Georgia and Maryland universities' OGCs interpretations and implementation of relevant law therefore raise concerns. The federal regulations state that IRBs must defer to state laws, but the present case indicates how state laws may not always explicitly address the issues faced by the IRB, and end up getting interpreted in highly subjective, narrow ways. The Georgia IRB and institution also expressed ongoing concern about how parents would react, even though the researchers responded that they would inform such a parent that they were following state law (i.e., IRBs may impede such research *despite* state law). Moreover, the Georgia CCO said it was open to another interpretation of the law, recognizing that its own initial sense of the law was only one among other potential interpretations. This case thus illustrates how institutions and IRBs may differ due to how they *interpret, apply* and *weigh* relevant laws.

Difficulties this study faced may have arisen partly because it investigates sexual behavior, and in particular, same-sex behavior. Among adolescents aged 17, 30% have had sex (Finer & Philbin, 2013), but only 43% of parents say they feel very comfortable talking with their children about sex in general (Planned Parenthood Federation of America, 2016). Given traditional taboos against sex before marriage, many adults feel uncomfortable and a visceral disgust (i.e., producing a "yuck response") about the possibility that their 16–17-year-old is sexually active and is gay or bisexual (George, 2012). The wide differences among IRB chairs concerning waiving parental permission for studies regarding sexual attitudes and behavior (George, 2012) suggest that many chairs may still feel uncomfortable about these issues. IRBs can encounter difficulties with studies on sexual issues among adolescents due to a few IRB members' personal discomfort (Klitzman, 2015).

IRBs should clearly focus on research ethics principles (of autonomy, beneficence, non-maleficence and justice), rather than visceral biases and emotional responses of moral disgust. Yet Leon Kass, former chairman of

the U.S. President's Council on Bioethics, and some religious organizations have argued that moral disgust is "an emotional expression of deep wisdom" (Kass, 2020). Other scholars have demonstrated, however, that these strong emotions can result from cognitive tendencies to maintain familiar social categories (Niemelä, 2011) and that disgust has historically been used to legitimate stigma and discrimination (e.g., homophobia and anti-Semitism) (Nussbaum, 2004).

This case also underscores how public health laws do not always reflect current science or key ethical principles or consensus. Many public health laws were written before the HIV epidemic existed, and therefore do not explicitly include HIV as a STI or venereal disease, though NIH, CDC and WHO all consider HIV to be an STI (U.S. DOH and Human Services, 2022). The fact that regulations do not explicitly mention HIV leaves room for ambiguity, and may be interpreted by IRBs and OGCs to mean that the statute does not apply to HIV. This case therefore suggests, too, needs to clarify or possibly change such laws.

Laws presumably reflect and embody a state's consensus concerning ethical values and responses to social, technological, or other developments. Some individuals may disagree with a law, but must conform to it, since society has determined that the good of the whole outweighs whatever harms the law may cause. Yet laws can lag behind shifts in ethical consensus and social and technological changes (Brazier, 2005). In recent years, for instance, recognition and acceptance of LGBTQ issues have been growing in many segments of society (Harms, 2011). The interpretations, applications and implementations of laws can also vary considerably. Hence, the specific applications of laws may not always be wholly ethical, and ethical behaviors may not always be deemed legal.

Clearly, IRBs and institutions vary in their responses to these issues—with the Massachusetts IRB very open to this research, while the Georgia one was not. One could argue that research on AMSM should only be done at those institutions that already have experience with such studies. However, AMSM may face varying challenges across different geographic regions. Research is thus needed through a wide range of institutions.

This case also highlights how investigators usually have relatively limited amounts of time in which to conduct a study (commonly 1–3 years), and must therefore balance the benefits of spending additional time trying to arrange to include adolescents against the harms and costs of delaying the study and longer-range benefits of maintaining effective working relationships with their IRB for future studies. For one multi-site study, IRBs varied in time to approval from 52 to 798 days (median 286) (Green et al., 2006). Unfortunately, for any one study, researchers may not want, or be able, to devote resources to challenging or opposing their IRB or institution, and instead feel needs to proceed with a study, and not contest an IRB's decision

(which could take several months, if not longer). Researchers are often hesitant to challenge IRB decisions, in part because of not wanting to antagonize IRBs, with whom they will presumably have to work with on multiple future projects, and not wanting to significantly delay and impede research (Klitzman, 1997).

Funders should consider these obstacles, too, allowing for additional time or extensions of grants when these barriers emerge. In addition, researchers should contact their IRB before even agreeing to serve as a research site for a study, to gauge their IRB's potential response. PIs may need to educate and communicate with, IRBs, OGCs CCOs, and others well in advance when controversial issues may be involved. The Georgia researchers here contacted the IRBs 1–2 months beforehand, but this case suggests that considerably more advance time (e.g., perhaps 3–6 months, if not longer) may be needed to fully resolve such issues. Still, such "testing the waters" requires additional resources—i.e., for the researchers to contact the IRB at institutions where they may not eventually even submit the protocol, due to these barriers.

This case also has several important implications for future research. The principal argument the researchers used in three of these sites was that the law allows adolescents to self-consent for certain procedures related to HIV testing and treatment. Researchers from the fourth site, Massachusetts also cited the potential harms to these participants if parental consent were required, the impracticability of requiring parental permission and the decreased confidentiality of the adolescents that would result. Researchers at others sites, in retrospect, could potentially have also used such additional, ethical arguments, along with articulation of the reduced scientific and therefore social benefit of the research if parental consent were required (since adolescents who would then participate might be less likely to be at highest risk for HIV acquisition), justice concerns (given data suggesting that adolescents at highest risk of becoming HIV infected and who might therefore be more likely to be excluded if parental permission were required are disproportionately Black and Latinx) and beneficence (that the study would benefit the participants themselves directly and this population more broadly).

However, it is not clear that additional ethical arguments would have altered IRBs' decisions, since two of the IRB responded to the protocol based on their own and their institution's interpretations of legal regulations, referring the protocol to the OGC, with decisions based wholly on legal, not ethical arguments. Hospital and university OGCs and CCOs focus to a large extent on protecting the institution from possible lawsuits (Peri, 2008; Saks & Landsman, 2009). Thus, it is not evident that additional ethical arguments would have altered these OGCs' and thus IRBs' decisions, but researchers in the future could and should still try.

The researchers planned to use the customary confidentiality protections (e.g., HIPAA) and did not specify additional unique or separate privacy

protections for adolescents. Yet none of the IRBs requested any such added protections, or mentioned needs for additional privacy protections as a reason for declining to approve the study.

While the researchers in Georgia engaged the IRB prior to submitting the proposal, the researchers in Massachusetts, Maryland and Alabama did not formally communicate with the IRBs prior to the submission. Such interactions in Maryland, and earlier such engagement in Georgia, may, however, possibly have been helpful, though whether the IRBs would have altered their adherence to strict and narrow interpretations of state laws remains unclear.

Regarding IRBs' potential concerns about parents later learning of their AMSM's participation, the parents may never find out. A researcher could tell parents who learn of their adolescent's participation that the study is designed to benefit the health of their adolescent and others (to avoid HIV infection) that the adolescent has certain rights and freely and voluntarily decided to participate, that among adolescents aged 15–17, 30% have had sex (Finer & Philbin, 2013), that harm reduction is vital, that negative attitudes toward LGBTQ issues among adolescents can harm these adolescents, and that the law doesn't oppose testing. Researchers could potentially add that around 75% of AMSM would not participate in HIV research if permission were required (C. B. Fisher et al., 2018), and that requiring such permission would thus significantly bias the sample and reduce the generalizability and usefulness of the entire study and thus its scientific and social value. Research could also offer assistance to adolescents who are wondering whether and how to disclose their participation (and perhaps their LGBTQ status) to their parents.

Unfortunately, the IRB barriers presented here may also discourage crucial efforts to study AMSM. Indeed, Gilbert et al. (2015), whose requests for waiver of parental permission in a study of PrEP among AMSM was approved by only 7 of 13 IRBs, found that many PIs doubted that their IRB would approve the research and they anticipated challenges in obtaining such approval.

This case underscores, too, needs for an improved external appeals system for researchers to be able to contest IRB decisions in a timely way. The federal regulations allow for a kind of "appeals system," in which individual IRBs can ask HHS to convene a panel of experts to determine if non-beneficial research on children that involves more than minimal risk can proceed. But that process can take months or years to make decisions, and the present case involves beneficial, rather than non-beneficial research, and is not more than minimal risk over standard of care (Ross, 2005). Moreover, this process needs to be instigated by an IRB, not a PI.

It is also unclear how single IRBs (sIRBs), which the federal government has recently mandated for federally funded multi-site studies (National Institutes of Health [NIH], 2016), will proceed in cases such as HPTN 078, in which states may differ in their relevant laws. Presumably, sIRBs may let individual local IRBs then make their own decisions, but inter-IRB variations, due partly

to personal biases or discomfort of one or a few IRB members, may impede principles of public health ethics.

While researchers should clearly follow pertinent governmental regulations, the HPTN 078 experience presented here highlights how the uses, interpretations and implementations of such laws can be highly subjective, and how IRBs should take into account the vital needs for research on the health needs of AMSM—the risks to AMSMs requiring parental permission and the benefits of not doing so. The Georgia OGC and IRB appear to have focused instead on legal considerations. It may be easy for an OGC to oppose research, but the loss to scientific and social benefits can be significant.

Local laws may themselves be idiosyncratic or unclear, underscoring needs to seek to change these at state or local levels. The Georgia law, for instance, is inherently illogical in allowing treatment but not testing since, obviously, testing is needed in order to justify treatment.

The examples of IRB responses presented here suggest as well needs to consider refinements and revisions to current laws. Advocates for AMSM should work with researchers and other stakeholders at institutional, governmental, and community levels to educate policymakers, public health departments, IRB chairs, members and staff, OGCs and CCOs about why waiving consent in certain studies can be acceptable

This case also highlights how international guidance documents are important, but may face challenges that need to be addressed. None of the researchers appear to have cited international ethics guidelines. In part, these documents lack legal standing, at least in the U.S., and U.S. IRBs can therefore choose to dismiss or ignore them. However, in the future, researchers should consider drawing on these documents in seeking IRB approval for such studies.

The researchers here could potentially have cited such guidance documents and ethical arguments more fully, which may have perhaps have helped persuade IRBs. The new UNAIDS and WHO *Ethical considerations in HIV prevention trials* (2021) and *HPTN ethics guidance in research* (Brown et al., 2021) will hopefully assist in reducing the barriers faced by HPTN 078 and persuade IRBs if reviewing such protocols today. The updated *HIV Prevention Trials Network ethics guidance for research* (Brown et al., 2021) states, for instance, that:

> It is advisable to ensure appropriate engagement of adolescent representatives, including involving them on existing advisory structures such as [Community Advisory Boards or Groups] or developing separate youth advisory boards to provide input on key study aspects such as recruitment and consent (Brown et al., 2021).

The HPTN 078 study did not do so, perhaps partly because this guidance was released only after the HPTN study was begun. The IRBs that rejected the researchers' requests did not mention this lack of such advisoryinput as

a reason, however such efforts may have helped. In future research, such a board may help persuade IRBs to allow waiver of parental permission.

UNAIDS and WHO guidelines also now state that,

> Parental consent for sensitive research can act as a barrier to enrollment and can cause social harms like parental sanction, and it might skew enrollment for low-risk adolescents (UN AIDS & WHO, 2021).

However, the document does not elaborate on what to do in such situations. Indeed, the next sentence of the document, rather than continuing to address the question of possible waiver of parental permission, states, "Every effort should be made to obtain the adolescent's informed decision to participate in the trial" (UN AIDS & WHO, 2021).

Hence, authors of future iterations of these documents might also consider how to address these legal challenges, emphasizing to CCOs OGCs and IRBs key ethical principles (e.g., of beneficence).

In sum, more attention and efforts to overcome these challenges are vital through heightened recognition of these challenges, including of the roles of institutional and legal contexts, and the ways various interpretations of these laws can impede important public health prevention endeavors to aid AMSM.

Acknowledgments

The authors would like to thank Theresa Gamble, PhD, Julian Dormitzer, RN BSN; Chris Root, BA, Kelly Lowensen, RN, MSN, ACRN and D. Scott Batey, PhD for their contributions to this manuscript, and Lundyn C Davis, Sayantanee Das, Jiseop Kim, Amanda Shen, Gabriella Smith, and especially Patricia Contino for their assistance with the preparation of this manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The HIV Prevention Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068619, UM1AI068613, UM1AI1068617), with co-funding from the National Institute of Mental Health, and the National Institute on Drug Abuse.

ORCID

Robert Klitzman http://orcid.org/0000-0002-6827-8063

References

Baral, S. D., Ketende, S., Schwartz, S., Orazulike, I., Ugoh, K., Peel, S. A., Ake, J., Blattner, W., & Charurat, M. (2015). Evaluating respondent-driven sampling as an implementation tool for universal coverage of antiretroviral studies among men who have sex with men living with HIV. *Journal of Acquired Immune Deficiency Syndrome*, *68*(2), S107–S103. https://doi.org/10.1097/qai.0000000000000438

Bauman, L. J., Mellins, C. A., & Klitzman, R. (2020). Whether to waive parental permission in HIV prevention research among adolescents: Ethical and legal considerations. *Journal of Law, Medicine & Ethics*, *48*(1), 188–201. https://doi.org/10.1177/1073110520917010

Boston College Law School's Juvenile Rights Advocacy Project. (2006). *Consent to medical treatment by minors in Massachusetts: A guide for practitioners*. Retrieved December 28, 2022, from https://www.mass.gov/doc/consent-tomedical-treatment-by-minors-in-massachusetts/download

Brazier, M. (2005). Where the law and the ethics conflict? *Research Ethics Review*, *1*(3), 97–100. https://doi.org/10.1177/174701610500100305

Brooks, R. A., Etzel, M. A., Hinojos, E., Henry, C. L., & Perez, M. (2005). Preventing HIV among Latino and African American gay and bisexual men in a context of HIV-related stigma, discrimination, and homophobia: Perspectives of providers. *AIDS Patient Care STDS*, *19*(11), 737–744. https://doi.org/10.1089/apc.2005.19.737

Brown, B., & Sugarman, J., & The HPTN Ethics Working Group. (Revised 2020, February, Updated 2021, December). *HPTN ethics guidance for research*. THE HIV HPTN Ethics Working Group. Retrieved January 11, 2023, from https://www.hptn.org/sites/default/files/inlinefiles/HPTN%20EWG_FINAL_EGD%20updates2021_02Dec2021_V3.1_0.pdf

Centers for Disease Control and Prevention. (2018). *HIV surveillance supplemental report: Estimated HIV incidence and prevalence in the United States, 2010-2015*. Retrieved December 20, 2022, from https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillancesupplemental-report-vol-26-1.pdf

Centers for Disease Control and Prevention. (2021, November 23). *PrEP for HIV prevention in the U.S*. Retrieved December 20, 2022, from https://www.cdc.gov/nchhstp/newsroom/fact-sheets/hiv/PrEPfor-hivprevention-in-the-US

Coombs, A., McFarland, W., Ick, T., Fuqua, V., Buchbinder, S. P., & Fuchs, J. D. (2014). Long-chain peer referral to recruit black MSM and black transgender women for an HIV vaccine efficacy trial. *Journal of Acquired Immune Deficiency Syndrome*, *66*(4), e94–e97. https://doi.org/10.1097/qai.0000000000000197

Council for International Organizations of Medical Sciences in collaboration with the World Health Organization. (2016). *International ethical guidelines for health-related research involving humans*. Retrieved December 20, 2022, from https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMSEthicalGuidelines.pdf

Finer, L. B., & Philbin, J. M. (2013). Sexual initiation, contraceptive use, and pregnancy among young adolescents. *Pediatrics*, *131*(5), 886–891. https://doi.org/10.1542/peds.2012-3495

Fisher, C. B., Fried, A. L., Ibrahim Puri, L., Macapagal, K., & Mustanski, B. (2018). Free testing and PrEP without outing myself to parents:" Motivation to participate in oral and injectable PrEP clinical trials among adolescent men who have sex with men. *PLoS One*, *13*(7), e0200560. https://doi.org/10.1371/journal.pone.0200560

Fisher, C. M., Irwin, J. A., & Coleman, J. D. (2014). LGBT health in the midlands: A rural/urban comparison of basic health indicators. *Journal of Homosexuality*, *61*(8), 1062–1090. https://doi.org/10.1080/00918369.2014.872487

George, A. (2012, July 11). *The yuck factor: Disgust's surprising power*. New Scientist. Retrieved December 20, 2022, from https://www.newscientist.com/article/mg21528731-800-the-yuck-factor-the-surprisingpower-of-disgust/

Georgia Code TITLE 31 – HEALTH CHAPTER 17 - CONTROL OF VENEREAL DISEASE § 31-17-7. (Last modified 2016, October 14). *Consent of minor to medical or surgical care or services; informing spouse, parent, custodian, guardian*. Retrieved December 28, 2022, from https://law.onecle.com/georgia/title-31/31-17-7.html

Gilbert, A. L., Knopf, A. S., Fortenberry, J. D., Hosek, S. G., Kapogiannis, B. G., & Zimet, G. D. (2015). Adolescent self-consent for biomedical human immunodeficiency virus prevention research. *Journal of Adolescent Health*, *57*(1), 113–119. https://doi.org/10.1016/j.jadohealth.2015.03.017

Goldman, J., & Katz, M. D. (1982). Inconsistency and Institutional Review Boards. *JAMA*, *248*(2), 197–202. https://doi.org/10.1001/jama.1982.03330020041027

Green, L. A., Lowery, J. C., Kowalski, C. P., & Wyszewianski, L. (2006). Impact of institutional review board practice variation on observational health services research. *Health Services Research*, *41*(1), 214–230. https://doi.org/10.1111/j.1475-6773.2005.00458.x

Guttmacher Institute. (Last updated January 1, 2022). *Minors' access to STI services*. Retrieved December 20, 2022, from https://www.guttmacher.org/state-policy/explore/minors-access-sti-services

Harms, W. (2011, September 28). *Americans move dramatically toward acceptance of homosexuality, survey finds.* uchicago news. Retrieved January 11, 2023, fromhttps://news.uchicago.edu/story/americansmove-dramatically-toward-acceptance-homosexuality-survey-finds

HIV Prevention Trials Network. (2020). *HPTN 078: Enhancing recruitment, linkage to care and treatment for HIV-infected men who have sex with men (MSM) in the United States.* HPTN HIV Prevention Trials Network. 2023. Retrieved March 1, 2022, from https://www.hptn.org/research/studies/hptn078

Kass, L. R. (1997). The wisdom of repugnance: Why we should ban the cloning of humans. *New Republic*, *216*(22), 17–26. PMID: 11654974.

Klitzman, R. (2015). *The ethics police? The struggle to make human research safe*. Oxford University Press.

Klitzman, R., Marhefka, S., Mellins, C., & Wiener, L. 2008. Ethical issues concerning disclosures of HIV diagnoses to perinatally infected children and adolescents. *The Journal of Clinical Ethics*, *19*(1), 31–42. PMID: 18552051; PMCID: PMC2770331 (No DOI). https://doi.org/10.1086/JCE200819106.

Knopf, A. N., Ott, M. A., Liu, N., Kapogiannis, B. G., Zimet, G. D., Fortenberry, J. D., & Hosek, S. G. (2017). Minors' and young adults' experiences of the research consent process in a phase II safety study of pre-exposure prophylaxis for HIV. *Journal of Adolescent Health*, *61*(6), 747–754. https://doi.org/10.1016/j.jadohealth.2017.06.013

Lee, M. G., & Quam, J. K. (2013). Comparing supports for LGBT aging in rural versus urban areas. *Journal of Gerontological Social Work*, *56*(2), 112–126. https://doi.org/10.1080/01634372.2012.74758

Levine, R. J. (1995). Adolescents as research subjects without permission of their parents or guardians: Ethical considerations. *Journal of Adolescent Health*, *7*(5), 287–297. https://doi.org/10.1016/1054139x(95)00175-r

MacKellar, D. A., Valleroy, L. A., Secura, G. M., Behel, S., Bingham, T., Celentano, D. D., Koblin, B. A., Lalota, M., McFarland, W., Shehan, D., Thiede, H., Torian, L. V., & Janssen, R. S., & the Young Men's Survey Study Group. (2005). Unrecognized HIV infection, risk behaviors, and perceptions of risk among young men who have sex with men: Opportunities for advancing HIV prevention in the third decade of HIV/AIDS. *Journal of*

Acquired Immune Deficiency Syndromes, *38*(5), 603–614. https://doi.org/10.1097/01.qai.0000141481.48348.7e

Mammel, K. A., & Kaplan, D. W. (1995). Research consent by adolescent minors and institutional review boards. *Journal of Adolescent Health*, *17*(5), 323–330. https://doi.org/10.1016/1054-139x(95)00176-s

Maryland Department of Public Health. (2018a, January 19). Subtitle 18 Human Immunodeficiency Virus (HIV) Infection and Acquired Immunodeficiency Syndrome (AIDS). *Notice of Proposed Action*, *45*(2), 90–94. Retrieved December 20, 2022, from https://health.maryland.gov/regs/Pages/Subtitle-18-HUMAN-IMMUNODEFICIENCYVIRUS-(HIV)-INFECTION-AND-ACQUIRED-IMMUNODEFICIENCYSYNDROME (AIDS)–(PREVENTION-AND-HEA.aspx

Maryland Department of Public Health. Treatment of Minors: Maryland Code Health General § 20-102. (2018, January 1). *Treatment for health-related problems*. Retrieved December 20, 2022, from https://codes.findlaw.com/md/health-general/md-code-health-gen-sect-20-102.html

Miller, R. L., Forte, D., Wilson, B. D., & Greene, G. J. (2006). Protecting sexual minority youth from research risks: Conflicting perspectives. *American Journal of Community Psychology*, *37*(3–4), 267–274. https://doi.org/10.1007/s10464-006-9053–4

Mustanski, B. (2011). Ethical and regulatory issues with conducting sexuality research with LGBT adolescents: A call to action for a scientifically informed approach. *Archives of Sexual Behavior*, *40*(4), 673–686. https://doi.org/10.1007/s10508-011-9745-1

Mustanski, B., Coventry, R., Macapagal, K., Arbeit, M. R., & Fisher, C. B. (2017). Sexual and gender minority adolescents' views on HIV research participation and parental permission: A mixed-methods study. *Perspectives on Sexual and Reproductive Health*, *49*(2), 111–121. https://doi.org/10.1363/psrh.12027

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979, April 19). *The Belmont report*. Retrieved December 28, 2022, from https://www.hhs.gov/ohrp/regulationsand-policy/belmont-report/read-the-belmontreport/index.html

National Institutes of Health. (2016, June 21). *Final NIH policy on the use of a single Institutional Review Board for multi-site research*. Retrieved December 20, 2022, from https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html

Niemelä, J. (2011). What puts the 'yuck' in the yuck factor? *Bioethics*, *25*(5), 267–279. https://doi.org/10.1111/j.1467-8519.2010.01802.x

Nussbaum, M. C. (2004, August 6). *Danger to human dignity: The revival of disgust and shame in the law*. The Chronicle of Higher Education. Retrieved December 20, 2022, from https://www.chronicle.com/article/danger-to-human-dignity-the-revival-of-disgust-andshame-in-the-law/

Office for Human Research Protections. (1993). *IRB guidebook*. Retrieved December 20, 2022, from http://wayback.archiveit.org/org745/20150930181805/http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm

Office for Human Research Protections. (2009, January 15). *Pre-2018 requirements Code of Federal Regulations*. Retrieved December 20, 2022, from https://www.hhs.gov/ohrp/regulations-andpolicy/regulations/regulatory-text/index.html

Office for Human Research Protections. (2019). *2018 requirements (2018 "Common Rule")*. Retrieved December 20, 2022, from https://www.ecfr.gov/on/2018-07-19/title45/subtitle-A/subchapter-A/part46

Peri, J. (2008). The wisdom of employed general counsel in higher education. *Widener Law Journal*, *18*(1), 191–204. (No DOI)

Planned Parenthood Federation of America. (Published 2011 October 3. Updated 2014, January 30, and 2016, October 28). *New poll: Parents are talking with their kids about sex but often not tackling harder issues*. Retrieved December 20, 2022, from https://www.plannedparenthood.org/about-us/newsroom/press-releases/new-pollparents-talking-their-kids-about-sex-often-not-tackling-harder-issues

Rennie, S., & Sugarman, J., & the HPTN Ethics Working Group. (2009, June 10). *HIV Prevention Trials Network ethics guidance for research*. THE HPTN HIV Prevention Network. 2023. Retrieved March 1, 2022, from https://www.hptn.org/sites/default/files/201605/HPTNEthicsGuidanceV10Jun2009_0.pdfchrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.hptn.org/sites/default/files/2016-05/HPTNEthicsGuidanceV10Jun2009_0.pdf

Ross, L. F. (2005). Lessons to be learned from the 407 process. *Health Matrix*, *15*(2), 401–421. PMID: 16238289.

Saks, M. J., & Landsman, S. (2020). The paradoxes of defensive medicine. *Health Matrix*, *30*(1), no page numbers listed. https://scholarlycommons.law.case.edu/healthmatrix/vol30/iss1/4/

Santelli, J. S., Smith Rogers, A., Rosenfeld, W. D., DuRant, R. H., Dubler, N., Morreale, M., English, A., Lyss, S., Wimberly, Y., & Schissel, A., & the Society for Adolescent Medicine. (2003). Guidelines for adolescent health research. A position paper of the Society For Adolescent Medicine. *Journal of Adolescent Health*, *33* (5), 396–409. https://doi.org/10.1016/j.jadohealth.2003.06.009

Schrag, Z. M. (2017). *Ethical imperialism: Institutional review boards and the social sciences, 1965–2009*. Johns Hopkins University Press.

The Society for Adolescent Medicine. (1999). Code of research ethics: Position paper of the Society for Adolescent Medicine. *Journal of Adolescent Health*, *24*(4), 277–282. discussion 283. https://doi.org/10.1016/S1054-139X(99)00003-8

U.S. Department of Health and Human Services. *HIVinfo*. Retrieved December 20, 2022, from. https://hivinfo.nih.gov/home-page

UN AIDS, & The World Health Organization. (2021, January 27). *Ethical considerations in HIV prevention trials*. Retrieved December 28, 2022, from https://www.unaids.org/en/resources/documents/2021/ethicalconsiderations-in-hiv-prevention-trials

Volz, E., & Heckathorn, D. D. (2008). Probability based estimation theory for respondent driven sampling. *Journal of Official Statistics*, *24*(1), 79–97. Retrieved December 20, 2022, from http://www.sverigeisiffror.scb.se/contentassets/ff271eeeca694f47ae99b942de61df83/pobability-based-estimation-theory-for-respondent-driven-sampling.pdf

World Health Organization. (2018). *Guidance on ethical considerations in planning and reviewing research studies on sexual and reproductive health in adolescents*. License: CC BY-NC-SA 3.0 IGO