Legal Barriers to Adolescent Participation in Research About HIV and Other Sexually Transmitted Infections

Whether adolescents can participate in clinical trials of pharmacologic therapies for HIV prevention, such as preexposure prophylaxis, without parental permission hinges on state minor consent laws.

Very few of these laws explicitly authorize adolescents to consent to preventive services for HIV and other sexually transmitted infections. Unclear state laws may lead to research cessation.

We have summarized legal, ethical, and policy considerations related to adolescents' participation in HIV and sexually transmitted infection prevention research in the United States, and we have explored strategies for facilitating adolescents' access. (*Am J Public Health*. 2016;106:40–44. doi:10.2105/AJPH.2015.302940)

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The second largest percentage (26%) of new HIV infections in the United States occurs among people aged 13 to 24 years, and most of those new infections occur in gay and bisexual young men (72%).[1] These rates of infection make high-risk adolescents an important target population for primary prevention. Used in conjunction with safer sex practices, preexposure prophylaxis (PrEP) has demonstrated effectiveness in preventing transmission in high-risk groups, such as men who have sex with men (MSM).[2] In the context of HIV, PrEP is defined as the use of antiretroviral medications in HIV-negative individuals to prevent HIV transmission. Using antiretroviral medications for prevention carries risks and can be fairly costly; therefore, current recommendations limit PrEP to those who are at an ongoing substantial risk of HIV infection, such as nonmonogamous MSM, serodiscordant couples, and intravenous drug users.[3]

For PrEP to be approved for use in adolescents who fall into these high-risk groups, studies must include adolescents. Parental permission is typically required for studies of minors that are funded by federal agencies that have adopted the Federal Policy for the Protection of Human Subjects (often referred to as the "Common Rule") or that are conducted by institutions that have agreed that all their research will comply with the Common Rule pursuant to a federal-wide assurance. Additionally, parental permission is generally required for studies of minors that are clinical investigations involving products the Food and Drug Administration (FDA) regulates.[4] Waivers of parental permission are possible for the first 2 categories of studies but not for the third.[4–6] Therefore, parental permission is required for most PrEP studies involving minors unless the minor is not considered a child under federal research regulations. This determination hinges on state minor consent laws, very few of which give explicit attention to consent to preventive services for HIV and other sexually transmitted infections (STIs).

These interlocking provisions, and state laws' lack of clarity on minors' consent for preventive services, have become significant legal barriers to conducting PrEP and other STI prevention research in the adolescent population. If parental permission is required for participation in this research, adolescents may not participate because they fear that asking their parents for permission is equal to notifying parents of their sexual orientation or that they are sexually active.[7] This can compromise scientific validity because of low enrollment rates or selection bias, which hinders important research to ascertain whether adolescents have different adherence rates, risk behaviors, or levels of understanding biomedical prevention methods than does the adult population.

An example from our own state illustrates the problems associated with unclear state laws along with inconsistent guidance for institutional review boards (IRBs). A protocol of a collaborative network funded by the National Institutes of Health and charged with the task of developing and implementing interventional clinical trials for HIV-infected and at-risk youths was submitted to an IRB in Texas. This protocol was an open label demonstration project and phase II safety study of preexposure prophylaxis use among MSM aged 15 to 17 years. A waiver of parental permission

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could not be obtained because the protocol was conducted under an investigational new drug application, which is subject to FDA regulations.

Because of the nature of the minor consent laws in Texas, minors could only be enrolled without parental permission if treatment for HIV was interpreted to include prevention. The investigators had multiple meetings with the IRB and consulted the institution's research ethics consultation service and legal counsel. Finally, after 5 months, agreement was reached that, although there is statutory ambiguity, the Texas definition of treatment could be interpreted to include prevention, and the IRB granted approval to conduct the research without parental permission. Unfortunately, the delay in IRB approval led to the Texas study site no longer being a viable option for the grantor. The unavailability of a research site that is located in a region with high rates of new HIV infection in youths has potential implications for the outcome of the study.

We summarize the current legal context and the issues raised for HIV and other STI prevention research involving adolescents, and we review relevant ethical and policy considerations. We conclude that there is a strong ethical and policy case for permitting adolescents to make decisions about HIV prevention and participate in HIV prevention research without parental permission, and we briefly explore strategies for facilitating adolescent access to STI prevention research, taking into account the relevant legal issues.

LEGAL CONTEXT

Parental permission is typically required for studies involving minors that comply with the Common Rule or that are clinical investigations involving products the FDA regulates. Eighteen federal agencies, such as the Department of Health and Human Services, have adopted the Common Rule, 15 of which have incorporated the policy in regulations. The regulations for Health and Human Services, which includes the National Institutes of Health, are codified at 45 CFR 46. Under these regulations, a waiver of parental permission can be obtained if (1) such a waiver does not adversely affect the rights and welfare of the child, (2) risks associated with research are minimal, and (3) the research could not practicably be carried out without the waiver.[5] Additionally, waiver is permissible if parental permission is not a reasonable requirement (e.g., for neglected or abused children) and the waiver is not inconsistent with federal, state, or local law, provided appropriate protective mechanisms are in place.[6] The comparable FDA research regulations, which apply to studies of drugs such as PrEP, do not permit waiver of parental permission.[4] Therefore, parental permission is required for PrEP studies involving minors and similar studies of therapies to prevent STIs, unless the minor is not considered a child under federal research regulations.

Both Health and Human Services and FDA regulations define a "child" as someone who is not legally able to consent to the treatment or procedure involved in the research according to the laws of the state where the research is conducted.[8,9] Accordingly, when an individual is younger than the age of majority (typically 18 years) but is legally authorized to consent to treatment under state law, that individual is not a child under the federal research regulations, and thus there is no requirement for parental permission to participate in research.

Some states have adopted the mature minor doctrine, which permits a minor to consent to or refuse care if it is established that the minor is mature enough to understand and appreciate the benefits and risks of that care.[10] These laws are applied on a case-by-case basis to allow minors who meet the maturity threshold to consent to health care generally. Other states grant minors general authority to consent to health care when parents are unavailable or unwilling to provide consent or when the minor is over a particular age threshold. However, only 17 states, including Delaware, Massachusetts, Nevada, Oregon, and West Virginia, have recognized the mature minor doctrine or granted general consent authority to large groups of minors.[11] Texas is among the states that have not taken either step.[12]

The alternative is to look to state laws that specifically define the circumstances under which individuals younger than the age of majority can legally give consent to health care. All 50 states and the District of Columbia have granted adolescents the legal authority to consent to the diagnosis and treatment of reportable infectious, contagious, or communicable diseases, including sexually transmitted diseases.[13] Moreover, 34 states have statutes that specifically authorize minor consent to HIV testing and treatment, or testing alone, through an HIV-specific statute or through the classification of HIV as an STI.[14] Five of those states (Arizona, Mississippi, New Mexico, New York, and Ohio) explicitly authorize minor access to HIV testing services but do not provide explicit authorization for HIV treatment.[14]

Only 7 states (California, Iowa, Kansas, Montana, Nebraska, North Carolina, and South Dakota) specifically authorize minors to consent to preventive services for STIs.[13] Additionally, many states permit minors to access nonpharmacologic STI prevention without parental permission, which is in line with US Supreme Court rulings extending the constitutional right to privacy to minors' access to contraception.[15]

Lack of clarity and variability across states are problematic not only clinically, when clinicians do not have guidance on prescribing HIV prevention to adolescents without parental consent, but also in the research context: multi-institutional studies are hindered because parental permission may be required in states where IRBs determine that prevention is not treatment under applicable state law. The issue of parental permission for participation in STI-related prevention research is a problem in this population. Perhaps most compelling, the youths most at risk for HIV infection (e.g., young MSM or unaffected partners in serodiscordant couples) would be unlikely to participate if parental permission was a requirement for their participation because these individuals are unlikely to have disclosed their sexual orientation or risk behaviors to their parents and may fear the repercussions of disclosure.

The Texas case highlights the implications of ambiguity in state law because of federal reliance on these laws to define a child. Without clear guidance regarding whether treatment includes prevention, IRBs are left

to interpret their state law, creating the potential for unjustified variation.[16] There is little evidence that general treatment-focused state laws were consciously crafted to exclude prevention. Rather, in most cases it is unclear whether treatment should be interpreted to encompass prevention. Hence, it is important to explore the underlying ethical and policy considerations.

ETHICAL AND POLICY CONSIDERATIONS

The ethical concepts of adolescent and parental autonomy and public health implications are important considerations in the evaluation of whether high-risk adolescents should be allowed to enroll in STI prevention research without parental permission.

Adolescent Autonomy

An important factor in determining whether parental permission should be required relates to adolescent autonomy, specifically adolescents' capacity to decide whether participating in research involving HIV PrEP and other STI prevention research is consistent with their values and best interests. Generally, children younger than the age of majority do not have the authority to consent to medical treatment or research participation without parental permission.[17,18] This is because it is presumed that children lack the capacity to make autonomous decisions and have not yet fully formed their own moral identity. They are treated as a vulnerable population in need of protection from harm. In the research context, parental permission is recognized as an important safeguard for protecting children from an unacceptable risk of harm.[19] With few exceptions, it is assumed that parents are most capable of ensuring that protection.[5,6,17] Thus, parental permission for research participation is generally both legally and ethically required. However, there are legal and ethical exceptions.

When adolescents are able to exercise the components of decision-making capacity as well as an adult, ethically they should be given authority over themselves. The chief components of decision-making capacity are paying attention to information, recalling information as needed, reasoning from present events to future likely consequences, appreciating that those consequences could happen to them, assessing those consequences on the basis of their values and beliefs, and expressing a preference on the basis of the previous components.[20] In the research context, the investigator has a duty to assess the adolescent's ability to weigh the risks and benefits from study participation. The role of the parents as decision-makers for the adolescent decreases as the adolescent's right to autonomy and capacity for independent decision-making increase.[21,22]

Several studies have compared the ability of adults and adolescents as young as aged 14 years to make informed decisions. In a study to evaluate developmental differences in competency to make informed treatment decisions using hypothetical treatment dilemmas, Weithron et al. found that adolescents aged 14 years did not differ from adults in their decision-making capacity related to treatment.[23] Similarly, in a study to evaluate minors' ability to understand their rights in research using hypothetical research vignettes, Bruzzese et al. found that 10th graders understood their rights as well as did adults.[24] Thus, minors are often granted the authority to make medical and research decisions for themselves, especially for reportable diseases, which pose a public health risk and for which minors are often reluctant to seek treatment because they fear loss of confidentiality.

Parental Autonomy

The considerations favoring respect for an adolescent's autonomy to make decisions about participation in HIV PrEP and other STI prevention research must be weighed against parents' claims to autonomy in raising their children. The US Supreme Court has affirmed deference to parents' decisions on the basis of a recognition that "natural bonds of affection lead parents to act in the best interests of their children."[17] Lainie Ross observes that parents generally have the right to raise their children as they see fit, and the state must have an overwhelming interest to override this right.[25] Moreover, Ross claims that state laws enabling minor consent place physicians in morally problematic situations in which they may be drawn into disrespecting what parents think is best, disregarding adolescents' need for further guidance, and colluding with adolescents against their parents.[25] Yet, Ross recognizes that adolescents do not always adhere to parental wishes and may engage in sexual behavior resulting in unwanted pregnancies or STIs.[25]

Indeed, the incidence of HIV infections from 2006 to 2009 increased by 21% among gay and bisexual males aged 13 to 29 years. Thus, HIV infection is a serious public health issue, which arguably gives the state an overwhelming interest in limiting the rights of parents.[1] Moreover, adolescents' participation in research could aid in expanding access to HIV prevention by providing important information that could be used to develop more prevention and treatment strategies for this age group.

Furthermore, a parental permission requirement may not be in the best interest of the adolescent. Adolescents are often not comfortable discussing their sexuality and sexual practices with their parents.[26] In fact, for many youths, parental involvement in or notification of their interest in or use of sexual health services is a deterrent to adolescents' continued use of these services.[7] Asking for parental permission for adolescents to participate in studies involving their sexuality may put adolescents at risk for experiencing negative consequences from parents if the adolescent does not want to answer parental questions regarding sexuality.[7]

Parental rights must be taken very seriously, but those rights are not absolute. Ultimately, if an adolescent has the capacity to make informed decisions and parental permission is not in the best interests of the adolescent, then it should not be required. Efforts should still be made to include parents in decision-making, with the minor's consent, and safeguards should be outlined in the research protocol to ensure that adolescents' vulnerabilities are addressed and young study participants are protected. Moreover, whether the confidentiality of health information obtained in the study will be maintained should be explicitly stated in the research protocol and consent form, and these statements should be in accordance with federal and state confidentiality laws. Like

minor consent, confidentiality of minors' health information is a complex issue, and state laws vary considerably and are often not in concordance with related minor consent laws (i.e., confidentiality may not be ensured even when the minor is authorized to consent).[27]

Public Health

The incidence of HIV infection in adolescents is a particular public health concern. The Centers for Disease Control and Prevention, state and local public health agencies, nongovernmental organizations, and researchers, clinicians, and health educators in the private sector have worked together to achieve an AIDS-free generation in the United States and have devoted significant time and energy to HIV testing, prevention, and treatment programs.[28] These efforts have paid off in reducing HIV incidence by more than two thirds since the height of the HIV epidemic in the United States. Yet, the current rate of HIV infection in youths suggests traditional preventive measures may not be as effective in the adolescent population. The rate of infection in MSM aged 13 to 29 years is particularly concerning.

Despite their contribution to new HIV infections, youths are relatively underrepresented in prevention research, particularly biomedical intervention studies.[2] Although the side effects and toxicities of antiretroviral medications have been evaluated in adolescents, the effectiveness of these medications in decreasing HIV transmission and the adherence rates of HIV-negative adolescents have not been evaluated. A parental permission requirement may make it impossible to obtain valid data because of selection bias or low response rates.[29] The same public health justification of reducing the incidence of HIV and other STI infections that supports granting adolescents the right to consent to testing or treatment applies to permitting adolescents to consent to HIV prevention research.

CONCLUSIONS

The rate of new HIV infection in adolescents is alarming, especially in the young MSM population. Research efforts to discover new drugs, prevention methods, and vaccines have made some progress in reducing the overall incidence of HIV infection in the United States, but these efforts need to include those most at risk—adolescents. Our analysis leads us to conclude that parental permission for adolescent participation in HIV preexposure prophylaxis and other STI prevention research is not ethically required and may undermine important interests, including the interests of adolescents themselves and public health. Other protections to minimize the risk to adolescents can and should be included in research protocols, such as the evaluation of the decision-making capacity of youths, the adoption of a community-based participatory research approach, careful attention to the development of youth-friendly protocols and consent procedures, and proper staff training.[7]

Unfortunately, especially when STI prevention research involves FDA-regulated products, unclear state laws together with the current federal research regulations leave IRBs confused about whether the parental permission requirement is applicable. Clarity does exist on several points. For example, all states and the District of Columbia have recognized the importance of permitting minors to consent to STI treatment. Furthermore, public health laws and policies clearly express a commitment to the prevention of HIV and other STIs, especially in high-risk populations, both to avoid needless suffering and to advance public health goals. Finally, more research on PrEP and other measures to prevent HIV and other STIs in high-risk adolescents is urgently needed.[2] Building on these points, we propose 2 strategies to address the legal barriers we have highlighted.

First, in states with existing minor consent provisions for STI treatment that do not expressly include prevention, we urge public health advocates and officials to partner with state legislators to promote amendments to minor consent statutes that would explicitly authorize minors to consent to preventive care related to STIs, including HIV. There is little reason to believe that legislators craft treatment-focused state laws to exclude prevention.

Nonetheless, the current ambiguity in many state laws obstructs important research, as in our Texas example, and creates barriers to receiving needed care in the clinical context. In the event of resistance related to fears of indiscriminate use of pharmacologic therapies such as PrEP in minors without parental oversight, legislators could be assured that recommendations for use of PrEP are carefully constructed to support limited, appropriate use and that any research conducted without parental permission will incorporate multiple protections for adolescent participants.

Second, absent clear evidence of a legislative intent to exclude prevention from treatment or an authoritative determination by a court that treatment excludes prevention, we believe that IRBs act reasonably and responsibly in concluding that treatment includes prevention in states with laws that authorize adolescents to consent to STI treatment, including HIV, but do not explicitly authorize minors to consent to preventive services. Therefore, pending changes in state law, we urge IRBs to adopt an open stance toward claims that the word "treatment" in state minor consent laws should be interpreted to encompass prevention. Consultation with the institution's legal counsel or research ethics consultation service, as in our example, is recommended to ensure proper interpretation of state law.

It would be helpful if the FDA and the Office of Human Research Protections provided guidance to foster greater consistency in IRB determinations within states that allow minors to consent to treating HIV and other STIs but do not explicitly address prevention. However, it is unlikely that either agency would want to preempt state law. IRB action that regulators support and the adoption of laws and policies that promote the inclusion of adolescents in prevention research would benefit adolescents and researchers and, ultimately, advance the important public health goal of an AIDS-free generation. AJPH

CONTRIBUTORS

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