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## Adolescent HIV Research Ethics in Resource-Constrained Settings: Low and Middle-Income Country Research Consortium Experience and Scoping Review

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### Contributors

JDT conceptualized the idea for the manuscript, with directional input from BGK, TDR, SKS, ECW, and SD. SD and JDT produced the initial draft and conducted the scoping review. Data on adolescent informed consent ethics provided by BGK, TDR, SKS, ECW, and JDT, with additional contributions by the wider PATC3H Consortium Adolescent Bioethics Working Group (see full list of contributors below). SD and JDT revised the manuscript with substantial edits and input from BGK, TDR, SKS, ECW, DFC, AS, GRD, PK, and CS. All authors approved the final draft.

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The comments and views of the authors do not necessarily represent the views of the Eunice Kennedy Shriver National Institute of Child Health and Human Development

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## Summary

**Background:** Adolescents in low- and middle-income countries (LMICs) have a high burden of HIV, increasing the importance of including adolescents in HIV research. Adolescence is a period of transition that introduces unique ethical challenges for HIV research. The aim of this paper is to describe the ethical-legal barriers to adolescent participation in HIV research studies and potential strategies for including adolescents in LMIC research studies.

**Methods:** We examined experiences from PATC3H, a research consortium focused on HIV prevention and treatment research in resource-constrained settings. The consortium includes studies in Brazil, Kenya, Mozambique, Nigeria, South Africa, Zambia, and Uganda. PATC3H researchers were asked to identify ethical and practical challenges for adolescent consent to research participation in these countries. We also used standardized scenarios to facilitate comparison of adolescent consent in these seven countries. Informed by our examination of PATC3H consortium experiences, we conducted a scoping review focused on solutions that could be used to enhance adolescent participation in LMIC HIV studies.

**Findings:** Our consortium experiences demonstrated many ethical challenges, including the following: inconsistent or absent guidance for the conditions under which adolescents can independently consent to research participation; guidelines that fail to account for the full array of adolescents' lives; and substantial variation in how ethical review committees assess adolescent research studies. Our scoping review identified several potential consent-related strategies to expand adolescent access to HIV research, including waiving parental consent requirements, allowing adolescents to provide independent research consent, and clarifying surrogate decision-making processes.

**Interpretation:** While there are several ethical and practical challenges in adolescent consent to HIV research participation in LMICs, these challenges can be addressed by alternative consent strategies. Guidance on the ethics of adolescent HIV research is needed to increase adolescent participation in research.

## Keywords

adolescents; HIV research; informed consent; low- and middle-income countries; research ethics; research participation

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## Introduction

The World Health Organization<sup>1</sup> and the Society for Adolescent Medicine<sup>2</sup> note that inclusion of adolescents in HIV research is a key priority. Given biological differences

between adults and children, there is a need to include adolescents in clinical research to determine treatment efficacy, safety and dosage.<sup>3</sup> Inclusion of adolescents in HIV research is particularly important in low- and middle-income countries (LMICs), where adolescents are at increased risk of HIV infection<sup>4-6</sup> and experience a substantial burden of HIV-related morbidity and mortality.<sup>7</sup>

Given the important behavioral, affective, cognitive, and physical changes that can affect adolescent decision-making abilities,<sup>8</sup> obtaining parental (or guardian) consent is typically required in addition to the adolescent's assent to participate in research. This dual consent/assent process provides the decision-making oversight of an adult with (presumably) the adolescent's best interest in mind, while at the same time recognizing the developing capacity of the adolescent to also make decisions on whether or not they agree to participate.<sup>9</sup> However, many adolescents face difficulties with participating in HIV studies because of country-specific laws, regulations and ethical practices regarding consent to research participation. Consider a 15-year-old girl who cannot negotiate barrier protection with her boyfriend, is seeking HIV testing, and is interested in joining an HIV prevention study she learns about at the testing site. Would she need parental (or guardian) consent to participate in the prevention study? The ethical-legal frameworks vary across LMICs. Some LMICs would not allow her to participate without explicit parental permission (e.g., Brazil), while others would allow her to participate without parental permission if she became emancipated through marriage or childbirth (e.g., Mozambique). Countries' consent processes also differentiate between consent to seeking care and consent for research participation. In some countries, she could consent to HIV testing without parental permission, but *not* to participating in the HIV prevention study (e.g., Kenya). In others, her ability to participate in the study without parental permission would depend on the ability of the researchers to justify this to an ethical review committee (e.g., South Africa). These differences suggest how ethical-legal consent requirements can impact adolescent participation in HIV studies across many LMICs.<sup>10</sup>

Despite the urgent need for adolescent participation in HIV research, there are few resources available to guide researchers to understand legal requirements and ethical recommendations for adolescent research. The existing landscape of legal and ethical frameworks in LMICs create several challenges related to adolescent consent to research participation, including the following: a lack of regulatory clarity and divergent approaches in ethical guidelines on research consent processes;<sup>11</sup> restrictions on including individuals younger than age 18 in studies without parental/guardian permission;<sup>12</sup> and a legal presumption that individuals who have reached a certain age (e.g. 18 years and older), achieved a certain status (e.g. marriage), or have certain conditions/responsibilities (e.g. pregnant, parenting) are capable of providing independent consent for research participation.<sup>13</sup> Given that systematic reviews<sup>14, 15</sup> and empirical studies<sup>16</sup> suggest that adolescents are under-represented and often systematically excluded from research, there is an urgent need to understand how consent processes may pose challenges to adolescent inclusion in HIV research, particularly in LMIC contexts.<sup>10</sup>

To address this gap, we examined the ethical-legal frameworks on adolescent consent to research participation in seven countries with PATC3H studies. We also conducted a

scoping review of potential strategies to enhance adolescent participation in HIV research. This analysis can inform the development of an ethical framework to ensure inclusion of adolescents in LMIC HIV research studies.

## Methods

Our analysis used data from two sources – a multi-national research consortium and a scoping review. The research consortium members submitted actual and anticipated challenges to a bioethics working group of the consortium and responded to a set of ethical scenarios from the perspective of their research setting. Actual challenges included problems encountered in organizing an HIV prevention research study for adolescents. Anticipated challenges were those ethical issues felt to be relevant in the specific LMIC setting.

The Prevention and Treatment through a Comprehensive Care Continuum for HIV-affected Adolescents in Resource Constrained Settings (PATC3H) consortium is supported by the *Eunice Kennedy Shriver* National Institute of Child Health and Development, the Office of Behavioral and Social Science Research, and the National Institute on Minority Health and Health Disparities at the US National Institutes of Health. The purpose of the consortium is to generate scientific knowledge in order to enhance HIV prevention and treatment for LMIC adolescents aged 10–24 years old.<sup>17</sup> The teams use a variety of individual, family, community, and structural interventions to enhance HIV outcomes across the prevention and treatment continuum. Consortium research studies are ongoing in Brazil, Kenya, Mozambique, Nigeria, South Africa, Uganda, and Zambia. A bioethics working group was composed of representatives from five of the seven study teams to better understand specific ethical challenges associated with adolescent HIV research in their respective settings. From monthly group discussions with core members of this working group, we gathered experiences of ethical challenges encountered in PATC3H studies, either anticipated by institutional review boards (IRBs) or experienced in the field. We also reviewed and summarized the ethical-legal frameworks for the inclusion of adolescents in research in each of the seven countries where PATC3H studies are conducted and focused specifically on adolescent informed consent to research participation, whether in the form of legislation or national ethics guidance documents. Additionally, to compare differences in adolescent research participation across the different settings of the consortium, we created two sets of scenarios (see Supplemental Data 1 and 2). Each scenario provided details about an adolescent interested in participating in an HIV study and then asked if this individual would be able to eligible to participate with specific reference to informed consent processes. The first set of scenarios focused on adolescents in various living arrangements, while the second focused on different adolescent key populations. PATC3H consortium investigators knowledgeable about regulatory and ethical in-country issues at each of the study sites were asked to provide programmatic data responding to these scenarios. These investigators had personal experience with IRB applications for adolescent HIV studies and/or a working understanding of regulatory and ethical requirements in the local contexts.

In addition to collecting scenario data from these sites, we organized a scoping review to identify potential strategies to enhance adolescent inclusion in HIV research. The scoping review followed the methodological framework for conducting a scoping study proposed by

Arksey and O'Malley.<sup>18</sup> The scoping review addressed ethical challenges identified by the PATC3H consortium. We searched PubMed, Google Scholar, and Embase on July 11<sup>th</sup>, 2019 and updated the search on October 17<sup>th</sup>, 2019. We used the search terms “ethics”, “LMIC”, “resource-constrained”, “HIV”, “adolescent”, “youth”, and “consent”. We included studies from high-income countries if the strategy proposed had relevance to the ethical-legal context of LMICs. No limitations were placed on publication date nor publication type (e.g. original research, systematic review).

## Results

### Local Ethical-Legal Contexts for Adolescent Participation: PATC3H Experiences

We observed substantial variation in the ethical-legal frameworks for adolescent informed consent in research participation in the seven LMIC countries (Table 1). While all seven countries require parental/guardian consent in addition to adolescent assent for individuals under the country's age of majority, exceptions to this general requirement vary widely. Most countries outline some provisions for waiving parental/guardian consent in instances where adolescents have the legal status of an adult (e.g. mature or emancipated) and/or where researchers can demonstrate that waiving parental consent would be the most appropriate course. The circumstances and eligible ages for which parental/guardian consent can be waived vary across the study sites, and three countries (Brazil, Mozambique and Zambia) do not appear to have explicit guidelines for waiving parental/guardian consent.

Ethical challenges associated with the existing regulatory frameworks include the following: inconsistent or absent guidelines for determining the ability of adolescents to independently consent to research participation; regulations/guidelines that fail to account for the full array of adolescents' living conditions/experiences; and substantial variation in the guidance to ethical review committees assessing adolescent studies. For example, ethics guidelines for obtaining parental consent waivers developed by the South African Department of Health are inconsistent with the South African National Health Act requirements to obtain parental/guardian informed consent for adolescents under age 18 (Table 1).<sup>19</sup> In Mozambique, the requirement to obtain parental consent for adolescents under age 18 does not fit with the living conditions experienced by many adolescents, including individuals who live and work away from their family home, or who may be married and heading their own households before the age of 18.<sup>20</sup> Finally, research ethics committees in Uganda must determine when a waiver of parental/guardian consent is justifiable on case-by-case basis.<sup>21</sup>

While the practical implications of these challenges varied across study sites, all sites reported barriers to adolescent inclusion due to informed consent processes. For example, variability in local ethical review committee decisions, denial of waivers for parental/guardian consent, and the exclusion of adolescents from research participation due to inability to meet parental/guardian consent requirements were all mentioned. Consent requirements vary between research site and may impact adolescent HIV research participation (Supplemental Table 1).

## Potential Strategies

Our scoping review identified several potential strategies to expand adolescent participation in HIV research studies, including waiving parental/guardian informed consent for adolescents for whom parental/guardian involvement may not be possible/appropriate, allowing adolescents to independently consent to participation (without parental involvement), and clarifying surrogate decision-making processes. Although none of these are a panacea, each could be implemented in LMIC settings to expand adolescent participation in HIV studies.

Waiving parental consent requirements is a potential strategy to increase adolescent participation in HIV research. Some HIV studies in non-LMIC contexts have successfully obtained IRB approval to allow parental consent to be waived for adolescents at high risk of HIV, including a study of preexposure prophylaxis (PrEP) adherence and safety among young men who have sex with men (MSM) and transwomen (ATN 113),<sup>22</sup> a study of HIV/STI prevention among African American youth receiving mental health services,<sup>23</sup> and a study of a text messaging-based HIV prevention strategy among gay, bisexual and queer adolescent males.<sup>24</sup> In an LMIC context, PATC3H studies in Nigeria were able to make use of federal guidelines to waive parental consent participation of adolescents between the ages of 14 and 17 years old in HIV studies.<sup>25</sup> In addition, the nationwide Brazilian adolescent PrEP study (PrEP 1519) involves adolescents between 15 and 17 years old, and obtained a waiver of parental consent for the use of PrEP.<sup>26</sup>

Another strategy to increase adolescent inclusion in HIV research studies is allowing adolescents to independently consent to participation without parental involvement. Evidence suggests that many adolescents have sufficient cognitive capacity for informed decision making participating in HIV research studies.<sup>27</sup> For example, some adolescents already have the ability to assess potential risks and benefits despite not yet being legal adults, and are already independently making decisions that impact their health, including decisions about accessing sexual and reproductive health services. Studies suggest that individuals as young as 14 years old and those of legal adult status (18 and 21 years old) did not differ in decision making capacity<sup>28</sup> and that adolescents age 14–17 years old demonstrate abilities associated with fully-informed self-consent.<sup>29</sup> Additionally, a study of decision-making among adolescents age 16–19 years old found that most adolescents already had the developmental capacity to understand and provide independent informed consent for a hypothetical HIV vaccine trial.<sup>30</sup> Age-based assumptions about decision-making capacity also imply that that parents/guardians are inherently better able to understand and assess the implications of research participation than adolescents. However, parents/guardians can vary in their ability to comprehend research, and may overestimate the risks associated with HIV research or be suspicious of researchers' intentions.<sup>31</sup>

Limiting adolescents' ability to independently consent to research participation may also be ethically problematic based on the assessment of risks versus benefits of participation. Some have made the case that if adolescents are legally able to consent to STI treatment without the need for parental consent, then they should also be able to independently consent to STI research participation, such as HIV research, if the benefits to participation outweigh the potential risks.<sup>32</sup> Additionally, excluding adolescents from research while still offering

them participation in testing and treatment may be ethically problematic as there may be unique treatment effects that will only be uncovered and addressed through research. In light of these considerations, the UNICEF Office of Research has recommended that national laws recognize adolescents' evolving capacities to make independent decisions about their health and allow adolescents to independently consent to research participation wherever possible (e.g. if a study is deemed lower-risk and the adolescent is assessed to be capable of providing informed consent).<sup>33</sup>

Studies have demonstrated that adolescents themselves support the option for independent adolescent consent in LMIC contexts as a strategy for enhancing adolescent inclusion in research. For example, a study conducted with adolescents in Kenya on consent for HIV research found that while the majority of adolescents preferred to involve their parents in the consent process, about a quarter recommended that adolescents be able to consent independently in order to include all those who may be eligible for research participation.<sup>34</sup> Other studies indicate that allowing adolescents to independently consent to research participation may be particularly important for engaging sexual and gender minority youth in HIV research.<sup>29, 35</sup>

Finally, surrogate decision-makers may increase adolescent participation in HIV research. Surrogate decision-makers are defined as individuals who have been given responsibility to act in the best interests of an adolescent and can provide consent in place of an adolescent's parent or legal guardian.<sup>36</sup> These individuals could include non-immediate family members, youth advocates, or those responsible for an adolescent. This strategy was used successfully by the Malawian site of the Girl Power study of youth-friendly health services for adolescent girls.<sup>37</sup> The study established a community club of individuals age 18 years and older who could serve as authorized representatives for granting consent to study participation in place of parents/guardians.<sup>38</sup> While surrogate decision-making may be particularly important in low-risk studies or where a parent/legal guardian cannot be identified (e.g. adolescents experiencing homelessness),<sup>39</sup> challenges remain with determining who can serve as a surrogate decision-maker. There is some evidence from LMICs to suggest that community consultation can be effective in identifying appropriate surrogate decision-makers for minors with unsupportive or absent parents.<sup>40, 41</sup> Community consultation and further consideration of surrogate decision making is warranted.<sup>42</sup> It may also be helpful to consider how legal authorities could serve as surrogate decision-makers in granting authorization to proceed with studies in which parental consent would not be possible to obtain. For example, a study of mental health among orphaned adolescents living with HIV in South Africa sought and received consent to proceed without the need for parental permission from the High Court of Johannesburg, which serves as the upper guardian of minors.<sup>43</sup>

## Discussion

Our analysis of the ethical-legal frameworks at PATC3H study sites demonstrates several barriers to inclusion of adolescents in HIV research. At the same time, waiving parental consent, allowing adolescents to provide independent informed consent, and clarifying surrogate decision making could all help to overcome some of these challenges. This study makes a contribution to the literature by including specific LMIC research scenarios,



drawing on the strengths and ethical/regulatory support of the PATC3H research consortium, and identifying potential strategies relevant in resource-constrained settings.

LMIC laws and related assumptions about capacity as an adult likely have a substantial impact on inclusion of adolescents in HIV research studies. There is variation in when children assume the legal status of an adult in different settings. For example, children legally become adults at 18 years old in Brazil, Kenya, South Africa, and Zambia. However, in Mozambique an individual may be considered an emancipated minor at 18 years old and only achieves legal adult status at 21 years old. A propensity score matched study found that legal age of consent below 16 years old was associated with an increased coverage of HIV testing.<sup>44</sup>

Rigid parental consent requirements can also decrease adolescent participation in HIV research.<sup>45</sup> For example, it may be inappropriate to obtain parental/guardian consent for studies involving adolescents engaged in transactional sex<sup>46</sup> and adolescents who are displaced or orphaned.<sup>47</sup> Requiring parental/guardian consent may pose a particularly strong barrier to HIV research participation for lesbian, gay, bisexual, transgender (LGBT) and non-binary adolescents due to concerns about negative reactions to disclosing their sexual/gender identity.<sup>29, 35, 48–50</sup>

Our scoping review suggests that alternative informed consent processes such as independent adolescent consent, waiving parental consent under select conditions, and surrogate decision-making may enhance adolescent inclusion in HIV research in LMICs. While some countries have provisions for allowing subsets of adolescents to independently consent to participate (e.g. sexual- or gender-minority adolescents in Kenya), others have limited recognition of circumstances where parental/guardian consent requirements could be waived (e.g. Brazil). Alternatives to parental consent can help HIV researchers to obtain crucial information on adolescent HIV prevention and treatment. For example, the registrational trials of HIV pre-exposure prophylaxis (PrEP) in at-risk minors then later allowed licensure of PrEP for adolescents at risk of HIV in the U.S.<sup>51</sup> Critically needed data on the safety and use patterns of PrEP among minors facing disproportionate risk of HIV were successfully obtained by implementing independent adolescent consent procedures that were thoughtfully deliberated and iteratively established before launching the trial.<sup>52</sup> To advance adolescent HIV prevention and treatment globally, future efforts are needed to understand the shared challenges of adolescent consent to HIV research participation in LMICs, with the goal of identifying strategies that would be both feasible and acceptable in these contexts.

Our analysis has several limitations that are worthy of consideration. First, our empirical examples only included seven sites and was not exhaustive. Second, many of the ethical issues related to adolescents are not well articulated in laws or well-known to institutional review boards or researchers. The experiences of PATC3H would be more knowledgeable about site-specific issues. At the same time, our group of research teams have a broad understanding of research ethics in these contexts and have provided more extensive feedback on the scenarios. Third, while this research was not limited to informed consent,

we found more examples and practical strategies related to informed consent. Further research is needed on adolescent ethical issues that go beyond informed consent alone.

Our study has implications for research and policy. From a research perspective, this analysis provides practical strategies to consider when designing adolescent HIV prevention studies in selected LMICs. Further research is needed to understand how best to include adolescents in HIV prevention research within other settings. From a policy perspective, guidelines focused on how best to include adolescents in LMIC HIV research are needed. This would require a consultative process with a range of stakeholders, including adolescents, ethical review committee members, and policy-makers. Continued engagement between PATC3H study teams and national policy-making stakeholders as part of the next phase of this research project may be able to address some of the barriers identified.

HIV researchers in LMIC settings experience a range of challenges with adolescent informed consent that can hinder adolescent inclusion in HIV studies. However, there are some potential strategies for addressing consent-related challenges that could be useful in LMIC contexts.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Ethical-legal frameworks related to adolescent informed consent in selected LMIC countries and related ethical challenges and practical implications for adolescent research participation.

Country	Framework for adolescent informed consent	Ethical challenges	Practical implications
Brazil	When a research participant is less than 18 years old, parental/guardian permission and minor assent are required for participation, except in very specific situations such as emancipation. <sup>53</sup> The informed consent must be signed in-person by the parent(s)/guardian(s), with a separate assent form signed by the minor. <sup>54</sup> Based on age of consent laws and regulations surrounding access to HIV-related care, adolescents are defined as individuals between ages 12–18 years, <sup>55</sup> however this definition of an adolescent is not readily applicable to the context of informed consent for research.	There is limited recognition in the current regulations for circumstances where waiving parental/guardian permission may be appropriate.	Collecting data on adolescents can be difficult due to the requirement to obtain written parental/guardian consent. This challenge is amplified among the most vulnerable adolescents (e.g. LGBT youth).
Kenya	Parental/guardian consent to participate in research is required in addition to the minor's assent for individuals under age 18 years and older than age 12 years. <sup>56</sup> Parental/guardian consent can be waived for emancipated minors (minors granted the status of adult by court order) <sup>57</sup> or mature minors (married, pregnant, mothers, or household head). <sup>56, 58</sup> National guidelines for conducting adolescent HIV/sexual health research also outline circumstances when a waiver of parental/guardian consent may be appropriate, such as if the child is a member of a key population (e.g. LGBT, MSM, sex workers, or persons who use drugs). <sup>59</sup>	National guidelines for adolescent HIV/sexual health research participation outline several ethical concerns pertaining to informed consent for vulnerable adolescents; for example, children of parents who have died of HIV (may require use of an independent advocate to determine if research participation is in the child's best interest), adolescents that are in school (must obtain support of education authorities, but they cannot provide participation permission), and adolescents belonging to specific populations (e.g. LGBT, MSM, sex workers, etc. who often face barriers in accessing health care and treatment). <sup>59</sup>	While the possibility of parental/guardian consent waivers make the inclusion of vulnerable adolescent populations more feasible, the current model reflects a 'life stages' approach to consent rather than a developmental one – i.e. assumes that an adolescent who is married/parenting/heading a household is more capable of independently consenting to participation than other adolescents.
Mozambique	An individual under age 21 is considered a minor. <sup>60</sup> However, minors may be eligible to independently consent to research studies by age 18, as this is the point at which an individual can be considered an 'emancipated minor' by law. <sup>60</sup> For individuals under 18 years old, consent needs to be obtained from a parent/guardian in addition to the minor's assent to participate. <sup>20</sup>	The requirement to obtain parental/guardian consent does not reflect the living situation of many minors; for example, a substantial proportion of girls between the ages of 15–19 in Mozambique are married, and many adolescents also live and work away from their family home. <sup>20</sup>	The requirement to obtain parental/guardian consent can result in a lengthy consent process. There may also be divergences in willingness to participate between the adolescent and their parent/guardian.
Nigeria	Due to conflict between the existing legal frameworks, there is no clear legislation specifically stating the minimum age of consent for research participation in Nigeria. <sup>25, 61</sup> The age at which an individual can consent differs between legislative acts, variously defining age 18 (1999 Constitution of the Federal Republic of Nigeria), age 16 (2003 Child Right Act), and age 14 (1958 Children and Young Persons Act) as the age of independent consent. <sup>25</sup> However, national guidelines established in 2014 recommend that individuals age 17 and older be allowed to independently consent to research participation, and that parental consent be waived for individuals 16 and younger (in therapeutic research) or 14 and younger (in non-therapeutic research) who are married, a head of household, emancipated, or experiencing abuse perpetrated by their parent/guardian. <sup>25</sup>	Existing legislation may be too broad in stipulating that persons and institutions acting in a child's 'best interest' are able to grant permission for. <sup>25</sup> An additional challenge with defining 'age of consent' is the tendency to conflate age of consent for sexual and reproductive health services with age of consent for sexual debut. <sup>62</sup>	Due to a lack of clear legal framework defining age of consent for research, parental/guardian permission tends to be the default requirement for individuals younger than age 18 (the age at which the Nigerian constitution defines adulthood). <sup>25</sup> However, there are often challenges with identifying a guardian who would be legally capable of providing this consent, as many adolescents in Nigeria live with surrogate caregivers. <sup>61</sup>
South Africa	Adolescent consent processes are outlined in multiple sources. The National Health Act requires parental/guardian consent for the participation of individuals younger than age 18, in addition to the minor's assent. <sup>63</sup> However, national ethical guidelines developed by the Department of Health <sup>64</sup> include provisions for waiving parental/guardian permission for individuals younger than age 18 in a variety of circumstances; for instance, if the risks are minimal, the child is	Due to legislative inconsistencies, there are no clear regulations specifying when adolescents may independently consent to research participation. <sup>19, 65</sup> RECs are in a difficult position when assessing research involving adolescents, and may require	Uncertainties and differences in local REC practices may exclude adolescents from participation in some South Africa HIV studies.

Country	Framework for adolescent informed consent	Ethical challenges	Practical implications
Uganda	<p>16+, researchers provided evidence of engagement with participating community members to indicate a waiver of parental permission is acceptable, and a Research Ethics Committee (REC) approved the waiver.<sup>61, 65</sup></p> <p>Individuals under age 18 require parental/guardian consent to participate in addition to the minor's assent. Mature minors are defined as individuals age 14–17 who have drug dependency or an STI; emancipated minors are defined as individuals under age 18 who are pregnant, married, have a child, or are self-sufficient.<sup>21</sup> A mature or emancipated minor may consent independently to research participation if two conditions are met: 1) The Institutional Research Ethics Committee (REC) approves the research study as acceptable based on community evidence, and 2) The protocol provides clear justification for involvement of mature/emancipated minors and for the need to waive parental/guardian consent.<sup>21, 66</sup></p>	<p>substantial justification and documentation of a study's consent processes.<sup>63</sup></p> <p>Provisions in the national guidelines to waive parental/guardian permission to participate in research depend greatly on the assessment of the reviewing REC, which must determine on a case-by-case basis whether a study would be "not objectionable to parents or guardians", and if the justification for including mature/emancipated youth is sufficient.<sup>21</sup></p>	<p>Even within prescribed guidelines there can be variation in which projects are granted waivers to include youth without parental/guardian permission and which are not.</p>
Zambia	<p>The National Health Research Act specifies that minors are individuals under the age of 18, and requires parental/guardian consent for both therapeutic and non-therapeutic research participation.<sup>67</sup> The Zambia National Guidelines for HIV Counseling and Testing note that individuals under age 18 who are married, pregnant, or parenting would be considered emancipated minors and thus capable of independent consent.<sup>68</sup></p>	<p>There is an absence of provisions for seeking a waiver of parental/guardian consent or guidance on when adolescents may provide independent consent to research participation. The need to obtain parental/guardian consent may require extensive community engagement to ensure the research is fully understood, which can be particularly challenging in rural locations with low levels of literacy.<sup>69</sup></p>	<p>Many research studies exclude adolescents.</p>