EDITORIAL REVIEW

Ethical considerations for research involving pregnant women with HIV and their children

Megan S. McHenry[a,b], Eric R. Masese[c], Daniel Kinyanjui[d], Edwin Were[e], James G. Carlucci[a,b], John M. Humphrey[b,f], Esther Wahome[b], Dennis Munyoro[b], Grace White[a], Amira Nafiseh[a], Kristen Cunningham[a], Madeline Cory[a], Mark Nyalumbe[b], Roselyne Ananda Ombitsa[b], Mary A. Ott[g,*] and Colin Halverson[h,*]

Pregnant and postpartum women with HIV (PPWH) and their children have historically been excluded from certain research in the name of protection. This may, however, inadvertently exacerbate health disparities. While calls for their inclusion have increased, additional practical guidance to achieve this goal is needed. Within this editorial, we provide practical recommendations for enabling PPWH and their children to participate ethically in research by identifying and addressing issues that potentially put them at risk. We ground this discussion in a framework that considers the various vulnerabilities that may exist when involving this population in research. These considerations were further informed by person-centered empirical data collected in Kenya, as well as reviews of the literature. Five key domains of consideration include: prioritizing confidentially, support for appropriate agency in decision-making, broad considerations related to respect for persons, community engagement, and appropriate oversight. We hope that the resulting guidance will inform future research practices, with implications for advancing ethical and inclusive research involving PPWH and their children.

AIDS 2025, **39**:1866–1877

Keywords: child, HIV, pregnant women, research ethics, review

Introduction

Globally, there are nearly 16 million children (ages 0–14 years) who have been born exposed to HIV [1]. Each year this number grows as approximately 1.3 million women with HIV become pregnant [2]. However, with the successful implementation of interventions for preventing vertical transmission, incident HIV infections

[a]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN, USA, [b]Academic Model Providing Access to Healthcare (AMPATH) Kenya, [c]Department of Sociology, Psychology, and Anthropology, Moi University, [d]Department of Mental Health and Behavioral Sciences, College of Health Sciences, [e]Department of Reproductive Health, Moi University School of Medicine, Eldoret, Kenya, [f]Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, [g]Arnhold Institute for Global Health, Department of Global Health, Icahn School of Medicine at Mount Sinai, New York City, NY, and [h]Center for Bioethics, Indiana University School of Medicine, Indianapolis, IN, USA.

Correspondence to Megan S. McHenry, MD, MS, FAAP, 705 Riley Hospital Drive, Room 5900, IN 46208, USA.

Tel: +1 317 944 7260; e-mail: msuhl@iu.edu

* M.A.O. and C.H. are co-senior authors.

Received: 5 February 2025; revised: 12 April 2025; accepted: 19 April 2025.

DOI:10.1097/QAD.0000000000004273

among children have decreased to around 120 000 per year [3]. Growing evidence demonstrates that children who are HIV-exposed but uninfected nonetheless have worse health and neurodevelopmental outcomes compared to their unexposed peers [4,5]. These challenges underscore the critical need for research to include pregnant and postpartum women with HIV (PPWH) and their children [4,5].

Such research presents unique challenges, largely due to the potential vulnerability of these populations. The Declaration of Helsinki defines vulnerability as the experience of greater risk of harm or being wronged [6]. Thinking about vulnerability has shifted from group-based vulnerability (e.g. children and pregnant persons) to characteristics and contexts that lead to vulnerability, such as poverty, medical illness such as HIV, and gender inequities [7]. Persons identified as vulnerable have often been excluded from research, due in part to increased regulatory requirements for inclusion, and in-part to concerns about increased risk of harm. However, there is increasing recognition that exclusion itself leads to harms. The Declaration of Helsinki now recognizes the potential harm of exclusion from research, which can perpetuate health disparities or limit access to effective treatments for populations, such as pregnant women and their children, who have been excluded from research in the past [6,8]. Researchers are, therefore, urged to focus on equitable access to research, balancing the potential risks of inclusion against the harms of exclusion when making recruitment and sampling decisions.

Understanding and addressing the vulnerabilities faced by PPWH and their children living in low-resource settings is essential in the design and conduct of ethical research. Vulnerabilities can arise from cognitive, medical, social, allocational, legal, and power-related factors, but PPWH and their children often experience multiple, overlapping vulnerabilities. The burden of living with HIV – including both physical effects such as chronic inflammation, neurologic sequelae, cardiac effects, and associated mental health burden – and the effort needed for treatment and care constitute a medical vulnerability [9–13]. HIV-associated stigma makes both PPWH and their children more susceptible to social exclusion, exploitation, stress and mental health disorders, and lack of access to resources, representing a social vulnerability [14,15]. An intersectional analysis reveals that PPWH are more likely to live in extreme poverty, experience gender inequality, and have limited access to quality healthcare [16]. For these reasons, any overarching principles of research ethics must be highly nuanced and contextualized to the lived experiences of PPWH and their children.

Globally, there has been a broad movement away from the exclusion of populations previously identified as 'vulnerable' toward more equitable access to research [6]. Simultaneously, there has been a movement to increase the involvement of communities and research participants themselves – including participants with vulnerabilities – in the application and contextualization of research ethics to work in their local contexts [17]. The majority of PPWH and their children are residents of countries struggling with postcolonization resource disparities, and therefore face additional vulnerabilities [6], such as allocation and infrastructural vulnerability. Members of the global research community must recruit these populations into their studies due to both a justice-based obligation to the communities and a science-based requirement for greater generalizability and representation.

In recent years, the HIV scientific community has made significant efforts to raise awareness about the need for including PPWH in research. Organizations such as the WHO, Pregnancy and HIV/AIDS: Seeking Equitable Study (PHASES) Project, International AIDS Society/Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) program, and the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network, have released ethics-based recommendations to enhance their inclusion [18–20]. These guidelines provide clear, actionable steps across a broad spectrum of research areas, including building capacity for research involving PPWH and supporting their inclusion in research. They also offer guidance to key stakeholders, including funders, industry, regulators, ethics committees, researchers, publishers, and other organizations [20].

Despite these impressive and ground-breaking efforts, there exist few concrete examples of how this guidance can be effectively and practically applied in real-world research settings beyond the recommendations with PHASES [19]. The present review focuses on identifying and addressing issues that put PPWH and their children at increased risk in research, as well as on providing practical considerations for research involving this population.

Development of research considerations for pregnant and postpartum women with HIV and their children

In 2019, we performed a systematic review of the empiric literature focused on ethical considerations of involving PPWH in research [21]. This review yielded only three articles. One provided key insights from HIV investigators and clinicians [22], and two studies included information directly gathered from PPWH [23,24]. The PHASES and 'Breastfeeding, Antiretroviral, and Nutrition' studies aimed to develop guidance to advance the health needs of pregnant women with and at risk for HIV through responsible research strategies [24,25]. These articles included the perspectives of women living with or at high risk for HIV, researchers, and clinicians. They highlighted the importance of adequate informed

consent, consideration of paternal involvement, access to research and treatment, and balancing risk (both intrinsic and extrinsic to the study itself). We then embarked on our own qualitative study of women with HIV who had participated in research during their pregnancy. Although cut short by the COVID-19 pandemic, we gained valuable perspectives from 12 women who described their motivations for participation, primarily altruism, and their greatest concerns, primarily disclosure of HIV status [26]. A more recent review of research focused on PPWH echoed these concerns, utilizing a relational ethics perspective that further acknowledges how PPWH are systematically disadvantaged and inseparable from their communities [27]. This review highlighted the communitarian and appropriate agentive values held by communities in many East African countries, including Kenya.

This foundational but limited literature sets the stage for a deeper and more directed analysis of the ethical conduct of research with PPWH and their children. To that end, we performed 75 one-on-one qualitative interviews and two multi-stakeholder participatory workshop, using a person-centered approach to gather empirical data on local experiences and local values regarding research. In-depth interviews were conducted from February to November 2024 and primarily included PPWH who had recently participated in research with their infants ($n = 29$), as well as with uninfected women who served as controls ($n = 16$). Other interviewees were members of communities directly impacted by such research, who were identified as salient groups by local experts and thought leaders. These interviewees included partners and individuals offering close support ($n = 12$), clinical providers ($n = 4$), research assistants ($n = 5$), village elders and chiefs ($n = 4$), and local and national ethics committee members ($n = 4$). All interviews were intended to allow PPWH and other interested parties to contribute to creating guidelines for ethical research engagement by providing their preferences and thoughts. The qualitative analysis of these interviews is presented elsewhere [28,29].

In April 2024, a two-day workshop was held, gathering 40 individuals to discuss issues and values in performing research with PPWH and their children. This workshop included PPWH, their male partners, community leaders, research assistants, and ethics committee members. After drafting the findings and recommendations, our team held a final workshop in November 2024 with 12 PPWH who had not previously participated in research. The women reviewed our findings and recommendations to evaluate how they aligned or conflicted with their concerns and considerations regarding research participation. These additional insights were utilized to refine the recommendations presented in this review.

Data from interviews and workshops were analyzed by a multidisciplinary team consisting of US and Kenyan research and clinical professionals with expertise in the following disciplines: adult and pediatric infectious disease, pediatrics, obstetrics, psychiatry, sociology and anthropology, adolescent medicine, ethics, and peer mentoring. The Chair of the Moi University Institutional Research and Ethics Committee was also a part of this team. This work was approved by local and international ethics review committees and written consent was obtained from participants.

Environmental context for research considerations

A person-centered approach to research and care includes recognition of individual strengths and vulnerabilities, life contexts, lived experiences, and preferences [30,31]. Using this approach, we also acknowledged the multidimensional nature of PPWH's experiences with research, which may include stigma and discrimination related to their HIV status [32], gender inequities, poverty, and high rates of gender-based violence [33], as well as increasing focus on their children [34,35]. We extended this approach by involving a broad range of additional stakeholders interacting with PPWH and their children, allowing those closely connected to their moral and practical worlds and medical decision-making to contribute insights on empowering PPWH across all stages of research engagement.

Global research guidelines, such as the Declaration of Helsinki and Belmont Report, are aligned with the values and ethical priorities, including autonomy, beneficence, and justice, local to the high-income countries in which they were originally formulated [17,36]. Because of the ascendance of autonomy in modern bioethics discourse, much of these regulations focus on informed consent, and perceptions of vulnerability focus on the ability of the individual to act autonomously and free from coercion, which does not sufficiently capture the impact of the research on individuals in societies where greater emphasis may be placed on interconnectedness within family and communities. In our Kenyan data, Ubuntu principles of interrelatedness are prioritized and valued in a way different from that of high-income countries. While the diverse viewpoints captured in our data may not be universally applicable to all research settings involving PPWH, neither are aspirationally global guidelines. Instead, our analysis offers contextually grounded insights that may be modularly applicable and adaptable across similar settings, including previously colonized regions where communitarian and agentive values inform everyday practice.

Recent updates to two influential international research guidelines, the Declaration of Helsinki and the Council for International Organizations of Medical Sciences (CIOMS), take a more person-centred approach than has historically been adopted and highlight key areas of

importance for research involving PPWH and their children. Most prominently, these foci include meaningful engagement with potential participants and communities as well as global equity [8]. However, making these high-level ethical principles actionable can be challenging, especially when the local context and its norms differ significantly from those in which these guidelines were developed. The proposed research considerations are not intended to replace these guidelines or other work in this area [37]; rather, their purpose is to operationalize these guidelines' general principles for PPWH and their children within the Kenyan context.

To frame and organize the structure of these considerations, we draw on Kipnis' bioethical taxonomy of vulnerability in research [38]. This approach addresses the specific sources of vulnerability, an individual's characteristics and environmental contexts, which contrasts with traditional group-based approaches that categorically exclude population groups from research (e.g. pregnant persons and children) despite internal heterogeneity. Our approach centers on equitable access to research for groups traditionally excluded. It focuses on characterizing the ways in which an individual might be vulnerable (e.g. poverty, medical illness, and gender inequities), and assuring appropriate protections and safeguards be in place, preserving the integrity of the research process and building on capacities and strengths within these settings. Kipnis outlines six types of vulnerability, including cognitive, juridic, deferential, medical, allocational, and infrastructural [39], all of which may be applicable for PPWH, with examples noted (Table 1).

The considerations we present are based in community values and the lived experiences of individuals living and working within these settings. This approach emphasizes the importance of local community voices and local institutional research ethics committees, consisting of individuals living and working within the communities they serve. However, despite the efforts of these local committees, it can be challenging to represent the full scope of PPWH and their children's experiences in research, as stigma and cultural hierarchies may limit candid representations. Through the following considerations, we aim to provide practical guidance for researchers and ethical committees and ensure that research involving PPWH and their children reflects an inclusive, respectful, and contextually grounded approach across settings.

Considerations for involving pregnant women with HIV and their children in research

The most critical issues and values we identified by the participants in the workshop were confidentiality, support for individual agency, access to care, community engagement, and appropriate oversight and guidance. We note that these critical issues and values were identified by participants themselves, and are framed differently than the bioethics principles of respect for persons, beneficence, and justice. For the purposes of this manuscript, we have adopted participants' enumeration of values and critical issues. We elaborate on each of these considerations below, and demonstrate the ways in which context, local values, and lived experiences can be interwoven. Additional practical examples and strategies are included in Table 1. Recommendations for addressing them were likewise informed by PPWH and key stakeholder perspectives. Although many are related to a broader category of respect for persons, the participants identified each of these as distinct concerns grounded within their lived experiences and local context.

Prioritizing confidentiality

Confidentiality is a mainstay in all research guidelines. Protection of personal and health information, as well as allowing for privacy of research activities, are fundamental elements of research protections and have clear guidance for their operationalization [40]. However, there are additional complicating factors related to confidentiality that should be considered by researchers working with PPWH, such as pervasive HIV stigma – internalized, experienced, and anticipated – in many Kenyan communities [41,42]. The potential for unwanted disclosure of one's HIV status through research participation is a related consideration, especially in communitarian societies marked by gender inequities where unwanted disclosure also has implications for one's partner, child, and her connection within society. Over 30% of Kenyan women with HIV experience intimate partner violence after disclosing their HIV status to their partners [43]. For this reason, most research teams avoid explicit disclosure of participants' HIV status. However, unintentional disclosure can still occur when research is performed by an organization that is well known within the community because of its history of HIV-related work. For example, logos on study personnel clothing, materials, or vehicles were identified by our participants as sources of unintentional disclosure, regardless of one's actual HIV status. Quality of research and its scientific validity can be hindered because of low rates of participation or follow-up related to.

Another manner by which unintentional disclosure may occur is through study documentation. Information sheets outlining research participation are often provided to research candidates to allow them to reference the information later. These documents are often required by ethics committees to contain key details, such as the title of the study, why that individual was recruited, and other information, any of which might potentially disclose their HIV status and therefore could be stigmatizing if discovered by another person. Additionally, these

Table 1. Practical examples of how to enact ethical considerations in research involving pregnant women with HIV.

	Potential scenario posing a challenge for PPWH	Considerations	Source of Information	Potential strategies to prevent or mitigate challenge
Cognitive vulnerability	PPWH reports understanding about study activities, risks, and benefits, but later, it is clear that she did not fully understand the study.	PPWH generally are less likely to complete primary and secondary education compared to their uninfected peers. This may make it more difficult to fully understand the study information unless additional effort is made. Additionally, the long-term nature of some studies may increase the chance to forget about study details and rights.	Literature review Key informant interview Authors experience and consensus	Use of information sheets and consent forms written in as simple language as possible to convey the document's main points. Use plain language and ensure that it is translated in the language the participant feels most comfortable with, even if it is not a national language. Also, consider culturally appropriate infographics and/or a verbal component of the consenting process. For long-term longitudinal studies, a periodic review of all study activities, reminder of ability to withdraw at any time, and possibly reconsenting.
	Due to limited prenatal care, PPWH may be approached for study enrolment during the delivery or immediate postpartum periods.	The period surrounding the delivery of a child can be filled with significant stress, discomfort, and an inability to carefully consider the nuances of study participation.	Key informant interview Authors experience and consensus	Ideally, PPWH should be recruited during an antenatal visit, when there is less pressure and stress within an interaction while prioritizing privacy. If this is not possible, researchers should consider sharing information about the study during the delivery and postpartum period but then invite the PPWH and their infants back at another time of their convenience to discuss the study information in more detail.
Allocational vulnerability	PPWH only wants to participate in clinical trial if they are placed in the intervention group and receive additional services and resources.	PPWH who lack resources may view research opportunities as a way to gain access to those resources, such as care and financial reimbursement. The biggest concern related to allocation vulnerability is undue inducement. For randomized clinical trials, the quality of evidence is dependent of a nonbiased sample. However, in many resource-limited settings, participation in research may be one of the few ways of accessing certain services or interventions.	Literature review Authors experience and consensus	Educate and remind participants about clinical equipoise; it would be unethical to conduct a trial if there was not genuine uncertainty about whether the intervention is any more less effective than the control. Also, consider other types of study designs that would ultimately allow for all participants to receive the treatment at some point in time (e.g. stepped-wedge). Consider providing a neutral benefit to the standard of care in the control groups that would not influence the primary outcome.
Juridic vulnerability	Partner of PPWH denies PPWH and child right to participate in research	In many paternalistic cultures, male partners' may not want their partner or child to participate in research. Rights and responsibilities for the guardian(s) of a child may differ across settings. Additionally, maternal deference to another guardian's refusal may depend on the closeness of the family unit (e.g. if the father lives with the child and supports family, more deference may be given)	Literature review Key informant interview Workshop discussion Authors experience and consensus	Assess whether involving the PPWH research without her partner's knowledge or consent would put her or her child at risk of harm (e.g. violence, abandonment, social ostracism). If so, consider deferring participation. Work with local ethics committees and community advisory boards, if available, to understand the sociocultural context and how decisions are typically made. If women often consult spouses, allow time and space for that discussion without making spousal approval a condition of participation.
	PPWH are found to participate in research much more often when their own clinical provider discusses it with them.	While key informants noted that they have a strong preference to have their own clinical providers discuss study activities with them, there is concern in the literature that this would cause undue influence.	Literature review Key informant interview	Depending on the setting and risk of the study, it may be appropriate for patient's own clinical providers to be directly involved in the research activities. Local institutional review boards can help guide this process if there is uncertainty.

Table 1 (*continued*)

	Potential scenario posing a challenge for PPWH	Considerations	Source of Information	Potential strategies to prevent or mitigate challenge
Medical vulnerability	A new easy-to-take, long-acting HIV medicine is available through a study and people are requesting to switch from their current regimen to this new drug.	Historically, lack of antiretroviral therapies would make PPWH particularly vulnerable to exploitation in early-stage trials. More recently, therapeutic misconceptions can affect medically vulnerable patients, assuming that whatever the research is studying is better than standard of care, which may be sub-optimal.	Literature review Key informant interview	During the enrolment process, make very clear that we do not know for sure whether this drug will work as well or better than one's current regimen. Clear guidance on monitoring of the medication and when they would discontinue its use should also be discussed.
Deferential vulnerability	PPWH hides participation in research from close contacts, including partner.	HIV stigma is still prevalent in many places in the world and disclosing your status to your partner may lead to domestic violence and/or abandonment.	Key informant interview Workshop discussion Authors experience and consensus	Obtain additional information from PPWH regarding their contact information, if they have a shared phone, and what would be the best way to address them. Determine a plan between the research team and individual PPWH for plans to contact and study visit scheduling.
	PPWH refer to research staff as doctors and nurses, in part due to study activities occurring within the clinical space.	While some research team members may be physicians and nurses, assumptions about positions and their roles may result in PPWH agreeing to participation because of their belief that it is a part of the healthcare services.	Key informant interview Authors experience and consensus	For research team activities taking place within clinic spaces, it is important to be clear about which activities are research and who is a part of the research team. A flyer with names, roles, and photos of team members can help.
Infrastructural vulnerability	PPWH are identified as having other pregnancy-related health conditions, such as hypertension or diabetes, during the course of planned research activities.	While most studies identify referral pathways if the condition of interest is identified during the course of a study, some health conditions may arise that are unrelated to study objectives. Within many resource-limited settings, simply referring to their primary care provider for further evaluation is not possible, due to the lack of preventive care and chronic disease management services.	Literature review Key informant interview Authors experience and consensus	Carefully review all variables that will be collected during the study (e.g. blood pressure, glucose, maternal depression, etc.). Ensure that if abnormalities are found in any of these conditions, that a clear, actionable referral pathway is created with the resources that are locally available. If specific care is not available, consider the ethics of identifying a condition without possible intervention.
	PPWH is found to be in an abusive relationship or living in destitution with an infant without food or support.	PPWH have higher incidence of intimate partner violence and rates of poverty compared to their uninfected peers.	Literature review Key informant interview Workshop discussion Authors experience and consensus	Prior to the start of a study, identify available resources for social support within local hospitals and organizations; understand the laws culture related to intimate partner violence; build relationships with the community leadership. These resources can then be tapped to when a study participant is in need. In our experience, the most support and benefit have come from communicating with local community leadership to help intervene in meaningful ways.

documents have the potential to introduce risk for participants who are not living with HIV but are included in a study's control arm. For example, in our research, a control participant reported intimate partner violence after her partner read a study information sheet and assumed she had secretly kept her HIV status from him. These risks can be mitigated by removing mention of HIV from the study materials.

Finally, when enrolling PPWH and their children in longitudinal research studies, implications for children who are orphaned during the period of observation must be considered. PPWH's risk of death during pregnancy and in the postpartum period is increased up to 10 times that of uninfected women [44]. An orphaned child might end up in the care of another family member who was not previously aware of the deceased participant's HIV status or research participation. When the research team enquires about the child as part of study follow-up, there is a question of whether the team is obligated to share the child's status. Absence of appropriate treatment and follow-up of children exposed to HIV may result in HIV transmission and early death. However, in areas with high HIV stigma, disclosing that the child was involved in HIV-related research, and thus disclosing their mother's status, may negatively impact the relationship between the adoptive family and the orphan, putting the child at risk. These situations should be approached with great care. Ideally, the preferences of individual mothers related to their child's participation in the event of loss to follow-up or maternal death should be ascertained and documented early in the enrolment process.

Support for appropriate agency

A common tenet of basic research ethics is to protect individuals with diminished autonomy [36]. Autonomy refers to the freedom and ability to make decisions without external influence or coercion. Although such protection is important, the prioritization of autonomy may not fully represent the values of PPWH living in communitarian contexts, such as in Kenya.

For participants in our study, promoting participant individual agency was prioritized, focusing on the capacity of individuals to make choices that shape their own lives, while allowing external influence from critical social structures. External influences, both positive and negative, may come from family members, close friends, neighbors, spiritual leaders, and other important relations. Within this context, decisions are often made with other parties or the community in mind, rather than strictly adhering to individual preferences and benefits. For example, a PPWH may desire to participate in research but her male partner, regardless of whether he is the father of her children, may not support their involvement. It was important for participants to have their decision-making agency supported, to have study staff recognize their ability to assess the situation and decide to defer, or to not defer, to their male partner.

Participants frequently described being caugt in a patriarchal and paternalistic culture, resulting in deferential vulnerability. Another example is that some PPWH decide to participate in research due to the perceived confusion about roles of on-site clinical and research personnel. In our study, research assistants were commonly addressed as doctors and nurses, despite introducing themselves as members of the research team. Such deference may strike a foreign researcher as ethically worrisome; however, assuming that PPWH will or should act fully autonomously without regard to these influences undermines cultural norms and values, places them at risk for harm, and may impact the validity of the study due to biased recruitment and/or high drop-out rates. Rather, our findings encourage researchers to acknowledge that decisions are often made in the context of relationships and to provide support for participants navigating these dynamics without coercion or fear of reprisal.

A candidate's agency is most critical during the informed consent process, which requires that potential participants fully understand risks and benefits of participation in research. So while cognitive vulnerability is a key concern across all research settings, it is especially important in low-income and middle-income countries (LMICs), where there are relatively low levels of health literacy are common [45]. This is exacerbated by gender inequities in education, where girls are less likely to complete primary or secondary school [46]. A variety of new methods to simplify information provided during the informed consent process have been developed to help combat this vulnerability. One such example is the visual informed consent used for the Children HIV-Exposed Uninfected – Research to Inform Survival and Health study in Western Cape, South Africa [47]. This document uses culturally appropriate illustrations of key study details, conveyed by cartoons in a colorful pamphlet written in multiple languages (Afrikaans, isiXhosa, or English), and the content was verbally reviewed with a study team member to enhance participants' understanding.

While ensuring use of appropriate language within the informed consent process is critical, researchers must also be aware that this is not a one-time event, but rather an ongoing conversation to keep participants informed over the course of the study. Researchers should adopt a model of dynamic consent, allowing participants to revise their decisions regarding research over time. PPWH and their infants have numerous clinical interactions in the peripartum period, and their social situations often change rapidly, which can make the recall of specific study activities and commitments difficult. Continued conversations about key elements of research participation are

critical and should emphasize the voluntary nature of research participation and the option of withdrawing consent at any time.

Juridic vulnerability, related to the agency of the child, can also arise when engaging PPWH in research. Within this context, mothers are asked to enroll their unborn child in longitudinal studies, which continue into childhood. Depending on the length of follow-up, researchers should consider eliciting assent from the child as he or she matures. Furthermore, they should consider whether consent fromother legal guardians (e.g. the father of the child) is needed for research involving children. However, within contexts where mother are typically the primary caregiver, father have varying levels of involvement, and there are high rates of domestic violence, empowering PPWH to identify a support person – who may or may not be the father of the child – might be a better and more relational approach that still consideres the interests of the child and creates a safety net if issues arise.

Medical vulnerability, allocational vulnerability, and access to care

Confidentiality and appropriate support for individual agency might broadly be categorized under the principle of respect of persons. However, for PPWH, within this context, additional dimensions of respect for persons require attention. First, acknowledging and addressing the medical vulnerability that PPWH may experience is critical. While advances in the care and treatment of HIV have led to dramatic decreases in HIV-related morbidity and mortality, resource constraints and social determinants of health still prevent many PPWH and their children from benefiting from these advances, and there is still no cure. This may lead PPWH to participate in studies in hopes that they and their children will receive 'enhanced' clinical care, which is a common belief about research, especially in LMICs where research studies often improve participants' access to critical healthcare services. Research may allow for more evaluations and time with specialized clinicians than what is available through standard clinical care in these settings, which corresponds to the infrastructure vulnerability experienced by participants. Furthermore, in our research studies, PPWH have reported educational benefits from the positive interactions with the research team, learning about research-related topics and being allowed to ask medical questions about their children. Nonetheless, such therapeutic misconception needs to be addressed within the informed consent process [48,49], even though it may be practically true that within settings with high medical scarcity and limited healthcare infrastructure, research participation has the potential to increase access to care and other resources.

Financial compensation

Allocational vulnerability, which can result from undue inducement through financial incentives for research participation, further contributes to the issue of respect for persons. Historically, financial compensation for participant travel, time, and engagement has been intentionally kept at an absolute minimum for fear of undue inducement. Around 40% of Kenyans live below the national poverty line [50], making undue inducement for high-risk research a particularly strong ethical consideration. Conversely, for low-risk research, limits on compensation can create unnecessary barriers to participation, leaving PPWH uncompensated for the costs of childcare, transportation, and missed wages. The paternalistic logic behind limiting financial incentives (viz. that it interferes with PPWH's capacity to make their own judgement about research risk) could be considered exploitative and signal a lack of respect for the participants themselves [37].

Balancing burdens and benefits

We have found altruism to be a major motivator for many PPWH to participate in research. In our study, PPWH voiced a desire to help improve knowledge and care for the community, even if it inconvenienced themselves. However, at times, overzealous study designs can translate to a much larger burden, and even exploitation. The number of investigations and time required for research participation is often considered only considered as the study activities begin rather than early during study design. For PPWH, research activities often coincide with their regularly scheduled HIV clinical care, which can result in prolonged days without the opportunity for rest or refreshments. Research teams must thoughtfully balance the goal of maximizing data yield during study visits with the comfort and preferences of the PPWH and their children.

Research design considerations

Furthermore, for all measured health outcomes, there should be a well developed plan for returning research results to participants in an acceptable, understandable, and safe format, with referral to available resources where appropriate. Returning results in this ethically robust fashion may be inconvenient for the research team in some settings due to its demands on time and labor, but it is nonetheless critical and must be accounted for during development of research protocols and associated budgets. This process may vary across settings, and certain information may be prioritized for communication; local input on how to operationalize this process is essential. For example, in our interviews, PPWH prioritized the return of information from common clinical procedures, such as imaging and lab work, regardless of the outcome. This contrasted with the local research protocol, which required only significant results warranting clinical referrals be communicated directly with families. Countenancing potential participants' attitudes toward the return of results during study design can even increase recruitment and retention. Both participants and researchers benefit when these expectations are clearly set during the informed consent process:

participants have a reliable system for learning pertinent information and the researchers can plan for the resources required for returning results. Demonstrating respect for research participants involves a broad spectrum of considerations, but at its core, a person-centered approach that acknowledges them as whole individuals who will be impacted by the research is essential to ethically responsible practices.

Community engagement

In recent years, the importance of meaningful community engagement in research has been increasingly recognized and codified in guidelines for the responsible conduct of research. Both the 2024 update of the Declaration of Helsinki and the 2016 update of the CIOMS guidelines have emphasized this topic [6,8]. Community engagement has the potential to reduce many dimensions of vulnerability and to enhance nearly all components of research ethics, including the informed consent process, trust-building for recruitment and retention, and determination of appropriate benefits, risks, and burdens [38]. As such, community enagement is becoming a necessary component of research development.

One common way of engaging community members is through the utilization of community advisory boards. Board members receive a voice in research design and execution to represent the interests and perspectives of patients, communities, and other key stakeholders. The formality and characteristics of these groups vary depending on the population of interest and funding available, but for PPWH, there are numerous recent examples spanning the research landscape (Fig. 1), including the PURPOSE 1 study, which took great lengths to include pregnant women in HIV research [51]. A potential alternative to formal boards in LMICs with high HIV prevalence is close consultation with mentor mothers. Mentor mothers are women with HIV who provide peer support to PPWH through the antenatal and postpartum period to enhance maternal health outcomes and prevent perinatal HIV transmission [52,53]. Through their lived experiences, local leadership within the community, and knowledge of the healthcare system, they provide valuable insights that can meaningfully contribute to development and implementation of research including PPWH.

In our research with key stakeholders about involving PPWH in research, the sentiment 'nothing about us, without us' rang clear. Study participants and community members expressed their desire to be a part of the decision-making process at multiple timepoints, ranging from shaping the focus and goals of research, to providing input on study activities and protocols, to determining how results are shared with the community. Furthermore, such inclusion allows for capacity strengthening of local experts and early-stage researchers involved in the study, ensuring appropriate distribution of benefits of research and protecting against abuse, misrecognition, and colonial imposition of values that may occur within the course of transnational research. This critical element improves the sustainability and impact of continued research and promotes justice comporting with local values.

Oversight and guidance

Ensuring ethical oversight, particularly at the local level, is essential to conducting research that optimizes benefits while minimizing risk. However, while our workshop, participants saw local research oversight as a priority, many were unaware of protections already in place. Additionally, chronic underfunding and limited workforce resources often challenge the feasibility of oversight by committees in both the sponsoring and host countries without external financial support. Nonetheless, dual review is necessary. The latest update to the Declaration of Helsinki underscores its importance, advocating for increased governmental and organizational funding to strengthen this critical infrastructure.

Meaningful community participation in research oversight is needed, particularly when enrolling vulnerable populations with stigmatizing conditions. A local institutional review board and community engagement together strengthens capacity at the local level, where the research is performed. It allows for community values to be identified and honored by those individuals most likely to understand and appreciate them, and for them to be applied successfully and with high fidelity to research design and implementation. By building capacity within local ethics review committees and deferring to them in cases of discordant assessments between sponsoring and host review committees, the authority to determine moral actions is yielded to the local communities that constitute the participants themselves rather than being imposed, as has traditionally been the case in colonial and postcolonial contexts.

It is also important to leverage other resources to guide decision-making and research development involving PPWH. The WHO recently created a toolkit to support antiretrovirals in pregnancy research, which includes a heavy focus on populations affected by HIV [54]. This toolkit provides specific information regarding community engagement and communication, study design, data harmonization, among other key topics to guide researchers focused on this population. Complementary to this is the recent Patient Safety Rights Charter published by the WHO, which outlines patients' rights within clinical settings and addresses some of the key vulnerabilities that PPWH face within clinical research [55].

In conclusion, while the broad dimensions of ethics may be universal, their actual operationalization is local. Key aspects of morally and sustainably impactful research

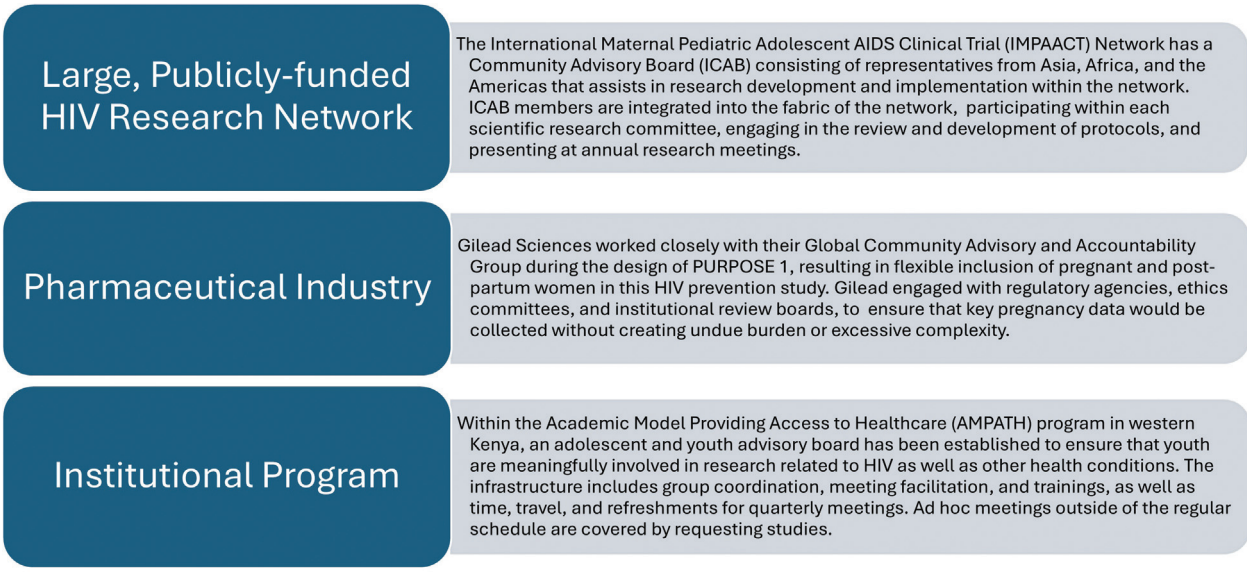

Fig. 1. Examples of community advisory boards, by level of organization.

include participant engagement across all aspects of research, close, equitable partnerships among funders, host sites, academic centers, and the communities engaged in the research. In sharing these considerations, we enhance the resources available regarding more person-centered and community-informed practices during the research development process. To that end, we have identified critical considerations that protect participant confidentiality, enable their agency to make decisions, respect their personhood, engage communities in design and execution, and provide appropriate oversight. In following this guidance, researchers can ensure that their work with PPWH and their children is highly ethical.

Acknowledgements

Thank you to the participants of our April and November 2024 workshops held on this topic in Eldoret, Kenya. We would like to acknowledge Michelle Haber at IMPAACT, Christoph Carter at Gilead, and Salim Bakari Ng'anzi, Hilda Cheserek, Victor Ng'eno, Edith Apondi, and Leslie Enane at AMPATH for providing descriptions of their respective community advocacy groups.

It is relevant to note that we use the terminology 'pregnant women' rather than 'pregnant persons'. This was not intended to exclude those who do not identify as women who become pregnant; rather, it more accurately represents the data on which these guidelines are based, which did not recruit pregnant or postpartum individuals who did not identify as women. Additional considerations are needed to encompass transgender and intersex viewpoints and preferences, both globally and specifically within many HIV-prevalent areas, as these individuals are marginalized and oppressed in distinctive and sometimes violent ways that require additional intersectional considerations in developing an ethical approach to their conscientious inclusion in research. Furthermore, due to the significant gender disparities in educational attainment, health outcomes, and representation in government and business in Kenya, we intend to focus preliminarily on issues associated with cis women as a group in this work.

Author contributions:

M.S.M. conceptulized and designed project; applied and was awarded funding as Principal Investigator; oversaw all study procedures; analyzed data; completed the first draft of the manuscript. E.R.M. contributed to the development of the data collection forms (interview guides); trained staff on performing the semi-structured interviews and led the workshop, which informed the study, contributed to data analysis, and edited manuscript draft. D.K. contributed to the development of the data collection forms (interview guides), served as site Principal Investigator for the study which informed the study, edited manuscript draft. E.W. contributed to the development of the study activities and data collection forms (interview guides), facilitated participant recruitment, reviewed manuscript draft. J.G.C. contributed to the conceptualization of the project, contributed to the design of the data collection forms, contributed to overall data analysis, provided edits and feedback for manuscript draft. J.M.H. contributed to the conceptualization of the project, contributed to the design of the data collection forms, contributed to overall data analysis, provided edits, and feedback for manuscript draft. E.W. contributed to

the design of the data collection forms; performed data collection; performed data analysis; reviewed manuscript. D.M. contributed to the design of the data collection forms, performed data collection, performed data analysis, reviewed manuscript. G.W. contributed to the development of the study activities and data collection forms (interview guides); planned and led ethics workshop; reviewed manuscript draft. A.N. contributed to the development of the study activities and data collection forms (interview guides); reviewed manuscript draft. K.C. coordinated study activities related to the data collection; lead the data analysis; provided feedback on manuscript draft. M.C. contributed to the management of the data; performed data analysis, reviewed manuscript draft. M.N. contributed to the design of the data collection forms, performed data collection, performed data analysis, and reviewed manuscript. R.A.O. coordinated all study activities related to the data collection in Kenya, provided conceptual feedback on ethics process, and reviewed manuscript. M.A.O. co-designed the conceptual framework for data collection; contributed to the development of data collection forms and workshop content, trained on analysis techniques; and provided substantial support in writing the manuscript as a senior author. C.H. co-designed the conceptual framework for data collection; contributed to the development of data collection forms and workshop content, trained on analysis techniques; provided substantial support in writing the manuscript as a senior author.

This work was funded through a supplemental grant awarded by the National Institutes of Health (NIH) Eunice Kennedy Shriver National Institute for Child Health and Human Development (NICHD) (R01HD104552–03S1, PI: McHenry). Dr Carlucci's time was supported through NIH/NICHD K23HD109056 (PI: Carlucci), Dr John Humphrey's through NIH/NICHD K23HD105495, and Dr Halverson's through NIH/National Human Genome Research Institute K01HG012408. The conclusions and opinions expressed in this article are those of the authors and do not necessarily reflect those of the National Institutes of Health or U.S. Department of Health and Human Services.

Conflicts of interest

There are no conflicts of interest.

References

1. UNAIDS. Elimination of mother-to-child transmission: Global Estimates of HIV-exposed children who are uninfected. In: *Prioritizing Neurodevelopment in Children with Perinatal HIV Exposure*. 2022.
2. World Health Organization. Data on the HIV response. World Health Organization. 5 February 2023. Available at: https://www.who.int/data/gho/data/themes/hiv-aids/data-on-the-hiv-aids-response. [Accessed 5 February 2023]
3. UNICEF. Global and regional trends: although strides have been made in the HIV response, children are still affected by the epidemic. Updated July 2024. Available at: https://data.unicef.org/topic/hivaids/global-regional-trends/#:~:text=In%202023%2C%20around%20120%2C000%20%5B83%2C000–170%2C000%5D%20children%20aged%200–14,with%20HIV%20to%201%2C370%2C000%20%5B1.1%20%E2%80%93%201.3%20million%5D. [Accessed 24 November 2024]
4. McHenry MS. Minding the gaps-next steps in care for children who are HEU. 2022.
5. McHenry MS, Oyungu E, Yang Z, Ombitsa AR, Cherop C, Vreeman RC. **Neurodevelopmental outcomes of young children born to HIV-infected mothers: a pilot study.** *Front Pediatr* 2021; **9**:697091.
6. World Medical Association. World Medical Association Declaration of Helsinki: Ethical principals for medical research involving human participants. 1964.
7. Iltis AS. **Introduction:vulnerability in biomedical research.** *J Law Med Ethics Spring* 2009; **37**:6–11.
8. Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans. Geneva 2016.
9. Nasi M, Pinti M, Mussini C, Cossarizza A. **Persistent inflammation in HIV infection: established concepts, new perspectives.** *Immunol Lett* 2014; **161**:184–188.
10. Rueda S, Mitra S, Chen S, Gogolishvili D, Globerman J, Chambers L, *et al*. **Examining the associations between HIV-related stigma and health outcomes in people living with HIV/AIDS: a series of meta-analyses.** *BMJ Open* 2016; **6**:e011453.
11. Nightingale S, Ances B, Cinque P, Dravid A, Dreyer AJ, Gisslén M, *et al*. **Cognitive impairment in people living with HIV: consensus recommendations for a new approach.** *Nat Rev Neurol* 2023; **19**:424–433.
12. Erqou S, Lodebo Bereket T, Masri A, Altibi AM, Echouffo-Tcheugui JB, Dzudie A, *et al*. **Cardiac dysfunction among people living with HIV.** *JACC Heart Fail* 2019; **7**:98–108.
13. Orza L, Bewley S, Logie CH, Crone ET, Moroz S, Strachan S, *et al*. **How does living with HIV impact on women's mental health? Voices from a global survey.** *J Int AIDS Soc* 2015; **18 (suppl 5)**:20289.
14. Turan B, Budhwani H, Fazeli PL, Browning WR, Raper JL, Mugavero MJ, Turan JM. **How does stigma affect people living with HIV? The mediating roles of internalized and anticipated HIV stigma in the effects of perceived community stigma on health and psychosocial outcomes.** *AIDS Behav* 2017; **21**:283–291.
15. UNAIDS. *Confronting inequalities: lessons for pandemic responses from 40 years of AIDS*. 2021. Available at: https://www.unaids.org/sites/default/files/media_asset/2021-global-aids-update_en.pdf. [Accessed 3 January 2025].
16. Rice WS, Logie CH, Napoles TM, Walcott M, Batchelder AW, Kempf MC, *et al*. **Perceptions of intersectional stigma among diverse women living with HIV in the United States.** *Soc Sci Med* 2018; **208**:9–17.
17. *Declaration of Helsinki: ethical principles for medical research involving research participants*. 2024. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki/. [Accessed 8 January 2025].
18. The PHASES Working Group. Ending the evidence gap for pregnant women around HIV & co-infections: a call to action. Available at: https://www.hivpregnancyethics.org/. [Accessed 4 April 2025]
19. Lyerly AD, Beigi R, Bekker LG, *et al*. **Ending the evidence gap for pregnancy, HIV and co-infections: ethics guidance from the PHASES project.** *J Int AIDS Soc* 2021; **24**:e25846.
20. World Health Organization. Call to accelerate the study of new drugs for HIV in pregnant and breastfeeding women. Available at: https://www.who.int/news/item/01–12–2021-call-to-accelerate-the-study-of-new-drugs-for-hiv-in-pregnant-and-breastfeeding-women. [Accessed 4 April 2025]
21. Raciti CG, Enane LA, Macdonald KR, Whipple EC, Ott MA, McHenry MS. **Ethical considerations for research involving pregnant women living with HIV and their young children: a systematic review of the empiric literature and discussion.** *BMC Med Ethics* 2021; **22**:38.
22. Krubiner CB, Faden RR, Cadigan RJ, Little MO, Lyerly AD, Abramson JS, *et al*. **Advancing HIV research with pregnant**

women: navigating challenges and opportunities. *AIDS* 2016; **30**:2261–2265.
23. Corneli AL, Piwoz EG, Bentley ME, Moses A, Nkhoma JR, Tohill BC, *et al*., UNC Project BAN Study Team. **Involving communities in the design of clinical trial protocols: the BAN Study in Lilongwe, Malawi.** *Contemp Clin Trials* 2007; **28**:59–67.
24. Sullivan KA, Little M, Rosenberg NE, Mtande T, Zimba C, Jaffe E, *et al*. **Women's views about a paternal consent requirement for biomedical research in pregnancy.** *J Empir Res Hum Res Ethics* 2018; **13**:349–362.
25. Corneli AL, Piwoz EG, Bentley ME, Moses A, Nkhoma JR, Tohill BC, *et al*. **Involving communities in the design of clinical trial protocols: the BAN Study in Lilongwe, Malawi.** *Contemp Clin Trials* 2007; **28**:59–67.
26. Raciti CG, Marsha J, Nafiseh AA, Masese ER, Apondi E, McHenry MS. **''If it benefits someone, it will be good:'' perspectives on research participation from pregnant women living with HIV.** *AIDS Care* 2023; **35**:366–373.
27. Weber AZ, Harrison A, Pellowski JA. **Systematic review of research focused on pregnant and postpartum women living with HIV: a relational ethics perspective.** *Bioethics* 2021; **35**:829–838.
28. Masese E. ''I am doing it for my child and myself'': empowering autonomy and ethical participation of pregnant women living with HIV and their children in clinical research. Presented at: *IAS 2023, the 13th IAS Conference on HIV Science. 2025*. 2025 [virtual].
29. White G. **Prioritization of holistic care by pregnant women and mothers of infants when considering HIV research engagement**. Presented at: *IAS 2023, the 13th IAS Conference on HIV Science, 2025*. 2025 [in person].
30. Duffy M, Madevu-Matson C, Posner JE, Zwick H, Sharer M, Powell AM. **Systematic review: development of a person-centered care framework within the context of HIV treatment settings in sub-Saharan Africa.** *Trop Med Int Health* 2022; **27**:479–493.
31. World Health Organization. WHO global strategy on integrated people-centred health services 2016–2026: placing people and communities at the centre of health services. 2015. Available at: https://interprofessional.global/wp-content/uploads/2019/11/WHO-2015-Global-strategy-on-integrated-people-centred-health-services-2016-2026.pdf. [Accessed 22 January 2025].
32. Cuca YP, Onono M, Bukusi E, Turan JM. **Factors associated with pregnant women's anticipations and experiences of HIV-related stigma in rural Kenya.** *AIDS Care* 2012; **24**:1173–1180.
33. Andrews C, Reuter TK, Marsh L, Velazquez JM, Jaoko W, Jolly P. **Intimate partner violence, human rights violations, and HIV among women in Nairobi, Kenya.** *Health Hum Rights* 2020; **22**:155.
34. Bukasa LL, Namiba A, Brown M, Ndu'ngu E, Nangwale M, Letting G, *et al*. **Setting the research agenda: involving parents in research on children who are HIV-free.** *J Int AIDS Soc* 2023; **26 Suppl 4 (Suppl 4)**:e26150.
35. Wedderburn CJ, Weldon E, Bertran-Cobo C, Rehman AM, Stein DJ, Gibb DM, *et al*. **Early neurodevelopment of HIV-exposed uninfected children in the era of antiretroviral therapy: a systematic review and meta-analysis.** *Lancet Child Adolesc Health* 2022; **6**:393–408.
36. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research. 1979.
37. Largent EA, Lynch HF. **Paying research participants: the outsized influence of ''undue influence''.** *IRB* 2017; **39**:1–39.
38. Adhikari B, Pell C, Cheah PY. **Community engagement and ethical global health research.** *Global Bioethics* 2020; **31**:1–12.
39. Kipnis K. Vulnerability in research subjects: a bioethical taxonomy. Ethical and policy issues in research involving human participants. Bethesda, MD: National Bioethics Advisory Commission; 2001:2.
40. UNAIDS. **The Privacy, Confidentiality and Security Assessment Tool: protecting personal health information**. 2019.
41. Kioko PM, Kamau MW, Obungu NA, Khabure EA, Simmelink AM, Geoffrey K, De Meijer FO. **HIV stigma in Kenya: a family medicine led community orientated primary care approach.** *Afr J Prim Healthcare Fam Med* 2021; **13**:e1–e3.
42. National Empowerment Network of People living with HIV/AIDS in Kenya. PLHIV Stigma Index 2.0 Kenya Country Assessment. 2021. Available at: https://www.stigmaindex.org/wp-content/uploads/2022/01/Kenya-SI-2.0-Report-2021.pdf. [Accessed 22 January 2025].
43. Colombini M, James C, Ndwiga C, Mayhew SH. **The risks of partner violence following HIV status disclosure, and health service responses: narratives of women attending reproductive health services in Kenya.** *Afr J Reprod Gynaecol Endosc* 2016; **19**:20766.
44. Lathrop E, Jamieson DJ, Danel I. **HIV and maternal mortality.** *Int J Gynaecol Obstet* 2014; **127**:213–215.
45. Malik M, Zaidi RZ, Hussain A. **Health literacy as a global public health concern: a systematic review.** *J Pharmacol Clin Res* 2017; **4**:555632.
46. Montenegro C, Wodon Q, Nguyen H, Onagoruwa A. **Missed opportunities: the high cost of not educating girls.** *The Cost of Not Educating Girls Notes Series* 2018.
47. Slogrove AL, de Beer ST, Kalk E, Boulle A, Cotton M, Cupido H, *et al*. **Survival and health of children who are HIV-exposed uninfected: study protocol for the CHERISH (Children HIV-Exposed Uninfected - Research to Inform Survival and Health) dynamic, prospective, maternal-child cohort study.** *BMJ Open* 2023; **13**:e070465.
48. Appelbaum PS, Roth LH, Lidz C. **The therapeutic misconception: Informed consent in psychiatric research.** *Int J Law Psychiatry* 1982; **5**:319–329.
49. Halverson CM, Ross LF. **Incidental findings of therapeutic misconception in biobank-based research.** *Genet Med* 2012; **14**:611–615.
50. The World Bank. Kenya poverty and equity assessment 2023. 2023.
51. Purpose Studies. Community advisors. Available at: https://www.purposestudies.com/community-advisors. (Accessed 4 April 2025)
52. Igumbor JO, Ouma J, Otwombe K, Musenge E, Anyanwu FC, Basera T, *et al*. **Effect of a Mentor Mother Programme on retention of mother-baby pairs in HIV care: a secondary analysis of programme data in Uganda.** *PLoS One* 2019; **14**:e0223332.
53. Carbone NB, Njala J, Jackson DJ, Eliya MT, Chilangwa C, Tseka J, *et al*. **''I would love if there was a young woman to encourage us, to ease our anxiety which we would have if we were alone'': adapting the Mothers2Mothers Mentor Mother Model for adolescent mothers living with HIV in Malawi.** *PLoS One* 2019; **14**:e0217693.
54. World Health Organization. Antiretrovirals in pregnancy research toolkit. World Health Organization. Available at: https://www.who.int/tools/antiretrovirals-in-pregnancy-research-toolkit. [Accessed 12 December 2024].
55. World Health Organization. Patient safety rights charter. Available at: https://www.who.int/publications/i/item/9789240093249. [Accessed 1 December 2024].