

Layered vulnerability and researchers' responsibilities: Learning from research involving Kenyan adolescents living with perinatal HIV infection

Mary Kimani

KEMRI Wellcome Trust Research Institute

Sassy Molyneux

KEMRI Wellcome Trust Research Institute

Anderson Charo

KEMRI Wellcome Trust Research Institute

Scholastica Zakayo

KEMRI Wellcome Trust Research Institute

Gladys Sanga

KEMRI Wellcome Trust Research Institute

Rita Njeru

KEMRI Wellcome Trust Research Institute

Alun Davies

KEMRI Wellcome Trust Research Institute

Maureen Kelley

University of Oxford University

Amina Abubakar

Aga Khan University

Vicki Marsh

`vicki.marsh@ndm.ox.ac.uk`

KEMRI Wellcome Trust Research Institute

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Abstract

Background

Carefully planned research is critical to building policies and interventions to counter the physical, psychological and social challenges young people living with HIV/AIDS regularly face, without increasing burdens. Through embedded social science research in an ongoing longitudinal cohort study on neurobehavioural outcomes in Adolescents Living with HIV/AIDS in Kenya, we develop an account of researchers' responsibilities towards young people involved in research, drawing on concepts of vulnerability and agency in the literature as 'interacting layers'.

Methods

Using qualitative research methods of in-depth interviews, group discussions, observations and a participatory workshop, we explored key stakeholders' views and experiences of vulnerability and resilience for young people living with HIV/AIDS. Our enquiry included domains of home and community, school, health clinic and research participation in Kilifi County in Kenya. The study involved 62 policy, provider, research and community-based stakeholders, including 27 young people living with HIV/AIDS and participating in research. Three linked research phases supported an iterative process of learning and enquiry, drawing on Framework Analysis.

Results

Young people faced many forms of vulnerability related to risks of stigmatisation across health clinics, schools and in homes. Sources of vulnerability were interrelated and cross sectoral with varying experiences of vulnerability and capacity for resilience that were importantly underpinned by access to social and economic resources. Interacting layers of vulnerability acted to progressively undermine wellbeing, leading to clusters of increasingly serious physical and mental health, social, educational and economic outcomes. Such vicious circles of vulnerability, or cascades, could be reversed, with positive inputs within and across sectors building resilience and leading to positive outcomes. Experiences of research participation reflected a potential to increase forms of vulnerability but importantly also to promote resilience for many young people.

Conclusions

The potential for experiences of research participation to exacerbate vulnerability and strengthen resilience for young people living with HIV/AIDS, through contributing to positive or negative cascades, has important implications for research planning. We argue that researchers' responsibilities include addressing structural causes of vulnerability for research participants living with HIV, giving examples of

strategies, and for the importance of embedded empirical ethics research to identify context-specific risks and opportunities.

1. Background

The rising rates of horizontal HIV infection and the improved survival of children with perinatal HIV infection have led to a high number of adolescents living with HIV (ALH) (1–3). For this group, adherence to antiretroviral medicines is lifesaving but often problematic, including through being negatively impacted by stigma and discrimination (1, 4). For many ALH, the fears and harms of stigma and discrimination remain common, manifested in three ways: anticipating that actions or inactions may be stigmatising; experiencing or perceiving other's actions as stigmatising; and internalising others' negative views about oneself (3–7). These challenges are particularly important given the formative nature of the adolescent period, when life experiences shape individual capabilities and human potential, as well as physical, emotional, cognitive and behavioural development (8). To address individual, family and societal-level challenges, evidence-based programmes of prevention, control and care are critical and require an understanding of how ALH can be involved fairly in needed research.

The dilemma of how to involve ALH in much-needed research exemplifies a well described 'vulnerability paradox' in research ethics, balancing the need for evidence-based policies and interventions for groups seen as vulnerable with concerns that their involvement in research will deepen underlying causes of vulnerability (9, 10). The concept of vulnerability in research ethics guidance has evolved over the past decade, moving from population-based accounts (for example, 'prisoners' and 'children') towards a more targeted and contextual evaluation of individual experiences within groups, identifying common, specified risks (9, 10). Thus, while ALH viewed as a 'population' may need extra protections related to their age and stage of development, these considerations should be placed in context. Important contextual elements include questions around emerging competence to make decisions, a need for legal protection as minors and related concerns around protecting young people's best interests while respecting their emerging agency or ability to choose and take action (10, 11). Further, within this sub-population of young people, there should be special attention to patterns of susceptibility to specific risks, such as stigma related to living with and treating HIV. Additionally, we know that for many individual young people, health, socioeconomic and cultural influences at individual, family, community and wider structural levels underpin patterns of vulnerability and resilience (12–14). Recognising this more complicated picture, definitions of vulnerability in research have increasingly accounted for individual and context-specific influences, informing more precise measures of what Hurst defends as a central criterion of 'an increased likelihood of incurring additional or greater wrong' (15) .

In this paper, we draw on Luna's (2009) account of vulnerability in the research ethics literature, identifying the need for a finely granular understanding of contextual influences on an individual's potential for vulnerability and the way that these influences may act as overlapping and interrelated 'layers', shifting across time and space (16). The use of 'layers' as a metaphor acts as a counter to forms of labelling or taxonomy that may be too rigid to capture the fluidity and interconnected nature of

influences on vulnerability in reality. Luna (2019) further elaborates an approach to understanding researchers' responsibilities through assessing levels of importance and urgency around specific forms of vulnerability, offering guidance to Ethics Review Committees (ERCs) and researchers (17). Through this analysis, Luna highlights a particularly important risk of the emergence of vicious cycles, described as a vulnerability cascade, in which potentially vulnerable individuals take actions that worsen their situation, often reflecting forms of agency constrained by sociocultural and economic influences.

Luna's account is a conceptual framework and as such requires further empirical understanding of how complex, layered sources of vulnerability in daily living are brought to the research experience and, in turn, might be balanced with other important values like agency and resilience to inform researcher responsibilities in real world research (18). We designed an empirical ethics study to explore these responsibilities, based on a research partnership between social and neurobehavioural scientists at the KEMRI Wellcome Trust Research Programme (KWTRP) in coastal Kenya (19). The empirical ethics study was nested within an ongoing longitudinal observational cohort study aiming to assess the impact of perinatal HIV infection on cognitive, educational, mental and social outcomes for ALH in Kilifi County (Adolescent Health Outcomes Study or AHOS) (20). Further, our empirical ethics research formed part of a multi-country collaborative project exploring Resilience and Empowerment in Maternal and Child Health Research (REACH) (21). Additional Information File 1 (titled 'A summary of the Adolescent Health Outcomes Study') provides details of AHOS, including the study aims, methods and approaches taken to addressing anticipated ethical issues, including through ancillary care planning.

Across the paper, we draw on Luna's account (2009) to share a nuanced understanding of the specific and multi-layered nature of vulnerability and resilience for young people living with HIV, including everyday experiences in school, in seeking health care, in life at home, in the community and during participation in AHOS. We bring these findings together to explore the relationship between vulnerabilities across everyday life and research participation. In so doing, we reference and build upon Luna's (2019) framing of researchers' responsibilities, including wider implications for research policy and practice, underlining the importance of institutional context and collaborative partnerships (17).

2. Study Methods

2.1 Study setting & population

Our study was based at the Kenya Medical Research Institute (KEMRI) Wellcome Trust Research Programme (KWTRP) in Kenya, a long standing international collaborative research programme with its main hub in Kilifi County, a largely rural area of coastal Kenya (19). Studies at KWTRP in Kilifi, including AHOS, often involve participants from surrounding areas, with research governance drawing on a collaborative partnership with the Kilifi County Health Team. The main economic activities across the county include petty trade, subsistence farming and fishing alongside emerging urban development, with rates of multidimensional poverty assessed at 35.6% (22, 23)

2.2 The empirical ethics study: Approach and methods

As an empirical ethics study, we used qualitative methods to explore vulnerability, resilience and agency in everyday life for ALH who joined AHOS, including influences from research participation. ALH in AHOS were largely school-going, attending day or boarding schools. As shown in Additional Fig. 1 (Additional Fig. 1, entitled 'Planned empirical ethics research foci for the study'), our study focused on three main domains in young people's lives - the school environment, HIV Comprehensive Care Clinics (CCCs) and home and community - alongside participation in AHOS, as well as wider structural and policy influences (24).

Figure 1: Planned empirical ethics research foci

2.3 Data collection, management and analysis

We collected data across three main research phases, with on-going analysis. To counter any potential for our research to exacerbate existing vulnerabilities and increase the potential for participation to be empowering for young people involved, we began by working with key stakeholders and least vulnerable ALH to learn about perceptions of vulnerability and resilience before involving a wider group, primarily through a participatory workshop as described below. Table 1 gives a summary of study methods, participants and numbers involved.

Table 1
Study participants and data collection activities

Types of participants	Data collection activity (number)	Number of participants
<i>Health related:</i> Clinical officers (2), nurse (1), Health policy and coordination of HIV activities (3)	IDI (6)	6
<i>School related:</i> School head (1), school matrons (2), teacher (1), teachers living with HIV (3)	IDI (4) Group interview (1)	7
<i>Community related:</i> Community health volunteers (2), mentor mothers (3), children officer (1), NGO project officer (1)	IDI (7)	7
<i>Family related:</i> Parents/caregivers	Focus group discussions(2) Group interview (1)	13
<i>AHOS related:</i> Recruitment staff (1), community liaison officer (1)	IDI (2)	2
<i>Adolescents:</i> Adolescents living with HIV	Group interview before workshop (1)	3
	Focus group discussions: Within (3) & after (2) workshop	24
Total number of participants		62

Additional Information File 2 includes the workshop objectives and outline programme (entitled 'Workshop objectives and outline programme'). Additional Information File 3 (entitled 'Data collection tools') includes the data collection tools used in this study.

Phase 1 included 15 in-depth interviews with key informants and two group interviews, one with ALH and the other with their main caregivers. In-depth interviews included policy and provider stakeholders working with ALH in the community, schools, CCCs and as part of AHOS (Table 1), identified purposively in relation to formal and informal roles, including through a snowballing process. In the health sector, we interviewed policy, management and provider stakeholders, working at County and facility levels, including from three CCCs providing services across urban (n = 1) and rural (n = 2) settings. We invited teaching and pastoral care staff from six purposively selected schools in Kilifi County, reflecting diversity in setting (urban vs. rural), pupil size, educational level (five primary and one secondary school) and status as day or mixed day and boarding schools. Across all sectors, interviews focused on identifying every day and research-related vulnerabilities and resilience for ALH and recommendations around research design and conduct. For focus group discussions (FGDs) with young people and their caregivers (as separate groups), we purposively selected ALH acting as 'HIV champions' in local CCCs, who were most likely to be able to reflect on their own and their contemporaries' situations, with some confidence. FGDs in Phases 1 and 3 explored understanding and experiences of participating in AHOS, probing around spontaneously shared accounts of everyday vulnerability.

Phase 2 included a one-day consultative workshop, drawing on Phase 1 findings and involved 24 ALH who were AHOS participants. Sampling aimed to maximize diversity of social and demographic characteristics (gender, age, geographic distribution, type of school attended). We held the workshop in a relaxed local hotel environment during a school holiday and included meals. Activities included group discussions and role-plays around experiences of AHOS participation in the morning, followed up in FGDs in the afternoon (n = 3). The workshop ended with a plenary discussion on the nature and aims of health research, using visual aids and using AHOS as an example, to build general understanding of research and address emerging issues.

Phase 3 involved four in-depth interviews and one group interview with key informants, two FGDs with workshop attendees and two FGDs with main caregivers, to clarify and take forwards findings from earlier phases.

In Phases 1 and 3, group discussions/interviews with ALH and caregivers lasted 40–90 minutes, with breaks for those involving ALH. Interviews with key stakeholders lasted 50–110 minutes. Data collection used Swahili, local (Mijikenda) or English languages, following participants' preferences. All interviews were audio recorded, transcribed verbatim and translated into English where necessary. Data analysis processes were ongoing, iterative and informed by a Framework Analysis approach, using Nvivo 10 software(25). Analysis involved the following steps: i) immersion in the data during collection; ii) the development, use and adaptation of *a priori* and emergent codes from an initial sample of rich transcripts by two researchers (MN and VM); iii) the development of analysis charts drawing on coded material; and

iv) data interpretation using the literature on vulnerability and resilience in ALH and global health research ethics (MN, AC, VM, SM).

2.4 Ethical considerations

We planned this study with high awareness of existing vulnerabilities for ALH and their families, and particular concern to protect young people's privacy and respond appropriately to challenges uncovered during our research. In so doing, we drew on ancillary care plans developed for the main AHOS cohort through collaborative partnerships with County Health and Social Care departments, included in Additional File 1. Similarly, our consent processes drew on approaches developed for AHOS, including that a known and trusted individual was responsible for communicating about the study with the young people and caregivers involved (see Additional File 1). Adult participants gave written informed consent before involvement, while young people gave verbal assent alongside adult caregivers' consent, including for participation in groups involving other ALH who were AHOS participants. All methods were performed in accordance with the Declaration of Helsinki. Heads of the Kilifi County Health and Education Departments and the Kilifi National AIDS and Sexually Transmitted Diseases Programme (NASCOP) supported study planning and conduct, and we communicated findings with these groups. The Kilifi County Research Governance office, the KEMRI Scientific and Ethics Review Unit (KEMRI/SERU/CGMR-C/084/3454) and Oxford University Tropical Medicine Research Ethics Committee (OXTREC 14–17) gave prior approval for the study.

3. Results

Following the framework used to guide data collection (Fig. 1, Additional File 1), we describe our findings on influences on vulnerability and resilience in relation to young people's experiences in the community and home, in school, in attending HIV/AIDS Comprehensive Care Clinics (CCCs) and in participating in AHOS. Across these four sections, we identify influences related to policies and organisational systems, and to interpersonal relations within these environments.

3.1 Community and home: Influences on ALH vulnerability and resilience

Many county-level HIV policy makers and community-based providers saw community-wide stigma and discrimination towards people living with HIV as becoming less marked over time. At the same time, negative attitudes were reportedly common across the community, including widespread inaccurate understandings of perinatal HIV that underpinned discriminatory behaviour, such as accusations of irresponsible sexual behaviour, as has been widely reported in different settings (26, 27). Key informants had experience of families feeling forced to move home when they suspected disclosure and stigma, sometimes having to move repeatedly, generating issues for continuity of care at CCCs and worsening outcomes. While poverty is common across rural areas of Kilifi county, ALH caregivers are particularly impacted, generating difficulties in accessing education, maintaining adequate nutrition and growth (core

to fears and experiences of stigma), paying fares to attend CCC and being able to afford a radio, watch or phone to support timing of ART doses (27, 28). Schooling could be impacted where girls were unable to afford sanitary towels and where hunger affected concentration in class. ALHs' responses to these challenges risked deepening their vulnerability, for example, in refusing to take ARTs because they did not have food, turning to commercial sex work or leaving school to look for paid work. Other reported responses reflected less constrained (but still non-ideal) forms of agency, for example, getting up very early to walk to school in the absence of fares (29). In this way, socioeconomic challenges in the home environment undermined ALHs' wellbeing and ability to cope with the multiple, often severe, challenges faced in everyday life, which we describe across the following sections.

Considerable diversity emerged around accounts of the types and levels of practical and emotional support available to ALH at home, including medicine taking, as has been shown elsewhere, including in Kenya (30–33). While some caregivers assumed that ALH could 'look after themselves' or 'harassed' those who forgot to take their ARTs, other families took their ARTS together. In one family, a young person reminded their parent about medication. We later discuss the privacy challenges faced by ALH in seeking time out of school to attend HIV/AIDS Comprehensive Care Clinics; caregivers could provide important support in this respect:

*My child doesn't even ask for a leave out [from school] if it's her time to come for the drugs, I usually call the teacher and inform him that my child had gone to the hospital and will come to school late.
(Caregivers FGD04)*

Encouraging ART adherence was particularly challenging if ALH were not aware of their status, reportedly common in low-resource settings. Some caregivers had insisted that CCC staff take responsibility for disclosing their child's status, contrary to national policy (34–36). Discriminatory attitudes were particularly described when affected young people were in the care of well-wishers or relatives outside their immediate family. It is notable that just over half of ALH participating in AHOS were orphans. Instances of prejudice and discrimination described included ALH being forced to keep their utensils separate from those of the wider household or sleep separate from other children in the home; caregivers selling food given for an ALH by local NGOs; and a 'sponsor' refusing to let an ALH placed in her care attend CCC. Elderly caregivers often struggled to provide an adequate diet for their charges given economic constraints, and faced difficulties in understanding and remembering ART regimes.

Across the county, government departments and NGOs provide important support to communities and families living with HIV, including through CCCs. While operating on fixed funding cycles, community-based NGO staff had particularly valued roles in acting as mentor mothers to families living with HIV/AIDS. This group also distributed designated support to families in NGO programs, ran motivational 'boot camps' for ALH, during which they would be encouraged to take their ARTs openly together, and set up support groups to help parents disclose their children's HIV status – a process seen as critical to ALH acceptance and wellbeing. Many such staff formed close and supporting relationships with the families and young people in their care, including supporting families in greatest need from their own pockets.

3.2 School environments: Influences on ALH vulnerability and resilience

Since AHOS participants were generally school going, those invited to join our study were primary or secondary school students in day, boarding or mixed facilities. The boarding school environment could be particularly challenging for ALH since, as shown earlier, family support was an important influence on young people's ability to thrive outside the home. The primary challenge for ALH in schools centered on efforts to maintain privacy in relation to their HIV status given actual and perceived risks of stigmatisation by students and staff, as reported from other parts of Kenya and sub Saharan Africa more widely (37–41). At the same time, staff could be a potential source of support to ALH, particularly members of the Kenya Network for Positive Teachers (KENEPOTE), a network set up within the Teachers Service Commission of Kenya in 2004 to support and empower this group (42). Across the following paragraphs, we first describe challenges related to organisational policies in schools, followed by influences on vulnerability and resilience from interpersonal relations.

Systems in place for managing routine medications and regulating student movements out of school, particularly in boarding schools, presented the main privacy risks for ALH and challenges to ART adherence. As noted elsewhere, particular challenges related to storage and access to ARTs in schools and securing permission to leave school to attend regular HIV/AIDS Comprehensive Care Clinic appointments (43). Notably, policies that required advance permission to be absent from school for health or other reasons, or to show a medical note to explain an absence, while reasonable at face value, generated important privacy risks for ALH. Young people described taking a series of strategies to counter privacy risks, such as missing ART doses, taking leave-outs without permission and accepting unfair punishments:

I just went to [started] that school just the other day. Better my former school where there was a teacher who also took drugs [ARTs], whenever he came here [CCC], we would see each other, he is the only person who knew. But at this other school, I'm still new and from the way I find them, it's like they are rumour mongers, so I won't say, I'll just go then come back, get caned and the story ends (ALH FGD07)

...at school I haven't trusted any teacher...that's why I always give an excuse of a headache or stomach ache for me to go to hospital when I go (to) maintain (refill) my drugs. (ALH FGD07)

Table 2 summarises our findings on organisational policies seen as challenging and students' reported responses to these. Of note in relation to these findings, while the Kenyan government banned corporal punishment in Kenyan schools in 2001, and enacted the Children's Act (44) which entitles children to protection from all forms of abuse and violence, corporal punishment is still used in Kenyan schools, when teachers believe it is for the child's good (45). For ALH, maintaining silence over HIV status in this way reflects a constrained form of agency in the face of discrimination and injustice, also described in high income settings (46).

Table 2
Challenging organisational policies in schools and students' coping strategies

<i>Challenging organisational policies</i>	<i>Coping strategies adopted by students</i>
<ul style="list-style-type: none"> • Public checking of students' bags at the start of a new term, when medicines might be tipped on the ground. • Requirements that all medicines are handed over to the matron for safe storage and dispensing. • Where medicines could be stored in dormitories, locking of these during the day, and the risk of discovery during random dormitory checks. • A requirement for formal permission to be out of school for health or other reasons, including attendance at Comprehensive Care Clinics, with a range of punishments if breached. • A lack of teaching support and punishment for failing to 'catch up', on missed classes. 	<ul style="list-style-type: none"> • Storing ARVs in school toilet blocks or outdoor hiding places, requiring special effort to access privately. • Putting ARVs in unmarked containers rather than labelled prescription bottles, risking confusion about identity. • Accepting physical punishment for being late to class (typically, 'caning') to allow a student to take ARVs in private between breakfast and class, rather than explain the reason for lateness. • Choosing to miss school to collect ARV refills without giving an explanation, choosing a risk of physical punishment rather than disclosure of their status; or explaining school absences as due to less stigmatizing conditions. • Using own time and borrowing other students' notes to try to catch up on missed classes.

The difficulties experienced by ALH in countering these challenges, for example in being seen by peers as needing regular medication was well illustrated by one caregiver:

They get a problem in taking the drugs at school because [other students] will see them and [they] may be asked 'What are these drugs for?'...you see our girls they always walk together everywhere, if they want to drink water or they go to the toilet (caregivers FGD)

School staff and policy makers also recognised the existence of stigma within schools and its consequences:

...this somehow really jeopardises suppression because at times when this information leaks out to these other students, they tend to either make fun or discriminate... one way or the other we don't get good outcomes. (Health policy maker 01)

The interpersonal challenges encountered by young people living with HIV/AIDS in schools have been widely described in the literature, including in sub Saharan Africa and from elsewhere in Kenya (37–41, 43, 46). Our data largely support existing accounts of stigma and discrimination likely to be experienced, and here we particularly focus on the reported attitudes and actions of peers and school staff that were core to the capacity of ALH to thrive in schools. As summarised in Table 3, alongside experiences of stigma and discrimination, some staff offered remarkable levels of support, potentially offering students a lifeline. While teachers who were themselves living with HIV/AIDS might try to support affected students, they also worried about and sometimes experienced stigma and discrimination themselves.

One such individual was described as being actively discriminatory towards ALH to limit risks of their own status being uncovered.

Table 3
Illustrative examples of interpersonal support and challenges for ALH in schools

<i>Discrimination/negative attitudes experienced</i>	<i>Positive support from staff</i>
<ul style="list-style-type: none"> • Teachers not allowing ALH to participate in certain activities such as games lessons and telling other students not to play with a student known to be HIV positive. • Teachers discussing students HIV status amongst themselves (reported by ALH and KENEPOTE members) • Peers refusal to sit next to or share personal items with others thought or known to be HIV positive; broadcasting information on students' or teachers' HIV status, including by writing on blackboards; and ridicule. • A participant who disclosed his HIV status to a close friend in confidence later entered the classroom to find his classmates discussing his status. 	<ul style="list-style-type: none"> • School staff helping ALH navigate challenges around the inspection of personal property and ARV storage, for example by undertaking ALH inspections or personally keeping; or ensuring day pupils had access to evening meals in school where food at home was known to be in short supply. • Staff helping ALH to navigate challenges in schools including paying transport costs and accompanying to CCC to ensure they received refills. • One boarding school matron supported four students living with HIV from school entry for four years, by ensuring their privacy in taking ARVs, access to a good diet, including making meals in her own house, and that the girls did not undertake heavy physical work at school. Since these girls were from the matron's home area, their 'special treatment' was widely accepted as a form of favouritism and did not generate stigma.

The risk attached to actions taken by students to protect their privacy in social spaces was well illustrated by one young woman who described her ARVs as 'headache tablets' to peers, and later felt obliged to share these with a friend who developed a headache. In the next section on experiences around visiting CCCs, we note a particular problem for ALH in accounting for the exact numbers of ARV tablets dispensed at a time, underlining additional challenges this young woman was likely to face in future.

3.3 HIV Comprehensive Care Clinics: Influences on ALH vulnerability and resilience

While the importance of well-functioning Youth Friendly Services at CCCs is clearly recognised, young people and other stakeholders in our study described a range of challenges typically encountered (47). In contrast to the school environment, privacy concerns were less prominent since attendance implied a positive HIV status for all clients, particularly where Youth Friendly Services (YFS) were in place. Instead, the main forms of vulnerability described related to negative staff attitudes, often influenced by underlying resource constraints. A core challenge for young people was the time spent in clinics, due to

high client-to-staff ratios. Access to specialist support, such as professional or adherence counselling, was particularly difficult since these services were available intermittently or required distant referral. During our observations, a clinician attended almost 100 clients in a day, with waiting times of up to six hours.

P3: At times the doctor may only be one/ P1: Yet there are many patients, so you won't be attended fast. You want to go back to school but there is only one doctor (ALH Group interview 01)

Across our study, CCC services were generally offered in one room where four to eight staff worked with clients across all age groups; accordingly, we noted many providers trying to communicate in 'whispers'. A lack of YFS heightened privacy concerns:

P3: When you just enter the door (of the CCC), all the eyes are on the entrance aah... you feel shy to walk up to thereP1: Others are even surprised..."Mh! A very small child using medicines [ARVs]? ...some women started talking, "Ah K's child is also using drugs" ...you know what, I don't like it. (ALH Group interview 01)

Given these constraints, individual CCC staff attitudes strongly influenced ALH experiences of attending these clinics and their capacity to manage lifesaving treatment. Supportive attitudes were commonly described, summarised in Table 4, including actions empowering ALH as a group as well as support for privacy, flexibility in approach towards individual young people and (often personal) contributions towards supporting ALH in difficulties:

...adolescents are very delicate...if an adolescent says 'I don't want X to see me' and then I say 'its ok who do you want to see you?'... you know most of them think that being HIV positive is the end of their life, no so I think we just need to understand them and walk with them as they come. (Health care provider IDI20)

Table 4
Individual CCC staff actions supporting ALH wellbeing

<i>CCC staff actions supporting ALH</i>
<ul style="list-style-type: none"> • Giving ALH a lead in planning outreach activities e.g. World AIDS Day. • Planning ALH-only CCC sessions, including during out-of-school hours/at same time as support groups to save time, transport costs and reduce privacy risks. • Waiting times at CCCs addressed by 'fast tracking' ALH wearing school uniforms. • Guardians/parents allowed to collect ARVs on ALH behalf for up to 2 months; ALH allowed to collect ARVs outside prior appointment times where a valid reason given; offering flexibility in clinic appointments when ALH attend on 'wrong' day (e.g. set appointments clash with important school events). • Individual CCC staff supporting ALH, including through: 'informal' task shifting strategies to reduce queues and allowing ALH to choose which provider to talk to at CCC. • Taking the initiative to develop and implement ART training for elderly caregivers. • Giving ALH in boarding schools enough ARTs to last to midterm or setting up a local CCC contact near to the school. • Supporting ALH privacy: visiting homes (on clinical indications) in the guise of a friend or selling items; suggesting ALH pad ARV bottles with cotton wool to prevent 'rattling' bringing attention to this medication. • Individual 'emergency support' in bringing urgent ARV supplies to homes at weekends and staff giving cash from their own pockets.

At the same time, ALH and caregivers described a series of important challenges linked to negative CCC staff attitudes. A frequently reported challenge arose from a CCC policy for staff to count remaining ART pills ('pill count') for each attending ALH to assess 'adherence' to a prescribed regime. Some staff reportedly dealt harshly with young people where mismatches occurred between expected and actual counts.

The one at the pharmacy, if you go there with a lot of drugs, they will quarrel [with] you so much, I don't know what! They will scold you... it's like they are a teacher now, you'll be scolded (P3) Yes, even if there are only two remaining (P1) Even if it's only one remaining (P2) (ALH Group interview 01)

Alternative explanations, such as errors in dispensing practices, seemed not to be explored. A similarly negative attitude could be associated with a finding of high viral loads, interpreted as reflecting 'non-adherence'. Suggesting risks of staff showing negative attitude, health providers in one CCC reportedly chose to use a back door to enter the facility to avoid public recognition, which was tellingly referred to as the 'stigma door'. As suggested earlier, resource constraints underpinned many structural challenges for CCCs, particularly staff levels and skills and physical space. In this way, when some trained adherence counsellors were described as 'reprimanding and blaming' rather than supportive, these behaviours could also be seen as signs of 'burnout' linked to high workloads:

... if a youth comes today and it's not his/her clinic day and the way I am already tired, your head is not working well, you can respond that youth badly. When you respond rudely to the client, you risk losing him/her. (Health care provider IDI 03)

3.4 AHOS participation: Influences on ALH vulnerability and resilience

Towards building a discussion of the ways in which research participation might potentially counter and exacerbate the everyday vulnerabilities described for ALH so far, in this section we describe findings around ALHs' experiences of being in AHOS, focusing on two core emerging themes around decision-making on joining the study and experiences of study procedures.

3.4.1 Deciding to join AHOS

The approach to informed consent and assent for AHOS (AdditionalFile 1) aimed to take account of the complex social, cultural and legal influences on ALHs' actual and assumed capacities for independent decision-making, reflecting agency. Influences included their emerging autonomy and age, given cultural and legal variations in assessments of maturity and around human rights (10, 48). Additional recognised challenges for AHOS included risks of inadvertent disclosure in approaching a young person who might be unaware of their HIV status and the need to seek consent from both caregiver and their teenagers as independent participants.

In practice, ALH were approached following discussions with their parents during regular CCC visits, to ensure that only ALH with perinatal infection and who were aware of their HIV status were invited. With initial parental agreement, in most cases an AHOS team member approached young people eligible to join the study with their parent or caregiver, at CCC or home. To build trust in the study, including around privacy, this team member had been recruited as a person known to CCC-users through an earlier 'mentor mother' role within a local NGO-led HIV/AIDS support programme. Throughout our study, we noted the positive relationship between AHOS participants and this - and other - AHOS team members, including young people's willingness to listen to their advice.

The formal AHOS consent process, including assent of the young person and consent of their caregiver or guardian, took place immediately prior to the first research clinic-based assessment, when the young person and their caregiver travelled to the research clinic. While there was reasonable clarity amongst ALH about the broad aims of and study procedures in AHOS, some young peoples' and caregivers' existing fears, such as worries about their 'thinking abilities' linked to memory and concentration, positively influenced some to join, as a way of accessing more information or advice. In some cases, a combination of parental authority traditional in this community and an assumption that participation might be beneficial seemed to generate prompt decision-making to join (48):

[How did you learn about the study?] I was told by my father over the phone ... he told me to come the following day, I was needed at KEMRI Kilifi, and I went because I know my status. (ALH FGD02)

3.4.2 Experiences of AHOS procedures

Participating families attended three annual research visits, each lasting half a day, over a two year period. As shown in Additional File 1, research procedures involved anthropometrics, clinical examination, blood sampling and responding to a series of questionnaires, using audio-computer assisted self-interviewing (ACASI) and a face-to-face interview. In general, ALH saw physical examinations as helpful, being more in-depth than those encountered at CCC, and the clinical staff undertaking examinations as respectful and engaging, rather than patronising or harsh. While some ALH found aspects of interviews, tasks and questionnaires ‘childish’, irrelevant or embarrassing, these procedures were generally seen in a positive light, as being individually informative and generally enjoyable. Since many ALH did not have regular access to computers at home or school, the ACASI-based tasks were often seen as an exciting “computer game”. Young people also saw research activities, particularly cognitive assessment tasks, as a form of learning, with a potential to compensate for missed classes:

I really thought about it, I miss school to come here?... When I got here I found the questions are the same as those in school so I felt good. Now I wonder if I had not gone, would I really get them [understand questions in school] or I would miss them? (ALH Group interview 01)

Perhaps the most common and strongest accounts around experiences of AHOS participation concerned the value young people placed on the open and friendly attitudes encountered at the research clinic, including reassurances around privacy:

They [staff] keep secrets...at the beginning you will be told there is no one who will know whatever you have said and it's true no one knows. It's only you and the computer...and the doctor...you feel very good (, ALH FGD02)

Whenever I go there I feel happy because they treat me nicely...when you go there everyone is free with you...there is a way you can ask someone something and their reply is cold that...I will feel afraid and even think of not coming back...but since they [KEMRI] treat me nicely, even as I say “hello” to their phone calls, I immediately dress up and go (ALH FGD02).

One ALH described the importance of feeling ‘noticed and remembered’ through setting up a study like this, focused on the needs of ALH. Also of great value to young people was the opportunity offered to meet peers, some of whom might be dealing with similar life challenges, with opportunities to share coping mechanisms.

At the same time, challenges emerged for ALH related to the time taken for AHOS appointments and difficulties experienced in explaining their participation to others. In relation to time, although research visits were much less frequent than routine CCC appointments, getting time out of school to attend AHOS appointments generated similar risks and challenges, including high levels of anxiety, risks of punishment linked to actions taken to avoid inadvertent disclosure and additional workloads in catching up missed schoolwork. Importantly, following an AHOS appointment, young people experienced

challenges in explaining the study (and their school absence) to others without risking disclosure of their HIV status. The study information sheet used in schools avoided reference to HIV to counter such privacy risks, instead talking about research on 'cognitive functioning'. In practice, class teachers often asked for more information about AHOS that ALH were ill placed to give without risking disclosure. The term 'cognitive functioning' also generated teasing as meaning 'mental health problems', which already vulnerable ALH found difficult to manage. As a result, in some instances ALH left school without permission to attend AHOS appointments, risking punishment for being absent without a good reason. As for CCC visits, they would also need to catch up on missed lessons in their own time.

4. Discussion

4.1 Risks of cascading vulnerability in everyday life

Across earlier sections, we have shown that sources of vulnerability and resilience for ALH in our study were interrelated and cross sectoral. In this way, access to social and economic resources importantly underpinned diverse, individual experiences of vulnerability and capacity for resilience. Thus, for example, micro-level policies in schools around ART storage and access and permission to attend CCCs prompted actions to protect privacy that could have perverse impacts on wellbeing. Maintaining silence over HIV status emerged as a response by young people to acts of discrimination and injustice, reflecting constrained forms of agency (29). Missing ART doses, taking time out of school without permission and accepting unfair punishments were detrimental to physical, emotional health and educational progress, which in turn could increase privacy risks and progressively worsen social, health and educational outcomes. Organisational policies at CCCs, intended to promote ART compliance, but potentially enacted in harsh ways, similarly undermined emotional wellbeing and could chip away at motivation to attend CCC or take ARTs regularly (47). Long waiting times at CCCs exacerbate the challenges in being away from school (for school-going ALH), as would the lack of underlying family support. Efforts and investments are clearly needed across different policy sectors to improve ALH's health and well-being, but inter-sectoral linkages are reportedly challenging to establish, undermining efforts to promote ALH welfare.

Our findings also illustrate young people's resilience through less constrained but still potentially harmful forms of agency adopted by ALH in response to anticipated or enacted stigma. Examples in our data include accepting less stigmatising health labels (such as epilepsy), sharing ARTs to support a claim to friends that these were headache tablets, switching CCCs (or schools) and refusing to be seen by certain CCC staff. We also see forms of what might be described as more positive agency, particularly through the actions of 'adherence champions' at CCCs, that is, young people who are living with HIV who choose to be open about their status to support other ALH. Notably, the actions of adherence champions reflect forms of agency that are reliant on a highly focused and supportive strategy, initiated and maintained through NGO support to NASCOP offices.

While the experiences of vulnerability we learned about reflect enormous challenges for affected young people who are trying to make their way in the world, we heard many positive accounts of youth-friendly policies and individuals working to promote the resilience and wellbeing of young people living with HIV in school and at CCCs. In relation to AHOS, we were struck by young people's delight in and appreciation of the friendly and respectful manner encountered in the research team and opportunities to spend time with their peers. The experiences of participating in AHOS stand out as instances of being respected, listened to and supported, made more important by the fears and experiences of stigma and blame encountered in many areas of their lives, particularly where underlying conditions of poverty and insecure family structures and relations are faced at home. Overall, research participation may have increased some forms of vulnerability for ALH - particularly those related to taking time out of school or being unable to answer questions about AHOS - but it seems likely to have promoted resilience for many young people.

Notably, the retention rate for AHOS has remained above 95% across the first year of its duration, supporting an interpretation that participation is valued. In studies where recruitment and retention rates are high, questions might be raised about the appropriateness of benefits involved. We argue that AHOS provides an example of a situation in which high retention rates and appreciation of resources offered do not imply that the benefits provided are 'too much'. Rather, the implication is that the everyday lives of this group of young people can be so challenging that their interactions with and support from researchers, which might be regarded as normal outside a context of such marked vulnerability, are instead interpreted as importantly self-affirming.

4.2 How should researchers' respond?

What emerges from this analysis is an understanding of the way that influences within and across sectors can interact to generate steadily worsening forms of vulnerability for ALH, leading to clusters of increasingly serious physical and mental health, social, educational and economic outcomes. At the same time, vulnerability cascades are reversible, so that positive inputs within and across sectors have the capacity to build increasing resilience and positive outcomes across these clusters. This raises a central ethical question about the appropriate scope of researchers' responsibilities towards potentially vulnerable individuals they hope to involve in studies: how should studies be designed to be responsive to and mindful of the unique risks, given that carefully planned research is key to identifying evidence-based interventions and policies that address risks of vulnerability?

In making arguments for researchers' responsibilities to understand and address specific risks of vulnerability and vulnerability cascades, we note some limitations for our study. Firstly, the most in-depth accounts of ALH vulnerability are not derived from young people themselves but other stakeholders, as a deliberate strategy to maximise the extent to which their involvement was likely to be a positive or empowering experience, and avoid increasing burdens for the most vulnerable in this group. Further, young people in this study were in school, while many affected teenagers may not have this opportunity, given health and socioeconomic challenges. Taken together these points suggest our analysis may be based on an underestimation of the burdens generally experienced by ALH in our context.

Luna's (2019) analysis frames researchers' responsibilities towards potentially vulnerable participants as a series of steps to characterise potential vulnerabilities in relation to their nature, their seriousness and probability, and assess researchers' responsibilities accordingly. The most serious forms of vulnerability, including cascading forms, should be most urgently addressed (17). It follows that researchers should seek to empower and strengthen the resilience of otherwise vulnerable participants as much as possible. Further, we have shown that sources of vulnerability and resilience may only become clear once a study is in progress, highlighting an important gap for global health research ethics in the 'post approval' space, and the importance of embedded empirical ethics research to inform responses. Drawing on the literature and the example of AHOS, in the following paragraphs, we discuss two broad responses that seem important for researchers working with ALH in this and other similar settings.

4.2.1 Grounding privacy strategies for research in 'real life' experience

Given the risks of cascading vulnerability in everyday life, our data underline that potentially the most important emerging ethical concern for research involving school-going ALH is ensuring that study participation does not increase existing privacy risks, including the need to provide or discuss reasons to be out of school that implicate their health. Added to the community engagement processes used to support AHOS, an important practical step could include greater engagement of ALH in developing strategies to support young people's capacity to talk about study participation in ways that do not risk a privacy breach in everyday life.

While protection of young people's privacy was core to ethical practice in AHOS, we note that strategies developed to protect young people's privacy during the informed consent process could generate an ethical challenge. ALH and their families already knew the individual undertaking much of the engagement for the study, as an HIV/AIDS community support volunteer who was also living with HIV/AIDS. As well as providing reassurance to families around privacy concerns, this strategy seems likely to have built trust in the research process itself, presenting a challenge to autonomy from the relationship already in place. Luna's (2019) emphasis on prioritising the most serious and urgent challenges for ALH suggests that a good balance was made in focusing on critically important privacy risks for ALH and their families, particularly given its evolving characteristic in this age group (10). This dilemma underlines the critical importance of ensuring that individual(s) in the team undertaking consent and interacting closely with ALH and their families have a high awareness of these autonomy risks, and - critically - the skills and institutional support to manage these.

4.2.2 Responding to structural injustices

Overall, our findings show very clearly that the most serious forms of cascading vulnerability faced by ALH in AHOS are largely structural and unrelated to research participation. Instead, existing forms and acts of stigma and discrimination, and the strategies young people adopt to contain these risks, work together across different domains of life to generate vicious - or potentially, virtuous - cycles. While AHOS

participation was generally seen as a positive experience, time spent on study participation - including travel - may clearly contribute to vulnerability, when added to the challenges experienced in attending CCC. Importantly, an interim analysis within AHOS has identified significantly poorer outcomes in cognitive, educational, and mental health across quantitative assessments for perinatally infected ALH in comparison to control groups². While educational outcomes are likely to reflect cumulative biological, social and economic influences in affected young people, it seems particularly important to limit time lost from class through CCC attendance and research participation. Planning research clinic visits for weekends and school holidays would limit this risk, but large cohort studies are unlikely to be feasible using this strategy. Overall, the risks and burdens of school-going ALH spending time at research clinics, even if infrequent, must be assessed alongside other reasons for school absence, as a cumulative phenomenon with important implications for their wellbeing.

In the short-term and more narrowly, researchers are argued to have 'ancillary care responsibilities' in relation to a range of reasonable forms of unmet health and social care need that participants experience during studies, including through setting up public sector and other referral pathways in advance of studies (49–51). Within AHOS, many short-term health care needs for ALH are addressed directly during clinical research assessments (such as prescribing courses of antibiotics) and there are well-developed referral systems to public sector partners for other health and social care needs (see Box 2). At the same time, public sector referrals do not cover all needs, sometimes leaving young people and their families unsupported or research teams to support in *ad hoc* ways that often generate ethical dilemmas for front line staff. We argue here and elsewhere for the importance of a grounded, structured policy response to ancillary care responsibilities in research in low resource settings, as an institutional responsibility to study participants and front line staff (52).

In addition, our study underlines a well-recognised responsibility for researchers to contribute to tackling underlying structural causes of unmet needs impacting the communities where they work (49–51, 53, 54). The preliminary findings from AHOS on poorer outcomes for this group of young people clearly illustrate how mindfully designed research can help contribute to critical knowledge around the layered vulnerabilities of a population, like these ALH in Kenya, helping to inform targeted interventions. The nature and extent of researchers' responsibilities in relation to existing forms of structural inequity may depend on the context, including the nature of the research and its social value, and the opportunities presented by the history and depth of researchers' involvement in research in a given setting. Specific to AHOS at KWTRP, a series of mechanisms aim to support the social value of research, including government and non-government stakeholder consultative workshops before and throughout the study, one element of which was a Young Persons Advisory Group drawn from local secondary schools in Kilifi (55). In addition, scientific governance mechanisms at institutional and national levels assess the social value of ethically challenging observational studies (such as AHOS), including opportunities to move rapidly towards policy or future intervention research that can more directly inform policy and support social value (48, 56–58). The continuing task for all researchers is to identify meaningful ways of supporting potentially vulnerable individuals and populations in ways that support their fair involvement

in studies, recognising the potential of careful empirical research as well as wide and meaningful consultative activities to inform such measures. While these relationships may be easier for well-established research institutions to build, a challenge emerges that the most vulnerable populations are likely to reside in remote areas without the infrastructure needed for collaborative research.

5 Conclusion

The potential for experiences of research to exacerbate vulnerability and strengthen resilience in the existing lives of young people living with HIV/AIDS, including through positive or negative cascades, has important implications for research planning. Drawing on Luna's 2019 account of vulnerability in research ethics, this empirical ethics study in coastal Kenya details the complex ways in which contextual, organisational and interpersonal influences at home, in the community, at school, in health care and in biomedical research settings may interact to impact the lives of young people living with HIV/AIDS who join studies. The findings importantly contribute to critical knowledge around the layered vulnerabilities of a specific population, like these ALH in Kenya, helping to inform targeted interventions across the disciplines of health care, education and social care as well as health research. Strong and on-going relationships between researchers and policy makers are critical to promoting the uptake of empirical ethics research findings into policy and practice. We argue that researchers' responsibilities include addressing structural causes of vulnerability for ALH research participants, giving examples of strategies, and for the importance of embedded empirical ethics research to identify context-specific risks and opportunities.

Abbreviations

ACASI	Audio computer-assisted self-interviewing
AIDS	Acquired Immunodeficiency Syndrome
ALH	Adolescent Living with HIV/AIDSs
AHOS	Adolescent Health Outcomes Study
ART	Antiretroviral Treatment
CCC	Comprehensive Care Clinic (for HIV/AIDS)
FGD	Focus group discussion
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
IDI	In-depth interview
KEMRI	Kenya Medical Research Institute

KEMRI SERU	Kenya Medical Research Institute Science and Ethics Review Unit
KEMRI CGRMC	Kenya Medical Research Institute Centre for Geographic Medicine, Coast
KENEPOTE	Kenya Network for HIV/AIDS Positive Teachers
KWTRP	Kenya Medical Research Institute-Wellcome Trust Research Programme
NASCOP	National AIDS and Sexually Transmitted Infection (STI) Control Programme
NGO	Non-Governmental Organisation
OxTREC	Oxford Tropical Research Ethics Committee
YFS	Youth Friendly Services

Declarations

Ethics approval and consent to participate

The Kilifi County Research Governance office, the KEMRI Scientific and Ethics Review Unit (KEMRI/SERU/CGMR-C/084/3454) and Oxford University Tropical Medicine Research Ethics Committee (OXTREC 14-17) gave prior approval for the study. The study was conducted in accordance with the Declaration of Helsinki. Adult participants gave written informed consent before involvement. Young people who were minors (under 18 years) gave verbal assent alongside adult caregivers' consent. Heads of the Kilifi County Health and Education Departments and the Kilifi National AIDS and Sexually Transmitted Diseases Programme (NASCOP) supported study planning and conduct.

Consent for publication: Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due the sensitivity of the data and the potential that aspects of this data set may infer identity of individual participants and may reflect sensitive areas in individuals' lives. Data will be made available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors were involved in the design of this study, and contributed to the analysis of data and development of the manuscript. MKi, AC, GS and SZ collected the data with support from VM, RN, AD and SM. AA gave particular support in embedding the study within the wider AHOS programme and facilitating partnerships with County-level HIV/AIDS policy makers and other stakeholders. MKi and VM developed the first draft of the manuscript. MKe gave particular support through facilitating wider learning for this study through the REACH consortium on vulnerability and resilience in research in low resource settings. All authors reviewed the manuscript.

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References

1. Sohn AH, Hazra R. The changing epidemiology of the global paediatric HIV epidemic: Keeping track of perinatally HIV-infected adolescents. *J Int AIDS Soc.* 2013;16:1–8.
2. UNICEF. Children and AIDS: Statistical Update. 2017;(December):0–3. Available from: www.childrenandaids.org
3. Enane L, Vreeman R FC. Retention and adherence: Global challenges for the long-term care of adolescents and young adults living with HIV. *Curr Opin HIV AIDS.* 2018;13(3):212–9.
4. Dahourou DL, Gautier-Lafaye C, Teasdale CA, Renner L, Yotebieng M, Desmonde S, et al. Transition from paediatric to adult care of adolescents living with HIV in sub-Saharan Africa: Challenges, youth-friendly models, and outcomes. Vol. 20, *Journal of the International AIDS Society. International AIDS Society*; 2017.
5. Lowenthal ED, Bakeera-Kitaka S, Marukutira T, Chapman J, Goldrath K, Ferrand RA. Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: A review of emerging challenges. Vol. 14, *The Lancet Infectious Diseases.* Lancet Publishing Group; 2014. p. 627–39.
6. Mburu G, Ram M, Oxenham D, Haamujompa C, Iorpenda K, Ferguson L. Responding to adolescents living with HIV in Zambia: A social-ecological approach. *Child Youth Serv Rev [Internet].* 2014;45(C):9–17. Available from: <http://dx.doi.org/10.1016/j.childyouth.2014.03.033>

7. Abubakar A, Van De Vijver FJR, Fischer R, Hassan AS, Gona JK, Dzombo JT, et al. "Everyone has a secret they keep close to their hearts": Challenges faced by adolescents living with HIV infection at the Kenyan coast Infectious Disease epidemiology. BMC Public Health [Internet]. 2016;16(1):1–8. Available from: <http://dx.doi.org/10.1186/s12889-016-2854-y>
8. Ahmed Zaky E. Adolescence; a Crucial Transitional Stage in Human Life. J Child Adolesc Behav. 2016;04(06):5–6.
9. Council for International Organizations of Medical Sciences. International Ethical Guidelines for Health-related Research Involving Humans. 2016.
10. Nuffield Council on Bioethics. Children and clinical research: ethical issues. 2015. 1–264 p.
11. World Medical Association. Declaration of Helsinki, Ethical Principles for Scientific Requirements and Research Protocols. Bull World Health Organ [Internet]. 2013;79(4):373. Available from: <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>
12. Sallis J, Owen N. Ecological Models of Health Behavior. In: Health Behavior: Theory, Research and Practice. John Wiley & Sons; 2015. p. 23–43.
13. Abubakar A. Biomedical Risk, Psychosocial Influences and Developmental Outcomes: Lesson for the Pediatric HIV Population. In: Serpell R, Marfo K, editors. Child Development in Africa: Views from Inside. Wiley Online Library; 2014. p. 23–41.
14. Enimil A, Nugent N, Amoah C, Norman B, Antwi S, Ocran J, et al. Quality of life among Ghanaian adolescents living with perinatally acquired HIV: A mixed methods study. AIDS Care - Psychol Socio-Medical Asp AIDS/HIV [Internet]. 2016;28(4):460–4. Available from: <https://doi.org/10.1080/09540121.2015.1114997>
15. Hurst SA. Vulnerability in research and health care; Describing the elephant in the room? Bioethics. 2008;22(4):195.
16. Luna F. Elucidating the Concept of Vulnerability: Layers Not Labels Author (s): Florencia Luna Source : International Journal of Feminist Approaches to Bioethics, Spring, 2009, Vol. 2, Published by : University of Toronto Press Stable URL : [https://www.js.2009;2\(1\):121–39](https://www.js.2009;2(1):121-39). Available from: https://www.jstor.org/stable/40339200?seq=1#metadata_info_tab_contents
17. Luna F. Identifying and evaluating layers of vulnerability – a way forward. Dev World Bioeth. 2019 Jun 1;19(2):86–95.
18. Abebe T. Reconceptualising children's agency as continuum and interdependence. Soc Sci. 2019;8(3).
19. KEMRI Wellcome Trust Research Programme [Internet]. [cited 2021 Aug 27]. Available from: <https://kemri-wellcome.org/>
20. Ssewanyana D, Newton CR, van Baar A, Hassan AS, Stein A, Taylor HG, et al. Beyond Their HIV Status: the Occurrence of Multiple Health Risk Behavior Among Adolescents from a Rural Setting of Sub-Saharan Africa. Int J Behav Med. 2020 Aug 1;27(4):426–43.

21. REACH: Resilience, Empowerment & Agency in Maternal & Child Health Research [Internet]. [cited 2021 Aug 27]. Available from: <https://www.ethox.ox.ac.uk/Our-research/major-programmes/reach/about-reach>
22. Ogega OM, Gyampoh BA, Oludhe C, Koske J, Kung'u JB. Building on foundations for climate services for sustainable development: A case of coastal smallholder farmers in Kilifi County, Kenya. *Clim Serv*. 2020 Dec 1;20.
23. World Bank. For the first time, the relative economic size of Kenya's counties is clear [Internet]. 2019 [cited 2021 Apr 8]. Available from: <https://blogs.worldbank.org/africacan/for-the-first-time-the-relative-economic-size-of-kenyas-counties-is-clear>
24. Stokols D. Translating social ecological theory into guidelines for community health promotion. *Am J Heal Promot*. 1996;10(4):282–98.
25. Green J, Thorogood N. Framework analysis. In: *Qualitative methods for health research* (4th ed). London: SAGE; 2018. p. 268–272.
26. Ashaba S; Cooper-Vince C; Vořechovská D; Rukundo G; Maling S; Akena D; Tsai A. Community beliefs HIV stigma and depression among adolescents living with HIV in rural Uganda. *African J AIDS Res* [Internet]. 2019;18(3):169–80. Available from: 10.2989/16085906.2019.1637912
27. Zgambo M; Kalembo F; Mbakaya B. Risky behaviours and their correlates among adolescents living with HIV in sub-Saharan Africa: A systematic review. *Reprod Health*. 2018;15(1).
28. Katana P V., Abubakar A, Nyongesa MK, Ssewanyana D, Mwangi P, Newton CR, et al. Economic burden and mental health of primary caregivers of perinatally HIV infected adolescents from Kilifi, Kenya. *BMC Public Health*. 2020 Apr 16;20(1).
29. Payne R. “Extraordinary survivors” or “ordinary lives”? Embracing “everyday agency” in social interventions with child-headed households in Zambia. *Child Geogr*. 2012;10(4):399–411.
30. Denison JA, Banda H, Dennis AC, Packer C, Nyambe N, Stalter RM, et al. The sky is the limit: Adhering to antiretroviral therapy and HIV self-management from the perspectives of adolescents living with HIV and their adult caregivers. *J Int AIDS Soc*. 2015;18(1):1–6.
31. Lachman JM, Cluver LD, Boyes ME, Kuo C, Casale M. Positive parenting for positive parents: HIV/AIDS, poverty, caregiver depression, child behavior, and parenting in South Africa. *AIDS Care - Psychol Socio-Medical Asp AIDS/HIV* [Internet]. 2014;26(3):304–13. Available from: <https://doi.org/10.1080/09540121.2013.825368>
32. Thurman TR, Kidman R, Nice J, Ikamari L. Family Functioning and Child Behavioral Problems in Households Affected by HIV and AIDS in Kenya. *AIDS Behav* [Internet]. 2015;19(8):1408–14. Available from: <http://dx.doi.org/10.1007/s10461-014-0897-6>
33. McHenry MS, Nyandiko WM, Scanlon ML, Fischer LJ, McAteer CI, Aluoch J, et al. HIV Stigma: Perspectives from Kenyan Child Caregivers and Adolescents Living with HIV. *J Int Assoc Provid AIDS Care* [Internet]. 2017;16(3):215–25. Available from: <https://doi.org/10.1177/2325957416668995>
34. National AIDS and STI Control Programme (NASCOP). Adolescents Package of Care in Kenya [Internet]. 2014. Available from:

<https://faces.ucsf.edu/sites/g/files/tkssra4711/f/AdolescentPackage.pdf>

35. Vreeman RC, Gramelspacher AM, Gisore PO, Scanlon ML, Nyandiko WM. Disclosure of HIV status to children in resource-limited settings: A systematic review. *J Int AIDS Soc.* 2013;16.
36. Vreeman RC, Nyandiko WM, Ayaya SO, Walumbe EG, Marrero DG, Inui TS. The perceived impact of disclosure of pediatric HIV status on pediatric antiretroviral therapy adherence, child well-being, and social relationships in a resource-limited setting. *AIDS Patient Care STDS.* 2010;24(10):639–49.
37. Kimera E, Vindevogel S, De Maeyer J, Reynaert D, Engelen AM, Nuwaha F, et al. Challenges and support for quality of life of youths living with HIV/AIDS in schools and larger community in East Africa: A systematic review. *Syst Rev.* 2019;8(1):1–18.
38. Kimera E, Vindevogel S, Rubaihayo J, Reynaert D, De Maeyer J, Engelen AM, et al. Youth living with HIV/AIDS in secondary schools: perspectives of peer educators and patron teachers in Western Uganda on stressors and supports. *Sahara J.* 2019;16(1):51–61.
39. Madiba S, Josiah U. Perceived Stigma and Fear of Unintended Disclosure are Barriers in Medication Adherence in Adolescents with Perinatal HIV in Botswana: A Qualitative Study. *Biomed Res Int.* 2019;2019.
40. Toska E, Cluver L, Orkin M, Bains A, Sherr L, Berezin M, et al. Screening and supporting through schools: Educational experiences and needs of adolescents living with HIV in a South African cohort. *BMC Public Health.* 2019 Mar 6;19(1).
41. Kimera E; Vindevogel S; Kintu M; Rubaihayo J; De Maeyer J; Reynaert D; Engelen A; Nuwaha F; Bilsen Jmmanuel. Experiences and perceptions of youth living with HIV in Western Uganda on school attendance: Barriers and facilitators. *BMC Public Health.* 2020;20(1).
42. UNDP Kenya. Journey to Zero: Stories from Teachers Living with HIV and AIDS in Kenya [Internet]. 2014 [cited 2021 Aug 28]. Available from: <https://www.ke.undp.org/content/kenya/en/home/ourwork/inecgr/successstories/Journey-to-Zero-Teachers-Living-with-HIV.html>
43. Apondi E, Wachira J, Ayikukwei R, Kafu C, Onyango J, Omollo M, et al. Barriers to ART adherence among school students living with HIV in Kenya. *African J AIDS Res.* 2021;20(3):232–7.
44. National Council for Law Reporting R of K. Children’s Act 2010 [Internet]. Available from: <http://www.childrenscouncil.go.ke/images/documents/Acts/Children-Act.pdf>
45. Mweru M. Why are Kenyan Teachers Still Using Corporal Punishment Eight Years After a Ban 2010. *Child Abus Rev.* 2010;19:248–58.
46. Fielden SJ, Chapman GE, Cadell S. Managing stigma in adolescent HIV: Silence, secrets and sanctioned spaces. *Cult Heal Sex.* 2011;13(3):267–81.
47. van Wyk BEDLC. Challenges to HIV treatment adherence amongst adolescents in a low socioeconomic setting in Cape Town. *South Afr J HIV Med.* 2019;20(1).
48. Marsh V, Mwangome N, Jao I, Wright K, Molyneux S, Davies A. Who should decide about children’s and adolescents’ participation in health research? The views of children and adults in rural Kenya. *BMC Med Ethics.* 2019;20(1):1–16.

49. Benatar S, Singer, Peter AS. A new look at international research ethics. *Br Med J*. 2000;321(7264):824–7.
50. Lavery J V., Bandewar SV, Kimani J, Upshur RE, Plummer FA, Singer PA. “Relief of oppression”: An organizing principle for researchers’ obligations to participants in observational studies in the developing world. *BMC Public Health*. 2010;10.
51. Merritt MW. Health researchers’ Ancillary Care obligations in low-resource settings how can we tell what is morally required? *Kennedy Inst Ethics J*. 2011;21(4):311–47.
52. Molyneux S, Sukhtankar P, Thitiri J, Njeru R, Muraya K, Sanga G, et al. Model for developing context-sensitive responses to vulnerability in research: Managing ethical dilemmas faced by frontline research staff in Kenya. *BMJ Glob Heal*. 2021;6(7):1–14.
53. Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries. Fair Benefits for Research in Developing Countries. *Science (80-)*. 2002;298(December):2133–4.
54. Hydner A, Merrit M. Ancillary Care for Public Health Research in Developing Countries. *JAMA*. 2009;302(4):429–31.
55. KWTRP. Schools Engagement Programme [Internet]. [cited 2021 Aug 31]. Available from: <https://www.tropicalmedicine.ox.ac.uk/study-with-us/tropmed-students/sep>
56. Betancourt TS, Meyers-Ohki SE, Charrow A, Hansen N. Annual research review: Mental health and resilience in HIV/AIDS-affected children - A review of the literature and recommendations for future research. *J Child Psychol Psychiatry Allied Discip*. 2013;54(4):423–44.
57. Njue M, Molyneux S, Kombe F, Mwalukore S, Kamuya D, Marsh V. Benefits in cash or in kind? A community consultation on types of benefits in health research on the Kenyan coast. *PLoS One* [Internet]. 2015;10(5):1–17. Available from: <http://dx.doi.org/10.1371/journal.pone.0127842>
58. Bhana A, Mellins CA, Small L, Nestadt DF, Leu CS, Petersen I, et al. Resilience in perinatal HIV + adolescents in South Africa. *AIDS Care - Psychol Socio-Medical Asp AIDS/HIV* [Internet]. 2016;28:49–59. Available from: <http://dx.doi.org/10.1080/09540121.2016.1176676>

Figures

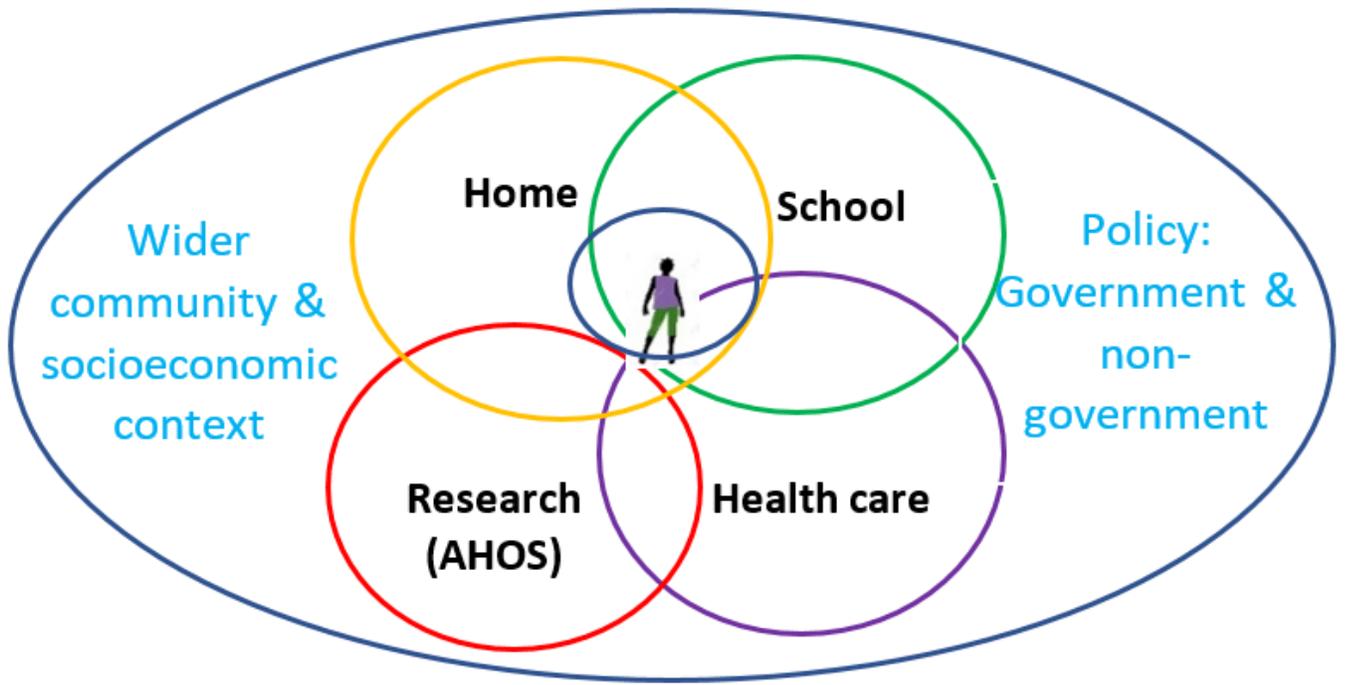


Figure 1

PLANNED EMPIRICAL ETHICS RESEARCH FOCI FOR THE STUDY

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