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Engagement of adolescent girls and young women into an early oral PrEP open-label study in Southern Africa: lessons learned from HPTN 082

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Abstract

Background Adolescent girls and young women (AGYW) in southern Africa face a high risk of HIV acquisition. Consistent use of daily oral pre-exposure prophylaxis (PrEP) can significantly mitigate this risk. We used the Good Participatory Practice Framework (GPP) to summarize lessons learned from engaging AGYW in an open-label PrEP trial, highlighting successful strategies that enhanced trial engagement.

Methods The HIV Prevention Trials Network (HPTN) 082 was an open-label study conducted from 2016 to 2018 that evaluated PrEP uptake and adherence in AGYW 16- to 25-year-old without HIV living in Cape Town and Johannesburg, South Africa, and Harare, Zimbabwe. Overall, 646 AGYW were screened for eligibility and 416 were enrolled. Fieldwork reflections, meeting summaries, Community Advisory Board (CAB) meeting minutes, and other project records were analyzed to synthesize lessons for stakeholder engagement relevant to PrEP introduction and service delivery.

Results Using the GPP framework, several key lessons were identified. Early and comprehensive engagement with a broad range of stakeholders throughout the trial was crucial. Youth stakeholders played a significant role in shaping communication materials, clinic design, the package of HIV and non-HIV care, and referral pathways for supportive services. Identifying myths and misconceptions during early stakeholder engagements allowed for tailored PrEP education materials and approaches for PrEP-naïve communities. Parents and caregivers emerged as an essential group to engage to ensure support, even when adolescents were of legal age to provide consent. Peers were identified as important sources of information, support and referral for screening during the trial. Innovations to enhance engagement and results dissemination included the development of youth-led videos and peer support clubs.

Conclusions Introducing daily oral PrEP for young African AGYW required multiple strategies that were culturally sensitive, age-appropriate, and inclusive of peers, partners, parents, and other influential adults. These strategies were

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essential for fostering a supportive environment for PrEP use and enhancing engagement in the trial. Lessons learned from PrEP introduction to AGYW in southern Africa have relevance for future trials and HIV prevention programs.

Trial registration ClinicalTrials.gov NCT02732730, 13 November 2018.

Keywords Pre-exposure prophylaxis, AGYW, GPP, Community engagement, HIV prevention, Clinical trials, Sub-Saharan africa

Background

In 2015, the World Health Organization (WHO) recommended daily oral pre-exposure prophylaxis ("PrEP") as part of a comprehensive HIV prevention package [1]. Countries adopted PrEP national guidelines for populations at risk [2]. Adolescent girls and young women (AGYW) aged 15 to 25 years old in sub-Saharan Africa are a priority population for PrEP, given high HIV incidence in this population [3, 4]. However following results from earlier trials that indicated very low PrEP adherence in younger women, there were concerns about whether AGYW desired PrEP and would use it consistently [5–7].

Following the WHO recommendations, countries including South Africa and Zimbabwe, initiated processes to support PrEP introduction into national programs. In South Africa, by oral PrEP was included as part of a package of care for sex workers by mid-2016, and oral PrEP had been introduced in 12 clinics in five South African provinces by the end of 2016. This introduction did not initially specifically include AGYW, and AGYW were only included in the PrEP program in South Africa in 2018 [8]. Zimbabwe adopted the WHO global guidance on PrEP in 2015, and subsequently launched revised guidelines that included PrEP in December 2016 but did not scale up PrEP provision until after 2017 [9].

Ahead of national PrEP introductions, and in part to understand factors influencing PrEP use in AGYW, several oral PrEP demonstration projects assessed PrEP uptake and adherence. The HIV Prevention Trials Network (HPTN) 082 study was one such study that aimed to demonstrate PrEP uptake and adherence among sexually active AGYW without HIV aged 16 to 25 living in Cape Town and Johannesburg, South Africa, and Harare, Zimbabwe (ClinicalTrials.gov NCT02732730). The study was initiated in October 2016 ahead of national PrEP guidelines and services for AGYW, as a vanguard study. Extensive community engagement and education was required to provide accurate information about PrEP, identify and address PrEP-related myths and concerns, and promote PrEP acceptance and adoption in AGYW in the study communities in South Africa and Zimbabwe.

Community outreach and engagement were considered essential given the barriers in access to routine health care services that AGYW experience including inconvenient opening hours (during school hour), challenges with transport to clinics, concerns about confidentiality, and judgmental attitudes about sexuality from health care providers [10, 11]. The UNAIDS/AVAC Good Participatory Practice (GPP) guidelines provide a framework for effective and systematic engagement with stakeholders in the design and conduct of clinical trials throughout the trial life cycle [12]. These guidelines were developed in part in response to the premature closure of two oral PrEP trials. Insufficient stakeholder engagement was viewed as one of the critical reasons for these closures, which were subsequently associated with delays in access to PrEP for vulnerable populations. Given this history, the HPTN 082 team was aware of the risks that inadequate community engagement could have in fueling negative beliefs and fostering community mistrust, with subsequent impacts on trial conduct and outcomes [13–15]. Furthermore, these negative impacts could extend beyond the trial and undermine the future uptake of PrEP in national programs. Additional considerations related to the sensitivity of inclusion of sexually active adolescents and youth in the study given the barriers that adolescents face in accessing quality reproductive health care in many countries in sub-Saharan Africa [10, 11]. Using the GPP framework, this manuscript reflects on lessons for stakeholder engagement and trial conduct from HPTN 082. We highlight lessons relevant for PrEP introduction and service delivery that enhanced PrEP uptake and continuation in AGYW. While the lessons learned relate to oral PrEP, many of these have relevance for the dapivirine vaginal ring, and long-acting injectable PrEP cabotegravir and lenacapavir for PrEP as these agents become increasingly available in sub-Saharan Africa (www.prepwatch.org/countries/).

Methods

Study design

The HIV Prevention Trials Network (HPTN) 082 was an open-label study of PrEP uptake and adherence conducted between October 2016 and October 2018 among 16- to 25-year-old women without HIV in Cape Town and Johannesburg, South Africa, and Harare, Zimbabwe, as previously reported [16]. Of 646 AGYW screened for eligibility, 451 AGYW were enrolled. Of these, 427 (95%) initiated oral PrEP, with 412 starting at enrolment and an additional 15 during follow-up. 31% had detectable tenofovir diphosphate levels at month 12. Overall, PrEP

uptake was high, but adherence and persistence were low over 12 months [16].

Study setting

HPTN 082 was conducted at three clinical research sites (CRS), including Emavundleni in Cape Town, Wits RHI Ward 21 in Johannesburg, South Africa, and Spilhaus in Harare, Zimbabwe. Established in 2006, the Emavundleni CRS is part of the Desmond Tutu Health Foundation (DTHF) and is in New Crossroads Township in Cape Town, South Africa. The Emavundleni team already had experience working with AGYW in other studies, and investigators had previous experience with PrEP studies, but the community team was PrEP-naive. The Wits RHI Ward 21 CRS was established in 2016 and is based in Hillbrow in inner-city Johannesburg. The community engagement team already had experience working with AGYW but was less familiar with PrEP, despite institutional experience conducting PrEP trials. The Spilhaus CRS, housed at the Zimbabwe National Family Planning Council Clinic at Harare Central Hospital, was established in 1994. HPTN 082 provided the team with the first experience of working with adolescents, although the site had previous PrEP trial experience. The study protocol was approved by the ethics review committees at each of the study sites in accordance with the Declaration of Helsinki.

Data sources and analysis

This paper is written from the perspective of the community engagement team members working in the field across the three HPTN 082 sites. Most of the authors were involved in all aspects of the HPTN 082 trial implementation and have first-hand experience in implementing GPP within trials. All authors consented to have their perspectives captured in this manuscript.

In September 2018, community team representatives from each of the three sites met to reflect on the lessons learned from community engagement during HPTN 082 and their relevance for future programs. Each site prepared a presentation highlighting their stakeholder engagement activities, organized into three stages preparedness, recruitment, and retention. Community engagement staff then collectively reviewed the challenges experienced during each stage. Subsequently, the authors supplemented this initial workshop report with insights gleaned from the review of meeting reports and minutes from trial inception to close out. These meetings included four in-person meetings before the start (May 2016), during (December 2016, October 2017), and towards the end of the study (September 2018). The community team also reviewed the minutes of protocol team calls throughout the study as well as work plans, training materials, monthly site-level community engagement reports, and Community Advisory Board (CAB) meeting minutes.

In January 2020, the lead author (MM) held virtual reflection sessions with each of the three community engagement teams to confirm combined findings and lessons learned at each site regarding engagement of AGYW and stakeholders in the trial, as well as particular experiences promoting oral PrEP as a novel HIV prevention intervention in these communities. In this manuscript we use the GPP definition of stakeholder, i.e. Individuals, groups, organizations, governments, or other entities that are affected by the outcome of a biomedical HIV prevention trial or that can influence proposed research through their input and actions [12].

The data was organized and analyzed according to the 16 practices of the GPP framework (Table 1). These practices are recommended for implementation across the trial life cycle with formative research activities, site selection, and protocol development being more relevant prior to trial start while stakeholder advisory mechanisms, stakeholder engagement plan, stakeholder education plan, stakeholder communications plan, issues management plan, informed consent process, standard of HIV prevention, access to HIV care and treatment, non-HIV related care, policies on trial-related harms, trial accrual, follow up and exit are important during trial implementation, and trial closure and results dissemination, and post-trial access to trial products or procedures relevant at study end. We summarize and present observations and lessons learned for community engagement throughout the life cycle of this vanguard open-label oral PrEP study for AGYW in three African sites (Table 1).

Results

Early collaboration with stakeholders

Sites did not engage in formal formative research activities per GPP guidelines most likely because they were established CRS with existing formal stakeholder engagement mechanisms in the form of established community advisory boards (CABs). GPP practices like protocol development and site selection had already been completed prior to stakeholder engagement, although stakeholder input throughout the trial influenced protocol implementation. Community teams engaged with CABs to identify additional relevant stakeholders that worked with youth or were influential in their access to health care. Youth CABs in particular were critical in identifying stakeholders that either provided services to young people e.g. clinics, schools, advocacy groups and peer educators, or were important gatekeepers e.g. ward counsellors and churches. The youth advisory boards included young people from the community aged 16–25 years; while it varied by site each CAB had 15–20 members and approximately half the members were female.

Table 1 Good participatory practice recommendations and lessons learned

GPP recommendation	Lessons learned
Formative research activities	Additional stakeholder mapping to identify youth service providers and groups.
Stakeholder advisory mechanisms	Pre-existing established community advisory boards including youth advisory boards. Early stakeholder engagement identified myths and misconceptions that were helpful to address subsequently through community education activities. Used in-person community dialogues to good effect.
Stakeholder engagement plan	All sites had plans that identified stakeholders and planned engagement events with those stakeholders that were updated periodically. Activities were reviewed on monthly calls and at regional meetings. These reviews helped to identify early challenges to trial implementation and PrEP use.
Stakeholder education plan	Educational activities were included in the engagement plan above. The absence of government endorsed PrEP education materials was a challenge. The team developed a video that included local young women to support PrEP education for participants. This video was also useful for sharing with stakeholders. .
Communications plan	Communication plans were included in the engagement plan above.
Issues management plan	Formal issues management plans were not prominent and did not specifically guide the process of issues management. Regular monitoring identified parents and caregivers as influential gatekeepers to PrEP use and participation in the study. Specific community dialogue events with parents and care givers helped resolve parent concerns before it became an issue.
Site selection	This process took place separately from site level activities. Working with experienced clinical research sites made it possible to build on existing experience and expertise, as well as leverage many established community relationships. This is an important consideration when conducting sensitive research.
Protocol development	This process took place somewhat separately from site level activities. The inclusion of local investigators in protocol development ensured relevance to the site population.
Informed consent process	A video was developed to enhance participant understanding of PrEP. Additional strategies were adopted at sites to enhance this process included waiting room group education session, the development of a study brochure summarizing key aspects of the study
Standard of HIV prevention	A package of prevention endorsed by youth advisors included condoms, STI testing and treatment, and contraception provision at the study site.
Access to HIV care and treatment	Stakeholder engagement informed the development of referral pathways for HIV care
Non-HIV related HIV care	Youth stakeholder involvement was essential for informing priorities for additional service needs e.g. access to mental health services, shelters for women experiencing intimate partner violence, housing advice units, and organizations that provided food parcels.
Policies on trial-related harms	There were no clinical trial insurance requirements as this was a phase IV study. Some sites required the presence of a distress protocol for handling distress resulting from questions about personal information. Social harm reporting was also a requirement of the protocol, and sites developed referral pathways to care based on relationships with local stakeholders for any events that required further medical or social intervention
Trial accrual, follow up and exit	Welcoming, confidential services delivered by non-judgmental providers and the offer of a comprehensive package of services enhances engagement in care. Peers played a critical role in disseminating accurate information and PrEP and referring potential participants for screening. Flexible scheduling of visits to account for specific adolescent development needs e.g. accommodating school hours or unanticipated travel enhance engagement in care. Peer support clubs were an important innovation that created a safe space for adolescents to normalize PrEP use, share experiences and solutions to challenges. Inclusion of non-health activities in these groups was valued by adolescents and reduced study fatigue and enhanced in engagement in care.
Trial closure and results dissemination	Participant-led videos were developed to support PrEP demand creation for the national programs in each country. Having materials that included adolescent voices was considered as important for increasing demand.
Post-trial access to trial products or procedures	Post trial access arrangements were challenging given that TDF/FTC was licensed in both countries, but PrEP programs were nascent and initially restricted to particular population groups.

Youth-friendly services were considered a critical element of sustained participant engagement in PrEP care. Youth CABs and local youth-focused organizations were instrumental in providing advice on youth-friendly communication materials, clinic design and clinic flow. They provided insights into language and communication style preferences. They advised that messages that labelled risky behaviors or populations were perceived as stigmatizing and judgmental. Consequently HPTN 082 communication materials were developed to be empowering

and sex positive, celebrating individual agency to make choices to protect one's health. Based on stakeholder feedback, all sites made adaptations to make study clinics more welcoming to young people. For instance, at Wits RHI, youth advisors and Youth CAB members conducted a walkthrough of the study clinic and identified aspects that might act as barriers to access and shared additional activities that they would like to access while in the clinic. At Spilhaus team, the team reached out to Pangea Zimbabwe AIDS Trust to learn how they structured their youth-friendly clinic given their limited experience with adolescent studies. There was an emphasis on creating welcoming spaces for youth through clear signage and entry points, training staff in non-judgmental attitudes, and providing comprehensive, integrated services for young women that included provision of contraception, condoms, and STI testing. Given that participants were anticipated to still be in secondary school or tertiary study, spaces for studying as well as internet access were provided, along with refreshments, in the clinic waiting rooms. Stakeholders also informed referral pathways for social and psychological services that were mapped out in advance. Through early stakeholder engagement the GPP requirements for an agreed standard of prevention, access to HIV care and treatment as well as non-HIV-related care specifically for an adolescent population were met.

The importance of stakeholder education plan on PrEP

Early stakeholder engagement reinforced the need for PrEP education. PrEP was a novel intervention at the time and many communities had little pre-existing knowledge about PrEP. Community teams were faced with the challenge of how best to explain PrEP and how it worked. In some cases, community members were not convinced that antiretrovirals could be used to prevent HIV infection. The community team found value in explaining PrEP in terms of known prevention interventions like contraception with which the community members were familiar. Initial stakeholder consultations also identified several community misconceptions about PrEP, including concerns that PrEP would undermine condom use, and that it would promote promiscuity and multiple sexual partnerships particularly among young women. The fact that initial PrEP programs in South Africa enrolled only sex workers, reinforced the potential for stigma associated with PrEP use. The association of antiretroviral pills with being identified as living with HIV was also voiced by stakeholders as another potential source of stigma.

These early insights allowed community teams to develop stakeholder education plans that addressed these common myths and misconceptions during routine community engagements. Initially there were no sources of government endorsed information about PrEP to refer community stakeholders to. In response, and also to enhance participant education and ultimately informed consent, the Wits RHI team developed a short video titled "Get PrEPared: What African Women Need to Know!" (https://www.youtube.com/watch?v=rHkQq--anmo) which was shared with participants who then for warded it to their peers. This brief video involved young women speaking to camera about the need for HIV prevention interventions for young women in Africa. It then provided a visual demonstration of how PrEP works. The video also emphasized the importance of condom use for prevention of pregnancy and sexually transmitted infections (STIs). The community team learnt that participants used the video to initiate disclosure conversations with family, partners and peers. The video was useful for providing standardized information about how PrEP works to stakeholders and during stakeholder events. The video had less utility outside South Africa because it required translation.

Community education events generally took the form of community dialogues. During these sessions organized at convenient times in community venues, PrEP was introduced as a new technology and framed as a positive intervention offered to young women to use independently to protect themselves. The sessions created opportunities for stakeholders to ask questions and engage with the content based on the relevance to them. Anticipating that community educators would be required to provide critical information about a new health technology in an accessible way to community members and potential participants, the study team organized a messaging workshop (May 2016). The goal was to further strengthen messaging given the community concerns that had already been identified. Included in this experiential training workshop was a values clarification exercise aimed at surfacing pre-existing beliefs, attitudes and biases among staff toward sexual activity in AGYW. This exercised clarified the importance of delivering non-judgmental, sex positive messages about PrEP for AGYW to community staff. At the workshop staff had the opportunity to practice their recruitment "pitches" in a safe space with peer feedback making it easier for community educators to have conversations about PrEP in the field when the time came.

With time, as PrEP programs evolved in country more government-endorsed information materials about PrEP became available. The lessons learned from vanguard studies about the need for sex positive, youth-friendly materials were incorporated into materials developed by the South African Department of Health. As one of the site community teams noted, it was challenging to conduct community education and outreach about PrEP in the absence of a national campaign. Once the South African Department of Health started providing print and

electronic information about PrEP, community education efforts became easier as PREP was normalized and legitimized in communities.

Issues identification and management

GPP guidelines refer to the need for an issues management plan that describes how research teams intend to manage issues of concern that could negatively impact the trial. While community teams did not really identify issues that would have necessitated the activation of an issues management plan, as the trial progressed the community identified that parents and caregivers were influential gatekeepers to AGYW PrEP use and participation in the trial. Early and ongoing parental buy-in was essential to facilitating recruitment and retention in care. Parents and caregivers with limited knowledge about PrEP were reluctant to provide parental consent for young women less than 18 years who wished to join the study. Parents shared many of the misconceptions and concerns about PREP voiced by other stakeholders. Even participants able to provide independent consent were strongly influenced by the opinions of parents and older family members. In some instances, participants would drop out of the study in response to negative comments by a parent or caregiver.

To address this, the community teams held meetings with parents, organized through school governing bodies, to provide PrEP education and to clarify AGYW involvement in the study. During these sessions it emerged that parents and caregivers were also concerned about the potential impact of study visits on school attendance. Community teams were able to point to the study areas on site as evidence of support for school attendance, as well as the efforts to facilitate study visits outside of school hours and on weekends. At the Emavundleni site, some parents worried that the autonomy created by reimbursing adolescent participants would dilute parental authority. Furthermore, Zimbabwean parents raised concerns about long-term fertility prospects after prolonged use of oral contraception. Through recognition of parents and caregivers as important additional stakeholders, and through dialogue and education, community teams were able to mitigate the potential negative impact of parent concerns on the trial conduct.

Lessons learned from trial accrual, follow-up and exit

Community teams learned to customize recruitment approaches for an adolescent population. For example, sites recognized the importance of spending time to ensure adequate informed consent and having materials in different media to explain the study and PrEP. Peer referral was observed to be a particularly important source of recruitment at all three sites. Community educators encouraged participants to bring partners, friends, or family members to study clinics to learn more about PrEP. The study clinic inadvertently became sites of AGYW knowledge and power, inverting traditional social arrangements where AGYW often have the least social power. Community teams leveraged this further by encouraging participants to share study information with their peers and invite them to the study clinic. Participants who referred participants for screening received a PrEP-branded T-shirt, regardless of screening outcome. This led to participants to self-select as PrEP ambassadors within their community, extending the study reach beyond the immediate community team and increasing PrEP awareness among young people in the community more generally. AGYW commented that it was helpful to receive information about PrEP from peers. The community team observed that this had an additional consequence of amplifying PrEP education in communities, thus increasing PrEP normalization, reducing stigma and making it acceptable for AGYW to take responsibility for their own protection and health.

Continued retention in care is essential to ensuring the optimal assessment of study outcomes. Community teams recognized early on that the first contact participants had with the site frequently influenced their expectations throughout study participation. Study staff were trained to build positive, non-judgmental relationships with adolescent participants at the first encounter. For instance, at Emavundleni, the person responsible for the initial recruitment of a participant became a case manager responsible for maintaining contact with that participant throughout the study. Participants who completed their scheduled visits and achieved study milestones e.g., the first 6 months of follow-up complete were given tokens of appreciation within a prescribed cost range approved by the Research Ethics Committee that would appeal to AGYW, e.g. lip balm, water bottles, and sling bags.

Reflecting on youth advisors' guidance on clinic design and flow, and in response to feedback from participants, study teams focused on optimizing participant retention by engineering study visits to be efficient and responsive to the needs of adolescent participants with busy lives. Study visits were scheduled before school, after school or on weekends to accommodate participants' other priorities and commitments. Booking appointments, batching visits e.g., only enrolment visits or only screening visits on a particular day, and ensuring adequate staff coverage, all contributed to reduced waiting times. Across all sites amenities such as childcare and commodities were made available to support study participants with children so they could attend their appointments without the burden of finding alternative childcare. Participant downtime was also optimized by providing access to free

computers, Wi-Fi and a place to work while waiting to be seen, and refreshments were provided too.

Community educators learned that adolescents often took unplanned travel or relocated outside of the study area for work, school or because their caregivers had relocated. Several strategies were developed to address this, including the capture and verification of adequate contact information not just for the participant but for one or more trusted alternate contacts. At enrolment, study teams invested time in exploring participant future plans and in anticipating travel for work, school or holidays. When participants missed visits because of relocation, study teams made arrangements to transport participants to site at convenient times. For example, at Spilhaus they conducted outreach in rural areas and transported participants who had moved to the rural areas to site. After the clinic visit, participants would be reimbursed for transport to return home.

Recognizing the importance of peer and social support to encourage ongoing engagement in care by adolescents, the study team developed peer support or "adherence clubs" aimed at sharing lessons learned and normalizing positive aspects of the PrEP experience. These sessions were optional and facilitated monthly in a venue at or close to the clinic site. In addition to providing adherence support, these clubs built on existing social networks and through additional peer support strengthened engagement in care for some. Participants gained from collective sharing of experience and solutions to challenges to PrEP use in the community. At Emavundleni, the clubs were also used to strengthen partnerships with other community stakeholders that provided services to adolescents in the community, e.g., the Zimele program that provided economic empowerment activities. Clubs were more effective in some communities than others, most likely where social cohesion was greater, because communities were smaller or more closed and participants were familiar with each other outside of the study. Acknowledging that some adolescents were rapidly fatigued by the singular focus on health messaging, the clubs adapted over time to focus on the broader interests of AGYW and the desire to have fun. Sites hosted quarterly events for participants that included an entertainment activity e.g., dance class, movie day, aerobics sessions, and a skills development activity e.g., writing a curriculum vitae, self-defense classes, and makeup tutorials. The events functioned to return people to care by offering the opportunity to complete a study visit on the same day and to strengthen social networks and peer support for participants.

Trial closure, results dissemination and post-trial access

Parents and caregivers raised concerns about post-trial access to PrEP given the nascent nature of the national program at the time of the study. Study teams were acutely aware of the importance of ongoing PrEP access for young women after the trial and identified this as a priority early on. By the end of the HPTN 082, participants at the South African sites were able to offer participants who wished to continue PrEP access to the POWER PrEP demonstration project. Some participants did not want to leave the familiarity of the trial for more routine services. In Zimbabwe access was more challenging initially but was possible by study end through the national program.

Sharing the lessons learned from this vanguard study about PrEP use in young women in Africa was important to the study team and participants. Each site developed short videos voiced by consenting participants who shared the benefits of PrEP that they had experienced. The goal of these videos was to build demand for PrEP among AGYW and to share the lessons learned from HPTN 082 with other vanguard studies and national programs. Unfortunately, the COVID pandemic disrupted many of the final plans for communication and dissemination of results from this study, but efforts were made to share findings with the community and national stakeholders.

Discussion

HPTN 082 trial was a vanguard open-label study of oral PrEP among AGYW in Southern Africa, and was introduced at a time before oral PrEP was widely available in communities. Community teams were challenged not just with standard recruitment, but with introducing a novel HIV prevention agent and generating demand for it in communities whose primary experience of antiretroviral therapy was for treatment. These challenges were compounded by the need to deliver this new agent to AGYW in settings where patriarchal values persist. Misconceptions and stigma that plagued trials quickly became apparent in these settings with concerns about side effects, the potential for risk compensation and the potential for PrEP to overturn social norms controlling young women's sexual behavior, the association of antiretroviral pills with HIV treatment and the related stigma all were expressed by community stakeholders [7, 14, 17]. Using the GPP framework to evaluate the community engagement response to these challenges, highlighted several important lessons for future research and programs with adolescents or with new prevention modalities.

Early stakeholder engagement was identified as critical. Sites already had an advantage as they had been conducting research activities in these communities over a prolonged period and had already built relationships and trust within communities. The importance of including youth advisors in stakeholder engagements was

emphasized due to their crucial role in expressing youth values, preferences, and perspectives, that ultimately influenced study communications, clinic design, and clinic flow. These findings align with a recent review that demonstrated the positive impacts of adolescent involvement in research, such as increased study relevance to adolescents, improved recruitment, the creation of more adolescent-friendly materials, enhanced data collection and analysis, and more effective dissemination. However, the authors of the review noted that while there is substantial evidence supporting the benefits of adolescent involvement in research, it is limited by a lack of rigorous evaluation, inconsistent reporting, and unclear evaluation methods [18].

The importance of stakeholder engagement for providing insights into concerns and misconceptions was essential to the development of community education approaches. Reflections on community education highlighted the importance of communication from trusted sources, and the value on in-person communication both with potential participants as well as with community members more generally. While information delivered through a range of media the community teams were able to leverage the longstanding trust between the sites that were all associated with local universities as sources of reliable information in the absence of government information. In some instances, where medical mistrust exists lack of trust in the research had to be overcome through regular personal engagements [19, 20].

Several important lessons were learned about working with adolescents. While it may seem obvious that parents and caregivers are important gatekeepers, their influence on participants who were considered adults was perhaps underestimated. Efforts to engage them reaped results for individual participants who received more social support but also helped to increase awareness about PrEP in communities more generally. The study was a reminder that adolescents are not just mini-adults and that an appreciation for their important developmental transition from children to adults needs to be accommodated in the way services are delivered, by being flexible, aware of the importance of education during this period, and a recognition that adolescents do not have complete control of their time or travel [21]. The investment in the provision of non-judgmental, youth competent services went a long way to retaining participants in care, ensuring that while PrEP persistence and adherence was not perfect it was much higher than that observed in the blinded trials. The study highlighted the importance of peers during adolescence, their influence and how this can be leveraged for the trial requirements of recruitment and continued engagement in care. The social support provided by the trials through "adherence clubs" allowed young women to share and normalize their experiences, ultimately empowering them to become sources of knowledge and ambassadors of this new technology in their communities. This reinforces an important principle of youth involvement in the development and delivery of services for youth and adolescents [18].

The GPP guidelines emphasize the importance of early collaboration with stakeholders, transparent and accurate communication, stakeholder education, and the involvement of key gatekeepers such as parents and community leaders [12]. By implementing GPP, research teams can navigate cultural nuances, address myths and misconceptions, and foster trust within communities, especially among AGYW. As the HIV prevention landscape continues to evolve, GPP remains a valuable framework for guiding community engagement efforts and ensuring the successful implementation of PrEP and other HIV prevention interventions. Using the GPP framework to organize these reflections highlighted the strong emphasis on planning and the development of plans at the start of the trial, although many of these practices are iterative. However, it also highlighted the relative paucity of practices at the end of the trial. At the time the team grappled with the issues of post-trial access for a product licensed for use in country but not yet available through programs. With the development of new HIV prevention products, the issue of national program access beyond access just for trial participants has increased in prominence [22]. Increasingly researchers and their community teams will need to respond to questions about country access to products that are being evaluated, and increasingly this will be an issue that needs to be planned for at the start of the trial.

There are some limitations to this analysis. The perspectives recorded as those of the community educators responsible for implementation of the trial. Although every effort was made to review meeting minutes and reports captured during the trial, these reflections may be subject to recall bias, with a greater recollection of successful strategies. The effectiveness of individual strategies was not assessed, but the manuscript highlights the consensus on the need for intentional design of community engagement strategies and activities prior to introducing new studies, products or services. These retrospective observations are still valuable for informing future community engagement strategies for interventions with adolescents and youth in South Africa and Zimbabwe, although some may need to be tailored for programmatic scale-up.

Conclusion

The HIV prevention landscape continues to evolve, and the need to effectively engage adolescents in HIV prevention options remains a high priority. The GPP guidelines are recommended to help research teams prepare,

recruit, and retain this population given their dynamic daily needs. The GPP lessons learned shared here provide insights into how to think about and develop effective community engagement strategies when introducing a new HIV prevention method or technology such as PrEP. There is no one-size-fits-all approach to engaging AGYW but a local-level understanding coupled with an understanding of the developmental needs of youth and adolescents is critically important for successful implementation. Lessons shared in this paper can also inform policy and programming for an expanding array of PrEP options.

Abbreviations

AGYW	Adolescent Girls and Young Women
CAB	Community Advisory Board
GPP	Good Participatory Practice
HIV	Human Immunodeficiency Virus
HPTN	HIV Prevention Trials Network
PrEP	Pre-Exposure Prophylaxis
STI	sexually transmitted infection
TB	Tuberculosis
WHO	World Health Organization

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Authors' contributions
The manuscript was conceptualized by MM, NM, SN, CC, NY, KH, MB, PM, TE, NH. The HPTN 082 study was designed by CCE and SDM. CCE, SDM, LGB, and NMG supervised trial activities. MM, with support from MNN and SDM, prepared the first draft of this manuscript, and all co-authors read, commented and approved the final manuscript.

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Data availability
All reflections with community teams, meeting minutes, and workshop summaries are stored at Wits RHI, South Africa. They are available from the study corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The overall HPTN 082 study was approved by the Human Research Ethics Committee of the University of the Witwatersrand, University of Cape Town, and University of Zimbabwe Joint Research Ethics Committee. All participants in the trial were required to provide written informed consent prior to trial participation.

Consent for publication
This paper is written from the perspective of community engagement team members from Spilhaus CRS, Emavundleni CRS, and Wits RHI Ward 21 CRS who consented to participate in all reflections and meeting discussions. They also gave permission for their insights shared to be published.

Competing interests
The authors declare no competing interests.

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