Gendered Lives, Constrained Choice and young African women's PrEP uptake and persistent use as a gender-responsive approach to HIV prevention

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Declaration

I, Elzette Rousseau, hereby declare that this thesis is my own work, and it has not been submitted to any other University for a degree or examination. Also, I hereby declare that all the sources of information I have used have been acknowledged and indicated in the reference list. In the case of multi-authored published papers, this constitutes work for which I was the lead author, and my specific contribution is outlined in the preface of this dissertation.

Signature: Signed by candidate

Date: 30 January 2024

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Preface

This thesis contains four published papers which were included for use as chapters, as per general provision 6.7 in the General Rules for the Degree of Doctor of Philosophy (PhD) of the University of Cape Town. The role of each author is listed under the title. My supervisor is Linda-Gail Bekker, Director of the Desmond Tutu HIV Centre and Professor in the Department of Medicine, University of Cape Town, South Africa. My co-supervisor is, Kathleen Sikkema, Professor and Chair of the Department of Sociomedical Sciences, Columbia University, New York, USA.

I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board to include the following publication(s) in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publication(s):

1. **Chapter Three from: Rousseau E, Katz AW, O'Rourke S, Bekker LG, Delany-Moretlwe S, Bukusi E, Travill D, Omollo V, Morton JF, O'Malley G, Haberer JE, Heffron R, Johnson R, Celum C, Baeten JM, and van der Straten A. Adolescent girls and young women's PrEP-user journey during an implementation science study in South Africa and Kenya. PloS One. 2021;16(10):e0258542.**

   Elzette Rousseau was the lead author, and conceptualised and conducted the data analysis. She was also the study coordinator and socio-behavioural scientist at the Cape Town site conceptualising and supervising study implementation and data collection.

   Ariana Katz collaborated in discussions around data analysis, data interpretation, and critically reviewed the manuscript.

   Shannon O'Rourke collaborated in discussions around data analysis, data interpretation, and critically reviewed the manuscript.

   Linda-Gail Bekker was co-investigator (and Cape Town site-PI) involved in study design, supported data collection and interpretation, and critically reviewed the manuscript.

   Sinead Delany-Moretlwe was co-investigator (and Johannesburg site-PI) involved in study design and reviewed the manuscript.

   Elizabeth Bukusi was co-investigator (and Kisumu site-PI) who was in study design and reviewed the manuscript.

Danielle Travill was Johannesburg site study coordinator, supervised the study, the data collection, and reviewed the manuscript.

Victor Omollo was the Kisumu site study coordinator, supervised the study, the data collection, and reviewed the manuscript.

Jennifer Morton was involved in study coordination and reviewed the manuscript.

Gabrielle O'Malley was a co-investigator involved in study design and critically reviewed the manuscript.

Jessica Haberer was a co-investigator involved in study design and reviewed the manuscript.

Renee Heffron was a co-investigator involved in study design and reviewed the manuscript.

Rachel Johnson was involved in study design and reviewed the manuscript.

Connie Celum was the Principal Investigator, was involved in study design, supported data interpretation, and critically reviewed the manuscript.

Jared Baeten was co-Principal Investigator, was involved in study design, supported data interpretation, and critically reviewed the manuscript.

Arianne van der Straten was co-investigator, was involved in study design, supported data analysis and interpretation, and critically reviewed the manuscript.

2. **Chapter Four from: Rousseau E, Wu L, Heffron R, Baeten JM, Celum CL, Travill D, Delany-Moretlwe S, Bekker LG, Bukusi E, Omollo V, van der Straten A, Morton JF, O'Malley G, Haberer JE, Johnson R, Roberts ST. Association of sexual relationship power with PrEP persistence and other sexual health outcomes among adolescent and young women in Kenya and South Africa. Frontiers in Reproductive Health. 2023 May 30;5:1073103.**

Elzette Rousseau was the lead author, conceptualised the study and analysis, and interpreted the data.

Linxuan Wu cleaned the data, ran the data analysis, and reviewed the manuscript.

Renee Heffron was a co-investigator involved in study design, supported the data analysis, and critically reviewed the manuscript.

Connie Celum was the Principal Investigator, was involved in study design, supported data interpretation, and critically reviewed the manuscript.

Jared Baeten was co-Principal Investigator, was involved in study design, supported data interpretation, and critically reviewed the manuscript.

Danielle Travill was Johannesburg site study coordinator, supervised the study, the data collection, and reviewed the manuscript.

Sinead Delany-Moretlwe was co-investigator (and Johannesburg site- was involved in study design and reviewed the manuscript.

Linda-Gail Bekker was co-investigator (and Cape Town site-PI) involved in study design, supported data collection and interpretation, and critically reviewed the manuscript.

Elizabeth Bukusi was co-investigator (and Kisumu site-PI) involved in study design and reviewed the manuscript.

Victor Omollo was Kisumu site study coordinator, supervised the study, the data collection, and reviewed the manuscript.

Arianne van der Straten, co-investigator, was involved in study design and critically reviewed the manuscript.

Jennifer Morton was involved in study coordination and reviewed the manuscript.

Gabrielle O'Malley was a co-investigator involved in study design and critically reviewed the manuscript.

Jessica Haberer was a co-investigator involved in study design and reviewed the manuscript.

Rachel Johnson was involved in study design and reviewed the manuscript.

Sarah Roberts was a co-investigator involved in study design, supported data analysis, data interpretation and critically reviewed the paper.

3. **Chapter Five from: Rousseau E, Bekker LG, Julies RF, Celum C, Morton J, Johnson R, Baeten JM, O'Malley G. A community-based mobile clinic model delivering PrEP for HIV prevention to adolescent girls and young women in Cape Town, South Africa. BMC Health Services Research. 2021 Dec;21(1):1-10.**

   Elzette Rousseau was lead investigator, lead author, conceptualised the study, designed the data analysis, conducted the study, cleaned and merged all data, and conducted the data analysis.

   Robin Julies supported data collection, supported data analysis, and critically reviewed the manuscript.

Connie Celum was the Principal Investigator and critically reviewed the manuscript.
Jennifer Morton was involved in study coordination and reviewed the manuscript.
Rachel Johnson reviewed the manuscript.
Jared Baeten was co-Principal Investigator, and critically reviewed the manuscript.
Gabrielle O'Malley was a co-investigator, supported data interpretation and critically reviewed the manuscript.
Linda-Gail Bekker was site PI, oversaw study design and implementation, and critically reviewed the manuscript.

4. **Chapter Six from: Rousseau E, Sikkema KJ, Julies RF, Mazer K, O'Malley G, Heffron R, Morton J, Johnson R, Celum C, Baeten J, Bekker LG. Exploring adolescent girls and young women's (AGYW) PrEP-user profiles: qualitative insights into differentiated PrEP delivery platform selection and engagement in Cape Town, South Africa. Journal of the International AIDS Society. 2024; 27(5): e26254**
Elzette Rousseau was lead investigator, lead author, conceptualised the study, designed and oversaw implementation, designed the data analysis, cleaned and merged all data, and conducted the data analysis.
Kathleen Sikkema was co-investigator, involved with study design and critically reviewed the manuscript.
Robin Julies supported data collection, supported data analysis, and critically reviewed the manuscript.
Katelyn Mazer supported data analysis and critically reviewed the manuscript.
Gabrielle O'Malley critically reviewed the manuscript.
Renee Heffron critically reviewed the manuscript.
Jennifer Morton was involved in study coordination and reviewed the manuscript.
Rachel Johnson reviewed the manuscript.
Connie Celum was the Principal Investigator and critically reviewed the manuscript.
Jared Baeten was co-Principal Investigator, and critically reviewed the manuscript.
Linda-Gail Bekker was site PI, oversaw study design and implementation, supported the data interpretation and critically reviewed the manuscript.

The candidate drafted all versions of each manuscript and was the lead and corresponding author on all the included papers. All co-authors critically reviewed and approved the submitted manuscripts. The principal investigators and supervisor for all the papers have confirmed to the University of Cape Town Doctoral Degrees Board that the included papers reflect the candidate's independent scientific work.

Signature:  **Date:** 30 January 2024

Student name: Elzette Rousseau **Student number:** RSSELZ001

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List of acronyms and abbreviations

AIDS	Acquired Immune Deficiency Syndrome
AGYW	Adolescent Girls and Young Women
ART	Anti-Retroviral Therapy
AVAC	AIDS Vaccine Advocacy Coalition
CAB	Community Advisory Board
CCT	Constrained Choice Theory
CMHC	Community Mobile Health Clinic
CT/NG	Chlamydia Trachomatis/Neisseria Gonorrhoea
DTHF	Desmond Tutu Health Foundation
FGD	Focus Group Discussion
TDF/FTC	Tenofovir Disoproxil Fumarate / Emtricitabine
HCP	Healthcare providers
HIV	Human Immunodeficiency Virus
HIVST	HIV Self-Test
HREC	Human Research Ethics Committee
IDI	In-depth Interview
IPV	Intimate Partner Violence
IRB	Institutional Review Board
KEMRI	Kenya Medical Research Institute
MOU	Maternity and Obstetrics Unit
MSM	Men who have Sex with Men
POWER	Prevention Options for Women Evaluation Research
PrEP	Pre-Exposure Prophylaxis
SOC	Standard of Care
SRH	Sexual and Reproductive Health
SRHS	Sexual and Reproductive Health Services
SRP	Sexual Relationship Power
SRPS	Sexual Relationship Power Scale
SSA	Sub-Sahara Africa
SSI	Social Science Interviewer

STI	Sexually Transmitted Infections
TTT	Tutu Teen Truck
VMMC	Voluntary Medical Male Circumcision
WHO	World Health Organization
WRHI	Wits Reproductive Health and HIV Initiative

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Abstract

While there is substantial momentum to scale up PrEP (pre-exposure prophylaxis) for HIV prevention in adolescent girls and young women (AGYW), this population is demonstrating difficulty in sustained PrEP use. PrEP use at the time of HIV exposure is critical for effectiveness. This thesis investigated AGYW's decision-making throughout the PrEP-user journey (from PrEP uptake to persistence or discontinuation). It reflected on the role of agency (personal and relational), gender, and PrEP access and how these facilitated or constrained PrEP use. The research used a multi-method approach, including pharmacy record review, in-depth interviews, and structured surveys. This cohort included 2550 AGYW participants (aged 16-25 years) of the POWER implementation study receiving oral PrEP for up to 36 months in Cape Town and Johannesburg, South Africa, and Kisumu, Kenya. The POWER study was designed to develop and evaluate scalable models of PrEP delivery.

Across analyses, PrEP uptake facilitators included PrEP integration with sexual and reproductive health services but were hampered by PrEP misconceptions and stigma in the community. Disclosure, social support, adolescent-friendly counselling, and convenient access were key enablers for PrEP persistence. Beyond this, AGYW were influenced by intrinsic (strong self-determination and autonomy finding PrEP adherence personally fulfilling) and extrinsic motivations (where PrEP use habits are influenced by external factors or rewards, social pressure, or fear of negative relational consequences). The research showed that AGYW's diversity in needs, habits, and lifestyles also influenced their PrEP access preferences, which led to the segmentation of this group into convenient, independent, social, or discreet PrEP users for optimised tailored service delivery. While the role of sexual relationship power in AGYW's PrEP continuation was also investigated, no significant influence was observed.

In conclusion, the findings suggest that AGYW are empowered to make positive PrEP use decisions when their agency is ignited and/or when AGYW are presented with access alternatives to choose from (differentiated models of PrEP delivery). AGYW's agency fluctuated in contexts of community stigma, non-disclosure, harmful relationship dynamics,

and emotional arousal; however, differentiated PrEP access created alternatives (a potential buffer zone) for these instances of limited agency.

1. Background and Literature Review

1.1 Epidemiology of HIV in Adolescent Girls and Young Women

It is well established that the HIV epidemic has a gendered pattern in eastern and southern Africa (ESA); it disproportionately affects adolescent girls and young women (AGYW, ages 15-24)[1-4]. The World Health Organisation (WHO, 2023) defines these gendered factors as: *"…the characteristics of women, men, girls, and boys that are socially constructed. Gender is hierarchical and produces inequalities that intersect with other social and economic inequalities. Gender inequality and discrimination faced by women and girls puts their health and well-being at risk."[5].* Gender differences, including differences in biology, physiology, socially constructed gender norms, economic inequalities, and unequal power relations, are critical social determinants of health and play a significant role in driving the HIV pandemic in AGYW [6, 7]. AGYW residing in urban informal areas who acquire HIV through heterosexual contact are at the most significant risk, with an incidence rate of 74% of infection in young people in eastern and southern Africa, with about 1000 new infections every day [8-11]. The existence of HIV hyper-endemics (settings with persistently high HIV incidence and HIV prevalence exceeding 15% of the population) in AGYW, along with accelerated youth population growth in Africa, makes preventing HIV a public health challenge that demands addressing [12].

A heightened HIV risk environment is created through the perfect storm of the epidemiological, neurobiological, social, and economic contexts of AGYW, specifically in ESA (Figure 1) [13]. Epidemiologically, many of these hyper-endemic areas also have an amplified STI epidemic (gonorrhoea, chlamydia, syphilis, trichomonas vaginalis), relatively low viral suppression rate in male partners, and low condom use, making every sexual encounter risky for AGYW [13-16]. Societal and relational associations of HIV infections in AGYW include age-disparate sexual relationships, multiple concurrent or serial partnerships, early sexual debut, substance abuse, and limited personal HIV risk perception. Of particular susceptibility to new HIV infections are young single women and those entering steady relationships [17]. Numerous studies have highlighted that young women are on the receiving end of patriarchal power and experience high levels of sexual violence and intimate partner violence or intimidation, exposing them to unsafe sexual practices, including low condom use [12, 18-21].

In addition, secondary school dropout, economic inequalities, unemployment and widespread poverty in African communities lead to AGYW engaging in transactional sex relationships [22]. Harmful gender norms also contribute to the stigma and healthcare providers' judgmental attitudes that AGYW face when accessing sexual and reproductive health (SRH) services [23-25]. All this is particularly prevalent during the adolescent and young adult neurobiological (brain) developmental period, characterised by high social motivation, reward sensitivity and delayed maturation of cognitive control regions of the brain, which can influence impulse control and, at times, may be exacerbated by poor cognitive skills and diminished self-control during emotionally salient situations. [26-28].

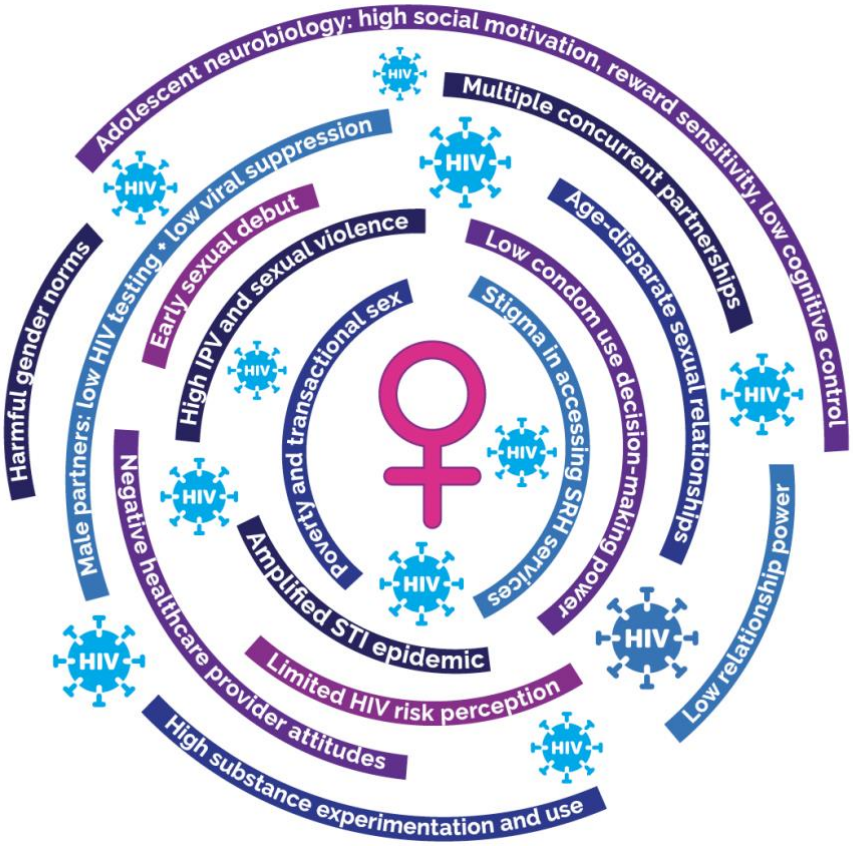


Figure 1. The perfect storm of heightened HIV risk environment for AGYW in Eastern and Southern Africa.
Visualisation created by candidate. AGYW experience multiple physiological, relational, social, neurobiological and economic factors that make them susceptible to HIV acquisition.

Given the ongoing high HIV incidence among AGYW within these contexts, a strong need exists for primary HIV prevention strategies to be gender-responsive, accessible, not need active

male cooperation, and can be applied outside of emotionally salient situations (i.e. at time of sexual encounter).

1.2 PrEP as HIV prevention in AGYW

Numerous HIV prevention interventions have been implemented in African communities. HIV prevention interventions fall into the categories of behavioural, structural, and, in more recent years, biomedical interventions [29]. Behavioural interventions aim to modify behaviours linked to increased HIV risk assuming that individual behaviour results from informed, rational, unconstrained decisions [30]. To date, behavioural interventions have primarily included attempts at delaying sexual debut, decreasing sexual partners, and increasing condom use [31]. Evidence suggests that behavioural interventions have minimal impact in reducing HIV incidence when social context and structural factors are not also taken into consideration [31, 32]. Structural interventions aim to target social and environmental factors, such as inequitable gender norms, poverty, food insecurity, or limited education and awareness, that may drive HIV acquisition. Structural interventions have included conditional cash transfers for keeping young people in school or community HIV awareness and education [29, 31]. Biomedical interventions include the use of suppressive antiretroviral therapy (ART) in people already living with HIV and antiretroviral-based pre-and post-exposure prophylaxis in people un-infected with HIV.

Biomedical science and technology development has made it possible for individuals to avoid diseases, including HIV. This increased focus on human control in transforming disease patterns makes understanding social factors increasingly important for improving population health [33]. ARV-based oral pre-exposure prophylaxis (PrEP) was first shown as effective in HIV prevention in 2010 in men who have sex with men (MSM) and subsequently shown as highly effective in various populations, including AGYW if taken regularly and at times of potential HIV exposure [34]. PrEP, as an HIV prevention method, allows users to take control of their health and mitigate health risks without dependence on their sexual partners. However, contradictory to this optimism that with PrEP AGYW may have the ability to prevent HIV, the early VOICE and FEM-PrEP randomised placebo-controlled clinical trials showed low PrEP usage [35-37]. Key conclusions from these trials and more recent PrEP demonstration

studies highlighted that this population encounters many barriers to PrEP use [35-37]. PrEP is a relatively new method of HIV prevention, and both anticipated and experienced stigma of PrEP use in AGYW, including stigma regarding serostatus and AGYW's sexual activity expressed through discrimination, intimate relationship dissolution, or even violence, is a deterrence for use [38-40]. Some researchers have posited that on an individual and interpersonal level, AGYW display poor HIV risk perception, which impacts their perceived interest and continued use of PrEP. A study found that young South African women's romantic feelings and relationship expectations influenced their perceptions of HIV risk within their partnerships, challenging the risk-framing of HIV prevention methods, including oral PrEP [27, 28, 41]. Furthermore, narratives from demonstration projects show that even though PrEP is user-controlled, AGYW still value their partners' perceptions of PrEP (often only predicted), influencing their PrEP use [42, 43]. Oral PrEP attributes such as the size of the pill and daily pill-taking burden towards a long-term desired outcome are added significant barriers for adolescents and young people due to young peoples' cognitive "present bias" and need for real-time rewards and results in exchange for behaviours [44, 45]. These barriers are further exacerbated by reported judgmental healthcare provider interactions and PrEP access barriers at clinics, including inconvenient times, locations, long queues, or fragmented services [46, 47]. AGYW's barriers to PrEP uptake and continued use are, in some instances, reminiscent of their hormonal contraception use barriers [48, 49].

1.3 PrEP delivery and access for AGYW in Eastern and Southern Africa

The World Health Organisation [50], as of September 2015, recommended that oral PrEP be offered to all population groups and people at 'substantial risk' of HIV infection, including AGYW as a particular key population and estimated this would involve approximately 3 million individuals. Oral PrEP was approved for use in both South Africa and Kenya in 2015. These two countries were the pathfinders for oral PrEP scale-up in Africa (figure 2). As of November 2023, PrEP Watch reported 1,175,293 PrEP initiations in South Africa and 481,376 in Kenya [51]. In South Africa, PrEP roll-out was initially targeted to selected sex worker sites, followed by men who have sex with men, serodiscordant couples, and AGYW. The roll-out in South Africa was directed by the National Department of Health targeting these populations in a phased approach over time [51]. Kenya was the first country in Africa to roll-out PrEP as a national

programme in the public sector. PrEP roll-out in Kenya was led by the government and started in 19 counties prioritised because of high HIV incidence, and with an initial special focus on serodiscordant couples [52]. The roll-out in both countries leveraged existing infrastructure in public HIV care and family planning clinics with added resources to facilitate widespread PrEP provision, including strong community engagement [53, 54].

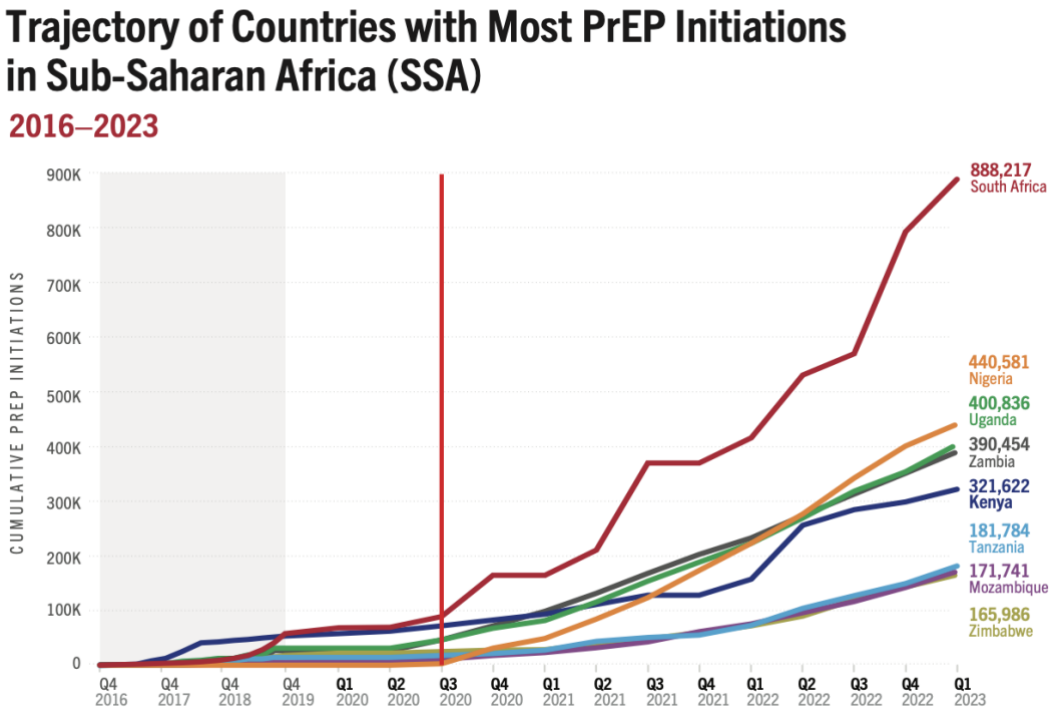


Figure 2. Trajectory of PrEP initiation with South-Africa and Kenya leading early implementation in the region [55].

While demonstration projects are showing high PrEP interest and initial uptake, young people under the age of 30 years, especially those from eastern and southern Africa, are showing difficulty in sustained PrEP use – an indication that biomedical HIV prevention will take more than just providing AGYW with a pill a day [32, 56-58]. A global meta-analysis showed that PrEP discontinuation within six months of initiation is 47% higher in this region [57].

The WHO has cautioned that gender influences people's access and experiences of healthcare: *"The way that health services are organised and provided can either limit or enable a person's access to healthcare information, support and services, and the outcome of those encounters. Health services should be affordable, accessible and acceptable to all, and they should be provided with quality, equity and dignity" (WHO, 2023)[5].* AGYW face

healthcare access barriers due to restrictions on their mobility, lack of decision-making power, discriminatory attitudes of healthcare providers (HCP) and communities, and inadequate awareness and preparation within health systems to attend to the specific health challenges and needs of young women and girls [5]. PrEP delivery in eastern and southern Africa has primarily been integrated into existing HIV treatment services within clinic-based public health services. PrEP delivery from these facilities is not always perceived as accessible or acceptable for all key populations, particularly so for AGYW. AGYW's healthcare access depends on the level of approachability, availability, and appropriateness of the service delivery [59, 60]. Health services options that have recently generated evidence-based acceptability data and improved adolescent prevention and treatment outcomes highlight a focus on adolescent-friendly services and community-based models tailored to reach key populations [61, 62]. The WHO [50] and, more recently, the IAS Lancet Commission on Global Health [59] emphasise the need for a paradigm shift from a "one-size-fits-all" model of HIV service delivery, recommending flexible, tailored, people-centred differentiated service delivery that effectively addresses the social and structural determinants of health. Differentiated models of service delivery have been implemented primarily in the HIV treatment cascade, including community-based adherence clubs and ARV home deliveries [63]. Delivering PrEP to AGYW across multiple community-based platforms or outlets is a promising innovation to potentially mitigate access barriers.

Furthermore, interventions need to be gender-responsive, which means recognising and addressing AGYW's different psycho-social needs and responding to their challenges and strengths in a rights-based, holistic way both during design and implementation. Gender-responsive healthcare places the person at the centre, reducing barriers to healthcare access, building the capacity of staff to respond to gender inequalities, and promoting women's participation in healthcare decisions [64, 65]. To this end, PrEP implementation studies have been called for to gauge AGYW's motivation for HIV prevention across PrEP delivery models, employing a variety of strategies to address the barriers young African women face to prevention uptake and persistent and effective use [66].

1.4 Persistent gaps in research and rationale

To date, most HIV prevention strategies need a high level of self-efficacy, agency, or influence within one's intimate relationship, for example, negotiating the use of male condom use or requesting partner HIV testing. This, unfortunately, means that AGYW also holds some of the lowest control over the prevention of HIV in heterosexual relationships. This thesis focused on understanding how AGYW can have more control in their sexual lives and, in particular, in the use of HIV prevention (Figure 3).

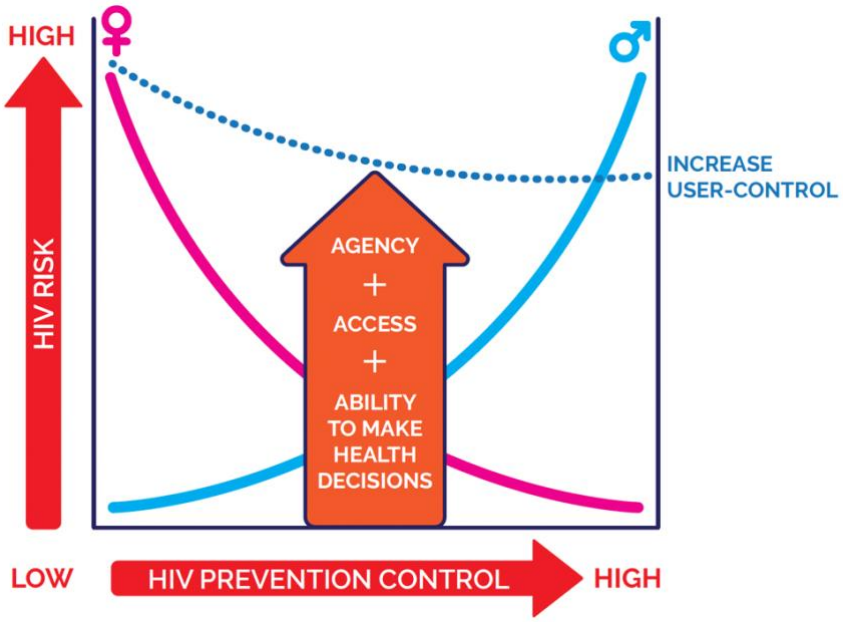


Figure 3. AGYW experience high HIV exposure risk and low prevention control
Visualisation created by the candidate. Compared to young men, AGYW experience higher HIV susceptibility but lower HIV prevention control. The thesis proposes that by increasing AGYW's agency, access, and ability to make health decisions, they will experience greater control in HIV prevention.

The AIDS Vaccine Advocacy Coalition's (AVAC) [42] recent report on *Breaking the Cycle of Transmission* highlighted that a shift is needed in young women from the focus on others' partner's desires and expectations toward a focus on the young woman herself. However, it is not a universal fact that young women are always passive in negotiating their sexuality, as described in some of the literature on young women and transactional sex, AGYW having multiple concurrent partnerships [67], and can take an active position concerning condom use, contraception choice, and family planning [23]. While there is substantial momentum

within the global HIV prevention community to scale up PrEP to AGYW who stand to benefit from it, the effectiveness of PrEP in high-incidence African locations depends on whether AGYW can independently access and effectively use PrEP. The integration of AGYW's perspectives into the uptake and use of PrEP and where PrEP fits into their broader lives and sexuality is critical in developing gender-responsive approaches to HIV prevention. This thesis aimed to broaden our understanding of the conditions that convert AGYW's intention to use PrEP into achieving this prevention goal and reflected on both individual behaviour and the societal and structural determinants that shape and influence those health decisions and outcomes [68]. In seeking deeper insights into AGYW's health and risk mitigation (protective) behaviour, I examined the factors influencing AGYW's PrEP use decision-making using Kabeer's Women's Empowerment Theory [69, 70] and Bird & Rieker's Constrained Choice Theory [68].

1.5 Guiding conceptual frameworks: The ability to make choices

In this thesis, I argued that effectively delivering PrEP needs a critical reflection of the obstacles (personal, relational and structural) constraining AGYW's agency from making protective health decisions. Choice and empowerment theory, as applied to HIV prevention research, is under-researched. Research on women's empowerment across various other fields outside of HIV research postulates that the ability to exercise choice rests on three interrelated dimensions: access to needed resources, agency (personal and relational), and achieving a desired outcome such as well-being or HIV prevention [70, 71] (Figure 4).

Resources (or opportunity structures) are the pre-conditions that allow for choice and include the availability of resources (PrEP services in this instance), how the resources are distributed, and whether AGYW's access to these resources is direct or via the authority of another person (sex partner or healthcare provider). Resources are the medium through which AGYW exercise their agency and achieve their desired well-being outcome (HIV prevention). Agency is a behavioural and psychological concept defined as the sense of being in control of one's own decisions, actions, and consequences [69]. Agency involves matching intentions (in this instance, HIV prevention), actions (taking PrEP), and outcomes (protection from HIV) [72]. It is the process by which choices are made and includes the meaning and motivations that

AGYW bring to their decision-making to reach a goal. As a result, agency is highest in environments of opportunity (enabling environments) but reduced when someone believes their voluntary actions will cause adverse outcomes (to themselves or their relationships) [72]. In this thesis, I was interested in the possible constraints and inequalities in AGYW's expression of agency (personal and relational) or access to resources (PrEP provision in accessible and acceptable service delivery models) and how this influenced their capability (or power) to make choices regarding HIV prevention (Illustrated in Fig 3).

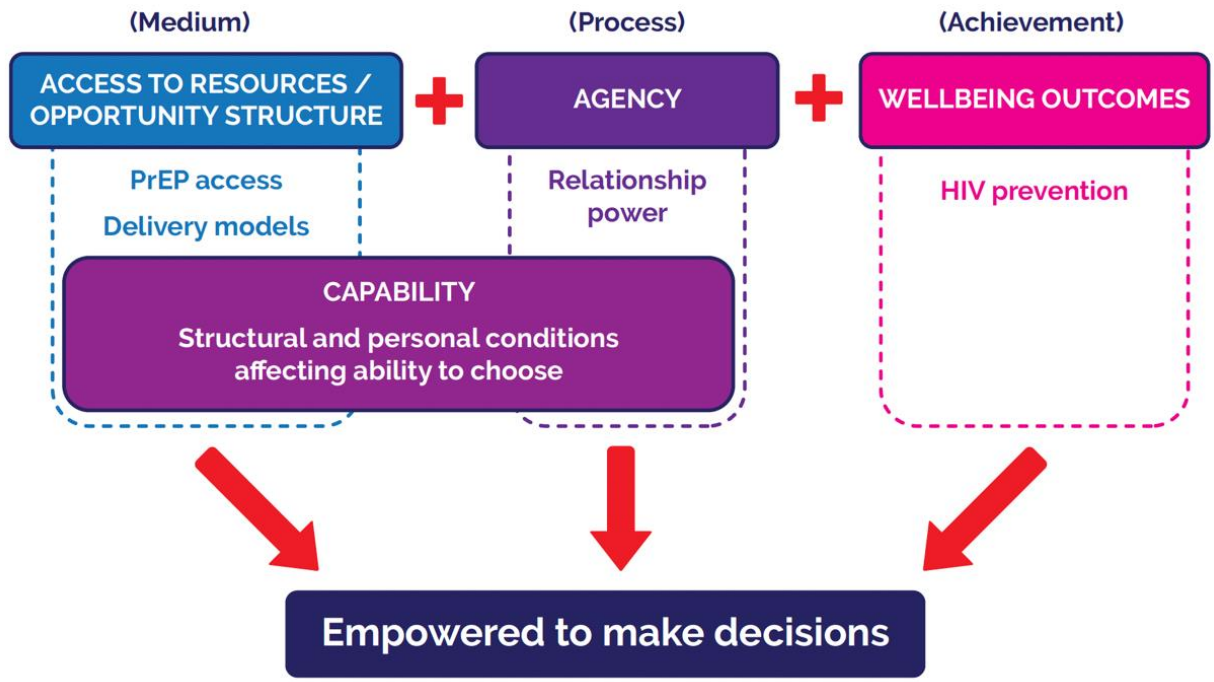


Figure 4. Empowered to make decisions: resources, agency and well-being outcomes
Visualisation created by candidate based on concepts from Kabeer (1999) [70]. Women are empowered to make decisions in the presence of three interrelated dimensions: access to resources, a sense of agency, and achieving a well-being outcome.

As illustrated in Figure 4, structural and personal conditions (agency) combined influence the capability to make decisions. Structural conditions (rules, guidelines, and distribution of resources in the healthcare system) shape the agency of individuals, while the agency exercised by individuals or groups may, in turn, modify or transform the structures. The position of AGYW in the social hierarchy in eastern and southern Africa, however, frequently hinders their expression of agency when it comes to sexual and reproductive health needs [73]. Norms regarding AGYW's sexuality are not just constructs perceived by them, but are

real structures and constraints embedded in systems such as public healthcare. The structural constraints experienced by AGYW in Kenya and South Africa which may influence their access, uptake and persistent use of PrEP are well documented and include travel distance to PrEP service points (clinics); low PrEP awareness and high stigma in the community; long waiting times in overcrowded clinics; limited adolescent friendly services availability; and lack of health care worker motivation to provide PrEP to young women [23, 74-77].

Therefore, the theoretical underpinnings of constrained choice theory [68] were also applied to create a health consciousness that recognised the role of gender, gender relations, and a sense of agency in health disparities. Constrained choice theory (CCT) recognises that social expectations for AGYW influence individuals' readiness and willingness to adopt preventative health behaviours (Figure 5). CCT aids in understanding what prevents or motivates an individual to prioritise sexual and reproductive health and considers the role of family, community, government (policy), and health systems in shaping the options individuals perceive in their everyday lives, how they rank and prioritise these options and thus their sense of agency to pursue health.

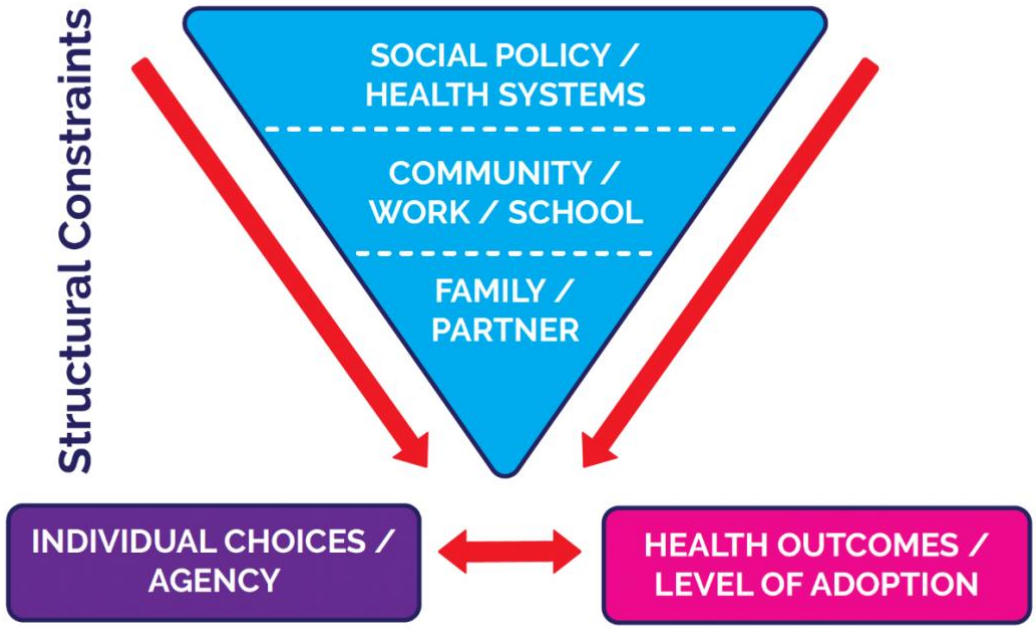


Figure 5. Constrained Choice Theory

Adapted from Bird & Rieker (2008). Gender and Health: The effects of constrained choices and social policies[68]. The sphere of action within which AGYW can make decisions about PrEP

use is set by the broad policy context, health systems and interacting relational and structural constraints. These forces intersect with AGYW's agency to affect the levels of adoption of PrEP.

1.6 Aims and Objectives

My thesis emanates from within a larger open-label oral PrEP implementation science project – the Prevention Options for Women Evaluation Research (POWER) study - providing PrEP to 3000 AGYW (aged 16 to 25 years old) for up to 36 months in Cape Town and Johannesburg, South Africa, and Kisumu, Kenya. The POWER study was designed to develop and evaluate scalable models of PrEP (daily oral emtricitabine/tenofovir disoproxil fumarate) delivery to African AGYW susceptible to HIV acquisition [78].

This thesis aimed to provide insights into the decision-making processes of AGYW offered PrEP as part of a gender-responsive approach to HIV prevention. I explored AGYW's experiences of gender relations and how these shaped their HIV risk perception, agency, and sexual health decision-making, specifically about PrEP uptake and persistent use. My objectives with this thesis included:

1. To understand AGYW's lived experiences of gender and decision-making in their PrEP-user journey from uptake to persistence (Paper 1 – Chapter 3)
2. To investigate associations between sexual relationship power and AGYW's PrEP use. (Paper 2 – Chapter 4)
3. To determine the role of agency, gender, and constrained choice in AGYW's preferences and use of PrEP delivery models. (Papers 3 and 4 - Chapters 5 and 6).

Chapter 2 describes the overall POWER implementation project and methods, while each manuscript included in this thesis (Chapters 3 to 6) further describes the specific methodology applicable to each chapter/paper in further detail.

1.7 Manuscripts included in this thesis.

The four results chapters included in this manuscript (Table 1) investigate AGYW's decision-making during PrEP uptake and persistence and reflect on the role of agency (personal and relational), gender, and access and how these facilitate or constrain PrEP use. Each paper addresses gaps in the literature and advances our understanding of AGYW's decision-making

and the opportunity structures (or enabling environment) that PrEP programmes need to implement to enhance AGYW's capability to start and continue PrEP during periods of heightened HIV risk.

Chapters 3 and 4 investigate the individual and relational factors influencing AGYW's PrEP uptake and persistence. Chapter 3 explores AGYW experiences and decision-making at critical moments along their PrEP-user journey from PrEP uptake to early use, persistence, PrEP pauses and restarts, and, sometimes, PrEP discontinuation. The paper highlights the facilitators and barriers to decision-making at each of these key moments and includes the influence of agency, gender, relationship dynamics, and accessibility of PrEP services. Chapter 4 narrows in on AGYW's intimate relationships and reports specifically on the association between AGYW's sexual relationship power and PrEP use. The role of PrEP access was highlighted in both these papers and stimulated a deeper investigation into the influence that access or lack thereof has on PrEP use in AGYW. As a result, Chapters 5 - 6 turn the attention to PrEP delivery structures, investigating community-based differentiated PrEP delivery to create gender-responsive healthcare. Chapter 5 presents a qualitative examination of AGYW's experience of PrEP delivery from the community-based mobile clinic model set up in Cape Town, South Africa, as part of the more extensive POWER study. During the analysis of this model and while the study was still actively enrolling, AGYW suggested an expansion of this model to include more PrEP delivery options. Towards the end of 2019, we expanded our PrEP delivery model to include a government clinic, a courier service, and a youth club. Chapter 6 shares the qualitative results of AGYW's experiences of using the different outlet modalities and an exploration of decision-making that facilitated or constrained the choice to use one of each of these PrEP delivery platforms offered. The findings of Chapter 6 highlight the diversity within even this targeted population and frame PrEP delivery to the AGYW target population as segmentations or profiles to be considered for future PrEP delivery demand creation and client-centered PrEP continuation, potentially allowing for enhanced tailoring.

Table 1. List of publications included in this thesis

Thesis Chapter	**Publication**
Chapter 3	Rousseau E, Katz AW, O'Rourke S, Bekker L-G, Delany-Moretlwe S, Bukusi E, *et al.* **Adolescent girls and young women's PrEP-user journey during an implementation science study in South Africa and Kenya.** PloS one. 2021;16(10):e0258542.

Chapter 4	Rousseau E, Wu L, Heffron R, Baeten JM, Celum CL, Travill D, et al. **Association of sexual relationship power with PrEP persistence and other sexual health outcomes among adolescent and young women in Kenya and South Africa.** Frontiers in Reproductive Health. 2023; 5:1073103.
Chapter 5	Rousseau E, Bekker L-G, Julies RF, Celum C, Morton J, Johnson R, *et al.* **A community-based mobile clinic model delivering PrEP for HIV prevention to adolescent girls and young women in Cape Town, South Africa.** BMC Health Services Research. 2021;21(1):1-10.
Chapter 6	Rousseau E, Sikkema KJ, Julies RF, Mazer K, O'Malley G, Heffron R, et al. **Exploring adolescent girls and young women's (AGYW) PrEP-user profiles: qualitative insights into differentiated PrEP delivery platform selection and engagement in Cape Town, South Africa**. JIAS. 2024; 27(5): e26254

2 Methodology

This research project was embedded within a larger open-label oral PrEP implementation science project – the Prevention Options for Women Evaluation Research (POWER) study - providing PrEP to AGYW in Cape Town and Johannesburg, South Africa, and Kisumu, Kenya. I served as the study coordinator and socio-bahvioural scientist at the Cape Town site in this project. This thesis aimed to track these AGYW's PrEP uptake and persistence, exploring their lived experiences of gender, PrEP decision-making processes, and factors enabling and constraining their access to PrEP. This research subject was investigated from an ontological and epistemological perspective of critical realism – mapping the context and understanding the patterns of the subjects' engagement. Critical realism proposes that multiple realities exist with common features and potential causal mechanisms that combine (across a group and phenomena) to generate observable events that can be evaluated in real-world evidence [79, 80]. A combination of quantitative and (primarily) qualitative observational designs were applied with data collected through medical record review, quantitative surveys and qualitative in-depth interviews or focus group discussions. This chapter describes the overall POWER implementation project and methods. The detailed methods and analysis for each included manuscript in this thesis are described in further detail in Chapters 3 to 6.

2.1 Study design and data source: the POWER study

Data for this thesis came from the POWER (Prevention Options for Women Evaluation Research) study. Each of the four manuscripts below is prefaced with a description of the

paper's contribution to the thesis, its novelty and the candidate's contribution to that paper. POWER was an implementation science study (2017-2022) of oral PrEP (tenofovir disoproxil fumarate/emtricitabine (TDF/FTC)), delivery to young women in South Africa and Kenya, supported by the University of Washington, Seattle, USA and USAID (AID-OAA-A-15-00034). South African and Kenyan regulatory authorities approved TDF/FTC as an HIV prevention method in 2016. POWER was a prospective, observational, open-label cohort study to evaluate delivery approaches, uptake, and persistence to PrEP, when delivered according to emerging standard of care (SOC) policies, among young women in South Africa and Kenya. Implementation partner organisations in the POWER study included the Desmond Tutu Health Foundation (DTHF in Cape Town), Wits Reproductive Health and HIV Initiative (WRHI in Johannesburg), and Kenya Medical Research Institute (KEMRI in Kisumu). Study sites included were an adolescent-friendly clinic (Ward 21) in the Johannesburg Hillbrow precinct, South Africa; a family planning clinic in Kisumu, Kenya; and an adolescent community-based mobile health clinic in Cape Town, South Africa. Papers 3 and 4 include data from the entire study cohort, while papers 5 and 6 include data from the Cape Town specific site. In 2019, the Cape Town site implemented a differentiated delivery model with a community-based mobile clinic, a fixed government health facility, a courier delivery service, and a youth PrEP club (Figure 6).

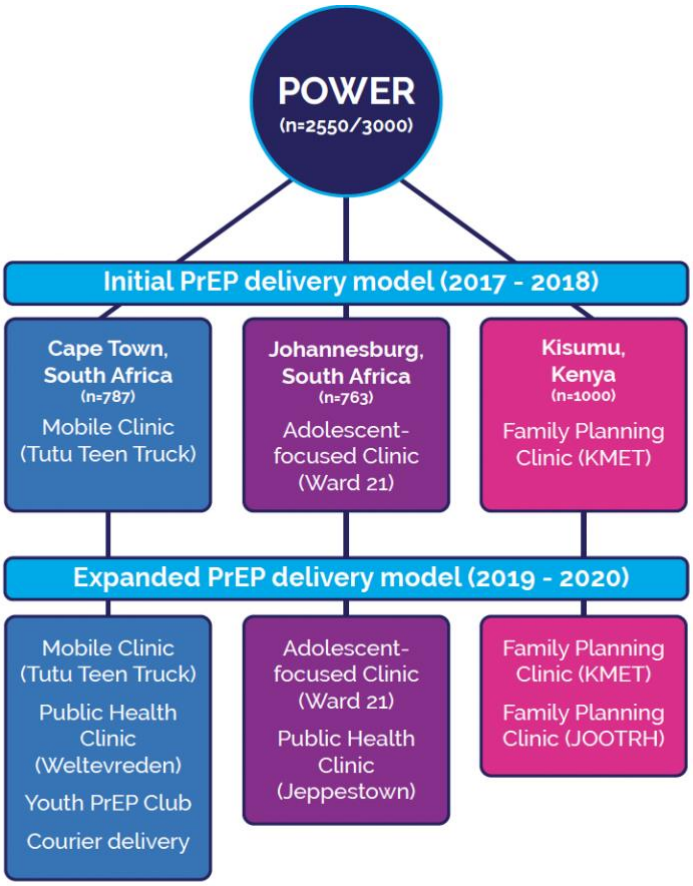


Figure 6. POWER study implementation timeline and research sites

Up to 1000 AGYW were included per site (n=3000 total), with a smaller number initiating PrEP. The inclusion criteria for enrollment in the parent POWER study were:

- Cis-gender woman
- Age 16-25
- Able and willing to provide written informed consent (we asked for a waiver of parental proxy consent for 16 – 17 year olds)
- Recently sexually active (defined as having had vaginal intercourse at least once in the previous three months)
- HIV uninfected based on negative HIV rapid tests on the date of enrollment

Women were ineligible for enrollment if they were pregnant as, at the start of the study, oral TDF/FTC was not yet approved for use in pregnant women in South Africa. Women were enrolled in the cohort based on their interest in HIV prevention and regardless of their decision to initiate or not initiate PrEP at enrollment or during follow-up. Follow-up was for

up to 36 months. Detailed study explanations were published by the principal investigator and study team in 2022 [78].

Specific study procedures are detailed in Tables 2 and 3. Study visits took place at enrollment, a visit one month after enrollment, and then quarterly after that for up to 36 months. At enrollment, HIV testing, according to national algorithms, was conducted to establish participant eligibility. Women who had symptoms potentially consistent with acute HIV infection (e.g., fever, rash, headache, pharyngitis) had enrollment deferred for 2-4 weeks, at which time repeat serologic testing was performed. At enrollment women were offered PrEP with the option to accept or refuse PrEP. At each visit, staff counselled all women about risk reduction and HIV prevention. At each visit, women had the option to accept PrEP or refuse PrEP. Regardless of their decision to use PrEP, all women enrolled in the cohort underwent the study procedures outlined below. At enrollment, demographic and behavioural information was collected. Medical history data, fertility intentions, and contraceptive use were collected during one-on-one sessions with staff counsellors. STI testing for chlamydia and gonorrhea were conducted via GeneXpert urine nucleic acid amplification tests. Participants had a urine pregnancy test when clinically indicated (e.g., missed menses, participant request).

At the Month 1 and then quarterly visits, all participants complete quantitative behavioral and clinical interviews about their interest in PrEP, contraceptive use, and fertility intentions. For follow-up visits, HIV-negative status was confirmed with a rapid HIV test (either health care professional administered or using a self-test). PrEP refills were issued upon confirmation of HIV-negative results. The timing of PrEP refills was ascertained at quarterly visits through review of the pharmacy records. Interim visits were allowed at any time during the study and were documented in participants' study records. To ensure as real-world an assessment of uptake and sustained use of PrEP as possible, retention procedures reflected local retention approaches used by local public health clinics.

Table 2. Procedures for PrEP delivery

	PrEP initiation visit	Month 1	Quarterly visits	6 monthly visits
HIV testing and counseling according to national algorithm	X	X	X	X
Risk reduction and condom provision	X	X	X	X
Contraception counseling and provision/referral according to national standard of care	X	X	X	X
Syndromic assessment of sexually transmitted infections and treatment according to national guidelines	X	X	X	X
Acute HIV assessment	X	X	X	X
PrEP provision (for women who take PrEP)	X	X	X	X
Effective PrEP use counseling (for women who take PrEP)	X	X	X	X
Urine pregnancy testing, as clinically indicated	[X]	[X]	[X]	[X]
Hepatitis B testing (for women initiating PrEP)	X			
Creatinine testing (for women who take PrEP)	X			X

Table 3. POWER study visit procedures

	Enrollment Visit	Month 1	Quarterly visits	6 monthly visits
Obtain informed consent	X			
Apply inclusion/exclusion criteria	X			
Collect/update locator information	X	X	X	X
Collect/update demographic information	X			
HIV testing and counseling according to national algorithm (Elisa test if positive rapid)	X	X	X	X
Risk reduction counseling and condom promotion and provision	X	X	X	X
Acute HIV assessment	X	X	X	X
Behavioral data collection	X	X	X	X
Medical history, fertility intentions, and contraception use data collection	X	X	X	X
Perform physical exam (as indicated)	[X]	[X]	[X]	[X]
STI Testing (gonorrhea, chlamydia)	X			X
Urine pregnancy testing (as clinically indicated)	[X]	[X]	[X]	[X]
Assess date of previous PrEP refill (if taking PrEP)		X	X	X
Collect adherence data (if taking PrEP)		X	X	X

2.2 Overview of data included and analytic methods

Study measures collected as part of the POWER study and follow-up visits are included in Supplementary Information 1. Measures related to the primary focus of PrEP use were collected at all study visits through medical and pharmacy records, while qualitative data was

collected at certain key times during the study period. Table 4 summarises the data collected and the sample size enrolled. Different sub-samples are included in different analyses of this thesis, as described in each chapter. The body of work in this thesis aims to provide an in-depth exploration of two outcomes: PrEP uptake and PrEP persistence in AGYW. PrEP persistence and effective PrEP use as a construct are complex, and the field of HIV prevention has used a range of definitions. PrEP persistence, however, cannot be limited to the expectation of daily adherence, similar to how people living with HIV take ARVs. PrEP persistence must be defined within the context of changes in risk for HIV infection and have the expectation of AGYW taking PrEP for HIV prevention only during time periods of potential exposure to HIV [81, 82]. In addition, recent research has indicated that fewer than daily oral PrEP dosing may also provide reasonable protection against HIV acquisition in women [83]. However, in the POWER study (and in the manuscripts listed in this thesis), PrEP uptake was defined as receiving a bottle of oral PrEP tablets at enrollment. Non-persistence on PrEP was defined as a gap of ≥ 15 days in PrEP availability for daily dosing as per pharmacy records [78].

Table 4. POWER study data included in this thesis

Data Collection Method	Data collected in POWER study	Data included in this thesis
Quantitative study data (n=2550)	• Demographics • Medical History • Sexual behaviour • HIV risk perception • Pharmacy: PrEP dispensed • Pharmacy: Contraception • Labs: HIV test result • Labs: Pregnancy test • Labs: STI test result • Labs Heb B and Creatinine • Sexual Relationship Power Scale • Alcohol and Recreational Drug Use • Self-esteem (PHQ-10) • Self-reported PrEP effective use • PrEP use disclosure • PrEP use experiences: side-effects • PrEP discontinuation reasons	<u>Paper 2/Chapter 4 (n=596)</u> • Demographics • Sexual behaviour • Pharmacy: PrEP dispensed • Pharmacy: Contraception • Labs: HIV test result • Labs: STI test result • Sexual Relationship Power Scale [84, 85]
Qualitative multi-site data	<u>IDI (n=104)</u> • Knowledge of PrEP • PrEP decision-making • Clinic experience • Experiences using PrEP • Relationships (family, friends, partners) • Social support • Stigma and Discrimination	<u>Paper 1/Chapter 3 (n=137)</u> • Knowledge of PrEP • PrEP decision-making • Experiences using PrEP • Relationships (family, friends, partners) • Social support • Stigma and Discrimination • Seroconversion (where applicable)

	• Seroconversion (where applicable) • PrEP in the future <u>FGD (n=33)</u> • PrEP decision-making • Experiences using PrEP • PrEP pause • PrEP restart • Social networks and social support mapping	• PrEP pause • PrEP restart <u>Paper 3/Chapter 5 (n=30)</u> • PrEP decision-making • Clinic experience • PrEP in the future
Qualitative Cape Town specific data	<u>IDI (n=26)</u> • Community PrEP perceptions • PrEP delivery platform decision-making • PrEP delivery platform barriers and facilitators • PrEP disclosure • Family influence in PrEP use and access • Peer influence in PrEP use and access • Sexual partner influence in PrEP use and access	<u>Paper 4/Chapter 6 (n=26)</u> • Community PrEP perceptions • PrEP delivery platform decision-making • PrEP delivery platform barriers and facilitators • PrEP disclosure • Family influence in PrEP use and access • Peer influence in PrEP use and access • Sexual partner influence in PrEP use and access

As indicated at the start of this chapter, mixed methods were employed in this thesis, with qualitative methodology used predominantly. This approach was chosen by the need to map the context and understand the complexities of AGYW's engagement with PrEP delivery services. Combining qualitative and quantitative research methodologies is becoming recognized as a necessity in public health as it allows the researcher to understand broad patterns in quantitative data while the narrative qualitative analysis generates a deeper understanding of the lived experience and potential underlying interactions [86]. A concurrent mixed-methods design was applied with quantitative and qualitative data simultaneously collected but analysed independently [86, 87]. The primary outcomes paper of the POWER study [78] (not included in this thesis, however, summarised below) and the investigation into the relationship between sexual relationship power (SRP) and continued PrEP use in Chapter 4 applied quantitative data analysis. Qualitative methodology and thematic analysis were applied in Chapters 3, 5 and 6 towards a more nuanced understanding of AGYW's experiences in their PrEP-user journey and engagement with differentiated models of PrEP delivery. The data collection and analysis strategy are described in each of these chapters. To ensure credibility and maximise the validity, multiple analysts/coders were used, and reliability of the qualitative data analysis was measured in Dedoose, with an average kappa >0.75. Finally, several limitations to the POWER study are alluded to within each of the manuscripts in Chapters 3-6.

2.3 A summary of the primary quantitative results of the POWER study to contextualise this thesis.

The clinical study outcomes of the POWER study were published by the principal investigators and study team in 2022 [78]. This section shares a summary of the primary quantitative results to contextualise the sub-analysis and follow-on investigations included in this thesis. The overall POWER cohort (n=2550) had a median age of 21 years and 66% did not know their sexual partner's HIV status. Consistent condom use was low, with a high prevalence of chlamydia (29%) and gonorrhea (10%). PrEP initiation was high (94%) among this group of AGYW, and 749 (31%) had a PrEP refill at one month. Of those who continued PrEP use beyond six months, one-fifth displayed short gaps in PrEP refills (PrEP pauses) Sixteen HIV seroconversions were observed (incidence 2.2 per 100 person-years). The overall conclusion of the primary study was that PrEP uptake is high when integrated with reproductive health services and primary care. Additional strategies are needed to simplify PrEP delivery and support adherence in African AGYW. Still, offering long-acting PrEP options may improve persistence in this population.

2.4 Ethical considerations

The research included in this thesis was approved by the human research ethics committees (HREC) of the University of Washington, the University of Cape Town, the Kenya Medical Research Institute, and the University of Witwatersrand. Prior to data collection, young women were informed about the focus and procedure of the parent research study and written informed consent was obtained for each of the additional sub-studies. Written informed consent as well as data collection was done in English or local languages: Xhosa in Cape Town, Zulu in Johannesburg, and Kiswahili or Dhuluo in Kisumu). Parental consent was waived in Kisumu and Cape Town for participants younger than 18 through an approved application to HREC. It is our contention that young women who are sexually active but who may not have disclosed this activity to their parents and guardians may well be at greatest risk for HIV acquisition. Therefore we motivated for our research to involve minors (age 16-17 years) as this is a sexually active population group and young women of this age are known to have unique difficulties obtaining medical services and advice. If we had involved only

adults aged 18 years or older, we do not believe we would have gained an adequate understanding of the unique needs and motivations of this specific population. In addition, by only involving minors who have disclosed their sexual status to legal guardians, we would have been unlikely to reach the most vulnerable adolescent population. Furthermore, the DTHF has been safely and effectively conducting HIV and SRH research among adolescents who are minors for more than a decade. They have developed robust strategies and operating procedures to ensure this research is conducted safely, ethically and effectively.

No reimbursement was offered to individuals except those participating in qualitative research. The reason for this is that POWER was an implementation science project that provided an "add-on" to SOC service. It was strongly felt by the study team and the community advisory board that reimbursing individuals for their role in this project would have distorted that service arrangement and undermined the real-world experience that was being investigated. The provision of reimbursement for the additional time spent in focus groups or IDIs, however, was easily explained and justified. These individuals were offered R150 as reimbursement for participation.

3 Adolescent girls and young women's PrEP-user journey during an implementation science study in South Africa and Kenya

Paper 1

Rousseau E, Katz AW, O'Rourke S, Bekker LG, Delany-Moretlwe S, Bukusi E, Travill D, Omollo V, Morton JF, O'Malley G, Haberer JE, Heffron R, Johnson R, Celum C, Baeten JM, and van der Straten A. Adolescent girls and young women's PrEP-user journey during an implementation science study in South Africa and Kenya. PloS One. 2021;16(10):e0258542.

Contribution to the thesis and novelty

This paper contributes to the first objective of the PhD, which is to describe the lived experiences of gender and decision-making in AGYW's PrEP-user journey from uptake to persistence. This first paper forms the backbone of my thesis, plotting AGYW's PrEP use beyond naïve statistics of uptake and persistence by highlighting the multiple decisions AGYW need to make beyond the initial decision to start PrEP. The paper's novelty lies in its discussion of the barriers and facilitators to PrEP use at each step starting at PrEP uptake and moving to early use, persistence and/or discontinuation. It further starts to highlight AGYW's experiences of PrEP pauses and restarts and how these could be either intentional or unintentional. These key moments in the PrEP-user journey remain a theme in the other papers included in this thesis and underline the complexity of decision-making and prevention persistence for AGYW in this context. This initial paper starts highlighting the role of influencers in AGYW's lives (partners, family, peers) while also emphasizing the role of individual decision-making based on internal versus external locus of control. Finally, the paper draws attention to the role of PrEP access (including the role of the health care provider and counselling) in AGYW's PrEP uptake and persistence, which contributed to the expansion of the project and the investigation of AGYW's access preferences in the later papers. Future expansion of the PrEP-user journey model will benefit from an in-depth exploration of the influence of systemic healthcare barriers when AGYW PrEP use is observed outside of a study setting.

Contribution of candidate

The paper was originally presented (poster exhibition) at the HIV Research for Prevention (HIVR4P) conference in January 2021 and was published as a manuscript later the same year. I conceptualized and wrote the piece, after they conducted the data analysis in collaboration with three of the co-authors. All the co-authors supported data interpretation and critically reviewed the manuscript.

Abstract

Successful scale-up of PrEP for HIV prevention in African adolescent girls and young women (AGYW) requires integration of PrEP into young women's everyday lives. We conducted interviews and focus group discussions with 137 AGYW PrEP users aged 16-25 from South Africa and Kenya. Individual and relational enablers and disablers were explored at key moments during their PrEP-user journey from awareness, initiation and early use through persistence, including PrEP pauses, restarts, and discontinuation. PrEP uptake was facilitated when offered as part of an integrated sexual reproductive health service, but hampered by low awareness, stigma and misconceptions about PrEP in the community. Daily pill-taking was challenging for AGYW due to individual, relational and structural factors and PrEP interruptions (intended or unintended) were described as part of AGYW's PrEP-user journey. Disclosure, social support, adolescent-friendly health counseling, and convenient access to PrEP were reported as key enablers for PrEP persistence.

3.1 Introduction

Globally, 1000 new infections occur daily in adolescent girls and young women (AGYW, ages 15-24), and HIV is the leading cause of death for women (15-49 years)[88]. In eastern and southern Africa, AGYW are disproportionately affected, accounting for 25% of all new infections. AGYW are 2.5 times more likely to acquire HIV through heterosexual sexual contact than their male peers [89]. Young people who are single or entering steady relationships are especially vulnerable to HIV acquisition [90]. Reducing HIV infection among AGYW is complicated by social factors that limit the ability of women to practice safer sex. These factors include a lack of communication between men and women regarding sexual health issues; gender inequality and violence in sexual relationships; difficulties with condom use negotiation; and overall low perception of HIV risk in AGYW [18, 19, 91, 92].

AGYW have welcomed oral pre-exposure prophylaxis (PrEP) as an HIV prevention method that will reduce HIV-related anxiety and increase their autonomy over their sexual health, independent of sexual partners' knowledge or approval [8-10]. While daily dosing of oral PrEP (emtricitabine/tenofovir disoproxil fumarate) reduces the risk of acquiring HIV by more than 95% when used consistently [93, 94], clinical trials in young African women have highlighted many barriers to use [35, 36, 95]. PrEP demonstration studies suggest that HIV-related stigma is pervasive, and confusing PrEP with antiretrovirals for treatment (ART) is common, creating a large deterrent to PrEP use [95-98]. Other barriers to PrEP uptake among AGYW include poor perception of HIV vulnerability, low awareness about PrEP, and lack of social support for PrEP use. Lower PrEP adherence has been noted among AGYW in relationships with intimate partner violence (IPV), in committed relationships where a sense of trust has been established, and situations where AGYW were hiding pill taking from their significant others [41, 45, 46, 99, 100]. Successful scale-up of PrEP in SSA will necessitate AGYW's ability to integrate PrEP into their everyday lives. This includes oral PrEP use among AGYW becoming more normalized along with AGYW accurately assessing their vulnerability for HIV acquisition and aligning their PrEP use to periods of HIV risk in what is called prevention-effective adherence [81].

Previous research on female-initiated HIV prevention technologies indicated that PrEP use integration will entail a focus on accessibility and practicalities of use, as well as the personal and relationship interests that influence uptake and continued PrEP use [101, 102]. During the POWER PrEP implementation science project in Kenya and South Africa, we conducted qualitative research to explore AGYW's PrEP-user journey [103] from awareness and initiation of PrEP to early use and persistence, including PrEP pauses, restarts, and discontinuation. This manuscript aims to highlight individual and relational enablers and disablers of PrEP engagement at each of these key moments along the PrEP user-journey.

3.2 Materials and methods

Research setting and study participants

The POWER (Prevention Options for Women Evaluation Research) implementation science study aimed to develop scalable and context specific PrEP delivery strategies for AGYW in Africa [27]. Between 2017-2020, 2550 AGYW enrolled on the POWER study at two family planning clinics in Kisumu, Kenya; an adolescent friendly clinic in Johannesburg; or a community mobile health clinic in Cape Town, South Africa. Inclusion criteria were being a cisgender woman, 16-25 years old (18-25 in Johannesburg), HIV uninfected, and sexually active at least once within the previous 3 months. Young women were given the option to start PrEP on the same day or delay PrEP initiation (PrEP initiation was not an enrollment requirement), with decision-making processes regarding PrEP uptake and persistence tracked for up to 36 months.

A subset of AGYW were purposively selected from this cohort for 104 in-depth interviews (IDIs) and six focus group discussions (FGDs; n=33). Qualitative participants were recruited based on their decision to initiate PrEP and their persistence with PrEP refills throughout the study, as established through pharmacy records. Quota sampling was employed to ensure eligible participants were chosen for the IDI's according to their unique PrEP-user journey experience and not necessarily to be representative of the overall POWER study cohort (Table 5). Using convenience sampling, participants who had at least one PrEP refill were recruited for FGD's during clinic visits toward the end of their study participation.

The research was approved by the human research ethics committees of the University of Washington, the University of Cape Town, the Kenya Medical Research Institute, and the University of Witwatersrand. Prior to data collection, young women were informed about the focus and procedure of the research, and written informed consent was obtained in English or local languages (Xhosa, Zulu, Kiswahili, or Dhuluo). Parental consent was waived in Kisumu and Cape Town for participants younger than 18.

Table 5. Participant categories

Participant Category	Definition	Number qualitatively interviewed[a]	Number in entire

		N=137	POWER cohort[b] N=2550 (%)
Early Acceptors	Participants who initiated PrEP at enrollment	24	2359 (93%)
Initial Decliners	Participants who declined PrEP at enrollment (but may or may not have started later)	23	183 (7%)
Persistors	Participants who initiated PrEP at enrollment and continued PrEP use over 6-month period with no gaps in pill coverage based on pill dispensing records	16	52 (3%)
Non-Persistors	Participants who initiated PrEP at enrollment and had a recently scheduled month 3 or month 6 visit and pharmacy records indicate late, missed or declined PrEP pill pick-up	23	2020 (92%)
Restarters	Participants who initiated PrEP and pharmacy records show a break in PrEP use for more than 30 days before a PrEP pill pick-up at a later clinic visit	5	384 (19%)
Special Cases	Participants whose unique circumstances or perspectives stood out and whose experiences could inform PrEP delivery, including participants who sero-converted to HIV	13	n/a
FGD participant	Participants who have had at least one PrEP refill were recruited for FGD's during clinic visits toward the end of their study participation	33	n/a

Participants selected for IDI's according to their unique PrEP-user journey experience based on PrEP pharmacy records.

[a]Participants could fall into more than one category, however participants here only indicated in categories originally recruited into.

[b]Celum, et al. (2021) [78]

Data collection

IDI (Supplementary Information 2) and FGD guides (Supplementary Information 3) were developed in English and translated into local languages. Interview guides included questions about the AGYW's PrEP-user journey experiences, including their awareness and interest in PrEP; the enablers and disablers to PrEP uptake and use; the influence of family, peers, intimate partners and other community on PrEP use; and the key points of support in the PrEP-user journey. The FGD guide included the use of an adapted vignette, with the goal of getting young women to express their personal views of PrEP through the lens of a fictional persona (Lebo in South Africa; Anyango in Kenya). The guide included questions about the persona's experiences, thoughts, and decisions to start, pause, restart, and discontinue PrEP as well as probes to understand differences between the persona and the participants' actual experiences.

All IDIs and FGDs were conducted face-to-face in the participants' preferred language by experienced social science interviewers who were independent of the demonstration study's clinical team. IDIs and FGDs lasted between 45-120 minutes and were audio recorded, then

simultaneously translated and transcribed, and English transcripts were quality controlled by bilingual research assistants.

Data analysis

An 'end-user journey' approach (based on the human-centered design framework: http://www.engagehcd.com/dpv-ring/) informed the codebook development [103]. The codebook was iteratively created to reflect the participants' unique experiences at each moment of the PrEP-user journey: PrEP awareness, uptake, early use (month 0-3), persistence (beyond 3 months), pause and restart, and discontinuation. Additional codes were included to capture themes such as risk perception, disclosure, social support, relationship dynamics, and stigma/misconceptions to understand how these influenced decisions during the PrEP-user journey. Transcripts were coded in Dedoose (Version 6.1.18, Los Angeles, CA: Socio-Cultural Research Consultants, LLC) and analyzed thematically [104] to explore how AGYW fit PrEP into their lives and to understand AGYW's needs at different key moments in their PrEP-user journey. Sections of independently coded transcripts were periodically compared by the four-person analysis team throughout the analysis process using the Dedoose Training Center with an average kappa of 0.76. Any disagreements were resolved through discussion until consensus was reached.

3.3 Results

Participants in the POWER qualitative sub-study included 137 AGYW aged 16-25 (median age = 21) from Johannesburg (n=46) and Cape Town (n=43), South Africa and Kisumu (n=48), Kenya who participated in IDI's (n=104) or FGD's (n=33). As illustrated in Table 6, the majority of young women were single with a partner (81%) and living with their parents or other family members (74%). Almost two-thirds of AGYW (63%) tested positive for a sexually transmitted infection (STI; either gonorrhea or chlamydia) at enrollment and 47% reported regular alcohol consumption. Seven young women (5%) were in known HIV serodiscordant relationships. Most young women receiving IDIs (59%; 61 of 104) had a PrEP interruption (i.e., following initiation, was not dispensed PrEP at an attended visit or was >14 days without pills due to a missed/late visit) during their use journey, with half (49%; 30 of 61) restarting PrEP within 30-60 days after pausing. Six young women interviewed seroconverted to HIV (either within the

first month of PrEP use and could have been infected at PrEP initiation); or later in the PrEP user-journey after missing a PrEP refill or taking a PrEP pause.

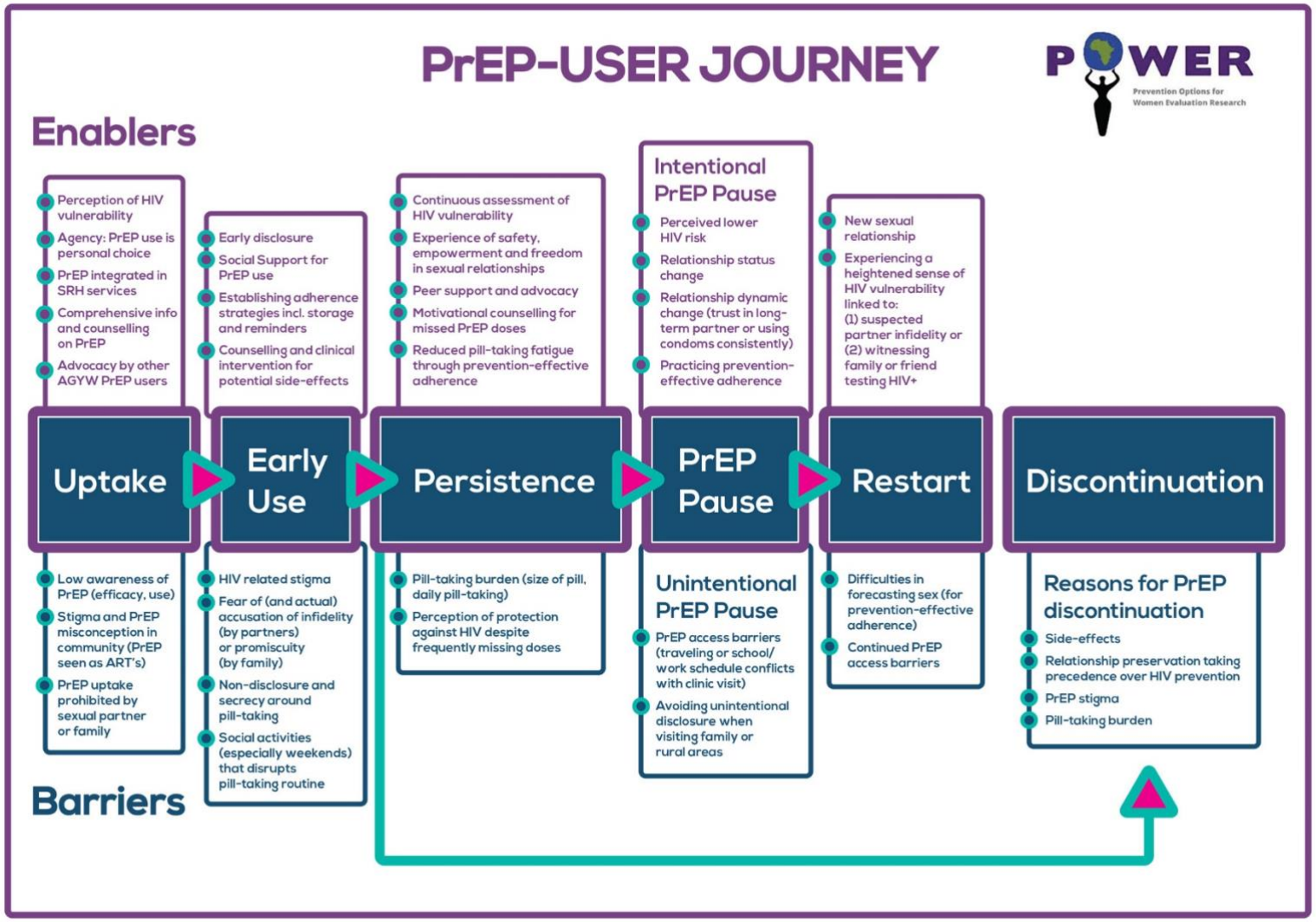
Table 6. Demographic and behavioural characteristics of participants

	N= 137 (%)
Age	
16-19	44 (32.4)
20-25	92 (67.6)
Relationship status	
Single, with partner	110 (80.9)
Single, no partner	2 (1.5)
Married, husband has one wife	21 (15.4)
Married, husband has multiple wives	2 (1.5)
Sexual partner's HIV status	
Sex partner is HIV+	7 (5.1)
HIV partner is not HIV+	48 (35.5)
Don't know sex partner's HIV status	81 (59.6)
Living situation[a]	
Parents	66 (48.9)
Other family	34 (25.2)
Sex partner	23 (17.0)
Friends	1 (0.7)
Alone	15 (11.1)
Other	6 (4.4)
Alcohol consumption	
Yes	64 (47.1)
no	72 (52.9)
STI at enrollment visit	
Gonorrhea and/or chlamydia	71 (63.4)
None	41 (36.6)

[a]AGYW could mark more than one category ('all that apply')

Qualitative results are described below according to key stages in young women's PrEP-user journey (illustrated in Fig 7).

Figure 7. AGYW's PrEP-user journey. Enablers and barriers at key stages in young women's PrEP user journey from PrEP uptake to early use and persistence or discontinuation, including periods of PrEP pauses and restarts.



3.3.1 AGYW's considerations for PrEP uptake

AGYW had a number of considerations before deciding to initiate, delay or decline PrEP: (1) prior awareness about PrEP; (2) perceptions of their HIV vulnerability; (3) ease of PrEP access; and (4) stigma and PrEP misconceptions in the community.

Initial PrEP awareness among AGYW in their communities

PrEP awareness was very low in the communities where participants resided, with AGYW primarily hearing about PrEP for the first time at the clinic where the POWER study took place, while seeking contraception or treatment for an existing STI.

> *"Because I did the research about that [efficacy], then they [staff at the clinic] told me it's true that the pill works, so I feel safe that I'm taking the pill which is making myself to be safe from men that are taking advantage of young women". (IDI, 20-year-old, Johannesburg)*

AGYW were generally enthusiastic to learn about PrEP and viewed it as something that young women have been waiting for.

> *"[PrEP is] the breakthrough that we have been waiting for especially as a youth" (IDI, 22-year-old, Johannesburg).*

AGYW's perception of HIV vulnerability

AGYW shared that knowledge of their vulnerability to HIV acquisition through a current sexual partner or sexual violence in their communities motivated them to consider PrEP uptake.

> *"Well, every girl is at risk of HIV and every day because we live in a horrible world, where we are raped, we are exposed to a lot of bad stuff, so I felt PrEP was just the answer you know, just prevent a disease and not to worry so much about it." (IDI, 20-year-old, Johannesburg).*

AGYW described their potential HIV exposure as due to their partners' multiple concurrent partnerships, unknown HIV status, and low condom use (either to avoid hostile condom negotiations or to please a long-term partner). They also described PrEP as an attractive option for young women when they are susceptible to peer pressure, seduced by older men when under the influence of alcohol, or because they are engaging in transactional sex.

> *"We always want to please our boyfriends or to please friends because of peer pressure. We engage in sex without using condoms. That is why I wanted to know more about PrEP" (IDI, 19-year-old, Cape Town)*

AGYW anticipated that their use of PrEP would provide a welcomed sense of safety, freedom and equalization of gender power in sexual encounters by enabling HIV prevention for AGYW independent from a male partner's consent or cooperation.

Ease of PrEP access and informed decision-making processes

AGYW who initiated PrEP indicated that the ease and convenience of getting PrEP on the same day of their clinic visit and as part of an integrated sexual and reproductive health (SRH) service facilitated uptake. Acceptance of PrEP was further facilitated when AGYW received counseling and comprehensive information, in an easily understandable manner, while being afforded the agency to decide for themselves if PrEP was appropriate for them. Early initiators of PrEP did so without consulting their family or partners. They believed PrEP to be a personal decision and that their sexual health should take precedence over others' opinions. They reported that making this decision for themselves boosted their self-esteem.

> *"It has made me feel proud about myself, because it was my decision to take PrEP...based on my own needs and not other people's [needs] - I saw that PrEP [is] good for me." (IDI, 19-year-old, Cape Town)*

Nevertheless, AGYW shared how important peer support was in generating PrEP interest, including seeing peers using PrEP themselves or noticing the presence and advocacy of other AGYW PrEP users at the clinic.

Stigma and PrEP misconceptions in the community

Stigma and misconceptions among families, peers and communities played a role in AGYW delaying uptake or declining PrEP. This included HIV-related stigma conflating PrEP for prevention and ART for treatment, anecdotes that women who take PrEP are promiscuous, cheating on their partners, or sex workers. These concerns resulted in some young women first establishing approval from family or partners before initiation PrEP during a subsequent return to the clinic.

> *The thing is, after that incident [hearing about PrEP from the clinic] I went to my mother and told her. And she said if I know it will help me, I should take it. Then I decided to come get it [the following day]. (IDI, 16-year-old, Cape Town)*

Conversely, for others, PrEP use was prohibited by sexual partners or family members and so they decided to not initiate.

> *"He [boyfriend] asked me why I should use it. "Don't you trust me?" he asked. "Do you have a side partner?" he continued. Those were the questions asked and I decided not to use it." (IDI, 21-year-old, Kisumu)*

Other concerns or considerations mentioned prior to initiating PrEP were around efficacy and potential side-effects, the burden of daily pill-taking, and duration of PrEP use. Young women indicated that in some instances taking more time to consider PrEP's relevance in their lives and learning more about PrEP's benefits in the media or from peers, convinced them to come back to the clinic and start PrEP.

3.3.2 Early PrEP use (0-3 months)

The early use phase was a period of adjustment for AGYW and included (1) disclosure; (2) seeking social support for PrEP use; and (3) thinking through pill-taking adherence strategies that suit their lifestyles.

Experiences of disclosure and social support

AGYW had a range of opinions and experiences regarding disclosure of their PrEP use to sexual partners, family, friends, and community. The benefits of disclosure after initiating PrEP were described as receiving social support for PrEP use and adherence reminders, which destigmatized taking PrEP in front of others. The primary deterrents and potential harms caused by disclosure included accusations of infidelity by partners; judgments about young women's sexual lives and behavior; or stigma/misconception of PrEP as ART. AGYW practiced selective disclosure, deciding who they felt comfortable disclosing to as well as whose knowledge of their PrEP use would be valuable for their adherence. Young women who avoided disclosure described having to hide pills and take them in secret which made consistent use difficult.

PrEP use was primarily disclosed to family or the people with whom AGYW cohabited. Mothers' support was of particular significance to AGYW and they appreciated when their parents encouraged them to make their own decisions about their health. Social support was described as beneficial to adherence and integrating PrEP into young women's daily routines during early use.

> *"It was supportive like at least there is someone who knows that I am taking them, I am not hiding this thing. Especially if my mother knows, then I am okay. About others and stuff, no, but just as long as my mother [knows]." (IDI, 18-year-old, Johannesburg)*

While AGYW felt that disclosure to family would be beneficial, they had concerns about disclosing PrEP use to their sexual partner(s). The main apprehensions related to disclosure causing conflicts, decreased trust, or potentially causing a breakup of their intimate relationships.

> *"My thoughts were that he [sexual partner] might not understand me and might think that I am sick [have HIV]. So, I was ashamed to tell him." (IDI, 20-year-old, Cape Town)*

Participants stated that this fear of partners' reactions caused young women to hide PrEP use or sometimes led to adjusting pill-taking times based on when they were meeting with a

sexual partner. In some instances, initial negative reactions from family or sexual partners at disclosure changed to acceptance and support when more information about PrEP and AGYW's reasons for use was provided to these significant others.

Early use adherence strategies and fitting PrEP into daily lives

AGYW shared strategies to integrate PrEP into their daily lives including pairing pill-taking with an existing daily activity (such as a television show or a specific meal); setting an alarm; or taking it with other medication such as contraception. A practical early use challenge was discreet PrEP storage, especially if a young woman was avoiding disclosure.

Missing pills at some stage during the PrEP-user journey was the norm and most missed doses were reported as unintentional due to unexpected circumstances or a disruption in their routine. Forgetting pills happened most frequently over weekends when AGYW were out with friends doing social activities, drinking alcohol, or staying over at a sexual partner's place.

> *"Ja, it [missing pills] happened, I had gone to a party [laughs] so I came back very late…I was just drunk and I had brought my friends home. I did not think about it [taking PrEP] that day." (IDI, 24-year-old, Johannesburg)*

3.3.3 Discontinuation

Fifty nine percent of the young women interviewed reported a PrEP interruption or discontinuation within the first 3 months of PrEP use. Reasons for PrEP discontinuation included (1) perceived side-effects and pill-taking burden, or (2) PrEP stigma and disapproval from family and sexual partners.

Perceived side-effects and pill-taking burden led to early discontinuation

Instances of discontinuation early in the PrEP-user journey occurred as a result of perceived side-effects (gastrointestinal, nausea, or headache) or the size of the pill, making swallowing challenging.

"I changed my mind because of the side effects… and the size [of PrEP pill]. My mother and aunt have their medications that they are taking but out of all these medications my PrEP pill was the biggest one... and I didn't feel well even when I was taking it." (IDI, 19-year-old, Cape Town)

Taking a pill daily for prevention was new to AGYW. The cognitive burden of daily pill taking and frequently forgetting doses discouraged continued PrEP use.

"It was difficult for me, because I kept on forgetting [to take PrEP] I am not used in taking pills all the time." (IDI, 20-year-old, Cape Town)

"Sometimes I just forget [to take PrEP], I don't know why… maybe because there will be no pain that will remind me that actually, it's paining now, go and drink these tablets and stuff." (IDI, 18-year-old, Johannesburg)

Stigma and disapproval from family, peers and sexual partners

Young women described how despite initial motivation to use PrEP, they ended up discontinuing when they experienced stigma and a lack of social support.

"The people in my life had the influence that PrEP is not something good, a lot of people. Like my mother because she is also against PrEP. So, as they think that PrEP is not good, I stopped PrEP." (IDI, 17-year-old, Cape Town)

In situations where AGYW experienced stigma from household members, maintaining a PrEP schedule was challenging as they attempted to take PrEP when they had privacy. This led to forgetting pills which was discouraging and sometimes concluded with discontinuation.

"…cause every time I take them [PrEP pills], my roommate used to ask me, 'why are you always taking pills', she didn't know anything about PrEP…And sometimes you will be embarrassed that maybe she would think that I am HIV positive or something. So that's why I decided that hey let me rather stop taking them [PrEP pills]." (IDI, 19-year-old, Johannesburg)

The importance of relationship preservation for AGYW was also described by young women in the FGDs, reflecting how HIV prevention decisions may be based on their anticipation of partners' negative responses to PrEP (disapproval with or without the threat of violence).

> *"Anyango stays with her husband who loves violence of which should he realize Anyango is using PrEP she will be badly beaten that day. He will accuse her of infidelity even though he is the one. So, she would not want the husband to know though it will be good if someone taught him about PrEP but Anyango herself can't." (FGD, Kisumu)*

Similarly, in South Africa a FGD participant indicated that Lebo may discontinue PrEP based on *"…pressure probably from her partner. He might say, 'if you are continuing [to take PrEP] sisi (sister), then I request that we break up then". (FGD, Cape Town)*

3.3.4 PrEP persistence

Persistence was a phase in the PrEP-user journey that included creating personal and social strategies to remain motivated in taking pills consistently over a prolonged period of time, while anticipating and adapting to changes in one's daily routine.

Sustaining motivation facilitates PrEP persistence

Sustained motivation for PrEP use was linked to AGYW continuously assessing and acknowledging HIV risk in their lives, along with forming clear intentions or reasons for PrEP use. AGYW shared how taking PrEP consistently allowed them to feel safe and more empowered, causing positive shifts in their relationship dynamics and sexual behaviour. Persistent PrEP users described increased comfort during sex without condoms and greater relational agency and communication with partners about HIV and dynamics around sex.

> *"I feel relaxed because that risk of getting HIV I have controlled." (IDI, 19-year-old, Kisumu)*

"I just feel PrEP is really helping, so I am not afraid [of HIV]… It has made me feel so comfortable [with my partner]". (IDI, 17-year-old, Kisumu)

Young women, however, shared that taking PrEP could feel like a big responsibility and at times they needed to motivate themselves to overcome the burden of daily pill-taking. Pill-taking fatigue was lessened for AGYW through either practicing prevention-effective adherence or motivating themselves to continue PrEP use during their current season of perceived high HIV risk, knowing it is impermanent.

Barriers to persistence

Convenience of accessing clinics for PrEP refills facilitated AGYW's continued engagement in SRH services, including PrEP persistence, while access barriers were frequently listed as reasons for PrEP interruptions. Young women shared how other obligations such as school and work often made it difficult to schedule their PrEP refill visits, leading to interrupted PrEP use and sometimes discontinuation. Participants in the FGD added that rumors about accessing PrEP from a local clinic also acted as a barrier to persistence.

"People will think that she is sick [has HIV] if she keeps going to the clinic, to fetch treatment [PrEP perceived as ARV's]." (FGD, Cape Town)

Non-persistors also seemed more affected by rumours and PrEP misconceptions and subsequently expressed doubts about PrEP's efficacy. Paradoxically, this group of young women also mentioned feeling protected despite frequently missing PrEP doses. Conversely, AGYW who persisted shared the positive emotions (e.g. feeling empowered, confident and safe in sexual encounters) they experienced while adhering to daily PrEP taking, and negative emotions (e.g. guilt and stress over HIV exposure) resulting from skipping pills.

Non-persistors particularly encouraged more peer advocacy and suggested that more young women should use PrEP openly to de-stigmatize PrEP and build peer support for use. AGYW who struggled with persistence also expressed their preferences for smaller pills or a more discreet option like an injection that would solve a few of their challenges including not

requiring home storage, avoiding issues around potential disclosure (no pills for partners or family to find), and less frequent clinic visits.

3.3.5 PrEP pause and restart

Young women described pauses of varying length in PrEP use (1-9 months) as either intentional or unintentional.

Intentional PrEP pauses

AGYW decided to take a PrEP pause 1) during phases of perceived lower risk of HIV; 2) when practicing prevention-effective adherence in their sexual relationships; 3) to avoid unintentional PrEP disclosure; or 4) during times when PrEP use was perceived as difficult to fit into their daily lives (e.g. seasonal travelling). Whereas five participants were specifically interviewed due to their experience of restarting PrEP, many more spoke about pausing and restarting PrEP and their views were included in this section too.

AGYW shared that they perceived lower HIV risk and took a PrEP pause during relationship status changes (i.e., going through a breakup, not dating anyone, or when their partner is out of town) or changes in relationship dynamics, such as starting to trust a long-term partner or using condoms more consistently. AGYW also shared about practicing prevention-effective adherence when a sexual partner worked in another area.

> *"You take it, after seven days that is when you can have sex with someone. This is because my partner is from [name of area] and whenever he is away, I can relax a bit [can pause PrEP use]. I will resume using it when he is coming back. He can tell me that he will come on such a day then it is up to me to plan myself for his coming." (IDI, 17-year-old, Kisumu)*

PrEP pauses were also common when AGYW traveled to visit family or their rural homes as a means to avoid unintentional disclosure and stigma:

"Sometimes maybe you visit [rural] home and then you don't take them because you are afraid that there is a person who will see that you are taking the pills…you will find that they will spread the news wide, they will say you are sick [have HIV], all that stuff. You will no longer be appealing." (IDI, 25-year-old, Johannesburg)

Seasonal PrEP pauses were discussed by young women in the FGDs too. Specifically, AGYW in South Africa indicated that they would like to pause PrEP use over the December holidays, as this was a time of travel and partying, making it difficult to fit oral PrEP into their lifestyles.

"Maybe in December, because it is the festive season. We have those 'big days'… she will forget it [to take PrEP], she is busy. During the festive season babe… it [taking PrEP] is just making things difficult for yourself. She won't even be able to carry that thing [pillbox] of hers" (FGD, Cape Town).

However, other young women in the same FGD group challenged seasonal PrEP pauses indicating that these were also seasons of heightened HIV risk and rather recommended a change in pill taking schedule.

"I think the schedule [of when she takes PrEP pills] would change. I would take it in the morning, because in the morning you are home, things [parties/events] start late. She must not take it [the PrEP pause], because she is not taking a break from sex." (FGD, Cape Town).

Unintentional PrEP pauses

AGYW experienced unintentional pauses primarily due to PrEP access barriers when traveling out of town; experiencing schedule conflicts (school or work commitments) with their PrEP refill visits; or when they lacked transport to a distant PrEP clinic.

"I was in the village and couldn't access it. I came back, and it took two months and a half [that she was off PrEP/away in the village). I told my friend that we need to go back [to clinic] for the drugs, and that is how we came for refills." (IDI, 24-year-old, Kisumu)

AGYW had various perspectives on protection from HIV acquisition and PrEP efficacy during PrEP pauses. Participants typically did not seek out counseling before a PrEP pause and made their own assessments regarding prevention-effective adherence.

Restarting PrEP

PrEP restarts after a pause occurred when AGYW: 1) reconciled with a past sexual partner; 2) started a new relationship; 3) restored access to PrEP services; or 4) experienced a heightened sense of HIV vulnerability. These feelings of increased HIV vulnerability were described when AGYW witnessed a family member or friend testing HIV positive or due to a sexual partner's behavior (e.g. instances of suspected multiple concurrent partnerships).

> *"I paused [PrEP use] because my sexual partner agreed that we will be using condoms, but after sometimes, he refused [condom use] and I started again to use PrEP." (FGD, Kisumu)*

AGYW, however, also described how despite understanding and practicing prevention-effective adherence, they sometimes experienced difficulties in forecasting sex, a drawback of this strategy. Young women in the FGDs agreed that Lebo/Ayango should return to the clinic for counseling on how to maintain daily PrEP use, or safely practice prevention-effective adherence as well as get tested for HIV and STI's before resuming PrEP use.

3.3.6 The role of counseling and healthcare providers in AGYW's PrEP-user journey

AGYW emphasized the importance of adolescent-friendly, non-judgmental, and supportive counselling at different stages during the PrEP-user journey. They highlighted that receiving clear and comprehensive information about PrEP, feeling supported by clinic staff, and knowing what to expect (including side effects) when taking PrEP were important and alleviated the initial concerns of AGYW. Young women shared that being able to ask questions about their SRH needs and intimate relationships to counsellors helped them prepare for potential use challenges and fitting PrEP into their daily lives.

"It was great because they [clinic staff] clearly explained to me, and I was very clear about what this pill is and for what, and how it works. So, I was interested [in taking PrEP] because I understood what it was all about." (IDI, 19-year-old, Cape Town)

Young women also appreciated the short waiting times and discretion when PrEP was dispensed at the study clinics.

"Coming to the clinic is not a big deal…it wasn't going to consume my time a lot. The other thing that motivated me was that when I went to the pharmacy, the tablets were put in an envelope. That already no one can know what I am picking from the pharmacy." (IDI, 23-year-old, Kisumu)

During the early use phase, AGYW could discuss with counsellors their decisions regarding disclosure, PrEP storage, and adherence strategies. Counselling and support at the clinic also helped AGYW to navigate PrEP stigma and misconceptions circulating in the community. AGYW also reported feeling supported by clinic staff to persist with PrEP when they felt demotivated by family, peers or sexual partners, and counselling promoted a focus on prioritizing AGYW's own health needs.

"She [counsellor] gave me courage [to take PrEP] and made me realize that I'm doing this for myself and not anyone else." (IDI, 24-year-old, Johannesburg)

Young women who experienced side-effects after starting PrEP reported it to the clinic staff who provided reassurance that these are transient, and prescribed medications and advice to alleviate the symptoms of early PrEP use. Counselling about potential side effects at the time of PrEP uptake reassured young women that their bodies would adapt, which encouraged them to continue PrEP use.

During the PrEP early use and persistence phases counseling was focused on encouraging young women to continue taking PrEP despite missed doses; thinking through adherence strategies when traveling or when out with friends or sexual partners; as well as how to deal with a lack of social support.

"Yes, I told them [about missing doses]. They said there is no problem but next time I have to take all my pills. I didn't feel bad because… she just said we are happy that you forgot once [to take PrEP] but next time we will be happy for you to take all of them [PrEP pills]." (IDI, 23-year-old, Johannesburg)

Young women in the FGDs viewed continued counselling and support as important for helping AGYW deal with adherence challenges and navigate PrEP restarts after a pause.

3.4 Discussion

This qualitative study highlighted enablers and barriers for AGYW in SSA during their PrEP-user journey, from awareness and initiation to discontinuation or persistence. Daily oral PrEP use was shown to be challenging for AGYW due to individual (side-effects), relational (prioritizing relationship preservation), social (stigma, lack of support, and difficulty fitting pill-taking into lifestyle), and structural factors (access). We found that AGYW valued informed decision-making regarding PrEP uptake and prevention-effective adherence. PrEP interruptions (voluntarily or involuntarily) were part of the PrEP-user journey and AGYW exercised their judgment to decide about when to use, pause or discontinue PrEP. Disclosure, social support, non-judgmental adolescent-friendly counseling, and convenient access to PrEP were key to persistence.

PrEP uptake was facilitated through AGYW's acknowledgement of HIV vulnerability in their lives and the benefits of being in control of HIV prevention in their relationships strongly influenced uptake and initiation. In addition, uptake was high when PrEP was offered as part of an integrated SRH service, but hampered by low awareness, stigma and PrEP misconceptions in the community. HIV prevention is embedded in social and interpersonal contexts [29, 105, 106] and AGYW in this study were found on a continuum from prioritizing their personal sexual health versus prioritizing others' opinions [107]. This was evident during PrEP uptake where some AGYW embraced PrEP as a user-controlled HIV prevention method, while others were compelled to negotiate social acceptance through establishing PrEP use

support from family or sexual partners before making this decision regarding their own sexual health. Research shows that AGYW's agency, the sense of being in control of one's own decisions, is highest in environments of opportunity (i.e., PrEP access, information and social support) and choice, but reduced when someone believes that their voluntary action will cause negative outcomes (to them or their relationships) [108]. We found that when strong personal agency was present in AGYW it positively affected the PrEP journey trajectory from uptake to persistence.

Early PrEP use (0-3 months) was an important period in the PrEP-user journey for establishing pill-taking strategies and seeking social support. Supportive and non-judgmental counseling was needed as a credible source for PrEP information at uptake and assisted AGYW during the early use phase to think through disclosure and dealing with potential early side effects. Unfortunately, young women who experienced a lack of (perceived or actual) social support or PrEP-related stigma, avoided disclosure and subsequently struggled with persistence [96, 109]. Similarly, AGYW whose sexual relationships were threatened by their PrEP use had more challenges with persistence, as reported in other research with female-initiated methods [41, 110-112]. In addition, AGYW need long-acting, discreet HIV prevention methods to reduce some of the barriers that daily pill-taking pose such as unintentional disclosure, cognitive and emotional burden, storage, and interference of competing life priorities such as having to fit the product into travels or weekend social life [113, 114].

Persistence on PrEP was facilitated by AGYW's continuous reevaluation of their HIV risk throughout the PrEP-user journey; family and peer support for PrEP use and reducing pill-taking fatigue through prevention-effective adherence. However, similar to previous research, for some AGYW, changes in relationship dynamics impacted their perception of HIV risk over time. Furthermore, the inability to accurately forecast sex complicated the practice of prevention-effective adherence [41, 107, 115, 116]. In this study, convenient PrEP access within an integrated SRH, adolescent-friendly service supported both PrEP pauses and sometimes discontinuation. This underscores other PrEP demonstration studies which suggest that improvement in PrEP access is critical for AGYW's PrEP journey [45, 117-119]. PrEP use interruptions (both intentional and unintentional PrEP pauses) were also observed when young women had challenges fitting PrEP into their daily lives or when attempting to

avoid unintentional PrEP disclosure to family or sexual partners [106, 120]. While PrEP discontinuation was often a result of perceived initial side effects, other factors like PrEP stigma, pill-taking burden, or relationship preservation also took precedence over AGYW's desire for HIV prevention. This highlights the importance of approaching biomedical prevention as a strategy that must fit into users' lives (and not the inverse). Research is needed to better understand pharmacological correlates of protection in AGYW as it has been established for men who have sex with men and transgender women [121-123]. If more forgiveness in oral PrEP adherence is demonstrated, this in turn may increase AGYW's options and allow for pill-taking variations, for those of whom daily dosing is not working.

Findings from this study indicated that more work on counseling AGYW regarding prevention-effective adherence, PrEP pauses, restarts and persistence is necessary. We suggest that healthcare providers accept "seasons of risk" and normalize PrEP interruptions without shaming AGYW, create adherence and HIV protection feedback opportunities for AGYW, and create an environment where young women feel comfortable sharing the relational and social conditions related to their PrEP use or interruptions. The value young women placed on informed decision-making regarding PrEP uptake, pauses, and restarts should guide approaches to PrEP implementation. Under these conditions, AGYW can increase personal agency and effective PrEP use [124, 125].

Our study had several limitations: it was qualitative and therefore inference regarding these findings cannot be applied outside of the study sample of AGYW and areas (urban and peri-urban areas in South Africa and Kenya). Our sample did not include participants who discontinued very early (before the month one clinic visit) and therefore our findings cannot be generalized to less engaged POWER study participants. The study, however, had a sizeable sample of 137 young women and triangulation was applied by gathering information from different data sources and data collection methods (IDIs and FGDs) in order to build a comprehensive understanding of AGYW's PrEP-user journey [126]. Social desirability might be a factor in this study since participants knew that PrEP adherence was desired and therefore might have exaggerated their interest and commitment to PrEP use. Additionally, our qualitative findings should be considered in combination with the quantitative results of this study, which revealed high initiation with modest levels of persistence [78].

In summary, this study characterizes the enablers and barriers at each of the key moments in AGYW's PrEP-user journey. We found that AGYW's ability to exercise decisions regarding initiation and persistence with oral PrEP required convenient and integrated access to PrEP; clear, understandable, and non-judgmental education, as well as personal and relational agency. These in turn helped AGYW carry out their choice to achieve the desired well-being outcome of feeling in control and safe from HIV infection. Young women desire comprehensive information on HIV prevention, and PrEP providers need to be aware of AGYW's developing self-identity within a social context with limited support for their sexual health decisions. Our findings highlight that AGYW's desire HIV prevention, but their PrEP-user journey is constrained by limited PrEP biomedical options (currently only daily oral PrEP) and service delivery models available to this population in SSA.

4 Association of sexual relationship power with PrEP persistence and other sexual health outcomes among adolescent and young women in Kenya and South Africa

Paper 2

Rousseau E, Wu L, Heffron R, Baeten JM, Celum CL, Travill D, Delany-Moretlwe S, Bekker LG, Bukusi E, Omollo V, van der Straten A, Morton JF, O'Malley G, Haberer JE, Johnson R, Roberts ST. Association of sexual relationship power with PrEP persistence and other sexual health outcomes among adolescent and young women in Kenya and South Africa. Frontiers in Reproductive Health. 2023 May 30;5:1073103.

Contribution to the thesis and novelty

This paper contributes to the second objective of the PhD, which is to investigate associations between sexual relationship power and AGYW's PrEP use. This objective aimed to investigate quantitatively the narratives from early PrEP trials that called attention to AGYW's intimate relationship dynamics and its influence on PrEP use. The paper's novelty lies in its use of the sexual relationship power scale to determine its influence on AGYW's PrEP persistence. At the outset my assumption was that the AGYW with higher sexual relationship power (and therefore greater control over their health behaviour and outcomes) will have higher PrEP persistence at 1 month and 6 months after PrEP initiation. However, as the study unfolded, I found that sexual relationship power was not associated with PrEP persistence and my conclusion was that persistent PrEP use is influenced by more than relational agency only. These results along with the findings from paper 1 motivated me to investigate the barriers and facilitators to AGYW's PrEP use beyond the role of intimate relationships and individual agency, to also include the role of PrEP access (as seen in papers 3 and 4).

Contribution of candidate

I was the lead author, conceptualized the study and analysis, and interpreted the data. All the co-authors critically reviewed the manuscript.

Abstract

Introduction: Gendered power inequalities impact adolescent girls' and young women's (AGYW) sexual and reproductive health (SRH) outcomes. We investigated the influence of sexual relationship power on AGYW's SRH outcomes, including HIV pre-exposure prophylaxis (PrEP) persistence.

Methods: The POWER study in Kisumu, Kenya, and Cape Town and Johannesburg, South Africa provided PrEP to 2550 AGYW (aged 16-25). AGYW's perceived power in their primary sexual relationship was measured among the first 596 participants enrolled using the Sexual Relationship Power Scale's (SRPS) relationship control sub-scale. Multivariable regression was used to test for 1) key sociodemographic and relationship characteristics associated with relationship power; and 2) the association of relationship power with SRH outcomes including PrEP persistence.

Results and Discussion: In this cohort, the mean SRPS score was 2.56 (0.49), 542 (90.9%) initiated PrEP; 192 (35.4%) persisted with PrEP at one month of which 46 (24.0% of 192) persisted at six months. SRPS were significantly lower among AGYW who cohabited with their sex partner (-0.14, 95% CI: -0.24 to- 0.04, p=0.01), or had ≥1 sex partner (-0.10, 95% CI: -0.19 to -0.00, p=0.05). AGYW with lower SRPS were more likely to not know their partner's HIV status (aOR 2.05, 95% CI: 1.27 to 3.33, p<0.01), but SRPS was not associated with PrEP persistence, STI infection, condom, or hormonal contraception use.

Conclusion: AGYW's reasons for initiating PrEP and reasons for continuously using PrEP may be different. While low relationship power was associated with perceived HIV vulnerability, AGYW's PrEP persistence may be influenced by more than relationship power.

4.1 Introduction

Gendered power inequalities impact young women's sexual and reproductive health (SRH) behaviours and their access to and use of preventative health interventions [127, 128]. Within intimate relationships, these power inequalities transpire through a male partner's

controlling behaviours over decisions regarding safe sex, timing of sex, and sexual consent [129]. In previous studies of African adolescent girls and young women (AGYW), low sexual relationship power has been associated with inconsistent condom use, lower contraceptive use, higher rates of pregnancy, physical and sexual violence, and acquisition of HIV and other sexually transmitted infections (STI) [13, 19, 128-133].

In sub-Sahara Africa (SSA), AGYW are disproportionately affected by sexual coercion, reproductive interference, and HIV, with this population experiencing an estimated 1000 new HIV infections daily [134, 135]. Relationship-level factors not only contribute to AGYW's susceptibility to HIV but also hinder them from adopting HIV prevention methods that need a high level of agency or influence within one's relationship [22, 41, 136]. Recent HIV prevention research has focused on the development of discreet, female-controlled methods. Oral PrEP (pre-exposure prophylaxis), when taken daily, provides highly effective HIV prevention without dependence on a sexual partner [93]. However, narratives from SRH and PrEP demonstration projects indicate that even though PrEP is user-controlled, AGYW often desire to disclose use and value their sexual partners' approval of PrEP [95, 137, 138]. This influences PrEP uptake [107, 125], while the fear of intimate partner violence (IPV) negatively influences PrEP persistence (continued daily adherence) [99, 117, 139]. A few studies in SSA have explored the influence of relationship power on SRH outcomes with mixed evidence [129]. The impact of relationship power on AGYW's PrEP persistence has not been evaluated in previous research and understanding the influence of relationship power may be important for developing strategies to support PrEP persistence in AGYW with continued HIV risk.

The POWER (Prevention Options for Women Evaluation Research) study in Kenya and South Africa offered PrEP to AGYW as part of integrated SRH services and evaluated PrEP uptake and persistence [78]. In this manuscript, we describe perceived sexual relationship power in the POWER study AGYW cohort and the key sociodemographic and relationship characteristics associated with relationship power. Secondly, we investigate the influence of relationship power on AGYW's PrEP persistence and other sexual health outcomes, including contraception use, condom use, knowledge of partner HIV status, and the presence of a curable STI.

4.2 Methods

Research setting and study participants

Between 2017 and 2019, 2550 HIV-uninfected AGYW (16-25 years) enrolled in the POWER study across four sites – two family planning clinics in Kisumu, Kenya; an adolescent-friendly clinic in Johannesburg (ages 18-25 only), and a mobile clinic in Cape Town, South Africa. Detailed study procedures have been described [78]. Eligible participants were HIV-negative, had a primary sex partner, and reported vaginal sex in the past three months. Follow-up occurred one month after PrEP initiation and then quarterly thereafter for up to 36 months.

Measurements

Demographic data on age, relationship status, partner cohabitation, number of sex partners, and number of children were assessed cross-sectionally at the enrolment visit. HIV vulnerability and SRH outcomes were assessed including participants' self-reported knowledge of partner HIV status, inconsistent condom use, hormonal contraceptive use, and presence of STI. Presence of a curable STI infection was defined as a positive GeneXpert urine nucleic acid amplification test result for *Chlamydia Trachomatis* (CT) and/or *Neisseria Gonorrhoea* (NG). Hormonal contraceptive (oral, injectable, or implant) use was categorized as either already using, wanting to start hormonal contraception, or neither on contraception nor wanting to start. Inconsistent condom use was defined as women self-reporting that they used condoms sometimes or never (versus always) in the previous three months. PrEP persistence was assessed among women who initiated PrEP, with non-persistence defined in the same manner as in the POWER primary analyses: ≥15 days gap in PrEP availability for daily dosing as per pharmacy records [78].

AGYW's perceived power in their primary sexual relationship was measured with the sexual relationship power scale (SRPS), widely used in HIV and reproductive health research [127, 140]. The SRPS draws from the Theory of Gender and Power and the Social Exchange Theory which defines power as the amount of control one person has over decision-making in the relationship and the amount of resistance in one partner that can potentially be overcome by the other [85]. The 15-item SRPS relationship control sub-scale was administered at enrolment to a convenience sample of the first approximately 150 participants at each site

(n=600) as part of an interviewer-administered survey. The subscale measured constructs of relationship control including physical violence, safe sex negotiation, relationship satisfaction, and relationship decision-making power on a 4-point Likert scale (1 = strongly agree to 4 = strongly disagree), with higher scores indicating more equal relationships [85]. Participants with more than one sex partner were asked to respond based on their relationship with their primary partner.

Analysis

Descriptive statistics were generated for women's demographics, behavioural characteristics, PrEP initiation, and persistence (at months one and six follow-up visits), and other SRH outcomes. The mean SRPS score for each young woman was calculated (possible range 1 to 4) and categorized by splitting the scale into tertiles that we labelled as lower, middle, and higher relationship power, following practices in the original paper and subsequent applications [85, 140-142]. Linear regression models were used to assess the association between each background characteristic and continuous SRPS scores at baseline. A multivariable model included age *a priori* plus all variables significant at the $p<0.1$ level in the bivariate analyses except for marital status, which was collinear with cohabitation. All subsequent analyses used an alpha of 0.05 to assess statistical significance.

To assess the association between SRPS score tertiles and PrEP and SRH outcomes, we used logistic regression models for binary outcomes and multinomial logistic regression models for the 3-level hormonal contraceptive use outcome. Due to low retention rates during follow-up and subsequent missing data for questionnaires and lab tests [78], analysis of SRH outcomes was conducted cross-sectionally using baseline data. The analysis of PrEP persistence was conducted prospectively with missed follow-up visits inherently indicating missed refills. Multivariable models adjusted for site and age *a priori* plus partner cohabitation based on the results of the analysis of sexual relationship power predictors. Odds ratios (OR) are presented with 95% confidence intervals (95% CI). De-identified data was captured in DFcollect (DF/Net Research Inc.) and imported into SAS v.9.4 (SAS Institute Inc.) for cleaning. R version 1.4.2 was used for all analyses. Internal consistency of the SRPS was calculated at 0.85 using Cronbach's alpha.

Ethics statement

The research was approved by the human research ethics committees of the University of Washington, University of Cape Town, Kenya Medical Research Institute, and the University of Witwatersrand. All participants provided written informed consent. Parental consent was waived for 16- and 17-year-old participants in Cape Town and Kenya, while participation at the Johannesburg site was limited to adults ages 18-25.

4.3 Results

Participant demographic and behavioural characteristics

A total of 599 of AGYW aged 16-25 years completed the SRPS questionnaire at enrolment and 596 were included in this analysis (3 were excluded as they did not have a primary sex partner). Table 7 presents participant baseline characteristics across the three implementation sites. The participants had a median age of 21 years, 78.7% were single with a partner, 20.5% were living with their partner, and 41.1% had a child.

At enrolment, 66.7% of participants did not know their partner's HIV status, 86.0% reported inconsistent condom use for the preceding three months, and 30.7% had an STI (CT/NG). Over one-third (37.8%) were on hormonal contraceptives and 23.1% wanted to start at that visit, while 39.1% were not interested in being on contraception. PrEP was initiated by 542 (90.9%) of AGYW at some point during their study participation, 192 (35.4% of 542) received a refill at one month, and 46 (24.0% of 192) persisted and obtained PrEP refills through six months of follow-up. The characteristics of participants in this analysis sample were similar to the overall POWER study cohort (N=2550).

Table 7. Participant background characteristics and descriptive SRH outcomes

	Overall	Cape Town	Johannesburg	Kisumu
Total number of participants	596	146 (24.5%)	150 (25.2%)	300 (50.3%)
Background characteristics				
Age (continuous), median (IQR)	21 (19-22)	20 (18-22)	21 (19-22)	21 (19-23)
	n (%)	*n (%)*	*n (%)*	*n (%)*
Age (categorical)				
16-17 years	48 (8.1%)	29 (19.9%)	0 (0.0%)*	19 (6.3%)
18-21 years	315 (52.8%)	70 (47.9%)	95 (63.3%)	150 (50.0%)
22-25 years	233 (39.1%)	47 (32.2%)	55 (36.7%)	131 (43.7%)

Marital Status				
Single, no partner	14 (2.3%)	5 (3.4%)	5 (3.3%)	4 (1.3%)
Single, with partner	469 (78.7%)	139 (95.2%)	141 (94.0%)	189 (63.0%)
Married, husband has one wife	103 (17.3%)	2 (1.4%)	4 (2.7%)	97 (32.3%)
Other	10 (1.7%)	0 (0.0%)	0 (0.0%)	10 (3.3%)
Lives with sexual partner				
No	470 (79.4%)	141 (97.9%)	137 (91.3%)	192 (64.4%)
Yes	122 (20.6%)	3 (2.1%)	13 (8.7%)	106 (35.6%)
>1 sex partner				
No	491 (82.8%)	131 (89.7%)	137 (91.9%)	223 (74.8%)
Yes	102 (17.2%)	15 (10.3%)	12 (8.1%)	75 (25.2%)
Number of living children				
0	349 (58.7%)	109 (75.7%)	100 (66.7%)	140 (46.7%)
>=1	245 (41.3%)	35 (24.3%)	50 (33.3%)	160 (53.3%)
SRH outcomes at enrollment				
Partner HIV status				
Unknown HIV status	397 (66.7%)	111 (76.0%)	77 (51.3%)	209 (70.0%)
Known, partner HIV positive	27 (4.6%)	8 (5.5%)	4 (2.7%)	15 (5.0%)
Known, partner HIV negative	171 (28.7%)	27 (18.5%)	69 (46.0%)	75 (25.0%)
Inconsistent condom use				
No (always use condoms)	83 (14.0%)	29 (19.9%)	25 (16.7%)	29 (9.8%)
Yes (sometimes/never use condoms)	509 (86.0%)	125 (80.1%)	125 (83.3%)	267 (90.2%)
STI (GC/NG) infection				
Negative	364 (69.3%)	72 (62.6%)	73 (64.6%)	219 (73.2%)
Positive	163 (30.7%)	43 (37.4%)	40 (35.4%)	80 (26.8%)
Hormonal Contraceptive				
On contraceptive	221 (37.8%)	65 (45.1%)	60 (42.3%)	96 (32.1%)
Wants contraceptive	135 (23.1%)	57 (39.6%)	44 (31.0%)	34 (11.4%)
Neither	229 (39.1%)	22 (15.3%)	38 (26.7%)	169 (56.5%)
SRH outcomes assessed during follow-up				
PrEP initiated ever				
No	54 (9.1%)	3 (2.1%)	5 (3.3%)	46 (15.3%)
Yes	542 (90.9%)	143 (97.9%)	145 (96.7%)	254 (84.7%)
PrEP persistent through 1 month				
No	350 (64.6%)	102 (71.3%)	84 (57.9%)	164 (64.6%)
Yes	192 (35.4%)	41 (28.7%)	61 (42.1%)	90 (35.4%)
PrEP persistent through 6 months**				
No	146 (76.0%)	37 (90.2%)	31 (50.8%)	78 (86.7%)
Yes	46 (24.0%)	4 (9.8%)	30 (49.2%)	12 (13.3%)

*Johannesburg only enrolled AGYW between the ages of 18-25

**PrEP persistence at 6 months was calculated including only participants who persisted through 1 month of PrEP use

Participants' sexual relationship power

This cohort had a mean SRPS score of 2.56 (0.49). SRPS score tertile ranges were 1.06-2.38 for the lower third, 2.38-2.75 for the middle third, and 2.75-3.69 for the higher third. Responses

to individual questions indicated that male partners had a substantial level of control in the relationships (Table 8): 60.4% agreed that their partners might be having sex with someone else, 33.6% believed that their partner had more say about important decisions, 28.9% indicated that their partner would get angry and 23.2% violent if asked to use a condom, 67.5% say that her partner always wants to know where she is, 35% tell her whom she can spend time with, 38.6% say that in disagreements their partner gets his way most times, and 18.6% reported that they felt trapped or stuck in their relationships. The mean score was significantly lower among participants from Kisumu (mean = 2.35) than from Cape Town (mean = 2.73) or Johannesburg (mean = 2.81, p<0.01).

Table 8. Sexual Relationship Power: Percentage of women who agree/strongly agree with individual items in the SRPS and the mean scale scores

	Total	Cape Town	Johannesburg	Kisumu	*p*
Total number of participants	596	146	150	300	
SRPS item = Strongly agree/Agree n (%)	*n (%)*	*n (%)*	*n (%)*	*n (%)*	
If I asked my partner to use a condom, he would get violent.	138 (23.2%)	12 (8.2%)	20 (13.3%)	106 (35.3%)	<0.01
If I asked my partner to use a condom, he would get angry.	172 (28.9%)	24 (16.4%)	27 (18.0%)	121 (40.3%)	<0.01
Most of the time, we do what my partner wants to do.	222 (37.2%)	31 (21.2%)	39 (26.0%)	152 (50.8%)	<0.01
My partner will not let me wear certain things.	225 (37.8%)	50 (34.5%)	45 (30.0%)	130 (43.5%)	0.01
When my partner and I are together, I am pretty quiet.	124 (20.8%)	32 (21.9%)	19 (12.7%)	73 (24.3%)	0.01
My partner has more say than I do about important decision that affect us.	200 (33.6%)	28 (19.3%)	31 (20.7%)	141 (47.3%)	<0.01
My partner tells me who I can spend time with.	210 (35.2%)	32 (22.1%)	33 (22.1%)	145 (48.5%)	<0.01
If I asked my partner to use a condom, he would think I am having sex with other people.	218 (36.6%)	50 (34.2%)	34 (22.7%)	134 (44.7%)	<0.01
I feel trapped or stuck in our relationship.	111 (18.6%)	17 (11.7%)	23 (15.3%)	71 (23.7%)	<0.01
My partner does what he wants, even if I do not want him tc	206 (34.6%)	28 (19.3%)	44 (29.3%)	134 (44.7%)	<0.01
I am more committed to our relationship than my partner is	179 (30.0%)	46 (31.7%)	56 (37.3%)	77 (25.7%)	0.03
When my partner and I disagree, he gets his way most of the	230 (38.6%)	42 (29.0%)	39 (26.2%)	149 (49.7%)	<0.01
My partner gets more out of our relationship than I do.	138 (23.2%)	30 (20.7%)	29 (19.3%)	79 (26.3%)	0.18
My partner always wants to know where I am.	402 (67.4%)	96 (66.2%)	84 (56.0%)	222 (74.0%)	<0.01
My partner might be having sex with someone else.	360 (60.4%)	92 (63.4%)	65 (43.3%)	203 (67.7%)	<0.01
SRPS Score (mean (SD))	***2.56 (0.49)***	***2.73 (0.41)***	***2.81 (0.48)***	***2.35 (0.44)***	***<0.01***

Demographic factors associated with sexual relationship power

In the univariable analysis, demographic factors significantly associated with lower sexual relationship power among AGYW included age, being from Kisumu, living with her sex partner, having children, and having more than one sex partner (Table 9). Study site (aOR -0.31, 95% CI: -0.40 to 0.21,p<0.01) and partner cohabitation (aOR -0.14, 95% CI: -0.24 to -

0.04, p<0.01) remained significantly associated with lower relationship power in the multivariable analysis.

Table 9. Demographic factors associated with sexual relationship power: univariable and multivariable analysis

		Univariable Regression		Multivariable Regression	
Factors	Mean SRPS (SD)	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value
Age, continuous	2.56 (0.49)	-0.02 (-0.03 to 0.01)	0.07	0.01 (-0.01 to 0.02)	0.69
Study site					
Cape Town	2.73 (0.41)				
Johannesburg	2.81 (0.48)	0.09 (-0.01 to 0.19)	0.09	0.08 (-0.02 to 0.18)	0.11
Kisumu	2.35 (0.44)	-0.38 (-0.46 to -0.29)	<0.01	-0.31 (-0.40 to 0.21)	<0.01
Marital Status*					
Single, no partner	2.61 (0.52)				
Single, with partner	2.64 (0.46)	0.03 (-0.21 to 0.28)	0.80		
Married, husband has one wife	2.25 (0.45)	-0.35 (-0.61 to -0.09)	0.01		
Other	1.93 (0.38)	-0.68 (-1.06 to -0.31)	<0.01		
Lives with sexual partner					
No	2.63 (0.47)				
Yes	2.31 (0.48)	-0.32 (0.42 to -0.23)	<0.01	-0.14 (-0.24 to -0.04)	0.01
Number of living children					
0	2.65 (0.48)				
>=1	2.44 (0.49)	-0.21 (-0.28 to -0.13)	<0.01	-0.07 (-0.15 to 0.01)	0.07
>1 sex partner					
No	2.59 (0.50)				
Yes	2.40 (0.42)	-0.19 (-0.29 to -0.09)	0.05	-0.10 (-0.19 to 0.00)	0.05

*Omitted from multivariable analysis due to collinearity with cohabitation

Relationship power and sexual reproductive health outcomes

Baseline sexual relationship power was not significantly associated with PrEP persistence at one (OR 0.72, 95% CI: 0.41 to 1.11, p=0.13) or six months (OR 0.79, 95% CI: 0.35 to 1.71, p=0.55) of follow-up (Table 10). In the cross-sectional analyses of baseline SRH outcomes, women with lower relationship power had twice the odds of not knowing a partner's HIV status than women with higher relationship power (aOR 2.05, 95% CI: 1.27 to 3.33, p<0.01). Additionally, women with lower relationship power were significantly more likely to report inconsistent condom use during the past three months (OR 1.95, 95% CI: 1.07 to 3.67, p=0.03) in the univariable model, but not in the multivariable model (aOR 1.29, 95% CI: 0.67 to 2.56, p=0.45). Relationship power was not associated with the presence of an STI (GC/NG) (aOR 0.93, 95% CI: 0.56 to 1.33, p=0.77). Compared to women with higher relationship power,

women with lower relationship power were less likely to be on hormonal contraception (OR 0.45, 95% CI: 0.29 to 0.72, p<0.01) or wanting to start hormonal contraception (OR 0.42, 95% CI: 0.25 to 0.72, p<0.01), although this was not significant in the multivariable analysis (aOR 0.65, 95% CI: 0.39 to 1.09, p=0.11).

Table 10. Associations between baseline sexual relationship power and PrEP and SRH outcomes: univariable and multivariable analyses

			Univariable Regression		Multivariable Regression*	
Outcomes	n/N	%	OR (95% CI)	p-value	OR (95% CI)	p-value
Prospective outcomes						
PrEP persistence through 1 month (N=542)						
Higher SRPS	74/184	40.2%	Ref		Ref	
Middle SRPS	62/186	33.3%	0.74 (0.49 to 1.14)	0.17	0.78 (0.50 to 1.22)	0.28
Lower SRPS	56/172	32.6%	0.72 (0.46 to 1.11)	0.13	0.69 (0.42 to 1.11)	0.12
PrEP persistence through 6 months (N=192)						
Higher SRPS	22/74	29.7%	Ref		Ref	
Middle SRPS	10/62	16.1%	0.45 (0.19 to 1.03)	0.07	0.8 (0.30 to 2.05)	0.64
Lower SRPS	14/56	25%	0.79 (0.35 to 1.71)	0.55	1.44 (0.56 to 3.77)	0.45
Cross-sectional outcomes						
Unknown partner HIV status (N=595)						
Higher SRPS	115/199	57.8%	Ref		Ref	
Middle SRPS	136/198	68.7%	1.6 (1.06 to 2.42)	0.02	1.32 (0.85 to 2.05)	0.22
Lower SRPS	146/198	73.7%	2.05 (1.35 to 3.14)	<0.01	2.05 (1.27 to 3.33)	<0.01
Inconsistent condom use (N=592)						
Higher SRPS	166/199	83.4%	Ref		Ref	
Middle SRPS	166/198	83.8%	1.03 (0.61 to 1.76)	0.91	0.91 (0.51 to 1.59)	0.73
Lower SRPS	177/195	90.8%	1.95 (1.07 to 3.67)	0.03	1.29 (0.67 to 2.56)	0.45
STI (GC/NG) infection (N=527)						
Higher SRPS	58/172	33.7%	Ref		Ref	
Middle SRPS	54/168	32.1%	0.93 (0.59 to 1.46)	0.76	1 (0.62 to 1.61)	0.99
Lower SRPS	51/187	27.3%	0.74 (0.47 to 1.16)	0.18	0.93 (0.56 to 1.53)	0.77
Contraceptive Use or Interest** (N=585)						
On contraceptive (vs. not on contraceptive) (N=450)						
Higher SRPS	83/142	58.5%	Ref		Ref	
Middle SRPS	76/149	51.0%	0.74 (0.47 to 1.18)	0.20	0.79 (0.47 to 1.30)	0.35
Lower SRPS	62/159	39.0%	0.45 (0.29 to 0.72)	<0.01	0.65 (0.39 to 1.09)	0.11
Wants contraceptive (vs. not on contraceptive) (N=364)						
Higher SRPS	53/112	47.3%	Ref		Ref	
Middle SRPS	45/118	38.1%	0.69 (0.41 to 1.16)	0.16	0.79 (0.44 to 1.43)	0.43
Lower SRPS	37/134	27.6%	0.42 (0.25 to 0.72)	<0.01	0.9 (0.48 to 1.68)	0.74

*Site, age, and lives with sexual partner were adjusted in multivariable regression

** Contraceptive results based on multinomial model: on contraception or wanting contraception vs. not on contraception

4.4 Discussion

In this PrEP implementation study, the cohort consisted primarily of young women who were single with a partner and showed high oral PrEP initiation, but low persistence. AGYW demonstrated high HIV vulnerability through reports of having a partner of unknown HIV status, inconsistent condom use, and multiple concurrent partnerships, and through the presence of a curable STI (CT/NG) at enrolment, which is compatible with other studies in similar contexts [128, 133, 135, 143, 144]. In this study, we explored the association of sexual relationship power with SRH outcomes and found that lower relationship power was associated with several factors linked to HIV vulnerability, which may have encouraged PrEP uptake, but relationship power did not predict PrEP persistence.

Intimate relationship dynamics are a known driver of PrEP uptake and may have supported PrEP interest in this cohort in which more than 90% initiated PrEP. Previous research in South Africa indicates higher PrEP interest and uptake in younger women in short-term relationships with higher-risk partners [128]. In this cohort, lower relationship power was associated with study site (Kenya), sex partner cohabitation, multiple concurrent relationships, and not knowing a partner's HIV status. Prior research has found that higher commitment relationships, where partners are co-habiting and have children (observed at higher rates in the Kisumu group), are more evident of male dominance, with some or no female partner autonomy [129, 142, 145] and may pose greater risks if partners did not approve of their use of SRH services and HIV prevention methods [117, 140, 145]. In addition, Kenyan women report higher rates of lifetime partner violence and adhere to more traditional and restrictive gender norms than Cape Town and Johannesburg, which lowers relationship power and reproductive health [146, 147]. Furthermore, having more than one sex partner has previously been connected to lower relationship power and higher IPV [148, 149]. In turn, this lower relationship power influences HIV vulnerability in that AGYW with lower relationship power are less likely to discuss or know their partner's HIV status and more likely to use condoms inconsistently with these partners [128]. This cohort had a slightly lower overall mean SRPS score than similar populations in SSA and displayed higher proportions of believing that their partner had other sexual partners and that their partner will get angry or violent when asked to use a condom [129, 148]. Previous research has shown that lower SRP is linked to HIV incidence, which may possibly account for the lower SRPS scores in this cohort of AGYW

who decided that their vulnerability to HIV is so high that PrEP as HIV prevention was sought [19, 129, 140, 148, 149]. Lower SRPS scores may be valuable in identifying AGYW with HIV vulnerability who could benefit from PrEP as an HIV prevention mechanism that is user-controlled and does not rely on a partner's permission. Understanding the role of AGYW's sexual relationship in the adoption of prevention behaviors and integrating support mechanisms for relationship power dynamics in SRH services may be beneficial in demand creation and uptake of PrEP among AGYW in need of prevention methods. In addition, HIV prevention may be further optimized for AGYW with lower relationship power by closing the HIV testing gap with their male partners.

In this cohort of African AGYW, relationship power did not predict baseline STI infection, condom use during the prior three months, or being on or wanting to start hormonal contraception. And sexual relationship power was not associated either positively or negatively with PrEP persistence. Recent research with AGYW PrEP users, including qualitative findings from this study, has shown that PrEP uptake and persistence early in the user journey are influenced by disclosure, social support, and PrEP stigma, all shaped to a degree by relationship dynamics and young women's need for relationship preservation [103, 150, 151]. Longer-term PrEP persistence in AGYW, however, is likely influenced by more factors than only sexual relationship power. Research highlights the role of accessibility of PrEP services, healthcare provider stigma, level of trust in an intimate relationship, pill-taking fatigue and desire for long-acting PrEP, and social support from the people sharing AGYW's living space (primarily family and not a sexual partner in this cohort), which in combination may have overwhelmed any effect of sexual relationship power on persistence [41, 105, 109, 152-154]. Supporting AGYW in effectively using PrEP will likely need a multi-faceted, yet tailored, response from providers of which intimate relationship dynamics will be a component.

This study had several limitations. Firstly, the SRPS questionnaire was only administered to AGYW interested in PrEP; therefore we could not test whether lower relationship power is a barrier to AGYW initiating PrEP, and our estimates of the level of relationship power in this population may not be generalizable to AGYW who are not interested in PrEP. Secondly, the SRPS questionnaire was interviewer-administered and social desirability might have

influenced women to underreport potentially stigmatizing relationship characteristics, including IPV and control in their relationships. Thirdly, AGYW's responses to the SRPS scale were based on their primary partner at baseline, which may be different from their partner at months one and six of PrEP follow-up. Finally, the overall study did not capture information on planned PrEP pauses and continued HIV vulnerability among those who discontinued PrEP; therefore, the practice of prevention-effective adherence (only taking PrEP during periods with actual HIV vulnerability) [82] may have been misinterpreted as lack of persistence in some instances.

To our knowledge, this is the first study to examine the association of sexual relationship power and PrEP persistence among AGYW in SSA. Taken together, these results suggest that AGYW's reasons for initiating PrEP and reasons for continuously using PrEP may be different. While relationship dynamics and their role in HIV vulnerability may influence PrEP uptake, AGYW's PrEP persistence may be influenced by more than relationship power. Identifying and addressing barriers and facilitators for effective PrEP use in AGYW in SSA remains an important research objective.

5. A community-based mobile clinic model delivering PrEP for HIV prevention to adolescent girls and young women in Cape Town, South Africa

Paper 3

Rousseau E, Bekker LG, Julies RF, Celum C, Morton J, Johnson R, Baeten JM, O'Malley G. A community-based mobile clinic model delivering PrEP for HIV prevention to adolescent girls and young women in Cape Town, South Africa. BMC Health Services Research. 2021 Dec;21(1):1-10.

Contribution to the thesis and novelty

This paper contributes to the third objective of the PhD, which is to determine the role of agency, gender, and constrained choice in AGYW's access to PrEP. This thesis is guided by the conceptual framework hypothesizing that AGYW's health decision-making rests on the combination of agency and access to resources. This paper focused on the Cape Town cohort and in a sub-sample qualitatively explored the barriers and facilitators of accessing PrEP from a community-based mobile clinic. Specifically, we explored agency in the form of self-efficacy (including making informed decisions), AGYW's agency in movement within the community, and resources needed to access PrEP. PrEP delivery from a mobile clinic was feasible and acceptable to AGYW and there was a recommendation for expanded differentiated community-based PrEP delivery for increased PrEP uptake and persistence in this population. At this recommendation from participants and in consultation with the community advisory board the project expanded as described in Paper 4 (Chapter 6). This finding also helped to inform the evolution of my thesis and the value of access relative to agency (as per Figure 4 in Chapter 1) for AGYW seeking PrEP.

Contribution of candidate

I was the lead author, conceptualized the study, designed the data analysis, conducted the study, and conducted the data analysis.

Abstract

Background: Daily doses of pre-exposure prophylaxis (PrEP) can reduce the risk of acquiring HIV by more than 95%. In sub-Saharan Africa, adolescent girls and young women (AGYW) are at disproportionately high risk of acquiring HIV, accounting for 25% of new infections. There are limited data available on implementation approaches to effectively reach and deliver PrEP to AGYW in high HIV burden communities.

Methods: We explored the feasibility and acceptability of providing PrEP to AGYW (aged 16-25 years) via a community-based mobile health clinic (CMHC) known as the Tutu Teen Truck (TTT) in Cape Town, South Africa. The TTT integrated PrEP delivery into its provision of comprehensive sexual and reproductive health services (SRHS). We analyzed data from community meetings and in-depth interviews with 30 AGYW PrEP users to understand the benefits and challenges of PrEP delivery in this context.

Results: A total of 585 young women started PrEP at the TTT between July 2017 – October 2019. During in-depth interviews, a subset of 30 AGYW described the CMHC intervention for PrEP delivery as acceptable and accessible. The TTT provided services at times and in neighbourhood locations where AGYW organically congregate, thus facilitating service access and generating peer demand for PrEP uptake. The community-based nature of the CMHC, in addition to its adolescent-friendly health providers, fostered a trusting provider-community-client relationship and strengthened AGYW HIV prevention self-efficacy. The integration of PrEP and SRH service delivery was highly valued by AGYW. While the TTT's integration in the community facilitated acceptability of the PrEP delivery model, challenges faced by the broader community (community riots, violence, and severe weather conditions) also at times interrupted PrEP delivery.

Conclusion: PrEP delivery from a CMHC is feasible and acceptable to young women in South Africa. However, to effectively scale-up PrEP it will be necessary to develop diverse PrEP delivery locations and modalities to meet AGYW HIV prevention needs.

Keywords: HIV prevention; pre-exposure prophylaxis (PrEP); adolescent girls and young women (AGYW); community mobile health clinic (CMHC); PrEP delivery models; sexual reproductive health services (SRHS)

5.1 Background

Despite the global acceleration of the HIV/AIDS response since 2010, 1.7 million new HIV infections occurred in 2018 [89]. In sub-Saharan Africa, adolescent girls and young women (AGYW) aged 15-24 years are at disproportionately high risk of acquiring HIV, accounting for 25% of new infections [88]. The benefit of pre-exposure prophylaxis (PrEP) for HIV prevention has been well-established. Daily doses of oral PrEP (Emtricitabine/Tenofovir Disoproxil Fumarate) have been shown to reduce the risk of acquiring HIV by more than 95% when adherence is high [93, 94]. PrEP effectiveness at the population level will depend on how well AGYW can access, adhere, and persist with PrEP [45, 155]. There are limited data available on implementation approaches to efficiently reach and deliver PrEP to women in high HIV burden communities, particularly adolescent girls and young women.

Adolescence into early adulthood is a period of significant physiological and psychological changes, and often the occurrence of sexual debut, making trustworthy and reliable sexual reproductive health services (SRHS) and information important [25, 156, 157]. Young women's health-seeking behaviours are shaped by their life contexts and relationship with the public healthcare system [24]. AGYW in South Africa have described barriers to SRHS access due to increased travel distance to health facilities, long waiting times at overcrowded facilities, negative healthcare provider attitudes about sexual activity among AGYW, negative social consequences resulting from a lack of privacy at SRHS delivery points, and limited availability of adolescent-friendly health services [23-25, 158, 159]. The challenges of reaching AGYW and supporting their PrEP use have similarly been described from initial PrEP clinical trials [35, 36, 160, 161]. Programs will have to overcome these barriers to successfully engage AGYW to utilize PrEP as an HIV prevention strategy.

Community-based mobile health clinics (CMHC) are an important model for delivering health services to vulnerable populations and impactful when providing differentiated, tailored and client-centered preventative health services [160, 162, 163]. In low- and middle-income countries, mobile health clinics have been deployed to provide a wide range of public health services; including cervical cancer screening in Thailand [164] and Brazil [165], maternal and child health care in Tanzania [166], primary health care in Namibia [167] and Malawi [168], mental health and diabetes screening and services in India [169, 170], and HIV screening and sexual and reproductive health services in South Africa [171-173]. CMHC that provide comprehensive integrated SRHS may be especially attractive to AGYW, providing flexibility in location to increase accessibility for these populations in resource-limited settings.

This paper describes a novel approach to delivering PrEP as an integrated component of community-based comprehensive SRHS to AGYW via a mobile health clinic in Cape Town, South Africa.

5.2 Methods

Study context

POWER (Prevention Options for Women Evaluation Research) is a PrEP implementation science project testing scalable models of PrEP delivery for young women, ages 16 – 25, in South Africa and Kenya. PrEP delivery is being incorporated into established health service settings, including an adolescent-friendly clinic (Johannesburg, South Africa), family planning clinics (Kisumu, Kenya) and a mobile clinic (Cape Town, South Africa) [78]. This manuscript intends to focus solely on PrEP delivery in the mobile clinic setting. While PrEP delivery at each of these sites follows national guidelines, the POWER study encourages the development and evolution of these delivery models to best fit the contexts of each site and to share ongoing lessons learned.

The intervention - Cape Town

In Cape Town, the POWER study integrated PrEP delivery into the SRHS provided by the Tutu Teen Truck (TTT) mobile health clinic. The TTT was originally developed in 2015 as an HIV testing and SRHS for adolescents and young people, geographically and logistically distinct

from government health facilities' day-to-day operations. The TTT is a Mercedes Sprinter and trailer clinic conversion with four consultation rooms delivering services in the densely populated, resource limited and high disease burden areas of Cape Town, South Africa.

The TTT aims to increase healthcare access of particularly vulnerable populations by providing services in locations and at times that build on where young women organically network, such as schools, community centers, and public transport hubs. Private, confidential, and non-judgmental adolescent friendly services are provided on the TTT by a clinical nurse practitioner, a professional nurse, and four lay health counselors. Services are tailored to the specific sexual and reproductive health needs of AGYW and include HIV testing, STI testing and treatment, and a range of contraception options (oral, injectable and implant). The TTT utilizes a m-health system (the Broccoli Biometric Profile and Benefits Management System) in which a young woman's medical record is linked to her fingerprint allowing for anonymized, current, and readily available medical information. A previous study of the TTT indicated that it is a highly acceptable SRHS for adolescents and young adults and preferred over primary health clinics [173].

PrEP delivery was integrated into the TTT sexual health services in July 2017 in consultation with the youth-CAB (community advisory board) to situate the specific intervention within communities largely naïve to PrEP as a biomedical HIV prevention method. AGYW self-presenting at the mobile clinic were invited to view an educational video[i] about HIV prevalence and risks in their community, and the effectiveness of PrEP for HIV prevention. During individual SRHS consultations, all HIV-negative AGYW were offered PrEP with the option to accept, delay, or refuse uptake. Point-of-care tests for HIV and pregnancy are conducted at every visit before PrEP is dispensed. Blood and urine samples are collected for verification of eligible creatinine clearance (at baseline and 6 monthly), Hepatitis B status (baseline only), and current STI infection (gonorrhea/chlamydia – baseline and 6 monthly) and sent off daily to BARC/Lancet laboratories for analysis via a courier pick-up service (see Figure 8). Follow-up visits are scheduled one month after PrEP initiation and then quarterly, with phone calls and WhatsApp communication for occasional visit reminders. The TTT rotation schedule between its delivery sites is intended to be fixed so that AGYW know when and where they can access follow-up services. The study team attended bi-monthly learning and

troubleshooting meetings to ensure the mobile clinic PrEP delivery operations and counseling messaging were adapted to the needs of AGYW within the specific communities of operation.

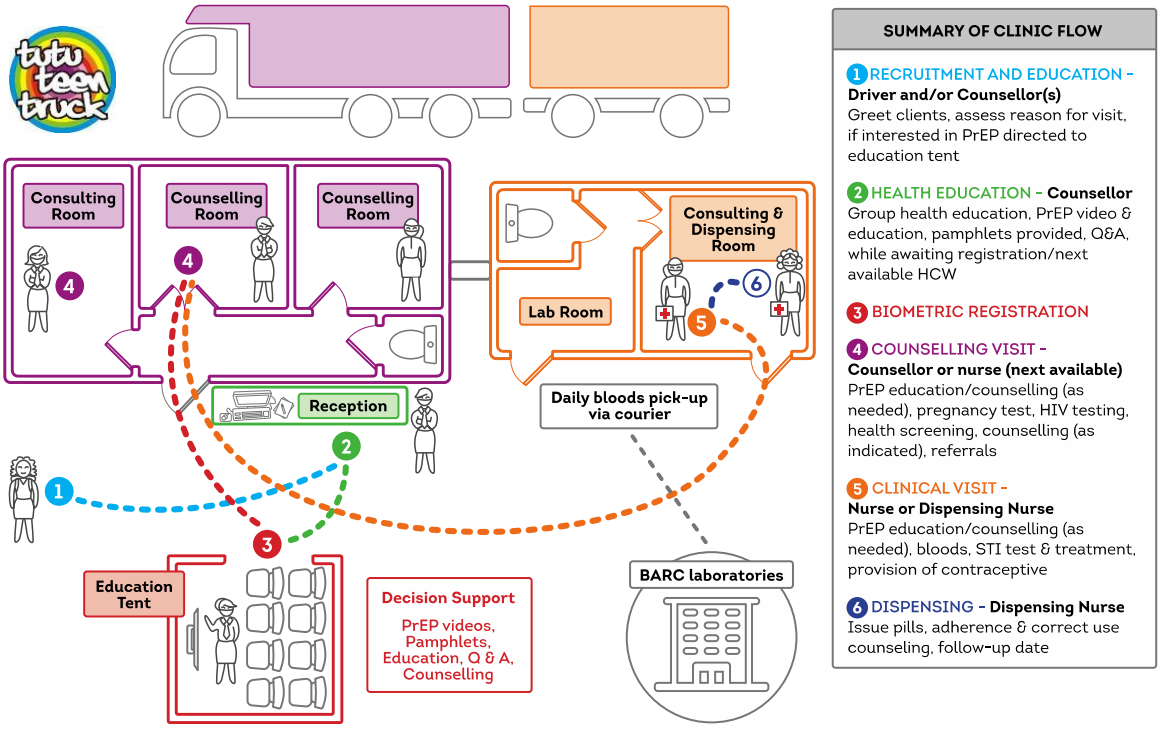


Figure 8. Layout and clinic flow in the Tutu Teen Truck (TTT) mobile clinic

Data collection and analysis

For this qualitative sub-study, we purposively selected and telephonically recruited 30 young women (53 were approached) from the PrEP demonstration cohort for in-depth interviews. RTI international applied quota sampling, established through pharmacy records, to include participants with early or continued PrEP use or who discontinued PrEP [150]. The thematic guide was developed by social scientists at RTI International (provided as Supplementary Information 2), pilot-tested at the study site, and translated into local languages. Interviews and discussions were conducted in participants' preferred language (English or IsiXhosa) by experienced female social science interviewers (SSI) independent of the demonstration study's clinical team. All research interviewers had university-level education and were fluent in English and isiXhosa. Young women were advised about the procedures and focus of the research and written informed consent was attained prior to any data collection. IDIs were conducted one-on-one, in a private community-based venue, lasting approximately 30-45min

and were audio-recorded and transcribed verbatim with sections pertaining to service delivery (clinic setting and logistics) extracted for thematic content analysis (Table 11). Interviews were conducted until saturation of themes was achieved. In addition, notes from six community meetings organized with AGYW receiving PrEP from the TTT and notes from field and study team meetings were included for triangulation analysis.

Table 11. Sample questions from qualitative guides

General Theme	Sample questions/prompts from qualitative guide
PrEP Decision-making	How did AGYW hear about PrEP in their community and/or what encouraged them to come to the clinic and start PrEP?
Clinic Experiences	AGYW asked to describe their clinic experiences, including accessibility, clinic procedures, counseling and support received from staff, and facilitators and barriers to starting and refilling PrEP from the clinic.
PrEP in the future	AGYW were asked about PrEP delivery strategies they think could be helpful for AGYW who want to take PrEP, including convenient locations and times of services and recommendations to clinic experience, PrEP counseling and information.

Relevant information pertaining to key themes of AGYW's experiences of accessing PrEP from a CMHC, and the benefits and challenges of PrEP delivery in this context was organized by two reviewers into major thematic themes using Dedoose[ii] software. Coding was partially deductive drawing from themes in the interview guide but also inductive with emerging themes added to the code book and applied to all transcripts. Throughout the analysis process, samples of the coded transcripts were reviewed by the coding team with any disagreements resolved through discussion until consensus was reached. Study visits medical and pharmacy records collected during young women's PrEP clinic visits were used to assess participants' PrEP uptake and patterns of use, and results from this analysis will be described in future studies.

Data collection was approved by the Human Research Ethics Committees of University of Cape Town (593/2016) and University of Washington IRB (00000950) and included a parental waiver of consent for participants younger than 18 years. The POWER study is ongoing; we report here early findings about CMHC delivery of PrEP for this population of AGYW.

5.3 Results

The mobile clinic's medical records indicate that a total of 1784 AGYW accessed SRHS between July 2017 – October 2019 and 585 (median age of 20 years) initiated PrEP on the same-day.

Baseline evidence suggests that the intervention reached the target population who were able to adequately assess their HIV vulnerability and self-select for PrEP initiation. For example, medical records of the AGYW who initiated PrEP indicated 80% (465) did not know their partner's HIV status; 85% (498) were unable to use condoms consistently; and 48% (259) tested positive for an STI (gonorrhea and/or chlamydia).

The 30 young women participating in the in-depth qualitative interviews had a median age of 20 (18-22) years. Table 12 presents the qualitative participants characteristics. Most AGYW were single with a partner and living with their parents.

Table 12. Demographic and behavioural characteristics of participants

	n (%)
Age	
16-19	17 (56.7)
20-25	13 (43.3)
Relationship status	
Single, with partner	28 (93.4)
Single, no partner	1 (3.3)
Married	1 (3.3)
AGYW lives with*	
Parents	24 (80)
Other family	6 (20)
Sex partner	1 (3.3)
Friends	1 (3.3)
Other	1 (3.3)

**AGYW could mark more than one category ('all that apply')*

Qualitative analysis highlighted five main themes describing the benefits of the CMHC intervention for PrEP delivery: acceptability and accessibility; trusting provider-community-client relationship; non-fragmented and integrated PrEP and SRHS; organic demand generation through AGYW network; and strengthened self-efficacy. A sixth theme was identified highlighting challenges of providing PrEP to AGYW via a CMHC model.

Acceptability and accessibility of mobile clinic PrEP delivery

Overall, AGYW described how being able to access services integrated in their community and daily lives made the service feel like a place of wellness and protection, rather than diseased-focused. The convenient community locations and high visibility of the TTT encouraged AGYW

to access SRHS including PrEP, while eliminating logistical barriers such as transport or difficulties in making appointments. Young women expressed that this made them feel like the service was focused on them and their health needs. Generally, the accessibility, visibility and convenience of the TTT made the services highly acceptable to AGYW and facilitated their uptake of SRHS including PrEP as described here:

> *"I used to see this truck regularly; it has been coming to [township name]. I have noticed it while even passing by [in] a taxi. There was this other time, with my friend we thought we should go and test. So when we got there we found out that they [the TTT] also offer family planning, you can test your blood pressure and many more. So we were interested and we tested and got PrEP."*

> *"It's easy because we get out of school then [the TTT] it's just next to the school."*

Young women shared that because the TTT operates at times convenient for them later in the day and the visits are short, it gives them time to still do their homework and chores. Young women valued the convenience and accessibility of the service:

> *"When we arrived there [at the TTT], we did not wait long time. They [clinic staff] attended to us immediately in a proper manner."*

> *"You get there [at the TTT] and they [clinic staff] serve you for example if you are there for family planning, after [receiving] that you leave. The other thing that makes it easy is that it [the TTT] is closer to us. We don't use transport when we are going to the truck… There are no queues [at the TTT], sometimes there will be a lot of people but they [clinic staff] try by all means to be quick."*

Furthermore, AGYW reported that the high visibility of the TTT and because it is "on their route" frequently acted as a reminder that they are due for a follow-up visit and could do it at that time of remembering without needing an appointment.

Trusting provider-community-client relationship

The TTT's community- and patient-centric design facilitated connection and trust between potential clients and health providers. AGYW indicated that services at the TTT are seen as

focused on young people making them feel comfortable asking questions about PrEP and sexual health while experiencing non-judgment and privacy. Coming from a community where discussions about sex are often a taboo, they welcomed having a reproductive health conversation with a trusted provider:

> *"As he [counsellor] was talking to me, it was as if I was a friend, he was sharing with me in an easily understandable manner. So, I asked lots of questions and he answered."*

> *"I feel I have found someone that can advise me about things that no one can talk to me about."*

> "*And when they [clinic staff] answer me they do it in a manner that I do not feel ashamed."*

> *"I was very comfortable because I am aware that whatever I have discussed with them [clinic staff] will not be discussed with other people."*

The biometric medical record system allowed for privacy as well as readily accessible client information, overcoming challenges with missing files or difficulty with re-entry when a client has not accessed services recently. Young women also related this feature to a trusting healthcare relationship, indicating their belief that the TTT could be trusted as a consistent service provider for AGYW's SRHS needs, with no concern about essential product stockouts like at their local primary healthcare clinics. One young woman emphasized her confidence in the reliability of TTT services, *"you will get from the TTT what you came there for*". Another young woman described her ease of picking up PrEP when she came to an unscheduled visit and conveyed her confidence that she would be able to receive her PrEP refill with ease as a result of the available electronic medical records:

> *"It was easy because they [clinic staff] don't make things difficult, they give you PrEP."*

Non-fragmented and integrated PrEP and SRHS

Integrated SRHS offered at the TTT encouraged AGYW to access a holistic prevention approach to their sexual health, with most young women indicating that they came to the TTT for contraception but then also started on PrEP the same day, or vice versa. Overall, young women highlighted the practicality of being able to access a range of services AGYW might need, including HIV testing, STI testing and treatment, PrEP, and contraception.

Furthermore, waiting times at the TTT are integrated with education allowing AGYW to be informed of their health choices by the time they reach the clinical staff.

> *"I know the staff there [at the TTT], and so I do not feel like its long [waiting times]. Because when I am there, I enjoy being there and, like, am always talking to people. And the staff is always explaining something new to us…[or] are showing us like the condom stuff and like there is this big book about contraceptives".*

Providing AGYW with educational information about HIV prevention, including PrEP, and contraception upfront assisted in triaging clients according to their PrEP and SRHS needs and ensures that they follow the most direct route of clinic flow within one clinic visit. A young woman shared her satisfaction with the convenience of integrated SRHS at the TTT:

> *"It was good because when you finish with one thing you enter another door immediately."*

Organic demand generation through AGYW networks

In the neighborhoods where the TTT operates, AGYW often attend their healthcare visits at the TTT as a group with friends. The TTT is seen as a place that is acceptable to go to with your friends and as being adolescent friendly.

> *"It's nice to be there [at the TTT]. What makes it nice is that when we visit we go as a group with friends. And there is also music. We will stand and listen, you see."*

The convenient location of the TTT to naturally occurring networks of AGYW, organically facilitated demand generation through young women already on PrEP disclosing their use to their peers and encouraging PrEP uptake. One young woman reported:

> *"[W]hen I arrived [at the TTT] there were some children who came to get PrEP and I was not aware [of PrEP] then. I asked these girls if this PrEP is a good thing to do. They said, 'yes, it is a good thing.' One was coming for the second time and the other for the third time, they all said they have not experienced any difficulties."*

Both AGYW and PrEP providers on the TTT reported young women frequently identified peers as influencing their decisions to start PrEP. This experience of AGYW already on PrEP inviting their friends, sisters, and cousins to visit the TTT caused a clear snowball effect in PrEP uptake on the TTT.

Enabling self-efficacy

AGYW indicated that the trusting relationship they fostered with the TTT along with the education in the waiting area and tailored services they received also fostered self-confidence and motivation to adopt increased health-seeking behavior. AGYW appreciated being informed adequately and in an adolescent-friendly and respectful manner and felt it promoted a sense of health ownership and that they have the ability to decide for themselves whether PrEP is an option for them.

> "*It is that they [clinic staff] do not get tired when you continue asking them questions. They keep on explaining until you understand, they explain in a way that you easily understand."*

> *"[T]hey [clinic staff] will do tests and tell you about PrEP [and] how it works. Then they will ask you if you would like to get it or not, the choice is entirely yours."*

Being informed and allowing AGYW to make choices about their health behavior in a manner that fits into their lives leads many young women to confidently merge their contraception and PrEP visit schedules making their SRH visits even more convenient for them.

Model challenge: mobility of services and young women

A sixth theme was identified highlighting challenges of providing PrEP to young women via a mobile health clinic model. The high mobility of the TTT, the lack of predictability in AGYW's lives, and the communities in which the TTT operates sometimes led to service delivery interruptions, negatively impacting AGYW's ongoing access to all SRHS including PrEP via the TTT. Healthcare providers shared that being part of a community means that the TTT experiences the same challenges that members of a community face. In the case of the TTT these included frequent political uprisings, violence hotspots and sometimes severe weather conditions preventing either the TTT or its clients from reaching service sites. While in general the TTT was viewed as highly accessible, some young women shared how the clinic's mobility caused unplanned PrEP use interruptions:

> *"I am still using it, but I have two weeks since I stopped taking the pills, because I couldn't get the truck on the date of the appointment*."

> *"If only it [the TTT] can be bigger …. We usually wait outside. Let's say it's raining; we can't sit outside and we also can't fit in their rooms so we will be forced to leave."*

AGYW typically experience limited autonomy in their movement; they mainly moved between school and home and generally did not have the financial resources or social freedom to travel to the TTT when it was outside of their neighbourhood. As a result, a young woman might have started PrEP when the TTT was outside her school but then when away during school holidays, it was difficult for her to obtain PrEP refills as a participant described here:

> *"[Sometimes] I do not have money to visit the truck. Or when my [PrEP refill visit] date is not close while they [TTT] visit our school, because I stay far from my school."*

AGYW's feedback about how they would like to receive PrEP services in the future frequently included suggestions to mitigate these access barriers, such as expanding delivery locations to include community PrEP clubs, inside their schools, community libraries, community care workers bringing PrEP to their homes, or having a courier drop their refills wherever they are when in need of PrEP.

"I was thinking, how about getting PrEP delivered door-to-door because sometimes when our [follow-up visit] dates are due we might not be around. We would be maybe travel[ing] to the other province for things like funerals, so when you need it, it would be nice if it can be delivered to your home when not around."

"I thought of asking someone [clinic staff] I know from the mobile truck, if [we] have forgotten our dates they [the TTT] should have a place where we can go and collect our pills."

5.4 Discussion

This is the first model of mobile, community-based delivery of PrEP integrated with contraception and other SRHS that has demonstrated feasibility and high acceptability among South African AGYW. CMHC in public health settings are known to increase healthcare access and improve health outcomes in target, yet hard-to-reach, populations such as AGYW in the HIV epidemic [174]. Across our participants' descriptions of PrEP uptake, the location of the CMHC intervention near where AGYW moved or gathered was highlighted as very important to their being able to access PrEP services. Beyond the convenience and material advantages of reducing transportation costs, our participants described how having the CMHC in their own community fostered trust, ownership, and positive health-seeking behaviour. This finding was similarly highlighted in a review of mobile health clinics in the United States, which found that location in surroundings familiar to the community fostered trust [174]. Scholars have postulated that by taking healthcare out of the hospital or doctor's office and bringing care to the people, the mobile health clinic acts as a vehicle for inclusion, creating empowered spaces for patients to become invested in their healthcare [175].

In addition to the convenience of PrEP uptake from a mobile clinic, AGYW emphasized the importance of services being delivered in an adolescent-friendly manner. Their descriptions of what they appreciated about the services covered many of the characteristics embedded in the World Health Organization (WHO)'s recommendation for adolescent-friendly services, including treating young people with respect, being non-judgmental and considerate of

adolescents needs, and providing appropriate and acceptable services accessible to young people at dedicated service delivery points. Research studies have indicated that further important components of these interventions are anonymized testing, flexible clinic hours, and centering services around AGYW's significant SRHS needs including contraception and STI treatment [24, 45]. This integration of PrEP and contraception services was of particular significance to young women. The TTT catered for the young women's comprehensive SRHS needs by providing point-of-care STI testing and treatment and minimizing the number of clinic visits AGYW need to make by integrating PrEP and contraception visits. Notably, while CMHC's are sometimes criticized for providing fragmented prevention services referring clients to primary health care clinics for additional care [174], the TTT was complimented for providing a non-fragmented service allowing for same-day PrEP start by using a courier lab service and an onboard pharmacy.

Although there are several advantages to the CMHC model for PrEP delivery, it is not an absolute solution. While the mobile clinic's seamless integration into the community facilitated the acceptability of this PrEP delivery model for AGYW, the CMHC was also negatively impacted by the challenges faced by the broader community, such as community riots, violence, and severe weather conditions. During these times, the TTT could not maintain its scheduled visits and return to a predictable schedule and routes was sometimes delayed causing gaps in SRHS delivery including PrEP supply to AGYW. In addition to the disruptions in the delivery described above, AGYW in disadvantaged communities tend to be highly mobile, moving to changing households with the school calendar or as their family or relationship circumstances change.

Mobile PrEP delivery via the TTT facilitated increased uptake of PrEP in AGYW, however, additional strategies are needed to support PrEP use continuation in young women. A differentiated model with various delivery options including CMHCs might meet AGYW's mobility and needs and mitigate supply interruptions which occur through reliance solely on the CMHC. The Tutu Teen Truck recently implemented a differentiated PrEP delivery model allowing AGYW to choose between four modes of PrEP delivery: 1) community-based mobile health clinic; 2) local government clinic; 3) community-based PrEP club; and 4) courier PrEP delivery service. These differentiated delivery models will need to pay special attention to

overcoming linkage/continuity challenges that have proven challenging for HIV and TB treatment from CMHC to static clinic sites [171, 176-178] and perhaps apply lessons learned from successful community-based ART distribution programs [179]. Future implementation research should move beyond scale-up strategies for PrEP to also include scale-out strategies where an established PrEP delivery intervention is rolled out to novel settings to enhance AGYW's uptake and persistence on PrEP [180].

The results presented in this paper are preliminary while the study is still ongoing in this community and cohort. Caution is needed with regard to generalizing our findings beyond AGYW in limited resource settings in South Africa, as attitudes and experiences across communities and groups might differ from this limited sample.

5.5 Conclusion

PrEP delivery from a mobile health clinic is feasible and acceptable to AGYW in South Africa. The Tutu Teen Truck facilitated a gender-responsive approach to delivering PrEP by providing a comprehensive service to AGYW's reproductive health needs, bringing the services close to young women considering their limited autonomy, and meaningfully involving AGYW in the planning of service uptake and continuation strategies. Additionally, positive provider-client interactions and trustworthy service delivery were combined in the model to strengthen self-efficacy and health-seeking behaviour among AGYW. However, findings also highlighted the importance of differentiated service delivery beyond CMHC as PrEP is scaled-up across South Africa. Diverse PrEP delivery locations and modalities will need to be developed so as to fit into the complex lives, mobility, and competing demands of AGYW and adapted to navigate contexts of chronic social instability in South Africa.

6. Exploring adolescent girls and young women's (AGYW) PrEP-user profiles: qualitative insights into differentiated PrEP delivery platform selection and engagement in Cape Town, South Africa

Paper 4

Rousseau E, Sikkema KJ, Julies RF, Mazer K, O'Malley G, Heffron R, Morton J, Johnson R, Celum C, Baeten J, Bekker LG. Exploring adolescent girls and young women's (AGYW) PrEP-user profiles: qualitative insights into differentiated PrEP delivery platform selection and engagement in Cape Town, South Africa. JIAS. 2024; 27(5): e26254

Contribution to the thesis and novelty

This paper contributes to the third objective of the PhD, which is to determine the role of agency, gender, and constrained choice in AGYW's preferences and use of PrEP delivery models. This paper focused on the Cape Town cohort and, in a sub-sample of PrEP persisters (AGYW using PrEP for ≥3 month), qualitatively explored PrEP delivery platform choice. This final cohort had the option of accessing PrEP from four different platforms (mobile clinic, government health facility, courier delivery, and youth PrEP club) with the intention of increasing PrEP access in a personalized fashion. The WHO, in recent years, has recommended differentiated HIV prevention to optimize PrEP access, acknowledging that the ideal option may vary by PrEP user. The framework of this thesis (and what we have seen in the findings of the previous papers) suggests that the availability of a resource (PrEP delivery platform) tells us about potential rather than actualized choice (Figures 3 and 4 in Chapter 1). In this final paper, I conducted an in-depth exploration of how access to PrEP services translates into the realization of the choice to continue using PrEP. While the previous papers explored the role of agency, gender, relationships, community, etc. on AGYW's decision to take PrEP, this paper explored how these factors influenced AGYW's access to service delivery platforms for their PrEP refills (persistent use). These concepts were explored by analysing AGYW as consumers. In so doing, I sought to understand the tradeoffs AGYW make between resource options when accessing PrEP by aligning PrEP utilization with their needs, lifestyles, attitudes, norms, behaviours, relationships, habits and perceived societal expectations. This paper is

novel in its use of market segmentation research methods to more clearly analyse AGYW's personalities and the choices they make when faced with PrEP delivery and access choices.

Contribution of candidate

The paper was originally presented (poster exhibition) at the International AIDS Society conference in July 2023 and recently published at the Journal of the International AIDS Society. I was the lead investigator and lead author, conceptualized the study, designed the data analysis, conducted the study, and conducted the data analysis.

Abstract

Introduction: Adolescent girls and young women (AGYW), a priority population for HIV prevention in Africa, show high interest but difficulty in sustained effective use of pre-exposure prophylaxis (PrEP). With ongoing PrEP scale-up focused on increasing access, it is important to understand what influences AGYW's choice of PrEP delivery platforms.

Methods: The POWER implementation study in Cape Town provided PrEP between 2017-2020 to AGYW (16-25 years) from any of four differentiated delivery platforms: mobile clinic, government facility, courier delivery, or community-based youth club. Healthcare providers at government and mobile clinics delivered comprehensive integrated sexual and reproductive health services. Courier and youth club platforms provided light-touch PrEP follow-up services incorporating rapid HIV self-testing. We conducted in-depth interviews with a purposive sample of AGYW who had ≥3 months of PrEP use based on pharmacy records and who accessed ≥2 PrEP delivery platforms. Thematic analysis explored their preferences, decision-making, and habits related to PrEP access to inform market segmentation.

Results: We interviewed 26 AGYW (median age 20) PrEP users between November 2020 - March 2021. Of these, 24 used mobile clinics, 17 courier delivery, 9 government health facilities, and 6 youth clubs. Qualitative findings highlighted four potential behavioural profiles. The "Social PrEP-user" preferred PrEP delivery in shared peer spaces such as youth clubs or adolescent-friendly mobile clinics, seeking affirmation and social support for continued PrEP use. The "Convenient PrEP-user" favoured PrEP delivery at easily accessible

locations, providing quick (courier) or integrated contraception-PrEP refill visits (mobile and government clinic). The "Independent PrEP-user" preferred PrEP delivery outside of traditional medical environments that offered control over delivery times that fit into their schedule such as the courier service. The "Discreet PrEP-user" highly valued privacy regarding their PrEP use (courier delivery) and avoided delivery options where groups of people wait for services or where unintentional disclosure was evident (youth club). Comfort with HIV self-testing had minimal influence on PrEP delivery choice.

Conclusions: Market segmentation of AGYW PrEP users characterizes different types of PrEP users and enhances tailored messaging and campaigns to reach specific segments and result in sustained PrEP use and HIV prevention benefits.

6.1 Introduction

The past five years have seen global inclusion of oral PrEP (pre-exposure prophylaxis) into national guidelines as a key biomedical HIV prevention method, with many countries poised to deliver services that are integrated, differentiated, and sometimes digitalized for optimal PrEP use [181]. In the South African context, adolescent girls and young women (AGYW) are a group with high HIV vulnerability, high interest and uptake of PrEP, but difficulty in continued use [182]. Frequently reported barriers to effective PrEP use in AGYW include community-level HIV-related stigma, relational barriers such as gender-based violence, disclosure concerns, and/or lack of social support, and access barriers including inconvenient locations, times of PrEP services and judgmental interactions with healthcare providers [40, 46, 103, 109, 117, 152, 182-185]. There has been a growing trend towards tailoring PrEP delivery, counselling, and support more closely to individuals' circumstances and needs to improve uptake and use.

In scaling up PrEP delivery, differentiated services (including non-clinic-based services) have been called for to increase access to PrEP for those who need it most. The World Health Organisation released updated guidelines in 2022 recommending simplified, demedicalized, differentiated PrEP delivery services, including the use of HIV self-testing (HIVST), that is person- and community-centered [181]. A systematic review of discreet choice experiments in key populations, including AGYW, has indicated that the most important attributes of

optimal PrEP access included cost, PrEP delivery independent of HIV treatment sites, PrEP services integrated with contraception provision, HIV testing that is quick with results available immediately, and services conveniently located and at times outside of normal clinic hours [186-188].

While research has highlighted the need for PrEP products to fit into AGYW's lifestyles and relationship dynamics [55, 106, 107], HIV prevention impact may be better if PrEP service delivery platforms match AGYW's diverse lifestyles and unique needs. Consumer segmentation is a widely used technique within marketing to align the demand and supply of services to groups of individuals with common priorities and needs based on their behavior, attitudes, and beliefs [189-191]. Market segmentation has previously been used in family planning counseling and for HIV prevention through voluntary medical male circumcision (VMMC) [192-194]. The POWER (Prevention Options for Women Evaluation Research) study provided PrEP to AGYW in Cape Town, South Africa via differentiated PrEP delivery models which included a mobile clinic, a government health facility, courier PrEP delivery, and a youth PrEP club. In relation to the POWER study, we explored AGYW PrEP-user preferences, decision-making, influences, and habits related to PrEP access from different delivery platforms to inform market segmentation.

6.2 Methodology

Research setting and study participants

The POWER implementation study was undertaken in Cape Town and Johannesburg, South Africa, and Kisumu, Kenya, to develop scalable PrEP delivery strategies for AGYW (aged 16-25 years). From June 2017 to September 2020, 2550 AGYW were enrolled across sites, 787 in Cape Town, with study procedures described previously [78]. The Cape Town site was based in townships and set up a community-based differentiated PrEP delivery model which included a mobile clinic, a government health facility, courier PrEP delivery, and a youth PrEP club option (Figure 9).

Prior to commencing the study, ethical clearance was provided by the University of Washington and the University of Cape Town. Participant written informed consent was

obtained in English or Xhosa before data collection, with parental consent waived for participants younger than 18 years.

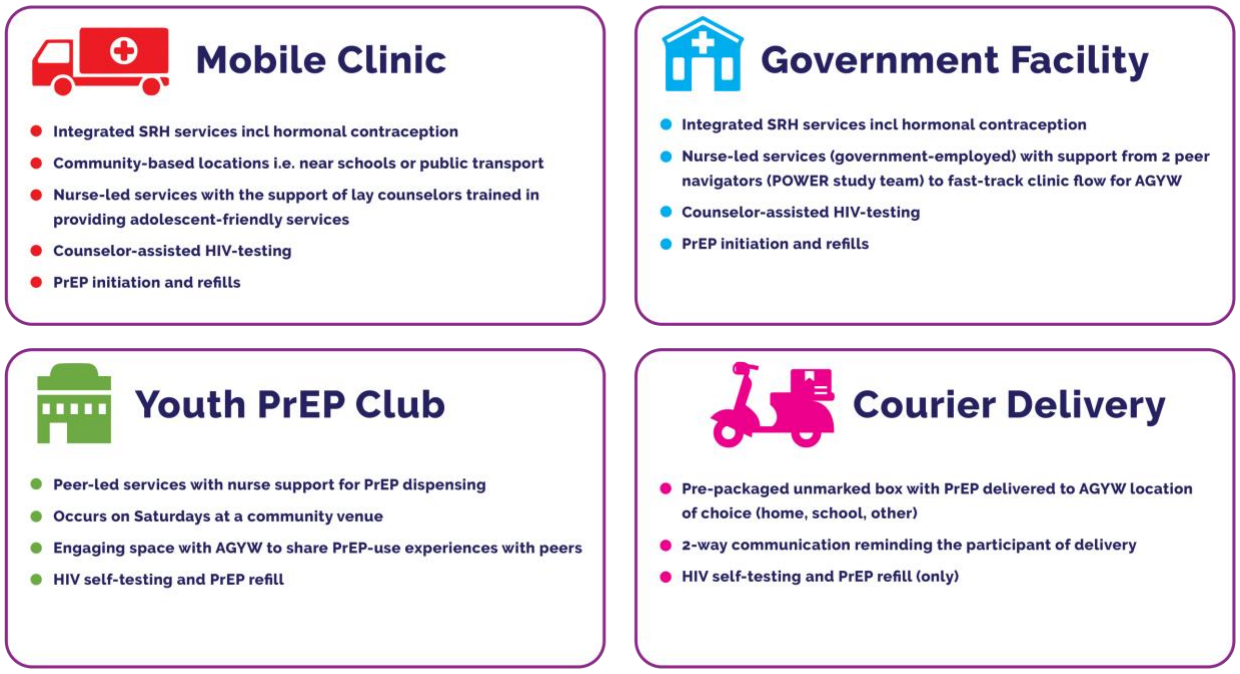
Study sites

The community-based mobile clinic provided PrEP as part of a nurse-led integrated sexual and reproductive health (SRH) service including hormonal contraception and point-of-care STI testing, previously described [195]. The government health facility provided public health services, including SRH services, and the POWER study team provided oral PrEP to this facility along with training on PrEP provision. A research administrator and two peer navigators from the study team were permanently placed at the facility to provide a friendly and fast-tracked service to AGYW and ensure study data capturing. The youth PrEP club occurred on Saturdays at a community venue and was led by a nurse providing additional education on PrEP and other SRH topics and created an engaging space for AGYW to share their PrEP use experiences with their peers. Participants accessing the community-based youth club could get their PrEP refills at this engagement in exchange for a completed HIV rapid self-test (HIVST) kit provided at the venue. The courier PrEP delivery option was fulfilled in collaboration with Iyeza Health[1] (a community-based courier service delivering chronic medication) and included 2-way communication via the Iyeza delivery App, which provided delivery reminders and allowed the participant to change the delivery date or location. Courier delivery included a pre-packaged unmarked box including a PrEP refill, a home pregnancy test, a rapid HIVST kit with instructions, and a referral mechanism should the test result be positive. The feasibility and acceptability of using the HIVST in this population had previously been confirmed [196].

In this PrEP delivery model, participants could use the mobile clinic and government health facilities for PrEP initiation or refills, while the courier service and youth club provided PrEP refills only. Participants' use of and movement between the four PrEP delivery platforms was tracked biometrically [195].

[1] www.iyezahealth.co.za

Figure 9. Differentiated PrEP delivery platforms



Subset with in-depth qualitative interviews

A subset of AGYW was purposively selected for in-depth interviews (IDIs) at the end of the study period. Using convenience sampling, qualitative participants were recruited for IDIs if they had continuously used PrEP for at least 3 months, based on pharmacy records, and used more than one of the four PrEP delivery platforms for their PrEP refills.

Data collection

Qualitative interviews followed semi-structured guides aimed at exploring the determinants of AGYW's choice and retention for each of the PrEP delivery platforms. Interview guides included questions related to their motivation to use a specific PrEP delivery platform, facilitators and barriers of each of the delivery platforms; and exploring the influence of sex partners, people the young women live with, and peers, in their decision to access PrEP from a particular platform (Supplementary Information 4). The IDIs were conducted face-to-face in either English or isiXhosa, based on participant preference, by experienced social science interviewers who were independent of the study's clinical team. The IDIs lasted between 30-60 minutes and were audio recorded, then simultaneously translated and transcribed, and English transcripts were checked by the qualitative team for accuracy.

Data analysis

The codebook was iteratively created to reflect participants' preferences, decision-making, and habits related to PrEP access from the various delivery platforms. Additional codes were included to capture themes such as the role of disclosure, relationship dynamics, PrEP perceptions, social support, and lifestyle in PrEP use decision-making. Transcripts were coded in Dedoose (Version 9.0.54, Los Angeles, CA: Socio-Cultural Research Consultant, LLC) by a three-person analysis team. Sections of independently coded transcripts were periodically compared throughout the analysis process with an average kappa of 0.80, indicating high reliability. Thematic analysis was applied to interpret AGYW's daily lives and PrEP access behaviours. Latent-level themes [197] emerged from the data describing AGYW PrEP users' preferences and decision-making.

6.3 Findings

Demographic and behavioral characteristics of sample

Participants in the POWER qualitative sub-study in Cape Town included 26 AGYW aged 16-25 (median age = 20), who primarily lived with their parents (69.2%) or other family members (23%). Participants accessed PrEP from a combination of delivery platforms, with most using the mobile clinic (92.3%) and courier PrEP delivery (65.4%), followed by the government health facility (34.6%) and youth PrEP club (23.1%). All young women in this cohort used hormonal contraception, with most (84.6%) using an injectable method needing regular (every 2 or 3 months) engagement with either the mobile clinic or government facility. HIVST was used during this study by 76.9% of participants to assess their HIV status at a PrEP refill.

Table 13. Demographic and behavioural characteristics of participants (N=26)

	N (%)
Age	
16-19	11 (42.3)
20-25	15 (57.7)
Living situation	
Parents	18 (69.2)
Other family	6 (23.1)
Sex partner	0 (0.0)
Other	2 (7.7)
Disclosed PrEP use to*	

People she lives with (parents/family)	23 (88.5)
Friend	26 (100.0)
Sex partner	11 (42.3)
PrEP delivery platform (ever used)**	
Mobile clinic	24 (92.3)
Government facility	9 (34.6)
Courier delivery	17 (65.4)
PrEP Club	6 (23.1)
HIV self-test (HIVST) experience	
Yes (used HIVST to assess HIV status during the study)	20 (76.9%)
No	6 (23.1%)
Hormonal contraception use	
Injectable	22 (84.6)
Implant	2 (7.7)
Oral	2 (7.7)

*AGYW could mark more than one category

**AGYW accessed multiple PrEP delivery platforms based on dispensing records

While the decision to use PrEP was highly personalized, AGYW who initiated and continued use had disclosure in common. Everyone in this cohort disclosed their PrEP use to a friend, while 88.5% disclosed to the people they lived with and 42.3% to a sex partner (Table 13). During the interviews, young women indicated that disclosure to the people they live with is important for adherence to the daily PrEP regimen. AGYW also shared their experiences of disclosure to sex partners, at times negotiating PrEP disclosure by framing it within the context of their HIV vulnerability due to high sexual violence in the community. Interestingly, AGYW highlighted that disclosure to a new partner when already on PrEP was easier than starting PrEP and disclosing use within an existing relationship.

> *"So, it made things easier that he knew from the beginning that I took PrEP, you see like instead of getting into a relationship and having to explain it further."* (Ayanda, 18-year-old)

Many (n=16, 61.5%) participants mentioned the pervasive stigma and misinformation surrounding PrEP in their communities and how it affected their PrEP access and use. A recurrent theme in the interviews was that AGYW's selection of a PrEP delivery platform depended on their needs at a specific time, driving PrEP interest while weighing the best fit of the platform choice into their lives.

"It depends on what you want for your life as a young woman, you will know where to get PrEP when you want to use it." (Avuyonke, 21-year-old)

Based on this AGYW cohort's needs, resources, relationships, and values, analysis of the narratives produced four PrEP-user segments: the convenient, the social, the independent, and the discreet PrEP-user (Figure 10).

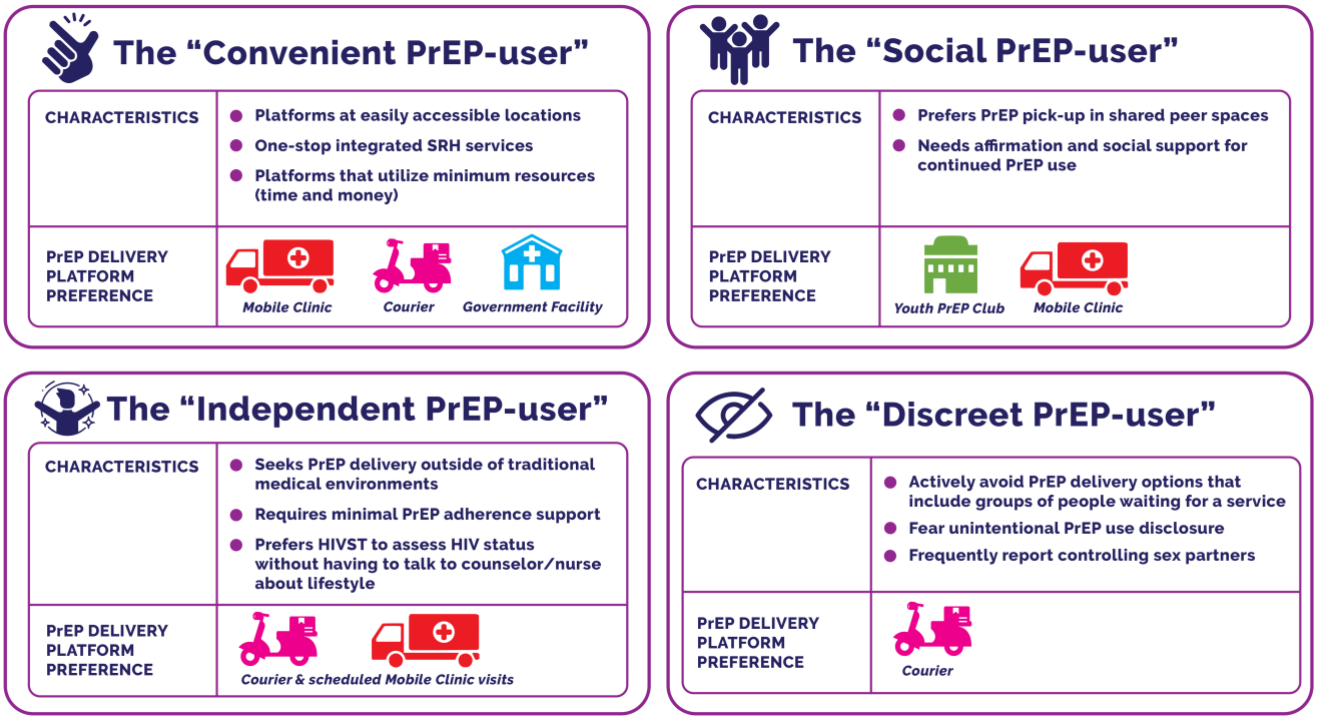


Figure 10. PrEP-user segments and their PrEP delivery platform preferences

The Convenient PrEP-user

The "Convenient PrEP-user" preferred PrEP delivery at easily accessible locations, providing quick and/or integrated service with contraception and PrEP refills in a single visit. For the convenient PrEP-user, using little time and financial resources to access PrEP was the highest priority. AGYW in this user segment most often used the mobile clinic available in their community at locations they frequent, such as schools, or courier delivery.

"It's because it's much closer to my township. So, I'd usually walk when I'm going there. So, it was easy for me in that way. Cause I don't even need transport." (Thando, 17-year-old)

"And the truck was like literally there outside my school, so I didn't have to travel for it, that was easier." (Ayanda, 18-year-old)

The mobile clinic was also deemed convenient for access to integrated SRH services without long queues and expedited PrEP refill visits.

"They give you your PrEP pills as well as contraceptives if you are using them. You don't wait for long without being attended to." (Lethu, 22-year-old)

"When you got there you knew that you wouldn't have to wait – you get there, and they've already prepared for you so that you can quickly get them [PrEP refill] and leave." (Aviwe, 24-year-old)

The government health facility was also perceived as an acceptable platform for integrated contraception-PrEP delivery if the facility was near where young women resided.

Courier PrEP delivery conveniently brought PrEP refills to a specified destination such as participants' homes (or other suitable locations) and did not move around like the mobile clinic. Participants also shared instances of shifting to the courier option when they relocated further away from the mobile clinic routes to attend a different school or university and during the covid-19 lockdown periods.

"When I had to come on my date, maybe I would not have money for transport firstly, then secondly you would find that we are busy with life, and I wouldn't be able to make time to come here. So, it's nice there because even if I am at a friend's place, or wherever I am…then at least they will transport them for me, and I can then take them… And also, during the Corona thing I also used the courier service." (Busisiwe, 19-year-old)

The Social PrEP-user

The "Social PrEP-user" sought PrEP delivery in shared peer spaces such as youth clubs or adolescent-friendly mobile clinics, that provided affirmation and social support for continued PrEP use. This group normally disclosed their PrEP use, however, for the purpose of validation of their PrEP use, with some needing social approval even before making the decision to initiate PrEP. The social PrEP-user valued opportunities to discuss adherence solutions and how PrEP was fitting into their lives and intimate relationships. Receiving PrEP in a peer environment at the youth clubs was seen as a space where they could overcome their concerns about community PrEP stigma.

> *"there are a lot of things we'd discuss, you see? Things that you weren't able to admit to your friends, but when you hear someone say something you were afraid to say, you also get that relief, you see?"* (Sammy, 24-year-old)

> "*It was fun and you can freely talk about anything. There was no one who can judge you or laugh at you. We were free to talk about anything. Healthcare workers [at mobile clinic] know how to work well with young people."* (Lethu, 22-year-old)

Some AGYW also preferred going for their PrEP refills with a friend or female family member, such as a sister or cousin, and at times encouraged their friends to start taking PrEP leading to greater perceived PrEP adherence support.

> *"Yes, my friends actually, they also actually went to take PrEP at some point. And then the support like that they also gave me is …I knew someone there knew that I was taking PrEP, so they would remind me (giggles) you see. And also like if there was something that I didn't understand sometimes, then they would also accompany me to the truck [mobile clinic] when I am fetching my things, then we can also ask the question together."* (Lusanda, 16-year-old)

Lastly, they appreciated the comradery of everyone being at the youth club for the same reason, in contrast to government facilities.

"Cos, if we're at the club, we're all brought together by PrEP, and we know what we are there for. Where(as) people are at the clinic for different reasons, some are there to look at you, the club is better." (Thando, 17-year-old)

The Independent PrEP-user

The "Independent PrEP-user" preferred PrEP delivery that was outside of traditional medical environments, allowing for a high level of control over PrEP refill times. The independent PrEP-user required minimal adherence support, believing that they can consistently and accurately assess their HIV vulnerability without the need to speak to a counselor about sexual behavior and relationship dynamics. Some AGYW in this group also liked using an HIV self-test, indicating that they valued knowing their HIV status and appreciated that they could do it at home in their own time.

"…the privacy, you do things alone and you are doing your thing. And no one is asking you certain questions that are unnecessary that you have to answer. Now you just do your thing, then take pictures and send it to them and then continue eating PrEP and then you go about your day." (Grace, 18-year-old)

Furthermore, the independent PrEP-user was often employed or busy looking for work, making it impossible to access government health facilities and mobile clinics with limited hours of operation. Young women in this category primarily chose the PrEP courier delivery option. They appreciated the advance contact with the courier service, allowing them to change or reschedule deliveries to a convenient time and/or location that will fit into their schedule and cut down on travel time and costs.

"The people [courier delivery] tell you when they are coming to you and you can say I'm not available you can come at a different time. They go according to your schedule." (Avuyonke, 21-year-old)

The Discreet PrEP-user

The "Discreet PrEP-user" was most concerned about stigma and people's perception of her as a PrEP-user, including her peers. Young women in this segment hardly disclosed their PrEP use and definitely not to their sex partners (often described as very controlling) which also led to skipping PrEP doses when with their partner. How people perceived them engaging with a specific delivery platform played a role in how and when they accessed PrEP. The discreet PrEP-user avoided delivery options that had groups of people waiting for services such as at the government health facility, or where unintentional PrEP use disclosure was evident like at the PrEP youth clubs.

> *"Sometimes there are children that come for their family planning, you will be shy to take PrEP in front of them. They will say you are taking PrEP in a nasty way even though you are doing the right thing."* (Ncumisa, 24-year-old)

Discreet PrEP-users accessed integrated SRH services where they could conceal their PrEP refill visit within their contraception appointment, but they mostly appreciated the privacy of the courier delivery.

> *"I was spotted going to collect pills in the clinic not knowing what pills I went to collect. But, when they spot the [courier delivery] car, they'll just ask what the car was here for, but they can't see what's inside [the box], and what we have [PrEP]."* (Yolanda, 20-year-old)

However, due to their heightened sensitivity to stigma and avoidance of disclosure, discreet PrEP-users will avoid and reschedule a courier PrEP delivery when there is any risk of unintentional disclosure.

> *"If the delivery person would call, and I am hanging out with people, I would silence my phone, but at the back of my head, I'll be thinking about how I need PrEP as I have run out… I'd answer if I'm on my own*." (Didi, 18-year-old)

6.4 Discussion

This qualitative study of AGYW continuous PrEP-users in South Africa highlighted four potential behavioural profiles (independent, convenient, social, and discreet PrEP-users) related to their engagement with specific PrEP delivery platforms. Although all the young women in this cohort reported an inclination towards continued PrEP use, their level of autonomy, resource constraints, and influence of others, shaped their access to PrEP services. Mobile clinics were the most used PrEP delivery platform, accessed by 92% of AGYW in this cohort. Mobile clinics have been described as acceptable and convenient for AGYW, especially those from under-resourced areas, by providing PrEP services at convenient times, at easily accessible locations, and integrated with contraception provision for optimal access [195, 198, 199]. The second most popular PrEP delivery platform was courier delivery, which AGYW selected for its privacy, convenience, and limited interaction needed, especially by AGYW considered to have a demanding lifestyle schedule or those avoiding PrEP use disclosure. The youth PrEP club, similar to other demonstration studies showed that supportive peer environments may increase adherence to PrEP, while also overcoming community stigma [200-202]. However, the PrEP club had a lower level of use compared to the other platforms and may be suited for a targeted sub-sample of AGYW. While the presence of peer navigators promoted AGYW accessing integrated SRH and PrEP services at the government health facility, this platform was still criticized for its lack of privacy and long waiting times, similar to other studies [23, 25, 77]. Comfort with HIV self-testing had minimal influence on PrEP delivery choice and was highly acceptable [203, 204], especially by the independent and convenient PrEP-users.

Previous research suggests that PrEP use in AGYW is influenced by both internal drivers and external circumstances [103]. Beyond that, we found that these intrinsic and extrinsic motivations along with AGYW's lifestyle habits also translate to their choice of PrEP delivery platform. AGYW in this study found themselves on a continuum of intrinsic (strong self-determination and autonomy finding PrEP adherence personally fulfilling) and extrinsic motivation (where PrEP use habits are influenced by external factors of either rewards, social pressure, or fear of negative consequences) [205-207]. Intrinsic motivation was most notable in the independent PrEP-user seeking PrEP delivery that fit into their schedule and require minimal adherence support. Previous research primarily associates independent PrEP-use

with men who have sex with men (MSM) and transgender populations [208-214], however, our findings suggest that some AGYW might also be suited for simplified, automated PrEP services, which in this study was courier delivery but could include PrEP delivery models that use telemedicine and pharmacies [188]. Extrinsic motivation was a factor for social PrEP-users, seeking peer-supported PrEP services that provide affirmation for continued PrEP. While community PrEP stigma was a crosscutting theme in the study cohort, the discreet PrEP-user especially avoided delivery options with a risk of unintentional disclosure, fearing stigma, discrimination, or negative consequences from controlling sex partners [96, 215]. While courier delivery was preferred by the discreet PrEP-user, similar to AGYW with low disclosure who struggles with consistent PrEP adherence [137, 151, 152, 216], this group at times missed PrEP refill visits when it threatened unintentional PrEP use disclosure. While it is generally accepted that people who display intrinsic motivation for their health behavior display better persistence [205], our findings suggest that PrEP delivery mechanism can be designed to also promote continued PrEP use in extrinsically motivated PrEP users – in this instance by providing high social reward services (youth PrEP club) or extremely private services (courier PrEP delivery and HIVST for discreet PrEP-users).

Akin to other demonstrations, our findings highlight that AGYW is a diverse group with different lifestyles, needs, habits, and levels of influence from those around them, which influence their engagement with service delivery platforms for both uptake and effective continued use of PrEP [118]. Understanding different market segmentations and how these influence AGYW's PrEP access will allow for tailored demand creation that creates the greatest likelihood that people will be connected to PrEP delivery platforms acceptable and feasible to them [189, 192]. In addition, when this information is made available to healthcare providers, adherence counselling can be geared towards AGYW's preferences and trade-offs regarding delivery platforms for PrEP refill visits for optimum use. This will also be important during the introduction of new biomedical PrEP modalities within a choice framework of HIV prevention options, where some methods (such as long-acting injectable cabotegravir) will be confined to a few delivery platforms where a healthcare provider can administer the therapy, while other long-acting methods such as the dapivirine vaginal ring will be amenable to multiple delivery platforms outside traditional facilities, including courier delivery, reinforcing convenience, independence, and discretion [217]. In the roll-out and scaling up of HIV

prevention for AGYW implementers are encouraged to consider both PrEP modality and PrEP delivery platform preferences. Successful market segmentation is a multi-phase process - the next step would be a further differentiation and validation of these PrEP-user segments through quantitative investigation of AGYW demographic and psychographic characteristics associated with these profiles.

Limitations

The primary limitation of this study is its qualitative design with a small sample of 26 AGYW and therefore caution needs to be applied in generalizing the results beyond this specific study population. In addition, the sample consisted of AGYW who had 3 months of sustained PrEP use, and different segmentation might apply to AGYW who struggle to use PrEP consistently or those who were interested in PrEP but did not initiate from any of these PrEP delivery platforms. Furthermore, the study cohort primarily lived with their parents or other family and therefore experienced low influence from sex partners on their PrEP delivery platform choice – this might look different in populations residing with their sexual partners.

6.5 Conclusion

This qualitative investigation of factors influencing AGYW's preferred PrEP delivery platform illuminated four key behavioral profiles: the independent, convenient, social, and discreet PrEP-user. By segmenting the market, we gain a deeper understanding of the different types of AGYW PrEP-users, enabling the development of targeted messaging and campaigns to best reach specific segments and result in sustained PrEP use and HIV prevention benefits.

7. Discussion and Recommendations

7.1 Introduction

The POWER study was implemented in South Africa and Kenya between 2017 and 2020 within limited-resource communities largely naïve to PrEP, despite a strong drive from WHO and other agencies to see scale-up of this biomedical HIV prevention method for AGYW in the regions most burdened by HIV. This thesis set out to explore AGYW's decision-making processes in PrEP uptake and the factors (particularly those related to being a young sexually active woman in Africa) that influence or constrain their PrEP uptake and persistence. This was explored through qualitative and quantitative investigation into AGYW PrEP users' experiences when offered PrEP within a differentiated service delivery model. The work in this thesis is the first of its kind to consider 1) AGYW's decision-making at key moments along the PrEP-user journey from uptake to persistence (including PrEP pauses and restarts); 2) the role of sexual relationship power in AGYW's PrEP use; and 3) segmenting (profiling) AGYW PrEP users based on their engagement with preferred differentiated PREP delivery models. This final chapter summarises the work's contribution, drawing together the essential findings and insights from the papers included and formulating a thesis which informs recommendations for PrEP scale-up in this key population and future research.

7.2 Assumptions and Limitations in this thesis

To attempt to predict at the outset of an intervention (providing "user-controlled" HIV prevention) precisely how it will change AGYW's lives runs into the risk of finding "outcomes" that do not truly reflect the potential of that intervention. As researchers and healthcare providers, we measure the achievement of AGYW's health outcome as PrEP uptake and consistent PrEP use. From the time of its introduction, oral PrEP was labelled as a user-controlled method that would mitigate AGYW's challenges of HIV prevention (condom negotiation, couples HIV testing, etc.) namely, an easy and discreet way of "simply taking one pill a day". Previous research highlighted that low adherence to PrEP was related to AGYW's inability to assess their HIV risk accurately [218, 219]. Throughout the studies included in this thesis (most notably during the exploration of the PrEP-user journey) and other research published during the same time, it becomes apparent that AGYW's conceptualisation of a "well-being" outcome moves beyond just taking a pill a day and achieving HIV prevention.

AGYW indicated that they do care about HIV prevention, evident in high PrEP uptake and stated recognition of acute knowledge of their partners' infidelity and the increased risk of HIV infection in the communities they reside in. While my premise at the start of my doctoral studies was that AGYW's PrEP decisions are constrained, I have come to the realisation through this work that AGYW are actively deciding what "well-being outcomes" mean to them. Particularly, I have learned that the focus on HIV prevention and PrEP use is narrow-in focus, with relationship preservation (and ensuring safety in a potentially volatile relationship) taking stronger precedence. With this has come the realisation that the answers received from AGYW when asked if they achieved their desired well-being outcomes, may well differ from my assumptions.

The POWER study was an observational implementation study and, therefore, prone to biases and loss to follow-up. In addition, the thesis applied a primarily qualitative methodology, and hence, inference regarding these findings can only be applied within the study sample of AGYW and chosen geographic areas and settings (peri-urban areas in South Africa and Kenya). Particularly, papers 3 and 4 were focused on the AGYW cohort in Cape Town, South Africa and additional care should be taken in applying these findings beyond this specific context. Furthermore, the findings of this thesis should be considered within the results of the primary, quantitative results of the POWER study, which revealed high initiation and very modest levels of persistence. The interpretation of these findings is further limited by the current lack of consensus in the field of reliable measures of prevention-effective PrEP use, which might have affected the interpretation of PrEP persistence. Finally, effective HIV prevention generally involves a health system and healthcare providers; however, this thesis focuses almost exclusively on the perspectives of PrEP users, and therefore, conclusions should not be drawn beyond this perspective.

7.3 Discussion of key findings

Primarily, the combination of investigations and papers included in this thesis aimed to uncover AGYW's decision-making power when it comes to HIV prevention. This section discusses the key findings and includes a reflection on agency and access to resources [70].

7.3.1 Decision-making is carried out between individuals, not only by them: The role of gender and agency in AGYW's PREP use

Oral PrEP is not a completely discreet HIV prevention method as it needs storage and daily pill-taking, which means AGYW considered their lifestyles and living conditions during PrEP uptake. Exploring AGYW's PrEP use experiences revealed that PrEP decision-making is often carried out between individuals (the AGYW and her partner, family, friends, or healthcare professional) not only by the individual herself. These significant "other" individuals were differently positioned concerning their influence on AGYW's decision-making processes, including how they either ignited or challenged AGYW's expression of agency. The studies also showed that AGYW who displayed PrEP persistence had disclosure in common, which is consistent with recent research [152, 220]. While the role of gender (the socially constructed behaviours, attitudes, and relative relationship power ascribed to women) did not impact AGYW's PrEP use as initially assumed, we see it present in some of AGYW's decision-making considerations.

There was evidence, particularly in papers 1 and 4, that when strong personal agency was present in AGYW, it positively affected the PrEP journey trajectory from uptake to persistence. **AGYW's sense of agency was ignited** when they received clear and comprehensive information about PrEP and felt supported by healthcare providers. AGYW shared how this fostered self-efficacy and a sense of health ownership, making them believe that they could decide for themselves whether PrEP was an option for them. This facilitated both PrEP uptake and continued effective use when AGYW had relevant information, e.g. on how to take an intentional PrEP pause and restart PrEP when needed, as seen in Papers 1 and 3. Recent research on the use of patient-centred decision tools that include comprehensive information on PrEP and contraception, including those that assist healthcare providers with counselling, has shown similar outcomes [221-223]. The translation of information into the agency to make effective health decisions might also be reflected in Paper 2. Here, AGYW with low sexual relationship power had an understanding of the effects of their low condom use and unknown partner HIV status and opted to start PrEP as a protective measure. These findings confirm that AGYW (from approximately ages 15-17 years) can make rational, deliberate and thoughtful decisions about their health, like starting PrEP, as stated in recent research on adolescent brain development [224]. In addition, as highlighted in other studies,

AGYW's knowledge of the efficacy of PrEP as an HIV prevention method was underlined throughout the included studies to make AGYW feel empowered in their relationships and feel like they were in control of their sexual health outcomes [125, 225, 226]. For some AGYW, this intrinsic motivation (strong self-determination and autonomy resulting from personal fulfilment of PrEP adherence) meant that minimal adherence support was needed with consequent streamlining of PrEP delivery (Paper 4).

The theoretical framework of this thesis [70] advises that agency is not only operationalised as decision-making but that **AGYW's agency can take the form of negotiation, deception and manipulation**. Similar to previous research, AGYW in this study frequently wanted to disclose their PrEP use to sex partners [137, 138]. However, AGYW in this study demonstrated their intimate knowledge of the exact resistance they would encounter in their relationships and spoke to their sexual partners about PrEP in ways they knew would be acceptable and lessen the resistance. AGYW found it easier to disclose PrEP use to casual or new sex partners than to indicate that they started PrEP within an existing relationship where issues of trust might already be in existence and controversial. AGYW in existing relationships, possibly to counter this difficulty, negotiated their PrEP use by framing it within the context of high sexual violence in their community and the notion that PrEP may protect them against rape from unknown perpetrators (papers 1 and 4).

While the key findings from the included papers showed these instances of strong intrinsic motivation for PrEP use, some AGYW were more extrinsically motivated, where external factors of either rewards, social pressure, or fear of negative consequences influenced PrEP use habits [205]. Extrinsic motivation was more prominent during PrEP uptake and early persistence and was influenced by disclosure, social support, and PrEP stigma. Extrinsic motivation was beneficial when AGYW found affirmation of their PrEP use in peer spaces, including when friends also took PrEP, as was seen in the 'social PrEP-user' in paper 4. **AGYW's sense of agency faltered** in instances of perceived or actual stigma, influencing PrEP uptake, effective use and discontinuation. Stigma was frequently connected to the expected gender roles and sexuality of AGYW, with PrEP being associated with sexual misbehaviour or infidelity, which may also result in violence. Recent investigations confirm that these gender norms around AGYW's sexuality often lead to young women relegating their needs and

desires, including their need to protect themselves from HIV through PrEP use [117, 227-229]. In this thesis, we saw instances where AGYW delayed PrEP uptake until they could establish approval from family or sex partners. This included some AGYW never initiating PrEP or instances of early PrEP discontinuation when a sex partner prohibited use, as some AGYW considered relationship-preservation crucial. In addition, similar to other studies, fear of a partner's reactions caused young women to hide their PrEP use, sometimes leading to multiple missed doses and inconsistent use when they were with their sexual partner [215]. The nature of oral PrEP, needing storage and daily pill taking, often needed disclosure to ensure effective continued use [152, 216, 230]. Therefore, this "user-controlled" but short-acting (daily) HIV prevention method required daily decision-making and multiple instances of exercising some form of agency along the PrEP use journey [231]. Missing pills at some stage during AGYW's PrEP use journey was the norm in the cohort included in this thesis. When AGYW's circumstances changed, including changes in living situation, change in partners, travelling, or even staying over at a sexual partner's place over weekends, the demand on agency changed and sometimes faltered, leading to unintentional PrEP pauses or even discontinuation.

7.3.2 Resources are a potential rather than actualised decision: The role of access

The POWER study aimed to evaluate scalable PrEP delivery approaches to AGYW. While global modelling studies present the effects that oral PrEP may have on the HIV pandemic, real-world implementation shows that adequate uninterrupted access to PrEP will need to be established to reach these goals, especially in AGYW [45, 232]. The theoretical underpinnings of this thesis propose that for AGYW to be empowered to make decisions, a combination of agency, access to resources, and well-being outcomes must be present. However, the framework also suggests that resources (opportunity structures, in this case, PrEP services) in themselves are unlikely to be empowering, but rather, they create the vantage point of alternatives to consider in AGYW's HIV prevention aspirations [69]. Papers 1 and 2 considered the role of gender and agency (personal and relational) on AGYW's PrEP uptake and use, while Papers 3 and 4 studied this in relation to AGYW's PrEP access.

AGYW stated that the choice to take PrEP felt like it was in the realm of possibility when they received adequate information that allowed for informed decision-making regarding

PrEP use and when it felt like the service was focused on them and considered their needs. This was enhanced by services where service delivery platforms were tailored to their needs. Similar to other studies, this included integrated SRH services, convenient services matched with AGYW's circumstances and lifestyle, same-day PrEP starts, and adolescent-friendly clinic staff [106, 233-238].

AGYW's access to PrEP services was constrained at times due to AGYW's limited autonomy in a social context with limited support for their sexual health. AGYW experienced access barriers when they encountered schedule conflicts (school or work commitments) or lacked the financial resources or social freedom to travel to the PrEP delivery site. In this thesis, I also explored whether access to PrEP services was direct or via the authority of another person. As mentioned earlier, when family or sexual partners prohibited PrEP use, this hampered PrEP access and uptake. Towards the end of the POWER study (paper 4) when an expanded differentiated PrEP delivery model was available, however, AGYW described few access barriers related to significant people in their lives. Access constraints were mainly indicated by the "discreet PrEP-users" with controlling partners and elevated community stigma concerns. However, within a differentiated PrEP delivery model, even these AGYW found an acceptable platform for continued PrEP access and use (at least three months of PrEP use as per sub-study inclusion criteria). Furthermore, contrary to initial assumptions, exploration of the influence of AGYW's sexual relationship power on their continued PrEP use (as shown in paper 2) found no significant impact. In addition, convenient, adolescent-friendly, person-centred services with approachable healthcare providers, ensured that there was no perceived health system authority barrier, a known deterrent to AGYW's PrEP access in traditional health service settings [40, 47, 239].

7.3.3 A hierarchy of decisions when it comes to AGYW's HIV prevention

Decision-making contexts come in interminable forms varying in significance, arousal, novelty, and cognitive demands required [240]. In this thesis, we saw examples of AGYW's decision-making agency ignited and situations where this agency faltered, and we saw instances when access to PrEP felt in the realm of possibility for AGYW and occasions when access was constrained. Research on brain development details that around the age of 15-17 years, adolescents reach the cognitive capacity to make deliberate, rational decisions similar

to adults when presented with adequate information in supportive (non-complex) environments [224, 240, 241]. Similarly, in this thesis, we established that AGYW are capable of the deliberate decision to initiate PrEP based on their HIV risk and perception of the necessary steps to effective PrEP use when in consultation with a supportive HCP. However, in line with adolescent brain development research, AGYW showed diminished decision-making performance in response to actual or perceived negative emotional stimuli (increasing complexity) in their social environments, affecting effective persistent PrEP use [240, 242, 243].

The nature of oral PrEP as an HIV prevention method requires daily decision-making and, therefore, the required agency and access to resources to execute this decision-making. AGYW stated the multiple facilitators and constraints they experienced in their PrEP use journey. These decisions were often (consciously or subconsciously) ranked based on AGYW's locus of motivation (extrinsic vs intrinsic), disclosure and social support, need for relationship preservation, potential violence in intimate relationships, community PrEP stigma, rapport with healthcare providers, continuous assessment of HIV risk, demands from social context (work and school), and travel away from home (where PrEP was generally stored and taken). This hierarchy of potentially emotionally stimulating decisions AGYW need to make after the initial deliberate decision to initiate PrEP is highly complex and probably why we see high early PrEP discontinuation in this population [57, 58]. Ultimately, AGYW have the capability to make protective health decisions. The extensive complexity (internal and social) inherent in their lived experiences as young women in Africa, however, constrain AGYW's decision-making, demanding a tailored, supportive approach to HIV prevention that reduces the decision-making burden for AGYW (Figure 11).

This thesis suggests that agency and access to resources exist on a spectrum, as portrayed in Figure 11. While this thesis confirmed that there is an unpredictability to agency (it is not guaranteed in situations of varying significance, arousal, relationship status, etc.), the availability of differentiated PrEP delivery platforms created alternatives (a potential buffer zone) that differently empowered AGYW could locate themselves in. This thesis showed that the number of decisions AGYW have to execute for continued PrEP use can be reduced by providing non-fragmented, integrated SRH services, bringing the services close to where

AGYW naturally gather, or automating PrEP access, for example, through courier PrEP delivery. The number of decisions AGYW need to make will potentially be reduced even further with the introduction of new longer-acting PrEP products [56, 244, 245]. The more options/alternatives AGYW have (PrEP products and PrEP delivery platforms), the fewer and less frequent decisions they will need to make.

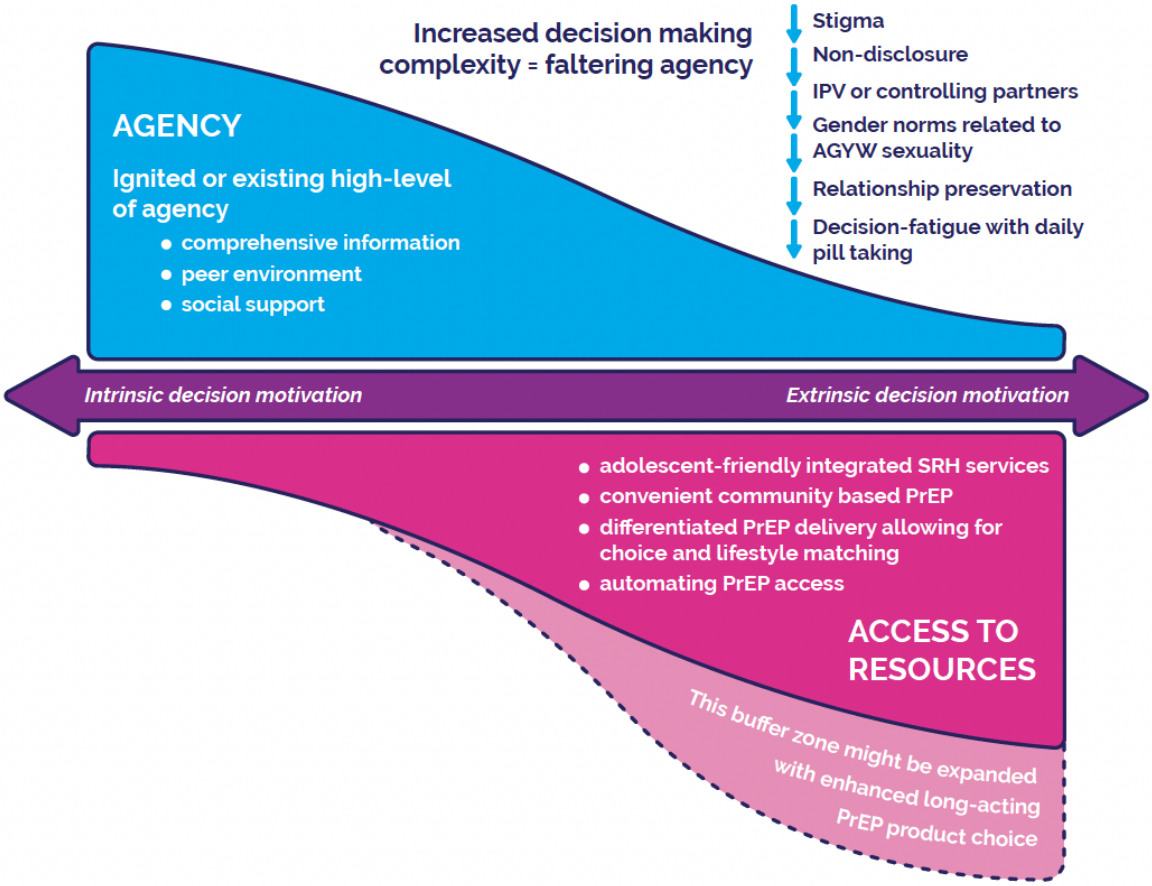


Figure 11. Spectrum of Agency and Access to Resources

7.4 Conclusions and Recommendations

My thesis explores the possible constraints and inequalities in AGYW's expression of agency (personal and relational) or access to resources (PrEP provision in accessible and acceptable service delivery models) in relation to AGYW's ability to make critical and lifesaving decisions regarding HIV prevention. This thesis has contributed to the field of PrEP delivery by expanding our understanding of the continuous, complex and diverse decision-making that needs to occur along AGYW's PrEP use continuum. Furthermore, to my knowledge, it was the first study to profile AGYW PrEP users to better understand decision-making (including the

trade-offs they make) when it comes to engagement with preferred differentiated PrEP delivery models. Notably, the findings presented in this thesis suggest that AGYW are empowered to make positive PrEP decisions when their agency is ignited (informed decision-making, positive extrinsic motivation, etc.) and/or it is enhanced (and buffered) when AGYW are presented with access alternatives to choose from (differentiated models of PrEP delivery). We also saw that AGYW's agency fluctuates (in instances of community stigma, non-disclosure, harmful relationship dynamics, emotional arousal, etc.); however, convenient, accessible, differentiated access to PrEP (bringing PrEP close to AGYW to fit their lives) may compensate for times of limited agency. We also learned that whilst we had the initial contention that sexual relationship power may play a significant role in AGYW's PrEP continuation, no such influence was observed in this study.

The POWER study focused on oral PrEP. Since then, other longer-acting products have become available to AGYW, including the dapivirine vaginal ring (approved in South Africa in 2022) and long-acting injectable cabotegravir (approved in SA in 2022 and pending approval in Kenya). This array of HIV prevention products available, especially longer-acting products may reduce the cognitive burden needed for continued protection. In taking forward these perspectives, several aspects require **further research**. They include:

- Understanding AGYW's decision-making in a choice framework that includes both PrEP product choice and PrEP delivery platform choice, including the development of decision tools to assist both users and providers in connecting AGYW with the best fit of PrEP product-platform combination to optimise effective PrEP use.
- Design (and advocate for) health systems that are feasible to deliver sustainable and affordable HIV prevention options to AGYW within community-based service delivery settings to reduce the burden on agency (and decision-making in this group, including multiple-product therapies (contraception-PrEP combinations).
- Translate AGYW PrEP-user profiles into tailored demand generation messages to optimise PrEP uptake and continuation through a tailored choice presentation.
- Mapping AGYW's trajectories of prevention-effective PrEP use towards developments of reliable and valid measures of PrEP persistence.

- To reach ambitious HIV prevention targets in AGYW, we will need to be nimble by launching research that anticipates evolving individual needs and preferences and harnesses emerging tools such as digital innovation and artificial intelligence.

The discussion section above also leads to several **recommendations for practice** tailored to the context of AGYW in South Africa and Kenya (with papers 3 and 4 of the thesis specifically related to Cape Town, South Africa (and should thus be generalised to other contexts with caution). Specific next steps could include:

- Implementing and evaluating PrEP service delivery options that can engage large populations of AGYW (including those at modest risk for HIV) that allow for simplified, community-based and automated PrEP services such as courier PrEP delivery and the use of telemedicine.
- Developing frameworks and service delivery models for differentiated PrEP engagement and re-engagement (after a PrEP pause or prolonged discontinuation).
- Evaluate PrEP access among gender-neutral youth populations (including heterosexual men, men who have sex with men, transgender people and other key populations) when offered the differentiated PrEP delivery platforms presented in this thesis.

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Supplementary Information 1. Clinical Research Forms for the POWER Study

Participant ID: ☐☐ – ☐☐☐☐ (Site / Participant) Visit Code ☐☐☐

ENROLLMENT

Date of initial visit: ☐☐ ☐☐ ☐☐ (dd mm yy)

A. Demographics

1. Date of birth: ☐☐ ☐☐ ☐☐☐☐ (dd mm yyyy)
2. Age: ☐☐ years
3. Marital status *(mark only one)*: ☐ single, no partner ☐ married (husband has one wife) ☐ widowed ☐ single, with partner ☐ married (husband has multiple wives) ☐ divorced/separated
4. Lives with *(mark all that apply)*: ☐ parent(s) ☐ sexual partner ☐ alone ☐ other family ☐ friend(s) ☐ other, specify: _____
5. # living children: ☐☐

B. Behavioral

1. Sex last 3 months: ☐ yes ☐ no → ***If no, go to item 2.***
   - 1a. If yes, # current sex partner(s): ☐
   - 1b. If yes, sex partner HIV+: ☐ yes ☐ no ☐ don't know
   - 1c. If yes, condoms: ☐ never ☐ sometimes ☐ always
2. Alcohol: ☐ yes ☐ no → ***If no, go to Section C.***
   - 2a. If yes, # drinks/week: ☐☐

C. Medical History

1. Height: ☐☐☐ cm
2. Weight: ☐☐☐.☐ kg
3. STI symptoms now: ☐ yes ☐ no
4. Ever pregnant: ☐ yes ☐ no
5. Pregnant now: ☐ yes ☐ no → ***If no, go to item 6.***
   - 5a. If yes, EDD: ☐☐ ☐☐ ☐☐ (dd mm yy)
6. Breastfeeding now: ☐ yes ☐ no
7. Trying to get pregnant: ☐ yes ☐ no

D. Family Planning

1. Family Planning—on now? ☐ yes ☐ no → ***If no, go to item 2.***

   If yes, method (*mark all that apply*):

   - ☐ 1a. oral
   - ☐ 1b. ring
   - ☐ 1c. injectable
   - ☐ 1d. implant
   - ☐ 1e. IUD
   - ☐ 1f. emergency contraceptive
   - ☐ 1g. diaphragm/cervical cap
   - ☐ 1h. tubal ligation/hysterectomy
   - ☐ 1i. condoms

2. Family Planning—wants today? ☐ yes ☐ no → ***If no, go to Section E.***

E. PrEP

1. Enrolled in HIV prevention trial: ☐ yes ☐ no
2. Prior PrEP study: ☐ yes ☐ no
3. Prior PEP use: ☐ yes ☐ no
4. Taking PrEP now: ☐ yes ☐ no
5. PrEP protects from HIV: ☐ yes ☐ no ☐ don't know
6. Medically eligible for PrEP: ☐ yes ☐ no
7. Signs/symptoms acute HIV: ☐ yes ☐ no
8. Willing to start PrEP: ☐ yes ☐ no, not at all ☐ no, thinking about it
9. Received pre-PrEP counseling: ☐ yes ☐ no ☐ not applicable
10. Accepted PrEP prescription today: ☐ yes ☐ no ☐ not applicable

F. Lab

1. HIV: ☐ positive ☐ negative ☐ indeterminate ☐ not done
2. Pregnancy test: ☐ positive ☐ negative ☐ not done
3. Gonorrhea: ☐ result pending ☐ not done
4. Chlamydia: ☐ result pending ☐ not done
5. HBV: ☐ result pending ☐ not done
6. Creatinine: ☐ result pending ☐ not done
7. Blood collected for DBS: ☐ yes ☐ no

TAKING PrEP AND HIV PREVENTION—ENROLLMENT

☐ Form not administered → ***End of form.***

Visit date: ☐☐ ☐☐ ☐☐ *dd mm yy*

1. Does anyone know you will be taking PrEP? ☐ yes ☐ no → ***If no, go to item 2.***

   1a. If yes, who? *(Mark all that apply)* ☐ sexual partner ☐ friend ☐ family ☐ other, specify: _____

2. How worried are you about getting HIV in the next year? **[Please read responses to participant]** ☐ not worried ☐ some worry ☐ a lot of worry

3. How worried are you about side effects from PrEP? **[Please read responses to participant]** ☐ not worried ☐ some worry ☐ a lot of worry

4. What fears or concerns do you have about taking PrEP every day? *(Mark all that apply)* **[Please read responses to participant]**

   ☐ *no concerns*
   ☐ *size/taste of pills*
   ☐ *people should not take drugs unless they are sick*
   ☐ *people might think I have HIV*
   ☐ *my partner will be upset*
   ☐ *effect on my fertility*
   ☐ *burdensome to take the tablet every day*
   ☐ *other, specify:*_____

ALCOHOL AND RECREATIONAL DRUG USE—ENROLLMENT

☐ Form not administered → ***End of form.***

Visit date: ☐☐ ☐☐ ☐☐ *dd mm yy*

1. Have you drunk any alcohol in the past year? ☐ yes ☐ no → ***If no, go to item 2.***

   1a. If yes, during the last year, have you had a feeling of guilt or remorse after drinking? ☐ yes ☐ no

   1b. If yes, during the last year, has a friend or family member ever told you about things you said or did while you were drinking that you could not remember? ☐ yes ☐ no

   1c. If yes, during the last year, have you failed to do what was normally expected of you because of drinking? ☐ yes ☐ no

   1d. If yes, during the last year, have you taken a drink in the morning when you first got up? ☐ yes ☐ no

2. Have you ever smoked cigarettes? ☐ never ☐ yes, ≤3 months ago ☐ yes, >3 months ago

3. Have you ever used other recreational drugs? ☐ never ☐ yes, ≤3 months ago ☐ yes, >3 months ago
   → ***If never, end of form.***

   3a. If yes, which one(s)? (*Mark all that apply*)

   ☐ *khat/cat/miraa*
   ☐ *marijuana/bhangi/dagga/cannabis*
   ☐ *heroin/brown sugar*
   ☐ *cocaine*
   ☐ *kuber*
   ☐ *shisha*
   ☐ *crack cocaine*
   ☐ *whoonga/nyoape*
   ☐ *crystal meth/tix*
   ☐ *mandrax*
   ☐ *ecstacy/MDMA*
   ☐ *other, specify:* _____

SEXUAL RELATIONSHIP POWER

☐ Form not administered → ***End of form.***

Visit date: ☐☐ ☐☐ ☐☐
dd mm yy

READ: I am now going to ask you some questions about your primary sexual relationship.
(If the participant does not identify a primary sexual relationship, check here.) ☐→ ***End of form.***

[Please read responses to participant]

1. If I asked my partner to use a condom, he would get violent.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
2. If I asked my partner to use a condom, he would get angry.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
3. Most of the time, we do what my partner wants to do.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
4. My partner won't let me wear certain things.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
5. When my partner and I are together, I'm pretty quiet.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
6. My partner has more say than I do about important decisions that affect us.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
7. My partner tells me who I can spend time with.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
8. If I asked my partner to use a condom, he would think I'm having sex with other people.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
9. I feel trapped or stuck in our relationship.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
10. My partner does what he wants, even if I do not want him to.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
11. I am more committed to our relationship than my partner is.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
12. When my partner and I disagree, he gets his way most of the time.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
13. My partner gets more out of our relationship than I do.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
14. My partner always wants to know where I am.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
15. My partner might be having sex with someone else.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*
16. My partner gives me money or supports me financially.	☐ *strongly agree*	☐ *agree*	☐ *disagree*	☐ *strongly disagree*

Supplementary Information 2. PrEP-user IDI guide

Thematic Guide: IDI with Young Women
Version 1.5, 25 March, 2019

Theme 1: Knowledge of PrEP *[For initial acceptors, restarters and refusers]*

1. How did you hear about PrEP at first? What do you know about PrEP?
    a. Where did you hear about or who told you about PrEP?
    b. Did you hear anything about PrEP in the media? (e.g. radio, advertising, social media?)
    c. What have you heard about PrEP?
        i. Who can take PrEP and why?
        ii. How is it taken?

2. What interested you about PrEP?
    a. What made you want to learn more about PrEP?

3. What encouraged you to come to the clinic?
    a. Was there anyone who motivated you to come?

Theme 2: PrEP Decision *[For initial acceptors/refusers, restarters and late acceptors]*

I'd like to ask about your initial decision about PrEP:

4. How did you decide if taking PrEP was right for you or not at the beginning?
    a. What were the pros and cons you considered when making the decision?
    b. How did people in your life influence your decision about whether or not to take PrEP? (e.g. partner, family, or friends)
    c. What health concerns did you consider when making your decision?
        i. Concerns or risk of getting HIV
        ii. Concerns from taking PrEP (side effects, long term health effects)
    d. How did the requirements for getting PrEP and taking it regularly influence your decision of whether or not to use it?
        i. ***[If this question is not clear, offer examples:]*** Accessing PrEP, time spent at the clinic; privacy; ability/willingness to take daily; forgetting; pill storage, pill burden, HIV testing

5. How did information from clinic staff influence your decision about PrEP?
    a. What did the counselors or the health provider tell you?
    b. Did you talk about any of your concerns about PrEP?

PrEP decision tool*:* Let's discuss a tablet/Ipad program you might have used while you were waiting for your appointment, which we're calling the "PrEP decision tool".

6. Did you use the decision tool? ***[If she did not use the tool, skip the rest of this section]***

7. How useful was the tool in helping you make decisions about taking or not taking PrEP? Please describe:
    a. Specifically, what section within the tool helped you decide?
    b. What information from the tool was the most useful to helping you to decide? Why?

8. What can be changed or improved with the tool?
    a. The content or sections of the tool itself ***(if participant has trouble remembering tool components, you may remind her of these)***:
        a. 1.0-3.0 **Opening screens** (including "Reasons Why")
        b. 4.0 **Options**: PrEP, Condoms, Decreasing my sex partners, Knowing if my partner has HIV, If my partner has HIV, he takes HIV medicines
        c. 5.0 **PrEP Versus PEP**
        d. 6.0-11.1 **Let's talk about PrEP** menu: What is it, Why take PrEP, How well does it prevent HIV, How do I take PrEP, What you need to know about PREP, True and False, etc.
        e. 12.1 **Learn More** – checking off options to talk to the clinic staff about
        f. 13.0 **Family planning**
    b. When and where it is used

[For initial refusers or if she states that didn't use PrEP]:

9. Can you imagine a situation in which you may want to use PrEP? If yes, please describe to me.

[For restarters and late acceptors only]:

10. What made you change your mind and decide to start using PrEP?
    a. Did you find out any information, including rumors, that made you change your mind about using PrEP? Could you explain?
    b. How did people in your life influence your decision to change your mind about using PrEP? (e.g. partner, family, or friends)
    c. Do you think a change in your ideas about your level of risk influenced your choice to start using PrEP? How?
        i. Risk of getting HIV
        ii. Risks from taking PrEP (side effects, long term health concerns)
    d. Did any other change in your life make it easier to take PrEP? (household, work, financial, other) How?
    e. Additional Probes for restarters:
    - How long were you off PrEP? How long since you resumed PrEP use?
    - Were there any new situations or change in circumstances that gave you motivation to restart?

11. Did anything happen at the clinic that made you decide to start using PrEP? Tell me more.

[For all participants]:

Theme 3: Clinic Experience

12. Now I would like to talk about your clinic visits. How easy or difficult was it to come to the clinic? What made it easy or difficult?

13. Describe what happens when you go to the clinic for a PrEP visit.
    a. How easy or difficult was it to get services and PrEP at the clinic? What made it easy or difficult?
    b. If you've gotten refills, how was it when you went to get refills? Where did you go?

14. Can you describe counseling and support you received on how to take PrEP?
    a. What were you told?
    b. What were the things you liked about it?
    c. What were the things you disliked about it?
    d. Do you feel they addressed your questions and concerns? Could you give me an example?

15. How do you think you were treated during this clinic visit?
    a. Can you give an example of what was good or bad?
    b. Do you feel that you have received any discrimination or judgment from clinic staff? If so, can you give an example?

16. How comfortable were you in discussing topics related to sex, HIV, PrEP and family planning with the clinic staff you interacted with during your POWER visit?
    a. Can you give an example of a time when you felt comfortable or uncomfortable talking about these topics? What makes/can make you feel more at ease?
    b. How comfortable were you asking the study staff questions?

Theme 4: Experiences using PrEP *[For anyone who took PrEP: initial acceptors, late acceptors, restarters, persistors, non-persistors, and seroconverters]*

Now I would like to talk about your experience using PrEP.

17. How has taking PrEP been for you?
    a. Tell me about the last time you took a pill… when was it, at what time, what were you doing, and where were you?
    b. Where have you been storing the pills? Any challenges with storage?

18. How has taking PrEP made you feel about yourself?
    a. How have you felt physically? (Any side effects? Any positive effects)
    b. How have you felt emotionally?
    c. How did you feel (emotionally/physically) during the PrEP pause?

19. How often do you take PrEP?

a. What are the things that have helped/made it easy for you to take PrEP? Please describe any strategies that you have used to help you take PrEP.
b. What are the things that have made it difficult for you to take PrEP?
    i. How have you dealt with these challenges?

20. How well do you think you are protected with the # of doses you've taken?

21. Tell me about a time you missed taking your PrEP pill.
    a. What caused you to miss doses?
    b. Did you talk to the clinic staff about it? If no, why not? If yes, what did they say? Was it helpful?
    c. What could help you to prevent missing doses?

[For restarters, non-persistors or for persistors who reveal gaps in use]

22. If you stopped using PrEP for any amount of time, or didn't take pills you picked up, what made you stop?
    a. Did you find out any information, including rumors, that made you change your mind about using PrEP? Could you explain?
    b. How did people in your life influence your decision to stop using PrEP? (e.g., partner, family, or friends)
    c. Were there any changes in your life (in your household, work, income, other) that made it harder to take PrEP?
    d. Do you think a change in your ideas about your level of risk influenced your choice to stop using PrEP? How?
        i. Risk of getting HIV
        ii. Risks from taking PrEP (side effects, long term health concerns)
    e. Was taking a pill daily difficult? Please describe your difficulties.
    f. Did you use other forms of protection while on the PrEP pause?
    g. Was stopping PrEP an active, intentional choice? Or was it due to circumstances out of your control?
    h. Are there any other reasons that caused you to stop taking PrEP?

23. Did anything happen at the clinic that made you decide to stop using PrEP? Tell me more.
    a. Did you continue to visit the POWER clinic during your PrEP pause?
    b. Did you have any worries about returning to the clinic after your PrEP pause?

24. Do you think you will use PrEP in the future? Why/Why not?
    a. Are there any barriers or facilitators in your life and personal relationships that act as barriers or facilitators to PrEP use?
    b. After restarting, what are your future goals for PrEP use? How can the clinic team support you?

Theme 5: Relationships

25. Now let's talk about your relationships. Are you currently in any relationships? (Main partner, casual partners)
    a. Tell me about your main partner and what your relationship is like.
    b. Do you have other partners?
        i. Tell me about your relationships with them.
    c. In the relationship(s) you're in, have you ever talked about HIV with your partner(s)?
        i. ***[If yes]*** Tell me more about the discussions you've had.
        ii. Have you ever had an HIV test together with your partner(s)?
            a. ***[If yes]*** Do you know your partner(s) HIV test status?
    d. Have you ever experienced any form of violence in your relationship(s)? (Physical, emotional, sexual, psychological)

26. Have you told anyone else that you are using PrEP or that you were thinking about using PrEP? Why/why not?
    a. ***[If yes]*** Who have you told? (partner, friends, family) And how did that go?
        i. Can you tell me about how people in your life have reacted to your use of PrEP?
        ii. Whose reaction has been most important?
        iii. Who supported you in taking PrEP? How?
        iv. Who discouraged your use of PrEP? What did they say?
        v. Who has supported your decision to restart PrEP? Did anyone oppose it?
        vi. Is there anyone important that you are hiding it (PrEP) from?
            1. Is there anyone important that you didn't tell? Why?
    b. ***[If no]*** What made you decide to keep your use of PrEP a secret?

27. What kind of support or advice have you received from clinic staff on talking about PrEP to your partner(s)/family?
    a. What did they tell you? Did they say how or whether to tell partner/ family?
    b. How did they address the challenges you faced?
        i. In what ways was the support helpful/adequate?
        ii. How could the support be improved?
    c. What kind of information about PrEP was available for you to give to partner(s)/family?
        i. What other resources would you like to give or to share with your partner(s)/family?

[If she took PrEP at all]:

28. Has using PrEP affected any of your family relationships? How?
29. Has using PrEP affected your sexual relationships? How? (e.g. decision-making, empowerment, communication)
    a. How about condom use with sexual partners? Has that changed?

Theme 6: Stigma and Discrimination

30. Now I would like to talk about what people in the community are saying about PrEP. Can you tell me about any things you have heard in your community about PrEP or this study? ***[This is however she defines community – can be neighborhood, peers, etc]***
    a. What kinds of ideas or rumors have you heard circulating?
    b. Who have you heard these from?
    c. How do you feel about what you've heard?
    d. ***[If untrue]*** What do you think is the best way to address these ideas/rumors?
        i. Who should address these?
        ii. Is there anything the clinic has done or could do to address community rumors or stigma?

[If she used PrEP]:

31. Can you tell me about any positive or negative social experiences you have had for using PrEP?
    a. What do they say?
    b. Who says those things? Tell more about these types of people. (Partner, family, friends, community, health care workers)
    c. How do you feel about what they say?
        i. Do you think what they say is true or false? Why?

Theme 7: Seroconversion ***[For seroconverters only]***

If it's okay with you, I'd like to talk about your HIV status.

32. What in your view might have contributed to you getting HIV?
    a. Can you tell me more about any particular time or event when you think you may have gotten HIV?
    b. Before getting infected, did you experience any changes in your personal life, behaviors, or circumstances that could have increased your chances of getting HIV?
        i. Changes in PrEP adherence
        ii. Changes in other prevention behaviors
        iii. Changes in relationships
    c. How do you feel being in POWER impacted your risk of getting HIV?
    d. How do you feel being on PrEP could have influenced your chances of getting HIV?

33. What support did you receive from the clinic staff when you got your HIV test results?
    a. Was it helpful? If yes, how? If not, how could it improve?

34. Tell me about your experiences with accessing HIV care.
    a. Have you been referred to an HIV care clinic?
    b. Have you been to an HIV care clinic yet?
        i. ***[If yes]*** How did the PrEP clinic staff support you in going there?
        ii. Are you currently on ART?

iii. ***[If yes]*** How was your experience with starting ART?

Theme 8: Advice *[**For Persistors, Non-Persistors, restarters, and Seroconverters who have been in the study for 3 months or more**]*

Now I would like to learn more about what you have said, or would say, to other young women about PrEP.

35. Have you ever advised other young women about using PrEP?
    a. ***[If yes]*** Who have you talked to? In what venues or spaces? (e.g. at school, on social media, in community groups)
    b. ***[If no]*** Why not?

36. What kind of advice have you given to other young woman about PrEP?
    [Interviewer: If the participant has never given advice, ask her to imagine what she might say if she were asked.]
    a. Should she take it?
    b. What should she know?
    c. How should she address any challenges that may come up using PrEP?
    d. Would you advise her to tell other people (partner, family, friends) about her PrEP use?
    e. What kind of changes in her life should she expect if she uses PrEP?
    f. What kind of advice would you give her about using condoms while using PrEP?

Theme 9: PrEP in the future *[**For persistors, non-persistors, restarters, and seroconverters who have been in the study for 3 months or more**]*

Now I want us to talk about what PrEP delivery should look like in the future.

37. Which locations or surroundings would be convenient and safe to go and get PrEP?
    a. How far would you be willing to travel to get PrEP?
    b. How long would a reasonable wait time be for a PrEP clinic appointment be?
    c. What locations and hours would be most convenient to get PrEP?

38. How can the clinic experience be made better?
    a. How should the clinic procedures be made better?
    b. How should the clinic space or environment be made better?
    c. How should the procedures for refills be made better?

39. What kind of provider would you prefer to go to for PrEP prescriptions and refills?
    a. Please describe to me your experience where you felt comfortable with a provider ***[To determine the characteristics of providers that she is comfortable with]***
    b. What would you change about clinic staff to make your experience more comfortable?

40. How could the clinic staff help young women store PrEP safely and privately at home?

41. What kind of information or counseling do you think could be helpful for young women who want to take PrEP?

42. What kind of social support from partner, friends, family, young women need to help them take PrEP?

[All participants]

Theme 10: As we finish

43. Do you have any other thoughts or questions? ***[Write down questions and make sure to answer them or refer the participants as needed].***

44. Are there any other questions we should have asked about how to improve delivery of PrEP or ease of use?

Supplementary Information 3. PrEP-user FGD guide

Thematic Guide: Focus Group Discussions with Young Women
Version 2.0; 19 April 2019

Theme 1: PrEP Journey: *To begin our conversation today, we'd like you to think about the following situation:*

Lebo [or alternate name appropriate for specific location], a young woman living in your community [village/township], is thinking about whether she wants to use PrEP.
We're now going to ask you various questions about Lebo and her PrEP user journey. Feel free to each choose different responses, there are no right or wrong answers. Use your responses to these first questions to help you think about what Lebo might do at each point in her PrEP user journey.
Let's first describe who Lebo is…

- Does Lebo go to school and/or is she working? Who does she live with (husband/sex partner or parents/family members)?
- How did she find out about PrEP in the first place? What did she hear? From whom?
    - Does she know if any of her friends are using PrEP? What do they say about it?

Now let's talk about what might come next after Lebo started thinking about whether or not to use PrEP.

- Why would she want to use PrEP? Why would she not want to use PrEP?
- Did she talk to other people about the possibility of her taking PrEP? What do you think they would have said?
- What does she need to consider before making her decision about whether to use PrEP?
    - Where would she find more information about PrEP?

Lebo [or alternate name] decides she wants to use PrEP.

- What was the primary reason she decided to use PrEP now?
- What concerns does she still have about PrEP?
- Where does she go to get PrEP? (If she says the POWER clinic, what if the POWER clinic didn't exist, where would she prefer to get PrEP?)
    - Why would she choose this place?
    - Any challenges with going there?
    - [If they haven't already talked about their personal experience] What about for you personally, what was it like for you to make the decision to start using PrEP?

Lebo [or alternate name] is now taking PrEP. Let's talk about what that's like for her.
[General experience, Disclosure & Stigma:]

- How would Lebo describe her experience of using PrEP?
  - What about taking PrEP does she find easy? Difficult? Please describe.
- Does she tell other people that she is on PrEP? Who? Why?
  - How would they react? What would they say? What would they do?
  - Is she feeling judged? By whom?
- Who does she decide (among her close friends/family/sex partner) **not** to tell about her PrEP use? Why?
- How has your experience been different than Lebo's?

[Acceptability & Adherence:]

- How does she remember to take her pills? Does she always take them? Does she forget? What makes her forget?
  - What support might she need to use PrEP as instructed?
- What is keeping her motivated to use PrEP?
  - Does she have any beneficial (positive) side effects from PrEP?
- What challenges might come up?
  - Does she have any unwanted (negative) side effects?
  - What about unwanted social experiences (stigma, discrimination, partner abuse)?
    How can she overcome those?
- When would Lebo pause using PrEP? For how long? Why the break? How often does she take breaks?
- [If haven't already talked about their personal experience] What about for you personally, what would lead you to take a break from using PrEP?
- Have you ever encountered stigma as a result of taking PrEP?
  - If yes, please describe the experience. Who was involved? What did they say? Where did this happen? How did it make you feel?

Lebo stops using PrEP.

- How long had she been using PrEP?
- What reasons or in what situations made her stop?
  - Were there other life situations that were more important to her than HIV prevention at that time?
- Who influenced her decision?
- How would she feel about herself after she stopped?
- What difference is there between stopping and taking a break from PrEP?
- [If haven't already talked about their personal experience] What about for you personally, what would make you stop using PrEP?

Lebo decides to start PrEP again.

- For how long was she off PrEP?
- What would lead her to decide to take PrEP again?

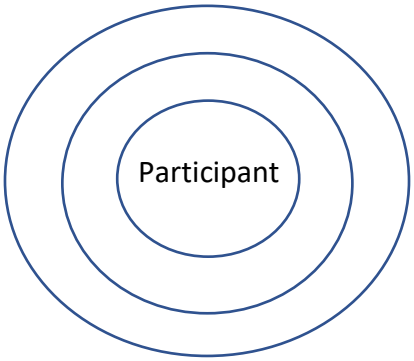
        - Is this the same or different from what led her to take PrEP the first time?
    - What advice would you give her about re-starting PrEP?

Thinking about your experience in POWER:

- What other personal experiences have you had with PrEP that is similar or different than Lebo that you'd like to share?
- When this study ends, are you still interested in taking PrEP? Why or why not?
    - [If yes] How do you plan to continue accessing PrEP?

Theme 2: Social Networks & Support Mapping: *Next, we'd like you to learn more from you about the people who are most important to you regarding your PrEP journey:*

- I have given each of you a piece of paper with "me" in the center and three circles drawn around it since you are the center of your social world.
- Using the stickers provided to you (e.g. best friend, friend group, mother, father, other family, sex partner, clinic counselor, doctor/pharmacist, religious leader, clinic staff, BLANK stickers to add others) on the inner circle place the stickers of the people who you think **would have or have had** the **biggest influence (positive or negative)** on your ability to take PrEP for as long as you are interested in taking it, **regardless of whether you have told them about your PrEP use in real life or not**. You can place as many or as few (even none) as you'd like.
    - Write in any additional people who have been or would be influential of your PrEP journey who aren't already covered by those listed on the stickers.
- Next, on the middle circle, place the stickers of the people who have or would have the next amount of influence.
- Finally, on the outer circle, place the stickers of the people who have or would have the least amount of influence on taking PrEP.
  Now, **marking only the stickers for the people who HAVE HAD influence on your PrEP user journey:** Use the RED highlighter to highlight those who had a negative influence on your PrEP use. Use the BLUE highlighter to highlight those who had a positive influence. If someone was influential both positively and negatively, highlight with both colors.



[After everyone has finished placing their stickers] **Let's start with the people you put in the inner circle.**

- Why are they the most influential? Are they supportive of your PrEP use? What have they said about it?
- What information do you think they need to be given in order to support your PrEP use?
    - Who should provide that information to them?
- What did you tell them? What would you like to tell them about your PrEP use that you haven't already? How important is it to tell them about your PrEP use?
    - What would you want them to do or say about your PrEP use?

Now let's talk about those whom you placed in the middle circle.

- Are they supportive of your PrEP use? What have they said about it?
- What information do you think they need or would need to support your PrEP use?
    - Who should provide that information to them?
- What did you tell them? What would you like to tell them that you haven't already? How important is it to tell them about your PrEP use?
    - What would you want them to do or say about your PrEP use?

Now let's talk about those whom you placed in the outermost circle.

- Are they supportive of your PrEP use? What have they said about it?
- What information do you think they need or would need to support your PrEP use?
    - Who should provide that information to them?
- What did you tell them? What would you like to tell them that you haven't already? How important is it to tell them about your PrEP use?
    - What would you want them to do or say about your PrEP use?

Theme 3: Wrap-up: *Before we end our conversation*,

- Is there anything else you'd like to share with me?
- Are there any questions you would like to ask me?

Thank you all very much for participating in this discussion today.

Supplementary Information 4. Differentiated model IDI guide

In-depth Interview (IDI) Guide Questions for young women

1. I'd like to start by first hearing a bit more about where you live. What is life like for a young woman in your community?
    - What are the highlights and what are the challenges?
    - Who influences sexual and reproductive health decisions for young women (such as whether to have sex; contraception use; HIV prevention)

2. What have you heard people say about PrEP in your community (if anything)?
    - Is there widespread knowledge/ awareness of PrEP/ PrEP research or other medical research in the community?
    - What are your reactions to what you have heard? How does this affect you?
    - What made you decide that PrEP was right for you?

3. In this study you are allowed to pick up your PrEP refills from different platforms including the Tutu Teen Truck, the Weltevreden clinic/local DoH clinic, the POWER adherence club, and the Iyeza courier service. Which of these PrEP pick-up platforms did you use and what motivated you to use this specific method?
    - How easy/difficult was it to access these services?
    - What are some of the challenges/barriers that you experienced which made it difficult for you to access this platform?
    - How did you overcome these challenges? What strategies did you try to ensure that you take your PrEP / come to study visits?
    - What are some of the things that made it easier/helped you to access/take the PrEP?
    - Overall, what would you say are the pros and cons of the specific platform you used?

4. Did you tell anyone that you were taking PrEP?
    - Is there a reason you told someone / did not tell anyone about it?
    - Did you receive any support from the person you told? What kind of support did you receive? How did that affect your PrEP use?
    - Did you receive any negativity from person that you told, what did they say? How did that affect your PrEP use?
    - How did the level of support you received affect which of the PrEP pick up platforms you used?

5. Tell me a bit about your living situation. Please describe the people you live with in your household.
    - Who do you live with?
    - What's your relationship to them?

- What aspects of your home made it easy or difficult to use PrEP?
    - How did the amount of privacy or lack of privacy you had affect your use?
    - How did the people who you live with influence your use?
- How does your living situation/people you live with influence which PrEP pick up platform you access?

6. I would also like to hear about your relationships. Let's start by having you think about your current relationship. What is it like?
    - How and where did you meet?
    - What attracted you to him/her?
    - What does your family think about your relationship?
    - What do your friends think about the relationship?
    - In your relationship who makes decisions about having sex? (incl. type of sex, timing of sex, frequency of sex, condom use)
    - Can you describe a situation where you made a decision around sex with your partner?
    - [*If they've had more than one partner*] How does it differ with different types of partners (e.g. casual, one night stand, long term, paying client)?
    - How does your partner influence your use of PrEP? Does your partner know you are taking PrEP? If so, what is your partner's opinion of PrEP?
    - How does your relationship influence which PrEP pick up platform you access?

7. Can you imagine yourself ever using one of the other PrEP pick-up platforms (name the ones the participant did not use)?
    - If yes, can you describe the scenario in which you could imagine wanting to use one of these services?
    - If no, what are the barriers/challenges in using each of the other PrEP pick-up platforms?

8. Where else do you think PrEP should be made available to young women like yourself?
    - Where would be most convenient or comfortable for you to get it?
    - What do you suggest other young women should do to successfully access and take PrEP?

[i] https://www.youtube.com/watch?v=c-vDZMzuLvY
[ii] Version 6.1.18, Los Angeles, CA: SocioCultural Research Consultants, LLC www.dedoose.com