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HIV Pre-Exposure Prophylaxis Uptake and Continuation Among 15-24-year-old Women in Mulago, Uganda

Dithan Kiragga
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Walden University

College of Health Sciences and Public Policy

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Dithan Kiragga

has been found to be complete and satisfactory in all respects,
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the review committee have been made.

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Walden University
2026

Abstract

HIV Pre-Exposure Prophylaxis Uptake and Continuation Among 15-24-year-old Women

in Mulago, Uganda

by

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MS, University of London, 2010

MPH, University of Liverpool, 2005

MBCHB, Makerere University, Kampala, 1995

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

February 2026

Abstract

Young women in Uganda face disproportionately high HIV risk compared to the general population. While pre-exposure prophylaxis (PrEP) demonstrates proven effectiveness, poor uptake and nonadherence limit its potential impact. This study examined the relationship between perceived HIV susceptibility, PrEP benefits, behavioral risk factors, service delivery models, and PrEP uptake and continuity among young women aged 15–24 in Uganda, guided by the health belief model. Data were abstracted from surveillance records at Mulago National Referral Hospital’s STI clinic from January 2024 to September 2025. Of $N=23,765$ young women screened (median age 21 years; 98.9% single or separated; 48.7% with primary education), 99.5% accessed screening through community-based services. However, only 3,958 (16.7%) initiated PrEP. Perceived HIV susceptibility was negatively associated with PrEP uptake ($aOR = 0.60$, 95% CI 0.55–0.65). All sociodemographic characteristics except marital status were significantly associated with PrEP uptake. HIV and STI incidence rates were 1.10 (95% CI 0.71–1.71) and 7.52 (95% CI 6.35–8.92) per 100 person-years at-risk, respectively. STI incidence was 61% ($aIRR = 1.61$, 95% CI 1.14–2.29) higher among participants with post-primary education than among those with primary education or less. Participants who were not married had a three-fold increase ($aIRR = 3.25$, 95% CI 1.32–7.99) in HIV incidence compared to those who were married. Only 117 (25%) were active on PrEP after 12 months, equivalent to a continuity rate of 6.48 (95% CI , 5.41 –7.77) persons per 100 person-years. The identified gaps indicate the need to strengthen PrEP adherence support and address misconceptions about HIV risk among young women in Uganda.

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Dedication

I dedicate this dissertation to my wife, Dr. Agnes Najjuko Kasirye Kiragga, and our children, Angel Donna Nantege, Isabella Favour Nabacwa, Jed Dithan Kiragga, and Shona Hannah Kirabo.

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Part 1: Overview

Introduction

The implementation of oral pre-exposure prophylaxis (PrEP) in Uganda, starting in 2017, faced significant challenges, hindering its effectiveness as a preventive measure against HIV transmission. Despite the revised national HIV guidelines recommending PrEP for HIV-negative individuals at substantial risk, access, uptake, and continuity remain significant obstacles. Studies have highlighted high HIV prevalence rates among vulnerable populations such as fisher folks (22%), truck drivers (25%), sex workers (37%), and people who inject drugs (16.7%), yet less than half of those at risk accept PrEP as a prevention method (Mayanja et al., 2022; Muwonge et al., 2020). Concerns over uptake and continuity further underscore the need for comprehensive interventions to address barriers to PrEP uptake and continuity.

As a relatively new program, PrEP delivery in Uganda began with a few accredited sites, focusing on all eligible clients. HIV prevention interventions targeting young women have only recently started integrating PrEP, as the focus has traditionally been on providing condoms, voluntary medical male circumcision (VMMC), family planning (FP), and STI treatment. The country established a national PrEP task force to streamline and coordinate the nationwide rollout of PrEP. The U.S. President's Emergency Fund for AIDS Relief (PEPFAR), Global Fund, and other stakeholders provided funding to scale up PrEP across accredited sites. Despite these significant investments, there continues to be a persistently low uptake of PrEP among young women aged 15-24 (Mayanja et al., 2022; Kyegombe et al., 2020), who account for a

significant proportion of new HIV diagnoses in the country. PrEP uptake remains suboptimal among this demographic, highlighting the need to address underlying barriers such as stigma, myths, misconceptions, and logistical challenges hindering access and utilization of this preventive measure.

Specific Problem

This dissertation explored and addressed the persistent barriers to the uptake and continuity of PrEP among young women in Uganda aged 15–24 years, a high-risk group for HIV, and proposed strategies to optimize PrEP uptake and continuity to improve its impact on HIV prevention efforts. Uganda faces a generalized HIV epidemic, with certain subpopulations, particularly adolescent girls and young women aged 15-24 years, disproportionately affected by HIV. Data from Uganda Population-Based HIV Impact Assessment (UPHIA) show that HIV prevalence in this age group is significantly higher than in the general population (Ssemata et al., 2024). Lunkuse et al. (2022) found that among fishing communities in Rakai, Uganda, there is an HIV prevalence rate of 19.7% among 15-24-year-olds, with women making up most of these numbers. Despite this, the uptake of HIV prevention services remains low, particularly among young women engaged in sex work, who are considered one of the highest-risk groups for HIV transmission in Uganda (Barnabee et al., 2023; Rutstein et al., 2020).

Moreover, studies consistently show that a substantial proportion of young women, particularly female sex workers (FSWs), enter sex work during adolescence (Dayton et al., 2023; Gombe et al., 2020). In Uganda, young women involved in high-risk sexual behavior are up to seven times more likely to contract HIV compared to their

peers (Barnabee et al., 2023; Thomas et al., 2024). These statistics underscore the need for evidence-based targeted HIV prevention interventions that are tailored to the unique needs of young women, especially in regions with high HIV prevalence.

The use of both oral and injectable antiretrovirals as PrEP is effective in preventing HIV across all sexual groups (Sidebottom et al., 2018). Oral prep is safe and effective when taken correctly, with very minimal resistance to HIV 1. However, the efficacy of oral preps is highly dependent on adherence, with low adherence rates noted among young women. A higher rate of adherence was noted among female sexual workers in Uganda. Higher adherence is associated with an increased risk perception of PrEP effectiveness in the real world. Oral PrEP has been less effective in young people and people of lower socioeconomic status, with these reporting higher discontinuation rates.

Existing research has identified several barriers to PrEP uptake, such as fear of side effects, stigma, and limited awareness of HIV risk. However, there is a gap in studies that explore the intersection of these barriers, particularly among young women aged 15-24. This demographic plays a key role in driving the HIV epidemic in Uganda. Most studies have either focused on isolated factors or on other groups, such as men who have sex with men (MSM) or adult women (Diabaté et al., 2021; Mbotwa et al., 2022). As a result, there is a significant gap in understanding the challenges young women face in accessing and continuing PrEP.

This study is therefore necessary because it fills a critical gap in the current literature on PrEP uptake and continuity in Uganda and similar settings. While

researchers have explored strategies to increase PrEP uptake (Muwonge et al., 2020; Sensalire et al., 2024), most have not comprehensively addressed the specific barriers faced by young women. This group remains underrepresented in HIV prevention research. Furthermore, studies have often focused on individual factors without considering the broader socioeconomic, cultural, and structural influences that intersect to shape young women's health behaviors. For instance, Sensalire et al. (2024) highlighted the effectiveness of a multi-tiered approach to addressing barriers to PrEP, including community engagement and training for health workers. Similarly, Muwonge et al. (2020) emphasized the role of healthcare providers in improving awareness and uptake. However, there is a need for more nuanced studies that focus specifically on young women whose experiences with PrEP are shaped by factors like gender inequality, socioeconomic status, and sexual health stigmas. By examining these factors through a gender-sensitive lens, this dissertation builds on existing frameworks to identify more effective, context-specific interventions for improving PrEP uptake and continuity among young women.

Uptake and continuity of PrEP are crucial for maximizing the benefits of this prevention method. Few studies have evaluated the long-term retention rates of PrEP users. Conflicting knowledge exists on whether young girls continue to come to clinics despite low rates of adherence to the pill itself (Tapsoba et al., 2022). Despite several options for HIV prevention, oral PrEP is still a preference. Uptake and continuity in care correlate with increased behavioral risk and self-reported adherence in the early days after initiation (Kagaayi et al., 2020; Mubezi et al., 2023). In addition, the findings of this

dissertation have the potential to make significant contributions to both policy and practice in HIV prevention, particularly in Uganda and similar contexts. By identifying the barriers and facilitators to PrEP uptake among young women, the study informs the development of targeted interventions that are more specific to the needs and experiences of this high-risk group.

Background

PrEP is a critical intervention in reducing HIV transmission, particularly among high-risk populations such as young women (Mayanja et al., 2022; Roberts et al., 2023). PrEP use among individuals at high risk of HIV infection can be efficacious in preventing transmission (Russ et al., 2021; Medina et al., 2023). However, uptake and continuity of PrEP remain challenges despite its efficacy.

Several structural and behavioral risk factors significantly influence PrEP uptake and continuation. Understanding the factors associated with PrEP uptake and continuation is crucial for enhancing PrEP accessibility and adherence among young women. Structural and behavioral HIV risk factors, such as early school dropout, food insecurity, inconsistent condom use, and engagement in commercial sex, have been closely linked to PrEP uptake amongst young women (Barnabee et al., 2023). Other studies have found that certain factors may be even more prominent for young women. Mayanja et al. (2022) noted that although PrEP uptake and adherence rates among young women were low, PrEP initiation was associated with increased sexual behavioral risks. The researchers also observed that only half of the young women population preferred oral PrEP, suggesting that this option may not be as significant a factor in PrEP uptake or

continuation as previously assumed.

Several studies collectively revealed a range of interconnected barriers to PrEP uptake and continuation. Gombe et al. (2020) found that concerns about side effects, limited awareness, stigma, and healthcare system challenges hindered the uptake and continuation of PrEP among high-risk individuals. Other health system barriers included the rapid pace of PrEP implementation programs, which lacked sufficient resources, and a lack of familiarity with prescribing PrEP (Estcourt et al., 2023). HIV-related stigma and limited access to health services are recurring themes in research examining the barriers to PrEP uptake and continuity.

Muwonge et al. (2020) noted that, in addition to safety concerns and forgetfulness, stigma and limited access were major obstacles to PrEP uptake. These challenges were not unique to young women but also affected other underrepresented groups. Russ et al. (2021) highlighted low HIV risk perception, stigma, and mistrust of the healthcare system as key barriers to PrEP use, particularly among Black men who have sex with men (BMSM). In addition to HIV-related stigma, Sensalire et al. (2024) revealed that concerns about PrEP side effects, adherence, and low HIV risk perception were key reasons clients rejected or discontinued PrEP. Not all stigma was related to HIV/AIDS. Other stigmas, such as those related to sexual activity and taking antiretrovirals, also hindered PrEP use (Giovenco et al., 2022; Velloza et al., 2020).

The research demonstrated that effective PrEP implementation for HIV prevention necessitates a multifaceted approach that addresses both individual and systemic challenges. Key facilitators include awareness-raising campaigns (Kayesu et al.,

2022), free access to PrEP and HIV testing (Diabate et al., 2020), and comprehensive training for health workers (Muwonge et al., 2020). Community delivery methods and alternative biomedical products tailored to meet end-users' needs are also crucial for enhancing PrEP uptake and continuity, especially during periods of restricted movement (Irungu et al., 2021; Mayanja et al., 2022). Comprehensive interventions and support systems are crucial to addressing barriers to PrEP use. Refining health worker training based on client feedback can better equip them to counsel clients on starting or continuing PrEP. Meanwhile, targeted program advertisements with messages that resonate with clients' experiences can further promote PrEP uptake and continuity (Gombe et al., 2022).

Strategies to improve PrEP uptake and continuity among young women include community-based service delivery models that can enhance PrEP education and HIV testing (Barnabee et al., 2023). These approaches also promote higher adherence through young women-centered refill services. Recommendations include offering PrEP in diverse settings to reach all those who need it, developing culturally sensitive training for healthcare professionals, and fostering collaboration among stakeholders (Estcourt et al., 2023; Jorgen et al., 2023). Sensalire et al. (2024) showed that a collaborative intervention significantly increased PrEP enrollment (from 64% to 89%) and continuity rates (from 51% to 78%). Velloza et al. (2020) found that over time, openly discussing PrEP with young women, supported by activities like counseling and adherence clubs, became empowering and helped them manage stigma. Still, all these efforts might fail to impact HIV incidence rates. Mayanja et al. (2022) showed that prioritizing PrEP for adolescents

had a minimal impact on HIV incidence rates, with only a slight increase (80.1% to 80.3%) in infections averted.

Key Constructs

The key dependent constructs are PrEP uptake and continuity among the high-risk group of Ugandan young women aged 15-24. Uptake refers to the adoption or initiation of PrEP among eligible users, while continuity is defined as the sustained use of PrEP among individuals who have initiated it during the risk period. In contrast, the key independent variables or constructs are perceived susceptibility to HIV, benefit of PrEP, socio-demographic factors, HIV behavioral risk factors, and the service access model. Susceptibility refers to a state of being exposed to a health problem. This perception is influenced by factors such as age, sex, genetic predisposition, and environmental exposure. The benefit of PrEP is measured through reduced risk for HIV and STI acquisition, HIV behavioral risk factors include the number of sexual partners, condom use, having a sexually transmitted infection in the last 12 months, being engaged to a partner in the HIV risk group, exposure to GBV, having sex in the past 6 months, having PEP in the last 6 months, and transactional sex. The PrEP delivery model for current users refers to access to the service at a facility or community.

Manuscript 1

The first manuscript examined the association between PrEP clients' perceived susceptibility to HIV and PrEP uptake among young women aged 15-24 in Uganda while controlling for social demographic factors. The dependent variable is the uptake of PrEP among young women (15-24 years) in Uganda. Uptake was measured based on whether

PrEP was initiated during the review period. This is a one-step (binary) categorical variable: Y (using PrEP) or No (not using PrEP).

I adopted a similar approach proposed by Balkus et al. (2015) to develop an HIV risk score. HIV susceptibility was assessed using a risk score estimated using variables on engagement in transactional sex, HIV status knowledge, number of sexual partners, STI history, pregnancy status, condom use, and injecting drug use. Number of sexual partners was grouped into ≤ 1 versus > 1 ; the rest of the variables were coded Yes (1) or No (0). The unfavorable value for each category was assigned a point value of 2, and 0 otherwise. A total score was calculated for each individual by summing up the scores, with higher values indicating higher risk. A susceptibility risk category was generated with a cut-off at the median. Multivariable logistic regression models were fitted to determine the effect of the susceptibility risk, adjusted for sociodemographic characteristics: age, marital status, education level attained, religion, residence (urban vs. rural), and service delivery model (facility or community)

Manuscript 2

The second manuscript aimed to characterize young women who were screened and initiated on PrEP and quantify the burden of HIV and STIs during the study period. It went a step further from the first manuscript by examining the relationship between HIV behavioral risk factors, the direct benefits of PrEP through assessment of the incidence of HIV and STIs in young women initiated on PrEP. Behavioral and social factors significantly influence both HIV and STI risk among young women. Understanding the

STI and HIV burden can inform targeted PrEP programs that integrate comprehensive sexual health services.

The exposure variables in the model were behavioral characteristics and incidents of HIV and STIs. Time-to-event methods (i.e., Kaplan Meier curves, log-rank tests, and Poisson models) were used to estimate HIV and STI burdens, estimated as incidence and defined as the number of HIV first incident STIs divided by person-years at risk (pya) per 100 person-years (pys), excluding those with a baseline prevalent infection from that calculation. Participant time to HIV and STI infections was explored using Kaplan-Meier curves and compared using log-rank tests. Univariate and multivariable Poisson models with a log link and exchangeable correlation were used to assess the crude and adjusted effects of participant characteristics on HIV and STI incidence.

Manuscript 3

The third manuscript assessed the impact of the PrEP service delivery model (health facility-based or community-based) on the continuity of PrEP among young women (15-24 years). The research question was “How do different PrEP service delivery modes (health facility-based or community-based) influence PrEP continuity among PrEP clients in Uganda, while controlling for sociodemographic factors?” The outcome variable was time to PrEP continuity, defined as the date of refill within 12 months of PrEP initiation. The exposure variables included demographic characteristics (age, marital status, education level, religion, and district of residence), and behavioral risk characteristics (number of sexual partners, knowledge of HIV status of sexual

partners, condom use during last sex, history and treatment of STIs, pregnancy, injecting drug history, and engagement in transactional sex).

Summary of Constructs

Benefits of PrEP: PrEP's efficacy in preventing HIV transmission is well-documented, but concerns about side effects and other factors affect uptake or continuation. The benefit of PrEP is measured through reduced risk for HIV and STI acquisition.

HIV behavioral risk factors: Risky behaviors such as the number of sexual partners, condom use, history of sexually transmitted infections, engaged to a partner in the HIV risk group, both casual and regular sex, history of injecting drugs, and transactional sex.

Model of access to PrEP services: Limited access to healthcare services, including PrEP, is a recurring barrier in the reviewed literature, with issues such as reaching the beneficiaries still noted as challenges.

Perceived susceptibility to HIV: Low HIV risk perception is a key barrier to PrEP uptake, particularly among high-risk individuals who may not recognize their vulnerability to HIV.

PrEP uptake among high-risk groups of people: Barriers such as stigma, healthcare system challenges, and low HIV risk perception hinder PrEP uptake across various high-risk groups, including young women.

PrEP uptake and continuity among young women in Uganda: Uptake and continuity rates among young women are generally low.

Overarching Theory

The theory that supports this study is the health belief model (HBM), proposed by Rosenstock (1974). This model suggests that individuals' health-related behaviors are influenced by their perceptions of the likelihood of health threats, social relationships, and the barriers to adopting recommended behaviors. According to Nganda et al. (2024), the model comprises several key tenets, from which the following have been selected for the study:

- Perceived susceptibility: The risk or the probability of acquiring an illness or encountering an undesirable outcome.
- Behavior risk factors: The exposure to and presence of disease can influence preventive behaviors, such as PrEP adoption.
- The benefits of PrEP: PrEP's efficacy in preventing HIV transmission is well-documented. I assessed the burdens of HIV and STIs in this study.
- Health care access options. Access can influence uptake and continuity in care.

Knowledge Gap

A significant gap exists in studies that focus on young women who face multiple, co-occurring risk factors for HIV acquisition, such as young women in sex work, those in violent relationships, or those with limited access to education or healthcare. These women face several challenges that may increase their risk and impair their ability to access and adhere to PrEP. A comprehensive understanding of this heterogeneity within the group of young women is lacking.

Studies that segment young women based on multiple intersecting risks (e.g., commercial sex work, rural/urban differences) and explore how these factors influence PrEP uptake could help create more targeted interventions for the most at-risk subsets of this Ugandan population. Sensalire et al. (2024) highlighted the effectiveness of a three-tier approach in addressing gaps in PrEP uptake and continuity, emphasizing the importance of tailored interventions. Similarly, Muwonge et al. (2020) explored PrEP delivery among diverse groups in Central Uganda, highlighting the role of health worker training in boosting awareness. However, there remains a need for research specifically targeting young women, who represent a significant proportion of new HIV diagnoses in the region (Barnabee et al., 2023; Kinuthia et al., 2023). Adolescents, often lacking agency in sexual decision-making and facing barriers to access, are particularly vulnerable to HIV (Hamilton et al., 2023; Mora et al., 2022). There is a need for both antiretroviral therapy (ART) and PrEP in combating HIV transmission within at-risk populations (Hamilton et al., 2023; Mora et al., 2022).

Furthermore, studies such as that of Barnabee et al. (2023) in Namibia, which investigate the safety of Tenofovir Disoproxil Fumarate (TDF)-based PrEP, provide valuable insights into structural and individual-level factors influencing PrEP uptake. However, these findings may only partially capture the unique challenges that young women face in accessing and adhering to PrEP. Therefore, the current study aimed to fill this gap by comprehensively assessing PrEP uptake and continuity among young women aged 15-24 in Uganda. Additionally, by building on existing frameworks, such as the three-tier approach proposed by Sensalire et al. (2024), the study developed targeted

interventions to improve PrEP uptake and continuity among young women, ultimately contributing to the effectiveness of HIV prevention efforts in Uganda and similar settings.

Overview of the Manuscripts

The factors influencing PrEP uptake and adherence operate at multiple levels (i.e., individual, behavioral, and structural). Each study allowed for examining these factors and developing relevant interventions at different levels, making it easier to design effective, tailored strategies. Together, these manuscripts are designed to work as complementary studies that address the overall study gap by examining PrEP uptake and continuity from different perspectives, including individual behavioral risk factors and structural/systemic barriers. By examining these factors in an integrated manner, the dissertation provides a comprehensive, multi-level understanding of the barriers and facilitators to PrEP uptake and continuity, with a specific focus on young women in Uganda.

The key problem of the three manuscripts was the lack of comprehensive studies focusing on the intersectionality of barriers and facilitators to PrEP uptake and continuity among young women aged 15-24. The findings from the three studies collectively inform the development of targeted interventions that address both individual and structural factors influencing PrEP use, thereby contributing to the effectiveness of HIV prevention efforts in Uganda and similar settings.

Manuscript 1

There is limited research on how perceived susceptibility to HIV influences PrEP

uptake among young women aged 15-24 in Uganda. While previous studies have explored individual factors and attitudes toward PrEP, few have specifically examined how susceptibility influences the initiation of PrEP. The research question is “What is the association between the perceived susceptibility to HIV and PrEP uptake among young women aged 15-24 in Uganda, while controlling for social demographic factors?”

This retrospective cross-sectional quantitative study was used to collect secondary data at the Mulago Sexually Transmitted Diseases (STD) clinic under the Most At-Risk Population Initiative (MARPI) from January 2024 to September 2025, using National PrEP data collection tools. Secondary data were abstracted from routine data for clients seeking HIV prevention services at the Mulago National Referral Hospital’s STI clinic, for 20,532 young women from January 2024 to September 2025. A minimum sample size of 385 young women was sufficient to estimate the outcomes in all three study objectives. This sample size was estimated using the Kish formula cited by Williams et al. (2021) for estimating a proportion in a cross-sectional study and assuming an expected outcome of 50% (to provide a maximum sample size), a 5% level of precision, a type-1 error of 5%, and a two-sided $\alpha = 0.05$.

Manuscript 2

There are limited studies on the association between HIV behavioral risk factors (number of sexual partners, condom use, history of sexually transmitted infections, engaged to a partner in the HIV risk group, GBV victims, history of sex in the past 6 months, history of PEP in the last 6 months and transactional sex) and the burden of HIV and STIs among young women in Uganda.

The research question is “What is the burden of HIV and STIs among young women aged 15-24 in Uganda who were screened and initiated on PrEP, while controlling for social demographic characteristics?” A retrospective study that employed was used to examine routine data for clients seeking HIV prevention services at the Mulago National Referral Hospital’s STI clinic, for 20,532 young women from January 2024 to September 2025. A total of 3,958 were started on PrEP during this period.

Manuscript 3

There is scarce information on how access to PrEP services affects PrEP continuity among young women who use PrEP in Uganda. The research question is “How do different PrEP service delivery models (health facility-based or community-based) influence PrEP continuity among PrEP clients in Uganda, while controlling for social-demographic factors?” A retrospective cross-sectional quantitative study targeting young women aged 15-24 enrolled in the MARPI clinic was used to collect secondary data. Secondary data were collected using the National PrEP data collection tools at the MARPI clinic. Secondary data were abstracted from routine data for clients seeking HIV prevention services at the Mulago National Referral Hospital’s STI clinic, for 20,532 young women from January 2024 to September 2025.

I sought a waiver of informed consent from the IRB. The study involved minimal risk to participants because I extracted and analyzed only non-personally identifying information (PII) data from the clinic database for young women who receive HIV prevention services at MARPI. Only the participant ID, a system-generated alphanumeric code, was used for tracking program participation; however, it could not be used to

identify individual participants. The study findings will inform the HIV prevention program for young women at high risk and will not change the services that participants receive at the clinic. For data extraction, no personal identifiers (such as participants' names, addresses, and telephone numbers) were included. Access to the extracted data was restricted. I signed confidentiality agreements to ensure that there are legal ramifications for violating the code of conduct and divulging study information. Ethical approval was obtained from the Walden University Institutional Board. In addition, Ethical clearance for the protocol was obtained from the Mildmay Uganda Research Ethics Committee (MUREC), and final approval of the protocol was granted by the Uganda National Council for Science and Technology (UNCST) prior to the commencement of the study.

Significance

The purpose of the study was to address the significant challenges hindering the effectiveness of HIV prevention efforts, particularly regarding the uptake and continuation of PrEP in Uganda. By comprehensively examining the barriers and facilitators to PrEP uptake and continuation among young women, the research contributes valuable insights to public health and HIV prevention.

By applying quantitative research methods and analyzing retrospective data, the study aimed to identify the underlying factors influencing PrEP uptake and continuation, including perceived susceptibility, demographic characteristics, behavioral risk factors, the benefits of PrEP, and the mode of access to healthcare services.

By identifying these factors, the research provides critical knowledge that can

inform the development and implementation of targeted interventions to improve PrEP uptake and continuation rates. Furthermore, by addressing gaps in the existing literature and building on previous research findings, the study contributes to advancing knowledge in HIV prevention and public health. The study will foster dialogue and collaboration among researchers, policymakers, healthcare providers, and community stakeholders by disseminating research findings through academic publications, conferences, and other professional forums.

By enhancing the understanding of the factors influencing PrEP uptake and continuation, the study informs the development of more effective HIV prevention strategies and interventions. By increasing PrEP uptake and continuation rates among young women, the research contributes to positive social change by reducing the incidence of HIV infections, improving health outcomes, and promoting overall well-being in communities affected by HIV/AIDS.

Summary

The study is a multi-level examination of the factors influencing PrEP uptake and continuity among young women in Uganda. The research is divided into three manuscripts. The first manuscript focused on individual-level factors and examined how young women's sociodemographic factors and perceived susceptibility to HIV influence the uptake of PrEP. It highlights the gap in research linking these perceptions with PrEP use. The second manuscript investigates behavioral risk factors and examines how risky sexual behaviors (e.g., number of sexual partners, condom use, history of sexually transmitted infections, engaged to a partner in the HIV risk group, GBV victims, history

of sex in the past 6 months, history of STIs and transactional sex), the benefit of PrEP and PrEP uptake among young women. The third manuscript examines how models of PrEP service delivery influence the continuity of PrEP use.

The three studies will employ retrospective, quantitative, cross-sectional designs. Secondary data for all three studies were collected using the National PrEP data collection tools at MARPI. The goal was to identify facilitators and barriers to PrEP uptake and continuity to inform targeted interventions to improve HIV prevention outcomes for young women in Uganda. The research contributes to public health knowledge by addressing key gaps in the literature and fostering collaboration among stakeholders, ultimately promoting positive health outcomes and contributing to social change in affected communities in Uganda.

Part 2: Manuscripts

**Manuscript 1: Perceived Susceptibility to HIV and Its Influence on PrEP Uptake
Among Young Women Aged 15-24 Years in Mulago, Uganda**

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Outlet for Manuscript

The target journal is *AIDS Care*, which is accessible at <https://www.tandfonline.com/journals/caic20/about-this-journal#open-access>. *AIDS Care* is an international, peer-reviewed, open-access journal. The journal contains scholarly research on HIV/AIDS, focusing on the planning, social, and psychological aspects of prevention, care, and treatment. It covers topics from various fields, including psychology, sociology, and health education. The journal seeks to publish research from diverse institutions worldwide to address the global impact of HIV/AIDS. This journal aligns with my manuscript content on PrEP uptake and continuation among young women in Uganda, as it focuses on multidisciplinary HIV/AIDS research, including social, psychological, and service-related factors. It emphasizes the global and societal impact of HIV, including topics such as HIV stigma, behavioral risk factors, and access to treatment services.

Authors can submit manuscripts in any format or layout, including Word and PDF, with figures and tables either embedded or separate, as long as the resolution is sufficient for review. Essential manuscript elements include an abstract, author details, figures, tables, and funding information. References can be in any format, but the citation style has to be consistent. The journal applies its own reference style upon acceptance. It requires me to provide a final editable version upon acceptance.

Abstract

Young women aged 15-24 account for a significant proportion of new HIV diagnoses in the region. Early identification of reasons for non-uptake of pre-exposure prophylaxis (PrEP) among young women enables the implementation of targeted interventions, thereby enhancing the effectiveness of the prevention program. The purpose of this study was to assess the relationship between the perceived susceptibility to HIV and PrEP uptake among young women (15-24 years), while controlling for social demographic factors. The Health Belief Model provided a theoretical framework for understanding the uptake of PrEP among young women in Uganda. Secondary data were abstracted from routine data for clients seeking HIV prevention services at the Mulago National Referral Hospital's STI clinic, for $N= 23,765$ young women from January 2024 to September 2025. The study found a statistically significant negative relationship between HIV susceptibility and PrEP uptake. Young women who had a high susceptibility to HIV were 40% ($aOR = 0.60$, $95\%CI 0.55-0.65$) less likely to take up PrEP compared to those with a low susceptibility. This counterintuitive finding, whereby individuals at the greatest objective risk are least likely to initiate preventive measures, challenges conventional assumptions about health-seeking behavior. The overall PrEP uptake was 16.7% per 100 person-years. And while this uptake represents nearly 4,000 young women initiating prevention, it indicates that five out of six eligible high-risk individuals are not accessing this life-saving intervention.

Introduction

The use of oral pre-exposure prophylaxis (PrEP) is an effective way to avert incident HIV cases among adolescent girls and young women (AGYW), who represent the largest proportion of people living with HIV (Butler et al., 2023; Hamilton et al., 2023). Globally, the aim is zero new infections among AGYW by 2030 (Russ et al., 2021). Since 2017, HIV incidence has declined thanks to diverse prevention options (Mahy et al., 2024). PrEP has been effective for key and priority populations (Muwonge et al., 2020; Ortblad et al., 2023). To further reduce the incidence of HIV, the World Health Organization (WHO) approved PrEP and issued guidelines for its implementation (Lanham et al., 2021; Mayanja et al., 2022).

Uganda launched its PrEP program in 2017, first targeting key populations that include female sex workers, men who have sex with men, people who inject drugs, transgender individuals, and prisoners, before later scaling the program to young women as a priority group. By 2023, the Ministry of Health reported that more than 200,000 people nationwide had initiated PrEP, although detailed age- and sex-disaggregated coverage data remain scarce (Matthews et al., 2023). The PrEP pathway begins with client screening and initiation, a process that can take up to 6 months before discontinuation.

Multiple factors have been identified as influencing PrEP uptake among young women at the individual, interpersonal, community, and structural levels. Studies in the East African region found low uptake and poor adherence to PrEP, with important factors including age, marital status, pregnancy, and religion (Estcourt et al., 2023; Heck et al.,

2022). At the individual level, HIV risk perception, knowledge of PrEP, attitudes toward the medication, and concerns about side effects and adherence burdens play a role (Barnabee et al., 2023; Camlin et al., 2020). Interpersonally, partner attitudes and power imbalances in relationships significantly impact a young woman's ability to access and utilize PrEP (Scorgie et al., 2020). Community stigma that associates PrEP with promiscuity or HIV-positive status creates additional barriers, especially where adolescent sexuality is socially sanctioned (Velloza et al., 2020). Finally, structural elements such as health-care access, provider attitudes, and service-delivery models determine whether at-risk young women can successfully initiate PrEP (Graybill et al., 2023).

Perceived susceptibility to HIV refers to the risk or probability of acquiring the infection, is theorized to drive demand for preventive services in health-behavior models (Rosenstock et al., 1974). Yet the relationship between perception and PrEP uptake is complex. Some research indicates that a higher perceived risk predicts PrEP initiation (Corneli et al., 2020), while other studies reveal a paradox in which individuals at the greatest objective risk tend to underestimate their susceptibility (Yellin et al., 2023). This mismatch between objective and subjective risk may help explain the suboptimal PrEP coverage among young women.

In Uganda, data on PrEP uptake among young women outside of research settings are scarce. Demonstration projects and clinical trials have illuminated acceptability and adherence, but little is known about uptake under routine programmatic conditions (Muwonge et al., 2021). This study sought to quantify PrEP uptake and its association

with HIV susceptibility among young women accessing prevention services at Mulago National Referral Hospital's STI clinic during the period 2024-2025. Specifically, I estimated the level of PrEP uptake among young women receiving services in the MRH STI clinic, assessed the effect of HIV susceptibility on PrEP uptake, and controlled for social-demographic variations. Identifying these associations can inform targeted strategies to expand PrEP coverage among this high-risk group, thereby contributing to efforts towards control of the HIV epidemic in Uganda and similar high-burden settings.

Methods

Study Setting

The STI clinic at Mulago National Referral Hospital is a high-volume site for HIV prevention services, including PrEP provision to at-risk populations. The clinic offers PrEP services integrated into routine STI services, employing both facility and community-based screening approaches, which provides a unique opportunity to examine PrEP uptake patterns across different service delivery models. The clinic's systematic data collection through the population-at-high-risk tracker enables analysis of demographic and behavioral factors associated with PrEP initiation.

Data Sources

The study was approved by the Walden University Institutional Review Board, the Mildmay Uganda Research Ethics Committee (MUREC), and the Uganda National Council for Science and Technology (UNCST) prior to its commencement. Secondary data were abstracted from the populations-at-high-risk tracker, a national surveillance system that collects and stores routine data from clients seeking HIV prevention services.

The tracker is a case-based surveillance system built on the District Health Information System (DHIS-2) platform, storing individual-level data on screening, enrolment, and follow-up for clients receiving services at public health facilities.

Assessment and Testing

At screening, healthcare workers assessed clients' PrEP eligibility through HIV testing and responses to questions on high-risk sexual behavior. HIV testing was offered to all clients who were not known HIV positives using the national HIV testing algorithm: Determine is the first test, and if reactive, Stat-Pak is used, and if discordant, a final tiebreaker is performed with Uni-Gold. Identified HIV positive clients were counseled and initiated on ART on the same day. HIV negative clients who were found to be at high HIV risk were initiated on PrEP. Clients were assigned an alphanumeric, unique number, which is used for tracking purposes at subsequent visits when they return for refills.

Estimating HIV Susceptibility

I adopted a similar approach proposed by Balkus et al. (2017) to develop an HIV risk score. HIV susceptibility was assessed using a risk score estimated using behavioral characteristics data, including transactional sex, HIV status knowledge, number of sexual partners, STI history, pregnancy status, condom use, and injecting drug use. The number of sexual partners was grouped into ≤ 1 versus > 1 ; the rest of the variables were coded Yes (1) or No (0). The unfavorable value for each category was assigned a point value of 2, and 0 otherwise. A total score was calculated for each individual by summing up the scores, with higher values indicating higher risk. A susceptibility risk category was

generated with a cut-off at the median.

Statistical Analysis

Participant characteristics were summarized using frequencies and percentages for categorical variables and medians with interquartile ranges (IQRs) for continuous variables, given the non-normal distribution of ages. Chi-square tests and t-tests were used to evaluate the association between participant characteristics and the uptake of PrEP for both categorical and continuous variables. To assess the associations between PrEP uptake (a binary outcome) and categorical predictors (age group, education level, marital status, district, religion, service delivery model, and HIV susceptibility category), the Pearson chi-square test of independence was used. For the continuous HIV susceptibility scores, the two-sample *t-test* was used after confirming approximate normality.

The effect of the participants' HIV susceptibility on PrEP uptake was assessed using binary logistic regression models. The outcome variable was PrEP uptake, defined as initiation of PrEP by young women who were found to be eligible after screening, and were offered and accepted PrEP. The primary exposure variable was HIV susceptibility, and the confounders were sociodemographic characteristics, i.e., age, education level, marital status, district of residence, and service model.

First, unadjusted logistic regression models were fitted with the outcome and each of the exposure variables to determine the crude effects of each variable on the outcome. A *p*-value < 0.05 was considered statistically significant for all analyses. A multivariable model fitted with the HIV susceptibility risk and confounders that achieved a *p*-value <

0.2 at the univariate level was used to estimate the adjusted effects on PrEP uptake. The variance inflation factor (VIF) was used to assess multicollinearity between the exposure variables, with a threshold of $VIF > 10$ indicating problematic collinearity. Effect estimates were summarized using adjusted odds ratios (aOR) and their 95% confidence intervals (CI). All data were analyzed using Stata IC 16.0.

Results

HIV Susceptibility and Social Demographic Characteristics

A total of 9,242 (38.9%) participants had high susceptibility to HIV. Median (interquartile range [IQR]) age was 21 (19-23) years. The majority were single or separated (98.9%), had attained primary education (48.7%), resided in Wakiso District (52.3%), and identified as Christian (94.8%). Nearly all participants (99.5%) were screened for PrEP through the community service model and/or hotspots (see Table 1).

Table 1*Participants' Sociodemographic Characteristics and HIV Susceptibility*

Characteristic	Screened for PrEP n (%)
Overall	23,765
Age (years)	
Median (IQR)	21 (19 - 23)
Age group	
15-19	6,240 (26.3)
20-24	17,525 (73.7)
Education level	
None	2,623 (11.2)
Primary	11,406 (48.7)
Secondary	8,981 (38.3)
Tertiary	421 (1.8)
Marital status (n=23,542)	
Married/cohabiting	269 (1.1)
Single /divorced/separated/widowed/separated	23,273 (98.9)
District	
Kampala	9,264 (39.0)
Wakiso	12,417 (52.3)
Other	2,084 (8.8)
Religion	
Christian	22,203 (94.8)
Moslem	1,220 (5.2)
Other	10 (0.04)
Type of service model	
Community	23,372 (99.5)
Health facility	125 (0.5)
HIV susceptibility	
Median (IQR)	2 (2-4)
Grouped	
Low	14,523 (61.1)
High	9,242 (38.9)

Note. N = 23,765 young women screened for PrEP from January 2024 to September 2025

Association Between PrEP Uptake and Participant HIV Susceptibility and Social Demographic Characteristics

Out of the 23,765 young women screened, only 3,958 (16.7%) initiated PrEP. PrEP uptake was more likely to be higher among participants who were young (18.8%), had no formal education (20.6%), were married/cohabiting (35.7%), and those who initiated PrEP at health facilities (64.8%). PrEP uptake was also highly likely (20.0%) among participants who had a low susceptibility to HIV (Table 2).

Table 2*Distribution of PrEP Uptake by Participant Characteristics and HIV Susceptibility*

Characteristic	PrEP uptake		p-value
	Yes	No	
Overall	3,958 (16.7)	19,807 (83.4)	
Age group			
15-19	1174 (18.8)	5,066 (81.2)	<0.001
20-24	2,784 (15.9)	14,741 (84.1)	
Education level			
None	239 (20.6)	2,084 (79.5)	
Primary	1,610 (14.1)	9,796 (85.9)	<0.001
Post primary	1,618 (17.2)	7,784 (82.8)	
Marital status			
Married/cohabiting	96 (35.7)	173 (64.3)	
Single /divorced/separated/ widowed/separated	3,760 (16.2)	19,513 (83.8)	<0.001
District			
Kampala	1,742 (18.8)	7,552 (81.2)	
Wakiso	1,736 (14.0)	10,681 (86.0)	<0.001
Other	480 (23.0)	1,604 (77.0)	
Religion			
Christian	3,508 (15.8)	18,695 (84.2)	<0.001
Other	291 (23.7)	939 (76.3)	
Type of service model			
Community	3,682 (15.8)	19,690 (84.3)	<0.001
Health facility	81 (64.8)	44 (35.2)	
HIV susceptibility			
Mean (SD)	2.5 (1.3)	3.1 (1.6)	<0.001
Low	2,898 (20.0)	11,625 (80.1)	<0.001
High	1,056 (11.4)	8,186 (88.6)	

Note. N = 23,765 young women screened for PrEP from January 2024 to September 2025

The Effect of HIV Susceptibility on PrEP Uptake

After adjusting for sociodemographic characteristics, there was a statistically significant negative relationship between HIV susceptibility and PrEP uptake.

Participants who had a high susceptibility to HIV were 40% (aOR = 0.60, 95% CI 0.55-0.65) less likely to take up PrEP compared to those with a low susceptibility. In addition, all sociodemographic characteristics except marital status were significantly associated with PrEP uptake.

Older participants (20-24 years) were 21% less likely (aOR = 0.79, 95% CI 0.73-0.86) to initiate PrEP compared to younger participants (15-19 years). PrEP uptake among participants with primary or post-primary education was 38% (aOR = 0.62, 95% CI 0.55-0.69) and 23% (aOR = 0.77, 95% CI 0.69-0.87) lower, respectively, compared to those without any formal education. Young women living in Wakiso district and other districts were 26% (aOR = 0.74, 95% CI 0.68-0.80) less likely and 47% (aOR = 1.47, 95% CI 1.31-1.67) more likely, respectively, to initiate PrEP compared to those living in Kampala district. Participants belonging to non-Christian denominations were 50% (aOR = 1.50, 95% CI 1.29-1.73) more likely to take PrEP than Christians. PrEP uptake was eight times higher (aOR = 8.04, 95% CI 5.38-12.02) among young women who were screened at health facilities compared to those in community outreaches (Table 3).

Table 3*Effects of Participant HIV Susceptibility on PrEP Uptake Adjusted for Sociodemographic**Characteristics*

Characteristic	Unadjusted OR (95%CI)	p-value	Adjusted OR (95% CI)	p-value
HIV susceptibility				
Low	1		1	
High	0.52 (0.48, 0.56)	<0.001	0.60 (0.55, 0.65)	<0.001
Age group				
15 – 19	1		1	
20 – 24	0.81 (0.76, 0.88)	<0.001	0.79 (0.73, 0.86)	<0.001
Education level				
None	1		1	
Primary	0.64 (0.57, 0.71)	<0.001	0.62 (0.55, 0.69)	<0.001
Post primary	0.80 (0.72, 0.90)	<0.001	0.77 (0.69, 0.87)	<0.001
Marital status				
Married/cohabiting	1		1	
Single /divorced/separated/ widowed/separated	0.35 (0.27, 0.45)	<0.001	0.90 (0.62, 1.29)	0.566
District				
Kampala	1		1	
Wakiso	0.70 (0.65, 0.75)	<0.001	0.74 (0.68, 0.80)	<0.001
Other	1.29 (1.15, 1.45)	<0.001	1.47 (1.31, 1.67)	<0.001
Religion				
Christian	1		1	
Other	1.65 (1.44, 1.89)	<0.001	1.50 (1.29, 1.73)	<0.001
Type of service model				
Community	1		1	
Health facility	9.84 (6.81, 14.23)	<0.001	8.04 (5.38, 12.02)	<0.001

Discussion

Summary of Principal Findings

This study provides critical insights into PrEP uptake patterns among 23,765 young women screened for HIV prevention services at Mulago National Referral Hospital's STI clinic between January 2024 and September 2025. The overall PrEP uptake of 16.7% among eligible young women, while representing a substantial absolute number of initiators, reveals a significant programmatic gap in converting screening and eligibility into actual initiation of prevention. This uptake is notably lower than the 20-35% typically reported in similar East African settings, suggesting potential barriers specific to the service delivery context or population characteristics at this facility (Barnabee et al., 2023; Gombe et al., 2020).

The most significant finding is the inverse relationship between HIV susceptibility and PrEP uptake. Young women categorized as having high HIV susceptibility were less likely to initiate PrEP compared to their low-susceptibility counterparts. This counterintuitive finding, whereby those at greatest objective risk are least likely to initiate prevention, challenges conventional assumptions about HIV risk perception and health-seeking behavior. Rather than reflecting individual choice or knowledge deficits, this pattern likely represents the overwhelming influence of structural barriers, anticipated stigma, economic dependence, intimate partner dynamics, and limited autonomy that disproportionately affect the most vulnerable young women.

The low PrEP uptake rate observed in this study falls within the lower range of rates reported across sub-Saharan Africa. A 2025 scoping review analyzing 58 studies on

PrEP delivery to young women in sub-Saharan Africa found that uptake rates in real-world programmatic settings typically range from 15% to 35%, with substantial variation based on service delivery models, population characteristics, and implementation contexts (Chen-Charles et al., 2025; Yi et al., 2021). Studies from South Africa implementing differentiated service delivery approaches have reported uptake rates ranging from 62% to 88% among young women enrolled in targeted prevention programs (Celum et al., 2020; Velloza et al., 2023). However, these higher rates often reflect selected populations with intensive support services rather than routine clinical care.

Furthermore, the study revealed a dramatic eight-fold difference in PrEP uptake by the service delivery model. Young women screened at health facilities were significantly more likely to initiate PrEP compared to those screened through community-based approaches. This finding is particularly noteworthy given that 99.5% of the cohort was reached through community screening, underscoring both the strength of community outreach for identification and the critical weakness in conversion to actual service uptake. The disparity suggests that while community models excel at reaching large numbers of at-risk individuals, the structured, private, and clinically assured environment of facility-based services may be essential for overcoming psychological and social barriers to PrEP initiation.

The inverse relationship between objective HIV risk and PrEP uptake, which is termed the 'PrEP paradox', has been documented across multiple contexts but remains inadequately addressed in prevention programming. Recent research from Kenya and South Africa found that young women at the highest risk often face the greatest barriers

to PrEP use, including anticipated stigma (fear of being perceived as HIV-positive or promiscuous), partner disclosure concerns, and economic dependence that limits autonomous health decision-making (Akullian et al., 2021; Butler et al., 2023). Studies examining PrEP stigma among users found that even current PrEP users harbor significant perceived stigma, with many fearing discrimination associated with PrEP use, suggesting that stigma operates as both a barrier to initiation and a challenge for persistence (Diabaté et al., 2021; Little et al., 2024).

Additional sociodemographic patterns emerged from the analysis. Older women showed lower PrEP uptake compared to their younger counterparts, potentially reflecting greater structural vulnerabilities, including economic responsibilities, partnership dynamics, and competing life demands. Educational attainment showed a complex relationship with uptake, with those having no formal education demonstrating higher initiation rates, possibly reflecting successful targeting through peer networks or greater perceived benefit due to fewer alternative protective options. Geographic variations between Wakiso and Kampala districts suggest that local service accessibility, mobility constraints, and district-specific HIV prevention programming may influence uptake patterns.

The finding that older women (20-24 years) showed lower uptake aligns with emerging evidence about age-stratified vulnerabilities. Research from Eastern and Southern Africa suggests that older women frequently encounter multiple structural barriers, including economic responsibilities for children or household members, partnership dynamics that restrict autonomy, and competing priorities that hinder

consistent clinic attendance (Butler et al., 2023; Giovenco et al., 2022). A 2025 study of pregnant and parenting young women in South Africa's Eastern Cape found that only 10% of HIV-negative pregnant/parenting women had ever taken PrEP despite 88% having recent HIV testing, highlighting missed opportunities, particularly among this higher-risk, older subgroup (Chen-Charles et al., 2025).

The eight-fold difference in uptake between facility-based and community-based screening models adds important nuance to the literature on differentiated service delivery. While the 2022 World Health Organization (WHO) guidance on differentiated PrEP service delivery emphasizes community-based approaches to improve accessibility, implementation studies from across sub-Saharan Africa reveal that community models often excel at identification and screening but struggle with conversion to actual service initiation. A 2024 systematic review of differentiated service delivery models during the COVID-19 pandemic found that successful PrEP scale-up required combining community outreach with streamlined facility-based initiation pathways, multi-month dispensing, and telehealth support (Njuguna et al., 2024). Recent studies from South Africa have found that young women value privacy, confidentiality, and professional healthcare interactions when deciding to initiate PrEP, factors that are more readily available in facility settings (Rousseau et al., 2021; Scorgie et al., 2021).

The pattern of higher uptake among young women with no formal education, while seemingly paradoxical, may reflect successful targeting through peer-based community networks that effectively reach marginalized populations. A 2024 study from Johannesburg found that community-based PrEP delivery through familiar peer networks

increased accessibility for young women with limited education, though persistence remained challenging without ongoing support (Naidoo et al., 2025). This finding underscores the importance of education-adapted communication strategies and peer support in PrEP programming.

These findings carry significant implications for HIV prevention policy and programmatic implementation in Uganda and similar high-burden settings. First, the pronounced PrEP paradox demands a fundamental shift from risk-based targeting to barrier-focused intervention. Simply identifying high-risk individuals is insufficient; programs must actively address the psychosocial, structural, and interpersonal barriers that prevent the most vulnerable from initiating prevention. This requires integration of stigma reduction interventions, economic empowerment programming, intimate partner violence screening and support, and models that enable discreet access to services.

Second, the stark disparity between community screening reach (99.5% of the cohort) and facility-based conversion success suggests an urgent need for hybrid service delivery models that combine the strengths of both approaches. Community-based screening should be systematically linked to immediate, same-day PrEP initiation opportunities—either through mobile services, rapid referral pathways with appointment accompaniment, or task-shifting to enable community health workers to initiate PrEP in non-facility settings. Uganda’s national PrEP guidelines should explicitly support such differentiated models with appropriate training, supply chain management, and monitoring systems.

Third, the age-stratified uptake patterns call for developmentally tailored

programming. Interventions for older women (20-24 years) must acknowledge and address their specific contexts, including motherhood, economic pressures, and partnership dynamics, through flexible service hours, childcare support, income-generating activities linked to HIV prevention, and couple-based counseling approaches. Programs should avoid a one-size-fits-all approach to young women and instead offer differentiated services tailored to each individual's life stage and circumstances.

Fourth, comprehensive stigma mitigation must become a central programmatic component rather than an ancillary concern. This includes community-level interventions to normalize PrEP use, healthcare provider training to reduce judgmental attitudes, integration of PrEP into routine sexual and reproductive health services to reduce its association with high-risk behavior, and promoting PrEP as a tool for wellness and empowerment rather than a marker of risky behavior. Media campaigns and community dialogues should emphasize PrEP as a rational health choice available to anyone who wants additional HIV protection.

Study Strengths and Limitations

Strengths

This study possesses several notable strengths that enhance the validity and generalizability of its findings. First, the large sample size (N = 23,765) drawn from routine programmatic data provides high statistical power and excellent external validity for real-world PrEP implementation in Uganda's public health system. The use of the national populations-at-high-risk tracker ensures standardized data collection, enabling comparison with other sites that implement similar surveillance systems. Second, the

study employed a validated HIV susceptibility scoring methodology adapted from established frameworks, allowing for systematic categorization of objective HIV risk. Third, the comprehensive multivariable analysis, controlling for sociodemographic confounders (age, education, marital status, district, and service model), enables a robust assessment of the independent associations with PrEP uptake. Fourth, the 21-month study period (January 2024-September 2025) provides sufficient temporal scope to capture programmatic patterns and seasonal variations. Finally, the inclusion of data from both facility-based and community-based service delivery models allows for comparative analysis of different implementation approaches.

Limitations

Despite these strengths, several important limitations must be acknowledged. First and most significantly, the reliance on secondary routine surveillance data means that crucial psychosocial variables known to influence PrEP decision-making were not available for analysis. These include perceived HIV-related stigma, partner attitudes toward PrEP, history of intimate partner violence, economic autonomy, social support networks, previous healthcare experiences, and actual knowledge about PrEP benefits and side effects. The absence of these variables limits my ability to elucidate the mechanisms underlying the observed PrEP paradox and prevents examination of potentially modifiable psychosocial factors. Future prospective studies should incorporate validated psychosocial measurement tools to better understand decision-making processes.

Second, this study focused exclusively on PrEP initiation (uptake) as the outcome,

without examining continuation, adherence, or persistence—the subsequent steps in the PrEP care cascade. Research across sub-Saharan Africa consistently demonstrates that while PrEP initiation may be achievable, sustained effective use remains challenging for young women. Understanding patterns of discontinuation and the factors that support persistence is essential for evaluating program effectiveness and would substantially strengthen conclusions about the impact of prevention. Future analyses should examine the complete PrEP cascade from screening through sustained use.

Third, the overwhelming predominance of community-based screening (99.5% of the cohort) creates a significant imbalance that may confound the comparison between service delivery models. Young women screened at facilities may represent a fundamentally different population with distinct characteristics (potentially higher health-seeking behavior, greater service awareness, or different risk profiles) that could account for some of the observed uptake difference beyond the service delivery model itself. Residual confounding by unmeasured factors related to service selection cannot be excluded. Future research should employ randomized or quasi-experimental designs to more definitively assess the causal impact of different service delivery approaches.

Fourth, the HIV susceptibility scoring system, while based on validated behavioral risk factors, may not fully capture individual risk perception or the lived experience of vulnerability. The discordance between objective and subjective risk is itself a critical factor in health behavior, and the inability to assess perceived personal risk limits interpretation of the PrEP paradox findings. Additionally, the binary categorization of susceptibility (high/low) based on a median split may obscure important

heterogeneity within risk categories.

Finally, this single-site study from an urban referral hospital may limit generalizability to rural settings, smaller health facilities, or other geographic regions of Uganda with different socio-cultural contexts, infrastructure, or HIV prevention programming. Multi-site studies encompassing diverse implementation contexts would strengthen evidence for national policy guidance.

Conclusions

This large-scale analysis of PrEP uptake among young women in Uganda reveals critical programmatic gaps that demand urgent attention. The 16.7% uptake rate, while representing nearly 4,000 young women initiating prevention, indicates that five out of six eligible high-risk individuals are not accessing this life-saving intervention. More concerning still is the pronounced PrEP paradox, whereby young women at the highest objective HIV risk are 40% less likely to initiate prevention, which fundamentally challenges the effectiveness of risk-based targeting approaches when structural and psychosocial barriers remain unaddressed.

The eight-fold difference in uptake between facility-based and community-based service models reveals both the power and the limitations of current differentiated service delivery strategies. While community outreach successfully identifies vulnerable populations at scale, conversion to actual service initiation requires the privacy, professional support, and clinical assurance that facility-based services provide. Future prevention programming must move beyond the false dichotomy of community versus facility services toward integrated hybrid models that combine the reach of community

engagement with the conversion efficiency of facility-based initiation.

To close the gap between need and initiation, HIV prevention efforts must pivot from risk identification to barrier mitigation. This requires multi-level interventions addressing individual (stigma reduction, PrEP literacy), interpersonal (partner communication, social support), community (stigma reduction, peer networks), and structural (service accessibility, economic empowerment, violence prevention) barriers. Differentiated service delivery models must be truly differentiated—tailored to the specific vulnerabilities, life circumstances, and preferences of distinct young women’s subgroups, rather than being implemented as standardized packages.

As Uganda works toward national and global HIV prevention targets, programmatic success will be determined not by the number of young women screened, but by the number who can access and sustain prevention methods despite the formidable barriers they face. Achieving this will require sustained political commitment, adequate resource allocation, health system strengthening, community engagement, and above all, a fundamental recognition that effective prevention must address the structural determinants of vulnerability rather than simply identifying those at risk.

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**Manuscript 2: Examining oral PrEP uptake and Associated Factors among
adolescent girls and young women attending STI clinic, Mulago National Referral
Hospital, Kampala District, Uganda**

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Outlet for Manuscript

The target journal is *AIDS Care*, which is accessible at <https://www.tandfonline.com/journals/caic20/about-this-journal#open-access>. *AIDS Care* is an international, peer-reviewed, open-access journal. The journal contains scholarly research on HIV/AIDS, focusing on the planning, social, and psychological aspects of prevention, care, and treatment. It covers topics from various fields, including psychology, sociology, and health education. The journal seeks to publish research from diverse institutions worldwide to address the global impact of HIV/AIDS. This journal aligns with my manuscript content on PrEP uptake and continuation among young women in Uganda, as it focuses on multidisciplinary HIV/AIDS research, including social, psychological, and service-related factors. It emphasizes the global and societal impact of HIV, including topics such as HIV stigma, behavioral risk factors, and access to treatment services.

Authors can submit manuscripts in any format or layout, including Word and PDF, with figures and tables either embedded or separate, as long as the resolution is sufficient for review. Essential manuscript elements include an abstract, author details, figures, tables, and funding information. References can be in any format, but the citation style has to be consistent. The journal applies its own reference style upon acceptance. It requires me to provide a final editable version upon acceptance.

Abstract

The scale-up of pre-exposure prophylaxis (PrEP) interventions within Uganda and other countries in sub-Saharan Africa has faced significant challenges that impact the effectiveness of HIV prevention efforts. Despite establishing national PrEP task forces and comprehensive rollout roadmaps, there remains persistently low uptake of PrEP among young women. This study investigated the association between the benefits, HIV behavioral risk factors, and PrEP uptake among young women (15-24) in Uganda. The health belief model provided a theoretical framework for understanding the uptake of PrEP among young women in Uganda. Secondary data were abstracted from routine data for clients seeking HIV prevention services at the Mulago National Referral Hospital's STI clinic, for $N=20,532$ young women from January 2024 to September 2025. HIV incidence of 1.13 per 100 person-years (pys) among young women on PrEP was a substantial reduction compared to the expected incidence without PrEP, but exceeds that observed in controlled trials where adherence was optimized. Married young women showed higher HIV incidence (2.17 vs. 0.80 per 100 py) compared to unmarried participants, with a 64% higher risk after adjustment. The STI incidence of 7.52 per 100 py revealed a substantial burden of bacterial infections, despite the use of PrEP. The findings suggest several programmatic modifications for optimizing PrEP delivery to young women. These include enhanced adherence support, integration of comprehensive sexual health services, and age-stratified interventions to address differential risk patterns.

Introduction

According to Omanga et al. (2023), 25% percent of new HIV infections in sub-Saharan Africa are among adolescent and young women (15-24 years). Young women were found to be 2.5 times more likely to acquire HIV through heterosexual contact than their male counterparts (Velloza et al., 2020). In sub-Saharan Africa, women and girls of all ages account for 63% of all new HIV infections (Lunkuse et al., 2022; Shimbire et al., 2024). In East Africa, it is estimated that 1.9 million young women (aged 15-24 years) are living with HIV (Haberer et al., 2024; Marthur et al., 2022).

In 2015, the World Health Organization (WHO) approved oral PrEP as an additional strategy for biomedical HIV prevention among HIV high-risk populations (Diabaté et al., 2021; Sensalire et al., 2024; Velloza et al., 2020). Despite the efficacy of PrEP, multiple challenges affect its real-world effectiveness among young women. Adherence remains suboptimal, with studies from Eastern and Southern Africa reporting continuation rates of less than 30% at 12 months (Celum et al., 2020; Gill et al., 2020). Furthermore, HIV incidence among PrEP users in programmatic settings often exceeds that observed in clinical trials, suggesting implementation gaps. A meta-analysis of PrEP demonstration projects found HIV incidence rates ranging from 0.8 to 3.7 per 100 person-years among young women, with higher rates associated with younger age, inconsistent PrEP use, and concurrent STIs (Estcourt et al., 2023; Mugo et al., 2023).

The relationship between STIs and HIV acquisition is particularly relevant for young women on PrEP. STIs, including syphilis, gonorrhea, and chlamydia, increase HIV susceptibility through multiple mechanisms that include disruption of mucosal barriers,

recruitment of HIV target cells to genital tissues, as well as increased viral shedding from HIV-positive partners (Sexton et al., 2018).

Studies from Kenya and South Africa have documented STI prevalence exceeding 20% among young women initiating PrEP, with incident STI rates of 15-30 per 100 person-years during follow-up (Rousseau et al., 2022). These high STI rates not only indicate ongoing sexual risk behavior but also represent missed opportunities for comprehensive sexual health services.

The burden of STIs among young women in Uganda remains inadequately characterized, particularly in the context of PrEP programs. Available data suggest a high prevalence of curable STIs, with studies reporting rates of 14.8% for chlamydia, 8.6% for gonorrhea, and 2.8% for syphilis among sexually active young women (Torrone et al., 2018). However, routine STI screening is not standard practice in most PrEP programs due to resource constraints, potentially missing opportunities for integrated HIV/STI prevention. The syndromic management approach used in many settings may miss asymptomatic infections, which constitute the majority of STIs in women (Mayanja et al., 2020).

Behavioral and social factors significantly influence both HIV and STI risk among young women. Transactional sex, reported by 15-40% of young women in East Africa, increases vulnerability through power imbalances that limit condom negotiation and partner selection (Kyegombe et al., 2019). Multiple concurrent partnerships, common among the youth still navigating economic pressures and social transitions, amplify transmission networks. Age-disparate relationships with older male partners who may

have higher HIV prevalence and resist condom use further compound the risk (Celum et al., 2022; Lewis et al., 2022). Understanding how these factors interact with PrEP use is crucial for optimizing prevention strategies.

This study aimed to characterize young women who were screened and initiated on PrEP uptake and quantified the burden of HIV and STIs during January 2024 to September 2025. Understanding these burdens in real-world settings can inform the implementation of targeted interventions to enhance PrEP effectiveness and integrate comprehensive sexual health services for young women.

Methods

Study Setting

The STI clinic at Mulago National Referral Hospital serves as a high-volume site for HIV prevention services, including PrEP provision to at-risk populations. The clinic's integration of PrEP into routine STI services, along with its use of both facility- and community-based screening approaches, provides an opportunity to examine PrEP uptake patterns across diverse service delivery models. Additionally, the clinic's systematic data collection through the population-at-high-risk tracker enables analysis of demographic and behavioral factors associated with PrEP initiation.

Data Sources

The study was approved by the Walden University Institutional Review Board, the Mildmay Uganda Research Ethics Committee (MUREC), and the Uganda National Council for Science and Technology (UNCST) prior to its commencement. Secondary data was abstracted from the populations-at-high-risk tracker, a national surveillance

system used to collect and store routine data from clients seeking HIV prevention services. The tracker is a case-based surveillance system built on the District Health Information System (DHIS-2) platform, which stores individual-level data on screening, enrolment, and follow-up for clients receiving services at public health facilities. At screening, participants were assessed by health care workers for PrEP using a set of standard questions for high-risk sexual behavior, including having multiple sexual partners, condomless sex, HIV status of sexual partners, engaging in transactional sex, substance use, and a history of STIs.

HIV testing was offered to all participants using the national HIV testing algorithm, which involves Determine as the initial test. If the result is reactive, Stat-Pak is used, and if the results are discordant, a final tiebreaker is performed with Uni-Gold. Identified HIV positive clients were counselled and initiated on ART on the same day.

HIV negative clients who were assessed to be at high HIV risk were initiated on PrEP. Syphilis testing was conducted with rapid plasma reagin (RPR) testing. A new diagnosis of syphilis was made by the study clinician by considering any previous RPR and treponemal results that were available in the participants' files. Participants were assigned an alphanumeric unique number for tracking at subsequent visits as they came for PrEP refills, which enabled the estimation of person-time under observation.

Statistical Analysis

Demographic and behavioral characteristics for participants were summarized using frequencies and percentages for categorical variables and medians with interquartile ranges for continuous variables. Survival analysis methods were used to

estimate HIV and STI burdens, estimated as incidence and defined as the number of HIV and STI first incidents divided by person-years at risk (PYA) per 100 PYA, excluding those with a baseline prevalent infection from that calculation. Participant time to HIV and STI infections was explored using Kaplan-Meier curves and compared using log-rank tests. A Poisson regression model with a log link and exchangeable correlation was used to assess the crude and adjusted effects of participant characteristics on HIV and STI incidence. The variables in the model included participant demographics and behavioral characteristics.

A p -value < 0.05 was considered statistically significant for all analyses.

Variables associated with HIV or STI incidence at $p < 0.20$ in univariable Poisson regression models were entered into the multivariable Poisson regression model to estimate the adjusted effects of participant characteristics. Effect measures were summarized using incident rate ratios (IRR) and adjusted incident rate ratios (aIRR), along with their 95% confidence intervals (CI). All data were analyzed using Stata IC 16.0.

Results

Baseline Social Demographic Characteristics

Median (interquartile range [IQR]) age was 21 (19-23) years. The majority had post-primary level education (43.07%) and were single or separated (97.5%). Most (73.9%) lived in the Kampala metropolitan area, which comprises Kampala, Wakiso, and the surrounding districts. Nearly all (97.9%) were enrolled through community outreach programs, with only 291 (7.7%) initiated at health facilities. About half reported being

engaged in transactional sex, just 9% knew the HIV status of their sexual partners, and nine out of ten reported having more than one sexual partner. Six percent reported having had a history of STIs, and a similar number had ever been treated for STIs. Only 710 (41.0%) reported using condoms during the last sex, 38(1.0%) had injected drugs at some point, and over 80% reported engaging in casual sex (Table 1).

Table 1*Baseline Social Demographic and Behavior Risk Factors*

Characteristic	N (%)
Total	3,958
Age (years)	
Median (IQR)	21 (19-23)
15-19	1,174 (29.7)
20-24	2,784 (70.3)
Education level	
None	539 (14.3)
Primary	1610 (42.7)
Post primary	1618 (43.0)
Marital status	
Married/cohabiting	96 (2.5)
Single /divorced/separated/widowed/separated	3,760 (97.5)
District	
Kampala	1,742 (44.0)
Wakiso	1,736 (43.9)
Other	480 (12.1)
Religion	
Christian	3508 (92.3)
Other	291 (7.7)
Type of service model	
Community	3682 (97.9)
Health facility	81 (2.2)
Client pregnant	
No	2137 (99.5)
Yes	10 (0.5)
Engaged in transactional sex	
No	2015 (50.9)
Yes	1943 (49.1)
Know the HIV status of the partner	
No	1369 (90.7)
Yes	141 (9.3)
Number of sexual partners in a month	
≤1	41 (4.9)
>1	792 (95.1)
History of STIs	
No	3706 (93.6)
Yes	252 (6.4)
Treatment of STIs	
No	3737 (94.4)
Yes	221 (5.6)
Used condom last sex	
No	1024 (59.1)
Yes	710 (41.0)
History of injecting drugs	
No	3920 (99.0)
Yes	38 (1.0)
History of sharing injecting materials	
No	1121 (97.5)
Yes	29 (2.5)
Pregnant	
No	2137 (99.5)
Yes	10 (0.5)
Sexual relationship type	
Both casual and regular	540 (18.3)
Casual	2411 (81.7)

Note. N = 3,958 were started on PrEP from January 2024 to September 2025

Benefits of PrEP

HIV and STI Incidence

Out of the 3,958 young women who started or continued PrEP during 2024-2025, 1,991 (49.9%) visited the clinic at least twice a year, contributing 1,768 py of observation. A total of 20 (1.0%) participants seroconverted, and 133 (6.7%) were diagnosed with STI infections during the 2024-2025 period. The survival distributions for HIV and STIs are depicted in the Kaplan-Meier curves in Figures 1 and 2.

Figure 1

Distribution of Time to HIV Infection

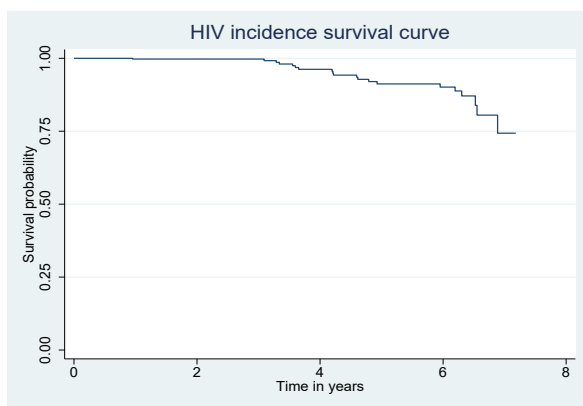
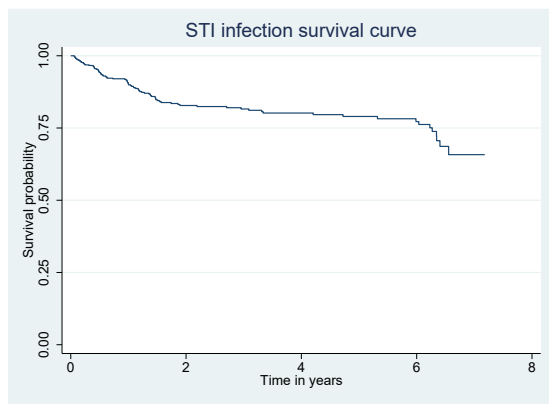


Figure 2

Distribution of Time to STI



Overall incidence rates were 1.13 (95%CI 0.73 – 1.75) and 7.52 (95%CI 6.35 – 8.92) per 100 py, for HIV and STIs, respectively. HIV incidence rate was higher among participants who were older (1.18 95%CI 0.73, 1.89 cases per 100 p-y), married (2.17 95%CI 1.04, 4.56), living in Kampala district (1.30 95%CI 0.81, 2.08), pregnant (3.78 95%CI 0.53, 26.86), who engaged in transactional sex (1.32 95%CI 0.85, 2.00), pregnant (3.78 95%CI 0.53, 26.86), and those who had a history of STIs (1.22 95%CI 0.79, 1.89).

On the other hand, STI incidence rate was higher among participants who were younger (11.00 95%CI 7.93, 15.24 cases per 100 py), had higher education (11.84 95%CI 9.35, 14.99), were not married (8.99 95%CI 7.54, 10.72), were living in Kampala district (8.00 95%CI 6.61, 9.69), those who were receiving PrEP services in the community (16.14 95%CI 13.44, 19.37), those who engaged in transactional sex (8.03 95%CI 6.73, 9.59), those who had a history of STIs (7.35 95%CI .35, 8.92) and those who had both causal and regular sexual relationships (25.93 95%CI 15.63, 43.01), see Table 2.

Table 2*HIV and STI Incidence Among Young Women*

Characteristic	HIV Number of events	Person-years	Incidence per 100 py (95% CI)	STI Number of events	Person- years	Incidence per 100 py (95% CI)
Overall	20	1,768	1.13 (0.73, 1.75)	133	1,768	7.52 (6.35, 8.92)
Age group						
15-19	3	327	0.92 (0.30, 2.84)	36	327	11.00 (7.93, 15.24)
20-24	17	1,441	1.18 (0.73, 1.89)	97	1,441	6.73 (5.51, 8.22)
Education level						
Primary and lower	9	836	1.08 (0.56, 2.07)	59	836	7.06 (5.47, 9.11)
Post primary	6	583	1.03 (0.46, 2.07)	69	583	11.84 (9.35, 14.99)
Marital status						
Married/cohabiting	7	322	2.17 (1.04, 4.56)	7	322	2.17 (1.04, 4.56)
Single/divorced/separated/ widowed/ separated	11	1,380	0.80 (0.44, 1.44)	124	1,380	8.99 (7.54, 10.72)
District						
Kampala	17	1,312	1.30 (0.81, 2.08)	105	1,312	8.00 (6.61, 9.69)
Other	3	456	0.66 (0.21, 2.04)	28	456	6.14 (4.24, 8.89)
Religion						
Christian	14	1,230	1.14 (0.67, 1.92)	119	1,230	9.67 (8.08, 11.58)
Other	2	220	0.91 (0.23, 3.64)	10	220	4.55 (2.45, 8.46)
Type of service model						
Community	2	713	0.28 (0.07, 1.12)	115	713	16.14 (13.44, 19.37)
Health facility	0	52	0	3	52	5.75 (1.85, 17.83)
Client pregnant						
No	15	1,060	1.41 (0.85, 2.35)	41	1,060	3.78 (2.78, 5.13)
Yes	1	26	3.78 (0.53, 26.86)	0	26	0
Engaged in transactional sex						
No	0	249	0	11	249	4.41 (2.44, 7.97)
Yes	20	1,519	1.32 (0.85, 2.0)	122	1,519	8.03 (6.73, 9.59)
Number of sexual partners						
≤1	0	6	0	0	6	0
>1	0	36	0	1	36	2.78 (0.39, 19.76)
History of STIs						
No	0	125	0	0	0	0
Yes	20	1,643	1.22 (0.79, 1.89)	133	1,767	7.35 (6.35, 8.92)
Sexual relationship type						
Both casual and regular	0	58	0	15	58	25.93 (15.63, 43.01)
Casual	1	583	0.17 (0.02, 1.22)	99	583	16.97 (13.94, 20.67)

Factors Associated with HIV and STI Incidence

Only marital status had a borderline association with HIV incidence. Non-married participants were 64% (aIRR = 0.36, 95% CI 0.12, 1.06, p -value = 0.063) less likely to seroconvert compared to those who were married. In the STI Poisson model, education level, marital status, and religion were significantly associated with STI incidence. But the age group had a borderline significant relationship with the risk of STIs. STI incidence was 61% (aIRR = 1.61, 95% CI 1.14-2.29, p -value = 0.007) higher among young women who had post-primary education compared to those who had primary education and no further education. Young women who were not married had a three-fold increase (aIRR=3.25 (1.32, 7.99, p -value=0.010) in HIV incidence compared to those who were married. Participants aged 20-24 years were 30% (aIRR=0.70, 95% CI 0.47, 1.03, p -value=0.069) less likely to have an STI infection compared to those aged 15-19 years (Table 3).

Table 3*Unadjusted and Adjusted Factors Associated with HIV and STI Incidence*

Characteristic	HIV			STI		
	Unadj. IRR (95%CI)	Adj. IRR (95%CI)	p-value	Unadj. IRR (95%CI)	Adj. IRR (95%CI)	p-value
Age group						
15-19	1	1		1	1	
20-24	1.29 (0.37, 4.39)	1.04 (0.23, 4.72)	0.962	0.61 (0.42, 0.99)	0.70 (0.47, 1.03)	0.069
Education level						
Primary and lower	1			1	1	
Post primary	0.96 (0.34, 2.69)			1.68 (1.19, 2.38)	1.61 (1.14, 2.29)	0.007
Marital status						
Married/cohabiting	1	1		1	1	
Single/divorced/separated/widowed/separate	0.37 (0.14, 0.95)	0.36 (0.12, 1.06)	0.063	4.14 (1.93, 8.86)	3.25 (1.32, 7.99)	0.010
District						
Kampala	1			1		
Other	0.51 (0.15, 1.73)			0.77 (0.51, 1.16)		
Religion						
Christian	1			1	1	
Other	0.80 (0.18, 3.52)			0.47 (0.25, 0.90)	0.52 (0.27, 0.96)	0.049
Type of service model						
Community				1		
Health facility				0.36 (0.11, 1.12)		
Client pregnant						
No		1				
Yes	2.67 (0.35, 20.25)	4.13 (0.53, 32.31)	0.177			
Engaged in transactional sex						
No				1	1	
Yes				1.81 (0.98, 3.37)	1.11 (0.56, 2.19)	0.761
Sexual relationship type						
Both casual and regular				1		
Casual				0.65 (0.38, 1.13)		

Discussion

This study provides critical real-world evidence on HIV and STI incidence among young women using PrEP in urban Uganda and reveals an HIV incidence of 1.13 per 100 person-years as well as a concerning STI incidence of 7.52 per 100 pys. These findings highlight both the protective effect of PrEP against HIV and the persistent vulnerability to STIs, underscoring the need for comprehensive sexual health approaches beyond HIV prevention alone.

HIV Incidence in the Context of PrEP Implementation

The observed HIV incidence of 1.13 per 100 person years (pys) among young women on PrEP represents a substantial reduction compared to the expected incidence without PrEP. Historical cohort studies from Uganda reported HIV incidence rates of 3.5-5.0 per 100 person-years among high-risk young women not on PrEP (Grabowski et al., 2022; Kagaayi et al., 2019). This suggests an approximate 70-75% reduction in HIV acquisition, aligning with effectiveness estimates from implementation studies across sub-Saharan Africa. The Partners Demonstration Project in Kenya and Uganda found similarly low incidence (0.2-2.3 per 100 pys) among women with high adherence (Heffron et al., 2017).

However, my incidence rate exceeds that observed in controlled trials where adherence was optimized. The iPrEx OLE and PROUD studies reported an incidence of less than 0.5 per 100 person-years with consistent PrEP use (Grant et al., 2014; McCormack et al., 2016). This gap between trial efficacy and real-world effectiveness

reflects implementation challenges, including suboptimal adherence, missed doses during high-risk periods, and potential drug resistance. Studies from South Africa's CAPRISA 082 trial found similar patterns, with HIV incidence of 1.9 per 100 pys despite PrEP provision, attributed primarily to inconsistent use (Mansoor et al., 2014).

The association between marital status and HIV incidence warrants careful interpretation. Married young women showed higher HIV incidence (2.17 vs 0.80 per 100 person-years) compared to unmarried participants, with a 64% higher risk after adjustment. This finding challenges the assumption that marriage is protective and aligns with emerging evidence from Eastern Africa. Mugwanya et al. (2021) reported similar patterns in Kenya, where married young women had 2.5-fold higher HIV risk, potentially reflecting reduced condom use in marriage, limited negotiating power with older spouses, and exposure to partners' external sexual networks. The "marriage paradox" described by Nabukenya et al. (2020) in Ugandan fishing communities found that married women often cannot negotiate safer sex or PrEP use due to trust expectations and gender norms.

STI Burden and Implications for Sexual Health

The STI incidence of 7.52 per 100 person-years reveals a substantial burden of bacterial infections despite PrEP use, consistent with rates reported across African PrEP programs. The HPTN 082 study in South Africa and Zimbabwe found STI incidence of 11.2 per 100 person-years among young women on PrEP (Delany-Moretlwe et al., 2022). My rates, while slightly lower, remain concerning given that STIs increase HIV susceptibility through biological mechanisms and indicate ongoing condomless sex.

The age-specific pattern of STI incidence, 11.00 per 100 person-years among 15–

19-year-olds versus 6.73 among 20–24-year-olds, mirrors findings from the DREAMS evaluation in Kenya, where younger adolescents had 1.8-fold higher STI risk (Gourlay et al., 2022). This may reflect biological vulnerability due to cervical ectopy, less experienced partner negotiation, and potentially riskier sexual networks. The 30% lower STI risk among older young women after adjustment suggests that developmental factors beyond simple age effects are at play.

Educational attainment emerged as an unexpected predictor, with post-primary education associated with a 61% higher incidence of STIs. This contradicts conventional assumptions about education as protective, but aligns with recent analyses from Tanzania, which show similar patterns (Francis et al., 2021). Potential explanations include increased mobility and sexual networking opportunities among the educated young women, false confidence in risk assessment, or selection bias where educated women are more likely to recognize symptoms and seek testing.

The protective effect of marriage against STIs (IRR 0.24) contrasts sharply with its association with higher HIV risk, which suggests different transmission dynamics. Married young women may have fewer partners, reducing STI exposure, while their HIV risk stems from partners' external exposures. This divergence, also noted in Malawian cohorts (Reed et al., 2024), highlights the complexity of risk within different partnership types and the need for nuanced prevention approaches.

Service Delivery Models and Outcomes

Although not statistically significant in adjusted analyses, the variation in outcomes between community and facility-based service delivery provides valuable

insights for program optimization. Community-based services showed a higher incidence of STIs (16.14 vs 5.75 per 100 person-years), possibly reflecting differences in client populations, screening intensity, or support services. Facility-based programs may provide more comprehensive sexual health services like regular STI screening, treatment, and counselling. These patterns align with findings from Eswatini's evaluation, which showed that facility-based PrEP services led to improved retention and clinical outcomes (Inghel et al., 2022).

Transactional Sex and Vulnerability

Nearly half (49.1%) of participants reported engaging in transactional sex, substantially higher than general population estimates of 15-25% among Ugandan young women (Lunkuse et al., 2022). While not independently associated with HIV/STI incidence after adjustment, this high prevalence indicates the economic vulnerabilities driving risk behavior. The lack of association may reflect successful PrEP protection despite high-risk behavior, or potentially that transactional sex in this population involves consistent partners rather than multiple casual encounters. Studies from Kenya's Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe (DREAMS) program found that combining PrEP with economic empowerment interventions reduced both transactional sex and HIV incidence (Gourlay et al., 2022).

Clinical and Programmatic Implications

My findings support several programmatic modifications for optimizing PrEP delivery to young women. First, the persistent HIV incidence despite PrEP provision necessitates enhanced adherence support. The 1.13% annual seroconversion rate, while

reduced from expected rates, indicates suboptimal protection. Programs should implement objective adherence monitoring through urine tenofovir testing or dried blood spot testing, as these have been demonstrated to be effective in several trials (Velloza et al., 2022).

Second, the high STI burden mandates integration of comprehensive sexual health services. Current syndromic management approaches overlook asymptomatic infections, which comprise 70-80% of STIs in women (Mayanja et al., 2020). Quarterly STI screening for PrEP users, as recommended by WHO but rarely implemented due to costs, could identify and treat infections that amplify HIV risk.

Third, age-stratified interventions are warranted given differential risk patterns. Younger adolescents (15-19) need enhanced STI prevention, potentially through more frequent screening and intensive counseling. Older young women (20-24) may benefit from couples-based interventions addressing partnership dynamics affecting HIV risk.

Fourth, the marriage-HIV risk association challenges current programming that often excludes married young women as “low risk.” Programs should recognize marriage-related vulnerabilities and develop culturally sensitive approaches for reaching married young women, potentially through antenatal care integration or male partner engagement strategies.

Study Limitations

There are some limitations that affect the interpretation of my findings. First, the observational design precludes causal inference about protective effects attributable specifically to PrEP versus other prevention behaviors. Without a control group of similar

young women who are not on PrEP, I cannot definitively quantify the effectiveness of PrEP in this setting.

Second, adherence data were unavailable, which prevented the conclusive assessment of the relationship between PrEP use patterns and breakthrough infections. HIV incidence varies from near zero with high adherence to rates approaching background incidence with poor adherence (de Vos et al., 2022). My inability to stratify by adherence likely obscures important heterogeneity in protection.

Third, STI testing relied primarily on syndromic presentation rather than routine screening, which likely underestimates the true incidence. Asymptomatic infections, particularly chlamydia and gonorrhea, may have been missed. The reported STI incidence should be considered a minimum estimate.

Fourth, the 50% retention for follow-up visits may introduce selection bias. Young women who remain engaged might differ systematically from those lost to follow-up in terms of risk behaviors, adherence, or health-seeking patterns. Studies from Sub-Saharan Africa have found that individuals who discontinued PrEP often had higher risk profiles (Tetteh et al., 2022).

Fifth, behavioral data relied on self-report, which is subject to social desirability bias, particularly for stigmatized behaviors like transactional sex or multiple partnerships. The true prevalence of risk behaviors may be higher than reported.

Finally, the single urban clinic setting limits generalizability. Rural young women face different risk contexts, including lower partner concurrency and potentially less access to health services. Multi-site studies are necessary to understand the effectiveness

of PrEP across diverse Ugandan settings.

Future Research Priorities

Our findings identify critical research gaps that require further investigation. Longitudinal studies with biomarkers of adherence could clarify the relationship between PrEP use patterns and breakthrough infections. Implementation research should test interventions to address the marriage-HIV risk paradox, potentially, through couples counselling or male partner engagement. Cost-effectiveness analyses of integrated PrEP-STI services versus HIV-only approaches could inform resource allocation decisions.

Additionally, qualitative research should explore how educational attainment influences sexual networks and risk behavior among young women. Studies of long-acting PrEP formulations (cabotegravir, dapivirine ring) may address adherence challenges identified in oral PrEP programs. Finally, evaluation of combination prevention packages that incorporate economic empowerment, PrEP, and STI management could identify synergistic approaches for comprehensive risk reduction.

Conclusions

This real-world evaluation of PrEP implementation among urban Ugandan young women demonstrates substantial but incomplete HIV protection, with breakthrough infections occurring at 1.13 per 100 person-years. The concurrent high STI burden (7.52 per 100 person-years) reveals ongoing vulnerability that calls for the adoption of comprehensive sexual health approaches beyond HIV prevention alone. Differential risk patterns by age, education, and marital status challenge conventional assumptions and demand nuanced, tailored interventions.

The unexpected vulnerability of married young women to HIV, contrasting with their protection from STIs, highlights complex transmission dynamics within different partnership types. Educational gradients in STI risk and age patterns in both HIV and STI incidence underscore the heterogeneity within the young women population, which necessitates stratified prevention approaches.

Achieving Uganda's ambitious HIV prevention targets requires optimizing PrEP delivery through enhanced adherence support, integrated STI management, and interventions that address social vulnerabilities. A significant number of individuals participating in transactional sex highlights the economic factors driving this behavior, underscoring the need for structural interventions that go beyond biomedical prevention methods. Success will be determined by not just how widely PrEP coverage is, but by sustained long-term effectiveness in reducing new HIV cases to nearly zero.

My findings show that while PrEP is valuable, it's not enough on its own for comprehensive HIV prevention among young women. To move forward, we need to combine biomedical, behavioral, and structural interventions that address the complex factors affecting young women's HIV risk. An AIDS-free generation for African young women can only be achieved through these comprehensive approaches.

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**Manuscript 3: Influence of PrEP Service Delivery Models on PrEP Continuity
Among Young Women in Uganda**

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Outlet for Manuscript

The target journal is *AIDS Care*, which is accessible at <https://www.tandfonline.com/journals/caic20/about-this-journal#open-access>. *AIDS Care* is an international, peer-reviewed, open-access journal. The journal features scholarly articles on HIV/AIDS, with a focus on the planning, social, and psychological aspects of prevention, care, and treatment. It covers topics from various fields, including psychology, sociology, and health education. The journal seeks to publish research from diverse institutions worldwide to address the global impact of HIV/AIDS. This journal aligns with my manuscript content on PrEP continuation among young women in Uganda, as it focuses on multidisciplinary HIV/AIDS research, including social, psychological, and service-related factors. It emphasizes the global and societal impact of HIV, including topics such as HIV stigma, behavioral risk factors, and access to treatment services.

Authors can submit manuscripts in any format or layout, including Word and PDF, with figures and tables either embedded or separate, as long as the resolution is sufficient for review. Essential manuscript elements include an abstract, author details, figures, tables, and funding information. References can be in any format, but the citation style has to be consistent. The journal applies its own reference style upon acceptance. It requires me to provide a final editable version upon acceptance.

Abstract

Despite being recognized as a highly cost-effective HIV prevention strategy, pre-exposure prophylaxis (PrEP) uptake and continuity remain suboptimal among young women, highlighting the urgent need to address underlying barriers and logistical challenges hindering access and utilization of this preventive measure. Maintaining continuity is essential because PrEP's effectiveness depends heavily on adherence and consistent access. This study examined the impact of PrEP service delivery models on PrEP adherence among young women aged 15-24. Andersen's behavioral model offers a theoretical framework for understanding the continuation of PrEP among young women in Uganda. Secondary data were abstracted from routine data for clients seeking HIV prevention services at the Mulago National Referral Hospital's STI clinic. A total of $N=2,495$ young women were on PrEP during the period from January 2024 to September 2025. This study revealed critically low PrEP continuation rates among young women in Uganda, with only 6.48% remaining on PrEP at 12 months despite substantial HIV risk in this population. There was a significant difference in continuation rates between facility-based (74.88 per 100 person-years) and community-based (11.04 per 100 person-years) service delivery. The findings suggest consideration for hybrid models that combine community outreach for awareness and screening with facility-based initiation and early support. Enrolled clients on PrEP need intense adherence counseling to improve continuity rates.

Introduction

According to Barnabee et al. (2023), the HIV pandemic remains one of the leading public health challenges globally. HIV is mainly spread through heterosexual sex. The World Health Organization (WHO) estimates that 69% of the people living with HIV are found in sub-Saharan Africa (Steven et al., 2024; Vithalani et al., 2018). Currently, Uganda is ranked 6th globally among countries highly burdened by HIV, with over one-third of the new infections found among young women (Mayanja et al., 2022).

Several HIV prevention strategies have been established. These main strategies have been developed in line with the risk involved in acquiring HIV. Pre-exposure prophylaxis (PrEP) is the main preventive strategy developed for HIV-negative people at risk of acquiring HIV (Roberts et al., 2023; Sensalire et al., 2024). The World Health Organization (WHO) approved the use of PrEP among HIV-negative people, but its effectiveness relies on its accessibility and proper adherence. The main key and priority populations eligible for PrEP include discordant couples, sex workers, fisherfolk, long-distance truck drivers, men who have sex with men, uniformed forces, and adolescent girls and young women (Ekwunife et al., 2022; Kagaayi et al., 2020).

PrEP continuity refers to the sustained and consistent use of PrEP medication among individuals at risk of HIV infection. Maintaining continuity is essential because PrEP's effectiveness depends heavily on adherence and consistent access. Interruptions, whether due to medication supply issues, healthcare access barriers, or personal challenges, can significantly reduce protection and increase vulnerability to HIV exposure (Mayanja et al., 2022; Tapsoba et al., 2022).

Several factors influence PrEP continuity among young women, including individual, structural, and policy barriers (Mubezi et al., 2023; Muhumuza et al., 2021). Individual-level barriers include low-risk perception, medication fatigue, side effects, mental health and substance use, and lack of knowledge. Structural and policy factors include socioeconomic status, such as unemployment and low income, which can hinder access to transportation for refills. Additionally, regional disparities, including limited PrEP availability in hard-to-reach and underserved areas, also pose challenges (Cooper et al., 2024; Mayanja et al., 2022).

Various strategies have been proposed to increase PrEP continuity. The key ones have focused on community-based programs to support ongoing engagement, health education to reduce stigma, and ongoing efforts to adopt long-acting injectable PrEP to alleviate the adherence burden (Dada et al., 2025; Mugwanya et al., 2023). All these strategies have been operationalized; however, PrEP uptake among young women remains a problem not only in Uganda but also in other high-burden countries in the sub-Saharan region, where the burden is highest among this population. In this study, I estimated the continuity of PrEP among young women who initiated and continued PrEP between January and December 2024. This period was chosen to enable us to estimate the proportion and rate of young women who remained on PrEP 12 months after initiation, as defined in the WHO guidelines.

Methods

Study Setting

The STI clinic at Mulago National Referral Hospital serves as a high-volume site

for HIV prevention services, including PrEP provision to at-risk populations. The clinic's integration of PrEP into routine STI services, along with its use of both facility- and community-based screening approaches, provides an opportunity to examine PrEP uptake patterns across diverse service delivery models. Additionally, the clinic's systematic data collection through the population-at-high-risk tracker enables analysis of demographic and behavioral factors associated with PrEP initiation.

Data Sources

The study was approved by the Walden University Institutional Review Board, the Mildmay Uganda Research Ethics Committee (MUREC), and the Uganda National Council for Science and Technology (UNCST) prior to its commencement. The data collection process described utilizes a robust surveillance system, specifically designed to track high-risk populations and monitor HIV prevention services. The surveillance system is a case-based surveillance platform that collects individual-level data on clients seeking HIV prevention services, built on the widely adopted DHIS-2 platform for scalability and reliability. Each client was assigned a unique alphanumeric identifier to enable precise tracking, and the system supports comprehensive data collection, including screening, enrollment, and follow-up visits. The data collection covered HIV testing and assessment of behavioral risk factors such as multiple sexual partners and condomless sex. HIV-negative clients identified as high-risk are initiated on PrEP, while those diagnosed as HIV-positive are counseled and initiated on antiretroviral therapy (ART) on the same day. This system offers multiple benefits, including improved data management for efficient client tracking and treatment monitoring, enhanced patient care through

timely interventions and targeted support, and valuable insights that inform and optimize HIV prevention strategies and public health programs.

Statistical Analysis

Demographic and behavioral characteristics of participants enrolled on PrEP were summarized using frequencies and percentages for categorical variables, and summary median with interquartile ranges for continuous variables. To estimate the PrEP continuity, survival analysis methods were used. PrEP continuity was defined as young women who started PrEP and continued to use it 12 months after initiation. Participants who did not reach 12 months were right censored. Data was analyzed for young women initiated on PrEP between January and September 2024, determining their active status by the end of September 2025.

PrEP continuity was explored using Kaplan-Meier curves, and the relationship with participant characteristics was explored using log-rank tests. PrEP continuity was summarized in the form of rates estimated by dividing the number of young women still on PrEP after 12 months by the total person-time at risk, and expressed as incidence rates per 100 person-years (pys).

To assess the crude and adjusted effects of participant demographic and behavioral characteristics on PrEP continuity, a Poisson regression model with a log link and robust standard errors was fitted, with person-time at risk included as an offset. The outcome variable was time to PrEP continuity, defined as the date of refill within 12 months of PrEP initiation. The exposure variables included demographic characteristics (age, marital status, education level, religion, and district of residence), and behavioral

risk characteristics (number of sexual partners, knowledge of HIV status of sexual partners, condom use during last sex, history and treatment of STIs, pregnancy, injecting drug history, and engagement in transactional sex).

Separate Poisson regression models with a log link, robust standard errors, and person-time at risk as an offset were fitted for each participant characteristic to estimate unadjusted incidence rate ratios (IRRs) for PrEP continuity. The variance inflation factor was used to assess collinearity between exposure variables. Effect measures were summarized using adjusted incident rate ratios (aIRR) and their corresponding 95% confidence intervals (95% CI). Variables with a p -value < 0.2 at the univariate level were added to the multivariate model. All data were analyzed using Stata IC 16.0.

Results

A total of 2,495 young women were on PrEP during the study period. Median (interquartile range [IQR]) age was 21 (19-23) years. The majority had post-primary level education (44.4%) and were single or separated (96.4%). Most lived in the Kampala metropolitan area, mainly Kampala (48.7%) and Wakiso (40.6%) districts. Nearly all (96.7%) were enrolled through the community outreaches, with just 76 (3.3%) initiated at health facilities. The majority (78.3%) reported engaging in transactional sex, just 16% knew the HIV status of their sexual partners, and >98% reported having more than one sexual partner. Four percent reported having had in the past STIs symptoms, and 211(8.5%) had been treated for STIs. Only 101 (30%) reported using condoms during the last sex, but only 19(0.8%) had injected drugs at some point, and over 80% reported engaging in casual sex (Table 1).

Table 1*Baseline Social Demographics of Young Women who were on Oral PrEP*

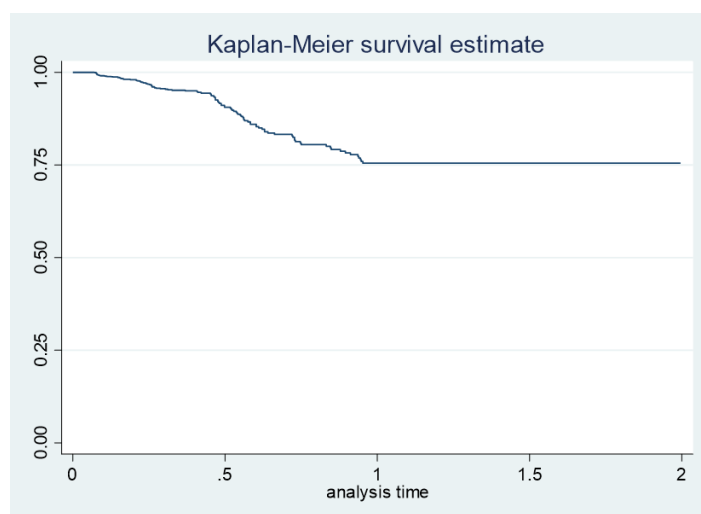
Characteristic	n (%)
Overall	2,495
Age (years)	
Median (IQR)	21 (19-23)
15-19	688 (27.6)
20-24	1,807 (72.4)
Education level	
None	331 (13.8)
Primary	1,006 (41.8)
Post primary	1,069 (44.4)
Marital status	
Married/cohabiting	89 (3.6)
Single /divorced/separated/widowed/separated	2,368 (96.4)
District	
Kampala	11,214 (48.7)
Wakiso	1,014 (40.6)
Other	267 (10.7)
Religion	
Christian	2,220 (91.6)
Other	201 (8.5)
Type of service model	
Community	2,221 (96.7)
Health facility	76 (3.3)
Client pregnant	
No	1,376 (99.4)
Yes	8 (0.6)
Engaged in transactional sex	
No	541 (21.7)
Yes	1,954 (78.3)
Know HIV status of partner	
No	271 (83.6)
Yes	54 (16.4)
Number of sexual partners in a month	
<=1	2 (1.9)
>1	103 (98.1)
History of STIs	
No	2,388 (95.7)
Yes	107 (4.3)
Treatment of STIs	
No	2,284 (91.5)
Yes	211 (8.5)
Used condom last sex	
No	231 (69.6)
Yes	101 (30.4)
History of injecting drugs	
No	2476 (99.2)
Yes	19 (0.8)
History of sharing injecting materials	
No	268 (99.3)
Yes	2 (0.7)
Pregnant	
No	1,376 (99.4)
Yes	8 (0.6)
Sexual relationship type	
Both casual and regular	234 (12.5)
Casual	1,632 (87.5)

PrEP Continuity During January 2024—September 2025

Out of the 2,495 young women who initiated and/or were continuing on PrEP by Dec 31, 2024, 1,925 (77.2%) had at least two refill visits at the clinic, contributing 1,805 pys. Of the 1,925 individuals who contributed analysis time, only 117 (6.1%) were still active on PrEP by the end of 1 year, equivalent to a continuity rate of 6.48 (95% CI 5.41–7.77) persons per 100 pys. The distribution is depicted in a Kaplan-Meier curve in Figure 1.

Figure 1

Kaplan-Meier Survival Estimate



Factors Associated with PrEP Continuity

PrEP continuity was twice as high among the young women compared to the older young women and tended to increase with higher education level. Also, PrEP continuity was three times higher among the single/widowed/or separated young women compared to those who were married. The continuity rates were 9 times higher among

young women who initiated care at health facilities compared to those in the community. Young women who were not pregnant had a two-fold higher continuity rate than those who were pregnant. And participants who had been treated for STIs had a two-fold increase in PrEP continuity than those who were not. Young women who engaged in transactional sex were less likely to continue on PrEP compared to those who did not. The characteristics that were significantly associated with PrEP continuity were age, type of service model, and STI treatment (Table 2).

Table 2*PrEP Continuity at 12 Months and Associated Factors*

Characteristic	PrEP active	Person-years	Incidence per 100 py (95% CI)	Unadjusted IRR (95%CI)	Adjusted IRR (95%CI)	p-value
Overall	117	1,805	6.48 (5.41, 7.77)			
Age group						
15-19	37	325	11.38 (8.24, 15.70)	1	1	
20-24	80	1,480	5.41 (4.34, 6.73)	0.48 (0.32, 0.70)	0.60 (0.37, 0.97)	0.038
Education level						
None	13	224	5.79 (3.36, 9.98)	1		
Primary	37	634	5.84 (4.23, 8.06)	1.01 (0.54, 1.90)		
Post primary	63	593	10.63 (8.30, 13.60)	1.83 (1.01, 3.33)		
Marital status						
Married/cohabiting	7	330	2.12 (1.01, 4.45)	1	1	
Single /divorced/separated /widowed/separated	106	1409	7.52 (6.22, 9.10)	3.55 (1.65, 7.62)	0.88 (0.30, 2.56)	0.813
District						
Kampala	68	1,351	5.03 (3.97, 6.38)	1	1	
Wakiso	36	388	9.27 (6.69, 12.85)	1.84 (1.23, 2.76)	0.93 (0.42, 2.04)	0.851
Other	13	66	19.72 (11.45, 33.96)	3.92 (2.16, 7.09)	1.07 (0.50, 2.30)	0.869
Religion						
Christian	106	1251	8.47 (7.00, 10.25)	1	1	
Other	10	231	4.32 (2.33, 8.03)	0.51 (0.27, 0.98)	1.19 (0.56, 2.54)	0.646
Type of service model						
Community	78	707	11.04 (8.83, 13.78)	1	1	
Health facility	39	52	74.88 (54.71, 102.49)	6.79 (4.62, 9.97)	8.93 (4.91, 16.23)	<0.001
Client pregnant						
No	67	1087	6.17 (4.85, 7.83)	1		
Yes	1	26	3.78 (0.63, 26.86)	0.61 (0.09, 4.42)		
Engaged in transactional sex						
No	24	248	9.66 (6.48, 14.41)	1	1	
Yes	93	1157	5.97 (4.88, 7.32)	0.62 (0.39, 0.97)	0.93 (0.48, 1.78)	0.822
History of STIs						
No	117	1805	6.48 (5.41, 7.77)			
Yes	0					
Treatment of STIs						
No	98	1680	5.83 (4.78, 7.11)	1	1	
Yes	19	125	15.22 (9.71, 23.86)	2.61 (1.60, 4.27)	2.39 (1.39, 4.12)	0.002
History of injecting drugs						
No	117	1805	6.48 (5.41, 7.77)			
Yes	0					
Sexual relationship type						
Both casual and regular	5	57	8.76 (3.64, 21.04)	1	1	
Casual	81	580	13.96 (11.23, 17.38)	1.59 (0.65, 3.93)	1.38 (0.54, 3.50)	0.501

Discussion

This study reveals critically low PrEP continuation rates among young women in Uganda, with only 6.48% remaining on PrEP at 12 months despite substantial HIV risk in this population. These findings highlight severe challenges in sustaining PrEP use among young women and raise important questions about the effectiveness of current PrEP delivery models in real-world settings.

Low Continuation Rates

The 6.48% continuation rate at 12 months observed in my study is substantially lower than rates reported in other sub-Saharan African settings. Studies from Kenya, South Africa, and Zimbabwe have reported 12-month continuation rates ranging from 25% to 40% among young women (Celum et al., 2022; Pyra et al., 2022; Were et al., 2021). Even in the HPTN 082 study, which faced challenges with adherence, the continuation rate at 12 months was approximately 25% (Beauchamp et al., 2024). My findings suggest that programmatic implementation in Uganda faces unique or amplified barriers compared to both research settings and other real-world programs.

The sharp distinction between the 77.2% who returned for at least one refill and the 6.48% who continued for 12 months indicates that initial motivation exists but rapidly wanes. This pattern aligns with the “PrEP cascade” framework described by Nunn et al. (2017), where the steepest drop-offs occur between initiation and early continuation. The Kaplan-Meier curve’s steep decline in the first three months mirrors findings from the POWER demonstration project, where most discontinuation occurred within 90 days (Kinuthia et al., 2023).

Age Patterns and Developmental Factors

Younger women (15-19 years) demonstrated significantly better continuation (11.38 per 100 person-years) compared to those aged 20-24 (5.41 per 100 person-years), with older young women having 40% lower odds of continuation after adjustment. This finding contradicts assumptions that older, more autonomous young women would show better adherence. However, it aligns with recent evidence from Mackworth-Young et al. (2025) in Zimbabwe, where younger adolescents who successfully navigated initial access barriers showed stronger persistence.

Several mechanisms may explain this counterintuitive age pattern. First, younger adolescents who overcome substantial barriers to PrEP initiation, including parental consent requirements, provider bias, and stigma, may represent a highly motivated and supported subset (Pilgrim et al., 2018). Second, school-going adolescents may have more structured routines that facilitate daily medication adherence, whereas young adults face competing priorities, including employment, relationship changes, and mobility (Camlin et al., 2020). Third, risk perception and prevention priorities may evolve across adolescence, with older young women potentially relying more on partner-based prevention strategies or experiencing “prevention fatigue” (Ridgeway et al., 2018).

Service Delivery Model Impact

The striking difference in continuation rates between facility-based (74.88 per 100 person-years) and community-based (11.04 per 100 person-years) service delivery represents one of my most significant findings. After adjustment, facility-based services showed nearly 9-fold higher continuation rates. This contradicts prevailing assumptions

that community-based services, by reducing access barriers, would improve retention (Ortblad et al., 2023).

Several factors may contribute to the superior performance of facility-based services. First, young women actively seeking facility-based PrEP may have higher intrinsic motivation and risk perception compared to those reached through community outreach. Second, facility-based services may offer more comprehensive counselling, clinical monitoring, and support services that reinforce continued care (Rousseau et al., 2021). Third, the clinical setting may confer greater perceived legitimacy and importance to PrEP use, while community-based distribution might inadvertently minimize its significance (Velloza et al., 2020).

These findings challenge current emphasis on differentiated service delivery models that prioritize community-based distribution. While such models may increase initial uptake, my results suggest they may compromise continuation without adequate support structures. The WHO's recommendation for "simplified" PrEP delivery (Beauchamp et al., 2024; O'Malley et al., 2021, 2021) may need reconsideration, at least for young women populations.

STI Treatment and Healthcare Engagement

Young women who had received STI treatment showed 2.39 times higher continuation rates after adjustment, suggesting that positive healthcare experiences and established clinical relationships facilitate PrEP persistence. This aligns with integration models, which demonstrate that STI treatment visits offer crucial opportunities for PrEP support and adherence counselling (Rousseau et al., 2021). The relationship between STI

treatment and PrEP continuation may reflect both higher risk perception among those with STI history and the benefits of integrated sexual health services.

Interestingly, STI history alone (without treatment) showed no events in my analysis, suggesting incomplete data capture or that untreated STIs represent a marker for healthcare avoidance that extends to PrEP discontinuation. This finding supports the arguments for integrating PrEP-STI services, as recommended by the Centers for Disease Control and Prevention (CDC).

High-Risk Behaviors and Continuation Patterns

Despite high baseline risk (95% reporting multiple partners, 49% engaged in transactional sex, and only 41% using condoms at last sex), continuation rates remained extremely low. This “prevention-risk paradox” has been observed in other PrEP programs, where those at the highest objective risk show the poorest adherence (Corneli et al., 2022). The lack of association between most risk behaviors and continuation suggests that risk exposure alone doesn’t sustain PrEP use.

The absence of continuation events among several high-risk subgroups (partner status knowledge, condom use, and drug injection) likely reflects data limitations rather than true zero continuation. However, it may also indicate that these highest-risk young women face overwhelming structural barriers, including stigma, violence, and economic instability, that make sustained PrEP use virtually impossible (Irungu et al., 2021; Muhumuza et al., 2021).

Implications for Programming

My findings suggest several critical modifications to current PrEP programming.

Rethinking Service Delivery Models

The superior performance of facility-based services challenges current trends toward community-based distribution. Programs should consider hybrid models that combine community outreach for awareness and screening with facility-based initiation and early support. The President’s Emergency Plan for AIDS Relief (PEPFAR) initiative provides a potential framework for such integration.

Age-Tailored Interventions

The better continuation rates among younger adolescents suggest the need for age-stratified approaches, as well as the need to intensify interventions as the young women grow older to reduce dropout rates. For 15- to 19-year-olds, leveraging existing motivation through peer support and school-based programs may be an effective approach. For 20- to 24-year-olds, addressing competing life priorities through flexible delivery and multi-month dispensing may improve adherence and continuation.

Early Intensive Support

The high rate of early discontinuation necessitates intensive support during the first three months. Interventions, such as the “PrEP persistence package” tested in Kenya, which includes SMS reminders, peer navigation, and flexible refills, have shown promise in improving early continuation (Pyra et al., 2022).

Integration with Sexual Health Services

The strong association between STI treatment and continuation supports comprehensive sexual health service integration. Programs should move beyond siloed

HIV prevention toward holistic approaches to sexual and reproductive health, as demonstrated by the successful Integration for Impact project (Mugwanya et al., 2023).

Study Limitations

First, the observational design precludes causal inference, and unmeasured confounders are likely to influence the observed associations. Second, substantial missing data for several variables (indicated by zero events) limited my analytical power and may have biased results. Third, I lacked data on the reasons for discontinuation, which prevented an understanding of whether stops were appropriate (for risk reduction) or problematic (due to access barriers). Fourth, the single urban clinic setting limits generalizability to rural populations where most Ugandan young women reside. Finally, I couldn't assess adherence among those continuing PrEP, and continuation without adherence provides no HIV protection.

Future Research Directions

My findings highlight critical research priorities. Mixed-methods studies should explore reasons for early discontinuation, distinguishing between individual choices and structural barriers. Implementation research should test strategies to support continuation, particularly during the critical first three months. Comparative effectiveness research should evaluate the impact of different service delivery models on both uptake and continuation. Additionally, studies should examine whether poor continuation reflects appropriate de-escalation when risk decreases versus missed prevention opportunities during ongoing risk.

Conclusions

This study reveals a crisis in PrEP continuation among Ugandan young women, with fewer than 1 in 15 continuing for 12 months despite substantial HIV risk. The findings challenge several assumptions underlying current PrEP programming, particularly those related to community-based delivery and age patterns. While expanding PrEP access remains important, our results demonstrate that access without continuation cannot achieve population-level HIV prevention impact. Urgent action is needed to redesign PrEP programs to support sustained use, particularly during the critical early months. Without dramatic improvements in continuation, PrEP's promise for HIV prevention among young women will remain unrealized, perpetuating the disproportionate HIV burden in this vulnerable population.

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Part 3: Summary

The factors influencing PrEP uptake and adherence operate at multiple levels (i.e., individual, behavioral, and structural). Each study enabled the examination of these factors and the development of relevant interventions at different levels, facilitating the design of effective, tailored strategies. Together, these manuscripts work as complementary studies that address the overall study gap by examining PrEP uptake and continuity from different perspectives, including individual behavioral risk factors and structural/systemic barriers. By examining these factors in an integrated manner, the study provides a comprehensive, multi-level understanding of the barriers and facilitators to PrEP uptake and continuity, with a specific focus on young women in Uganda. The findings from each manuscript will inform the development of targeted interventions that address both individual and structural factors influencing PrEP use, thereby contributing to the effectiveness of HIV prevention efforts in Uganda and similar settings.

Manuscript 1

This large-scale analysis of PrEP uptake among young women in Uganda reveals critical programmatic gaps that demand attention. The 16.7% uptake rate, while representing nearly 4,000 young women initiating prevention, indicates that 5 out of 6 eligible high-risk individuals are not accessing this life-saving intervention. More concerning still is the pronounced PrEP paradox, whereby young women at the highest objective HIV risk are 40% less likely to initiate prevention, which challenges the effectiveness of risk-based targeting approaches when structural and psychosocial barriers remain unaddressed.

The eight-fold difference in uptake between facility-based and community-based service models reveals both the power and the limitations of current differentiated service delivery strategies. While community outreach successfully identifies vulnerable populations at scale, conversion to actual service initiation requires the privacy, professional support, and clinical assurance that facility-based services provide. Future prevention programming must move beyond the false dichotomy of community versus facility services toward integrated hybrid models that combine the reach of community engagement with the conversion efficiency of facility-based initiation.

To close the gap between need and initiation, HIV prevention efforts must pivot from risk identification to barrier mitigation. This requires multi-level interventions addressing individual (stigma reduction, PrEP literacy), interpersonal (partner communication, social support), community (stigma reduction, peer networks), and structural (service accessibility, economic empowerment, violence prevention) barriers. Differentiated service delivery models must be truly differentiated—tailored to the specific vulnerabilities, life circumstances, and preferences of distinct young women’s subgroups, rather than being implemented as standardized packages.

As Uganda works toward national and global HIV prevention targets, programmatic success will be determined not by the number of young women screened, but by the number who can access and sustain prevention methods despite the barriers they face. Achieving this will require sustained political commitment, adequate resource allocation, health system strengthening, community engagement, and above all, a fundamental recognition that effective prevention must address the structural

determinants of vulnerability rather than simply identifying those at risk.

Manuscript 2

This real-world evaluation of PrEP implementation among urban Ugandan young women demonstrates substantial but incomplete HIV protection, with breakthrough infections occurring at 1.13 per 100 person-years. The concurrent high STI burden (7.52 per 100 person-years) reveals ongoing vulnerability that calls for the adoption of comprehensive sexual health approaches beyond HIV prevention alone. Differential risk patterns by age, education, and marital status challenge conventional assumptions and demand nuanced, tailored interventions.

The unexpected vulnerability of married young women to HIV, contrasting with their protection from STIs, highlights complex transmission dynamics within different partnership types. Educational gradients in STI risk and age patterns in both HIV and STI incidence underscore the heterogeneity within the young women population, which necessitates stratified prevention approaches.

Achieving Uganda's HIV prevention targets requires optimizing PrEP delivery through enhanced adherence support, integrated STI management, and interventions that address social vulnerabilities. A significant number of individuals participating in transactional sex highlights the economic factors driving this behavior, underscoring the need for structural interventions that go beyond biomedical prevention methods. Success will be determined by not just how wide PrEP coverage is but by sustained long-term effectiveness in reducing new HIV cases to nearly zero.

My findings show that while PrEP is valuable it is not enough on its own for

comprehensive HIV prevention among young women. To move forward, biomedical, behavioral, and structural interventions need to be combined to address the complex factors affecting young women's HIV risk. An AIDS-free generation for African young women can only be achieved through these comprehensive approaches.

Manuscript 3

This study reveals a crisis in PrEP continuation among Ugandan young women, with fewer than 1 in 15 continuing for 12 months despite substantial HIV risk. The findings challenge several assumptions underlying current PrEP programming, particularly those related to community-based delivery and age patterns. While expanding PrEP access remains important, results demonstrate that access without continuation cannot achieve population-level HIV prevention impact. Action is needed to redesign PrEP programs to support sustained use, particularly during the critical early months. Without dramatic improvements in continuation, PrEP's promise for HIV prevention among young women will remain unrealized, perpetuating the disproportionate HIV burden in this vulnerable population.

Dissemination Plan and Use of the Findings

The study's findings will be disseminated in the form of reports, abstracts, and manuscripts at national and international conferences, as well as in peer-reviewed journals. I will also leverage meetings of existing structures, such as national and subnational technical working groups (TWGs), to further disseminate these findings. Key stakeholders in the TWGs will include MARPI, MoH, development partners, regional referral hospitals, and districts. Other considerations include:

The research study comprises three manuscripts that will be published in leading journals in Uganda and Africa. One target journal is AIDS Care. AIDS Care is an international, peer-reviewed, open-access journal. The journal contains scholarly research on HIV/AIDS, focusing on the planning, social, and psychological aspects of prevention, care, and treatment. I will also organize dissemination meetings through webinars targeting public health practitioners. The research contributes to public health knowledge by addressing key gaps in the literature and fostering collaboration among stakeholders, ultimately promoting positive health outcomes and contributing to social change in affected communities in Uganda and Africa.

Finally, through the Baylor Foundation Uganda (Baylorfoundationuganda.org) links. Baylor College of Medicine Children's Foundation Uganda (BFU) supports 45 districts in Uganda and is part of the Network from Texas Children's Medical Centre, USA. I will share on the BFU website and organize dissemination meetings through CMEs for staff and partners.

Risk Mitigation Plan

To protect study personnel and participants against potential diseases or outbreaks of COVID-19, Ebola, or Mpox within the MARPI clinic setting, mitigation measures were instituted that included training in adherence to infection prevention and control measures at the study site, compliance with regular updates from the WHO and MOH, and adherence to public health guidelines.

The sensitive nature of HIV information and the vulnerability of the target population (young women aged 15 - 24) also required careful handling. To mitigate this

risk, as noted in the waiver for informed consent, all data were anonymized, and only the participant IDs will be used. Access to the dataset was restricted. Additionally, ethical approvals from the Walden University IRB, Mildmay REC, and UNCST were obtained prior to the commencement of the study. A waiver of informed consent was requested due to the minimal risk nature of the study.

Other potential risks included incomplete or poor-quality records from the Mulago Sexually Transmitted Diseases (STD) clinic and misinterpretation of the secondary data. I addressed these data quality concerns by working closely with MARPI data officers to verify and validate any entries before conducting the data analysis.

Community Engagement Plan

I had minimal engagement with the community, as the study employed secondary data, and I did not directly interact with the study participants. However, during the secondary data collection phase, I sought one-on-one feedback from facility staff to help contextualize my interpretation of the data. Additionally, to promote the future adoption of the findings, I will engage the MARPI clinic leadership to invite community members and other stakeholders during the dissemination of results.

Timelines and Budget

The main activities of the study included (i) preparation and submission of a protocol to IRB for ethical approval; (ii) Engaging facility team to enable access and extraction of data; (iii) data extraction; (iv) data management and analysis; (v) abstracts writing; (vi) manuscript writing and (vii) dissemination at national and international conferences. I estimate that the study will take 30 weeks (approximately 4 months) from

the time of ethical approval of the protocol. The duration of each activity is shown in

Table 1.

Table 1

Timeframe

#	Activity	Month 1	Month 2	Month 3	Month 4	Responsible persons
1.	Prepare and submit a protocol to the IRB for ethical approval	X	X			PI
2.	Engage the facility staff for data extraction		X			PI and site manager
3.	Data extraction		X			PI and site staff
4.	Data management and analysis		X			PI
5.	Abstracts writing			X		PI
6.	Manuscripts writing			X		PI
7.	Present study findings at national and international conferences				X	PI and site manager
8.	Attend meetings to disseminate findings to key stakeholders				X	PI and site manager

Table 2

Budget

#	Activity	Units	Unit cost (\$)	Total Amount (\$)
1.	Prepare and submit a protocol to the IRB for ethical approval	2 submissions	250	500
2.	Train/engage the data extraction team	1 day	100	100
3.	Data extraction	3 data collectors	100	300
4.	Data management and analysis	1 PI and 3 co-investigators	50	200
5.	Abstracts writing	1 PI	100	100
6.	Manuscripts writing	1 PI	200	200
7.	Present study findings to national and international conferences	2 conferences	500	1,000
8.	Attend meetings to disseminate findings to key stakeholders	3 meetings	200	600
	Total Amount			\$3,000

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