Original Paper

Digitally Enabled Hybrid Delivery of HIV Preexposure Prophylaxis in Gauteng Province, South Africa: Mixed Methods Feasibility and Acceptability Study

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Abstract

Background: Facility-based preexposure prophylaxis (PrEP) services often deter potential users through privacy and stigma concerns, travel requirements, waiting times, and restricted operating hours. Digital models may help address some of these barriers, but evidence on hybrid digital and telemedicine PrEP pathways for general adult populations in African settings remains limited.

Objective: This study aims to assess the feasibility and acceptability of a digitally enabled hybrid oral PrEP delivery pathway combining digital engagement and HIV self-testing (HIVST) with home-based nurse assessment, virtual physician prescribing, pharmacist dispensing, courier delivery of medication, and HIVST-supported follow-up in Gauteng province, South Africa.

Methods: We used a multiphase mixed methods design. In May 2023, 127 adults recruited through convenience sampling via an online platform and community pharmacies participating in the PPREPP-SA (Pharmacy-Delivered Preexposure Prophylaxis in South Africa) implementation project in Johannesburg and Cape Town completed a market survey. In June 2023, study staff invited adults who were available and willing to participate at pharmacies in both cities; 30 completed formative interviews, which were analyzed descriptively. During implementation (July 2023-July 2024), users self-enrolled through the online platform, and website analytics and programmatic data described progression to PrEP initiation (n=155). At 6 to 7 months—the midpoint of the 13-month follow-up period—criterion-based purposive sampling was used to select users from 3 engagement groups: active, missed appointment, and lost to follow-up. Seven users completed midline interviews. In addition, one senior manager from the online platform completed a key informant interview. Preimplementation interviews were analyzed descriptively, midline interviews were analyzed thematically, and findings were integrated using a joint display.

Results: Among the 127 market survey respondents, 96 (75.6%) preferred pharmacy-based PrEP, whereas 17 (13.4%) selected online access; 83 (65.4%) were willing to pay for PrEP-related services. During implementation, 567 users ordered an HIV self-test, 457 (80.6%) received it, 253 reported a nonreactive result, 192 requested a nurse visit, 157 completed the visit, and 155 initiated PrEP. Initiation represented 61.3% (155/253) of users reporting a nonreactive result and 27.3% (155/567) of all users who ordered a test. Among the 155 participants who initiated PrEP, 97 (62.6%) were assigned male at birth, 123 (79.4%) had tertiary education, and 110 (70.9%) were employed. Privacy, discretion, and convenience supported acceptability. The absence of clearly identifiable addresses, courier delivery and laboratory delays, scheduling difficulties, and communication breakdowns between participants and study staff affected progression through the pathway. Participants and the platform stakeholder also raised concerns about affordability, poststudy access, and financial sustainability.

Conclusions: The digitally enabled hybrid PrEP pathway supported PrEP initiation among users who valued privacy and convenience. Its feasibility was conditional on coordination among multiple service components. Wider implementation will

require streamlined clinical and logistical processes, equitable digital access, flexible delivery or collection options, and sustainable financing that complements existing pharmacy- and facility-based PrEP services.

Trial Registration: ClinicalTrials.gov NCT07006246; https://clinicaltrials.gov/study/NCT07006246

JMIR Form Res 2026;10:e88059; doi: 10.2196/88059

Keywords: HIV prevention; HIV self-testing; online delivery; telemedicine; telehealth; e-commerce; home-based care; acceptability; preexposure prophylaxis; PrEP; HIV; feasibility

Introduction

Daily oral preexposure prophylaxis (PrEP) is highly effective in preventing HIV acquisition when taken as prescribed [1]. However, uptake and continued use are suboptimal among people at substantial risk of HIV acquisition [2-5]. South Africa introduced oral PrEP in 2016, initially for sex workers, before progressively expanding access to other key and priority populations and subsequently to all people who could benefit from PrEP [6]. By 2025, approximately 1.7 million oral PrEP initiations had been recorded in South Africa; however, an estimated 140,000 new HIV infections still occurred in the previous year [7,8]. The World Health Organization (WHO) recommends differentiated service delivery models that simplify PrEP delivery and provide person-centered alternatives to conventional facility-based care [9].

The COVID-19 pandemic accelerated the adoption of telehealth in many countries and demonstrated its potential to maintain access to health services when in-person care was restricted [10-14]. Telehealth has increasingly been used to support several components of the PrEP cascade, including eligibility screening, counseling, prescribing, and adherence support, including in the United States and Brazil [15,16]. In both studies, high acceptability of telehealth PrEP services among men who have sex with men (MSM) and transgender individuals was attributed to convenience, privacy, and reduced travel distances. Telehealth models were also instrumental in maintaining PrEP services during the COVID-19 pandemic, with noted improvements in retention and adherence [17,18]. Telehealth services integrated into virtual platforms have also been piloted for PrEP delivery in Malaysia and the United States, demonstrating promising results [19,20]. In both pilots, clients valued the efficiency and stigma-free experience of accessing PrEP services through the platforms.

Most studies on telehealth models and online PrEP delivery to date have been conducted in middle- to high-income countries and have primarily focused on MSM and transgender populations [15-20]. However, little is known about the feasibility and acceptability of online PrEP delivery for broader adult populations in sub-Saharan Africa (SSA), including heterosexual men and women, who also experience substantial barriers to accessing facility-based PrEP services. These barriers include fears of associated stigma, travel distances, waiting times, limited hours of operation, and health worker attitudes [21-24]. An online pharmacy and telehealth model for PrEP and postexposure prophylaxis (PEP) delivery, the first in the region to our knowledge, was recently piloted in Kenya and reported high acceptability among clients who initiated PrEP and PEP [25], suggesting that these models may be feasible in the SSA setting.

In South Africa, as of 2024, most households exclusively use mobile phones (91%) and have at least one form of internet access (79%), while almost 1 in 5 (17.4%) have a fixed internet connection at home [26]. High internet penetration has driven rapid growth in South Africa's e-commerce sector and the expansion of courier networks to support home deliveries [27]. These factors, along with user preferences for greater autonomy in accessing PrEP services [28-30], create a possible opportunity for web-based PrEP delivery as an alternative to facility-based PrEP access. Research in our African setting is critical to identify and address disparities in infrastructure and internet access among underprivileged communities, ensuring that the benefits of online PrEP services are equitably realized [31].

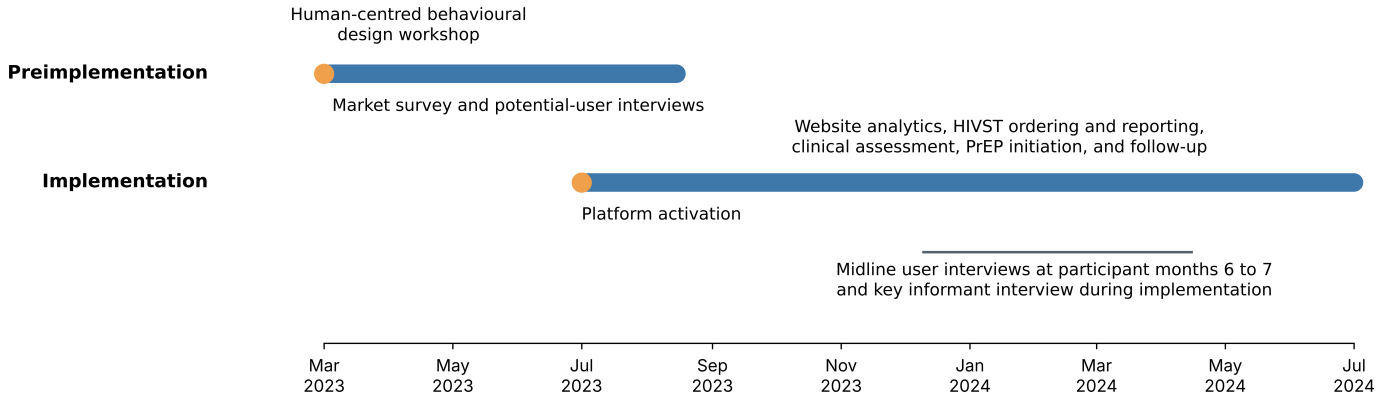
We developed a digitally enabled, hybrid PrEP delivery pathway for adults aged 18 years or older in Gauteng province, South Africa. This study assessed the feasibility of progressing users from digital engagement and HIV self-testing (HIVST) to PrEP initiation and explored the acceptability, operational challenges, and sustainability of the model from the perspectives of potential users, enrolled users, and an e-commerce platform stakeholder.

Methods

Study Design and Setting

We used a multiphase mixed methods design comprising sequential preimplementation and implementation phases, with quantitative and qualitative data collected within each phase. The digitally enabled PrEP pathway was developed within a broader implementation program (PPREPP-SA [Pharmacy-Delivered Preexposure Prophylaxis in South Africa]), which evaluated differentiated PrEP delivery through community pharmacies and online services [32]. Formative activities conducted during the preimplementation phase drew on the broader program's existing pharmacy sites and informed the development of the digitally enabled pathway evaluated during the implementation phase. The present analysis focuses specifically on this pathway, with quantitative and qualitative findings integrated to identify areas of convergence, complementarity, and discordance. Figure 1 presents the study phases, activities, and principal data collection points covering the early analysis period from March 2023 to July 2024.

Figure 1. Study phases and principal data collection activities from March 2023 to July 2024. HIVST: HIV self-testing; PrEP: preexposure prophylaxis.



We partnered with King Online (Red Button Consulting Pty Ltd), a South African health and wellness e-commerce company established in 2013. King Online sells health, sexual and reproductive health, and home-testing products. Before this study, the company had distributed HIVST kits in partnership with Ezintsha and Population Services International (PSI). For this study, the King Online website served as an entry point to the PrEP pathway. In this manuscript, the term "online platform" refers specifically to the King Online website.

Preimplementation Phase

Formative Human-Centered Behavioral Design Workshop

In March 2023, members of the study team participated in a 2-day human-centered behavioral design workshop attended by behavioral scientists, researchers, clinicians, digital health developers, and implementation partners [33]. The workshop examined barriers to PrEP uptake and continued use among gay, bisexual, and other men who have sex with men (GBMSM). Proposed intervention components included simplified service delivery, home delivery of medication, digital tools adapted to different user journeys, and communication approaches intended to improve PrEP awareness and engagement. As the workshop focused on GBMSM, its findings were treated as preliminary design inputs rather than assumed to apply to the broader adult population targeted by the study. The relevance of the proposed components to adult men and women was subsequently explored through the market survey and interviews with potential users.

Market Survey

In May 2023, a cross-sectional market survey was administered to adults aged 18 years or older who accessed the online platform or community pharmacies participating in PPREPP-SA [32] in Johannesburg and Cape Town. Participants were recruited using convenience sampling. The self-administered survey collected information on participants' sociodemographic characteristics, HIV testing practices, awareness of PrEP, preferred locations for accessing PrEP, views on the availability of PrEP information, and willingness to pay for PrEP-related services. Participants recruited through community pharmacies accessed the survey via a web link presented on an electronic tablet, whereas website users accessed it electronically through the online platform.

In-Depth Interviews With Potential Users

In June 2023, potential users were recruited from all community pharmacies participating in PPREPP-SA in the 2 cities. These existing program sites were not selected through convenience sampling. Within these sites, study staff invited interested adults aged 18 years or older to participate in interviews discussing the proposed PrEP delivery pathway. Participation was based on availability and willingness, constituting convenience sampling at the participant level. We aimed to interview 30 individuals, an a priori sampling target set before recruitment, because these interviews were formative and intended to inform the development of a PrEP delivery pathway rather than to develop theory. We planned to conduct approximately 15 interviews in each city to capture views from both locations. Recruitment ended once the target was reached and the team was satisfied that the range of preferences, anticipated barriers, and suggestions relevant to designing the pathway had been covered. Interviews were conducted by 2 study researchers trained in qualitative and mixed methods (KEO and AN). Neither interviewer had an established relationship with participants before recruitment, and no one other than the participant and interviewer was present. Individual semistructured interviews were conducted in private rooms at participating pharmacies, in participants' preferred language, and lasted approximately 30 to 45 minutes. Interviews were audio-recorded with permission and supplemented by field notes recorded during or immediately after the interview. The interview guide explored sexual health-seeking behavior, PrEP knowledge, motivations for PrEP uptake, anticipated barriers, preferences for online, pharmacy-based, and conventional facility-based services, and recommendations for implementation.

Application of Preimplementation Findings

The multidisciplinary implementation team comprised software developers, project managers, pharmacists, nurses, doctors, and social scientists and participated in weekly planning meetings from April to June 2023 to review findings from the workshop, market survey, and user interviews before activating the online platform. Findings were compared across sources to identify recurring barriers and preferences

and assess their relevance to the broader adult population. Proposed intervention components were reviewed against user preferences, operational feasibility, and clinical and regulatory requirements, with agreed actions documented in meeting notes. These findings informed the platform design, including PrEP information, demand-creation messages, delivery options, and support for PrEP initiation and follow-up.

Implementation Phase

Recruitment and HIVST

The online platform homepage was activated on July 1, 2023, and included a PrEP banner linked to a dedicated study information page. Recruitment strategies included search engine optimization, social media advertising on platforms such as Facebook and Instagram, advertisements on campus radio stations, and distribution of QR codes. Interested users could review the study details and, if they resided in Gauteng province, opt in and add a free blood-based HIV self-test (CheckNOW; Abbott), which detects HIV-1 and HIV-2 antibodies, to their online shopping cart for courier delivery. Each kit included the manufacturer's standard instruction leaflets for performing the HIV test. Two days after delivery confirmation, participants received an SMS message containing a link to an online form which they could report their HIVST result and request an in-person nurse visit. Nonresponders received an SMS reminder on day 5 and a final telephone reminder from study staff on day 7.

Users were eligible for a nurse visit if they were aged 18 years or older, reported a nonreactive HIVST result, and wanted to initiate PrEP. Although WHO guidance permits PrEP initiation following a nonreactive HIVST, the South African guidelines in effect during the study required provider-administered HIV testing before PrEP initiation [34]. The in-person nurse visit was included to meet this national requirement. In South Africa, an HIVST is considered a screening tool and not a diagnostic test. Users reporting a reactive result were therefore contacted by study staff and referred to a clinic or facility of their choice for provider-administered testing. Under the national serial testing algorithm in effect during the study, a reactive first rapid test was followed by a second, different rapid assay to confirm the result [35].

PrEP Initiation and Specimen Collection

A trained study nurse traveled to the participant's home or another private location selected by the participant within Gauteng province. During the visit, the nurse obtained written informed consent for study participation, reviewed the participant's medical history, provided HIV risk-reduction counseling, performed provider-administered, blood-based rapid HIV testing (Determine HIV-1/2; Abbott), assessed clinical eligibility for PrEP, and conducted syndromic screening for sexually transmitted infections (STIs). Participants with STI symptoms were managed or referred in accordance with applicable clinical guidance [36]. Medical history was obtained as per routine service delivery and included conditions present at enrollment and previously diagnosed conditions, such as STIs; no specific recall periods were applied to self-reported conditions. Sexual behavior questions were adapted from the national PrEP risk-assessment tool [34] for personal HIV vulnerability identification and did not use a specified recall period. Participants with a reactive provider-administered HIV test did not initiate PrEP and were referred for confirmatory testing.

The nurse collected baseline blood samples for hepatitis B and renal function assessments where clinically indicated [34]. Specimens were labeled at the point of collection and transported by the nurse to the contracted laboratory after the visit in accordance with the laboratory's specimen-handling requirements. The laboratory processed the specimens and transmitted the results securely to the study clinicians. Participants were not required to transport specimens or attend the laboratory.

Sex assigned at birth was self-reported; gender identity was not assessed. Participants assigned female at birth received contraception counseling and were offered oral contraceptive options where appropriate. Participants who selected injectable contraception were referred to a health facility because administration required an in-person follow-up visit.

Prescribing, Dispensing, and Delivery

Study nurses employed by the project did not have the necessary authorization to prescribe or dispense PrEP remotely under South African medicine regulations [37]. While in the presence of the study participant, the study nurse initiated a video call with a study-assigned doctor. The doctor reviewed the participant's clinical information in the project database and, if the participant was clinically eligible, prescribed tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg. The nurse provided information on PrEP delivery and follow-up requirements to those prescribed PrEP. Participants did not receive the PrEP package from the nurse at the end of this visit. Rather, a study partner pharmacy dispensed a 1-month supply of PrEP, along with oral contraception and/or STI treatment, where indicated. The dispensed package also contained an HIVST and a dried blood spot (DBS) collection kit for use during follow-up. Only participants who were prescribed PrEP had a package delivered by courier. After delivery confirmation, a pharmacist or pharmacy assistant telephoned participants to provide instructions on PrEP use, potential side effects, and management of missed doses. This call was conducted only at initiation. The interval from the nurse visit to receipt of the PrEP package was calculated as the number of calendar days between the clinical visit and courier-confirmed delivery.

PrEP Continuation Procedures

Participants were scheduled for follow-up for up to 13 months, with the first follow-up at month 1 and subsequent follow-ups every 3 months (months 4, 7, 10, and 13) in accordance with the national PrEP follow-up schedule [34]. At these scheduled follow-up time points, participants wishing to continue PrEP were asked to perform an HIVST and collect a DBS sample for HIV RNA testing

to provide study-specific confirmation of their self-reported negative HIVST result, as national guidelines at the time did not support the use of HIVST for PrEP continuation. DBS collection enabled HIV RNA testing without requiring a nurse to visit the participant for provider-administered HIV testing. Ten days before each refill was due, participants received an automated SMS text message containing a link to an online follow-up form. The form collected the participant's self-reported HIVST result, intention to continue PrEP, self-reported adherence, and HIV risk information.

Participants collected the DBS specimen using the kit and instructions provided, after which they scheduled the collection of the DBS card using the follow-up form. A courier collected the completed DBS card and transported it to the contracted laboratory. The laboratory processed the specimen and securely transmitted the result to the study clinicians. Participants with confirmed negative results had a telephone consultation with the doctor, after which the partner pharmacy dispensed and couriered the prescribed PrEP refill. This process was repeated at the scheduled follow-up points. Participants reporting a reactive HIVST result or having a detectable DBS result were linked to a health facility of their choice for confirmatory testing and antiretroviral therapy.

Midline User and Stakeholder Interviews

Midline in-depth interviews were conducted at approximately 6 to 7 months after enrollment, at the midpoint of the planned 13-month follow-up period. This timing allowed participants to reflect on PrEP initiation and follow-up/refill experiences while the study was ongoing. Participants were eligible if they had initiated PrEP through the hybrid pathway, had reached approximately 6 to 7 months of follow-up, and were classified in 1 of 3 predefined engagement categories: active in follow-up, missed scheduled appointments, or lost to follow-up. Study records were used to identify eligible participants. For these midline users, we set an a priori sampling target of approximately 10% of eligible participants. The aim was to describe how implementation worked in practice across the range of engagement experiences; rather than to establish how common any experience was. Criterion-based purposive sampling was used to select participants from each engagement category to capture variation in pathway experience and continuation status, and study staff invited selected participants by telephone. A senior manager from the online platform was interviewed as a key informant due to their central role in platform implementation.

Midline interviews were led by KEO and AN, together with other study team members trained in qualitative interviewing. Interviews followed the same semistructured procedures described for the preimplementation interviews but were conducted by telephone. The midline interview guide focused on reasons for enrolling in PrEP through the hybrid model, experiences of using the model, operational challenges, and recommendations. The key informant interview guide focused on the rationale for establishing the platform, operational experience, strategies used to enhance uptake, and sustainability.

Quantitative Data Management and Analysis

Google Analytics was used to measure overall traffic to the online platform and engagement with the PrEP product page. Market survey responses, online HIVST reporting forms, and participant information collected during PrEP initiation and follow-up were stored in REDCap (version 15.5.5), a secure, web-based electronic data-capture platform for research studies [38]. Data were exported from REDCap and managed and analyzed using Stata SE (version 18.0; StataCorp). We describe online platform engagement and the PrEP initiation cascade by calculating the number and proportion of users progressing to each stage, as well as the losses at each stage. Characteristics of participants enrolled in and initiated on PrEP are described using frequencies and percentages; age was assessed using the Shapiro-Wilk test and summarized using the median and IQR due to nonnormal distribution. No inferential or multivariable analyses were undertaken because this formative analysis was designed to describe feasibility and acceptability rather than test associations. Persistence and adherence outcomes were not included in this early analysis.

Qualitative Data Management and Analysis

Audio recordings were uploaded to a password-protected online drive accessible only to authorized study staff. Interviews were transcribed verbatim in the language used by the participant and translated into English where necessary. Transcripts and translations were quality-checked against the audio recordings before analysis. Transcripts were not returned to participants for correction, and participants were not asked to comment on the final themes. All qualitative data were managed and coded using MAXQDA 2022 (VERBI software GmbH) and analyzed thematically, drawing on Braun and Clarke [39], using a combined deductive and inductive coding approach. The preimplementation and implementation-phase interview datasets were analyzed separately as they addressed different study periods and purposes. The preimplementation potential-user interviews were analyzed descriptively as a formative qualitative component, focusing on recurring preferences, anticipated barriers, implementation considerations, and recommendations that could inform pathway development. For the midline dataset, KEO and AN independently familiarized themselves with the transcripts and generated the primary codes. Deductive codes were informed by the study objectives and interview guide, whereas inductive codes captured unanticipated experiences and implementation issues raised by participants. KEO and AN compared coding output, discussed differences in interpretation, refined code definitions, and grouped related codes into candidate themes. STL-E, a senior mixed methods researcher, served as a third analytic reviewer. She reviewed the coding structure, candidate themes, and interpretations against the coded data, interview questions, and study objectives. Differences in interpretation were resolved through discussion and iterative refinement. Recruitment for the midline interviews continued across the predefined engagement categories until the team

judged that the principal experiences and implementation issues relevant to the research questions were sufficiently covered and no materially new issues were identified.

During mixed methods interpretation, the qualitative themes were compared with the quantitative findings. The research team examined areas of convergence, complementarity, and discordance between the quantitative and qualitative findings.

Ethical Considerations

The study received ethical approval from the University of the Witwatersrand Human Research Ethics Committee (reference 230107). All participants provided written informed consent, which allowed voluntary participation and the right to discontinue participation at any time. Participant confidentiality and anonymity were upheld throughout the research process. Participants received reimbursement of ZAR 405 (US $22.50) for in-depth interviews. All study-related services, including courier fees, PrEP consultations and medication, HIV testing, and laboratory assessments offered through the model, were provided free of charge to the participants.

Results

Preimplementation Phase

Market Surveys

A total of 127 potential PrEP clients completed the market surveys (Table 1). The median age was 28 (IQR 22-35) years, and just over half were female respondents (n=65, 51.2%). Most respondents had education beyond secondary school (n=91, 71.7%) and (n=66, 51.9%) were formally employed.

Table 1. Characteristics and preexposure prophylaxis (PrEP) service preferences of preimplementation market survey respondents.

Characteristics	Total
Age (y), median (IQR)	28 (22-35)
Age group (y; n=127), n (%)	
18-35	86 (67.7)
>35	41 (32.3)
Sex (n=127), n (%)	
Male	62 (48.8)
Female	65 (51.2)
Education (n=127), n (%)	
Primary	3 (2.4)
Secondary	33 (25.9)
Postmatric	91 (71.7)
Employment (n=127), n (%)	
Student	34 (26.8)
Permanent	51 (40.2)
Temporary	15 (11.8)
Unemployed	27 (21.3)
Do you test for HIV? (n=127), n (%)	
Yes	109 (85.8)
No	18 (14.2)
If yes, where do you test for HIV? (n=109), n (%)	
Self-test	4 (3.7)
Local clinic	61 (55.9)
Doctors' room	22 (20.2)
Other	22 (20.2)
Are you aware or have you heard of PrEP (n=127), n (%)	
Yes	62 (48.8)
No	65 (51.2)
Source of PrEP information (n=62), n (%)	
Television	4 (6.5)
Social media	20 (32.3)
Pharmacy	6 (9.7)
Clinic	19 (30.6)

Characteristics	Total
Other	13 (20.9)
Do you think there is enough information available on PrEP? (n=127), n (%)	
Yes	29 (22.8)
No	98 (77.2)
If you are interested in PrEP, where would you like to receive it? (n=127), n (%)	
Pharmacy	96 (75.6)
Local government clinic	8 (6.3)
Online	17 (13.4)
Other	6 (4.7)
Would you pay for PrEP? (n=127), n (%)	
Yes	83 (65.4)
No	44 (34.6)
How much are you willing to pay for PrEP? (ZAR, n=83), n (%)	
Less than 200 (<US $11)	58 (69.9)
200-300 (US $11-US $17)	17 (20.5)
Over 300 (>US $17)	8 (9.6)

Most respondents (109/127, 85.8%) reported having previously tested for HIV. Among the 109 respondents reporting previous testing, 61 (55.9%) had tested at local clinics, 22 (20.2%) at a doctor's practice, and 22 (20.2%) at another location. Only 4 (3.7%) reported having used an HIVST. Fewer than half of the respondents (62/127, 48.8%) had heard of PrEP and of these, social media was the primary source of PrEP information (20/62, 32.3%), closely followed by clinics (19/62, 30.6%). Most respondents (98/127, 77.2%) felt that there was insufficient information available on PrEP.

Of the 127 respondents asked where they would prefer to access PrEP services if interested in starting PrEP, 96 (75.6%) selected a pharmacy. Online access was the second most preferred option (n=17, 13.4%), while 8 (n=6.3%) selected a local government clinic and 6 (4.7%) selected another option, such as a private medical practitioner. Most clients (n=83, 65.4%) indicated a willingness to pay for PrEP-related services. Of these 83 respondents, 58 (69.9%) were willing to pay an amount less than ZAR 200 (US $11), whereas the remaining 25 (30.1%) were willing to pay an amount exceeding ZAR 200 (US $11), though a specific payment interval was not specified for these amounts.

Descriptive Formative Findings From Potential-User Interviews

Thirty potential users participated in the preimplementation interviews. Their median age was 22 (IQR 20-30) years, and 73.3% (22/30) were female respondents. The descriptive formative analysis identified recurring expectations that digitally enabled and home-supported PrEP could offer convenience, privacy, and discretion. Participants anticipated that receiving some services at home could reduce travel, clinic waiting times, stigma, and the risk of unwanted disclosure.

One participant explained the perceived privacy of the pathway:

> *It is a better option because the nurse will come to you and do everything. And no one will know.* [20-year-old female, potential user interview]

Another participant described the convenience of avoiding travel:

> *It would work for me. Because have you seen today's weather? So, I wouldn't have to leave the house.* [26-year-old female, potential-user interview]

Participants also anticipated operational barriers. A principal concern was the difficulty of delivering services to informal settlements or other locations without formal or clearly identifiable addresses:

> *Some of the houses don't have addresses….Someone might find interest, but then they don't have the proper address to locate them.* [18-year-old female, potential-user interview]

Potential users of PrEP emphasized the importance of improving the platform's visibility and user engagement.

> *Yes, I've seen. I think they should have a section where people, just like this pharmacy, is has site where you have to write your review about your experience at the pharmacy. They should have that.* [20-year-old female, potential user interview]

Implications for Implementation

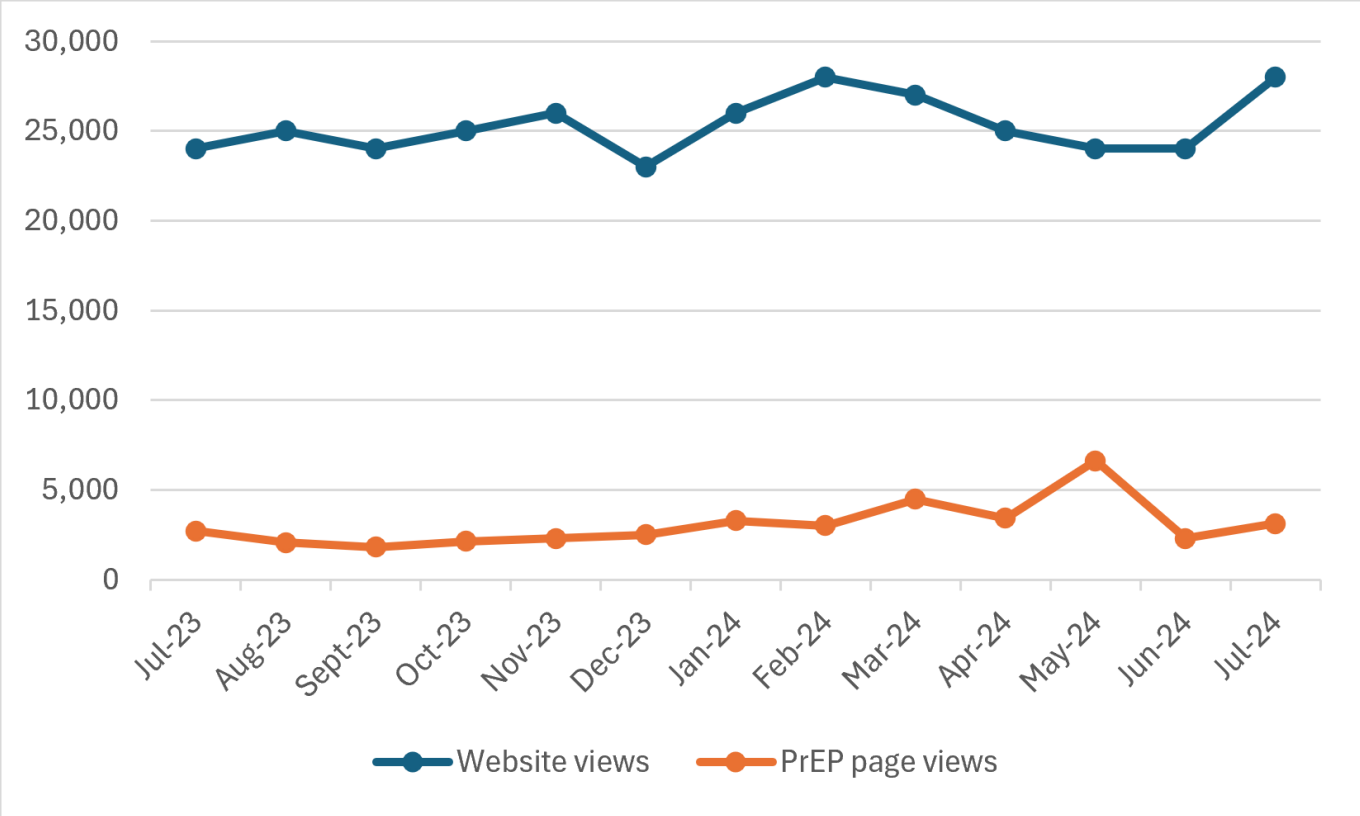
The survey and descriptive formative interview findings were complementary. Although online access was not the preferred option, the perceived privacy and convenience suggested that it could meet the needs of a selected subgroup. These findings informed the hybrid pathway evaluated during the implementation phase.

Implementation Phase

Online Platform Engagement

The online platform was activated in July 2023. During the 6 months preceding implementation (January to June 2023), the online platform received an average of approximately 22,000 views per month. Between July 2023 and July 2024, the website received 329,000 views, corresponding to an average of 25,308 views per month. The dedicated PrEP page received 39,737 views, representing 12.1% of all website views and an average of 3057 views per month. Monthly views of the PrEP page generally increased after implementation began and reached a peak of 6622 views in May 2024 (Figure 2). These analytics describe exposure to and engagement with the PrEP page. They do not indicate how many unique individuals viewed the page or whether a page view resulted in HIV self-test order or progression through the PrEP initiation pathway.

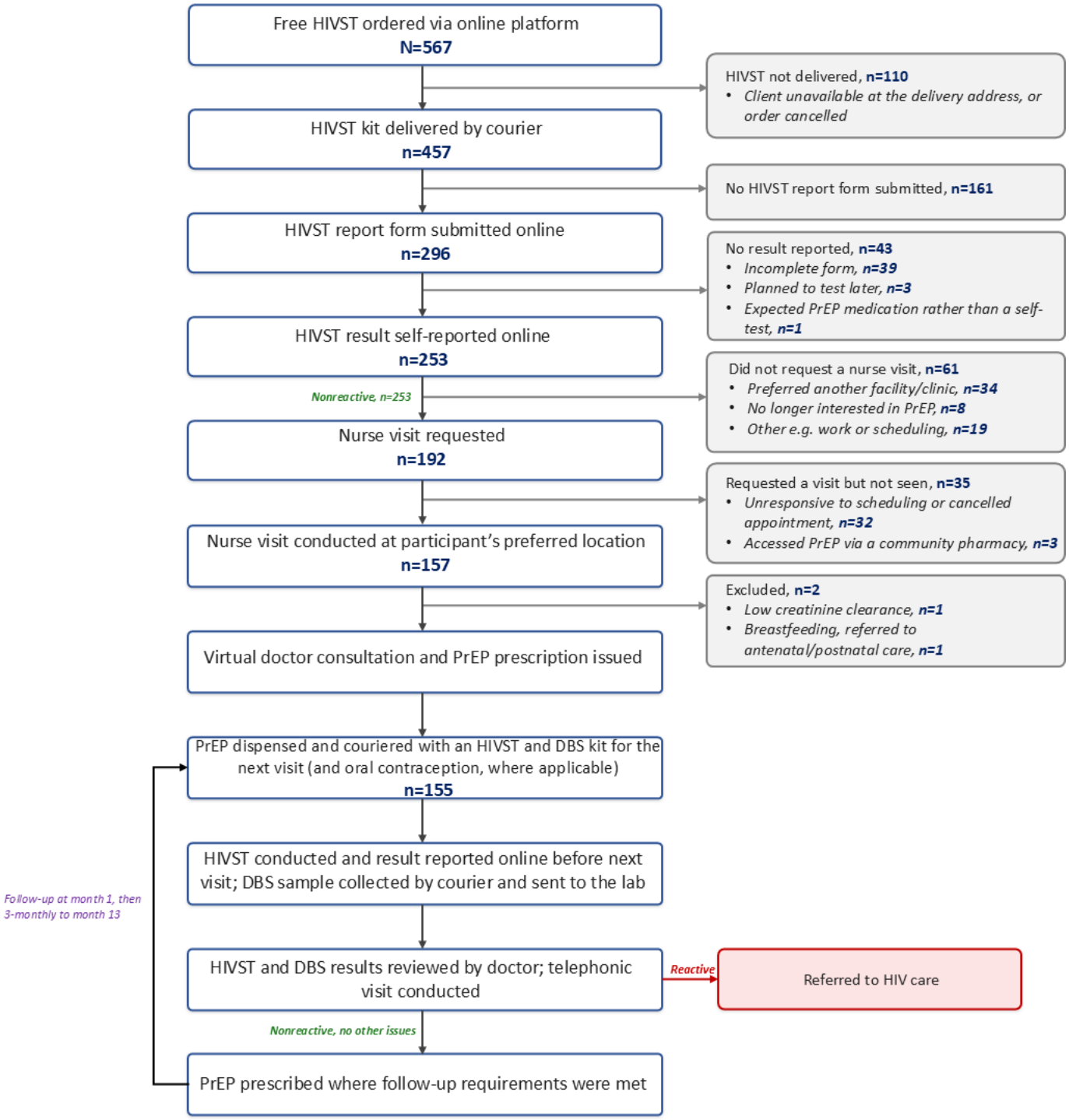
Figure 2. Online platform analytics from July 2023 to July 2024. PrEP: preexposure prophylaxis.



Progression Through the PrEP Initiation Pathway

A total of 567 users ordered a free HIVST through the online platform during the implementation period (Figure 3). Courier records confirmed successful delivery to 80.6% (457/567) of users. The remaining 110 orders were not delivered because users were unavailable at the delivery address or had canceled their orders.

Figure 3. Flow of participants through the digitally enabled hybrid preexposure prophylaxis (PrEP) pathway during the implementation phase. Gray boxes indicate the numbers and reasons why participants did not proceed to the next step; the red box indicates exit from the PrEP pathway due to a reactive HIV result during the follow-up phase, with referral to HIV care. The follow-up loop shows the procedures scheduled at month 1 and every 3 months thereafter; PrEP continuation, adherence, and persistence outcomes were not evaluated in this analysis. DBS: dried blood spot; HIVST: HIV self-testing.



Among the 457 users who received an HIVST, 296 (64.8%) submitted an online HIVST reporting form. The remaining 161 users did not submit a form despite receiving an automated reminder and a telephone call from the study team. Among those who submitted a form, 253 (85.5%) reported an HIVST result. Of the 43 users who submitted a form without reporting a result, 3 indicated that they intended to test later, 1 expected to receive PrEP medication rather than an HIV self-test, and 39 submitted an incomplete form. HIVST use could not be determined for these 39 users or for those who did not submit a reporting form.

All 253 self-reported HIVST results were nonreactive. Of these users, 192 (75.9%) requested an in-person nurse visit. Among the 61 users who did not request a visit, 34 preferred to obtain PrEP from a clinic or another health facility, 8 were no longer interested in initiating PrEP, and 19 reported other reasons, including work or scheduling constraints.

Of the 192 users who requested a nurse visit, 157 (81.8%) completed the nurse assessment visit. Among the 35 users who requested a visit but were not seen, 32 were unresponsive to scheduling attempts or canceled their appointments, and 3 chose to access PrEP through a community pharmacy. Of the 157 users who completed the nurse assessment, 155 (98.7%) were eligible, enrolled in the study, and initiated PrEP. Two users did not initiate PrEP: 1 had low creatinine clearance, and 1 was breastfeeding, which was an exclusion criterion under the study protocol at the time. Overall, 61.3% (155/253) of users who reported a nonreactive HIVST result initiated PrEP, and 27.3% (155/567) of users who ordered an HIV self-test ultimately initiated PrEP and received their first PrEP package. The average delivery time for the PrEP package was 2.5 (SD 2.1) days after the nurse visit.

Characteristics of Participants Initiating PrEP

A total of 155 participants initiated PrEP between July 2023 and July 2024 (Table 2). The median age was 31 (IQR 27-38) years, and 97 (62.6%) were assigned male at birth. Most participants were single or had never married (127, 81.9%), had completed tertiary education (123, 79.4%), and were employed (110, 70.9%). Most participants reported a monthly income above ZAR 5000 (US $305; n=123, 79.4%), while 105 (67.7%) did not have private medical insurance.

Table 2. Baseline characteristics of participants initiating preexposure prophylaxis (PrEP) through the digitally initiated hybrid pathway, July 2023 to July 2024 (N=155).

Characteristic and category	Values
Sociodemographic factors	
Age (y), median (IQR)	31 (27-38)
Age category (y), n (%)	
18-25	26 (16.8)
26-35	82 (52.9)
≥36	47 (30.3)
Sex assigned at birth, n (%)	
Male	97 (62.6)
Female	58 (37.4)
Marital status, n (%)	
Single (never married)	127 (81.9)
Currently married	17 (10.9)
Divorced	5 (3.2)
Cohabiting	4 (2.6)
Other	2 (1.3)
Employment status, n (%)	
Employed	110 (70.9)
Not employed	27 (17.4)
Self-employed	18 (11.6)
Education level, n (%)	
Secondary	32 (20.6)
Tertiary	123 (79.4)
Income level (ZAR monthly), n (%)	
More than 5000	123 (79.4)
Less than 5000	32 (20.6)
Private medical insurance, n (%)	
Yes	50 (32.3)
No	105 (67.7)
Medical history, n (%)	
Medical condition(s)	
Yes	24 (15.5)
No	131 (84.5)
History of STI[a] diagnosis	
Yes	6 (3.9)
No	149 (96.1)
PrEP history	

Characteristic and category	Values
Yes	34 (21.9)
No	121 (78.1)
Screening/testing results, n (%)	
Syndromic STI screening	
Negative	155 (100)
HIV rapid test	
Negative	155 (100)
Sexual behavior, n (%)	
Condomless sex	
Yes	92 (59.4)
Multiple sexual partners	
Yes	46 (29.7)
Sexually active	
Yes	151 (97.4)
Sex with HIV-positive partner	
Yes	12 (7.7)
Sex with partner of unknown HIV status	
Yes	52 (33.5)
Sex under influence of alcohol/drugs	
Yes	45 (29.0)
Age disparate relationship (partner >5 y older)	
Yes	30 (19.4)

[a]STI: sexually transmitted infection.

Most participants were initiating PrEP for the first time (121/155, 78.1%). Twenty-four participants (15.5%) reported a current or previously diagnosed medical condition. Six participants (3.9%) reported having previously received an STI diagnosis. No participants had symptoms consistent with an STI during syndromic screening at the PrEP initiation visit.

Most participants reported being sexually active (n=151, 97.4%). More than half reported condomless sex (n=92, 59.4%), while 46 (29.7%) reported having multiple sexual partners. Other reported behaviors included sex with a partner of unknown HIV status (n=52, 33.5%), sex under the influence of alcohol or drugs (n=45, 29.0%), sex with a partner living with HIV (n=12, 7.7%), and an age-disparate relationship with a partner more than 5 years older (n=30, 19.4%).

Midline User and Stakeholder Interview Findings

Overview of Midline Interviews

A total of 55 participants met the midline eligibility criteria. Fifteen were approached by telephone, of whom 7 were interviewed, representing all 3 engagement categories (2 active participants, 2 who had missed scheduled appointments, and 3 who had been lost to follow-up). The remaining participants approached were unreachable or declined to participate. The median age of the 7 participants interviewed was 28 (IQR 24-31) years, and 4 (57.1%) were female participants. One senior manager from the online platform also participated in a key informant interview. Three overarching themes were identified: acceptability and motivations for PrEP uptake; operational feasibility and implementation challenges; and sustainability and potential scale-up.

Acceptability and Motivations for PrEP Uptake

Participants generally described the hybrid pathway as acceptable because it offered privacy, discretion, convenience, and reduced reliance on facility-based services. Receiving services at home reduced travel and clinic waiting times and allowed participants to access PrEP without disclosing their use to other people. Participants also valued the convenience of HIVST, communication with study staff, and delivery of medication to a location of their choice.

One participant described the privacy offered by home delivery:

> *Online is best because you get PrEP from the comfort of your home. It's like your own secret.* [24-year-old female, online PrEP user]

Some participants reported that the digitally initiated pathway made obtaining PrEP easier than accessing conventional facility-based services:

> *It just made getting PrEP 10 times easier for me.* [31-year-old female, online PrEP user]

The stakeholder echoed this view, recognizing the online platform as a valuable, differentiated service delivery option:

So, PrEP being initiated online, I think it's a relatively good initiative [Stakeholder KII, online platform]

Operational Feasibility and Implementation Challenges

Participants generally reported positive interactions with the study team and appreciated the convenience of combining remote engagement with home-supported clinical and delivery services. Nevertheless, the hybrid structure created operational dependencies across the online platform, study staff, nurse, virtual doctor, laboratory, pharmacy, and courier service.

Reported challenges included unsuccessful or delayed communication and delays in specimen collection and laboratory processing. One participant described a communication breakdown involving the collection of follow-up specimens:

They said they'll come and pick up some tests, and they never really came. I thought maybe they had stopped the program. [21-year-old female, online PrEP user]

The stakeholder similarly identified delivery timelines, laboratory processes, and coordination among service providers as important operational challenges. The requirement for an in-person nurse visit and separate prescribing, dispensing, and courier steps reduced the immediacy normally associated with an e-commerce service. Participants recommended clearer communication, more reliable scheduling, and a single, consistent channel for updates.

Participants and stakeholders also noted that home delivery could be difficult in informal settlements or other areas without formal street names or clearly identifiable addresses. Suggested improvements included flexible delivery times, alternative delivery or collection points, evening or weekend clinical appointments, and closer coordination among the clinical, pharmacy, laboratory, and courier components.

Sustainability and Potential Scale-Up

Participants expressed concern about whether they would continue to have access to PrEP after the study ended. Although PrEP and related services were provided free of charge during the study, participants were uncertain about the future cost of consultations, laboratory testing, medication, and delivery.

The online platform stakeholder explained that the pathway was more viable when operational costs could be distributed across the platform's broader business:

The only reason it works with us is because PrEP is one of 15,000 products that we sell. Our cost is spread across multiple products. [Stakeholder KII, online platform]

The stakeholder indicated that a stand-alone online PrEP service could face difficulty generating sufficient revenue to cover clinical, laboratory, logistics, and administrative costs. Potential approaches to sustainability included cross-subsidization within larger e-commerce or pharmacy platforms, public financing, insurance reimbursement, and formal collaboration with government health services.

Participants also recommended increasing awareness of the pathway, improving its visibility online, and creating a mechanism through which users could provide feedback about their experiences. However, they distinguished limited awareness of the service from limited access to internet-enabled devices or affordable data. This distinction indicated that demand-creation activities alone would not address digital exclusion.

Overall, the midline interviews indicated that the hybrid pathway was acceptable to the selected users interviewed, particularly because of its privacy and convenience. Its operational feasibility and sustainability, however, depended on reliable coordination across its digital, clinical, laboratory, pharmacy, and delivery components, as well as affordable and equitable access for potential users.

Integration of Findings

Quantitative and qualitative findings from the preimplementation and implementation phases were compared during interpretation to identify convergence, complementarity, and discordance. Table 3 presents a mixed methods joint display, showing where qualitative findings converged with, complemented, or differed from quantitative patterns in service preferences, pathway progression, operational losses, and willingness to pay.

Table 3. Integration of quantitative and qualitative findings from the preimplementation and implementation phases.

Study phase and topic	Quantitative findings	Qualitative findings	Integrated finding
Preimplementation preferences and anticipated acceptability	Among 127 market survey respondents, 96 (75.6%) preferred pharmacy-based PrEP[a], while 17 (13.4%) preferred digitally enabled access. Most respondents (98, 77.2%) believed that insufficient information about PrEP was available.	Potential users valued privacy, convenience, reduced travel, and avoidance of unwanted disclosure. They also emphasized the need for clear PrEP information and greater visibility of the pathway.	The survey and formative interviews showed divergence between overall service preferences and anticipated acceptability: digitally enabled access was selected by a minority, while privacy, convenience, and reduced risk of unwanted disclosure were valued by potential users.

Study phase and topic	Quantitative findings	Qualitative findings	Integrated finding
Engagement and PrEP initiation	A total of 567 users ordered an HIV self-test, 457 received it, 253 reported a nonreactive result, and 155 initiated PrEP. Initiation represented 61.3% (155/253) of those reporting a nonreactive result and 27.3% (155/567) of all users who ordered a test.	Users who initiated PrEP valued privacy, convenience, home-supported access, and reduced dependence on facility-based services.	Quantitative progression and interview accounts converged in showing that the pathway could support PrEP initiation among selected users who progressed through the required steps, with privacy and convenience prominent in their accounts.
Operational barriers and pathway losses	Of 567 HIV self-test orders, 110 were not delivered. Of the 192 users who requested a nurse visit, 35 did not complete the visit.	Participants and the stakeholder reported unclear addresses, scheduling difficulties, communication breakdowns, and delays involving courier and laboratory processes.	Qualitative accounts complemented the cascade data by identifying address, scheduling, communication, courier, and laboratory problems that could plausibly contribute to losses at different stages.
Affordability and sustainability	Among the 127 survey respondents, 83 (65.4%) were willing to pay for PrEP-related services. Among those willing to pay, 58 (69.9%) preferred to pay less than ZAR 200 (US $11).	Users were concerned about continued access after the study. The stakeholder indicated that the pathway was viable partly because its costs were distributed across the platform's broader product range.	Willingness-to-pay responses were complemented by concerns about poststudy access and the stakeholder's description of operational costs, indicating that willingness to pay did not equate to demonstrated affordability or financial sustainability.

[a]PrEP: preexposure prophylaxis.

Discussion

Principal Findings

This study demonstrated that a digitally enabled hybrid PrEP delivery pathway using HIVST as an entry point for PrEP initiation is both feasible and acceptable among a selected group of adults in Gauteng province, South Africa, particularly because it offered privacy and convenience. However, progression depended on successful coordination among the digital platform, in-person clinical assessment, remote prescribing, laboratory services, pharmacy dispensing, and courier delivery. Feasibility was therefore conditional on the performance of the complete hybrid system rather than the online platform alone.

The preimplementation and implementation findings together suggest that digitally enabled PrEP could complement rather than replace existing service delivery options. Pharmacy-based access remained the preferred option among most survey respondents, while those who selected and experienced the hybrid pathway valued its discretion and convenience, demonstrating that an alternative entry point into PrEP services can reach users who value person-centered PrEP delivery [9,28].

HIVST provided a useful entry point to the pathway, consistent with evidence from other differentiated PrEP programs in similar settings. A study in South Africa among adolescent girls and young women showed HIVST supported PrEP refills during the COVID-19 lockdown, and in the MY DAWA (MYDAWA Trading Ltd) online pharmacy platform in Nairobi, Kenya, more than 90% of PrEP and PEP users opted for HIVST over rapid provider testing to initiate PrEP or PEP [25,29]. Losses after HIVST result reporting were largely attributed to scheduling difficulties for the nurse visit, which was required under current Department of Health requirements for a provider-confirmed negative rapid testing before PrEP initiation. The present study demonstrates how HIVST can support entry into a hybrid pathway for a broader adult population but highlights that, in the current regulatory environment, a digitally enabled pathway may still require in-person and other physical service components to comply with clinical guidance on appropriate HIV testing.

The in-person nurse assessment and separate prescribing, laboratory, pharmacy, and courier processes reduced the immediacy normally associated with an e-commerce service. Similar telehealth PrEP programs have also retained in-person components by combining telehealth with external specimen collection, laboratory services, and pharmacy or mailed medication delivery [40-42]. The findings suggest that successful hybrid delivery does not require the complete elimination of in-person contact. Instead, in-person components should be limited to those that are clinically necessary and efficiently integrated with the digital pathway. Further refinement of the pathway may therefore reduce the time required to initiate PrEP while retaining the convenience and discretion offered by digital delivery.

Operational challenges involving scheduling, communication, specimen collection, laboratory processes, and delivery affected users' ability to progress through the pathway. These challenges indicate that improving the website alone would be insufficient. Implementation should focus on coordination across service providers, flexible appointment times, alternative delivery or collection locations, and a consistent communication channel. Such adaptations may be particularly important for users living in informal settlements or locations without clearly identifiable addresses.

The characteristics of participants who initiated PrEP suggest that digitally enabled pathways may be accessible to people with internet-enabled devices, affordable data, stable

delivery locations, and sufficient flexibility to complete the required clinical procedures. Digital delivery could therefore reduce some barriers to PrEP while creating others. Wider implementation should include measures to support people with limited connectivity and should retain pharmacy- and facility-based alternatives to avoid widening existing inequalities in access.

The findings also distinguish user acceptability from financial sustainability. Participants valued the pathway, but the amounts that potential users were willing to pay were unlikely to cover all clinical, laboratory, dispensing, delivery, and administrative costs. Comparable hybrid PrEP programs generally depend on public or research funding, insurance reimbursement, and medication-assistance programs rather than user payments alone [41,43,44]. Sustainable implementation may similarly require cross-subsidization within larger pharmacy or e-commerce platforms, public or donor support for clinical and laboratory services, insurance reimbursement, or formal public-private partnerships.

Limitations

This study has several limitations. First, market survey respondents and potential-user interview participants were recruited using convenience sampling, and the survey included users recruited through both the online platform and community pharmacies. These findings should therefore not be interpreted as population-level estimates of demand for digitally initiated PrEP. Second, the preimplementation interview sample was predominantly female, whereas participants who initiated PrEP were predominantly assigned male at birth. This difference limits direct comparison between anticipated acceptability before implementation and the experiences of those who used the pathway. Third, only 7 online PrEP users and 1 platform stakeholder participated in the midline interviews. The qualitative findings provide contextual depth but may not represent the experiences of all users or the perspectives of other relevant stakeholders, including clinicians, laboratory staff, couriers, policymakers, and potential implementation partners. Fourth, participants required access to an internet-enabled device, affordable data, and a location where clinical and delivery services could be provided. People with greater digital access, stable delivery addresses, and sufficient flexibility to complete the pathway may have been more likely to initiate PrEP. This selection may limit transferability to rural populations, people living in informal settlements, and those with limited connectivity or fewer economic resources. Fifth, the quantitative analysis was descriptive and did not examine factors associated with progression or loss at different stages of the pathway. Reasons for nonprogression were obtained from routinely collected programmatic data and were not available for all users. The quantitative and qualitative findings were integrated during interpretation, but the different preimplementation and implementation samples prevented direct individual-level linkage of the 2 datasets. Sixth, all PrEP-related services were provided free of charge during the study. Consequently, reported willingness to pay does not establish actual affordability or demand under routine service conditions. The study was also implemented through a single e-commerce platform in 1 predominantly urban province, which may limit transferability to other platforms and settings. Finally, this early analysis assessed progression through PrEP initiation and identified operational barriers affecting the pathway. It did not evaluate adherence, continuation, persistence, clinical outcomes, cost-effectiveness, or sustainability over the full follow-up period.

Implications for Practice and Policy

Digitally enabled hybrid PrEP delivery should complement rather than replace facility-based services. Policy should enable trained providers to complete more components of PrEP initiation, and the integration of HIVST, where permitted, could streamline delivery at a single service point while reducing unnecessary in-person contact. Implementation should strengthen coordination and communication, provide flexible appointment and collection options, and improve access for users facing digital or logistical barriers. Sustainable delivery will likely require public financing, insurance reimbursement, and public-private partnerships. Future implementation research should assess costs, continuation, persistence, clinical outcomes, and equity under routine service conditions.

Conclusions

The digitally enabled hybrid PrEP pathway supported PrEP initiation among users who valued privacy and convenience. However, its feasibility was conditional on coordination across multiple service components, with substantial losses occurring at several stages of the pathway. Wider implementation will require streamlined clinical and logistical processes, flexible delivery or collection options, equitable digital access, and a sustainable financing model that complements existing pharmacy- and facility-based PrEP services.

Acknowledgments

The authors acknowledge the PPREPP-SA study team, King Online, and all participants who contributed to this study.

Generative AI Use

Generative AI tools, including Claude (Opus 5.5 [Anthropic]) and ChatGPT (OpenAI), were used for language editing, grammar correction, and shortening selected passages. They were not used to generate or analyze study data. The authors reviewed and revised all AI-assisted text and take full responsibility for the manuscript.

Funding

This work was supported, in whole or in part, by the Gates Foundation (INV-037064). The conclusions and opinions expressed in this work are those of the authors alone and shall not be attributed to the foundation. Under the foundation's grant

conditions, a Creative Commons Attribution 4.0 license has already been assigned to the authors' accepted manuscript version that may arise from this submission.

Data Availability

Data will be made available upon request.

Authors' Contributions

Conceptualization: TN, KEO, STL-E, AT
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Formal analysis: MS, TW, KEO, AN, STL-E
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Writing – original draft: TN, KEO, MAM
Writing – review & editing: TN, KEO, STL-E, MAM, TC, MS, CH, AT

Conflicts of Interest

None declared.

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Abbreviations

DBS: dried blood spot
GBMSM: gay, bisexual, and other men who have sex with men
HIVST: HIV self-testing
MSM: men who have sex with men
PEP: postexposure prophylaxis
PPREPP-SA: Pharmacy-Delivered Preexposure Prophylaxis in South Africa
PrEP: preexposure prophylaxis
PSI: Population Services International
SSA: sub-Saharan Africa
STI: sexually transmitted infection
WHO: World Health Organization

Edited by Stephanie Law; peer-reviewed by Robin McGowan, Tiffany Lillie; submitted 19.Nov.2025; initial comments to author 30.Mar.2026; final revised version received 22.Sep.2026; accepted 23.Sep.2026; published 26.Nov.2026

Please cite as:
Nyamuzihwa T, Oladimeji KE, Mkansi MA, Wonderlik T, Nyatela A, Seleka M, Collings T, Hendrickson C, Lalla-Edward ST, Tembo A
Digitally Enabled Hybrid Delivery of HIV Preexposure Prophylaxis in Gauteng Province, South Africa: Mixed Methods Feasibility and Acceptability Study
JMIR Form Res 2026;10:e88059
URL: https://formative.jmir.org/2026/1/e88059
doi: 10.2196/88059

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