Jabula Uzibone: Protocol for an Implementation Study of Transgender-Specific Differentiated HIV Service Delivery Models in the South African Public Primary Healthcare System

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Abstract

Background: Almost 60% of transgender people in South Africa are living with HIV, compared with 18% of reproductive age adults. Ending the HIV epidemic will require that key populations, including transgender people, successfully access HIV prevention, treatment, and care. However, transgender people often avoid health services due to facility-based stigma and lack of availability of gender-affirming care. Transgender-specific differentiated service delivery (TG-DSD) may improve engagement and facilitate progress toward HIV elimination. Wits RHI, a renowned South African research institute, established 4 TG-DSD demonstration sites in 2019, with funding support from the US Agency for International Development (USAID). These sites offer unique opportunities to evaluate implementation of TG-DSD and test the effectiveness of TG-DSD on HIV outcomes.

Objective: The Jabula Uzibone study seeks to assess the implementation, effectiveness, and cost of TG-DSD for viral suppression and prevention-effective adherence.

Methods: This observational, mixed methods, prospective implementation study collects baseline and 12-month site observation checklists (n=8 sites) and key informant interviews (6/site, n=48) at the 4 TG-DSD sites and 4 standard sites to explore implementation. We will enroll 600 transgender clients at TG-DSD (n=300) and standard (n=300) sites: 200 with HIV on antiretroviral therapy and 100 HIV-negative for each site type. Participants complete interviewer-administered surveys quarterly, and blood is drawn at baseline and 12 months for HIV RNA testing among participants with HIV and tenofovir levels among participants on PrEP. A subset of 30 per site type will also complete in-depth interviews at baseline and 12 months. Within each site type, 15 will be living with HIV and 15 will not. Qualitative analyses will explore aspects of implementation; regression models will compare HIV outcomes (viral suppression and prevention-effective adherence) by site type. Structural equation modeling will test whether HIV outcomes are mediated by stigma and/or gender affirmation. A micro-costing approach will estimate the cost per service user served and per service user successfully treated at TG-DSD relative to standard sites, as well as the budget needed for broader implementation of TG-DSD.

Results: As of June 28, 2024, 489 transgender participants have been enrolled: 216 are living with HIV and 279 are HIV-negative; 15% (75/489) are gender non-conforming, 15% (72/489) are transgender men, and 70% (342/489) are transgender women. We anticipate baseline enrollment will be complete by August 31, 2024, and the final study visit will take place no later than August 2025.

Conclusions: Jabula Uzibone will provide actionable data to inform HIV policies and health facility practices in South Africa and generate the first evidence for implementation of TG-DSD in sub-Saharan Africa. Study findings also may inform how other countries could utilize TG-DSD strategies to increase care engagement of transgender people and advance global progress towards HIV elimination goals. Clinical Trial: Not applicable

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Keywords: HIV prevention, HIV Care, pre-exposure prophylaxis, antiretroviral therapy, gender-affirmation

Introduction

HIV Among Transgender People

Transgender people are a key population with a disproportionate burden of HIV. Globally, transgender women have an estimated HIV prevalence of 19.9% with a 66-fold greater odds of HIV compared with other adults, a prevalence that has not decreased over the past decade despite introduction of HIV pre-exposure prophylaxis (PrEP) [1, 2]. Transgender men also face elevated HIV prevalence with an estimated global prevalence of 2.6% and a 6.8-fold increased odds of HIV [2]. South Africa has the largest HIV epidemic in the world, where more than 7 million people are living with HIV. [3] Nearly 18% of general population adults have HIV, and prevalence is estimated to be three-fold higher (58%) among transgender people [3]. A recent integrated bio-behavioral respondent driven sampling study (*Botshelo Ba Trans*; N=888) estimated HIV prevalence in transgender women to be 46% in Buffalo City and Cape Town and 63% in Johannesburg [4-6]. Unfortunately, transgender men and nonbinary people have been largely overlooked in the HIV response – with no available prevalence data from South Africa.

Engaging transgender people in HIV care and prevention is necessary to reach global goals for ending the HIV epidemic by 2030. Global 2020 targets toward ending the HIV epidemic were missed, and often left behind key populations, such as transgender people. For example, in 6 of 13 countries reporting HIV data on transgender people to UNAIDS, less than half of transgender women were able to access HIV prevention services [7]. The 2021–2026 Global AIDS Strategy aims to leave no one behind in the HIV response [8]. Therefore, UNAIDS has set more ambitious targets for 95% of people with HIV (PHIV) to be diagnosed, 95% of diagnosed PHIV to be on antiretroviral therapy (ART), and 95% of PHIV on ART to achieve sustained viral suppression (i.e., 95-95-95) by 2025 [9]. Since key populations accounted for 65% of new HIV infections globally and 35% within sub-Saharan Africa in 2020, UNAIDS emphasized the importance of reaching key populations, including transgender people, to achieve these goals [10, 11]. Because stigma and discrimination are known drivers of HIV, UNAIDS also set targets for 2025 that include <10% of health workers reporting negative attitudes toward key populations and <10% of key populations reporting experiences of stigma and discrimination [12]. However, interviews with more than1,400 transgender people in South Africa in 2023 revealed that only 7% felt safe and comfortable when accessing healthcare; 72% no longer get services because of disrespect from health facility staff; 65% reported that health facility staff were unfriendly; and 10% had been denied healthcare outright [13].

Although South Africa has the world's largest HIV epidemic, it has achieved 92% of PHIV being aware of their status, 72% of PHIV on ART, and 66% of PHIV virally suppressed [14]. Unfortunately, South Africa does not disaggregate HIV continuum data for transgender people. In 2019, a study that combined data from transgender women and men who have sex with men in sub-Saharan Africa (including Cape Town and Soweto, South Africa) found 56% of PHIV knew their status, 34% were on ART, and 28% were virally suppressed [15]. Another combined study of transgender women and men who have sex with men in Johannesburg found that 47% were virally suppressed. Modelling data from 2021 indicate South Africa will not reach the HIV elimination threshold (incidence <0.1%) without engaging key populations [16]. While 97% of South African transgender women with HIV in a 2018 study (N=213) had been prescribed ART, 69% reported experiencing ART interruptions [17]. Modeling has indicated that halving the rate of ART interruptions in South Africa would substantially reduce new infections, accelerating progress toward ending the HIV epidemic [18].

Available data among transgender men [19] and transgender women [20, 21] have found sub-optimal levels of ART adherence and viral suppression, even in high-income countries. For example, a U.S.-based study of transgender men with HIV found that while 93% had been prescribed ART, only 60% maintained viral suppression over the course of 12 months [19]. Similarly, a US study of transgender women found that while 80% reported ART adherence, only 59% achieved viral suppression [21]. Disaggregated data on viral suppression among transgender people in South Africa are scant. However, an observational cohort study including 24 transgender women from South Africa, Kenya, and Malawi found that 25% of TW were virally suppressed at baseline and 62.5% were suppressed at 12-months [22].

UNAIDS 2025 targets call for 95% of people at risk to use combination HIV prevention, including PrEP [9]. However, PrEP uptake is low among transgender women. A large (N=728) U.S.-based longitudinal study of transgender women's adherence to PrEP during periods of sexual risk (also known as prevention-effective adherence) found it to be less than 20% [23]. A smaller South African study (N=213) found that less than half of HIV-negative transgender women reported they had heard of PrEP and only 11% reported taking PrEP [24]. Qualitative interviews with transgender women in the study (n=36) identified health facility-based anti-transgender stigma as a barrier to care-seeking. [24] While PrEP data on transgender men in sub-Saharan Africa are unavailable, research in high income countries has found that PrEP-eligible transgender men report low PrEP use (~11%) [25, 26], and healthcare provider stigma is associated with decreased access to HIV prevention services [27]. Our team found no published data on PrEP engagement among gender nonbinary people.

Multiple studies with transgender people have concluded that stigma and limited access to gender-affirmation are associated with increased HIV risk and low engagement in HIV care and prevention services [19, 28-30]. Access to gender affirming hormone therapy (GAHT) is a priority for many transgender people, often deemed more important than HIV care or prevention [31]. Yet, a recent study with transgender women in South Africa found that only 17% had access to GAHT [24]. Research has also found that the use of gender-affirming language by healthcare providers positively impacts transgender patients health care experiences, quality of care, mental health and likelihood of seeking preventative services [32].

Differentiated Service Delivery

Transgender-specific differentiated service delivery (TG-DSD) is a promising strategy to overcome barriers to HIV service engagement among transgender people. DSD is a term used to refer to client-centered approaches that tailor HIV services to reflect the needs of specific populations [33]. Building blocks of DSD include adaptations to when (e.g., frequency of clinical visits), where (e.g., health facility, community), by whom (e.g., nurses, community health workers), and what (e.g., ART, PrEP, counseling) services are offered based on the needs of the individual client [34]. When implemented at scale, DSD is intended to simplify and adapt HIV services across the prevention and treatment continuum in ways that better serve client needs, improve client outcomes, and reduce burdens on the health system. [33] UNAIDS 2025 targets call for 90% of PHIV and people at risk to be linked to people-centered, context-specific, integrated services, i.e. DSD [9].

DSD sites may differentiate services according to client clinical characteristics (e.g., newly diagnosed with HIV, stable on ART), subpopulations to which they belong (e.g., pediatric, pregnant, key population), and context in which they live (e.g., concentrated/generalized epidemic, rural/urban setting) [34]. The World Health Organization (WHO) promotes the use of DSD for key populations to increase service acceptability, quality and coverage, and reduce costs [35]. Facilities across sub-Saharan Africa have implemented a variety of DSD models for different subpopulations [36-38].

However, South Africa is the first in the region to implement TG-DSD models that tailor services to the specific needs of transgender people, including the need for GAHT.

Because GAHT is a priority for transgender people, guidance on DSD for key populations from WHO [39] and the International AIDS Society [40] recommend inclusion of GAHT in DSD for transgender people. Promising research in Peru, Thailand, and the United States suggest that integration of GAHT services with HIV care and/or prevention can improve engagement with HIV services [41-44]. However, the evidence base is limited to case studies or protocols lacking outcome data [41, 43, 45, 46]; cross-sectional associations between use of GAHT and engagement in HIV services [47, 48]; or outcomes and perceptions of services at a single site [42, 44, 49]. No published studies compare HIV outcomes at TG-DSD sites versus standard service delivery (SSD) sites; and no published studies of TG-DSD have been conducted in sub-Saharan Africa, the region with the greatest burden of HIV [36].

A recent review of DSD models called for a deeper understanding of their mechanism of effect and noted that while the success of DSD implementation may differ based on a variety of factors, few studies have evaluated comparative implementation or cost [50]. To inform ongoing efforts to achieve UNAIDS goals and leave no one behind, data are needed on the effectiveness of TG-DSD models for improving engagement in HIV services and on implementation barriers, facilitators, acceptability, feasibility, and cost.

Wits RHI demonstration sites provide a unique opportunity to evaluate TG-DSD in sub-Saharan Africa [51]. Over the last several years, Wits RHI has collaborated with transgender-led organizations in four municipal areas (Gauteng, Cape Town, Nelson Mandela Bay, Buffalo City) in South Africa to implement a TG-DSD site in each area (N=4 sites). Each site integrates gender-affirming care, including GAHT, with a full package of facility-based and community-based (mobile) HIV care and prevention services – consistent with WHO key population and DSD guidelines [51-53]. All staff receive training on the provision of non-stigmatizing, gender-affirming services. Clinicians receive additional competency training in gender-affirming medical care. These real-world sites, currently supported by programmatic (non-research) funds from USAID, provide an important opportunity to conduct much-needed implementation research [33, 35, 54]. Findings will not only directly inform the future direction of DSD strategies in South Africa but also advance the knowledge base on *if* and *how* TG-DSD models work and the cost of implementation.

A robust evidence base supports DSD among non-key populations. A systematic scoping review of DSD for HIV treatment included 40 publications (18 from South Africa) involving over 240,000 participants spanning 9 countries in sub-Saharan Africa [36]. The review found that a variety of DSD models were effective for improving viral suppression and retention in care compared with SSD. DSD improved acceptability and, in some cases, reduced the cost of care to clients. While these data provide a strong scientific premise for evaluating DSD models, none of the evaluated DSD models focused on key populations.

Study Aims and Hypotheses

This study entitled, *Jabula Uzibone* (a Zulu phrase that can be translated into English as “Be Happy, See Yourself”), is designed to fill an important gap in data on implementation, effectiveness, and cost of TG-DSD models in sub-Saharan Africa. It has the following aims:

Aim 1: Assess barriers, facilitators, acceptability, and feasibility of TG-DSD.

Aim 2: Evaluate the effect of TG-DSD on viral suppression and prevention-effective adherence, testing stigma and gender affirmation as mediators.

Hypothesis 1. Rates of viral suppression (HIV RNA <50 copies/ml) are more likely to increase among transgender people on ART at TG-DSD sites than among transgender people on ART at SSD sites, over the 12-month study period.

Hypothesis 2: Rates of prevention-effective adherence (measured by tenofovir levels >700 fmol/punch among participants on PrEP and/or no condomless intercourse among HIV-negative participants who are not taking PrEP) are more likely to increase among participants at TG-DSD sites than among those at SSD sites, over the 12-month study period.

Hypothesis 3: Stigma and gender affirmation will mediate relationships between service delivery models (TG-DSD vs. SSD) and HIV outcomes (viral suppression and prevention-effective adherence).

Aim 3: Estimate the cost associated with TG-DSD versus SSD using a micro-costing approach to determine the cost per service user served and per service user successfully treated at TG-DSD sites relative to SSD sites, as well as the budget needed for successful South Africa-wide implementation.

Methods

Overall Study Design

Jabula Uzibone is an observational, multi-site, mixed methods, prospective implementation study. To meet the first aim, we will assess implementation of TG-DSD models and SSD models at the facility level using standardized observation checklists at 8 facilities (1 DSD site and 1 SSD site per area in all 4 areas). We will examine implementation, acceptability, feasibility, barriers to and facilitators of TG-DSD via key informant interviews (KIIs; n=6 per site) with health facility staff. At the client level we will conduct in-depth interviews (IDIs) with 30 transgender people (15 from DSD sites and 15 from SSD sites) drawn from the longitudinal cohort enrolled for Aim 2 (**Table 1**).

Table 1. Sample Sizes for Longitudinal Cohort of Transgender People (N=600)

HIV Status	TG-DSD[a] sample (n=300)	SSD[b] sample (n=300)	TOTAL (N=600)
Living with HIV	200	200	400
HIV-negative	100	100	200

[a]TGD-DSD = transgender-differentiated service delivery; [b]SSD = standard service delivery

To meet the second aim, we will enroll a cohort of 600 transgender people (**Table 1**) and follow them for 12 months. Of the 600 transgender people enrolled, 400 will be transgender people living with HIV. This will include 200 who receive ART at TG-DSD sites and 200 who receive ART at SSD sites in the same area as the TG-DSD sites. We will also enroll 200 transgender people without HIV. This will include 100 participants without HIV at TG-DSD sites (and 100 without HIV at SSD sites in the same area as the TG-DSD sites. Each participant will complete a quarterly survey to assess engagement in HIV prevention and care, changes over time in experiences of gender affirmation, as well as experiences of stigma.

For participants on ART, we will measure HIV RNA levels (i.e., viral load) at baseline and 12 months. For participants on PrEP, we will measure tenofovir (TFV) levels at baseline and 12 months. For HIV-negative participants who are not on PrEP, we will assess self-reported condomless sex. Prevention-effective adherence is defined as being HIV-negative and meeting one of the following criteria: a) adherent to PrEP based on TFV-levels; b) self-report of consistent condom use in the prior

30 days; or c) self-report of no anal or vaginal sex in the prior 30 days. See **Table 2** for a list of data collection activities organized level of analysis, participant type, and month of enrollment.

Table 2. Data Collection Activities by Level of Analysis, Participant Type, and Month of Enrollment

Level	Baseline	Months 3, 6, and 9	Month 12
Facility Level (n=8)			
TG-DSD[a] sites (n=4) SSD[b] sites (n=4)	Checklists (n=8 sites) KIIs[c] (6/site, n=48)	Quantitative Survey	Checklists (n=8 sites) KIIs[c] (6/site, n=48)
TGP living with HIV (n=400)			
Care at TG-DSD[a] sites (n=200) Care at SSD[b] sites (n=200)	HIV RNA level Quantitative Survey IDI[d] (15/arm, n=30)	Quantitative Survey	HIV RNA level Quantitative Survey IDI[d] (15/arm, n=30)
TGP without HIV (n=200)			
Care at TG-DSD[a] sites (n=100) Care at SSD[b] sites (n=100)	TFV[e] level Quantitative Survey IDI[d] (15/arm, n=30)	Quantitative Survey	TFV[e] level Quantitative Survey IDI[d] (15/arm, n=30)

[a]TGD-DSD = transgender-differentiated service delivery; [b]SSD = standard service delivery [c]KII=key informant interview [d]IDI=in-depth interview; [e]TFV=tenofovir

To meet the third aim, we will estimate the incremental costs of DSD implementation compared with SSD from the provider perspective by conducting a bottom-up analysis of the resources used and costs accrued by the TG-DSD cohort and comparing them to the costs of SSD established in recent studies. [55, 56] We will also calculate the cost per successful outcome (suppressed viral load for those on ART and prevention effective adherence for those without HIV) and the total budget required for a national rollout of TG-DSD.

Ethics Approval

Ethics approval was received for this study from the University of Witwatersrand Human Research Ethics Committee (M220420) and from the Duke University Health System Institutional Review Board (Pro00113320). All participants complete a written informed consent process after eligibility screening and prior to any data collection activities. Participants receive 300 rand for each study visit.

Study Frameworks

This study uses the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) [57, 58] implementation science evaluation framework and the Gender Affirmation Framework [59]. Data collection and analysis for all aims are guided by RE-AIM. Key measures and analyses for Aim 2 are also guided by the Gender Affirmation Framework – a conceptual framework that outlines mechanisms by which TG-DSD is expected to improve HIV outcomes.

RE-AIM is often used to guide evaluation of implementation strategies [57]. It is well-suited for studies of projects that are in the implementation process [58] and guides our selection of study measures [60]. The first four RE-AIM domains are listed in **Table 3** with examples of research questions for each domain. These domains (reach, effectiveness, adoption, and implementation) are most applicable to this study, while the fifth domain, maintenance, will not be addressed.

Table 3. RE-AIM Domains and Example Research Questions	
Domain	Example Research Questions
Reach	Is the intervention reaching the desired population?
Effectiveness	Does the intervention accomplish its goals?
Adoption	To what extent are the people who should deliver the intervention participating?
Implementation	To what extent is the intervention consistently implemented?

The Gender Affirmation Framework provides a model for drivers of HIV outcomes. Gender affirmation is a process of recognition and support for one's gender identity [59]. Gender affirmation has 4 core facets: medical (e.g., GAHT, surgery), psychological (e.g., self-acceptance, sense of alignment with one's gender), social (e.g., use of desired name and pronouns, wearing clothes associated with one's gender identity), and legal (e.g., change of name and/or gender marker on legal documents) [61].

The Gender Affirmation Framework posits that anti-transgender stigma leads to social oppression and psychological distress. Social oppression reduces access to gender affirmation while psychological distress increases the need for gender affirmation. The gap between access and need drives behaviors that increase HIV vulnerability. Significant relationships between unmet gender affirmation needs and HIV risk behavior as well as ART interruptions are well documented [59, 62-65]. This framework informs our hypothesis that TG-DSD will reduce stigma and increase gender affirmation, thereby increasing engagement in HIV services and improving HIV outcomes (i.e., viral suppression and prevention-effective adherence) among transgender people. Our measures of stigma as well as medical (i.e., GAHT) and psychological gender affirmation will be used to test hypothesis 3 for Aim 2.

Transgender Differentiated Service Delivery Models

Wits RHI provides TG-DSD models at four sites. Two are stand-alone sites; and two are in park homes on an SSD facility campus. All TG-DSD sites offer GAHT in an integrated HIV and primary care package, which includes both facility-based (fixed) services and community-based (mobile) services. All services are free to clients.

Details of the care provided at those sites have been published elsewhere [51], and an overview is provided in **Table 4**. Each site employs peer navigators, community liaison officers, professional nurses, a social worker, a site manager, and community health workers. Each site also employs a sessional physician and psychologist. Services have been designed and delivered in collaboration with local transgender community-based organizations. All cadres of staff (clinical, non-clinical, professional, and lay) complete transgender sensitization training conducted by transgender-led community organizations. These trainings build staff skills in providing non-stigmatizing, transgender-friendly services. Trainings take place upon hire and routinely thereafter during in-service sessions.

Table 4. Wits RHI TG-DSD Sites and Models of Care in South Africa				
	Guateng	**Cape Town**	**Nelson Mandela Bay**	**Buffalo City**
Model	Stand alone	Stand alone	Co-located with SSD	Co-located with SSD
Urban/Rural	Urban	Urban	Peri-urban and rural	Peri-urban and rural
Gender-affirming hormone therapy (GAHT)	Provided on-site	Provided on-site	Provided on-site	Provided off-site
Clinical services	Primary health care; sexually transmitted infections screening and treatment; tuberculosis screening; HIV treatment and prevention; GAHT			
Ancillary services	Psychosocial support; referral to post-violence care, legal support, and			

	substance use services
Full-time staff	4-10 peer navigator; 0-2 community liaison officers; 1 social worker; 0-2 community health workers; 2 nurses; 1 site manager
Sessional staff	1 physician, 1 psychologist
Community partnerships	Local transgender community organizations; Local AIDS Councils
Community Leadership	Community Advisory Boards comprising transgender advocates/ activists who guide and monitor services

Where possible, transgender people are appointed in all staff cadres. Most community health workers and peer navigators are transgender people. Program-specific Facebook and WhatsApp groups provide information on services and events to the community. Transgender-friendly health information, education and communications printed materials are available.

Clinical services related to GAHT are provided only at the facility. The client comes to the facility monthly for the first 3 months on hormones for laboratory testing, side effect assessment, and dose adjustments. After the third month, when clients are on a stable dose, they return to see the medical provider at month 6, then every 6 months subsequently for monitoring. Multi-month dispensing of hormones is currently a challenge in South Africa due to stock shortages; therefore, clients on GAHT return monthly for dispensing visits only.

In addition to facility-based GAHT and HIV services, each TG-DSD site provides mobile HIV services in the community throughout their catchment area. These mobile services are offered in a van equipped with exam rooms and basic medical equipment. Mobile teams include a peer navigator, a community health worker, and a professional nurse. They offer primary health services, HIV testing and counselling, and multi-month dispensing of ART and PrEP.

Standard Service Delivery Models

Public primary health care centers in South Africa provide SSD through a professional nurse-based, physician-supported infrastructure of over 3,500 clinics and community health centers, available within five kilometers of more than 90% of the population and free at the point of care [66]. Primary health care centers are the first point of entry for healthcare access. These facilities provide a comprehensive package of basic services including maternal, child and reproductive health, HIV and tuberculosis testing and treatment – including ART, screening and care for non-communicable diseases and treatment of common ailments. The primary health care system is supported by community teams, referred to as Ward-based Primary Health Care Outreach Teams. These teams are allocated to specific wards according to the size, geography, and social and structural considerations. They provide health information to the community and screen and refer those who need further management to corresponding primary health care facilities [67]. Despite a progressive constitutional and legal framework, transgender people continue to face stigma and discrimination when they access SSD sites for healthcare [68-70]. GAHT is not available in public primary health care facilities. In general, access to GAHT is limited in South Africa, where it is only provided by specialist endocrinologist at tertiary facilities; and transgender people may face waiting times of up to 20 years or more to access gender-affirming surgery in the public sector [71, 72].

Study Procedures

Facility-level eligibility, recruitment, and data collection

We have enrolled all 4 Wits RHI TG-DSD sites listed in **Table 4**. In collaboration with district health departments, we have recruited one SSD site within the catchment area of each DSD site for a total of 4 TG-DSD sites and 4 SSD sites. SSD sites are similar to TG-DSD sites in urbanicity, socioeconomic status of client population, and types of HIV services offered (i.e., both ART and PrEP). We shared information about the study with the district and SSD site leadership and invited them to participate in the study. Study staff will visit all 8 recruited sites (TG-DSD and SSD) to complete a standardized observation checklist at baseline and 12 months. Checklist items include: the number, type and role of staff; content and frequency of staff training; facility hours, amenities (e.g., number of rooms) and community outreach efforts; standard policies, and procedures for delivery of HIV and STI testing, PrEP, ART, and GAHT services – including, but not limited to counseling, prescribing, dispensing, laboratory monitoring, tracking, and visit frequency; sex and gender documentation on clinical forms and records; the number of transgender clients; number of TGP prescribed GAHT; number of transgender people prescribed PrEP; number of transgender people prescribed ART; availability and use of psychosocial services; and cost of service delivery.

Leadership at each recruited site facilitate recruitment of 6 staff members per site (n=48) to complete a key informant interview (KII) at baseline and 12 months. Eligible staff members are 18 years of age or older and work for one of the TG-DSD sites or a selected SSD sites. We enroll one person in each role at each site – i.e., peer navigator, community liaison officer, social worker, community health worker, nurse, and site manager. If a staff member leaves between baseline and 12 months, we will interview another person in the same role for the 12-month time point. We contact potential key informants via email and/or WhatsApp and invite them to participate.

An experienced qualitative researcher conducts the KIIs after the informed consent process. A semi-structured KII guide will be used to organize the interview. KIIs last approximately 60 minutes and include open-ended questions that explore facilitators, barriers, strengths, and weaknesses of the DSD and SSD approaches; and recommendations for improving service delivery. At the end of the qualitative interview, participants complete a brief, interviewer-administered quantitative tool measuring anti-transgender stigma [73] and validated measures of intervention acceptability, feasibility, and appropriateness [74, 75]. KIIs are audio-recorded with permission of the participant and notes are taken during and after the interview to facilitate accuracy and appropriate analysis. Where possible, interviewers are fluent in local languages. When interpretation is required, a trained study staff member interprets during the interview.

We collect data on the costs of implementation at all TG-DSD sites by conducting a bottom-up analysis of the resources used and costs accrued by all transgender cohort participants who receive TG-DSD. We also collect facility-level data on overhead cost items such as space, administration, and utility costs, and allocate these to the service and our cohort based on the number of visits. We use our extensive database of public sector prices and salaries, as well as information on staff levels at each site, to estimate the public sector costs; these are data we have used in other costing studies in South Africa [55, 76, 77].

In collaboration with local transgender organizations, trained transgender people recruit their peers from their social networks via social media posts, WhatsApp groups, and word-of-mouth. Eligibility criteria include age ≥18 years, identity as a gender different from sex assigned at birth, and residence in the catchment area for one of the enrolled health facilities. Participants must either be living with HIV and prescribed ART or HIV-negative and PrEP-eligible (whether or not they are currently taking PrEP). We use stratified sampling to ensure enrollment of 400 participants on ART and 200 participants who are HIV-negative. Within those strata, we further ensure that half are individuals

who receive care at a TG-DSD sites and the other half are transgender people who receive care at an SSD site in the same catchment area.

Once a specific stratum (e.g., transgender person with HIV at TG-DSD site) is full, new potential participants who fit that stratum are longer eligible to participate. We use quotas to ensure that no TG-DSD site makes up less than 20% of TG-DSD participants. At the enrollment visit, participants are re-screened for eligibility, including rapid HIV testing to confirm self-reported HIV status.

Client-level eligibility, recruitment, and data collection

Participants complete study data collection visits with the study team in a dedicated room at the site or in the community. Over the 12-month study period, participants complete five study visits: baseline, 3, 6, 9, and 12 months. At each visit, trained study staff administer electronic tablet-based quantitative surveys lasting 30 minutes. Surveys assess the key measures listed in **Table 5**. Survey data are collected and managed using Research Electronic Data Capture (REDCap), which synchronizes with the encrypted cloud-based server at Wits RHI, where it is stored for analysis.

Table 5. Key Quantitative Survey Measures

Construct	Measure	Citation
Implementation Outcomes		
Acceptability	Acceptability of Intervention Measure (AIM)	Weiner et al. 2017 [75]
Feasibility	Feasibility of Intervention Measure (FIM)	
Appropriateness	Intervention Appropriateness Measure (IAM)	
Enacted Stigma		
Health facility stigma	Brief health facility stigma tool	Nyblade et al. 2013 [73]
Experienced Stigma		
Transgender-specific stigma	Gender Minority Stress and Resilience measure	Testa et al. 2015 [78]
Intersectional stigma	Intersectional Discrimination Index	Scheim et al. 2019 [79]
Gender Affirmation		
Psychological	Psychological Gender Affirmation Scale	Sevelius et al. 2021 [80]
Prevention-effective Adherence [23]		
Sexual behavior	“Have you had anal or vaginal sex in the past 30 days?”	---
Condom use[a]	“How often did you use condoms when you had sex?”	---
PrEP adherence[b]	How many days have you missed PrEP pills in the last 30 days ?”	---

a. This question is only asked of participants who report sex in the past 30 days.
b. This question is only asked of participants who self-report taking PrEP.

At the baseline and 12-month visits, all participants have blood drawn by a professional nurse for laboratory analysis. Sera from participants on ART are tested for HIV RNA. HIV RNA levels < 50 copies/ml are the threshold for viral suppression, consistent with South African national guidelines [81]. Dried blood spots (DBS) from participants on PrEP will be tested for tenofovir diphosphate levels [82, 83]. Levels > 700 fmol/punch are consistent with ≥4 doses per week and will be used as a marker for adherence [84, 85].

A subset (n=30) of enrolled transgender participants who complete the quantitative survey and laboratory analyses at baseline are invited to participate in longitudinal qualitative in-depth interviews (IDIs) at baseline and 12 months. IDIs are most appropriate for eliciting detailed accounts

of participant experiences and perceptions of service delivery models. The open-ended nature of IDIs provide the opportunity to more deeply explore issues relevant to the study aims.[156] Embedding qualitative data collection within implementation research can enrich the understanding of how and why service delivery models work or do not work [86, 87]. Longitudinal interviews are important to study how participants experience, interpret, and respond to the service delivery model over time [88].

We invite participants to take part in IDIs using stratified purposive sampling [89]. We stratify by care model, i.e., 15 who receive care at TG-DSD sites and 15 who receive care from SSD sites. Within each stratum, we purposively sample to ensure diversity by HIV status, catchment area, and gender identity (transgender women, transgender man, gender nonbinary). A topical guide structures the interview. Open-ended questions, followed by prompts, are used to elicit participant narratives. Study staff with training and experience in qualitative research conduct the IDIs. Each IDI explores perceptions of DSD vs. SSD models of care; satisfaction and/or concerns related to type of care received; experiences with GAHT, if any; experiences with ART or PrEP, as appropriate; and recommendations for service improvement. Follow-up IDIs will explore how participant experiences and perceptions have changed over time and provide an opportunity to clarify earlier responses. With participant permission, all interviews are digitally audio-recorded. Interviewers write field notes and narrative summaries after each interview that supplement the transcripts. Participants' qualitative data are linked with the survey data to allow for integration with their quantitative measures of stigma and gender affirmation.

Participant tracking and retention rely on multiple strategies. At enrollment and each subsequent study visit, we document contact details for participants (e.g., phone numbers, addresses, WhatsApp, social media profiles) in order to communicate study reminders and re-engage participants who may miss a study visit. If participants are unable to come to the study site for data collection, research staff support retention by accompanying mobile health facility staff into the community and collecting study data there. We provide modest financial remuneration and refreshments to incentivize participation and retention. We have hired transgender study staff to create a welcoming and affirming environment for study participation. Gender-affirming stigma reduction training of research staff facilitates strong staff-participant rapport to encourage retention. Participants are provided referral to counseling services if they demonstrate psychological distress while engaging with study staff.

Overall Approach to Data Analysis

Data analysis will include both qualitative and quantitative data. **Table 6** outlines the relationships between the RE-AIM framework domains and the types of data to be collected.

Table 6. Relationship between RE-AIM Domains, Study Aims, and Data Collection

Domains (Aim)	Level	Data Type/Source	Example Qualitative Questions and Quantitative Measures[a]
Reach (1)	Facility	Site checklist	Number of transgender people who receive GAHT, ART, and/or PrEP from the site
		KIIs[b] with health staff	What factors contribute to the engagement of transgender people at TG-DSD?
Adoption (1)	Facility	KIIs[b] with health staff	What barriers/facilitators affected staff implementation of TG-DSD?
Implementation (1, 3)	Facility	Site Checklist	Number and type of staff and their roles in implementation. Availability of GAHT on site. Frequency of stigma reduction training. Cost of

			service delivery (infrastructure, labs, visits, etc.)
		KIIs[b] with health staff	How was TG-DSD implemented and adapted over time? AIM, IAM, FIM implementation science measures[a]
	Client	IDIs[c] with TGP[d]	Tell me about the services you received at the site?
Effectiveness (2)	Facility	KIIs[b] with health staff	What changes in use of HIV services (e.g., ART/PrEP uptake and adherence) did you notice when TG-DSD was implemented? Health facility stigma scale by Nyblade[a]
	Client	IDIs[c] with TGP[d]	Tell me about your experience receiving care at the site.
		Survey with TGP[d]	Intersectional stigma scale by Scheim[a] Psychological Gender Affirmation scale by Sevelius[a] GAHT use by self-report.
		Lab test with TGP[d]	HIV RNA level by serum analysis (for TGP on ART) TFV level by DBS (for TGP on PrEP)

[a]See Table 5 for more information about quantitative survey measures
[b]KII = key informant interview
[c]IDI = in-depth interview
[d]TGP = transgender participants

Qualitative interview (KII and IDI) recordings will be transcribed and translated into English. The transcripts, field notes, and narrative summaries will be uploaded into qualitative data management software, Atlas.ti, to facilitate analyses. During regularly scheduled meetings, the study team will review field notes, transcripts, and summaries, discuss emerging themes, and revise interviewing and coding strategies, as needed.

Statistical analysis of quantitative data will be performed using STATA and MPlus. Data exploration of key variables will be conducted to assess for implausible values and determine whether statistical assumptions (e.g. normal distributions of data) for planned statistical analyses are satisfied. Categorical variables will be reported as frequencies and percentages, with means and standard deviations or medians and interquartile ranges reported for continuous variables. Patterns of missing data will be examined, including testing for differences between participants with and without missing data. A series of sensitivity analyses will be conducted to evaluate the robustness of conclusions drawn from the primary models to departures from the missing at random assumption by comparing the magnitude of the primary effect. In the rare situation that more than 10% missing data is observed, we will use multiple imputation, as appropriate. We will specify two-sided tests, 0.05 significance level ($\alpha = 0.05$), and compute 95% confidence intervals throughout.

Qualitative Data Analysis for Aim 1

Qualitative transcripts from the KIIs with health facility staff and IDIs with TGP will be analyzed to assess barriers, facilitators, acceptability, and feasibility of TG-DSD. To identify preliminary results quickly, we will use a framework-guided rapid analysis in which transcripts are summarized in a structured template [90, 91]. The template will include a section for each of the four aspects of this aim: barriers, facilitators, acceptability, and feasibility.

For full analysis, *a priori* codes based on the interview guides and key implementation constructs from RE-AIM will be used to generate the initial codebook [86]. Two independent analysts will code a subset of transcripts and meet weekly to discuss the textual context, update the codebook, assess inter-rater reliability, and generate analytic memos. Once the codebook is finalized, the remainder of

the transcripts will be systematically coded. Code summaries will be consolidated into matrices by each category of variation (e.g. site) to identify salient themes [92]. Any differences in code density will be explored after coding completion from baseline to 12 months and by site characteristics such as district, urbanicity, and population size.

Codes and associated quotes will be examined within and across transcripts to identify patterns and recurrent themes related to the implementation constructs [93]. After preliminary findings have been shared with key stakeholders for member-checking [94]. deductive in-depth content analyses will be conducted with open coding followed by focused coding. Once coding is complete, we will use visualization features of Atlas.ti to map out differences in code density by service delivery model.

To take advantage of the longitudinal nature of the data, we will apply multiple analytic approaches to the constant comparison technique as outlined by Lewis [95]. We will review the narrative summaries for each participant over time to look for within-individual changes. We will read across the transcripts for each time period to look for themes unique to specific time periods; and we will compare all data across service delivery models (TG-DSD vs. SSD). Analytical memos will describe emergent themes and track the analytic process. Peer debriefing, triangulation with quantitative data, member-checking, and memos will support rigor [96].

Sample sizes for qualitative inquiries are designed to collect enough data to reach theoretical saturation – defined as the point at which no new themes emerge from ongoing data collection [97]. Samples sizes as low as 6 can achieve saturation when the study population is homogeneous. However, a sample size of 12-20 is typically needed, fewer for longitudinal studies. To account for diversity by site, role, gender identity, education level, etc., we have chosen a sample size of 48 individuals for KII participants, for a total data set of 96 KIIs (including baseline and 12 month). We have selected a smaller sample size of 15 per arm (n=30) for IDIs with transgender clients since they will share similarities which will produce a robust data set of 60 total IDIs for analysis.

Quantitative Data Analysis for Aim 1

Standardized checklists from DSD and SSD sites will be examined using descriptive statistics. We will perform chi-square tests or Fisher's exact tests for associations between categorical variables. We will perform unpaired student's *t* tests to compare continuous variables or outcomes between two groups. We will perform Wilcoxon rank-sum tests, if data are not normally distributed.

In the DSD sites, to assess acceptability and perceived feasibility of implementing the differentiated care model, staff at each implementing site will complete a brief survey with implementation outcome measures at 12 months. The Acceptability of Intervention Measure (AIM), the Intervention Appropriateness Measure (IAM), and the Feasibility Intervention Measure (FIM) will be used to quantitatively measure implementation outcomes related to the TD-DSD model [75]. Each measure consists of 4 items with response options on a Likert scale from 1 (completely disagree) to 5 (completely agree), for a possible summary score range from 4 to 20. Higher scores indicate greater acceptability and feasibility.

Descriptive statistics will be used to characterize each measure overall and by site. Based on a score of 4 (agree) for all 4 items in the scale, a summary score ≥16 on each scale would be consistent with overall agreement that the strategy was acceptable or feasible respectively [75]. Therefore, we will test the hypothesis that the overall mean score for each measure (AIM and FIM) is ≥ 16 using a one-sample t-test. If score data deviates from normality (skewed or non-normal), we will conduct a one-sample Wilcoxon signed test. We will conduct a secondary analysis to test for significant changes in baseline and 12-month scores across sites using paired sample t-tests for normally distributed data or Wilcoxon signed rank tests if the data are non-normal.

Using data from both study arms, facility-based stigma will be measured using the brief health facility stigma tool [73]. Each item includes 4 response options on a Likert scale that ranges from "never" to "most of the time." Higher scores indicate greater facility-based stigma. Descriptive statistics will be generated as outlined above for the implementation outcome measures. We will compare mean summary scores at TG-DSD sites vs. SSD sites at baseline and at 12 months, using two-sample t-tests if normally distributed or Wilcoxon rank tests if non-normal. Exploratory analyses will include Pearson's correlation analyses and bivariate regression to assess associations between site characteristics (e.g., location, urbanicity), including facility-based stigma scores, and the above-mentioned implementation outcome scores.

Qualitative and Quantitative Data Integration for Aim 1

Qualitative and quantitative data will be integrated using results-based convergent synthesis in which they will be analyzed separately then merged using joint display [98-100]. Qualitative themes will triangulate and provide context for facility stigma scores, and implementation measures. Data from the checklists will be integrated into the joint display to assess visually any relationships between site features and the relationship between TG-DSD and HIV outcomes. Integrated displays will be used to identify implementation patterns. The qualitative code density (frequency of each code) will be displayed by service delivery model (TG-DSD vs. SSD). Visualization will facilitate identification of similarities and differences in participant experiences across models.

Data Analysis for Aim 2

We will use quantitative methods to evaluate the effectiveness of TG-DSD for viral suppression and prevention-effective adherence and to assess stigma and GAHT use as potential mediators. As noted above, our first hypothesis is that rates of viral suppression are more likely to increase among transgender people on ART at TG-DSD sites than among transgender people on ART at SSD sites, over the 12-month study period.

The primary outcome measure is the proportion of transgender people on ART with viral suppression (HIV RNA < 50 copies/ml). Descriptive analyses will summarize HIV viral suppression comparing participants at TG-DSD vs. SSD sites as well as by gender identity at baseline and 12 months. Percent distributions will be computed for categorical variables and means, ranges, standard deviations, medians, and interquartile ranges will be presented for continuous variables stratified by attendance at TG-DSD vs. SSD sites. The primary estimate for this aim is the absolute difference in the change in proportion of virally suppressed during the study period between participants at TG-DSD sites and those at SSD sites. A difference-in-difference (D-i-D) analysis will be conducted to account for anticipated differences between groups at baseline (TG-DSD vs. SSD). Additionally, we will compare differences at 12 months taking into account baseline values to enhance the robustness of the estimators of the differences in the two groups.

A mixed-effects binomial model will be fit, where the binary viral load suppression status of each client/patient is regressed on fixed effects for time (baseline vs. 12 months), TG-DSD vs. SSD site, the time by site model interaction, and client level covariates (age and gender identity). Additionally, random intercepts for each of the sites will be included in the model to account for within-site correlation. The D-i-D estimator is the estimated regression coefficient for the time by service delivery model interaction term. All models will account for clustering and be adjusted for relevant confounders in baseline covariates.

The second hypothesis is that rates of prevention-effective adherence are more likely to increase

among HIV-negative transgender people on at TG-DSD sites than among those at SSD sites, over the 12-month study period. We will follow the same steps outlined above for the primary hypothesis. However, we define the outcome measure (prevention-effective adherence) as the proportion of (a) participants on PrEP with TFV levels >700 fmol/punch and (b) participants who are not on PrEP who report no condomless intercourse during the prior 30 days. The estimate will be the absolute difference in the change in proportion who achieve prevention-effective adherence during the study period comparing those at TG-DSD versus SSD sites. Additionally, we will estimate the difference between TGD-DSD and SSD sites at 12 months, taking into account baseline values.

Clients who receive SSD services on enrollment may switch to TG-DSD over time, thereby reducing the sample size of the SSD arm and creating a threat to internal validity. In order to identify and account for switches over time, we will update information about where the participant is receiving care at every study visit. Participants who transfer from an SSD site to a TG-DSD site will be censored after the date of their last visit for the primary analysis. It would be inappropriate and unethical to require participants to continue receiving care at a specific site, therefore we will use careful tracking to inform an exploratory dose-response analysis that takes into consideration the amount of time a participant received care at the TG-DSD sites. The amount of time receiving care at the TG-DSD site will be the independent variable with the change in outcome from baseline to 12-months as the dependent variable.

The third hypothesis is that stigma and gender affirmation will mediate relationships between service delivery models (TG-DSD vs. SSD) and HIV outcomes (viral suppression and prevention-effective adherence). Mediation analyses will be used to investigate whether any association between service delivery models and HIV outcomes are significantly mediated by stigma (measured using Nyblade, Testa, and Scheim scales in **Table 5)** and/or gender affirmation (measured using the proportion of participants on GAHT and the Sevelius Gender Affirmation scale in **Table 5**). Structural equation modelling will be used for this analysis. Structural equation modelling provides tests of the direct and indirect paths from the independent variable to the dependent variables [101]. The independent variable will be the service delivery model (TG-DSD vs. SSD); and the dependent variables will be change from baseline to 12 months in the mediators (stigma and gender affirmation measures) and change from baseline to 12 months in the outcomes (difference in viral suppression and difference in prevention-effective adherence). Structural equation models will test direct paths (e.g. from serviced delivery model to viral suppression) and indirect paths (e.g. from service delivery model to stigma and from stigma to viral suppression). The basic model to be tested for this analysis is in **Figure 1.** We will assess standard fit statistics for the overall model: Model Chi-square, Adjusted Goodness of fit, Comparative Fit Index, and Standardized Root Mean Square Error of Approximation.

Exploratory Analyses for Aims 1 and 2

We will conduct 3 exploratory analyses: (i) Using longitudinal data from baseline, 3, 6, 9 and 12 months, we will perform mixed effects regression modeling to analyze changes in stigma scores, psychological gender affirmation scores, and GAHT use over time by service delivery model. Mixed effects regression is most appropriate for clustered longitudinal data as it captures correlations of repeated measures using random effects that describe cluster-specific trends over time [102]. (ii) As sample size allows, we will assess HIV outcomes by subgroups. The D-i-D model, used to test H1 and H2 above, will be fit separately for subgroups defined by (a) gender identity, (b) sex assigned at birth, (c) individual care facility, and (d) co-located vs. stand-alone TG-DSD sites. (iii) The association between 12-month HIV outcomes (viral suppression rates and prevention-effective adherence rates) and implementation metrics from Aim 1 will be examined graphically for the four TG-DSD sites by plotting the HIV outcomes at each site versus means scores on the AIM, IAM, and

FIM, respectively.

The use of difference-in-difference analyses implicitly assumes that TG-DSD sites are either comparable to SSD sites (other than the DSD approach) or that we can readily adjust for any differences. However, if we find that groups differ on important characteristics, we will use Inverse Probability of Treatment Weighting (IPTW) to adjust for the covariates in the effect estimation to mitigate potential bias.

Data Analysis for Aim 3

We will use the data from the micro-costing exercise as well as existing data on SSD costs to estimate the incremental cost of TG-DSD over SSD from the healthcare system perspective. Integrating data collected for Aim 2, we will then calculate the cost per successful outcome (defined as viral suppression for those participants on ART or prevention-effective adherence for the HIV-negative participants at month 12) and the cost of producing an additional client with a successful outcome. Finally, using any available size estimates for the overall transgender population in South Africa [103], we will then calculate the total budget required for a national roll-out of TG-DSD in South Africa, incremental to the country's HIV budget on which we will have real-time data.

Statistical Power

Power analyses and sample size calculations were based on the primary outcome of viral suppression (Aim 2). No viral load data are available for transgender people in South Africa disaggregated from other key populations. The only South African data that includes transgender women and uses the current nationally recommended threshold for viral suppression includes cisgender men who have sex with men. Nonetheless, the study found a viral suppression rate of 47% [104]. One study of transgender people receiving TG-DSD in South Africa found that those on GAHT were three times more likely to be virally suppressed compared to TGP who are not on GAHT [51]. This suggests an effect size of at least 20%. We consider an effect size as low as 15% to be clinically significant. Based on these data, **Table 7** presents the anticipated number of virally suppressed transgender people on ART at baseline and 12 months, stratified by TG-DSD vs. SSD sites.

Table 7: Anticipated sample sizes (SS) and viral load suppression (VLS) at baseline and 12-months for transgender people who receive care at TG-DSD[a] vs. SSD[b] sites

	SS pre-intervention	% VLS pre-intervention	SS post-intervention[1]	% VLS post-intervention	Difference
TG-DSD	200	65	175[c]	85	20
SSD	200	61	175[c]	66	5

[a]TGD-DSD = transgender-differentiated service delivery; [b]SSD = standard service delivery
[c]Assuming there will be some attrition as accounted for in sample size calculation

The presented estimates are pooled across all sites based on aforementioned data and an assumed difference in the absolute change in viral load suppression between intervention and control sites of 15%. Using a ratio (r=1), $\alpha = 0.05$, power = $1 - ß = 0.08$ and p_1 = viral suppression in the SSD and p_2 = viral suppression in the TG-DSD group and difference of p2-p1 = 0.15, the minimum sample per group will be: $n_{TG\text{-}DSD} = n_{SSD}$=172 for total minimum sample size of 344. Adjusting for loss to follow-up of ~10%, a sample of 200 in each group for a total of 400 transgender people on ART will provide adequate statistical power for planned analyses.

Loss to follow-up is a challenge for any longitudinal study. We will make every effort to minimize

loss to follow-up by collecting multiple forms of contact, reaching out monthly to update contacts, collecting data in the field as well as the study site, and providing remuneration for study participation. We will enroll a larger sample size than required by the power calculations to allow for potential loss to follow-up without loss of statistical power.

Results

Jabula Uzibone study enrollment began in November 2023. As of June 28, 2024, 489 transgender participants have been enrolled: 216 are living with HIV and 279 are HIV-negative. The majority (70%; 342/489) are transgender women; 15% (72/489) are transgender men; and 15% (75/489) are gender nonbinary. We anticipate baseline enrollment will be complete by August 31, 2024, and the final study visit will take place no later than August 2025.

Discussion

We anticipate that the *Jabula Uzibone* study will demonstrate that TG-DSD is associated with higher rates of viral suppression and prevention-effective adherence compared with SSD. Further, we expect qualitative and quantitative results to indicate that these associations are mediated by gender-affirmation and stigma reduction. Importantly, we expect to find that broader implementation of key aspects of TG-DSD models, including cost, are feasible, acceptable and appropriate.

Prior studies of DSD models support their effectiveness for improving retention in care and viral suppression for people living with HIV in sub-Saharan Africa [105]. However, the largest systematic review assessing DSD implementation barriers and facilitators excluded key populations [106]. This study will fill the critical gap in data on DSD for transgender people, a key population, as well as provide the first data on use of DSD for HIV prevention services.

This study is limited by its non-randomized, observational nature. Because TG-DSD is already being offered at Wits RHI sites in South Africa, sites cannot be randomized. While randomized controlled trials (RCTs) are considered the highest standard of scientific evidence, an RCT is not feasible in this situation. If an RCT were possible, it would run the risk of producing findings that cannot be replicated in less controlled settings. *Jabula Uzibone* will generate rich data on implementation strategies and intervention effectiveness in real world conditions.

Assessment of prevention-effective adherence among HIV-negative participants who are not prescribed PrEP relies on self-reported sexual behaviors. Recall and social desirability bias may affect the accuracy of self-report. Despite this limitation, our choice to measure overall prevention-effective adherence (rather than limiting measures to TFV-levels among participants on PrEP) allows for broader applicability of findings to the real lives of transgender people whose sexual behavior and indication for PrEP shift over time [23].

In addition to dissemination in scientific journals and relevance conferences, results from this study will be shared directly with both transgender community organizations and the National Department of Health in South Africa. *Jabula Uzibone* will provide actionable data to inform HIV policies and health facility practices in South Africa and generate the first evidence for implementation of TG-DSD in sub-Saharan Africa. Study findings also may inform how other countries could utilize TG-DSD strategies to increase engagement of transgender people in care and advance global progress towards HIV elimination goals.

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with and providing services for transgender people.

Data Availability

The datasets generated during the current study will be available from the senior author upon reasonable request one year after completion of data collection.

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Conflict of Interest

The authors declare that they have no competing interests.

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Abbreviations

AIM: Acceptability of Intervention measure
AIDS: Acquired Immune Deficiency Syndrome
ART: antiretroviral therapy
D-i-D: difference-in-difference
DSD: differentiated service delivery
FIM: Feasibility of Intervention measure
GAHT: gender affirming hormone therapy
HIV: Human Immunodeficiency Virus
IAM: Intervention Appropriateness measure
IDI: in-depth interview
KII: key informant interview

PHIV: people with HIV
PrEP: pre-exposure prophylaxis
RE-AIM: Reach, Effectiveness, Adoption, Implementation, Maintenance
RNA: ribonucleic acid
SSD: standard service delivery
TFV: tenofovir
TG-DSD: transgender-specific differentiated service delivery
TGP: transgender people
UNAIDS: Joint United Nations Programme on HIV and AIDS
USAID: United States Agency for International Development
WHO: World Health Organization

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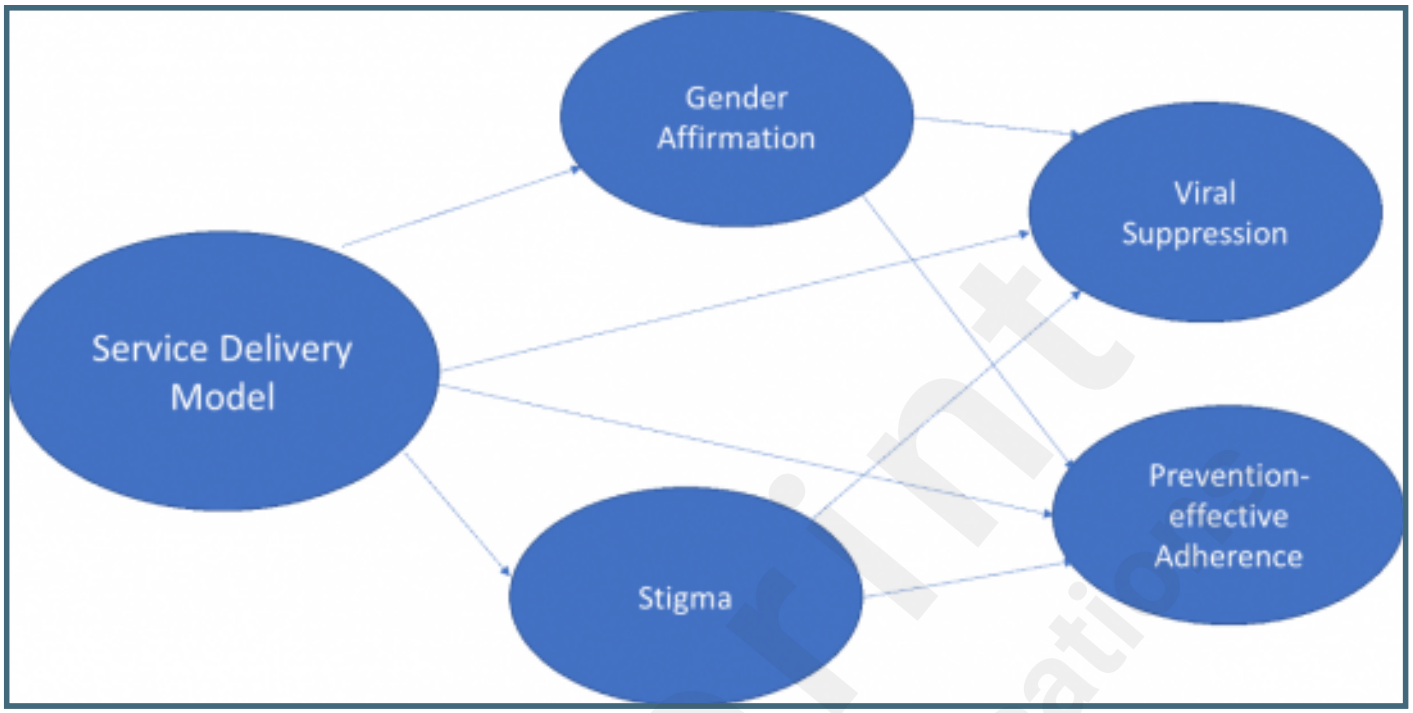
Supplementary Files

Figures

Structural equation model to test stigma and gender affirmation as mediators of relationships between service delivery type and HIV outcomes.



Multimedia Appendixes

NIH Reviews.
URL: http://asset.jmir.pub/assets/e5e068220f9a8285c227d64a93f69d4b.pdf

TOC/Feature image for homepages

Recruitment card for Jabula Uzibone.