

Evaluation of the Tu'Washindi na PrEP intervention to reduce gender-based violence and increase pre-exposure prophylaxis uptake and adherence among Kenyan adolescent girls and young women: Protocol for a cluster-randomized controlled trial.

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Table of Contents

Original Manuscript..... 5

Supplementary Files..... 46

 Figures 47

 Figure 1..... 48

 Figure 2..... 49

 Figure 3..... 50

 Figure 4..... 51

 Multimedia Appendixes 52

 Multimedia Appendix 1..... 53

 CONSORT (or other) checklists..... 54

 CONSORT (or other) checklist 0..... 54

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Abstract

Background: Adolescent girls and young women (AGYW) constitute a priority population disproportionately affected by HIV, accounting for 25% of annual HIV incidence among adults in Kenya. Although oral PrEP is effective in reducing HIV acquisition, its protective benefit has been limited among AGYW in sub-Saharan Africa because of low uptake, adherence, and persistence. Intimate partner violence (IPV) and relationship power inequities are both widespread among AGYW and contribute to higher HIV incidence and lower PrEP utilization. Interventions are needed to support sustained PrEP use among AGYW by addressing IPV and relationship dynamics.

Objective: This study aims to test the effectiveness of a Tu'Washindi na PrEP (We are Winners with PrEP), a multilevel community-based intervention, to increase uptake and adherence to PrEP and reduce IPV among AGYW in Siaya County, Kenya.

Methods: The Tu'Washindi na PrEP intervention was co-designed by our team and AGYW using participatory methods and includes three components delivered over 6 months: an eight-session, empowerment-based support club for AGYW, community sensitization targeted toward male partners, and PrEP education events for couples. The intervention will be evaluated using cluster-randomized controlled trial across 22 administrative wards in Siaya County, Kenya, enrolling 72 AGYW per ward (total N=1,584). The primary objectives are to test the effectiveness of the intervention on PrEP uptake and adherence immediately post-delivery (month 6 post-enrollment) and 6 months later (month 12). As secondary objectives we will test the intervention effect on IPV. A rigorous process evaluation will explore mechanisms of change, contextual factors, and implementation considerations to inform future refinement and scale-up, using programmatic data, participant questionnaires, and qualitative interviews with participants and providers (Aim 3).

Results: Data collection started in September 2022. As of December 2024, enrollment has been completed in 16 of 22 study wards, with 1150 of 1584 participants enrolled (73%). We anticipate that data collection will be completed in May 2026 and results will be available by mid-2027.

Conclusions: The study builds directly on our promising formative and pilot research to develop the evidence base for this youth-designed, multi-level HIV prevention intervention. If effective, Tu'Washindi will be ideally positioned for sustainable

integration into existing youth-focused programming to expand and support PrEP use in this priority population. Clinical Trial: Clinicaltrials.gov (NCT05599581); Current protocol: Version 7.0, 22 October 2024

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Original Manuscript

Evaluation of the *Tu'Washindi na PrEP* intervention to reduce gender-based violence and increase pre-exposure prophylaxis uptake and adherence among Kenyan adolescent girls and young women: Protocol for a cluster-randomized controlled trial.

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Methods: The *Tu'Washindi na PrEP* intervention was co-designed by our team and AGYW using participatory methods and includes three components delivered over 6 months: an eight-session, empowerment-based support club for AGYW, community sensitization targeted toward male partners, and PrEP education events for couples. The intervention will be evaluated using cluster-randomized controlled trial across 22 administrative wards in Siaya County, Kenya, enrolling 72 AGYW per ward (total N=1,584). The primary objectives are to test the effectiveness of the intervention on PrEP uptake and adherence immediately post-delivery (month 6 post-enrollment) and 6 months later (month 12). As secondary objectives we will test the intervention effect on IPV. A rigorous process evaluation will explore mechanisms of change, contextual factors, and implementation considerations to inform future refinement and scale-up, using programmatic data, participant questionnaires, and qualitative interviews with participants and providers (Aim 3).

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Trial registration: Clinicaltrials.gov (NCT05599581); **Current protocol:** Version 7.0, 22 October 2024

Key Words: adolescent girls and young women; HIV prevention; pre-exposure prophylaxis; adherence; Kenya; intimate partner violence



Main text (Word count: 7475)

Introduction

Optimizing the effectiveness of proven biomedical prevention interventions is critical to decreasing the high incidence of HIV among adolescent girls and young women (AGYW) ages 15-24 in sub-Saharan Africa (SSA), a priority population for HIV prevention. More than one in four new HIV infections in this region are among AGYW [1], who are over twice as likely to acquire HIV as their male counterparts. [2] Oral pre-exposure prophylaxis (PrEP) is an effective, female-initiated biomedical HIV prevention intervention, but its protective benefit has been limited among AGYW across sub-Saharan Africa by challenges to uptake, adherence, and persistence. [3-17] In western Kenya, a study of AGYW attending family planning clinics found that, 76% met PrEP eligibility criteria, but only 4% initiated PrEP [16], and the proportion of AGYW persisting with PrEP for 3 months post-initiation ranges from 5%–37% across studies. [7, 10, 11, 15, 17] In samples of PrEP users at an average of 6 months post-initiation, only 4-8% had tenofovir diphosphate (TFVdp) levels suggesting high adherence. [17-19] The public health impact of PrEP will be determined by concurrent interventions that address critical barriers to uptake and adherence.

AGYW who live in a context of heightened gender inequality and risk of intimate partner violence (IPV) represent a large subpopulation who are uniquely vulnerable to HIV infection. IPV is widespread among AGYW in western Kenya: 19% report experience of sexual IPV in the past year, 25% report physical IPV, and 34% report emotional IPV. [20-22] Experience or fear of IPV in sexual relationships is associated with having limited relationship power [22, 23] and with 28%–55% higher HIV incidence in AGYW and adult women. [23-25] Studies have found that IPV and other partner-related social harms are associated with 1.5- to 2.5-fold higher risk of poor adherence to oral PrEP and the dapivirine ring for HIV prevention. Similar to HIV treatment and contraception, [21, 22, 26-31] IPV and relationship inequality introduce barriers to uptake of and adherence to PrEP at multiple levels. At the individual level, restricted access to information and health services, poor negotiation skills, low self-efficacy, and fear of violence or relationship dissolution hinder adoption of health-promoting behaviors. [32-34] Dynamics at the partner

level, such as poor communication and low decision-making power, limit disclosure about PrEP use and reduce partner support, which can impact adherence. [35-37] These challenges are further compounded at the community level by a lack of PrEP awareness, inequitable gender norms, and stigma associated with taking PrEP, which contribute to partner and community opposition to female PrEP use. [38-41] A multilevel context-specific intervention to address barriers to PrEP use is needed to ensure that AGYW experiencing relationship inequality and IPV benefit from this effective biomedical prevention strategy.

In response, our intervention, *Tu'Washindi na PREP* (We are winners with PrEP), was designed in close partnership with local AGYW and incorporates strategies targeted to address relationship dynamics and IPV at multiple levels. [42-44] This intervention has three components: an empowerment-based Support Club for AGYW, PrEP education events for couples offered in the context of a health fair ("Buddy Days"), and community sensitization about PrEP targeted toward AGYW's partners. [42] The pilot cluster randomized controlled trial (cRCT) of *Tu'Washindi* at six DREAMS Safe Spaces demonstrated feasibility, high acceptability, implementation with fidelity, and promising effects on PrEP and IPV outcomes. [45] PrEP uptake and adherence were both approximately twice as high in the intervention arm as in the control arm ($p < 0.05$). [46] Although adherence was still lower than desired in the intervention arm, with Wisepill openings on 25% of days on PrEP, they still represented substantial improvement over programmatic outcomes. [17, 18] We also observed less frequent or severe IPV among intervention arm participants. [46]

Because our pilot findings suggested that *Tu'Washindi* shows promise as an acceptable intervention that can be implemented with fidelity to promote PrEP uptake and adherence among AGYW without concomitant increases in IPV, we designed a fully powered effectiveness trial to determine whether these gains translate to increases in biomarker measures of PrEP adherence and whether the intervention can reduce IPV risk.

Study Objectives

The objectives of the current study are to test the effectiveness of the multilevel *Tu'Washindi* intervention to increase effective PrEP use and reduce IPV among Kenyan AGYW by addressing

relationship dynamics and partner opposition to PrEP. A process evaluation will assess the implementation processes and theorized mechanisms of change influencing intervention effectiveness and identify implementation challenges and strategies to facilitate future scale-up in programmatic settings to maximize public health impact. Study findings will contribute to the limited evidence base for effective PrEP adherence interventions to reduce HIV acquisition in this priority population.

Methods

Design

This study has a two-arm parallel cRCT design (Figure 1). We have randomized 22 administrative wards in a 1:1 ratio and aim to enroll about 72 AGYW from each (total N=about 1,584) to receive either the *Tu'Washindi* intervention plus usual HIV prevention services, or usual HIV prevention services alone. Because of the urgent need for interventions to support PrEP use among AGYW in a real-world context, the intervention is delivered outside of DREAMS to evaluate its impact on AGYW accessing PrEP from Ministry of Health (MoH) facilities. This pragmatic study design enables us to determine effectiveness of the intervention when layered onto ongoing county-wide HIV prevention programming. [47] After informed consent and baseline data collection, the *Tu'Washindi* intervention is implemented in each intervention cluster while the control cluster continues with usual HIV prevention services. Participants are followed for 12 months, with data collection visits at intervention midline (Study Month 3), intervention endline (Study Month 6), and at 6 months post-intervention (Study Month 12). A prospective process evaluation is being conducted to characterize intervention implementation, explore theorized mechanisms of change, and capture contextual factors influencing study outcomes.

Study Setting

Siaya County is located in the former Nyanza Province in western Kenya, along the shores of Lake Victoria. The county is primarily peri-urban and rural, and agriculture and fishing are the main economic activities. [48] Siaya County has the second highest HIV incidence in Kenya (2.5% per year); it is the site of 12% of new HIV infections but comprises just 2% of the national population. [49] The former Nyanza Province also has the highest prevalence of gender-based violence in Kenya: 22% of women aged 15-49 have reported sexual violence and 56% have reported physical violence at least once since age 15. [50]

Study Organization

The Tu'Washindi study leadership is comprised of investigators from RTI International and Impact Research and Development Organization (IRDO) and meets monthly. This group is ultimately responsible for the design and conduct of the trial, including intervention updates, protocol preparations and revisions, and protocol and safety monitoring. The trial management committee meets weekly and is responsible for the day-to-day conduct of the trial. It includes the Principal Investigator (PI) and Site PI, Project Director, and Project Coordinator, Intervention Leads, and quantitative and qualitative data management teams. The University of North Carolina Center for AIDS Research Clinical Pharmacology and Analytical Chemistry Core is responsible for analysis of the dried blood spot (DBS) samples. The study is further supported by a five-member national-level Technical Advisory Committee (TAC) who meet annually and advise on design considerations to ensure a smooth transition from research to implementation if the intervention is effective; a 15-member Youth Advisory Board (YAB) that meets quarterly and provides feedback on study design and methods, data collection tools, and recruitment and retention of study participants; and a 12-member Stakeholder Advisory Board (SAB) made up of PrEP technical staff from MoH and other delivery partners, IPV referral agency representatives, and other community leaders that meets twice yearly to advise on effective integration of the study into existing structures and on linkage to PrEP and other referral services.

Cluster Randomized Controlled Trial Component

Site selection and randomization

The study clusters comprise 22 of the 30 administrative wards in the county. The 30 wards were categorized into five strata based on community type (peri-urban, rural fishing, or rural non-fishing) and whether the proportion of girls on PrEP is above or below the median, using MoH programmatic data. (Although the geography and PrEP use criteria define 6 strata, only 1 ward in the county fell within the urban, low PrEP use stratum. Because it was not possible to create a pair of intervention and control wards in this stratum, it was excluded.) The 22 study wards were purposively selected to ensure an even number of wards within each stratum and a balanced distribution of wards across strata. Randomization was completed by RTI statisticians

once the 22 study wards are selected and placed into strata. Within each stratum, wards were randomly allocated to the intervention or control arms in a 1:1 ratio. After randomization, we created pairs of intervention and control wards within each stratum and determined the order in which they would be enrolled in the study based on the location of each ward, to minimize the risk of contamination while ensuring the feasibility of implementation. Subsequently, one intervention and control site pair were randomly selected from each stratum for inclusion in the qualitative component. Allocation was revealed to investigators before community mapping (see below) and to participants after their enrollment into the study.

Eligibility Criteria

To be eligible, potential participants must be females aged 15-24, currently in a sexual relationship with a male partner for at least 1 month, vulnerable to HIV per a modified version of the DREAMS eligibility screening tool. To reflect the population most likely to participate in this intervention in a programmatic setting, they must be either taking PrEP or interested in PrEP (i.e., thinks she would benefit from PrEP but is not currently taking it). Additionally, they must be residents of the applicable study ward; willing and able to attend support clubs; willing and able to provide adequate contact information; fluent in English, Dholuo, or Kiswahili; and able and willing to provide informed consent (or assent and parental consent for non-mature minors aged 15-17). Potential participants are excluded if they are living with HIV (by self-report); planning any long-term travel or relocation in the next 12 months; or have any condition that the site PI or designee determines would preclude participation.

Individuals who do not meet the criteria for participation in this trial (screen failure) because of criteria that are likely to change over time may be rescreened. Examples include not being resident of the ward or not being interested in PrEP.

Recruitment and Screening

Recruitment occurs simultaneously in each pair of wards before moving on to the next pair and focuses on the catchment areas of two to four health facilities in each ward. Prior to recruitment, community mapping is conducted to identify key stakeholders, referral resources, locations where AGYW gather, and locations where men gather. Recruitment takes place at

venues identified through community mapping, including health facilities, schools, churches, DREAMS Safe Spaces, youth groups, and community markets. To ensure that the study findings are generalizable to AGYW across the 15-24-year age range, we aim to enroll at least 25% of the study sample from the 15-19-year age group who have lower rates of PrEP utilization but similar HIV incidence to the 20-24-year age group [51, 52]. Attendees interested in the study are invited to see the Research Assistant after the recruitment meeting to discuss questions, obtain additional information, and schedule an appointment for informed consent, eligibility screening, and, if eligible, for enrollment.

Retention

Once a participant is enrolled in the study, the study team makes every reasonable effort to retain her, to minimize bias associated with loss to follow-up. To ensure high retention, IRDO tracks retention rates and follows standard study operating procedures detailing strategies such as clear explanation of the visit schedule at all visits, collection of detailed locator information with multiple means to contact participants, appropriate and timely visit reminders, offering weekend hours for study visits, and conducting immediate follow-up on missed visits through phone, home or other off-site visits.

Intervention and Control Conditions

Intervention Design: Tu'Washindi was developed by our team using a participatory process with AGYW and service providers in Siaya County to ensure that it was responsive to AGYW's stated needs for PrEP support in the context of their relationships. [42] The intervention components are informed by social cognitive theory [53] in combination with a socioecological framework for PrEP introduction [54] to address factors at the individual, partnership, and community levels that influence AGYW's response to IPV and their PrEP use (Figure 2).

Social cognitive theory informs Support Club activities to enhance individual-level behavioral capability (e.g., knowledge and skills to use PrEP, IPV safety planning), improve outcomes expectations (e.g., that PrEP use will prevent HIV without threats to safety or relationship security), and increase self-efficacy to use PrEP safely and consistently. At the partnership level, Support Clubs also aim to develop skills for healthy communication and PrEP disclosure. Drama

activities are integrated into each session to allow participants to practice these skills and build self-efficacy. AGYW follow suggested storylines from the intervention manual, developed by youth in the formative phase [42], to create and enact plays about overcoming partner-related barriers to PrEP use, including one to be performed at the Buddy Day. Buddy Days also work at this level to facilitate disclosure and build male partner support for PrEP use by engaging couples in discussions about PrEP, healthy relationships, and promoting HIV prevention as part of family well-being. To increase men's receptiveness to information provided at the Buddy Day or from their female partners, community sensitization events deliver accurate information about PrEP (e.g., safety, effectiveness, and eligibility), discuss common myths and misperceptions, and encourage men to support their partners' PrEP use. [55] At the community level, the community sensitization activities aim to increase PrEP knowledge, reduce PrEP stigma, and reduce the acceptability or normalization of IPV as a response to AGYW's PrEP use. Support Clubs aim to increase social assets, including peer support for PrEP use and access to IPV resources in the community. **Figure 3** illustrates the intervention's alignment with the conceptual framework.

Intervention delivery: Prior to delivery, the intervention manual and training tools were updated to reflect lessons learned during the pilot and the change to implementation outside of DREAMS. Because age restrictions on PrEP in DREAMS did not permit us to pilot the intervention with adolescent girls ages 15–17 years, we also pretested the activities with 12–15 adolescent girls in this age range over a 1-month period to obtain feedback on comprehension and relevance of the content and how best to support participation.

Delivery takes place in four phases, with activities in two wards concurrently in Phase 1 and three wards concurrently in phases 2–4. In each ward, the intervention is conducted over a 6-month period with intervention implementation beginning about one week after enrollment concludes. Each new phase of the intervention commences immediately after activities in the previous phase are concluded. This phased approach minimizes staff burden and allows for close monitoring of implementation to identify and correct problems early on.

The intervention activities include:

- Sensitization of MoH clinics: Prior to study initiation in each intervention ward, we collaborate with the facility in-charges from each of the two to four health facilities selected for study recruitment to identify PrEP delivery staff and schedule a ½ - 1 day training to introduce the study and discuss relationship-related challenges to PrEP use, with the goal of ensuring that the counseling support offered at the clinics complements the messages provided through the intervention. We also review PrEP adherence and couples' counseling and disclosure approaches to more comprehensively address adherence challenges commonly experienced by AGYW.
- Intervention staffing and training: Within each ward, the intervention is delivered by a set of two to four "Mentors" (women slightly older than the participants who have completed at least some secondary education and are rooted in their communities), an experienced male community organizer, and clinicians and counselors with experience in PrEP provision to AGYW. Staff supervisors train each cadre over 1-3 days to review the intervention manual and to practice the required activities.
- Community sensitization sessions are conducted by the community organizer approximately weekly over the first 3 months of the intervention period, lasting about 60 minutes to 90 minutes each. Sessions take place in places where AGYW's male partners are known to gather. [56] Content focuses on PrEP information and dispelling myths and rumors. When time allows, additional content on healthy relationship communication is also included. Clinicians may attend larger sessions to support the organizer.
- Buddy Days take place around Month 3 of the intervention period, with about two to three events per ward to maximize participation. The sessions are co-facilitated by the community organizer and clinician and include provision of information about PrEP; facilitated discussion of reasons to support AGYW's PrEP use, healthy relationship communication, and acceptability of IPV; and an interactive drama, designed and performed by volunteer *Tu'Washindi* participants based on story guides in the intervention manual, to illustrate real-world partner-related challenges to PrEP use. The co-facilitators foster audience engagement both during and after the performance by soliciting reflections on the drama, discussions of alternate storylines, and experiences

from audience members. [57] To encourage and destigmatize participation, Buddy Days are open to all community members and offer health services such as HIV testing services (HTS) and screening for hypertension, and diabetes. All AGYW and their partners who attend the Buddy Day together as a couple also receive a small basket of foodstuffs worth about \$5 USD as an incentive.

- Support Clubs meet for approximately eight 2-hour sessions over the 6-month intervention period, facilitated by the mentor or by participants with mentor support. Three to four clubs are offered at varying times and locations to maximize convenience and maintain a small enough number of attendees (18–24) to build community and trust. The clubs aim to be youth-friendly and nonjudgmental, with an emphasis on ground rules and confidentiality, and support for PrEP uptake and adherence are integrated throughout. Each interactive, participatory session follows the same basic format: a check-in and activity to build community; recap of the previous session; a new topic related to PrEP and relationships, led by the mentor, clinician, or counselor (*Table 1*); drama activities; and a closing activity to reflect on lessons learned and build confidence and support.

Table 1. Sample Support Club Topics and Co-Leaders

Session	Topic	Leader(s)
1	PrEP information	Mentor and Clinician
2	Disclosure	Mentor and Counselor
3	Undisclosed PrEP use	Mentor and Clinician
4	Healthy relationships	Mentor and Counselor
5	IPV and PrEP use	Mentor and Counselor
6	Open session ^a	Mentor
7	Open session ^a	Mentor
8	Future goals, closing ceremony	Mentor

^a Participants' choice of topics.

- Monitoring and quality assurance. Intervention delivery is closely monitored for quality and fidelity. Staff supervisors will observe at least 15% of community sensitization activities, 100% of Buddy Days, and at least 20% of Support Clubs using activity-specific observation forms to document assessments of fidelity (adherence to the intervention manual), quality of facilitation (e.g., facilitator maintains focus, nonjudgmental delivery),

participant engagement, and any factors that may have affected implementation. Intervention staff receive feedback and coaching after each observed session. Findings inform staff retraining and implementation refinement for subsequent phases. For example, provider training may be bolstered if gaps are identified.

Usual care services: Participants in the intervention and control clusters will have access to a range of evidence-based HIV prevention services offered in the county, including Global Fund-supported services such as HTS, syndromic management of sexually transmitted infections (STIs), family planning and post-violence care services; ongoing DREAMS programming; and PrEP. [58] Participants in both arms receive information about available services and are referred to these services upon request. PrEP is available to AGYW ages ≥ 15 at more than 100 MoH facilities throughout the county, [59] and all participants who choose to use PrEP in the study access it through these MoH facilities. In keeping with our study design, this choice of usual services as the comparator condition is realistic, ethical, and relevant [60] because it represents a wide range of evidence-based services to reduce HIV risk. However, PrEP uptake and persistence have been suboptimal in this context, indicating that the intervention is warranted and that the comparator condition is not sufficiently robust to preclude our ability to detect an effect. [61]

Data collection

Data collection visits occur simultaneously in each pair of wards at enrollment, and months 3, 6, and 12 (*Table 2*). At enrollment, interviewer-administered questionnaires assess socio-demographics, relationship characteristics, IPV, behavioral HIV risk factors, and history of PrEP use. Follow-up questionnaires repeat measures to document changes in relevant characteristics, attitudes, and behaviors.

DBS samples are collected via fingerprick at Months 6 and 12 from all participants who report initiation or continuation of PrEP since the last visit. For participants who report discontinuation of PrEP, reasons for discontinuation are recorded, but DBS are not collected. Due to storage and transport challenges, DBS samples are also not collected for participants who have relocated outside the county and have follow-up visits conducted by phone or at a remote location. DBS

samples are stored in freezers at the IRDO laboratory and then shipped to the laboratory at the University of North Carolina Center for AIDS Research Clinical Pharmacology and Analytical Chemistry Core for quantification of drug concentrations by liquid chromatography-tandem mass spectrometry technology. [62]



Table 2: Participant Timeline

	BL M0	M1	M2	3MFU M3	M4	M5	6MFU M6	M7	M8	M9	M10	M11	12MFU M12
Assess and/or confirm eligibility	X	X											
Informed Consent	X												
Enrollment	X												
Locator information and update	X			X			X			X			X
Quantitative Data Collection													
Sociodemographic and behavioral characteristics	X			X			X					X	
PrEP use history	X			X			X						X
IPV	X			X			X						X
Hypothesized mechanisms of action ^a	X			X			X						X
Laboratory Assessment (Dried Blood Spots)							X						X
Tu'Washindi Intervention													
Community Sensitization Session (Weekly)		X	X	X									
Buddy Days				X									
Support Clubs (once or twice per month)		^b XX	^b XX	X	X	X	X						
Qualitative Data Collection													
In-depth interviews (subset of participants)							X						X
Safety Monitoring													
Standardized Assessments				X			X						X
Short in-person or telephone contact visit										X			
Reporting of IPV, injuries, social harms, or other relevant concerns		X	X	X	X	X	X	X	X	X	X	X	X

BL= Baseline appointment; M = Month; MFU= Month follow up appointment; ^a Also part of process evaluation; ^b Two Support Clubs per month;

Process Evaluation Component

The mixed methods process evaluation utilizes implementation data, quantitative AGYW participant questionnaires, exit surveys with men who attend intervention activities, qualitative in-depth interviews (IDIs) with AGYW participants, their male partners, and intervention

providers, and a project diary. Our process evaluation framework (*Figure 4*) highlights the key evaluation components, relationships between them, and key measures and data sources. [63-66]

Participants and Eligibility

Eligibility criteria for AGYW are described above. Participants in exit surveys or male partner IDIs must be males aged 15 years or older. Additionally, exit survey participants must have attended a study Buddy Day or community sensitization event and have been present for at least half of the event, while IDI participants must be a sexual partner of an AGYW clinical trial participant and that AGYW participant must have provided permission for the study staff to contact the male partner. Intervention providers must be aged 18 or older and have been involved in delivering Tu'Washindi intervention activities. Additionally, all participants must be fluent in English, Dholuo, or Kiswahili; and willing and able to provide informed consent, and not have any condition that the site PI or designee determines would preclude participation.

Participant Selection and Recruitment

Exit Surveys: At all intervention sites, all men who attend a Buddy Day event as a couple are approached while waiting for incentive distribution and asked to complete a survey. A research assistant approaches about 20% of men who attend community sensitization events and asks them to complete survey after the event.

IDIs: For each of the five intervention and control ward pairs randomly selected for qualitative research, we use data captured at Month 3 to purposively select a subset of AGYW participants ($n = 30$; 4 per intervention ward and 2 per control ward) who are behaviorally eligible for PrEP, per self-report, and have attended at least one support club meeting (intervention wards only). We aim to ensure representation of PrEP users and non-users and those with and without a history of IPV. Participants who are selected for IDIs are contacted by a Research Assistant prior to their Month 6 visit, informed that they have been selected, and invited to participate in the IDI.

Based on information provided by the AGYW at the month 6 visit, we purposively select male partners ($n=20$; 4 per intervention ward) for IDIs to represent a range of exposure to the Buddy

Days and community sensitization activities.

Male partners are only contacted with the permission of the AGYW participants, who provide contact information. A Research Assistant then contacts the male partner and invites him to participate in the IDI. Study staff do not disclose the PrEP use status of AGYW to any partner whom they recruit for the IDIs.

Intervention providers are purposively selected for IDIs by the Study Coordinator to represent a variety of job functions, including mentors, community organizers, counselors, and clinicians (n=20, 4 per intervention ward).

Data collection

Implementation data includes staff hiring and training records; minutes from YAB, SAB, and TAC meetings; and study activation checklists to track activities, materials, and systems required for successful implementation, such as community introductions, final intervention manuals, and vetted lists of referral agencies. Providers maintain activity logs and attendance records for each meeting or event, and supervisors record minutes from feedback and coaching meetings. Quality and fidelity of intervention activities is documented on observation forms as described above.

Participant questionnaires are administered to AGYW at each visit to assess mechanisms of change (for all participants) and perceived intervention quality (intervention arm) or potential contamination (control arm). The hypothesized mechanisms of change include PrEP self-efficacy and outcome expectations, PrEP knowledge, healthy communication, disclosure of PrEP use to male partner and partner reaction, community knowledge of PrEP, PrEP stigma, and social assets.

Exit surveys are brief, anonymous, quantitative, interviewer-administered questionnaires that gather information on men's views of PrEP, their willingness to support their partner's PrEP use, and feedback on intervention activities.

IDIs are conducted in a private location and facilitated by trained female interviewers following a semi structured guide.

- *Serial IDIs* with AGYW participants are conducted at two timepoints (Months 6 and 12). Key topics include relationship quality and experiences of IPV, patterns of PrEP use and barriers and facilitators to PrEP access and use, experiences with the intervention, and perceptions of how the intervention has affected the hypothesized mechanisms of change and study outcomes.
- *Male partner IDIs* take place at the end of the intervention period and explore men's experiences with the intervention. Interviews also aim to identify mechanisms through which their attitudes towards PrEP were shifted, or reasons why they were not.
- *Intervention provider IDIs* are conducted at the end of intervention delivery to elicit their perceptions of the adequacy of inputs (e.g., training and resources), fidelity and quality of delivery, and challenges and perceived benefits to delivering each intervention component.

A program diary is maintained by the Study Coordinator to record external events (e.g., elections, police activity, festivities, health campaigns) and internal events (e.g., increased funding or supply stockouts) that may affect intervention delivery or study outcomes. Prior to intervention implementation in each ward, the Study Coordinator identifies a set of sources including study staff, health facility personnel, community members or others who are well-positioned to provide this contextual information, and contacts them at regular intervals to record any updates.

Data Management

Most questionnaire data is collected on tablets using REDCap or collected on paper forms and entered into REDCap at the study offices, with hard copies securely stored at the field site. [67, 68] RTI implements a quality assurance plan, including routine generation of quality control reports by the data manager and communication of findings for resolution. IDIs are audio-recorded, with debriefing reports completed immediately after each interview and quickly shared with the study team to highlight preliminary findings. Interviews are translated and transcribed at the study site. Electronic copies of forms are securely transmitted to RTI and reviewed for quality control, with weekly query resolutions.

Sample size considerations

The study is powered to identify an absolute difference of 15% between intervention and control arms for the primary outcomes: the proportion with effective PrEP use at month 6 and month 12. Power calculations were conducted using simulations based on the logistic model with normally distributed ward (cluster) effects and assuming 11 wards per treatment arm with type 1 error of 0.025 to account for separate analyses at each of two time points. With 60 subjects per ward, we will have $\geq 80\%$ power to detect a 15% difference in the outcome as long as the SD for ward variation is $\leq 10\%$ and the level of effective PrEP use in control wards remains $< 50\%$ (far higher than observed in recent trials and demonstration projects). To allow for up to 20% loss to follow-up, our total sample size will be 1,584 participants: 72 AGYW in each of 22 wards (11 wards per arm).

Data Analysis: Clinical Trial

Outcomes and hypotheses

The primary outcomes of the study will be the proportion of study participants with effective PrEP use, defined in *Table 3*, evaluated immediately post-intervention, at Month 6, and at Month 12 to gauge the persistence of intervention effect. TFVdp levels will be dichotomized by CPAC laboratory specialists to delineate between consistent (≥ 4 doses per week) versus inconsistent (< 4 doses per week) adherence. [69] **Aim 1 hypothesis:** The proportion of participants with effective PrEP use at (a) Month 6 and (b) Month 12 will be *higher* in the intervention versus control arm.

The secondary outcomes of the study will be the proportion of participants reporting any IPV and severe IPV (*Table 3*) between enrollment and Month 6, and between Month 6 and Month 12, and the difference in IPV intensity scores at Months 6 and 12. **Aim 2 hypotheses:** The proportion of participants reporting any IPV and severe IPV and IPV severity scores will all be *lower* at both timepoints in the intervention arm versus control arm.

In exploratory analyses, we will first explore effect modification by age (15–19 vs. 20–24) and DREAMS participation (current, former, or never) for the primary and secondary outcomes. Second, we will break down the primary outcome into steps along the continuum (PrEP uptake, execution, and persistence) and IPV outcomes by type—physical, sexual, emotional, and economic—to understand where the intervention had its strongest effects. Third, we will compare the proportion of participants per arm with emtricitabine triphosphate (FTCtp) levels indicating consistent PrEP adherence over the past 2 weeks. Comparing TFVdp and FTCtp levels will yield insights on adherence patterns over both a long and short window of time prior to collection. We will also analyze the alignment of adherence measures with HIV risk perception and behavior to better understand adherence patterns.

Table 3. Overview of Key Measures for cRCT. Collected at enrollment and Months 3, 6, and 12 unless otherwise noted.

Measure	Method
Primary Outcomes	
Effective PrEP use (biomarker assessment)	% of all study participants with biomarker TFVdp levels indicating consistent PrEP use (≥ 4 doses per week) for the past 2 months. [69, 70] Represents a composite outcome of PrEP initiation and high execution to capture these key steps in the HIV prevention continuum. Collected at Months 6 and 12 only.
Secondary Outcomes	
IPV prevalence	% of participants reporting IPV since the last study visit, measured with the WHO Violence Against Women instrument (VAWI) [71] and classified by the STRIVE Consortium definition [72]: any act of severe physical or sexual violence, or ≥ 2 acts of moderate physical violence.
IPV severity	% of participants reporting any sexual or severe physical IPV since the last study visit, measured with WHO VAWI. [71]
IPV intensity	Continuous score calculated from the number of specific violent acts reported and the reported frequency of each act (0=never; 1=once; 2=a few times; 3=often) since the last study visit, measured with WHO VAWI. [71]
Exploratory Outcomes (sub-components or alternate measures of primary and secondary outcomes)	
PrEP uptake	% of participants initiating PrEP <i>among those not on PrEP at baseline</i> , self-reported and validated by MoH records.
PrEP execution	% of participants with TFVdp levels indicating consistent use <i>among those reporting current PrEP use</i> .
PrEP persistence	% of participants with any detectable TFVdp <i>among those who ever initiated PrEP</i> . Participants who self-report discontinuation will be categorized as having undetectable TFVdp levels.
Recent PrEP use (biomarker)	% of all study participants with biomarker FTCtp levels indicating consistent PrEP use (≥ 4 doses per week) for the past 2 weeks. Collected at Months 6 and 12 only.
IPV type	% of participants reporting each IPV type (physical, sexual, emotional, economic) since the last visit, per WHO VAWI. [71]

Analysis approach

Descriptive and bivariate statistics will be used to compare participant characteristics in the intervention and control arms and those who completed the study versus those lost to follow-up. Outcomes will be modeled using an intent-to-treat approach with mixed effect logistic and linear regression models. Model predictors will include treatment assignment, randomization strata, and a random effect for ward (cluster) within stratum that is assumed to be independent and normally distributed with mean zero. If the cluster randomization does not adequately balance baseline characteristics across arms, we will conduct exploratory analyses controlling for those characteristics. We will analyze the data from each of two time points separately and the primary outcomes analyses will use a type I error rate of 0.025 at each time point.

Missing Data

In any situation with missing data, we will do appropriate secondary analyses that adjust for variables that may be related to the missingness mechanism. If missing data rates are higher than anticipated (over 10%), we will include covariates that are related to missingness in regression models. We will also perform sensitivity analyses to assess the potential impact of the missing data.

Data analysis: Process Evaluation

Quantitative data

Implementation inputs, process, and outputs will be analyzed descriptively, and we will draw comparisons across intervention wards. Intervention effects on each mechanism of change will be modeled individually following the approach described for the cRCT. We will regress each mechanism on the exposure (intervention arm assignment), controlling for baseline levels of the mechanism. If the primary analyses show no effect of the intervention on PrEP or IPV outcomes, the results will inform our interpretation of whether the intervention failed to affect the intended mechanism or whether the change in mechanism did not lead to the hypothesized outcome. If the primary analyses suggest a positive intervention effect on PrEP or IPV outcomes, we will conduct causal mediation analysis. [73, 74] Coverage, uptake, and exit survey data on

perceived impact will also be evaluated as moderators of intervention effectiveness at the site level in exploratory analyses of mechanisms of change.

Qualitative data

The coding process will involve a core group of about 2-5 analysts from IRDO and RTI who will develop one or more codebook(s) and establish qualitative coding procedures. Data will be coded using a qualitative software package such as DedooseTM. A set of preliminary codes will be developed based on key themes or topics identified *a priori* and the findings highlighted in the debriefing reports for each of the three datasets (e.g., AGYW, male partners, and providers). Each group member will apply the initial set of thematic codes to a common transcript, discuss their coding experiences, and agree on expanding and modifying code names and definitions when necessary. We will continue with an iterative process of revising the codebook(s) as we continue to read and code the data. Once finalized, the codebook(s) will be used for a final recoding of all transcripts.

A pre-selected number of transcripts will be double-coded by two coders to establish intra-coder and inter-coder reliability. Following this process, the coding team will discuss discrepancies, which will ultimately be resolved through consensus. This process will continue until the inter-coder reliability is at least 80%. Thereafter the remaining texts will primarily be coded by one analyst only, with one or more rounds of consistency checks and regular discussions among the coding team to ensure that coding remains standardized and reliable.

Comprehensive listings of all coded quotations for every code or code “family” will be generated in the qualitative analysis software. Coding memos will be used to summarize and explore the relationship between the constructs of the evaluation framework (e.g., the relationship between implementation processes and hypothesized mechanisms of change, or between mechanisms of change and outcomes). Analysts will also review and analyze coded serial IDI content within each participant’s dataset to look specifically for patterns over time. The findings and interpretations of the data will be critically discussed until there is group consensus on the dominant themes and meanings contained in the data. [75]

Integrated synthesis of quantitative and qualitative data

For each construct of the evaluation framework, findings from the qualitative and quantitative analyses will be integrated to build a more comprehensive picture of whether the target intervention inputs, processes, and outputs were achieved, whether these resulted in the

hypothesized changes in mechanisms of action, whether these changes resulted in the intended outcomes, and how external contextual factors influenced implementation, thereby both evaluating the success of study implementation and testing the theory of change.

Study Monitoring

Protocol Oversight

The study team continuously reviews recruitment and follow-up data to ensure compliance with the protocol and ethical standards. The IRDO Study Coordinator regularly monitors protocol compliance at study sites. The IRDO Internal Research Monitor conducts quarterly spot checks of 100% of informed consent forms and 10% of data files. Any issues are documented in quality control logs and reviewed with the study staff. Protocol deviations or violations are reported to the study leadership and IRB within 5 business days.

Data and Safety Monitoring Board (DSMB)

The trial is monitored by a DSMB composed of four members: a statistician, a medical doctor, a researcher with content expertise in IPV, and a researcher with expertise in PrEP use among AGYW. All DSMB members are independent from any professional or financial conflict of interest with the research project, study investigators, and study institutions. The DSMB established a charter that outlines their responsibilities and meets approximately semiannually to review data quality and integrity, protocol adherence, participant safety, study conduct, and progress. Based on their review, they make recommendations on study continuation and modifications.

Safety Monitoring

This study adheres to the World Health Organization (WHO) Ethical and Safety Recommendations for Intervention Research on Violence Against Women. [76] All data collection staff receive training on IPV assessment, recognizing warning signs of immediate danger, discussing sensitive topics with participants, managing distressed participants, legal reporting requirements, and referral protocols. We aim to ensure that all communication with participants protects against unintentional disclosure of PrEP use, study participation, or reported IPV and does not place participants at additional risk of harm. To increase

confidentiality, the study is presented to the community and to participants as a study on HIV prevention methods in young women, and the focus on IPV is not advertised.

The MoH clinics conduct clinical safety monitoring for PrEP according to Kenyan guidelines. The present study focuses on monitoring for adverse events that could be associated with the intervention, including IPV, social harms, serious adverse events (SAEs), and unanticipated problems. All instances of these events are recorded on case report forms and followed up until resolution or 30 days after the participant exits from the study. These adverse events are reviewed monthly by the protocol team and reported to the institutional review board (IRB) and DSMB according to their established protocols.

All staff have been trained to respond to any reports of IPV and social harms using the WHO's LIVES approach: Listening, Inquiring, Validating, Ensuring safety, and Supporting through referrals. [77] Staff follow up by phone or during subsequent visits to check on referral uptake and provide additional assistance if needed. Participants who report being in immediate danger or feeling unsafe returning home are offered an immediate escorted referral to vetted rescue/shelter services, and study staff follow up with the participant weekly until their situation is resolved or stabilized, or until 30 days after their exit from the study. If staff have concerns about the safety of a participant's enrollment, they alert the site PI or designee to make a final determination about eligibility.

Ethical Considerations

The trial is being carried out in accordance with International Council on Harmonization Good Clinical Practice and the United States Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46).

Ethics Approval

The study protocol and associated documents have been reviewed and approved by the Maseno University Ethical Review Committee (MUERC; ref MSU/DRPI/MUERC/00991/21). The RTI International Committee for Human Subjects Research established a reliance on MUERC for the study under a signed IRB authorization agreement. No amendment to the protocol or informed consent forms is implemented without prior ethics committee approval. Protocol

violations are reported in writing to MUERC in accordance with their policy.

Informed Consent Process

IRDO study staff obtain informed consent/assent from all participants taking part in the cRCT or IDIs. Study staff explain the study purpose and procedures, risks and benefits to eligible participants, and compensation for participation. They emphasize that participation is voluntary, that there is no penalty if the individual decides not to participate. Participants aged 18 and above provide written consent in English, Kiswahili, or Dholuo. The IRB has granted a waiver of parental consent for AGYW who meet the criteria for "mature minors" outlined in MoH guidelines for Conducting Adolescent HIV Sexual and Reproductive Health Research in Kenya [78], and for male partners aged 15-17 to take part in IDIs, because they constitute a minimal risk research activity. All minors may choose to involve their parent in the consent process. For minors not meeting the above criteria, or who involve their parents, we obtain parental consent and child assent. The IRB has also granted a waiver of written consent for the brief and anonymous exit interviews focused on program acceptability.

Confidentiality

All study procedures occur in private settings. Each participant receives a unique study identification number, and personally identifiable information does not appear on study data. All electronic data and study records are stored on secure, password-protected devices and uploaded to a secure RTI project server. Access to the system is restricted to trained study staff. Hardcopy data, consent and contact information forms with personally identifiable information are kept in separate double-locked files at the site and not transmitted to RTI.

To minimize confidentiality risks during follow-up visits, we use contact methods agreed to by participants, including aliases for study staff. To protect confidentiality during group activities, participants are asked to follow ground rules and pledge not to disclose others' personal details outside the group. At each session's start and end, participants are reminded to respect confidentiality and that there is a risk that others may disclose what they say.

Participants' study information will not be released without their written permission, except as required by law or as necessary for review, monitoring, and/or auditing by

- Representatives of the US Federal Government, including the US Office of Human Research Protections, the National Institutes of Health (NIH) and/or contractors of the NIH, and other local, US, and international regulatory entities
- Representatives of RTI
- Study staff
- Site IRBs

Criteria for early termination of study participation

Participants can withdraw from the study at any time for any reason. The PI, site PI, or designee may also withdraw participants for safety or non-compliance reasons, with the DSMB notified of such terminations. Efforts are made to complete a final evaluation for participants who withdraw. Staff document withdrawal reasons in study records. Participants who withdraw may rejoin and resume intervention or follow-up visits up to their original exit date, with PI and DSMB consultation.

Study Discontinuation

The study may be suspended or terminated at any time by the NIH, RTI, site IRBs, or other authorities due to funding issues or significant concerns, such as DSMB recommendations. If this occurs, the PI will be notified in writing with the reasons, and will inform participants, the IRB, and the sponsor. The study may resume if safety, protocol compliance, and data quality issues are resolved and approved by the relevant parties.

Dissemination and Use of Findings

Study findings will be disseminated to the study communities, the scientific community, and HIV service and advocacy organizations via peer review publications, professional meetings, research briefs, and stakeholder meetings. All media, presentations and publications resulting from data collected during this study will be collaborative in nature but require approval from the study leadership. All publications will be submitted to PubMed Central, in accordance with NIH Public Access Policy.

Results

The study was funded in August 2021, and data collection started in September 2022. As of December 2024, enrollment has been completed in 16 of 22 study wards, with 1150 of 1584 participants enrolled (73%). We anticipate that data collection will be completed in May 2026 and results will be available by mid-2027.

Discussion

This study offers four key innovations. First, it offers the opportunity to address the lack of evidence-based interventions that explicitly confront the role of IPV and relationship dynamics in supporting PrEP use among AGYW. Current interventions have focused largely on instrumental adherence support (e.g., pill-taking reminders and strategies), motivational interviewing, and peer support, with limited evidence of success. [5, 19, 79-84] If found effective, the *Tu'Washindi* intervention will be one of the first to successfully address critical partner-related barriers to uptake and adherence and to directly involve male partners to build support for AGYW PrEP use. Second, our intervention approach is youth-designed and tailored to meet the specific needs of AGYW, qualities that have been specifically called for in recent literature to address shortcomings in existing interventions. [85, 86] The intervention components of male engagement and couples' education were added to the design in direct response to the formative research findings, and our participatory design methods resulted in high intervention acceptability and uptake among AGYW and high ratings for relevance and perceived effectiveness. Third, our multilevel approach recognizes that IPV and relationship power create barriers to HIV prevention at the individual, partnership, and community levels. *Tu'Washindi* supports AGYW to respond to experienced or anticipated IPV at each level by fostering self-efficacy, improving relationship communication, developing support systems, and encouraging action to maintain safety and HIV prevention adherence. [87-89] Fourth, we assess short- and long-term adherence with biomarker measurements of two active PrEP metabolites, TFVdp and FTCtp to gain a more thorough understanding of AGYW adherence behavior. Although the field has focused on TFVdp levels to classify long-term (i.e. previous 1-3 months) PrEP adherence, [90] FTCtp concentrations can delineate between consistent (≥ 4 doses/week) versus inconsistent (< 4 doses/week) PrEP adherence over 2 weeks prior to sample collection with $\geq 89\%$ accuracy. [91] Thus we will have the ability to classify AGYW on the basis of short-term (2-week) adherence in addition to the long-term (2-month) adherence measured by TFVdp levels.

Our intervention and evaluation have been designed from the start to facilitate scalability,

sustainability, and rapid adoption. *Tu'Washindi* was designed to be delivered by trained community members with support from clinicians and counselors, and to integrate into ongoing national or donor-funded youth-focused programs prioritizing HIV prevention. The proposed study employs a pragmatic, rather than exploratory, design to maximize generalizability and ensure results are applicable to real-world settings. [47, 92] In addition, our design includes a rigorous process evaluation to document implementation process, quality and fidelity of delivery, resource requirements, and contextual factors to provide valuable guidance to program and policy stakeholders who wish to replicate or adapt the intervention outside of the research setting. In combination, the intervention design and process evaluation approach will reduce the "know-do gap" [93] and accelerate *Tu'Washindi*'s translation from research to practice.

Several limitations to this study should be noted. First, there is a risk of PrEP and HIV test kit stockouts in MoH clinics, which could interfere with adherence and complicate interpretation of results. We will carefully document stockouts as part of the program diary, and study staff will help link participants to other sources of PrEP provision if necessary. Second, cluster randomized studies carry a risk that individual participant characteristics may differ at baseline in important ways. Our design stratifies on two important community characteristics (i.e., geographic type and baseline PrEP use) to reduce this risk, and our analysis plan incorporates exploratory analyses to control for baseline differences between randomization arms.

Tu'Washindi has demonstrated feasibility and acceptability in pilot research and shows promise to promote PrEP use and reduce IPV among AGYW. The proposed study builds directly on our intervention development work to conduct a rigorous effectiveness trial, a critical step in developing the evidence base for this youth-designed, multilevel HIV prevention intervention. Our rigorous process evaluation will clarify mechanisms of change, and implementation considerations to inform policy and practice. If effective, *Tu'Washindi* will be ideally positioned for sustainable integration into existing youth-focused HIV prevention programming to expand and support PrEP uptake and adherence in this priority population.

Declarations

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Authors' contributions: **Sarah Roberts:** Conceptualization, methodology, writing-original draft, supervision, project administration, funding acquisition; **Alexandra Minnis:** conceptualization, methodology, writing – original draft, supervision; **Erica Browne:** methodology, software, formal analysis, data curation, writing – original draft; **Sue Napierala:** conceptualization, methodology, investigation, supervision, writing – original draft;; **Elizabeth Montgomery:** conceptualization, methodology, supervision, writing – original draft; **Lina Digolo:** methodology, writing- review and editing; **Mackenzie Cottrell:** methodology, resources, investigation; writing – review and editing; **Jacqueline Ndirangu:** methodology; supervision; project administration; writing – review and editing; **Joyce Boke:** investigation, supervision, writing- reviewing and editing; **Kawango Agot:** conceptualization, methodology, supervision, resources, writing – original draft; project administration.

Availability of data and material: The research tools, protocols, standard operating procedures, analytic code, codebooks, and de-identified data generated in this study will be made available to other investigators upon request. Before access is to de-identified participant data is granted, a Data Sharing Agreement will be implemented to ensure that the data will be used for the proposed purpose and that no attempts will be made to identify participants.

Competing interests: The authors declare that they have no competing interests

Abbreviations:

AGYW	Adolescent girls and young women
CFR	Code of Federal Regulations

cRCT	Cluster randomized controlled trial
DBS	Dried blood spots
DREAMS	Determined, Resilient, Empowered, AIDS-free, Mentored and Safe
DSMB	Data and Safety Monitoring Board
FTCtp	Emtricitabine triphosphate
HIV	Human immunodeficiency virus
IDI	In-depth interview
IPV	Intimate partner violence
IRB	Institutional review board
IRDO	Impact Research and Development Organization
MoH	Ministry of Health
MUERC	Maseno University Ethical Review Committee
NIH	National Institutes of Health
PI	Principal investigator
PrEP	Pre-exposure prophylaxis
SAB	Stakeholder Advisory Board
SAE	Serious adverse event

TAC	Technical Advisory Committee
TFVdp	Tenofovir diphosphate
WHO	World Health Organization
YAB	Youth Advisory Board

Multimedia Appendix 1: SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents

References

1. UNAIDS. Communities at the centre: defending rights, breaking barriers, reaching people with HIV services. Geneva: UNAIDS, 2019.
2. UNAIDS. We've got the power: women, adolescent girls, and the HIV response. Geneva: UNAIDS, 2020.
3. Blaschke TF, Osterberg L, Vrijens B, Urquhart J. Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. *Annu Rev Pharmacol Toxicol*. 2012;52:275-301. PMID: 21942628. doi: 10.1146/annurev-pharmtox-011711-113247.
4. Celum C, Gill K, Morton J, Stein G, Myers L, Thomas K, et al. Incentives conditioned on tenofovir levels to increase adherence among young women on PrEP in Cape Town. 10th IAS Conference on HIV Science; July 21-24; Mexico City, Mexico 2019.
5. Celum C, Mgodini N, Bekker LG, Hosek S, Donnell D, Anderson P, et al. PrEP use in young African women in HPTN 082: effect of drug level feedback. 10th IAS Conference on HIV Science; July 21-24, 2019; Mexico City, Mexico 2019.
6. Cover J, Obong'o C, Obanda R, Kariithi E, Madiang O, Brady M, et al. Individual and contextual factors associated with PrEP adherence among Kenyan adolescent girls and young women 23rd International AIDS Conference (AIDS 2020); 6-10 July; Virtual Conference 2020.
7. de Dieu Tapsoba J, Zangeneh SZ, Appelmans E, Pasalar S, Mori K, Peng L, et al. Persistence of oral pre-exposure prophylaxis (PrEP) among adolescent girls and young women initiating PrEP for HIV prevention in Kenya. *AIDS Care*. 2020 Sep 21:1-9. PMID: 32951437. doi: 10.1080/09540121.2020.1822505.
8. Gill K, Johnson L, Dietrich J, Myer L, Marcus R, Wallace M, et al. Acceptability, safety, and patterns of use of oral tenofovir disoproxil fumarate and emtricitabine for HIV pre-exposure prophylaxis in South African adolescents: an open-label single-arm phase 2 trial. *Lancet Child Adolesc Health*. 2020 Dec;4(12):875-83. PMID: 33222803. doi: 10.1016/S2352-4642(20)30248-0.
9. Haberer JE, Bangsberg DR, Baeten JM, Curran K, Koechlin F, Amico KR, et al. Defining success with HIV pre-exposure prophylaxis: a prevention-effective adherence paradigm. *AIDS*. 2015 Jul 17;29(11):1277-85. PMID: 26103095. doi: 10.1097/QAD.0000000000000647.
10. Kinuthia J, Pintye J, Abuna F, Mugwanya KK, Lagat H, Onyango D, et al. Pre-exposure prophylaxis uptake and early continuation among pregnant and post-partum women within maternal and child health clinics in Kenya: results from an implementation programme. *Lancet HIV*. 2020 Jan;7(1):e38-e48. PMID: 31813837. doi: 10.1016/S2352-3018(19)30335-2.
11. Kyongo JK, Kiragu M, Karuga R, Ochieng C, Ngunjiri A, Wachihi C, et al. How long will they take it? Oral pre-exposure prophylaxis (PrEP) retention for female sex workers, men who have sex with men and young women in a demonstration project in Kenya. *J Int AIDS Soc*. 2018 Jul;21(Suppl 6):e25148. doi: <https://doi.org/10.1002/jia2.25148>.
12. Masyuko S, Mukui I, Njathi O, Kimani M, Oluoch P, Wamicwe J, et al. Pre-exposure prophylaxis rollout in a national public sector program: the Kenyan case study. *Sex Health*. 2018 Nov;15(6):578-86. PMID: 30408432. doi: 10.1071/sh18090.
13. Mukui I. Understanding PrEP effectiveness in different populations in the context of public health programs. HIV Research for Prevention (R4P); 21-25 October, 2018; Madrid, Spain. p. Presentation SY04.3.
14. Oluoch LM, Roxby A, Mugo N, Wald A, Ngure K, Selke S, et al. Does providing laboratory confirmed STI results impact uptake of HIV pre-exposure prophylaxis (PrEP) uptake among Kenyan adolescents girls and young women? A descriptive analysis. *Sex Transm Infect*. 2020 Sep 11. PMID: 32917766. doi: 10.1136/sextrans-2020-054637.
15. Rousseau-Jemwa E, Bekker L-G, Bukusi E, Delaney-Moretlwe S, Omollo V, Travill D, et al. Early

persistence of HIV pre-exposure prophylaxis (PrEP) in African adolescent girls and young women (AGYW) from Kenya and South Africa. HIV Research for Prevention Conference; 21-25 October, 2018; Madrid, Spain.

16. Sila J, Larsen AM, Kinuthia J, Owiti G, Abuna F, Kohler PK, et al. High awareness, yet low uptake, of pre-exposure prophylaxis among adolescent girls and young women within family planning clinics in Kenya. *AIDS Patient Care STDS*. 2020 Aug;34(8):336-43. PMID: 32757980. doi: 10.1089/apc.2020.0037.
17. Were D, Musau A, Mutegi J, Ongwen P, Manguro G, Kamau M, et al. Using a HIV prevention cascade for identifying missed opportunities in PrEP delivery in Kenya: results from a programmatic surveillance study. *J Int AIDS Soc*. 2020 Jun;23 Suppl 3:e25537. PMID: 32602658. doi: 10.1002/jia2.25537.
18. Tapsoba JD, Cover J, Obong'o C, Brady M, Cressey TR, Mori K, et al. Continued attendance in a PrEP program despite low adherence and non-protective drug levels among adolescent girls and young women in Kenya: Results from a prospective cohort study. *PLoS Med*. 2022 Sep;19(9):e1004097. PMID: 36095005. doi: 10.1371/journal.pmed.1004097.
19. Celum CL, Gill K, Morton JF, Stein G, Myers L, Thomas KK, et al. Incentives conditioned on tenofovir levels to support PrEP adherence among young South African women: a randomized trial. *J Int AIDS Soc*. 2020 Nov;23(11):e25636. PMID: 33247553. doi: 10.1002/jia2.25636.
20. Kenya National Bureau of Statistics, Ministry of Health, National AIDS Control Council, Kenya Medical Research Institute (KEMRI), National Council for Population and Development, I. C. F. International. Kenya Demographic and Health Survey 2014. Nairobi, Kenya: Kenya National Bureau of Statistics, 2015 1111111111.
21. Mathur S, Okal J, Musheke M, Pilgrim N, Patel SK, Bhattacharya R, et al. High rates of sexual violence by both intimate and non-intimate partners experienced by adolescent girls and young women in Kenya and Zambia: Findings around violence and other negative health outcomes. *PLoS One*. 2018;13:1-13. PMID: 30212561. doi: 10.1371/journal.pone.0203929.
22. Pulerwitz J, Mathur S, Woznica D. How empowered are girls/young women in their sexual relationships? Relationship power, HIV risk, and partner violence in Kenya. *PLoS One*. 2018;13(7):e0199733. doi: 10.1371/journal.pone.0199733.
23. Jewkes RK, Dunkle K, Nduna M, Shai N. Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. *Lancet*. 2010 Jul 03;376(9734):41-8. PMID: 20557928. doi: 10.1016/S0140-6736(10)60548-X.
24. Kouyoumdjian FG, Calzavara LM, Bondy SJ, O'Campo P, Serwadda D, Nalugoda F, et al. Intimate partner violence is associated with incident HIV infection in women in Uganda. *AIDS*. 2013 May 15;27(8):1331-8. PMID: 23925380. doi: 10.1097/QAD.0b013e32835fd851.
25. Li Y, Marshall CM, Rees HC, Nunez A, Ezeanolue EE, Ehiri JE. Intimate partner violence and HIV infection among women: a systematic review and meta-analysis. *J Int AIDS Soc*. 2014;17:18845. PMID: 24560342. doi: 10.7448/IAS.17.1.18845.
26. Allsworth JE, Secura GM, Zhao Q, Madden T, Peipert JF. The impact of emotional, physical, and sexual abuse on contraceptive method selection and discontinuation. *Am J Public Health*. 2013 Oct;103(10):1857-64. PMID: 23948012. doi: 10.2105/AJPH.2013.301371.
27. Bergmann JN, Stockman JK. How does intimate partner violence affect condom and oral contraceptive use in the United States? A systematic review of the literature. *Contraception*. 2015;91(6):438-55. doi: 10.1016/j.contraception.2015.02.009.
28. Hampanda KM. Intimate partner violence and HIV-positive women's non-adherence to antiretroviral medication for the purpose of prevention of mother-to-child transmission in Lusaka, Zambia. *Soc Sci Med*. 2016 Mar;153:123-30. PMID: 26896876. doi: 10.1016/j.socscimed.2016.02.011.
29. Maxwell L, Devries K, Zions D, Alhusen JL, Campbell J. Estimating the effect of intimate partner violence on women's use of contraception: a systematic review and meta-analysis. *PLoS One*. 2015;10(2):e0118234-e. PMID: 25693056. doi: 10.1371/journal.pone.0118234.

30. Sprague C, Hatcher AM, Woollett N, Black V. How nurses in Johannesburg address intimate partner violence in female patients: understanding IPV responses in low- and middle-income country health systems. *J Interpers Violence*. 2015 Jun 19;32(11):1591-619. PMID: 26092654. doi: 10.1177/0886260515589929.
31. Stephenson R, Bartel D, Rubardt M. Constructs of power and equity and their association with contraceptive use among men and women in rural Ethiopia and Kenya. *Glob Public Health*. 2012;7(6):618-34. PMID: 22568536. doi: 10.1080/17441692.2012.672581.
32. Brown JL, Young AM, Sales JM, DiClemente RJ, Rose ES, Wingood GM. Impact of abuse history on adolescent African-American women's current HIV/STD-associated behaviors and psychosocial mediators of HIV/STD risk. *J Aggress Maltreat Trauma*. 2014 Feb;23(2):151-67. PMID: 25505369. doi: 10.1080/10926771.2014.873511.
33. Hatcher AM, Stöckl H, Christofides N, Woollett N, Pallitto CC, Garcia-Moreno C, Turan JM. Mechanisms linking intimate partner violence and prevention of mother-to-child transmission of HIV: A qualitative study in South Africa. *Soc Sci Med*. 2016 11//;168:130-9. PMID: 27643847. doi: <http://dx.doi.org/10.1016/j.socscimed.2016.09.013>.
34. Salazar LF, Crosby RA, DiClemente RJ, Wingood GM, Lescano CM, Brown LK, et al. Self-esteem and theoretical mediators of safer sex among African American female adolescents: implications for sexual risk reduction interventions. *Health Educ Behav*. 2005 Jun;32(3):413-27. PMID: 15851547. doi: 10.1177/1090198104272335.
35. Lanham M, Wilcher R, Montgomery ET, Pool R, Schuler S, Lenzi R, Friedland B. Engaging male partners in women's microbicide use: evidence from clinical trials and implications for future research and microbicide introduction. *J Int AIDS Soc*. 2014;17(3 Suppl 2):19159. PMID: 25224618. doi: 10.7448/IAS.17.3.19159.
36. Montgomery ET, van der Straten A, Stadler J, Hartmann M, Magazi B, Mathebula F, et al. Male partner influence on women's HIV prevention trial participation and use of pre-exposure prophylaxis: the Importance of "understanding". *AIDS Behav*. 2015 May;19(5):784-93. PMID: 25416076. doi: 10.1007/s10461-014-0950-5.
37. Stadler J, Delany-Moretlwe S, Palanee T, Rees H. Hidden harms: women's narratives of intimate partner violence in a microbicide trial, South Africa. *Soc Sci Med*. 2014 Jun;110:49-55. PMID: 24721447. doi: 10.1016/j.socscimed.2014.03.021.
38. Hartmann M, Otticha S, Agot K, Wanga B, Oginga F, Minnis A, et al. Unpacking the role of gender-based violence as a barrier to pre-exposure prophylaxis use among adolescent girls and young women in the DREAMS program in Kenya through qualitative storytelling. *International Workshop on HIV & Adolescence; Nairobi, Kenya2019*. p. Abstract 35.
39. van der Straten A, Stadler J, Luecke E, Laborde N, Hartmann M, Montgomery ET, Team V-CS. Perspectives on use of oral and vaginal antiretrovirals for HIV prevention: the VOICE-C qualitative study in Johannesburg, South Africa. *J Int AIDS Soc*. 2014;17(3 Suppl 2):19146. PMID: 25224610. doi: 10.7448/IAS.17.3.19146.
40. van der Straten A, Stadler J, Montgomery E, Hartmann M, Magazi B, Mathebula F, et al. Women's experiences with oral and vaginal pre-exposure prophylaxis: the VOICE-C qualitative study in Johannesburg, South Africa. *PLoS One*. 2014;9(2):e89118. PMID: 24586534. doi: 10.1371/journal.pone.0089118.
41. Velloza J, Khoza N, Scorgie F, Chitukuta M, Mutero P, Mutiti K, et al. The influence of HIV-related stigma on PrEP disclosure and adherence among adolescent girls and young women in HPTN 082: a qualitative study. *J Int AIDS Soc*. 2020 Mar;23(3):e25463. PMID: 32144874. doi: 10.1002/jia2.25463.
42. Hartmann M, Otticha S, Agot K, Minnis AM, Montgomery ET, Roberts ST. Tu'Washindi na PrEP: working with young women and service providers to design an intervention for PrEP uptake and adherence in the context of gender-based violence. *AIDS Educ Prev*. 2021;33(1):(In press).
43. Otticha S, Hartmann M, Agot K, Minnis A, Roberts ST. Working with young people to design and implement an intervention for PrEP uptake and persistence. *23rd International AIDS Conference (AIDS 2020);*

6-10 July; Virtual Conference2020. p. Abstract PED1220.

44. Roberts ST. Tu'Washindi na PrEP: understanding how relationship dynamics and intimate partner violence influence PrEP use among young women in Kenya. HIV Research for Prevention (R4P); Madrid, Spain2018. p. Satellite symposium presentation.
45. Minnis AM, Agot K, Hartmann M, Otticha S, Montgomery ET, Roberts ST. Feasibility and Acceptability of the Novel Tu'Washindi Intervention to Increase PrEP Use among Adolescent Girls and Young Women in Siaya County, Kenya. *AIDS Behav.* 2024 Jun 5. PMID: 38836985. doi: 10.1007/s10461-024-04390-3.
46. Roberts ST, Hartmann M, Minnis AM, Otticha SO, Browne EN, Montgomery ET, Agot K. Breaking down relationship barriers to increase PrEP uptake and adherence among adolescent girls and young women in Kenya: safety and preliminary effectiveness results from a pilot cluster-randomized trial. *J Int AIDS Soc.* 2023 Dec;26(12):e26198. PMID: 38123866. doi: 10.1002/jia2.26198.
47. Treweek S, Zwarenstein M. Making trials matter: pragmatic and explanatory trials and the problem of applicability. *Trials.* 2009 2009/06/03;10(1):37. doi: 10.1186/1745-6215-10-37.
48. Republic of Kenya. County Government of Siaya. 2015 [updated 2019; cited 2020 01 May]; Available from: <http://www.siaya.go.ke/>.
49. Kenya Ministry of Health. Kenya HIV prevention revolution road map. Nairobi: 2014.
50. DHS. Kenya Demographic and Health Survey. Nairobi, Kenya: Kenya Bureau of National Statistics, 2015.
51. Ohiomoba RO, Owuor PM, Orero W, Were I, Sawo F, Ezema A, et al. Pre-Exposure Prophylaxis (PrEP) Initiation and Retention Among Young Kenyan Women. *AIDS Behav.* 2022 Jul;26(7):2376-86. PMID: 35061115. doi: 10.1007/s10461-022-03576-x.
52. Council KNSDC. Translating Progress into Success: A Decade of Progress Report, 2013-2023. Nairobi: Kenya National Syndemic Diseases Control Council, 2024.
53. Bandura A. Social cognitive theory and exercise of control over HIV infection. In: DiClemente RJ, Peterson J, editors. New York, NY: Plenum Publishing Corp; 1994. p. 25-59.
54. Mathur S, Pilgrim N, Pulerwitz J. PrEP introduction for adolescent girls and young women. *Lancet HIV.* 2016 Sep;3(9):e406-8. PMID: 27562739. doi: 10.1016/S2352-3018(16)30115-1.
55. Agot K, Hartmann M, Otticha S, Minnis A, Onyango J, Ochillo M, Roberts ST. "I didn't support PrEP because I didn't know what it was": Inadequate information undermines male partner support for young women's pre-exposure prophylaxis use in western Kenya. *Afr J AIDS Res.* 2022 Oct;21(3):221-30. PMID: 36102052. doi: 10.2989/16085906.2022.2049831.
56. Doyle AM, Floyd S, Baisley K, Orindi B, Kwaro D, Mthiyane TN, et al. Who are the male sexual partners of adolescent girls and young women? Comparative analysis of population data in three settings prior to DREAMS roll-out. *PLoS One.* 2018;13(9):e0198783. doi: 10.1371/journal.pone.0198783.
57. Health Communication Partnership Zambia. Theatre facilitation manual. 2008.
58. Saul J, Bachman G, Allen S, Toiv NF, Cooney C, Beamon TA. The DREAMS core package of interventions: a comprehensive approach to preventing HIV among adolescent girls and young women. *PLoS One.* 2018;13(12):e0208167-e. PMID: 30532210. doi: 10.1371/journal.pone.0208167.
59. Ministry of Health, National AIDS & STI Control Program. Guidelines on use of antiretroviral drugs for treating and preventing HIV infection in Kenya 2018 edition. Nairobi, Kenya: NASCOP; 2018.
60. Freedland KE, King AC, Ambrosius WT, Mayo-Wilson E, Mohr DC, Czajkowski SM, et al. The selection of comparators for randomized controlled trials of health-related behavioral interventions: recommendations of an NIH expert panel. *J Clin Epidemiol.* 2019 2019/06/01;110:74-81. doi: <https://doi.org/10.1016/j.jclinepi.2019.02.011>.
61. The United States President's Emergency Plan for AIDS Relief (PEPFAR). 2019 annual report to Congress. Washington, DC: U.S. Department of State Office of the U.S. Global AIDS Coordinator and Health Diplomacy; 2019.

62. Schauer AP, Sykes C, Cottrell ML, Prince H, Kashuba AD. Validation of an LC-MS/MS assay to simultaneously monitor the intracellular active metabolites of tenofovir, emtricitabine, and lamivudine in dried blood spots. *J Pharm Biomed Anal.* 2018;149:40-5.
63. Plummer ML, Wight D, Obasi AIN, Wamoyi J, Mshana G, Todd J, et al. A process evaluation of a school-based adolescent sexual health intervention in rural Tanzania: the MEMA kwa Vijana programme. *Health Educ Res.* 2007 August 1, 2007;22(4):500-12. doi: 10.1093/her/cyl103.
64. Power R, Langhaug LF, Nyamurera T, Wilson D, Bassett MT, Cowan FM. Developing complex interventions for rigorous evaluation--a case study from rural Zimbabwe. *Health Educ Res.* 2004 October 1, 2004;19(5):570-5. doi: 10.1093/her/cyg073.
65. Busza J, Chiyaka T, Musemburi S, Fearon E, Davey C, Chabata S, et al. Enhancing national prevention and treatment services for sex workers in Zimbabwe: a process evaluation of the SAPH-IRe trial. *Health Policy Plan.* 2019 Jun 1;34(5):337-45. PMID: 31157368. doi: 10.1093/heapol/czz037.
66. Hatcher AM, McBride RS, Rebombo D, Munshi S, Khumalo M, Christofides N. Process evaluation of a community mobilization intervention for preventing men's partner violence use in peri-urban South Africa. *Eval Program Plann.* 2020 Feb;78:101727. PMID: 31639542. doi: 10.1016/j.evalprogplan.2019.101727.
67. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. *Journal of Biomedical Informatics.* 2019 2019/07/01/;95:103208. doi: <https://doi.org/10.1016/j.jbi.2019.103208>.
68. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics.* 2009 2009/04/01/;42(2):377-81. doi: <https://doi.org/10.1016/j.jbi.2008.08.010>.
69. Devanathan AS, Dumond JB, Anderson DJC, Moody K, Polisen AJ, Schauer AP, et al. A Novel Algorithm to Improve PrEP Adherence Monitoring Using Dried Blood Spots. *Clin Pharmacol Ther.* 2023 Apr;113(4):896-903. PMID: 36622798.
70. Anderson PL, Glidden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med.* 2012;4:151ra25. PMID: 22972843. doi: 10.1126/scitranslmed.3004006.
71. Garcia-Moreno C, Jansen HA, Ellsberg M, Heise L, Watts CH, W. H. O. Multi-country Study on Women's Health and Domestic Violence against Women Study Team. Prevalence of intimate partner violence: findings from the WHO multi-country study on women's health and domestic violence. *Lancet.* 2006 Oct 07;368(9543):1260-9. PMID: 17027732. doi: 10.1016/S0140-6736(06)69523-8.
72. Heise AL, Hossain M. STRIVE technical brief: measuring intimate partner violence. London, UK: London School of Hygiene and Tropical Medicine, 2017.
73. VanderWeele T, Vansteelandt S. Conceptual issues concerning mediation, interventions and composition. *Stat Interface.* 2009 01/01;2(4):457-68. doi: 10.4310/SII.2009.v2.n4.a7.
74. Valeri L, Vanderweele TJ. Mediation analysis allowing for exposure-mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychol Methods.* 2013 Jun;18(2):137-50. PMID: 23379553. doi: 10.1037/a0031034.
75. Ryan GW, Bernard RH. Data Management and Analysis Methods. In: Denzin N, Lincoln Y, editors. *Handbook of Qualitative Research.* 2nd ed. Thousand Oaks: Sage Publications; 2000. p. 769-802.
76. Ethical and safety recommendations for intervention research on violence against women. Building on lessons from the WHO publication Putting women first: ethical and safety recommendations for research on domestic violence against women Geneva: World Health Organization, 2016.
77. World Health Organization. Health care for women subjected to intimate partner violence or sexual violence: a clinical handbook. Switzerland: World Health Organization, 2014.

78. National AIDS and STI Control Program (NASCOP), Kenya Medical Research Institute (KEMRI). Guidelines for conducting adolescents sexual and reproductive health research in Kenya. Government of Kenya Ministry of Health, 2015.
79. Amico KR, Mansoor LE, Corneli A, Torjesen K, van der Straten A. Adherence support approaches in biomedical HIV prevention trials: experiences, insights and future directions from four multisite prevention trials. *AIDS Behav.* 2013 Jul;17(6):2143-55. PMID: 23435697. doi: 10.1007/s10461-013-0429-9.
80. Amico KR, Mugavero M, Krousel-Wood MA, Bosworth HB, Merlin JS. Advantages to using social-behavioral models of medication adherence in research and practice. *J Gen Intern Med.* 2018 2018/02/01;33(2):207-15. doi: 10.1007/s11606-017-4197-5.
81. Amico KR, Wallace M, Bekker LG, Roux S, Atujuna M, Sebastian E, et al. Experiences with HPTN 067/ADAPT study-provided open-label PrEP among women in Cape Town: facilitators and barriers within a mutuality framework. *AIDS and Behavior.* 2016 Jun 17:1-15. PMID: 27317411. doi: 10.1007/s10461-016-1458-y.
82. Amico RK, McMahan V, Goicochea P, Vargas L, Marcus JL, Grant RM, Liu A. Supporting study product use and accuracy in self-report in the iPrEx study: next step counseling and neutral assessment. *AIDS and Behavior.* 2012 2012/07/01;16(5):1243-59. doi: 10.1007/s10461-012-0182-5.
83. Balán IC, Lentz C, Giguere R, Mayo AJ, Rael CT, Soto-Torres L, et al. Implementation of a fidelity monitoring process to assess delivery of an evidence-based adherence counseling intervention in a multi-site biomedical HIV prevention study. *AIDS Care.* 2020:1-10. doi: 10.1080/09540121.2019.1709614.
84. Delany-Moretlwe S, Chersich M, Harvey S, Stangl A, Baron D, Columbini M, et al. Empowerment clubs did not increase PrEP continuation among adolescent girls and young women in South Africa and Tanzania - Results from the EMPOWER randomised trial. *AIDS* 2018; Amsterdam, Netherlands 2018. p. Abstract FRAE0108LB.
85. Mannell J, Willan S, Shahmanesh M, Seeley J, Sherr L, Gibbs A. Why interventions to prevent intimate partner violence and HIV have failed young women in southern Africa. *J Int AIDS Soc.* 2019 2019/08/01;22(8):e25380. doi: 10.1002/jia2.25380.
86. Gibbs A. Tackling gender inequalities and intimate partner violence in the response to HIV: moving towards effective interventions in Southern and Eastern Africa. *African Journal of AIDS Research.* 2016 2016/07/15;15(2):141-8. doi: 10.2989/16085906.2016.1204331.
87. Campbell C, Mannell J. Conceptualising the agency of highly marginalised women: Intimate partner violence in extreme settings. *Global Public Health.* 2016 2016/02/07;11(1-2):1-16. doi: 10.1080/17441692.2015.1109694.
88. Mannell J, Jackson S, Umutoni A. Women's responses to intimate partner violence in Rwanda: rethinking agency in constrained social contexts. *Global Public Health.* 2016 2016/02/07;11(1-2):65-81. doi: 10.1080/17441692.2015.1013050.
89. Logie CH, Daniel C. 'My body is mine': qualitatively exploring agency among internally displaced women participants in a small-group intervention in Leogane, Haiti. *Global Public Health.* 2016 2016/02/07;11(1-2):122-34. doi: 10.1080/17441692.2015.1027249.
90. Anderson PL, Liu AY, Castillo-Mancilla JR, Gardner EM, Seifert SM, McHugh C, et al. Intracellular tenofovir-diphosphate and emtricitabine-triphosphate in dried blood spots following directly observed therapy. *Antimicrob Agents Chemother.* 2018 Jan;62(1). PMID: 29038282. doi: 10.1128/AAC.01710-17.
91. Anderson D, Prince H, Poliseno A, Moody K, Saunders A, Sykes C, et al. An exploration of adherence measures to detect recent changes in Truvada® dosing patterns. *Reviews in Antiviral Therapy & Infectious Diseases* 2019;4:Oral abstract 14.
92. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ.* 2015 May 8;350:h2147. PMID: 25956159. doi: 10.1136/bmj.h2147.

93. Lambdin BH, Cheng B, Peter T, Mbwambo J, Apollo T, Dunbar M, et al. Implementing implementation science: an approach for HIV prevention, care and treatment programs. *Curr HIV Res.* 2015;13(3):244-9. PMID: 25986374. doi: 10.2174/1570162x1303150506185423.
94. Pettifor A, Lippman SA, Selin AM, Peacock D, Gottert A, Maman S, et al. A cluster randomized-controlled trial of a community mobilization intervention to change gender norms and reduce HIV risk in rural South Africa: study design and intervention. *BMC Public Health.* 2015 Aug 6;15:752. PMID: 26245910. doi: 10.1186/s12889-015-2048-z.
95. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ.* 2015 Mar 19;350:h1258. PMID: 25791983. doi: 10.1136/bmj.h1258.

Figures

Figure 1. Study Design Overview

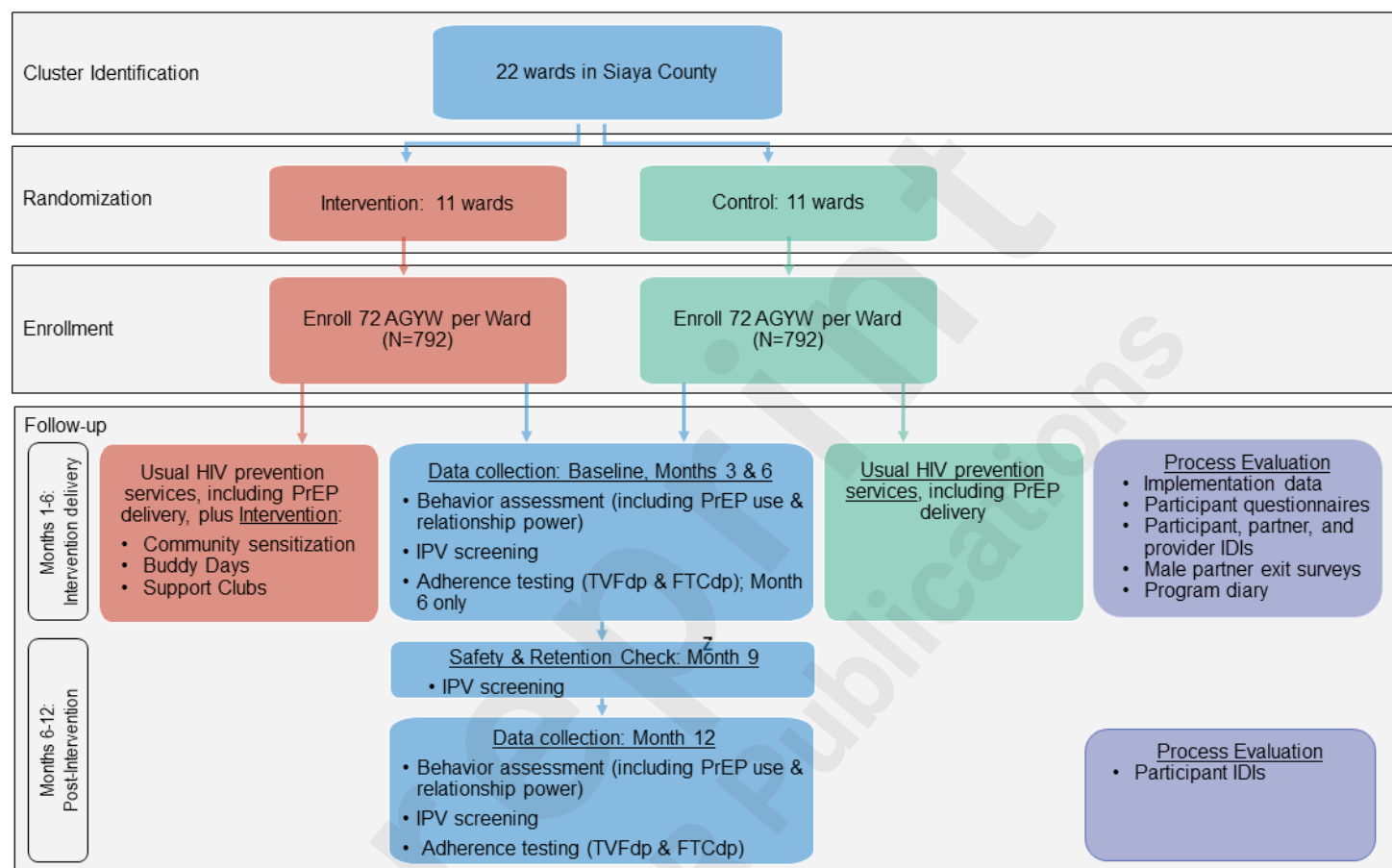


Figure 2. Conceptual Framework. Adapted from Pettifor et al, BMC Public Health 2015 and Mathur, Pilgrim and Pulerwitz, Lancet HIV 2016 [54, 94]

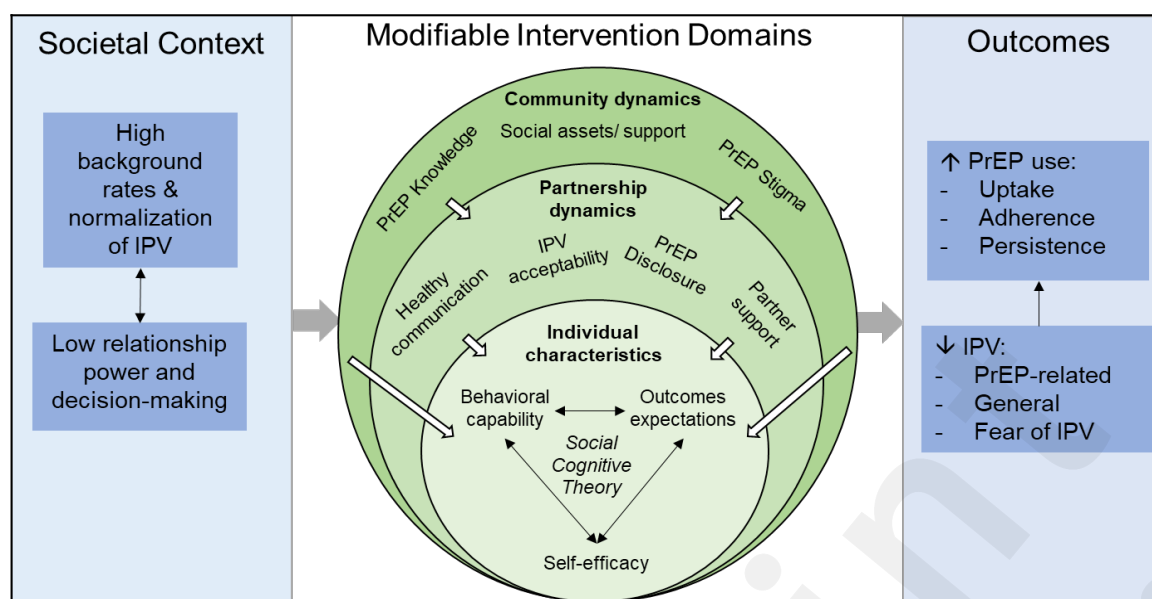
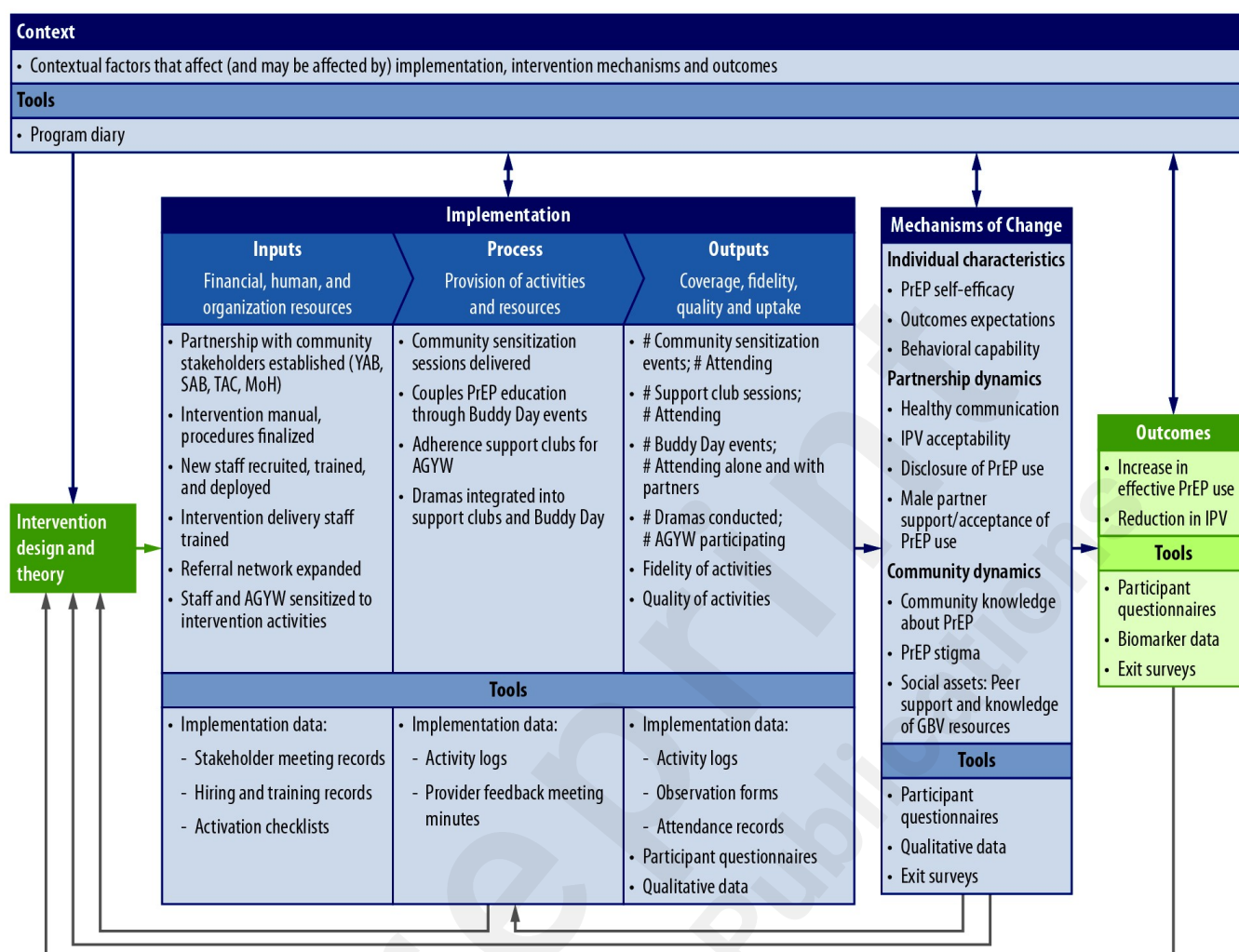


Figure 3. Mapping of Intervention Components to Conceptual Framework

Level	Domain	Community Sensitization	Buddy Day	Support Clubs
Individual	Behavioral capability			•
	Outcomes expectations		•	•
	Self-efficacy			•
Partnership	Healthy communication		•	•
	Reduce IPV acceptability	•	•	•
	Disclosure of PrEP use		•	•
	Partner support or acceptance	•	•	
Community	PrEP knowledge	•	•	
	Stigma	•		
	Social assets			•

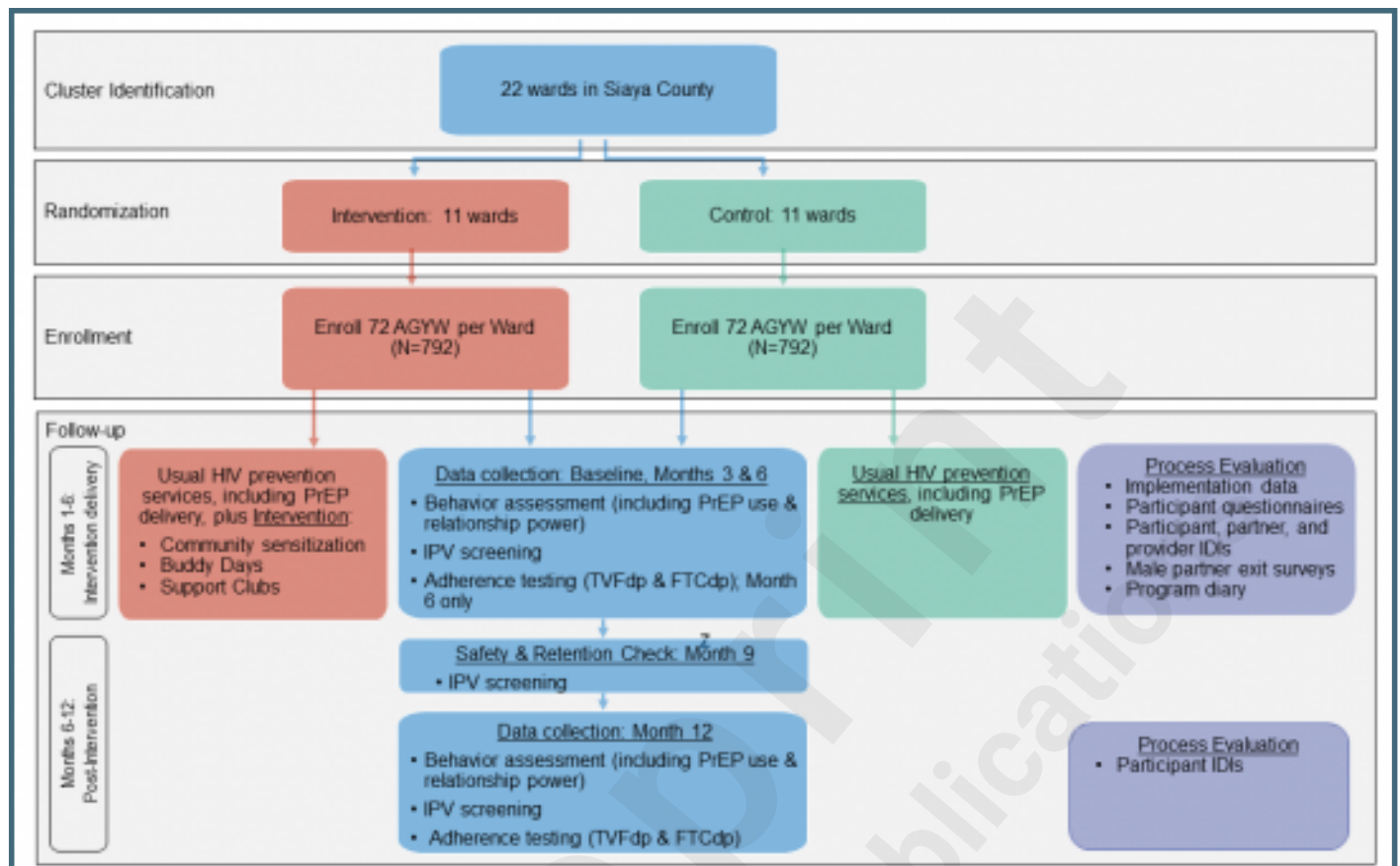
Figure 4. Process Evaluation Framework and Key Measures. Adapted from the Medical Research Council guidelines for process evaluation of complex interventions. [95]



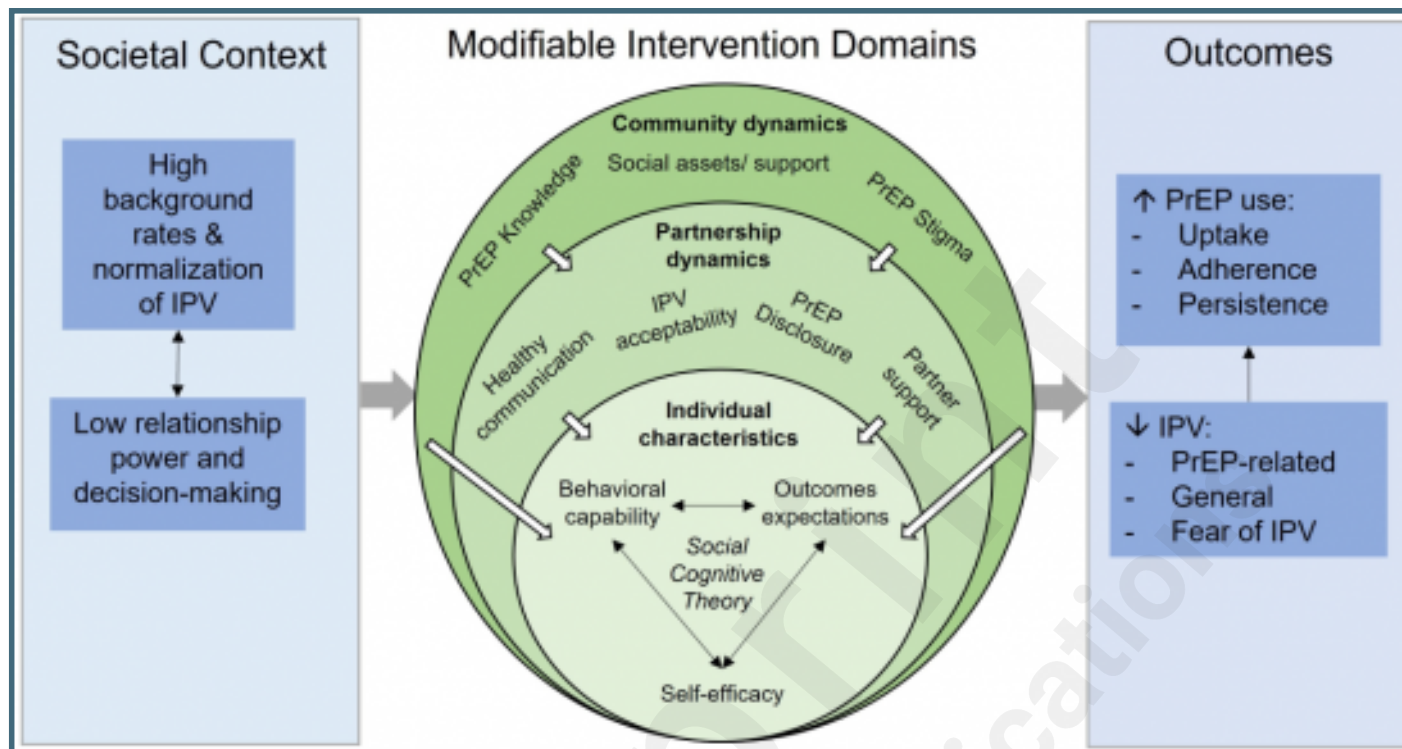
Supplementary Files

Figures

Study Design Overview.



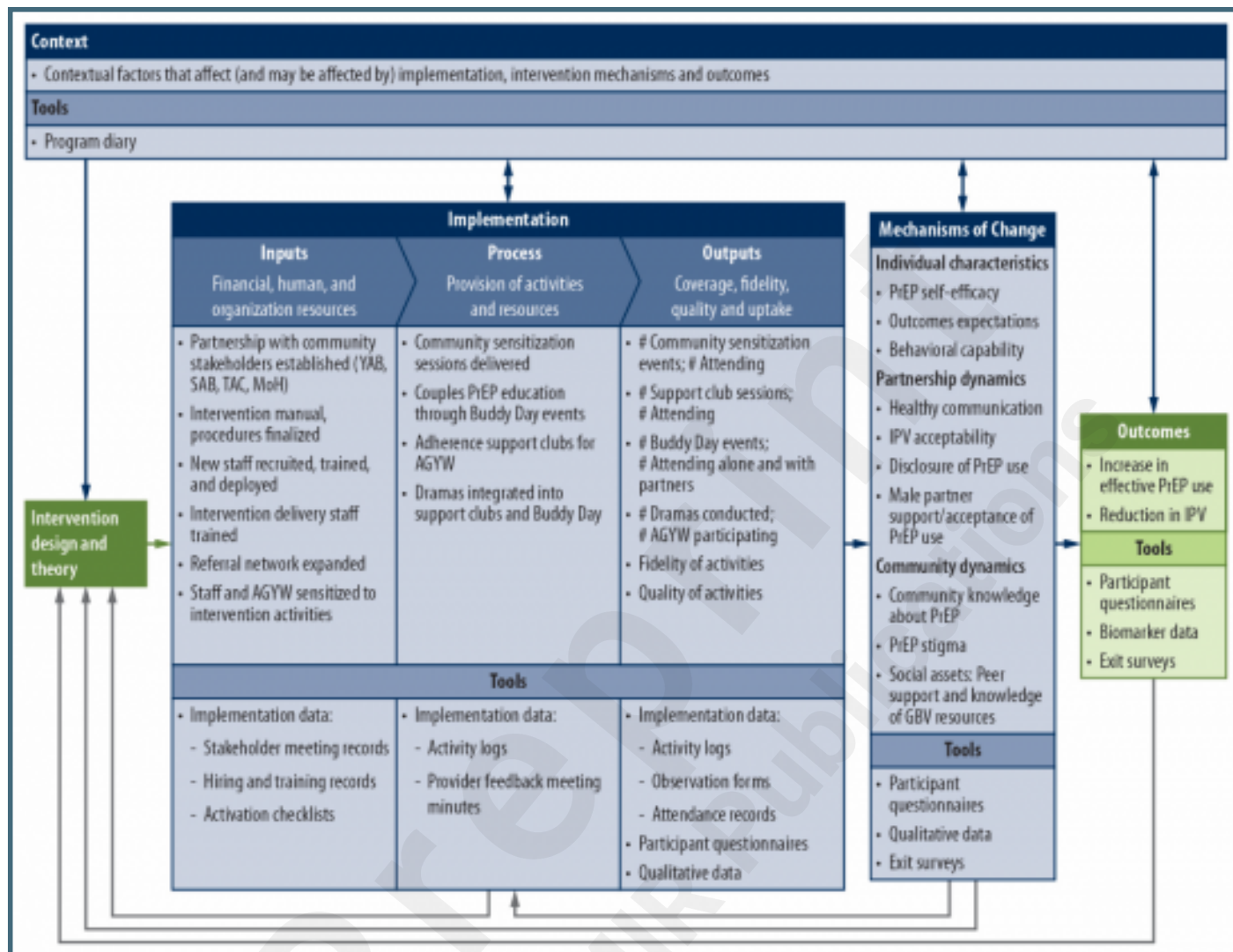
Conceptual Framework. Adapted from Pettifor et al, BMC Public Health 2015 and Mathur, Pilgrim and Pulerwitz, Lancet HIV 2016. [54, 94].



Mapping of Intervention Components to Conceptual Framework.

Level	Domain	Community Sensitization	Buddy Day	Support Clubs
Individual	Behavioral capability			•
	Outcomes expectations		•	•
	Self-efficacy			•
Partnership	Healthy communication		•	•
	Reduce IPV acceptability	•	•	•
	Disclosure of PrEP use		•	•
	Partner support or acceptance	•	•	
Community	PrEP knowledge	•	•	
	Stigma	•		
	Social assets			•

Process Evaluation Framework and Key Measures. Adapted from the Medical Research Council guidelines for process evaluation of complex interventions. [95].



Multimedia Appendixes

Peer-review report by the Center for Scientific Review HIV/AIDS Intra- and Inter-personal Determinants and Behavioral Interventions Study Section (National Institutes of Health, USA).

URL: <http://asset.jmir.pub/assets/46747a1ac076a2dfe12fe5c8d42cadbc.pdf>



CONSORT (or other) checklists

SPIRIT Checklist.

URL: <http://asset.jmir.pub/assets/ac19955366146137f00cf57ef3ab2eea.pdf>