



A cluster randomized trial to reduce HIV risk from outside partnerships in Zambian HIV-Negative couples using a novel behavioral intervention, “Strengthening Our Vows”: Study protocol and baseline data

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ABSTRACT

Background: Heterosexual couples contribute to most new HIV infections in areas of generalized HIV epidemics in sub-Saharan Africa. After Couples' Voluntary HIV Counseling and Testing (CVCT), heterosexual concordant HIV negative couples (CNC) in cohabiting unions contribute to approximately 47% of residual new infections in couples. These infections are attributed to concurrent sexual partners, a key driver of the HIV epidemic in Zambia.

Methods/design: Ten Zambian government clinics in two of the largest cities were randomized in matched pairs to a Strengthening Our Vows (SOV) intervention or a Good Health Package (GHP) comparison arm. SOV addressed preventing HIV infection from concurrent partners and protecting spouses after exposures outside the relationship. GHP focused on handwashing; water chlorination; household deworming; and screening for hypertension, diabetes and schistosomiasis. CNC were referred from CVCT services in government clinics. Follow-up includes post-intervention questionnaires and outcome assessments through 60 months. Longitudinal outcomes of interest include self-report and laboratory markers of condomless sex with outside partners and reported sexual agreements. We present baseline characteristics and factors associated with study arm and reported risk using descriptive statistics.

Results: The mean age of men was 32 and 26 for women. On average, couples cohabited for 6 years and had 2 children. Baseline analyses demonstrated some failures of randomization by study arm which will be considered in future primary analyses of longitudinal data. An HIV/STI risk factor composite was not different in the two study arms. Almost one-quarter of couples had an HIV risk factor at baseline.

Discussion: In preparation for future biomedical and behavioral interventions in sub-Saharan Africa, it is critical to understand and decrease HIV risk within CNC.

1. Introduction

Most incident HIV infections in sub-Saharan Africa (SSA) occur in cohabiting heterosexual couples, including discordant and concordant HIV negative (HIV-) couples [1,2]. Couples' Voluntary Counseling and Testing (CVCT) was developed by CDC [3] in collaboration with the

Rwanda Zambia HIV Research Group and endorsed by WHO for HIV prevention in 2012 [4]. In Zambia, a demonstration project in 73 government health centers provided CVCT to 207,428 couples of whom 13% were concordant HIV+, 8% were discordant (DC), and 79% were concordant negative couples (CNC). CVCT reduced transmission in both DC and CNC. Though the DC remained at comparatively higher risk (1.78/100 Couple-Years HIV incidence after CVCT + condoms + ART)

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Abbreviations

ART	Anti-Retroviral Treatment
CAB	Community Advisory Board
CAS	Condomless Anal Sex
CDC	Centers for Disease Control and Prevention
CFHRZ	Center for Family Health Research in Zambia
CVCT	Couples' HIV Voluntary Counseling and Testing
CNC	Concordant HIV-negative couples
DHS	Demographic Health Survey
GHP	Good Health Package
MSM	men who have sex with men
PrEP	Pre-Exposure Prophylaxis
RPR	Rapid Plasma Reagin
STI	Sexually Transmitted Infections
SOV	Strengthening Our Vows
SSA	sub-Saharan Africa
V0–V5	Visit 1-Visit 5
WHO	World Health Organization

than the CNC (0.53/100 CY), the CNC were a much larger percentage of all couples. As a result, 47% of the new infections that occurred after CVCT were in CNC and 53% were in DC [5].

Having multiple and concurrent partners results in extended sexual networks which increases opportunities for HIV transmission [6,7], and multiple, concurrent partnerships are one of the key drivers of the Zambian HIV epidemic [8]. In Zambia's 2013-2014 Demographic Health Survey (DHS), approximately 20% of men and 1% of women who are married/cohabiting report having two or more partners in the past 12 months [9]. This is similar to literature from other countries that show men report more multiple and concurrent partners than women [10,11]. Couples-based HIV interventions tailored for CNCs could enhance the impact of CVCT to further reduce HIV risk in this group.

Other prevention modalities, like pre-exposure prophylaxis (PrEP), have been shown to reduce HIV transmission. However, PrEP implementation has been slow due to costs, clinic capacity, communication and awareness, supplies, and access [5,12]. Additionally, from the end-user perspective, drug adherence, access, side effects, stigma, and perceptions of safety and effectiveness pose challenges to uptake [13, 14]. In Zambia, given the low incidence of HIV following CVCT [5], CNC do not qualify for PrEP based on WHO Guidelines.

Previous work with negotiated agreements in western couples provided the template for our work. Much of this work was done with men who have sex with men (MSM) couples, in whom the majority of new infections are also acquired from a main partner [15–17]. Gass et al. found that MSM were more likely to have condomless anal sex (CAS) with the main partner [18]. In 1999, Crawford et al. reported that when sexual partners engage in negotiated safety agreements, they usually did not practice unsafe sex [19]. In 2001, the same group interviewed MSM with regular partners and found a variety of agreements including negotiated safety (29%); no CAS (34%); and unsafe sex (11%) [20]. Kippax et al. published similar findings from the pre-HAART era, with 91% of concordant HIV- men reporting no outside CAS with use of a negotiated agreement in 82% [21,22]. A 2014 longitudinal study by Darbes et al. found that higher investment in sexual agreement and communication were among the factors that significantly predicted less CAS with outside partners for seroconcordant MSM couples [23]. Hoff et al. and Gomez et al. have assessed predictors of broken agreements [24] and the effects of relationship characteristics and serostatus differences on sexual agreements in MSM couples [24–26]. Mitchell et al. explored the influence of substance use on adherence to sexual agreements among MSM [27]. Stephenson et al. found that partnered HIV-MSM were less likely to seek regular HIV testing compared with MSM in

an open relationship [28]. In a 2015 qualitative study of heterosexual clients attending Sexually Transmitted Infections (STI) services in the US, Stephenson et al. showed high levels of willingness to be jointly tested and counseled for HIV and to discuss sexual agreements [29].

We developed the Strengthening Our Vows (SOV) intervention to reduce HIV risk among Zambian CNC through modeling and supporting negotiation for sexual agreements between husband and wife. This intervention is relevant and timely as couple-based strategies may be more impactful than individually focused approaches in reducing sexual risk behaviors but no study has yet evaluated sexual agreements in heterosexual African couples [30–32]. In this randomized trial, we include a comparator arm with an intervention focused on neglected tropical and non-communicable diseases, in keeping with UN Development goals [33].

2. Methods

2.1. Pre-trial planning

2.1.1. Focus groups and interviews

The pre-pilot and pilot phases for developing SOV were conducted from 2011-2014. We present the summary of the phases in Table 1. Focus groups and individual interviews were conducted with convenience samples of heterosexual CNC, CNC in which one or both partners had become HIV infected due to exposure outside the relationship, and CVCT counselors. All participants provided written informed consent. Focus groups with couples were sex-separated with facilitators and note takers of the same gender as participants to encourage candid discussions on concurrent partners and relationship agreement in the context of HIV prevention. These trained facilitators and note takers were senior counselors, who spoke the local languages Nyanja and Bemba, and had extensive training and experience in CVCT and conducting focus groups and interviews. Focus groups with couples were done in a local language while focus groups with CVCT counselors included both men and women and were conducted in English. Focus group sessions were audio recorded but not transcribed verbatim. Rather, recordings were reviewed later and compared against notes to ensure accuracy of thematic identification. Interviews were conducted with each spouse separately in the local language and were not recorded.

Focus groups and interviews typically lasted from 30 to 60 min. At end of each session, study staff met, reviewed the participants' responses, and noted repeating themes. Recruitment for focus groups concluded when saturation of themes was reached. The purpose of the formative work was to discuss counselor's experiences managing concurrent partners during CVCT; highlight couples and counselors' perceptions of negotiated sexual agreements as an HIV prevention strategy; determine feasibility and acceptability of sexual agreements for CNC; identify threats in a union that might lead to a potential HIV exposure from concurrent partners; explore issues that may impact facilitating sexual agreements with CNC; and develop a pragmatic behavioral intervention to guide couples on taking preventative actions to protect their marriage from HIV exposure from outside partners.

From the pre-pilot phase, we identified key considerations and themes such as discussing hypothetical concurrent partners in the abstract during counseling; not disclosing outside partners without spouse's permission; providing discrete referrals for CVCT with outside partners; ensuring gender balance when discussing threats that lead to HIV exposure; and ensuring neutrality and confidentiality throughout counseling. Important messages highlighted by participants included an emphasis on the window period between exposure and seroconversion during which individuals are very contagious, and alternatives to monogamy including testing with outside partners prior to sex and using condoms during all outside sexual contacts. Interviews with men and women of seroconverted CNC highlighted threats that might lead to potential HIV exposure outside the relationship such as traveling, the desire for extra money and goods, post-partum abstinence, discord

Table 1
Phases of formative work for strengthening our vows.

Phase	Time frame	Participants	Facilitated by	Topics	Key Considerations/Themes for Intervention/Activities
Pre-Pilot FGD	Dec 2011–May 2013	CVCT Counselors in GRZ clinics, 11 sessions, 29 M, 91 F and 13 sex not indicated	CFHRZ counselors	Frequency of discussions on concurrent partnerships during CVCT, counseling couples on concurrent sexual partners, and developing concurrent partner modules	<ul style="list-style-type: none"> •Counseling couples on scenarios for risk reduction and concurrent partners using abstract examples •Ensuring the intervention allows for opportunities for spouses who want to disclose outside partnerships with spouse and facilitate testing at CVCT with those outside partners •Ensuring counseling messaging targets HIV prevention and concurrent partnerships equally between men and women as it is sometimes assumed that only men are involved in extramarital affairs •Ensuring counselors do not interject their personal opinions or judgements into the counseling sessions •Training counselors on concurrent partnerships to ensure they are comfortable with the messages •Providing additional training to counselors to ensure confidentiality and disclosure with individuals/couples in context of multiple concurrent partners
IDI	Jan 2012–Feb 2012	HIV Concordant Negative Couples, 4 M and 3 F	CFHRZ nurse counselors/physicians	Initial feedback on whether couples would want to discuss outside partners	<ul style="list-style-type: none"> •Initial interviews showed couples seemed to be open to discussing outside partners
FGD	Jul 2012–Jun 2013	HIV Concordant Negative Couples, 16 sessions, 31 M and 31 F	gender-matched counselors (CFHRZ and GRZ)	Discussion with spouse about outside partners, relationship contracts, benefits and disadvantages of discussing outside partners with spouse, how they would like counselor to bring up outside partners during counseling, how concurrent partners impact HIV transmission, how can we better facilitate this, what are the top 3 things you would like included if you created your own contract	<ul style="list-style-type: none"> •Partners open to having concurrent partners discussed during counseling •Preferences to discussing concurrent partners using abstract examples • Ensuring discreteness when testing with outside partners at the clinics; no special procedures • Counseling should encourage disclosure only if partner wants to • Partners were open to their spouses protecting them and testing with outside partners but may not want to know themselves • Couples generally supporting the concept of relationship contracts as it set limits and helps to maintain relationship • Partners stating that though concurrent partners exist it is not a social norm • Discussing concurrent partnerships could help someone realize their HIV risk • Ensuring confidentiality • Emphasizing counseling should not focus on blame but risk reduction and protecting spouse
IDI	Feb 2014–Apr 2014	7 HIV seroconvertors ^a and 3 spouses, 5 M and 5 F	CFHRZ nurse counselors/physicians	CVCT knowledge, impact of testing program on the couple, threats to avoiding exposure to HIV, coping with situation, advice/recommendations to friends in similar situation	<ul style="list-style-type: none"> • Emphasis on window period as participants seemed surprise of themselves or spouse becoming infected in a short period of time 1–2 months • Threats that led to partner seroconversion: traveling spouse; desire for extra money, goods; desire to be paid attention to; taking spouse for granted • Testing with outside partners together is important before engaging in sex; one should not take verbal indication of being test to be truth. •If outside partner refuses to test, use condoms
Pilot FGD @ V1	Feb 2014–Mar 2014	HIV Concordant Negative Couples, 8 sessions, 30 M and 30 F	gender-matched counselors (CFHRZ and GRZ)	Piloting “Strengthening Our Vows” Intervention	<ul style="list-style-type: none"> •Developing intervention visit length and logistic planning for the visit •Conducting mock intervention •Identifying potential threats to remaining HIV free: lack of money or goods; traveling for work; dissatisfaction with spouse; peer and family influence; and alcohol use

(continued on next page)

Table 1 (continued)

Phase	Time frame	Participants	Facilitated by	Topics	Key Considerations/Themes for Intervention/Activities
FUP IDI @ V2	Mar 2014	HIV Concordant Negative Couples, 18 M and 17 F	CFHRZ and GRZ counselors	Piloting post-intervention questionnaire	<ul style="list-style-type: none"> •Receiving feedback from the CFHRZ counselors on intervention guide after pilot focus groups •Incorporating strategies to communicate risk non-verbally; introduction of yellow card as a non-verbal communication cue •Introducing CFHRZ team to draft post intervention questionnaire •Administering post intervention questionnaires in an open-ended format until saturation of responses reached •Assessing comprehension, comfort, timing of post-intervention questionnaires •Receiving feedback from the CFHRZ counselors on the post intervention visit flow •Refining questionnaire based on counselor feedback and couple responses

Abbreviations: CFHRZ, Center for Family Health Research in Zambia; FGD, focus group discussions; GRZ, Government Republic of Zambia; IDI, in-depth interviews; M, male; F, female.

^a 1 concordant negative HIV couple where both spouses seroconverted.

within the marriage, and inattentive spouses. Some participants mentioned that, as long as their spouse protected them from HIV, they did not need to know the details of their outside sexual contacts. These findings were incorporated into the intervention and open-ended, post-intervention questionnaire that would be used during the pilot phase with CNC. During the pilot phase, staff were trained on the draft tools. We performed mock intervention and post intervention visits with CNC to assess visit flow, length of visit, and further refined the questionnaire based on responses from couples and feedback from counselors. During this period, identifying potential threats to remaining HIV free and using a non-verbal communication cue were further explored and incorporated into the intervention and post-intervention questionnaire.

The construct of the questionnaires used to assess the impact on SOV was based on our 27 years of experience on sexual behavior in cohabiting Zambian heterosexual couples. These questionnaires were consistent with our previous work with regard to measurement of standard behavioral outcomes, such as outside partners, condom use, alcohol use, joint testing and self-reported STI treatment.

2.1.2. Intervention and comparator content

The intervention and comparator arm materials included client videos and complementary counselor flip charts. The structure of the video and flip chart aligned in terms of headings, pause points, and content covered; the flip chart provided counselor structure to highlight key important points during pauses. This was done through group brainstorming as well as questions and answers. All materials were translated into local languages, Bemba and Nyanja and content was equivalent to or below 8th grade level. Video run-time for each arm was approximately 1 h. We present the intervention content in Table 2.

The SOV video was structured in two segments and included the HIV prevention agreements within the plans: “Together HIV Free” and “Protecting My Spouse” with guidance to finalize the plan in “Making Your Plan.” The first segment included the same content presented separately to men only and women only groups. “Together HIV Free” focused on keeping HIV from entering the marriage by 1) not having sexual partners outside of the relationship, 2) testing jointly with outside partners and only having sex with those who are also HIV-, and/or 3) using condoms every time with an outside partner [34,35]. “Protecting My Spouse” discussed ways to avoid passing the virus on in the event of an unprotected sexual exposure to an outside partner with HIV + or unknown HIV status and included 1) abstaining from sex with the spouse or 2) using condoms consistently with the spouse until HIV retest after the “window period” of 30 days. The “window period” was emphasized in the video as a particularly infectious period prior to development of

anti-HIV antibodies.

For the second segment, husbands and wives were brought together into one group to view and discuss six scripted video scenarios depicting hypothetical couples with various risk factors identified from the formative research. Each video scenario highlighted different potential threats to remaining HIV free including longstanding outside partners (“old boyfriends/girlfriends”); traveling and working away from home; alcohol use [36–38]; receipt of attention, money and gifts; and sexual inactivity due to wife’s postpartum abstinence and menstruation. The creation of the scenarios was guided by the harm reduction approach where potential real-life threats to remaining HIV free are acted out and couples discussed and used various strategies from “Together HIV Free” and “Protecting My Spouse” to prevent HIV from entering the union. There were pauses in the video after each scenario for counselors to use the flip chart for further discussion of the HIV risk the couples in each scenario faced; what actions could reduce risk of HIV; and what couples could agree to do to prevent HIV in the future. The video also featured communicating the need for using “Protecting My Spouse” and included tips on how to deal with difficult communication and disclosure. An alternative and unique concept for communicating the need to use the “Protecting My Spouse” plan was the “yellow card”, a visual cue derived from soccer, to signify a non-verbal signal to the spouse about a potential HIV exposure and need for caution. The familiarity and understanding of the use of the yellow card in soccer made it a neutral tool for men and women to use given the sport’s popularity in Zambia. The yellow card, which all intervention couples received, was used in scenarios to illustrate how the card can be used to indicate the need to have a conversation about a potential HIV exposure and need for an alternative/interim plan to ensure protection from HIV within the relationship. The final part of the video, “Making Your Plan”, asked couples to discuss risk reduction plans together and return in one to two weeks for a counseling session to finalize their agreement and ‘take their vows’. Vows were an opportunity for the couple to discuss and identify their mutual agreement and commitment to keeping each other HIV free and to provide both partners with an opportunity to verbally communicate directly to their partner regarding their agreement and commitment.

Flip chart-based GHP had been previously developed for use at government clinics to improve follow-up testing rates after CVCT [39] and covered education, prevention and screening of diarrheal diseases, intestinal helminths, hypertension, diabetes, and schistosomiasis. The diseases were chosen as they are common health issues in Zambia in addition to being a simple, low cost service that could be easily integrated into CVCT. For this study, we further expanded GHP to include

Table 2
Intervention content.

Visit	Video segments	SOV arm	GHP arm
V01	Part 1	<p>Watch 1 h SOV intervention video</p> <p>Separate into men and women groups; facilitated by same sex counselor using a complimentary flipchart to the video</p> <p>“Together HIV Free” plan</p> <p>Be monogamous and only have sex with your spouse</p> <p>Always use a condom with outside partners and/or</p> <p>Only have sex with outside partners if you have tested with those partners and you know that they are also HIV- “Protecting My Spouse” plan</p> <p>Abstain/NOT have sex or use condoms with their spouse until HIV retest in 1 month after the potential exposure</p> <p>If continuing to have sex with other partner(s)also</p> <p>Test for HIV as a couple with that other partner(s). Some couples test for HIV with their spouse and their boy/girlfriend at the same time</p> <p>Abstain from sex or use condoms with the other partner until they know that partner’s HIV status</p> <p>Consider ending the relationship with the boyfriend or girlfriend.</p>	<p>Watch 1 h GHP comparator video</p> <p>Separate into men and women groups; facilitated by same sex counselor using a complimentary flipchart to the video</p> <p>“Everyone has an equal responsibility in keeping our family healthy”</p> <p>Importance of household roles in maintaining good household health</p> <p>Health education (risk groups; information on transmission and mechanism of action; signs and symptoms) for Diarrhea and Worms, hypertension, diabetes, and schistosomiasis were covered.</p> <p>Modifiable lifestyle choices for prevention of hypertension and diabetes were emphasized</p> <p>Illustration of portion control with salt and sugar measurements</p> <p>Proper Handwashing technique with practical</p> <p>Water chlorination 5L and 20 L with practical</p> <p>Health screenings hypertension, diabetes and schistosomiasis</p> <p>Barriers to implementing GHP</p>
	Part 2	<p>Couples All Together</p> <p>Six scripted scenarios covering potential threats to remaining HIV free:</p> <p>Longstanding outside partners; traveling and working away from home; alcohol use; receipt of attention, money and gifts; and sexual inactivity due to wife’s postpartum abstinence and menstruation</p> <p>“Making Your Plan”</p> <p>3-way agreement</p> <p>Each person commits to keeping yourself and your spouse HIV free</p> <p>Counselors commit to helping you achieve this goal</p>	<p>Couples All Together</p> <p>Game: GHP review (mini-quiz (6 questions)) non-graded</p> <p>Couples talked about what the phrase “Everyone has an equal responsibility in keeping our family healthy” meant to them</p> <p>Receipt of commodities: low sodium salt, deworming pills for family, chlorine and hand soap</p> <p>Treatment and referral for any abnormal result</p> <p>3-way agreement</p> <p>Each of you commits to keeping yourself and your household healthy</p> <p>Counselors commit to help you achieve this goal</p> <p>The success of implementing these strategies is ultimately your responsibility as individuals and as a family.</p>

Table 2 (continued)

Visit	Video segments	SOV arm	GHP arm
V05	Part 1		<p>The ultimate responsibility of this agreement lies with you individually as well as a couple</p> <p>Not assigning blame if a partner makes a mistake, but trying to focus on the original agreement from today of keeping HIV out of the marriage</p> <p>Couples asked to agree that if someone makes a mistake, they will put the health of one another first. After that, you can also discuss how to minimize future threats. Can you agree to that?</p> <p>Encourage coupled to go home and discuss and decide on plans together</p> <p>Couples given yellow card</p>
		<p>All couples watch SOV video for 1 h</p>	<p>Encouraged couples to go home and think about keeping a healthy household, keep this key message in mind: “Everyone has an equal responsibility in keeping our family healthy”</p> <p>All couples watch GHP video for 1 h</p>

more health education content on each of the diseases; practicum for handwashing and water treatment with chlorine; and barriers to applying GHP at home. Pauses were incorporated throughout the video in key areas to cover flip chart talking points and allow for questions. Similar to SOV, GHP had two segments, with couples being separated into groups of men only and women only in the first segment and being brought back together in the second segment. The first segment opened with the theme “Everyone has an equal responsibility in keeping our family healthy” and covered each health topic; risk groups; information on transmission and mechanism of action; signs and symptoms; key facts and statistics; and prevention strategies. Modifiable lifestyle choices related to diet, salt intake and physical activity were emphasized for prevention of hypertension and diabetes. Schistosomiasis education highlighted how freshwater areas within a city could be potentially infected as a recent study had shown active infection in 10% of Lusaka adults [40]. Pauses in the video also allowed counselors to demonstrate and for participants to practice proper handwashing techniques, preparation of potable water by measuring chlorine for 5L and 20L containers, and portion size of salt and sugar. The second segment consisted of mini quiz game where couples were asked about content covered and practiced preparing chlorinated water and handwashing. This segment closed with couples talking about what the theme “Everyone has an equal responsibility in keeping our family healthy” meant to them. Participants were provided with a bottle of chlorine, hand soap and deworming pills for the family to take home.

2.1.3. Rationale for the comparator

The comparator GHP was designed to be unrelated to HIV but to include a similar format (videos and group discussions) and to require a similar amount of time with beneficial health messaging unrelated to HIV, STI or sexual behavior. All couples received CVCT prior to joining the study. Post-test counseling in CVCT covered HIV risk reduction strategies with basic messaging on monogamy, alcohol awareness, condom use with outside partners, and repeat HIV testing if exposed. The GHP arm was family focused while SOV was couple focused.

2.2. Study objectives

This trial has primary and secondary objectives related to both the

intervention, Strengthening Our Vows, and the comparator, Good Health Package.

2.2.1. Primary objectives

1. Compare the impact of ‘Strengthening our Vows’ (SOV) negotiated sexual agreement intervention versus a comparison arm on reduction in a composite of HIV risk factors from concurrent partners. The HIV risk factors include incident HIV and sexually transmitted infections (STIs) diagnosed and by self-report of outside treatment as well as

- self-report of outside partners, condom and alcohol use during sex with outside partners, knowledge of outside partner HIV status, and joint HIV testing with outside partners
2. Describe the types of risk couples report for acquisition of HIV in the marriage and the HIV prevention agreements SOV couples develop to reduce those risks
3. In the comparison arm that receives a “Good Health Practices” (GHP) intervention focusing on prevention of neglected tropical and non-communicable diseases, measure improvement in knowledge of

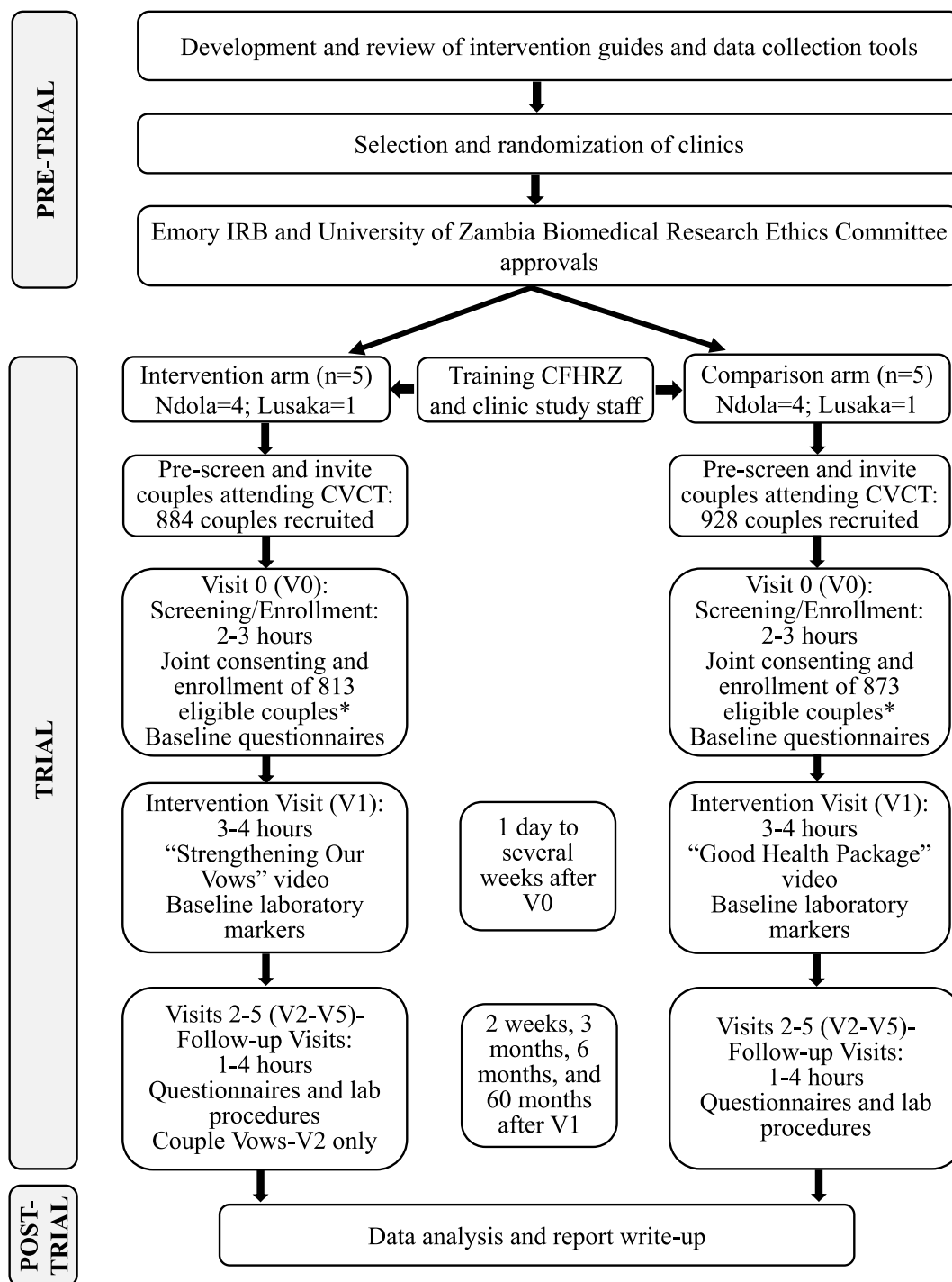


Fig. 1. *Reasons for exclusion (couples may be excluded for multiple reasons): not CNC (8); age (23); not available for follow-up (21); cohabiting <3 months (20); not willing to participate (14); not willing to provide contact information (5); unable to understand study (1); false couple (23); did not return for enrollment (16); outside acceptable window for enroll (6); impairment (2); co-enrolled (3); unknown (3).

prevention and treatment of diarrheal and respiratory diseases, intestinal helminths, hypertension, diabetes, and schistosomiasis

2.2.2. Secondary objectives

1. Assess the ability of an e-fingerprinting system to enhance follow-up and detection of study outcomes, multiple enrollments and potential spillover effect
2. Disseminate and incorporate successful strategies learned from the SOV and GHP into current CVCT and Couples' Family Planning Counseling guidelines

2.3. Ethics

Approval for this trial has been granted by the OHRP-registered University of Zambia Biomedical Regulatory Ethics Committee and Emory University Institutional Review Board. This trial is registered at the US National Institutes of Health ([ClinicalTrials.gov](https://clinicaltrials.gov)) as NCT02744586. Couples viewed a verbatim reading of the informed consent on a video, met with a counselor to discuss any questions or clarifications, and jointly signed consent. A unique alphanumeric ID was implemented for all data gathering tools. Locator information was stored separately from data to maintain privacy and confidentiality. As stated in the informed consent, couples may withdraw from the study at any time without losing their entitled benefits. The study involves some risks and discomforts, such as blood draws, answering personal questions, and discussions at home related to study topics. Participants may opt out of questions or discussions if they are not comfortable and can seek additional counseling at the clinic, individually or with their spouse. Information a spouse provides individually is confidential and is only disclosed to the spouse with explicit permission. Initial and ongoing training and supervision of the study team is conducted to mitigate risk.

2.4. Community advisory board (CAB)

Before the beginning of the trial, the study team engaged the CABs in Lusaka and Ndola to review protocol, informed consents and discuss recruitment. The CAB has representation from media; education; health; faith-based institutions; law enforcement, young adults; community leaders; people living with HIV; as well as at-risk HIV populations. The CAB continues to be updated throughout the trial on study progress. At each meeting, a light lunch and an honorarium are given.

2.5. Trial design overview

We illustrate the trial design and procedures in [Fig. 1](#). This is a clinic-randomized trial among CNC. We selected government health clinics as the unit of randomization since the intervention is provided in a group setting. Clinics in matched dyads were randomly assigned to either intervention or comparison arm via a coin toss. Eligible couples attending their neighborhood clinics automatically received the arm assignment for the clinic. At the final visit, the alternative intervention is offered so that participants can benefit from both interventions.

2.6. Clinic selection and randomization

The cluster randomized trial comprises urban, government health clinics in Ndola and Lusaka Zambia which provided Couples' HIV Voluntary Counseling Testing (CVCT) services in collaboration with the Center for Family Health Research in Zambia (CFHRZ). Of 55 clinics offering CVCT, 10 clinics were selected based on urban location (catchment population of 10,000–145,000 people) from "The 2012 List of Health Facilities in Zambia" preliminary report (Republic of Zambia Ministry of Health, 2012). The first selection criteria were that the clinics be far enough apart to have low risk of spillover and that in the aggregate they have the volume of CVCT that would ensure recruitment

of a sufficient number of couples for the trial.

To detect possible patient spillover due to bus routes and walking trails not reflected on maps, the study team and drivers mapped transport routes to high-volume clinics and checked with clinic staff about their clientele to ensure that chances of spillover would be low. Clinics were then matched by clinic volume (number of couples tested), distribution of couple HIV serostatus, and follow-up testing rates in the year following CVCT [39]. The five dyads were randomized via coin toss by an unbiased staff member not directly involved with the clinics. Coin toss was done for the first clinic in each dyad. The second clinic in the dyad received the opposite arm by default.

2.7. Study population

Couples who received CVCT services at the clinics in Ndola ($n = 8$) and Lusaka ($n = 2$) were pre-screened. Those meeting initial eligibility at pre-screen were invited for screening, enrollment, receipt of SOV intervention/GHP comparator, and follow-up.

2.8. Trial procedures

Trial procedures are outlined in [Fig. 1: Trial Design and Procedures](#). Trial procedures for couples include a baseline visit (V0), intervention visit (V1) and four post-intervention visits (V2–V5).

2.8.1. Staff training and quality assurance

As in our past training programs, we administered pre and post-didactic training tests [41] to select government clinic nurses and counselors who worked with us on CVCT. The purpose of the pre and post tests were to identify knowledge gaps and assess knowledge uptake after training. The trainees for this study were selected by our team based on their experience and performance with the CVCT program. Trainees who passed the didactic test proceeded to practicums observed by trainers and including obtaining informed consent, leading the video group discussion, and administering questionnaires. The flip chart provided to the counselor for use during video sessions included explicit instructions to ensure that important topics were emphasized during Q and A and were consistently delivered over time. It is traditional in Zambia for counselors and nurses to use "call and response" [42] when doing health talks in the clinics, which is an excellent way to ensure audience participation and comprehension. Each clinic was staffed by a senior research nurse who provided ongoing monitoring and mentorship to ensure fidelity to the study procedures. In addition, "mystery couples" [43] were selected from among community health workers who had collaborated with the research team for many years. They were trained on checklists of procedures to pay attention to and interviewed by study trainers after each visit. Their feedback was relayed to the research nurse for inclusion in oversight duties.

2.8.2. Study reimbursement

At each visit, couples receive study reimbursement to cover time at clinic and transport, as described in the informed consent. Reimbursement is 30 kwacha (approximately 3 USD) per person. An additional 20 kwacha (approximately 2 USD) per person is given as a lunch allowance for longer study visits.

2.8.3. Pre-screening at CVCT

At CVCT services in government health centers, couples underwent pre-test counseling, HIV rapid testing per national guidelines adapted for couples (screening with HIV with Alere Determine HIV1/2 and confirmation with either Trinity Biotech Uni-Gold HIV or Standard Diagnostics (SD) Biotline HIV-1/2 3.0), and post-test counseling provided by government counselors. Couples received HIV results together and were counseled per their couple HIV status according to CDC and WHO guidelines [3,4]. Each couple was given a unique couple ID during CVCT, which they maintained throughout the trial. Eligible and

interested couples were referred for additional screening procedures.

2.8.4. Visit 0 (V0): screening and enrollment

2.8.4.1. Screening. Screening and enrollment procedures based on Inclusion and Exclusion Criteria, Table 3 occurred on Saturday or Sunday when the clinics were less busy and group activities could be conducted without disruption to regular clinic flow. This visit lasted 2–3 h. Participants were given a membership card recording their study ID, appointment dates, and fingerprints.

2.8.4.2. Enrollment. A baseline questionnaire was administered to each spouse separately by a gender-matched counselor and included socio-demographic characteristics (income, number of persons/children in the household and literacy) and past and recent sexual history questions were asked related to HIV risk behaviors, such as age at sexual debut, number of lifetime sexual partners, frequency of sex with spouse, outside partners since married, condom use with outside partners, alcohol use during sex with outside partners and ever being treated for an STI. In addition, to measure unrelated outcomes addressed in the comparator arm, participants were asked about roles in the household for daily activities (collecting and treating water, preparing and purchasing food, taking care of sick persons, changing baby's nappy, washing dishes and handling animals). Spouses were also asked about knowledge and behavior related to communicable and non-communicable diseases addressed in the GHP comparison program. Couples consented to storage of blood, urine and vaginal swab samples.

2.8.5. Visit 1 (V1): intervention visit

Participants were scheduled for the intervention one or two weekends after enrollment. Testing for HIV was repeated as described above in CVCT in addition to syphilis testing with SD Syphilis 3.0 Bioline and microscopic exam of wet mount for detection of vaginal trichomoniasis. Quality control testing was performed at our research laboratories with wet mount microscopy for vaginal trichomoniasis and IMMUNOTREP RPR® by Omega Diagnostics for syphilis. While laboratory tests were underway, couples in both intervention and comparison arms attended their arm specific video group sessions. The content and format of the videos and discussions is presented above. Participants with positive syphilis tests were provided with treatment at no cost. This visit lasted 3–4 h.

2.8.5.1. Intervention arm: Strengthening Our Vows (SOV). At the end of

Table 3
Inclusion/exclusion criteria.

Inclusion Criteria	Exclusion Criteria
1. Heterosexual, both partners HIV negative	1. Either partner has a condition, in opinion of investigator, that would prevent informed consent or affect reaching study objectives
2. Women aged 18–45 and men aged 18–65 years of age	2. Either partner HIV-positive or with indeterminate HIV rapid test results
3. Cohabiting 3 months or greater	3. May seek health care at a clinic randomized to the opposite arm of the clinic they would enroll in
4. Not taking any anti-retrovirals as Post or Pre-Exposure Prophylaxis	
5. Interested in participating	
6. Able and willing to provide informed consent	
7. Willing to answer questions on risk factors	
8. Available for duration of the study	
9. Willing and able to be reached by phone or home visit	
10. Willing and able to provide locator/contact information for retention and be contacted by study team	

the visit, each spouse was offered a yellow card to use in the event of an outside sexual exposure and provided with condoms. They were invited to revisit the issues raised in the video and group discussion at home and to develop an agreement to remain HIV-free as a couple. They were scheduled for a counseling session one to two weekends later to finalize their agreement and take their vows.

2.8.5.2. Comparison arm: Good Health Package (GHP). Following the video and group discussion, couples were screened for hypertension via blood pressure cuff and diabetes (glucose) and schistosomiasis (blood) via urine dipstick. Individuals were provided with immediate treatment with praziquantel if blood was detected in the urine. Any participant with abnormal screening results, i.e., blood pressure greater than/equal to 140/90 mmHg and/or glucose on urine dipstick greater than/equal to 500 mg/dl was provided with additional lifestyle and dietary counseling, low sodium salt, and referral for further clinical assessments as indicated. Each couple received deworming tablets for the family, chlorine for water treatment, and hand soap. They were scheduled for a follow-up visit one to two weekends later to assess changes in knowledge and behavior.

2.8.6. Visit 2 (V2): follow-up visit

In the SOV arm at V2, each spouse was interviewed separately by a gender-matched counselor. The questionnaire covered knowledge of strategies which included recall of topics covered during intervention and questions related to the 30-day “window period” for HIV and the importance of abstaining or using condoms for this 30-day period if HIV exposed. Spouses responded to a series of questions related to discussion of plans “Together HIV Free” and “Protecting My Spouse” with their spouses and whether they made their plan. These questions ranged from discussions at home in terms of the environment, length of discussion, agreement on the plan, discussion initiator, and comfort discussing these plans. The counselors read strategies for the “Together HIV Free” plan (monogamy, always using condoms with outside partners, testing with outside partners and/or knowing their HIV status) and “Protect My Spouse” plan (following an unprotected outside exposure, abstain from sex with spouse or use condoms for 1 month until HIV retest) and participants reported which components were a part of their agreement. Respondents reported whether they had challenges communicating their plans effectively and if there were any threats to their ability to remain HIV free in the union. After the interview, each partner was asked whether there was any information they had shared with the interviewer that they would NOT want discussed when the couple was brought together. Counselors for the two partners met separately to compare notes, brought the couple together, and reinforced and congratulated couples on successful negotiations while avoiding disclosure of confidential information. Spouses then recited the standardized SOV vows to each other, which include not exposing themselves to HIV outside the marriage and if potentially becoming exposed to HIV, keeping the spouse safe during the window period until repeat test was done. The citing the vows together gave the couple an opportunity to practice direct communication of their plans in a supportive environment with the counselor. This process further emphasized positive communication about keeping HIV out of the marriage from outside partnership through using the plans.

In the GHP arm, men and women were interviewed separately to assess change in knowledge and behavior related to components of the GHP intervention.

2.8.7. Visit 3-visit 5 (V3–V5): follow-up visits

Follow-up visits are scheduled 3 months (V3); 6 months (V4); and 60 months (V5) after intervention (V1). Each spouse is administered a questionnaire that includes sexual behavior questions that make up the HIV risk factor composite; these include reported sex with outside partners since participating in the intervention (for V2) or since the last

visit (for V3, V4 and 5), HIV status (if known) of those outside partners, HIV testing with outside partners, condom use and alcohol use during outside exposures; and STIs including syphilis, genital ulcers, gonorrhea and genital discharge, which were diagnosed at or treated between study visits. Laboratory testing is done for HIV and STI using same tests outlined in enrollment procedures. Follow-up visits last between 1 and 4 h.

2.8.8. V5

At V5 after data collection regarding HIV risk behaviors and laboratory testing for HIV and STI, participants in each arm will receive the video-intervention from the other arm (i.e., SOV participants receive the GHP video intervention and GHP participants receive the SOV video intervention).

The construct of the questionnaires used to assess the impact on SOV was based on our 30 years of experience on sexual behavior in cohabiting Zambian heterosexual couples. These questionnaires were consistent with our previous work with regard to standard behavioral outcomes, such as outside partners, condom use, alcohol use, and self-reported STI treatment.

3. Retention

3.1. Retention strategies

3.1.1. Locator cards, appointment books, and late lists

Couple's locator information and phone numbers are updated throughout the trial. Phone numbers are verified by counselors during the visit. Appointments are recorded on couple's membership card and an internal appointment book. Couples with phones receive reminder texts prior to study visits and are called on the day of the visit if late for appointment. Appointments are rescheduled as needed. Late lists are generated to follow-up couples who miss appointments. Couples are contacted via SMS, phone call and/or home visit.

3.1.2. Couple identification

At enrollment and at each follow-up visit, right and left index and thumbprints of each spouse are taken manually using paper and fingerprint ink. Manual records are used real-time at the clinic for participant identification by comparing the ink fingerprints on the membership card issued at enrollment with the fingerprint obtained on the day of the follow-up visit.

We also captured electronic fingerprints [44] using tablet-based biometric software and a Lumidgm scanner. Tablets from participating clinics are brought to the research sites in Lusaka and Ndola for data upload as neither wifi nor adequate cellular reception are available at the clinics. Unique and anonymous numbers (not fingerprint images) are stored on a password secured website. This ensures that couples have not been enrolled in more than one clinic, and that the participants who return for follow-up are those who were enrolled with that identifier. Confirmation that the correct couple was interviewed at each follow-up visits is done post-hoc using this electronic database.

4. Sample size and power calculation

Power calculations were based on Hussey and Hughes [45] assuming enrollment of 1800 couples and a conservative 58% retention. Conservative retention estimates are based on our many years of experience with cohort studies in Zambia. Loss to follow-up is expected to be high due to high rates of relocation [46]. Expected outcomes are based on the literature. The calculations in Table 4 show risk in the intervention group and detectable risk ratio for 80% and 90% power with intraclass correlation value of 0.10.

Table 4
Power calculation.

Risk Control	Risk Intervention	Risk ratio detected	Power
15%	5%	0.53	80%
	6.5%	0.43	90%
20%	11%	0.55	80%
	12%	0.60	90%
25%	14%	0.56	80%
	15%	0.60	90%

5. Data management

Questionnaire data is managed using Microsoft Access and Research Electronic Data Capture (REDCap) electronic data capture tools hosted at Emory University [47] with IT support from Research and Woodruff Health IT Division grant support (UL1 TR000424). All laboratory data is managed in Microsoft Access. Data cleaning is conducted in REDCap as well as queries generated in Microsoft Excel and Microsoft Access. Data analysis is conducted using SAS 9.4 (SAS Institute, Cary, N.C.).

6. Baseline data analyses

6.1. Baseline sociodemographic, reproductive health characteristics, sexual history and behavioral characteristics by study arm

To assess the success of randomization and the resulting equivalency of participants in the two arms, baseline characteristics are compared between SOV and GHP for socio-demographic, contraceptive, reproductive and sexual behavioral characteristics including baseline HIV risk factors (Tables 5 and 6). A Couple HIV Risk Factor composite was created to indicate whether either or both partners self-reported any baseline HIV risk factors, defined as previous treatment for STI, outside partners since marriage, and condom and alcohol use with outside partners. Comparison of baseline characteristics by arm are done using *t*-test for continuous variables and Chi-Square for categorical variables. Each covariate in bivariate analysis is compared by study arm using generalized estimating equations (GEE) and presented as crude odds ratios (cOR) with 95% confidence intervals (CI). GEE is used to account for clustering. Any imbalances in baseline characteristics by trial arm will be considered as possible confounders in future analyses of the impact of the intervention on HIV/STI risk. To bolster the assumptions for the power calculations above, the composite Couple HIV Risk Factor is compared in the two arms.

7. Planned data analyses

7.1. Communication of plans to remain HIV free between SOV spouses post intervention

We will compare responses between spouses at V2 one to two weeks after the SOV intervention to assess knowledge retention. More importantly, we will compare responses from each spouse regarding their discussion of the two plans "Together HIV Free" and "Protecting My Spouse" at home. The questions will explore actions and communication, individually or jointly, as it relates to plan selection; disclosure of plan to spouse; identification of threats to remaining HIV free; protection of spouse in case of HIV exposure; barriers to using the plans; and the importance of remaining HIV free. Comparisons in responses between spouses will be assessed using logistic regression.

7.2. Knowledge uptake in Good Health Package health topics

We will compare baseline to V2 (one to two weeks post intervention), V3 (three months post intervention), and V4 (six months post intervention) and V5 (60 months post intervention) in the GHP arm to assess

Table 5
Baseline sociodemographic and reproductive health characteristics by study arm.

	Total (N = 1686)		Intervention Arm (N = 813)		Comparison Arm (N = 873)		p-value ^a	95% CI			
	Mean	SD	Mean	SD	Mean	SD		cOR	LL	UL	p-value
Man age (mean, years)^b	31.9	7.8	32.1	7.8	31.7	7.8	0.39	1.01	0.99	1.02	0.39
Woman age (mean, years)^b	26.2	6.7	26.4	6.8	26.0	6.5	0.21	1.01	0.99	1.02	0.21
	N	%	N	%	N	%					
Man's Income											
Yes	1662	99%	793	98%	869	100%	0.001				
No	24	1%	20	2%	4	0%					
Man's income (IQR, ZMW)^c	800	800	700	800	900	1000	0.0001	0.99	0.98	0.99	0.002
Woman's Income											
Yes	1132	67%	492	61%	640	73%	<0.0001	Ref			
No	553	33%	320	39%	233	27%		1.79	1.45	2.19	<0.0001
Woman's income (IQR, ZMW)^c	250	650	200	500	350	900	<0.0001	0.95	0.94	0.97	<0.0001
City of Residence											
Lusaka	334	20%	174	21%	160	18%	0.11	1.21	0.95	1.54	0.11
Ndola	1352	80%	639	79%	713	82%		Ref			
Man vernacular literacy (Bemba or Nyanja)											
Easily	1255	74%	556	68%	699	80%	<0.0001	Ref			
With Difficulty/Not at all	431	26%	257	32%	174	20%		1.86	1.49	2.32	<0.0001
Woman vernacular literacy (Bemba or Nyanja)											
Easily	927	55%	358	44%	569	65%	<0.0001	Ref			
With Difficulty/Not at all	758	45%	454	56%	304	35%		2.37	1.95	2.89	<0.0001
Man reads or understands English											
Easily	1070	63%	470	58%	600	69%	<0.0001	Ref			
With Difficulty/Not at all	616	37%	343	42%	273	31%		1.60	1.31	1.96	<0.0001
Woman reads or understands English											
Easily	716	42%	275	34%	441	51%	<0.0001	Ref			
With Difficulty/Not at all	969	58%	537	66%	432	49%		1.99	1.64	2.43	<0.0001
Couple: Years Cohabiting^b	5.9	5.8	6.2	5.8	5.5	5.8	0.01	1.02	1.00	1.04	0.01
Couple: Number of people in household^d	4.6	2.1	4.8	2.1	4.4	2.2	0.001	1.08	1.03	1.13	0.002
Couple: Number of children <16 years old in household^d	2.1	1.7	2.3	1.6	1.9	1.6	<0.0001	1.15	1.09	1.23	<0.0001
Self-Reported Pregnancy											
Yes	450	27%	143	18%	307	35%	<0.0001	Ref			
No	1236	73%	670	82%	566	65%		2.54	2.02	3.19	<0.0001
If not pregnant, current contraceptive method											
IUD	12	1%	4	1%	8	1%	0.062				
Implant	198	16%	97	14%	101	18%					
Injectable	283	23%	159	24%	124	22%					
Pills	134	11%	64	10%	70	12%					
Tubal Ligation	1	0%	0	0%	1	0%					
None/Condom/Other	608	49%	346	52%	262	46%					

Ref indicates reference group.

^a *Two-tailed t-test for continuous variables, chi-square test for categorical variables with cell counts ≥ 5 , Fisher's exact test for categorical variables with cell counts < 5 .

^b Per one year increase.

^c Per 1 person or 1 child increase.

^d Per one child increase.

knowledge and implementation of strategies for keeping their family healthy. Responses will be compared between men and women as it pertains to knowledge and application of strategies in water chlorination, handwashing, deworming, prevention of schistosomiasis, and prevention and management of diabetes and hypertension. In addition, barriers, roles in household as it relates to these areas, and the perceived importance of these strategies will be assessed. Comparisons in responses between spouses will be assessed using logistic regression.

7.3. Retention

We will present retention statistics of couples and indicate reasons for withdrawals and lost to follow-up. In addition, we will assess predictors of follow-up by comparing socio-demographic, reproductive and sexual history, and behavioral characteristics of couples completing baseline only versus couples with follow-up.

7.4. Impact of the intervention during 60 months of follow-up

At two weeks, three months and 6 months post-intervention, HIV/

STI incidence and risk behaviors will be compared in the SOV and GHP arms. Given this short time frame of follow-up (for context, couples had been together for 6 years at the time they entered the study during which 24% had at least one partner reporting a risk factor as shown in Table 6) we do not anticipate very high levels of risk behavior. Thus, we will combine any reported risk behavior (outside partners, condom use with outside partners, alcohol use with outside partners, knowledge of outside partner HIV status, joint HIV testing with outside partners) or STI diagnosis (HIV, RPR, trichomonas diagnosed in the study or any STI treatment elsewhere) from either partner at V2, V3, and/or V4 into one composite outcome indicating one or more risk factors identified for the relationship, regardless of if it was from one or both partners..

The ongoing long-term follow-up is 60 months after the intervention and we do anticipate more reported risk behaviors and incident STI in this longer time frame. This will allow more detailed comparisons of individual risk factors between arms.

For outcomes assessed up to 6-months or 60 months, outcomes of interest will be described by study arm and compared using t-tests for continuous variables (e.g., number of outside partners) and Chi-Square tests for categorical variables (e.g., risk factor yes/no, composite

Table 6
Baseline sexual history and behavioral characteristics by study arm.

	Total (N = 1686)		Intervention Arm (N = 813)		Comparison Arm (N = 873)		p-value ^a	95% CI			
	Mean	SD	Mean	SD	Mean	SD		cOR	LL	UL	p-value
Man lifetime sex partners (mean)^b	5.1	8.9	5.5	11.3	4.8	5.8	0.11	–			
Man lifetime sex partners (IQR)^b	4.0	3.0	4.0	4.0	3.0	3.0	0.11	1.01	1.00	1.03	0.11
Woman lifetime sex partners (mean)^b	1.9	1.5	2.0	1.4	1.9	1.6	0.18	–			
Woman lifetime sex partners (IQR)^b	1.0	1.0	2.0	1.0	1.0	1.0	0.18	1.05	0.97	1.12	0.23
Man age at first sexual intercourse (mean, years)^c	18.7	4.0	18.6	4.0	18.7	4.1	0.62	0.99	0.97	1.02	0.62
Woman age at first sexual intercourse (mean, years)^c	17.7	2.6	17.3	2.5	18.0	2.6	<0.0001	0.88	0.85	0.92	<0.0001
Couple number of times sex with spouse in last 1 month^d	12.5	10.1	10.2	7.8	14.5	11.5	<0.0001	0.95	0.94	0.96	<0.0001
Man Outside Partners Since Married											
Yes	200	12%	99	12%	101	12%	0.70				
No	1486	88%	714	88%	772	88%					
If yes, man's number of outside partners (mean)	2.0	2.2	2.3	2.8	1.7	1.3	0.07	1.06	0.79	1.42	0.70
Man Condom use with outside partners since married											
Yes without condoms	136	8%	76	9%	60	7%	0.03	1.37	0.96	1.95	0.08
Yes with condoms	64	4%	23	3%	41	5%		0.61	0.36	1.02	0.06
No	1486	94%	714	88%	772	88%		Ref			
Man alcohol use during sex with outside partners											
Yes with alcohol	93	6%	38	5%	55	6%	0.07				
Yes without alcohol	107	6%	61	8%	46	5%					
No	1486	88%	714	88%	772	88%					
Woman outside partners since married											
Yes	19	1%	7	1%	12	1%	0.32				
No	1666	99%	805	99%	861	99%					
If yes, woman's number of outside partners (mean)	1.5	0.8	1.7	1.1	1.3	0.5	0.31	0.62	0.24	1.59	0.32
Woman condom use with outside partners since married											
Yes without condoms	10	1%	4	0%	6	1%	0.63				
Yes with condoms	9	1%	3	0%	6	1%					
No	1666	99%	805	99%	861	99%					
Woman alcohol use during sex with outside partners											
Yes with alcohol	4	0%	1	0%	3	0%	0.59				
Yes without alcohol	15	1%	6	1%	9	1%					
No	1666	99%	805	99%	861	99%					
Man ever treated for STI											
Yes	209	12%	98	12%	111	13%	0.68				
No	1477	88%	715	88%	762	87%					
Woman ever treated for STI											
Yes	74	4%	31	4%	43	5%	0.27				
No	1611	96%	781	96%	830	95%					
HIV Risk Factor by spouse^l											
No man and woman HIV risk	1285	76%	622	77%	663	76%	0.40				
Yes man only HIV risk	311	18%	154	19%	157	18%					

(continued on next page)

Table 6 (continued)

	Total (N = 1686)		Intervention Arm (N = 813)		Comparison Arm (N = 873)		p-value ^a	95% CI			
	Mean	SD	Mean	SD	Mean	SD		cOR	LL	UL	p-value
Yes woman only HIV risk	44	3%	16	2%	28	3%					
Yes man and woman HIV risk	45	3%	20	2%	25	3%					
Couple HIV Risk Factor[†]											
Yes	400	24%	190	23%	210	24%	0.75	0.97	0.77	1.21	0.75
No	1285	76%	622	77%	663	76%	Ref				

Ref indicates reference group.

†HIV Risk Factor and Couple HIV Risk Factor includes man and woman's baseline self-reports of previous treatment for STI, outside partners since married, condom use with those outside partners, and alcohol use during sex with those outside partners.

^a Two-tailed *t*-test for continuous variables, chi-square test for categorical variables with cell counts greater than or equal to 5, Fisher's exact test for categorical variables with cell counts less than 5.

^b Per one person increase.

^c Per one year increase.

^d Per 1 sex act increase.

outcome). In our primary analysis, the effect of the intervention on outcomes of interest will be evaluated using crude logistic regression models and GEE methods. In sensitivity analyses, a multivariable model will estimate the impact of the intervention on outcomes of interest adjusting for any imbalances by study arm identified at baseline (described in the Results section and presented in Tables 5–6).

8. Results

We present trial flow from randomization to intervention participation in Fig. 1. We have enrolled 1686 couples (813 in SOV arm and 873 in GHP arm) in 10 clinics in Ndola and Lusaka. The average number of enrolled couples per clinic is 168.6 (range 112–224). We show baseline socio-demographics, reproductive and sexual history and behavioral characteristics by study arm in Tables 5 and 6 respectively.

9. Bivariate analysis

Baseline Sociodemographic and Reproductive Health Characteristics by Study Arm (Table 5): Significant differences in bivariate comparisons were found between the SOV and GHP arms in income, literacy, duration of cohabitation, number of people and children in the household, and current pregnancy. In summary, couples in the GHP comparison arm had higher men's and women's literacy in the vernacular and English, higher men's income, higher women's employment, fewer people and children living in the home and higher self-reported pregnancy. The two arms did not differ by residence (Lusaka vs. Ndola) or modern contraceptive use among non-pregnant women.

Baseline Sexual History and Behavioral Characteristics by Study Arm (Table 6): There were few differences between SOV and GHP arms in sexual history, risk behaviors and STI histories. Variables not significant in bivariate analysis included number of lifetime sexual partners, man's age of sexual debut, alcohol use during sex with outside partners, and ever being treated for an STI. Women in the SOV arm had a younger age at first sexual intercourse and couples in the SOV arm reported fewer sexual contacts within the marriage in the last month. A composite score including history of STI, outside partners, condom use with outside partners, and alcohol use during sex with outside partners in either spouse showed no difference between the two groups. Twenty-four percent of couples had at least one risk factor including 18% with only the man having a risk factor, 3% with only the woman, and 3% with both partners reporting a risk factor since the union began.

10. Trial status

The trial started recruitment and enrollment in January 2016. Follow-up for the trial is ongoing.

11. Discussion

We describe a protocol for testing the impact of 'Strengthening Our Vows', an innovative behavioral intervention to reduce HIV risk among HIV concordant negative couples in Zambia through reduction in exposure from concurrent sexual partners. To our knowledge this is the first couple-based HIV prevention trial to look at the impact of sexual agreements in heterosexual African couples. Our study covers important gaps in the literature as it pertains to a health outcome in a high prevalence, resource limited setting, and addresses challenges associated with uptake and continued use of sexual agreements.

The majority of new HIV infections in sub Saharan Africa occur in cohabiting couples and CVCT has been recommended for HIV prevention by WHO since 2012. To date, only Rwanda has nationalized CVCT in antenatal clinics, where >80% of pregnant women have been tested with partners since 2013 [48] thus resulting in prevention of an estimated 70% of all new infections [1,2]. Research and implementation programs in several countries confirm that CVCT is feasible [5,49–59], recently summarized in a review of uptake of couples' testing [60]. Several clinical trials have provided CVCT in order to recruit discordant couples for biomedical prevention interventions [61,62] or concordant positive couples into treatment interventions [63] but prevention and treatment efforts to date have focused on HIV-infected couples.

A combination approach to HIV prevention has been adapted for specific risk groups such as female sex workers (FSW) and youth [64–69]. These targeted interventions ideally focus limited resources on those at highest risk. Examples in couples include treatment-as-prevention in the HIV + partner in discordant couples [70], PrEP in the HIV- partner if the HIV + partner does not have an undetectable viral load [61], and male circumcision in uninfected men married to HIV + women [71]. Given the low incidence of HIV in CNC after CVCT, cost-benefit analyses preclude PrEP in this group. Similarly, given limited access and low uptake in many areas [72–74] men in concordant HIV- unions would be a lower programmatic priority for male circumcision compared with single men or men with HIV + spouses.

Though unprotected sex with concurrent partners remains the primary mode of HIV acquisition in heterosexual CNC in Africa, couples lack evidence-based pragmatic, communication and action-focused strategies to aid in their decision-making to protect their marriages from HIV. Our 'Strengthening Our Vows' approach aims to incorporate this combinative strategy with CVCT, an already proven, cost-effective strategy and adapts strategies previously used to provide a platform for couples to discuss concurrent partnerships and HIV prevention [75, 76].

In a review of 48 studies of HIV- MSM couples by LeBlanc et al., negotiated safety included the following components: joint HIV testing

and counseling; explicit relationship boundaries with either monogamy allowing no condom use within the couple, or consistent condom use with outside partners; and a communication plan in the event the agreement was breached [77]. Though this review was published after our trial began, it describes an approach very similar to our intervention.

The literature on negotiated sexual agreements has grown since we began our trial and new findings will inform our analyses. Rogers et al. assessed measures of love, trust, and conflict style as they relate to agreement type, satisfaction with a breaking of agreements [78]. Mitchell et al. found that MSM cited rewards of sexual agreements included honesty, communication, clear expectations, intimacy and trust. Challenges included stigma about having an open agreement; awkwardness and jealousy [79]. Hoff et al. found positive relationship dynamics are associated with less risk with partners outside the relationship, but were associated with greater odds of condomless anal sex (CAS) with primary partners [80]. Feinstein also found that MSM who were seriously dating their partner and those with monogamous agreements were most likely to report condomless anal sex within the union (CAS) [81]. Hoff explored relationship quality and sex life enhancement motives and found the former associated with less CAS and the latter with more CAS outside the primary relationship [82]. Perry et al. found that decision-making power relative to one's partner was not associated with any agreement outcome, but that younger and lower earning MSM partners more frequently broke their agreements but the latter more often disclosed breaks [83]. Gusakova found that while monogamous couples had more positive attitudes toward communication about sexual agreements, the perceived impact of broken safety agreements in this group were less clear [84].

Young partnered US men who have sex with men \pm women reported a need for skills training in negotiating sexual agreements [85]. To add to this complexity, dynamics change as relationships evolve: Mitchell et al. reported that desire for sexual exploration, events with other men, past relationships, other couples and duration of the union affect the context of agreements, highlighting the importance of maintaining open communication [86]. Given that outside exposures do happen even with monogamous agreements, prevention efforts should help couples mutually agree to integrate HIV testing into their sexual agreement [87]. A qualitative study of MSM in South Africa found sexual agreements permitting non-monogamy with female partners only, suggesting heteronormative societal pressures [88].

Responses describing the type of agreement a couple has do not always agree when partners are interviewed separately: Gamarel et al. found 45% of transgender women and their cisgender primary male partners had different perceptions of what their agreement was [89]. Studies in African heterosexuals have examined concordance in reporting sexual behaviors and risks. In Uganda, questions with high or substantial couple agreement included condom use at last sex and frequency of condom use while low or fair couple agreement was found in decision-making regarding condom use, wanting more biological children and deciding when to have sex [90]. This is similar to our own findings with Rwandan couples [91]. Other studies have focused on couples with one or both partners HIV+ [92–96] and have examined patterns of communication in couples and enhanced male involvement in HIV prevention with pregnant women [97–100], though without a specific focus on negotiated agreements [51,101–104].

Studies on sexual agreements with heterosexual couples are more limited and mostly assess feasibility of sexual agreements, self-reported monogamy agreements, or perceptions of western providers about agreements [105,106]. In a comprehensive scoping review of the primary literature on sexual agreements, including negotiated safety, Rios-Spicer and colleagues identified several knowledge gaps including the need to expand sexual agreements research beyond MSM populations and the need to better understand agreement breaks and break disclosure [75].

CVCT reduces incident HIV infections in Zambia CNC and during post-test counseling sexual agreements are often spontaneously

developed by the couples that primarily focus on monogamy. Current counseling guidelines do not include structured support for negotiated agreements, how to protect individuals and their spouses from threats to monogamy or how to react to potential outside HIV exposures if they happen.

The addition of cost-effective, sustainable strategies to the existing HIV prevention toolkit are critical as funding for HIV continues to decline. This is especially true in resource limited settings. Though we have not performed cost analysis for this added component, we have shown that CVCT is feasible on a large scale [48], cost-effective [5], and able to be integrated into routine services [107]. In addition to feasibility and cost-effectiveness, we have shown that HIV and unplanned pregnancy prevention efforts can be mutually leveraged with integrated couples-focused programs [108]. Lastly, we have also shown that the addition of services such as hygiene, sanitation, and prevention of neglected and non-communicable diseases to CVCT is feasible [39]. Such an integrative, preventive public health package that not only encompasses multiple health topics (HIV/STIs, family planning, hygiene and sanitation, and prevention of neglected and non-communicable diseases) but also includes both spouses is ideal and captures the spirit of the UN Sustainable Development Goals [33].

Our intervention is novel, timely and integrative with minimum anticipated costs. An added strength of the study is that baseline couple HIV risk is not statistically significant between the two arms. This demonstrates that as it relates to the primary outcome of interest, the arms appear to be balanced. We acknowledge that the trial sample size being based on individuals and not clusters as well as sample size adjustments in early enrollment to increase couples instead of clinics may impact power. To account for potential loss of power, we have extended the follow-up period to 60 months. The number of clusters are limited due to budgetary constraints.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.conctc.2021.100850>.

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References

- [1] K.L. Dunkle, R. Stephenson, E. Karita, E. Chomba, K. Kayitenkore, C. Vwalika, et al., New heterosexually transmitted HIV infections in married or cohabiting couples in urban Zambia and Rwanda: an analysis of survey and clinical data, *Lancet* 371 (9631) (2008) 2183–2191.
- [2] K.L. Dunkle, L. Greenberg, A. Lanterman, R. Stephenson, S. Allen, Source of new infections in generalised HIV epidemics – Authors' reply, *Lancet* 372 (9646) (2008) 1300–1301.
- [3] Couples HIV Counseling and Testing Intervention and Training Curriculum, U.S. Centers for Disease Control and Prevention, 2007. <http://www.cdc.gov/globalaids/resources/prevention/chct.html>.
- [4] World Health Organization, Guidance on Couples HIV Testing and Counseling: Recommendations for a Public Health Approach, 2012. <http://www.who.int/hiv/pub/guidelines/9789241501972/en>.
- [5] K.M. Wall, M. Inambao, W. Kilembe, E. Karita, B. Vwalika, J. Mulenga, et al., HIV testing and counselling couples together for affordable HIV prevention in Africa, *Int. J. Epidemiol.* 48 (1) (2019) 217–227.
- [6] UNAIDS, Practical Guidelines for Intensifying HIV Prevention: towards Universal Access, UNAIDS, Geneva, Switzerland, 2007. http://data.unaids.org/pub/manual/2007/20070306_prevention_guidelines_towards_universal_access_en.pdf.
- [7] A.B. Kharsany, Q.A. Karim, HIV infection and AIDS in sub-saharan Africa: current status, challenges and opportunities, *Open AIDS J.* 10 (2016) 34–48.
- [8] Zambia National AIDS Council U, Global Health HIV/AIDS Program, World Bank, Zambia HIV Prevention Response and Modes of Transmission Analysis, 2009.
- [9] Zambia Central Statistical Office. Zambia Demographic Health Survey, 2013–2014.
- [10] International Organization for Migration FHI, UNAIDS, UNIFPA, UNICEF, WHO, Zambia National AIDS Council, Tropical Disease Research Centre, Gender and Concurrent Sexual Partnerships in Zambia: Preliminary Analysis Findings, 2010. https://www.k4health.org/sites/default/files/MCP_Zambia-Preliminary_Results_2010.pdf.
- [11] D.T. Halperin, H. Epstein, Concurrent sexual partnerships help to explain Africa's high HIV prevalence: implications for prevention, *Lancet* 364 (9428) (2004) 4–6.
- [12] R.M. Pinto, K.R. Berringer, R. Melendez, O. Mmje, Improving PrEP implementation through multilevel interventions: a synthesis of the literature, *AIDS Behav.* 22 (11) (2018) 3681–3691.
- [13] R. Eakle, P. Weatherburn, A. Bourne, Understanding user perspectives of and preferences for oral PrEP for HIV prevention in the context of intervention scale-up: a synthesis of evidence from sub-Saharan Africa, *J. Int. AIDS Soc.* 22 (Suppl 4) (2019), e25306.
- [14] F.M. Koehlin, V.A. Fonner, S.L. Dalglis, K.R. O'Reilly, R. Baggaley, R.M. Grant, et al., Values and preferences on the use of oral pre-exposure prophylaxis (PrEP) for HIV prevention among multiple populations: a systematic review of the literature, *AIDS Behav.* 21 (5) (2017) 1325–1335.
- [15] U. Davidovich, J. de Wit, N. Albrecht, R. Geskus, W. Stroebel, R. Coutinho, Increase in the share of steady partners as a source of HIV infection: a 17-year study of seroconversion among gay men, *AIDS* 15 (10) (2001) 1303–1308.
- [16] U. Davidovich, J.B. de Wit, W. Stroebel, Assessing sexual risk behaviour of young gay men in primary relationships: the incorporation of negotiated safety and negotiated safety compliance, *AIDS* 14 (6) (2000) 701–706.
- [17] P.S. Sullivan, O. Hamouda, V. Delpech, J.E. Geduld, J. Prejean, C. Semaille, et al., Reemergence of the HIV epidemic among men who have sex with men in North America, Western Europe, and Australia, 1996–2005, *Ann. Epidemiol.* 19 (6) (2009) 423–431.
- [18] K. Gass, C.C. Hoff, R. Stephenson, P.S. Sullivan, Sexual agreements in the partnerships of internet-using men who have sex with men, *AIDS Care* 24 (10) (2012) 1255–1263.
- [19] J. Crawford, S. Kippax, P. Van de Ven, Sexual agreements between men in relationships, *Focus* 14 (5) (1999) 5–7.
- [20] J.M. Crawford, P. Rodden, S. Kippax, P. Van de Ven, Negotiated safety and other agreements between men in relationships: risk practice redefined, *Int. J. STD AIDS* 12 (3) (2001) 164–170.
- [21] S. Kippax, J. Crawford, M. Davis, P. Rodden, G. Dowsett, Sustaining safe sex: a longitudinal study of a sample of homosexual men, *AIDS* 7 (2) (1993) 257–263.
- [22] S. Kippax, J. Noble, G. Prestage, J.M. Crawford, D. Campbell, D. Baxter, et al., Sexual negotiation in the AIDS era: negotiated safety revisited, *AIDS* 11 (2) (1997) 191–197.
- [23] L.A. Darbes, D. Chakravarty, T.B. Neilands, S.C. Beougher, C.C. Hoff, Sexual risk for HIV among gay male couples: a longitudinal study of the impact of relationship dynamics, *Arch. Sex. Behav.* 43 (1) (2014) 47–60.
- [24] C.C. Hoff, D. Chakravarty, S.C. Beougher, T.B. Neilands, L.A. Darbes, Relationship characteristics associated with sexual risk behavior among MSM in committed relationships, *AIDS Patient Care STDS* 26 (12) (2012) 738–745.
- [25] C.C. Hoff, S.C. Beougher, D. Chakravarty, L.A. Darbes, T.B. Neilands, Relationship characteristics and motivations behind agreements among gay male couples: differences by agreement type and couple serostatus, *AIDS Care* 22 (7) (2010) 827–835.
- [26] C.C. Hoff, D. Chakravarty, S.C. Beougher, L.A. Darbes, R. Dadasovich, T. B. Neilands, Serostatus differences and agreements about sex with outside partners among gay male couples, *AIDS Educ. Prev.* 21 (1) (2009) 25–38.
- [27] J.W. Mitchell, C. Boyd, S. McCabe, R. Stephenson, A cause for concern: male couples' sexual agreements and their use of substances with sex, *AIDS Behav.* 18 (7) (2014) 1401–1411.
- [28] R. Stephenson, D. White, L. Darbes, C. Hoff, P. Sullivan, HIV testing behaviors and perceptions of risk of HIV infection among MSM with main partners, *AIDS Behav.* 19 (3) (2015) 553–560.
- [29] R. Stephenson, C. Finneran, T. Goldenberg, P. Coury-Doniger, T.E. Senn, M. Urban, et al., Willingness to use couples HIV testing and discussion of sexual agreements among heterosexuals, *SpringerPlus* 4 (2015) 169.
- [30] J. Burton, L.A. Darbes, D. Operario, Couples-focused behavioral interventions for prevention of HIV: systematic review of the state of evidence, *AIDS Behav.* 14 (1) (2010) 1–10.
- [31] N. El-Bassel, W.M. Wechsberg, Couple-based behavioral HIV interventions: placing HIV risk-reduction responsibility and agency on the female and male dyad, *Couple Family Psychol.: Res. Pract.* 1 (2) (2012) 94–105.
- [32] N.E. Rosenberg, B.M. Hauser, J. Ryan, W.C. Miller, The effect of HIV counselling and testing on HIV acquisition in sub-Saharan Africa: a systematic review, *Sex. Transm. Infect.* 92 (8) (2016) 579–586.
- [33] United Nations, Transforming Our World: the 2030 Agenda for Sustainable Development, 2015.
- [34] A.M. Corbett, J. Dickson-Gomez, H. Hilario, M.R. Weeks, A little thing called love: condom use in high-risk primary heterosexual relationships, *Perspect. Sex. Reprod. Health* 41 (4) (2009) 218–224.
- [35] K.M. Wall, W. Kilembe, B. Vwalika, L.B. Haddad, S. Lakhi, U. Onwubiko, et al., Sustained effect of couples' HIV counselling and testing on risk reduction among Zambian HIV serodiscordant couples, *Sex. Transm. Infect.* 93 (4) (2017) 259–266.
- [36] M.E. Coldiron, R. Stephenson, E. Chomba, C. Vwalika, E. Karita, K. Kayitenkore, et al., The relationship between alcohol consumption and unprotected sex among known HIV-discordant couples in Rwanda and Zambia, *AIDS Behav.* 12 (4) (2008) 594–603.
- [37] N.P. Ntombela, A.B.M. Kharsany, A. Soogun, N. Yende-Zuma, H.P. Kohler, L. R. McKinnon, Prevalence and risk factors for HIV infection among heterosexual men recruited from socializing venues in rural KwaZulu-natal, South Africa, *AIDS Behav.* Feb 11 (2021), <https://doi.org/10.1007/s10461-021-03182-3>. PMID: 33575900.
- [38] M.N. Nyabuti, M.L. Petersen, E.A. Bukusi, M.R. Kanya, F. Mwangwa, J. Kabami, et al., Characteristics of HIV seroconverters in the setting of universal test and treat: results from the SEARCH trial in rural Uganda and Kenya, *PLoS One* 16 (2) (2021), e0243167.
- [39] N.L. Czaicki, J. Davitte, B. Siangonya, R. Kastner, N. Ahmed, N.H. Khu, et al., Predictors of first follow-up HIV testing for couples' voluntary HIV counseling and testing in Ndola, Zambia, *J. Acquir. Immune Defic. Syndr.* 66 (1) (2014) e1–7.
- [40] K.M. Wall, W. Kilembe, B. Vwalika, C. Dinh, P. Livingston, Y.M. Lee, et al., Schistosomiasis is associated with incident HIV transmission and death in Zambia, *PLoS Neglected Trop. Dis.* 12 (12) (2018), e0006902.
- [41] K.Y. Wu, M. Oppert, K.M. Wall, M. Inambao, M.K. Simpungwe, N. Ahmed, et al., Couples' voluntary HIV counseling and testing provider training evaluation, *Zambia, Health Promot. Int.* 33 (4) (2018) 580–588.
- [42] D. Lemoy, Teach like a Champion, Jossey-Bass, 2005.
- [43] A. Larsen, K.S. Wilson, J. Kinuthia, G. John-Stewart, B.A. Richardson, J. Pintye, et al., Standardised patient encounters to improve quality of counselling for pre-exposure prophylaxis (PrEP) in adolescent girls and young women (AGYW) in Kenya: study protocol of a cluster randomised controlled trial, *BMJ open* 10 (6) (2020), e035689.
- [44] K.M. Wall, W. Kilembe, M. Inambao, Y.N. Chen, M. McHoongo, L. Kimaru, et al., Implementation of an electronic fingerprint-linked data collection system: a feasibility and acceptability study among Zambian female sex workers, *Glob. Health* 11 (2015) 27.
- [45] M.A. Hussey, J.P. Hughes, Design and analysis of stepped wedge cluster randomized trials, *Contemp. Clin. Trials* 28 (2) (2007) 182–191.
- [46] M.C. Kempf, S. Allen, I. Zulu, N. Kancheya, R. Stephenson, I. Brill, et al., Enrollment and retention of HIV discordant couples in Lusaka, Zambia, *J. Acquir. Immune Defic. Syndr.* 47 (1) (2008) 116–125.
- [47] P.A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J.G. Conde, Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support, *J. Biomed. Inf.* 42 (2) (2009) 377–381.
- [48] E. Karita, S. Nsanzimana, F. Ndagije, K.M. Wall, J. Mukamuyango, P. Mugwaneza, et al., Implementation and operational research: evolution of couples' voluntary counseling and testing for HIV in Rwanda: from research to public health practice, *J. Acquir. Immune Defic. Syndr.* 73 (3) (2016) e51–e58.
- [49] E.L. Sibanda, M. Tumushime, J. Mufuka, S.N. Mavedzenge, S. Gudukeya, S. Bautista-Arredondo, et al., Effect of non-monetary incentives on uptake of couples' counselling and testing among clients attending mobile HIV services in rural Zimbabwe: a cluster-randomised trial, *Lancet Global Health* 5 (9) (2017) e907–e915.
- [50] J.M. Belus, D.H. Baucom, T. Carney, E.A. Carrino, W.M. Wechsberg, A South African couple-based HIV prevention program: preliminary evidence of the long-term effects, *J. Assoc. Nurses AIDS Care* 30 (6) (2019) 648–657.
- [51] I.S. Speizer, W.A. Zule, T. Carney, F.A. Browne, J. Ndirangu, W.M. Wechsberg, Changing sex risk behaviors, gender norms, and relationship dynamics among couples in Cape Town, South Africa: efficacy of an intervention on the dyad, *Soc. Sci. Med.* 209 (2018) 95–103.
- [52] M.K. Kumwenda, E.L. Corbett, J. Chikovore, M. Phiri, D. Mwale, A.T. Choko, et al., Discordance, disclosure and normative gender roles: barriers to couple testing within a community-level HIV self-testing intervention in urban blantyre, Malawi, *AIDS Behav.* 22 (8) (2018) 2491–2499.

- [53] M. Kababu, E. Sakwa, R. Karuga, A. Ikahu, I. Njeri, J. Kyongo, et al., Use of a counsellor supported disclosure model to improve the uptake of couple HIV testing and counselling in Kenya: a quasi-experimental study, *BMC Publ. Health* 18 (1) (2018) 638.
- [54] V. Nannozi, E. Wobudeya, N. Matsiko, J. Gahagan, Motivators of couple HIV counseling and testing (CHCT) uptake in a rural setting in Uganda, *BMC Publ. Health* 17 (1) (2017) 104.
- [55] W. Kilembe, K.M. Wall, M. Mokgoro, A. Mwaanga, E. Dissen, M. Kamusoko, et al., Implementation of couples' voluntary HIV counseling and testing services in Durban, South Africa, *BMC Publ. Health* 15 (2015) 601.
- [56] W. Kilembe, K.M. Wall, M. Mokgoro, A. Mwaanga, E. Dissen, M. Kamusoko, et al., Knowledge of HIV serodiscordance, transmission, and prevention among couples in Durban, South Africa, *PLoS One* 10 (4) (2015), e0124548.
- [57] C.M. Audet, M. Blevins, Y.M. Chire, M.H. Aliyu, L.M. Vaz, E. Antonio, et al., Engagement of men in antenatal care services: increased HIV testing and treatment uptake in a community participatory action program in Mozambique, *AIDS Behav.* 20 (9) (2016) 2090–2100.
- [58] L. Nakiire, S. Kabwama, R. Majwala, J.K. Bbale, I. Makumbi, J. Kalyango, et al., Factors associated with utilisation of couple HIV counselling and testing among HIV-positive adults in kyoga fishing community Uganda, may 2017: cross sectional study, *AIDS Behav.* 24 (10) (2020) 2935–2941.
- [59] A. Kamali, M.A. Price, S. Lakhi, E. Karita, M. Inambao, E.J. Sanders, et al., Creating an African HIV clinical research and prevention trials network: HIV prevalence, incidence and transmission, *PLoS One* 10 (1) (2015), e0116100.
- [60] T.G. Haillemariam, S. Nathan, C.N. Seifu, P. Rawstorne, Uptake of couples HIV testing and counselling among heterosexual couples in Sub-Saharan Africa: a systematic review and meta-analysis, *AIDS Care* 32 (2) (2020) 137–147.
- [61] R. Heffron, K. Thomson, C. Celum, J. Haberer, K. Ngunjiri, N. Mugso, et al., Fertility intentions, pregnancy, and use of PrEP and ART for safer conception among east African HIV serodiscordant couples, *AIDS Behav.* 22 (6) (2018) 1758–1765.
- [62] J.R. Lingappa, E. Kahle, N. Mugso, A. Mujugira, A. Magaret, J. Baeten, et al., Characteristics of HIV-1 discordant couples enrolled in a trial of HSV-2 suppression to reduce HIV-1 transmission: the partners study, *PLoS One* 4 (4) (2009), e5272.
- [63] C.M. Audet, E. Graves, E. Barreto, C. De Schacht, W. Gong, B.E. Shepherd, et al., Partners-based HIV treatment for seroconcordant couples attending antenatal and postnatal care in rural Mozambique: a cluster randomized trial protocol, *Contemp. Clin. Trials* 71 (2018) 63–69.
- [64] J. Buttolph, I. Inwani, K. Agot, C.M. Cleland, P. Cherutich, J.N. Kiarie, et al., Gender-specific combination HIV prevention for youth in high-burden settings: the MP3 youth observational pilot study protocol, *JMIR Res. Protoc.* 6 (3) (2017) e22.
- [65] F.M. Cowan, C. Davey, E. Fearon, P. Mushati, J. Dirawo, S. Chabata, et al., Targeted combination prevention to support female sex workers in Zimbabwe accessing and adhering to antiretrovirals for treatment and prevention of HIV (SAPPH-IRE): a cluster-randomised trial, *Lancet HIV* 5 (8) (2018) e417–e426.
- [66] D. Kerrigan, J. Mbwambo, S. Likindikoki, W. Davis, A. Mantsios, S.W. Beckham, et al., Project shikamana: community empowerment-based combination HIV prevention significantly impacts HIV incidence and care continuum outcomes among female sex workers in iringa, Tanzania, *J. Acquir. Immune Defic. Syndr.* 82 (2) (2019) 141–148.
- [67] M.O. Kuteesa, H.A. Weiss, A. Abaasa, S. Nash, R.N. Nsubuga, R. Newton, et al., Feasibility of conducting HIV combination prevention interventions in fishing communities in Uganda: a pilot cluster randomised trial, *PLoS One* 14 (3) (2019), e0210719.
- [68] M. Maskew, L. Jamieson, G. Mohomi, L. Long, C. Mongwenyana, C. Nyoni, et al., Implementation of Option B and a fixed-dose combination antiretroviral regimen for prevention of mother-to-child transmission of HIV in South Africa: a model of uptake and adherence to care, *PLoS One* 13 (8) (2018), e0201955.
- [69] K.F. Ortblad, C.E. Oldenburg, Tailoring combination HIV prevention for female sex workers, *Lancet HIV* 5 (8) (2018) e406–e407.
- [70] S.H. Eshleman, S.E. Hudelson, A.D. Redd, R. Swanson, S.S. Ou, X.C. Zhang, et al., Treatment as prevention: characterization of partner infections in the HIV prevention trials network 052 trial, *J. Acquir. Immune Defic. Syndr.* 74 (1) (2017) 112–116.
- [71] J. Fox, P.J. White, J. Weber, G.P. Garnett, H. Ward, S. Fidler, Quantifying sexual exposure to HIV within an HIV-serodiscordant relationship: development of an algorithm, *AIDS* 25 (8) (2011) 1065–1082.
- [72] J. Mark, J. Kinuthia, A.O. Osofi, M.A. Gone, V. Asila, D. Krakowiak, et al., Male partner linkage to clinic-based services for sexually transmitted infections and HIV, *Sex. Transm. Dis.* 46 (11) (2019) 716–721.
- [73] C. Maibvise, T.R. Mavundla, A model to promote the uptake of male circumcision as an HIV-preventive measure in high HIV and low male circumcision prevalence settings, *Health SA* 24 (2019) 1070.
- [74] C.T. Nxumalo, G.G. Mchunu, Zulu men's conceptions, understanding, and experiences of voluntary medical male circumcision in KwaZulu-natal, South Africa, *Am. J. Men's Health* 14 (2) (2020), 1557988319892437.
- [75] R. Rios-Spicer, L. Darbes, C. Hoff, P.S. Sullivan, R. Stephenson, Sexual agreements: a scoping review of measurement, prevalence and links to health outcomes, *AIDS Behav.* 23 (1) (2019) 259–271.
- [76] N.M. Leblanc, J.W. Mitchell, J.P. De Santis, Negotiated safety - components, context and use: an integrative literature review, *J. Adv. Nurs.* 73 (7) (2016) 1583–1603.
- [77] N.M. Leblanc, J.W. Mitchell, J.P. De Santis, Negotiated safety - components, context and use: an integrative literature review, *J. Adv. Nurs.* 73 (7) (2017) 1583–1603.
- [78] E. Rogers, M.J. Mimiaga, R. Garofalo, E. Brown, A. Bratcher, T. Wimbly, et al., A dyadic perspective on sexual agreements among same-sex male couples in the United States, *AIDS Behav.* 24 (11) (2020) 3107–3123.
- [79] J.W. Mitchell, J.Y. Lee, C. Woodyatt, J. Bauermeister, P. Sullivan, R. Stephenson, Perceived challenges and rewards of forming a sexual agreement among HIV-negative male couples, *Arch. Sex. Behav.* 45 (6) (2016) 1525–1534.
- [80] C.C. Hoff, C.K. Campbell, D. Chakravarty, L.A. Darbes, Relationship-based predictors of sexual risk for HIV among MSM couples: a systematic review of the literature, *AIDS Behav.* 20 (12) (2016) 2873–2892.
- [81] B.A. Feinstein, T.V. Dellucci, P.S. Sullivan, B. Mustanski, Characterizing sexual agreements with one's most recent sexual partner among young men who have sex with men, *AIDS Educ. Prev. : Off. Publ. Int. Soc. AIDS Educat.* 30 (4) (2018) 335–349.
- [82] C.C. Hoff, D. Chakravarty, L. Darbes, T.B. Neilands, Studying the motivations behind sexual agreements: a first look at the motivations behind agreement (mba) scale for male couples, *J. Sex. Res.* 56 (6) (2019) 718–727.
- [83] N.S. Perry, D.M. Huebner, B.R. Baucom, C.C. Hoff, Relationship power, sociodemographics, and their relative influence on sexual agreements among gay male couples, *AIDS Behav.* 20 (6) (2016) 1302–1314.
- [84] S. Gusakova, K. Chin, E. Ascigil, T.D. Conley, D. Chakravarty, T.B. Neilands, et al., Communication patterns among male couples with open and monogamous agreements, *Arch. Sex. Behav.* 50 (4) (2020) 1419–1431.
- [85] K.E. Gamarel, L.A. Darbes, O. Kutsa, L.B. Hightow-Weidman, P. Sullivan, R. Stephenson, Perspectives from young partnered gay, bisexual, and other men who have sex with men on the adaptation of couples HIV testing and counseling (CHTC), *AIDS Behav.* 25 (2020) 836–846.
- [86] J.W. Mitchell, J.Y. Lee, C. Woodyatt, J. Bauermeister, P. Sullivan, R. Stephenson, Illuminating the context and circumstances of male couples establishing a sexual agreement in their relationship, *Am. J. Men's Health* 11 (3) (2017) 600–609.
- [87] J.W. Mitchell, J.Y. Lee, C. Woodyatt, J. Bauermeister, P. Sullivan, R. Stephenson, Decisions about testing for HIV while in a relationship: perspectives from an urban, convenience sample of HIV-negative male couples who have a sexual agreement, *Arch. Sex. Behav.* 46 (4) (2017) 1069–1077.
- [88] Z. Essack, I. Lynch, C.J. Kaunda, R. Stephenson, L. Darbes, H. Van Rooyen, Power relations in sexual agreements among male couples in Southern Africa, *Cult. Health Sex.* (2019) 1–16.
- [89] K.E. Gamarel, S.L. Reisner, L.A. Darbes, C.C. Hoff, D. Chakravarty, T. Nemoto, et al., Dyadic dynamics of HIV risk among transgender women and their primary male sexual partners: the role of sexual agreement types and motivations, *AIDS Care* 28 (1) (2016) 104–111.
- [90] K.A. Muldoon, S. Kanters, J. Birungi, R.L. King, M. Nyonyintono, S. Khanakwa, et al., 'He said, she said': assessing dyadic agreement of reported sexual behaviour and decision-making among an HIV sero-discordant couples cohort in Uganda, *J. Fam. Plann. Reprod. Health Care* 43 (2) (2017) 142–146.
- [91] K.M. Hageman, E. Karita, K. Kayitenkore, R. Bayingana, A. van der Straten, R. Stephenson, et al., What the better half is thinking: a comparison of men's and women's responses and agreement between spouses regarding reported sexual and reproductive behaviors in Rwanda, *Psychol. Res. Behav. Manag.* 2 (2009) 47–58.
- [92] N. Chitalu, M. Mumbi, R. Cook, S.M. Weiss, D. Jones, The impact of key HIV intervention components as predictors of sexual barrier use: the Zambia partner project, *J. Int. Assoc. Phys. AIDS Care* 15 (1) (2016) 51–58.
- [93] R. Cook, R. Hayden, S.M. Weiss, D.L. Jones, Desire for fertility among HIV-seroconcordant and -discordant couples in Lusaka, Zambia, *Cult. Health Sex.* 16 (7) (2014) 741–751.
- [94] D. Jones, D. Kashy, N. Chitalu, C. Kankasa, M. Mumbi, R. Cook, et al., Risk reduction among HIV-seroconcordant and -discordant couples: the Zambia NOW2 intervention, *AIDS Patient Care STDS* 28 (8) (2014) 433–441.
- [95] D. Jones, S.M. Weiss, K. Arheart, R. Cook, N. Chitalu, Implementation of HIV prevention interventions in resource limited settings: the partner project, *J. Community Health* 39 (1) (2014) 151–158.
- [96] S. Vamos, R. Cook, N. Chitalu, M. Mumbi, S.M. Weiss, D. Jones, Quality of relationship and sexual risk behaviors among HIV couples in Lusaka, Zambia, *AIDS Care* 25 (9) (2013) 1102–1108.
- [97] K. Hampanda, A. Helova, T. Odwar, T. Odeny, M. Onono, E. Bukusi, et al., Male partner involvement and successful completion of the prevention of mother-to-child transmission continuum of care in Kenya, *Int. J. Gynaecol. Obstet.* 152 (3) (2021) 409–415.
- [98] A.M. Hatcher, L. Darbes, Z. Kwena, P.L. Musoke, A.J. Rogers, G. Owino, et al., Pathways for HIV prevention behaviors following a home-based couples intervention for pregnant women and male partners in Kenya, *AIDS Behav.* 24 (7) (2020) 2091–2100.
- [99] Z. Kwena, L. Kimbo, L.A. Darbes, A.M. Hatcher, A. Helova, G. Owino, et al., Testing strategies for couple engagement in prevention of mother-to-child transmission of HIV and family health in Kenya: study protocol for a randomized controlled trial, *Trials* 22 (1) (2021) 19.
- [100] J.M. Turan, L.A. Darbes, P.L. Musoke, Z. Kwena, A.J. Rogers, A.M. Hatcher, et al., Development and piloting of a home-based couples intervention during pregnancy and postpartum in southwestern Kenya, *AIDS Patient Care STDS* 32 (3) (2018) 92–103.
- [101] J.M. Belus, D.H. Baucom, T. Carney, E.A. Carrino, W.M. Wechsberg, A South African couple-based HIV prevention program: preliminary evidence of the long-term effects, *J. Assoc. Nurses AIDS Care* 30 (6) (2019) 648–657.
- [102] J.M. Belus, D.H. Baucom, W.M. Wechsberg, Individual and relationship predictors of couple-level sexual concurrency in heterosexual South African couples, *Arch. Sex. Behav.* 49 (3) (2020) 999–1015.

- [103] J.M. Belus, T. Kline, T. Carney, B. Myers, W.M. Wechsberg, Measuring relationship functioning in South African couples: a strategy for improving HIV prevention efforts, *Sex. Relatsh. Ther.* 35 (1) (2020) 2–14.
- [104] I.A. Doherty, B. Myers, W.A. Zule, A.M. Minnis, T.L. Kline, C.D. Parry, et al., Seek, Test and Disclose: knowledge of HIV testing and serostatus among high-risk couples in a South African township, *Sex. Transm. Infect.* 92 (1) (2016) 5–11.
- [105] N.M. Leblanc, J. McMahon, Perceived facilitators and barriers to couples' HIV testing and counseling in U.S. Clinical settings: perspectives from U.S. Health providers, *J. Assoc. Nurses AIDS Care* 30 (3) (2019) 279–291.
- [106] N.M. Leblanc, J. Mitchell, Providers' perceptions of couples' HIV testing and counseling (CHTC): perspectives from a U.S. HIV epicenter, *Couple Family Psychol.* 7 (1) (2018) 22–33.
- [107] M. Inambao, W. Kilembe, L.A. Canary, N.L. Czaicki, M. Kakungu-Simpungwe, R. Chavuma, et al., Transitioning couple's voluntary HIV counseling and testing (CVCT) from stand-alone weekend services into routine antenatal and VCT services in government clinics in Zambia's two largest cities, *PLoS One* 12 (10) (2017), e0185142.
- [108] K. Malama, W. Kilembe, M. Inambao, A. Hoagland, T. Sharkey, R. Parker, et al., A couple-focused, integrated unplanned pregnancy and HIV prevention program in urban and rural Zambia, *Am. J. Obstet. Gynecol.* 222 (4s) (2020). S915.e1-S.e10.